Protocol C5091003

A PHASE 2B, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, PARALLEL GROUP, DOSE RANGING STUDY TO EVALUATE VIROLOGICAL RESPONSE AND SAFETY OF ORAL PF-07817883 IN NON-HOSPITALIZED SYMPTOMATIC ADULT PARTICIPANTS WITH COVID-19

Statistical Analysis Plan
(SAP)

Version: **1.0**

Date: 12 May 2023

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1.0/ 12 May 2023	Protocol Amendment 2; 14 April 2023	NA	SAP original version

2. INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study C5091003. Text taken verbatim from the protocol is italicized.

2.1. Modifications to the Analysis Plan Described in the Protocol

None.

2.2. Study Objectives, Endpoints, and Estimands

Type	Objective	Endpoint	Estimand
Virological response - Primary	*To describe the effect of PF-07817883 treatment versus placebo on SARS-CoV-2 RNA levels in NP samples in nonhospitalized symptomatic adult participants with COVID-19.*	*Change from baseline in SARS-CoV-2 RNA level on Day 5.*	*E1: The estimand is the difference between the PF-07817883 dose groups and placebo in mean change from baseline in SARS-CoV-2 RNA level in NP samples in the population of nonhospitalized, symptomatic, adult participants with COVID-19 who have SARS-CoV-2 RNA level ⩾4 log10 copies/mL at baseline. This analysis will exclude data after use of prohibited COVID-19 medications and after study treatment discontinuation.*
Virological response - Secondary	*To describe the effect ofPF-07817883 treatment versus placebo on SARS-CoV-2 RNA levels in*	*Change from baseline in SARS-CoV-2 RNA level on Days 3, 10 and 14.*	*E1: The estimand is the difference between the PF-07817883 dose groups and placebo in mean change from*

Type	Objective	Endpoint	Estimand
	NP samples in non-hospitalized symptomatic adult participants with COVID-19.		*baseline in SARS-CoV-2 RNA level in NP samples in the population of non-hospitalized, symptomatic, adult participants with COVID-19 who have SARS-CoV-2 RNA level ⩾4 log10 copies/mL at baseline. This analysis will exclude data after use of prohibited COVID-19 medications and after study treatment discontinuation.*
Safety	*To describe the safety and tolerability of PF-07817883 relative to placebo in the treatment of non-hospitalized, symptomatic, adult participants with COVID-19.*	• *Incidence of TEAEs.* • *Incidence of SAEs and AEs leading to discontinuations.* • *Incidence of clinically significant abnormal laboratory values, vital signs, and ECGs.*	*NA*
Tertiary/Exploratory	*To assess the effect of PF-07817883 treatment on the duration and severity of signs and symptoms in nonhospitalized, symptomatic, adult participants with COVID-19.*	• *Proportion of participants with any targeted signs/ symptoms attributed to COVID-19 over time.* • *Proportion of participants with any targeted severe sign or symptom attributed to COVID-19 over time.* • Proportion *of participants with sustained alleviation of all targeted signs/symptoms over time.* • Proportion *of participants with*	*NA*

Type	Objective	Endpoint	Estimand
		sustained resolution of all targeted signs and symptoms over time. • *Duration of targeted COVID-19 sign or symptom.* • Proportion of participants with *progression to a worsening status in 1 or more self-reported COVID-19-associated symptoms over time.* • *Proportion of participants with symptom rebound* over time.	
Tertiary/Exploratory	*To assess the effect of PF-07817883 treatment on COVID-19-related medical visits, hospitalization or death and all-cause mortality in nonhospitalized, symptomatic, adult participants with COVID-19.*	• *Proportion of participants with COVID-19 related medical visits or hospitalization, over time.* • *Proportion of participants with death (all cause) over time.* • *Number of days in hospital and ICU stay in participants with COVID-19 related hospitalization over time.*	*NA*
Tertiary/Exploratory	*To determine the PK of PK-07817883 in non-hospitalized, symptomatic, adult participants with COVID-19*	• *PF-07817883 PK in plasma and whole blood (if feasible)*	*NA*
Tertiary/Exploratory	*To describe the effect of PF-07817883*	• *Change from Day 5 in SARS-CoV-2 RNA*	*NA*

Type	Objective	Endpoint	Estimand
	treatnent versus placebo on SARS-CoV-2 RNA levels in NP samples in non-hospitalzed symptomatic adult participants with COVID-19.	*level at Days 10, 14, and 21.* • *Change from baseline in SARS-CoV-2 RNA level at Days 21 and 33.* • *Proportion of participants with SARS-CoV-2 RNA level <LLOQ in NP samples over time.* • *Proportion of participants with viral rebound at Day 10, Day 14, or Day 21.*	
Tertiary/Exploratory	*To describe the effect of PF-07817883 treatment on infectivity of SARS-CoV-2 collected from NP samples.*	• *Change from baseline in SARS-CoV-2 infectious titer on Days 3, 5, 10 and 14, and Days 21 and 33 (if data permit).*	*NA*

2.2.1. Primary Estimand(s)

E1 *(primary analysis estimand): The estimand is the difference between the PF-07817883 dose groups and placebo in mean change from baseline in SARS-CoV-2 RNA level in NP samples in the population of non-hospitalized, symptomatic, adult participants with COVID-19 who have SARS-CoV-2 RNA level ≥4 log10 copies/mL at baseline. This analysis will exclude data after use of prohibited COVID-19 medications and study treatment discontinuation.*

E2 *(estimand for supplementary analyses): The estimand is the difference between the PF-07817883 dose groups and placebo in mean change from baseline in SARS-CoV-2 RNA level in NP samples in the population of non-hospitalized, symptomatic, adult participants with COVID-19. This will exclude data after use of prohibited COVID-19 medications and study treatment discontinuation.*

Note that for E1 and E2, partial participant data accumulated prior to use of prohibited COVID-19 medications or treatment discontinuation is included in the analysis.

The timepoints used in each model & estimand will be specified in the respective analysis section.

2.2.2. Secondary Estimand(s)

The E1 estimand will be applied to change from baseline in SARS-CoV-2 RNA level on Days 3, 10 and 14.

2.3. Study Design

This is a Phase 2B, double-blind, randomized, placebo-controlled, parallel group, dose ranging study to assess the effect of PF-07817883 treatment on SARS-CoV-2 RNA level reduction in NP samples in non-hospitalized, symptomatic, adult participants with COVID-19. Approximately 228 eligible participants with a confirmed diagnosis of SARS-CoV-2 infection are planned to be randomized into the study to ensure approximately 180 participants with baseline SARS-CoV-2 RNA level ⩾4 log10 copies/mL complete the study. Participants will be randomized in a 1:1:2:2 ratio to receive PF-07817883 100, 300, or 600 mg, or placebo orally q12h for 5 days (10 doses total). Study visits should take place at the investigational site.

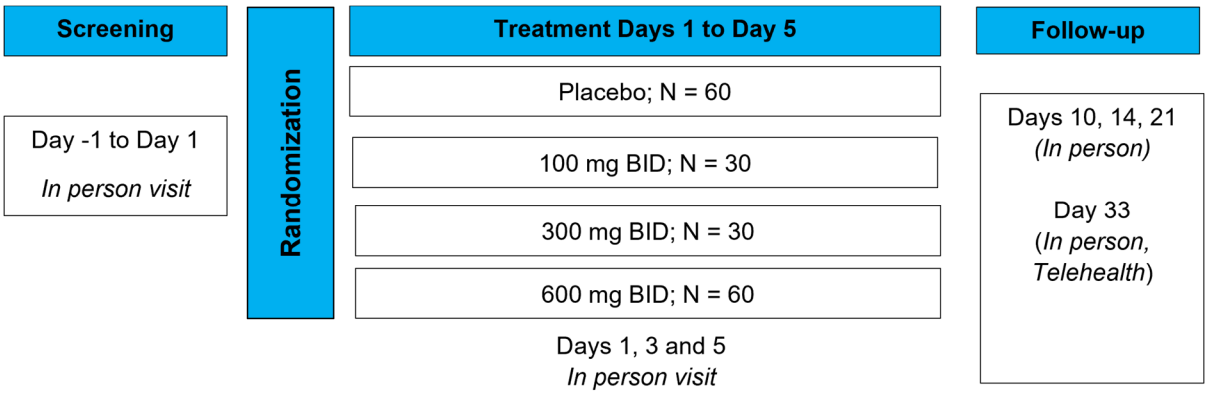
The total study duration is up to 5 weeks and includes a screening period of no more than 48 hours before randomization, study intervention for 5 days and a 4-week follow-up period after the last administration of the study intervention.

An independent IRC will review unblinded data to ensure the safety of participants throughout the duration of the study, as specified in the IRC Charter. In addition to safety reviews, the IRC will review the following:

- *A planned formal interim analysis for virological response and safety may be performed after approximately 50% or more participants complete their study* participation *(including viral load assessment) through Day 5. The timing of the interim analysis will be contingent on the recruitment rate.*

Subsequent to the planned interim analysis, there will be 1 planned analysis for reporting the results of this study. The primary analysis will be performed after all participants have completed the Day 33 visit.

Figure 1. Study Design



N=number of completers.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint(s)

- *The primary efficacy endpoint is the change in SARS-CoV-2 RNA level from baseline to Day 5 as measured in NP samples.*

3.2. Secondary Endpoint(s)

- *Change from baseline in SARS-CoV-2 RNA level on Days 3, 10 and 14.*
- *Incidence of TEAEs.*
- *Incidence of SAEs and AEs leading to discontinuations.*
- *Incidence of clinically significant abnormal laboratory values, vital signs, and ECGs.*

3.3. Other Endpoint(s)

- *Proportion of participants with any targeted signs and symptoms attributed to COVID-19 over time.*
- *Proportion of participants with any targeted severe sign or symptom attributed to COVID-19 over time.*
- *Number of participants with sustained alleviation of all targeted signs/symptoms over time.*
- *Number of participants with sustained resolution of all targeted signs and symptoms over time.*
- *Duration of targeted COVID-19 sign or symptom.*
- *Progression to a worsening status in 1 or more self-reported COVID-19-associated symptoms over time.*
- *Proportion of participants with symptom rebound at Day 10, 14, and 21.*
- *Proportion of participants with COVID-19 related medical visits or hospitalization, over time.*
- *Proportion of participants with death (all cause) over time.*
- *Number of days in hospital and ICU stay in participants with COVID-19 related hospitalization over time.*
- *PF-07817883 PK in plasma and whole blood (if feasible).*

- *Change from Day 5 in SARS-CoV-2 RNA level at Day 10, Day 14, and Day 21.*
- *Change from baseline in SARS-CoV-2 RNA level at Days 21 and 33.*
- *Proportion of participants with SARS-CoV-2 RNA level <LLOQ in NP samples over time.*
- *Proportion of participants with viral rebound at Day 10, Day 14, or Day 21.*
- *Change from baseline in SARS-CoV-2 infectious titer on Days 3, 5, 10, and 14, and Days 21 and 33 (if data permit).*

3.4. Baseline Variables

Baseline visit (Day -1 to Day 1) will be defined as the latest measurement taken prior to start of study drug, within the baseline window as defined in Appendix 2.1.

For Viral Load data, Baseline visit is set up according to study days of Screening (Day -1) to Baseline (Day 1). Only results that are within 1 hour post start of dosing will be treated as Baseline data.

For laboratory Assessments, ECGS, and vital signs: baseline window will be Day -1 to Day 1. For COVID-19 signs and symptoms, baseline will be Day 1.

The following baseline variables may be used in efficacy analyses:

- Baseline serology status defined as positive or negative.
- Baseline SARS-CoV-2 RNA level.

3.5. Safety Endpoints

The safety endpoints of this study are:

- Incidence of treatment-emergent adverse events (TEAEs).
- Incidence of treatment-emergent SAEs and AEs leading to discontinuation.
- Incidence of clinically significant abnormal laboratory values, vital signs, and ECGs.

CaPs will be used for the analysis of standard safety data.

3.5.1. Adverse Events

An adverse event (AE) is any untoward medical occurrence in a study participant administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. An adverse event is considered a treatment-emergent adverse event (TEAE) if the event started on or after the study medication start date and time.

3.5.2. Laboratory Data

To determine if there are any clinically significant laboratory abnormalities, the hematological and clinical biochemistry and other safety tests will be assessed against the criteria specified in the Pfizer reporting standards. This assessment will take into account whether each participant's baseline test results are within or outside the laboratory reference range for particular laboratory parameter.

3.5.3. Vital Signs

Vital signs measure include temperature, pulse rate, respiratory rate, oxygen saturation level and blood pressure.

3.5.4. Electrocardiogram

A triplicate ECG will be collected at baseline prior to dosing. Other ECGs will be collected at times specified in the Schedule of Activities.

3.5.5. Height and Weight

Height and weight will be measured and recorded at screening.

3.5.6. Medical History

Medical history in addition to COVID-19 disease history and demographics will be collected at screening. Complete medication history of all prescription or nonprescription drugs (including vaccinations), and dietary and herbal supplements taken within 30 days prior to the planned first dose will be collected. All COVID-19 vaccinations received at any time prior to the planned first dose will also be collected.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database and classifications will be documented per standard operating procedures.

Population	Description	Applicable Analysis
Enrolled (Randomized or assigned to study intervention)	*"Enrolled" means a participant's, or their legally authorized representative's, agreement to participate in a clinical study following completion of the informed consent process and randomization to study intervention. A participant will be considered enrolled if the informed consent is not withdrawn prior to participating in any study activity after screening. Potential participants who are screened for the purpose of determining eligibility for the study, but do not participate in the study,*	

Population	Description	Applicable Analysis
	are not considered enrolled, unless otherwise specified by the protocol.	
FAS	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention. Participants will be analysed according to the study intervention to which they were randomized.*	Sensitivity analysis (Section 6.1.1.2) Tertiary analyses (Section 6.3) Baseline summaries (Section 6.5.1, 6.5.2)
SAS	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention. Participants will be analyzed according to the intervention they actually received.*	Analyses of AEs, Labs, vital signs and ECGs (Section 6.2)
PK analysis set	*All enrolled participants who received at least 1 dose of PK-07817883 and in whom at least 1 concentration value is reported*	Analysis of PK

Defined Analysis Set	Description	Applicable Analysis
MFAS	*All participants in the FAS who have SARS-CoV-2 RNA level ⩾4 log_{10} copies/mL at baseline.* *Participants will be analyzed according to the study intervention to which they were randomized.*	Primary analysis (Section 6.1.1.1, includes MMRM & dose-response model) Secondary analysis (Section 6.2.1)

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Hypotheses and Decision Rules

The primary hypothesis is to test whether or not there is a difference in mean change of SARS-CoV-2 RNA level from baseline to Day 5 between the PF-07817883 dose groups and the placebo group using the Bayesian dose-response model:

Null hypothesis: $H_0\ \mu_{PF\text{-}07817883} - \mu_{placebo} = 0$

Alternative hypothesis: $H_a\ \mu_{PF\text{-}07817883} - \mu_{placebo} < 0$

Where $\mu_{PF\text{-}07817883}$ *and* $\mu_{placebo}$ *are mean change of SARS-CoV-2 RNA level from baseline to Day 5 for each PF-07817883 dose groups and placebo group.* A one-sided alpha of 0.1 will be used.

5.2. General Methods

Descriptive statistics for all efficacy and safety endpoints by treatment group and visit will be provided.

The number of participants screened will be reported. The number of participants randomized to the double-blind treatment phase, completing the study drug administration, completing the study, and discontinued the study will be summarized for the FAS for each treatment group.

Baseline demographic and other characteristics will be tabulated for the FAS and summarized by treatment group. Quantitative variables will be described by standard descriptive statistics (mean, standard deviation, median*, minimum, and maximum), and qualitative variables will be summarized by frequency tables with number and proportion in each category (with the corresponding sample sizes).*

5.2.1. Analyses for Binary Endpoints

For binary endpoints, the proportion of participants with the event will be summarized for each group with exact 80% CIs. For the one-sample proportions Blyth-Still-Cassella will be used for the calculation of CI and for the difference of proportions Chan and Zhang method will be used for the calculation of CI.

5.2.2. Analyses for Continuous Endpoints

For continuous endpoints, an MMRM model will be used to analyze change from baseline outcomes.

An unstructured covariance matrix will be used to estimate the variances and covariance within participant across time points. If convergence is not obtained or model fit is not adequate, then other covariance structures will be investigated as necessary. The Kenward-Roger approximation will be used for estimating degrees of freedom for the model parameters.

Missing values (e.g. due to censoring) will be implicitly imputed as part of the MMRM model fitting.

The Least Squares Means (LSMeans) together with 80% confidence intervals, standard errors and p-values (2-sided) will be obtained for each treatment group at each time point.

Differences in LSMeans between each treatment group of PF-07817883 relative to placebo at each time point, together with 80% confidence intervals, standard errors and p-values (2-sided), will also be obtained.

5.2.3. Analyses for Categorical Endpoints

For categorical endpoints, proportion of participants (and 80% CI) *for each category will be summarized for each treatment group.*

5.2.4. Analyses for Time-to-Event Endpoints

Time to event endpoints may be summarized graphically using Kaplan-Meier plots for each treatment group.

5.2.5. Emax Model

The 4-parameter dose-response Emax model will be used to characterize the change from baseline dose-response relationships with dose included as a continuous variable.

The model structure will take the form:

$$CFB = (E_0) + \frac{(E_{max}) \times dose^{Hill}}{ED_{50}{}^{Hill} + dose^{Hill}}$$

E_0 is the placebo effect, *dose* is the randomized dose, E_{max} is the maximum effect, ED_{50} is the dose producing 50% of the maximum effect and *Hill* is the slope parameter.

The model will be applied to the raw LSMean results from the primary MMRM model (Section 6.1.1.1) utilizing a Bayesian methodology approach with non informative priors.

Estimates of the model parameters of E_0, E_{max}, ED_{50}, and *Hill* and their 80% credible intervals will be produced.

The posterior medians and 80% credible intervals (10^{th} and 90^{th} percentiles of the relevant posterior distribution) will be reported for each randomized dose (including Placebo) and their differences relative to placebo. Both will be reported in tables and plotted in separate figures.

If convergence cannot be obtained or visual inspection of the data does not support a dose-response Emax relationship, then the hill parameter will be assumed to be 1 and removed from the model (giving a 3-parameter dose-response Emax model). If it is still the case that convergence cannot be obtained or visual inspection of the data does not support a dose-response Emax relationship, then the results from the MMRM model described in Section 6.1.1.1 will be reported.

5.3. Methods to Manage Missing Data

Missing SARS-CoV-2 RNA level will not be imputed in general. MMRM will be used to analyze SARS-CoV-2 RNA level data to handle Missing at Random (MAR), and it allows for inclusion of participants with partial longitudinal data in the analysis.

For efficacy endpoints related to sustained alleviation/resolution of COVID-19 targeted sign/symptoms, missing data at baseline will be treated as mild.

All missing and partial dates will be programmatically handled according to Pfizer standards. No other missing data will be imputed.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint(s)

The primary efficacy endpoint is the change in SARS-CoV-2 RNA level from baseline to Day 5 as measured in NP samples.

6.1.1.1. Main Analysis

The primary analysis will utilize a Bayesian Emax model applied to the estimates from the MMRM analysis.

Change from baseline in SARS-CoV-2 RNA level at Day 5 will first be analyzed using Estimand 1 and MMRM model. The MMRM model will be fitted to the change from baseline at all post-treatment timepoints up to Day 5 using MFAS with fixed effects including treatment, time (ie, visit day*), interaction of time by treatment, and baseline SARS-CoV-2 RNA level.* Covariates in the model will be selected based on the distribution of the data and clinical relevance, and may include days since symptom onset (≤3 vs. >3 days), vaccination status (partitions to be defined based on data), recency of vaccination (within last 6 months or not), and baseline serology. Covariates may also be excluded if there are model fit issues.

LSmeans (and 80% CIs and p-values) will be summarized.

If no more than 50% of participants in any treatment arm have SARS-CoV-2 RNA levels below LLOQ at Day 5, *a Bayesian Emax model will then be fitted to the Day 5 LSmeans and SEs from the MMRM analysis* using non-informative prior distributions for the placebo (E0), the difference in response (difTarget) between the highest dose (600 mg q12h) and placebo, and the residual standard deviation (sigma).

The fitted curve will be graphically displayed with 80% credible bands. The posterior medians and 80% credible intervals (10th and 90th percentiles of the relevant posterior distribution) will be reported for each randomized dose (including placebo) and their differences relative to placebo. If the Bayesian Emax model cannot be fitted to the data, or the data do not support a dose-response, the model may be simplified as outlined in Section 5.2.5, or the analysis may not be performed and the primary results for the study will be based on the MMRM results at Day 5. *No adjustments will be made for multiplicity in the MMRM model.*

If more than 50% of the participants in any treatment arm have SARS-CoV-2 RNA levels below LLOQ at Day 5, an alternative Bayesian Emax model will instead be fitted that uses the proportion of participants with SARS-CoV-2 RNA levels below LLOQ at Day 5. The proportions used in the Bayesian Emax model will be estimated using 80% CIs (where participants with missing SARS-CoV-2 RNA levels at Day 5 will be treated as non-responders).

Analysis will be conducted using the MFAS population.

6.1.1.2. Sensitivity/Supplementary Analyses

The MMRM analysis and Bayesian Emax dose-response models described in Section 6.1.1.1 *will be repeated using the FAS instead of MFAS and use the E2 estimand strategy* (ie, include all participants regardless of baseline SARS-CoV-2 RNA level). The MMRM model will include baseline and all post-baseline visits through Day 5 (ie, baseline, Day 3, Day 5), the Bayesian Emax model will be based on MMRM (or proportion) results at Day 5.

6.2. Secondary Endpoint(s)

6.2.1. Change from Baseline in SARS-CoV-2 RNA Level on Days 3, 10, and 14

The MMRM analysis described in Section 6.1.1.1 will be repeated using the MFAS and FAS and use the E1 and E2 estimand strategy respectively to assess change from baseline in SARS-CoV-2 RNA level on Days 3, 10, and 14. The MMRM model will have the identical specification except the MMRM model will be fitted to the change from baseline at all post-treatment timepoints up to Day 14.

6.2.2. Incidence of Treatment-Emergent Adverse Events (TEAEs)

The incidence of TEAEs will be summarized by treatment group, by system organ class (SOC) and preferred term (PT) using the SAS population.

6.2.3. Incidence of Treatment-Emergent SAEs and AEs Leading to Discontinuation

The incidence of SAEs and AEs leading to discontinuation will be summarized by treatment group using the SAS population.

6.2.4. Incidence of Clinically Significant Abnormal Laboratory Values, Vital Signs and ECGs

Analysis of adverse events, laboratory abnormalities, vital signs and ECG abnormalities will use the SAS population.

6.3. Tertiary/Exploratory Endpoint(s)

6.3.1. Proportion of Participants with Any Targeted Signs/Symptoms Attributed to COVID-19 Over Time

Proportion of participants (and 80% CIs) with any targeted signs/symptoms attributed to COVID-19 will be summarized for each sign and symptom by severity as specified below, using the FAS population.

The severity of any targeted sign/symptom will be derived based on the maximum severity of the targeted symptoms. The proportion of participants with any severe targeted signs/symptoms attributed to COVID-19 will be summarized overall, by treatment group, and by visit. A participant with severe score for any targeted symptoms post-baseline will be counted as severe. Additionally, the following analysis will be performed overall, by treatment group, and by visit:

- Proportion of participants reporting the presence of each targeted sign and symptom at Days 3, 5, 7, 14, and 28 that is mild, moderate, severe, or total category.

- Proportion of participants reporting the presence of any targeted sign and symptom at Days 3, 5, 7, 14, and 28 that is mild, moderate, severe, or total category.

6.3.2. Proportion of Participants with Any Targeted Severe Sign or Symptom Attributed to COVID-19 Over Time

See Section 6.3.1.

6.3.3. Proportion of Participants with Sustained Alleviation of All Targeted Signs/Symptoms Over Time

Proportion of participants (and 80% CI) with sustained alleviation of all targeted signs/symptoms over time through Day 29 will be summarized, using the FAS population.

Sustained alleviation of all targeted COVID-19 signs/symptoms is defined as the event occurring on the first of 4 consecutive days when all symptoms scored as moderate or severe at study entry are scored as mild or absent AND all symptoms scored mild or absent at study entry are scored as absent.

For symptoms with no reported severity in baseline, the symptom will have to be absent at later timepoints in order to be counted as sustained alleviated (missing severity at baseline will be treated as mild).

Participants who are hospitalized for the treatment of COVID-19 or death from any cause during the 29-day period will be classified as not achieving sustained symptom alleviation.

Day 26 is the last possible day sustained alleviation can be achieved (definition includes data from the subsequent three days) and Day 29 is the last day participants report their daily signs and symptoms.

6.3.4. Proportion of Participants with Sustained Resolution of All Targeted Signs/Symptoms Over Time

Proportion of participants (and 80% CI) with sustained resolution of all targeted signs/symptoms over time will be summarized, using the FAS population.

Sustained resolution is defined as when all targeted symptoms are scored as absent for 4 consecutive days. The first day of the 4 consecutive-day period will be considered the First Event Date.

For symptoms with no reported severity in baseline, the symptom will have to be absent in order to be counted as sustained resolution (missing severity at baseline will be treated as mild).

Participants who are hospitalized for the treatment of COVID-19 or death from any cause during the 29-day period will be classified as not achieving sustained resolution.

Day 26 is the last possible day sustained resolution can be achieved (definition includes data from the subsequent three days) and Day 29 is the last day participants report their daily signs and symptoms.

A similar analysis may be conducted for resolution (remain resolved for ≥24 hours) of the 5 symptoms group (Details in Appendix 5).

6.3.5. Duration of Each Targeted COVID-19 Sign/Symptom

Duration of each targeted COVID-19 signs/symptoms is defined as (First Date when the symptom achieved sustained alleviation/resolved)-(First Dose Date) + 1 for each participant with baseline severity of mild, moderate, or severe. Missing severity at baseline will be treated as mild.

Duration of each targeted COVID-19 sign/symptom with a mild or worse severity will be summarized for each treatment group.

For the duration of each targeted COVID-19 sign/symptom, a Kaplan-Meier analysis providing the median and quartiles will be provided for each treatment group. Number of participants and median time to sustained alleviation/resolution of each targeted sign/symptom by treatment group will be included.

For a participant (baseline severity of mild, moderate or severe) that either completes Day 29 of the study or discontinues from the study before Day 29 without sustained symptom alleviation/resolution (censored), censoring date will be at the last date on which sustained symptom alleviation/resolution is assessed:

- Duration of each targeted COVID-19 symptom is calculated as (Censoring Date) –(First Dose Date) +1 or Day 26 whichever occurs first.

Participants who are hospitalized for the treatment of COVID-19 or death from any cause during the 29-day period will be classified as not achieving sustained resolution/alleviation and will be censored at Day 26.

Analysis will be conducted using the FAS population.

6.3.6. Proportion of Participants with Progression to a Worsening Status in 1 or More Self-Reported COVID-19-Associated Symptoms Over Time

Participants will record a daily severity rating of their symptom severity over the past 24 hours based on a 4-point scale in which 0 is reported if no symptoms were present; 1 if mild;

2 if moderate; and 3 if severe. Vomiting and diarrhea will each be rated on a 4-point frequency scale where 0 is reported for no occurrence, 1(mild) for 1 to 2 times, 2 (moderate) for 3 to 4 times, and 3 (severe) for 5 or greater.

Progression to a worsening status for any targeted symptom will be derived programmatically based upon increasing severity (ie, the first time any targeted symptoms worsen after treatment relative to baseline):

Progression to worsening (Yes/No)	
Increasing severity	Yes
Not increasing severity	No

The proportion of participants (and 80% CI) with progression (increasing severity for any targeted symptom) by Day 29 will be summarized by treatment group.

Analysis will be conducted using the FAS population.

6.3.7. Proportion of Participants with Symptom Rebound Over Time

Proportion of participants (and 80% CI) with symptom rebound by Day 29 will be summarized.

Symptom rebound is defined as *the first day of at least two consecutive diary entries after Day 5* (regardless of missing entries in between) *where there is any symptom (regardless of severity) after achieving short symptom recovery, or if a patient is hospitalized after achieving short symptom recovery*. *Short symptom recovery* is defined as *the first day of at least two consecutive diary entries* (regardless of missing entries in between) *where all targeted symptoms are absent*. If a hospitalization event occurs prior to the short recovery day, this patient is considered not having short symptom recovery by Day 29.

Analysis will be conducted using the FAS population.

6.3.8. Proportion of Participants in Each Category of Global Impression Questions and Anchor Items Over Time

The proportion of participants answering “yes” to the patient-reported global impression items a) return to usual health and b) return to usual activities will be summarized by treatment group at Day 3, 5, 7, 14, and 28.

The proportion of participants in each category of c) overall COVID-19 related symptoms (none, mild, moderate, severe) will be summarized by treatment group at Day 3, 5, 7, 14, and 28.

The proportion of participants in each category of the fatigue, shortness of breath, and cognitive function anchor items (none, mild, moderate, severe, very severe) will be summarized by treatment group for each weekly assessment (i.e., Day 7, 14, 21, 28).

Analyses will be conducted using the FAS population.

6.3.9. Proportion of Participants with COVID-19-Related Medical Visits or Hospitalization Over Time

Proportion of participants with COVID-19 related medical visits or hospitalization through Day 29 will be summarized by treatment group.

Analysis will be conducted using the FAS population.

6.3.10. Proportion of Participants with Death (All-Cause) Over Time

Proportion of participants with death (all cause) through Day 29 will be summarized by treatment group.

Analysis will be conducted using the FAS population.

6.3.11. Number of Days in Hospital and ICU Stay in Participants with COVID-19-Related Hospitalization Over Time

Health resource utilization data will be summarized by treatment group through Day 29. This will include number (days) of hospital stay and number (days) of ICU stay. The analyses will be done using the FAS population. Descriptive statistics (ie, mean, median, range) will be used to summarize this endpoint).

6.3.12. PF-07817883 PK in Plasma and Whole Blood (If Feasible)

Summary statistics (N, geometric mean, geometric CV, median, arithmetic mean, CV, minimum, maximum) of concentrations of PF-07817883 at nominal time of collection as defined in SoA for each treatment arm will be calculated. The post-dose concentrations of PF-07817883 may be presented graphically (boxplot by treatment at each nominal time point post-dose).

For each individual, a blood to plasma (B/P) ratio will be calculated by dividing concurrent (i.e. Day 1, 60 min post-dose) whole blood PF-07817883 concentration with the plasma PF-07817883 concentration. A geometric mean B/P ratio of all individuals in the trial will be calculated. The plasma equivalent PF-07817883 concentration by microsampling will be calculated by dividing with the individual B/P ratio. As a sensitivity analysis, the plasma equivalent concentration will also be calculated using the geometric mean B/P ratio. Summary statistics (N, geometric mean, geometric CV, median, arithmetic mean, CV, minimum, maximum) of the whole blood concentrations, plasma equivalent concentrations by microsampling using individual B/P ratio and plasma equivalent concentrations by microsampling using geometric mean B/P ratio at nominal time of collection as defined in SoA for each treatment arm will be calculated.

To determine correlation in concentrations derived from time matched Tasso M-20 microsapling and traditional venous plasma sampling, Bland Altman scatterplot analysis will be performed to evaluate the bias and SD of the bias between the mean differences and to estimate an agreement interval within a 95% confidence limit. A concentration correlation analysis will be conducted with the same dataset. A population PK modeling may be performed with the concentration data from this study alone or combined with data from other studies. In addition, a relationship between exposures and efficacy/safety endpoints may be evaluated using population PK/PD approach. Any population analyses conducted will not be part of the clinical study report (CSR) and may be reported separately.

6.3.13. Change from Day 5 in SARS-CoV-2 RNA Level at Days 10, 14, and 21

The MMRM analysis described in Section 5.2.2 will be repeated using the change in SARS-CoV-2 RNA level from Day 5 at Days 10, 14, and 21. Analysis will be done using the FAS Population.

6.3.14. Change from Baseline in SARS-CoV-2 RNA Levels at Days 21 and 33

The change from baseline in SARS-CoV-2 RNA levels at Days 21 and 33 will be summarized descriptively using the FAS population.

6.3.15. Proportion of Participants with SARS-CoV-2 RNA Level <LLOQ in NP Samples Over Time

The proportion of participants with SARS-CoV-2 RNA level <LLOQ in NP samples will be summarized at each timepoint. Analysis will be conducted using the FAS population.

6.3.16. Proportion of Participants with Viral Rebound at Day 10, Day 14, or Day 21

The proportions of participants with viral rebound at Day 10, Day 14, or Day 21 will be summarized and analysis will be conducted using the FAS population. The denominator will be the evaluable population with non-missing Day 5 and Day 10, 14, or 21 SARS-CoV-2 RNA level.

Within the population of Day 5 virologic responders (Day 5 VL <LLOQ or ≥ 1 log_{10} copies/mL decline from baseline to Day 5), virologic rebound for Day 10, 14, or 21 is defined as:

1) *Day 5 VL <LLOQ AND at Day 10, 14, or 21 VL ≥LLOQ;*

   OR

2) *Day 5 RNA ≥LLOQ AND Day 10, 14, or 21 RNA ≥0.5 log_{10} copies/mL increase from Day 5.*

6.3.17. Change from Baseline in SARS-CoV-2 Infectious Titer on Days 3, 5, 10, and 14, and Days 21 and 33 (If Data Permit)

Analyses will be addressed in the VAP.

6.4. Subset Analyses

No subset analyses are planned.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

The demographic characteristics will be summarized by treatment group within the MFAS and FAS. This will include age, gender, race, ethnicity, baseline height, baseline weight, and baseline BMI. All baseline disease characteristics will be summarized by treatment group within the MFAS and FAS.

6.5.2. Study Conduct and Participant Disposition

Participant evaluation groups will be presented for all screened participants, and participant disposition will be summarized within the FAS population. The number of participants screened and randomized will be presented. The number of participants treated, completing and discontinuing by study phase (treatment period and follow-up), as well as the number of participants in each analysis set will be summarized by treatment group. For participants who did not complete the study, the reasons for withdrawal from the study will be presented.

6.5.3. Study Treatment Exposure

Duration of treatment will be summarized within SAS population.

The duration of treatment will be calculated as follows: Duration of treatment = Date of last dose of study drug - date of first dose of study drug +1.

6.5.4. Prior and Concomitant Medications and Nondrug Treatments

The frequency of prior and concomitant medications will be summarized by treatment based on the WHO-drug coding dictionary within SAS population in accordance with Clinical Data Interchange Standards Consortium (CDISC) and Pfizer Standards (CaPS).

6.6. Safety Summaries and Analyses

Standard summary tables and listings will be generated in accordance with Clinical Data Interchange Standards Consortium (CDISC) and Pfizer Standards (CaPS) for safety reporting for the following parameters: adverse events, lab parameters, vital signs, discontinuations from study, discontinuations from treatment, and treatment duration.

6.6.1. Adverse Events

AEs will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA).

6.6.2. Laboratory Data

Descriptive statistics will be summarized by treatment group over time as well as mean change from baseline for laboratory parameters within SAS population.

Laboratory shift tables from baseline will be presented for the following laboratory abnormalities at baseline: D-dimer levels, Liver function tests (ALT/AST), Creatinine Clearance (combined Scr +Scys), platelets, albumin, and total proteins.

All laboratory data will be reported in accordance with Clinical Data Interchange Standards Consortium (CDISC) and Pfizer Standards (CaPS) for safety reporting.

6.6.3. Vital Signs

All vital signs data will be descriptively summarized by treatment group within SAS population and reported in accordance with Pfizer data standard for safety reporting.

Categories for Vital Signs (Post-Dose)

Systolic BP (mm Hg)	min. <90	
Systolic BP (mm Hg) Change from Baseline	max. decrease ≥30	max. increase ≥30
Diastolic BP (mm Hg)	min. <50	
Diastolic BP (mm Hg) Change from Baseline	max. decrease ≥20	max. increase ≥20
Supine Pulse Rate (bpm)	min. <40	max. >120

6.6.4. Electrocardiograms

Changes from baseline for the ECG parameters HR, QTcF, PR interval, and QRS complex will be summarized by treatment group *and* visit. *The frequency of uncorrected QT values above 500 ms will be tabulated.*

The number (%) of participants with maximum post-dose QTcF values and maximum increases from baseline in the following categories will be tabulated by treatment:

Categories for Safety QTcF Assessment

Degree of Prolongation	**Mild (msec)**	**Moderate (msec)**	**Severe (msec)**
Absolute value of QTcF (msec)	>450 and ≤480	>480 and ≤500	>500
Increase from baseline in QTcF (msec)		>30 and ≤60	>60

7. INTERIM ANALYSES

7.1. Introduction

A planned formal interim analysis for virological response and safety may be performed to assess SARS-CoV-2 RNA level after approximately 50% or more participants, ie, at least 114 participants with baseline SARS-CoV-2 RNA level ≥4 log_{10} copies/mL, complete their study participation (including viral load assessment) through Day 5. The timing of the interim analysis is contingent on the recruitment rate.

Additional interim analysis may be performed for internal business decision-making or regulatory requests. Before any interim analyses are conducted, the final number and timings of interims, the details of the objectives, decision criteria, information dissemination plan, and method for maintaining the study blind as per Pfizer's SOPs will be documented and approved in an IRC charter and interim analysis plan.

7.2. Interim Analyses and Summaries

The interim analyses will be detailed in the interim analyses plan.

8. REFERENCES

1. Thomas, N. and Wu, J. (2019). clinDR: Simulation and Analysis Tools for Clinical Dose Response Modeling. R package version 1.9. https://CRAN.R-project.org/package=clinDR

2. Deo R, Choudhary MC, Moser C, et al. Symptom and Viral Rebound in Untreated SARS-CoV-2 Infection. Ann Intern Med. 2023;10.7326/M22-2381.

9. APPENDICES

Appendix 1. Summary of Efficacy Analyses

Endpoint	Analysis Type	Population	Data inclusion and rules for handling incurrent events and missing data	Analysis model
Change from baseline in SARS-CoV-2 RNA level on Day 5	Summary	FAS	Observed data	N/A
	Main analysis	MFAS	Estimand E1	MMRM from baseline to Day 5 and Bayesian Emax model at Day 5
	Sensitivity/supplementary analysis	FAS	Estimand E2	MMRM from baseline to Day 5 and Bayesian Emax model at Day 5
Change from Baseline in SARS-CoV-2 RNA level on Days 3, 10, and 14	Summary	FAS	Observed data	N/A
	Main Analysis	MFAS & FAS	Estimand E1 & E2	MMRM from baseline to Day 14 (includes Day 3, 5, 10)
Proportion of participants with any targeted signs/symptoms attributed to COVID-19 over time	Summary	FAS	Observed data	N/A
Proportion of participants with any targeted severe sign or	Summary	FAS	Observed data	N/A

Endpoint	Analysis Type	Population	Data inclusion and rules for handling incurrent events and missing data	Analysis model
symptoms attributed to COVID-19 over time				
Proportion of participants with sustained alleviation of all targeted signs/symptoms over time	Summary	FAS	Observed data	N/A
Proportion of participants with sustained resolution of all targeted signs/symptoms over time	Summary	FAS	Observed data	N/A
Duration of each targeted COVID-19 sign/symptoms prior to sustained alleviation/resolution	Kaplain Meier	FAS	Observed data	N/A
Proportion of participants with progression to a	Summary	FAS	Observed data	N/A

Endpoint	Analysis Type	Population	Data inclusion and rules for handling incurrent events and missing data	Analysis model
worsening status in 1 or more self-reported COVID-19 associated symptoms over time				
Proportion of participants with symptom rebound at Day 10, 14, and 21	Summary	FAS	Observed data	N/A
Proportion of participants with COVID-19 related medical visits or hospitalization, through over time	Summary	FAS	Observed data	N/A
Proportion of participants with death (all cause) through over time	Summary	FAS	Observed data	N/A
Number of days in hospital and ICU stay in participants with COVID-19 related	Summary	FAS	Observed data	N/A

Endpoint	Analysis Type	Population	Data inclusion and rules for handling incurrent events and missing data	Analysis model
hospitalization over time				
Change in SARS-CoV-2 RNA level at Days 10, 14, and 21 from Day 5.	Summary	FAS	Observed data	MMRM
Change from baseline in SARS-CoV-2 RNA levels at Days 21 and 33	Summary	FAS	Observed data	N/A
Proportion of participants with SARS-CoV-2 RNA level <LLOQ in NP samples over time	Summary	FAS	Observed data	N/A
Proportion of participants with viral rebound at Day 10, 14, or 21	Summary	FAS	Observed data	N/A

Appendix 2. Data Derivation Details

Appendix 2.1. Definition and Use of Visit Windows in Reporting

The following table defines the visit windows and labels to be used for reporting:

Visit number	Visit Label	Definition [Day Window]
2	Baseline Day	=Day 1, with a window of Day -1 to Day 1
3	Day 3	=Day 3, with a window of ±1 days, (ie, days 2 to 4)
4	Day 5/EOT	=Day 5, with a window of ±1 days, (ie, days 4 to 6)
5	Day 10	=Day 10, with a window from days 7 to 11
6	Day 14	=Day 14, with a window from days 12 to 17
7	Day 21	=Day 21, with a window from days 18 to 24
8	Day 28	=Day 28, with a window from days 25 to 33

- *Labs, Viral load, Vital Signs, and ECG: Baseline window will be Day -1 to 1. Signs and symptoms baseline will be Day 1.*
- *If multiple readings fall into the same window, choose the one closer to the target day. If equidistant, then select the later one after the target day.*
- *Labs, If multiple observations without time or at the same time fall on the same day after the windowing logic has been applied, average observations. If different times on the same day, select the later one.*
- *When data from study Day 4 has an overlap between Day 3 and Day 5 windows, decision made is to assign the window according to the nominal visit. The rule will not be applicable to other study days 2 and 3 for Day 3 window, and days 5 and 6 for Day 5 window.*

Appendix 3. Bayesian Statistical Methodology Details

Emax model (Section 5.2.5).

A dataset (either .txt or .csv) of the following format should be produced by programming from proc mixed for use in R by the reporting statistician and QC statistician. Note, column headers should be labelled as specified below (including capitalization), as R is case sensitive:

Dose	Mean	SE
0	x.xx	x.xx
100	x.xx	x.xx
300	x.xx	x.xx
600	x.xx	x.xx

The residual standard deviation at Day 5 from the unstructured covariance matrix from the associated MMRM will also be provided to the statisticians.

The 4-parameter Emax model will be fit using the latest version of the clinDR package[1]. This analysis will be conducted by the study statistician. A different statistician will conduct QC of the analysis. The outputs of the analysis will be provided as .txt files to the programming team for inclusion in the final CSR table and figure formats.

Prior distributions will be specified for the placebo response (E_0), and the difference in response between the highest dose (*dTarget*=600 mg) and placebo, denoted by *difTarget*. Non-informative priors will be used for these parameters. Note that the E_{max} parameter is derived from the other parameters and is thus not explicitly supplied. The residual standard deviation, *sigma*, is assigned a uniform prior distribution over a range we are confident will include the population value.

Parameter	Prior
E_0	Normal(Mean = 0, SD = 100)
difTarget	Normal(Mean = 0, SD = 100)
sigma	Uniform(lb = 0.01, ub = 100)

In addition, the projected ED_{50} is P_{50} = ~100 mg based on data from the C5091001 study. The distribution of the Hill parameter is the predictive distribution from the meta-data. The current distributions are listed below. They are the default distributions in clinDR. These default distributions will be updated if the meta-data and their analysis are updated before the completion of the current study.

Parameter	Prior
log(Hill)	*t*(Mean = 0, SD = 0.84, df = 5)
log(ED_{50})	log(P_{50}) + *t*(Mean = 0, SD = 1.74, df = 5)

The default burn-in and number of samples will be utilized along with thinning of 20, which will include 3 chains to assess convergence. Model diagnostics will be examined including trace and auto-correlations plots. If these raise concerns over model convergence, additional burn-ins, samples and thinning will be attempted to improve convergence. The final diagnostic plots will not be included in the clinical study report.

The following R code is included as an example that will be used as a basis for the analysis:

```
library(clinDR)
compileStanModels()
mmrmRes <- read.csv("LSmeans.csv",header=T,stringsAsFactors=F)
# Determine 'effective' subject numbers based on MMRM SD at Day 5E:
mmrm_sd <- x.xxx # Provided by programming
mmrmRes$N <- trunc((mmrm_sd/mmrmRes$StdErr)^2,0)

# Set-up priors and MCMC options:
prior_mmrm <- emaxPrior.control(epmu=0, epsca=100, difTargetmu=0, difTargetsca=100, dTarget=600, effDF=9999, p50=100, sigmalow=0.1, sigmaup=100)
mcmc_mmrm <- mcmc.control(chains=3,thin=20,seed=169)

### Run Emax model: ###
emaxMMRM <- fitEmaxB(mmrmRes$Estimate,mmrmRes$dose,prior_mmrm,modType=4,count=mmrmRes$N,msSat=mmrm_sd^2,mcmc=mcmc_mmrm)

# Diagnostics and output:
stan_trace(emaxMMRM$estanfit) # Look at trace
stan_dens(emaxMMRM$estanfit) # Look at densities
stan_ac(emaxMMRM$estanfit) # Look at autocorrelation
```

```
summary(emaxMMRM) # Summary of model parameters
plot(emaxMMRM) # Look at fitted vs. observed data
emaxMMRMout <- predict(emaxMMRM,dosevec=mmrmRes$dose,clev=0.80) # Get dose predictions
```

Model parameters, posterior medians and 80% credible intervals as specified in Section 5.2.5 will be output and provided back to the programming team after QC is complete.

The statistical summary for analysis (Emax) of CFB for viral load at Day 5 will take the following form:

			Difference to placebo	
Treatment Group	Posterior Median	80% CI	Difference	80% CI
Placebo				
100 mg				
300 mg				
600 mg				

The supporting statistical output will take the following form:

	Mean	SE	L80	U80
e50				
lambda				
emax				

	Mean	SE	L80	U80
e0[1]				
Sigma[1]				
difTarget				

Appendix 4. Statistical Methodology Details

The following SAS code is to be used as a guide for implementation.

Example SAS code for MMRM Model:

```
proc mixed data = dataset method=reml;
        class subject treatment visit covar;
        model cfb = treatment base visit base* visit visit *treatment covar /ddfm=kr residual outp=resid_out;
        repeated time /subject=subjid type = un;
        lsmeans treatment*time/diff cl alpha=0.1;
        ods output lsmeans=lsmeans_out;
        ods output diffs=diffs_out;
        ods output CovParms=CovParms_out;
run;
```

Note that the "covar" argument will include all or some of the covariates described in Section 6.1.1.1.

Appendix 5. Signs and Symptoms Attributable to COVID-19

Daily Sign and Symptom Collection	Entry Criterion #4 Targeted (used for study entry)	Daily Signs and Symptom Collection	Targeted Symptom Analysis	5 Symptom Analysis*
Stuffy or runny nose	X	X	X	X
Sore throat	X	X	X	X
Cough	X	X	X	X
Feeling hot or feverish	X	X	X	X
Fatigue (low energy or tiredness)	X	X		X
Shortness of breath or difficulty breathing	X	X	X	
Shortness of breath (difficulty breathing) while resting		X		
Shortness of breath (difficulty breathing) while physically active		X		
Chest pain		X		
Low energy or tiredness after physical activity		X		
Difficulty concentrating		X		
Chills or shivering	X	X	X	
Muscle or body aches	X	X	X	
Diarrhea (loose or watery stools)	X	X	X	

Daily Sign and Symptom Collection	Entry Criterion #4 Targeted (used for study entry)	Daily Signs and Symptom Collection	Targeted Symptom Analysis	5 Symptom Analysis*
Nausea (feeling like you wanted to throw up)	X	X	X	
Vomiting (throw up)	X	X	X	
Headache	X	X	X	
Loss of smell		X		
Loss of taste		X		

*Resolution of symptoms will be assessed as follows: for preexisting symptoms that were present before the onset of COVID-19 and considered by the patient to have worsened at baseline, severe symptoms at baseline must have improved to moderate or better (including no symptoms), moderate symptoms at baseline must have improved to mild or better (including no symptoms), and mild symptoms at baseline must have remained mild or better (including no symptoms) and for preexisting symptoms that were present before the onset of COVID-19 and considered by the patient not to have worsened at baseline, severe symptoms at baseline must have remained severe or improved (including no symptoms), moderate symptoms at baseline must have remained moderate or improved (including no symptoms), and mild symptoms at baseline must have remained mild or better (including no symptoms). Symptoms other than the above (those not occurring before the onset of COVID-19 or those that occur at or after baseline) must have completely resolved. Patients will be considered to have achieved resolution if the 5 COVID-19 symptoms remain resolved for ⩾24 hours.

Appendix 6. List of Abbreviations

Abbreviation	Term
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the curve
BMI	body mass index
BP	blood pressure
B/P	blood to plasma
CaPS	CDISC and Pfizer Standards
CDARS	Clinical Data Analysis and Reporting System
CDISC	Clinical Data Interchange Standards Consortium
CFB	change from baseline
CI	confidence interval
CRF	case report form
CSR	clinical study report
CV	coefficient of variation
DR	dose response
ECG	electrocardiogram
ET	early termination
FAS	full analysis set
ICU	intensive care unit
IRC	internal review committee
LLOQ	lower limit of quantitation
LS	least-squares
LSM	least-squares mean
MAR	missing at random
MedDRA	Medical Dictionary for Regulatory Activities
MFAS	modified full analysis set
MMRM	mixed-effects model with repeated measures
N/A	not applicable
NP	nasopharyngeal
PD	pharmacodynamic(s)
PK	pharmacokinetic(s)
PRO	patient-reported outcome
PT	preferred term
QC	quality control
QTc	corrected QT
QTcF	corrected QT (Fridericia method)
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation

Abbreviation	Term
SE	standard error
SoA	schedule of activities
SOP	standard operating procedure
TEAE	treatment-emergent adverse event
VAP	virology analysis plan
VL	viral load
WHO	World Health Organization