Protocol C5091008

A Phase 1, Open-Label, 2-Period, Fixed Sequence Study to Estimate the Effect of Itraconazole on the Pharmacokinetics of PF-07817883 in Healthy Adults

Statistical Analysis Plan
(SAP)

Version: 1

Date: 30 May 2023

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NOTE: *Italicized* text within this document has been taken verbatim from the Protocol.

1. VERSION HISTORY

Table 1 Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 / 30 May 2023	Amendment 1 19 Apr 2023	N/A	N/A

2. INTRODUCTION

PF-07817883 is a potent and selective inhibitor of the SARS-CoV-2 M^{pro} that is currently being developed as an oral treatment for patients with COVID-19.

The purpose of the study is to estimate the effect of itraconazole, a strong CYP3A4 inhibitor, on the PK of PF-07817883 in healthy adults. Results from this study will provide guidance for dosing recommendations with concomitant medications that have CYP3A inhibitory potential.

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study C5091008.

2.1. Modifications to the Analysis Plan Described in the Protocol

None.

2.2. Study Objectives, Endpoints, and Estimands

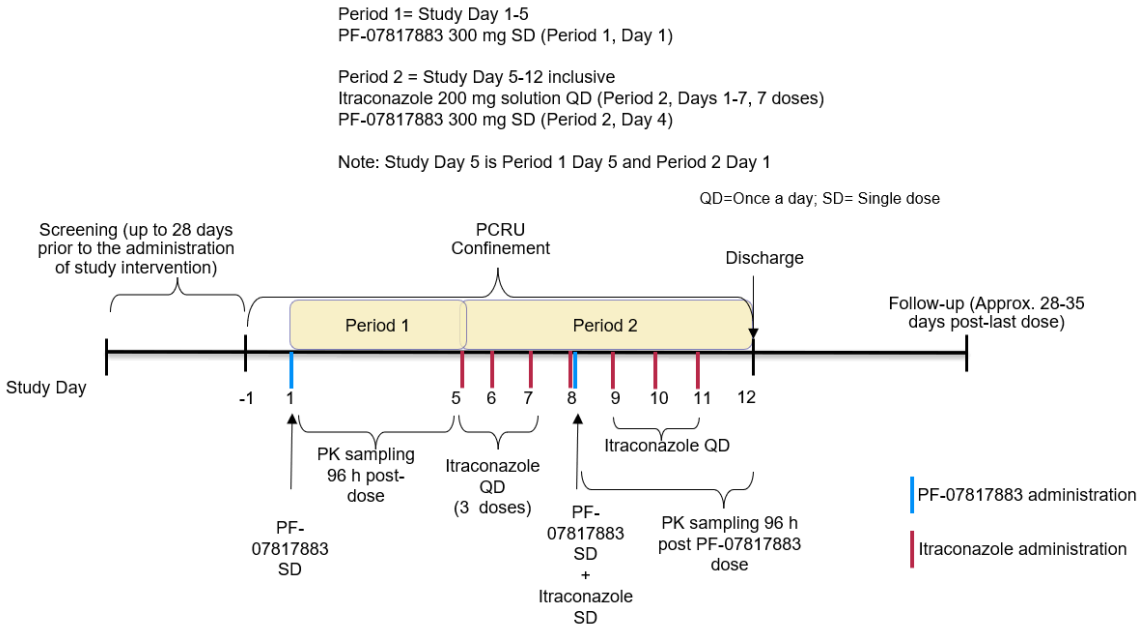
The following are the objectives and endpoints in this study. Estimand framework will not be applied to this Phase 1 study in healthy participants.

Objectives	*Endpoints*
Primary:	***Primary:***
• *To estimate the effect of multiple doses of itraconazole 200 mg QD on the PK of PF-07817883 following a single oral dose of PF-07817883 300 mg*	• *PF-07817883 plasma PK parameters: C_{max} and AUC_{inf} (if data permits, otherwise AUC_{last}) with itraconazole (test) versus without itraconazole (reference)*
Secondary:	***Secondary:***
• *To evaluate the safety and tolerability of PF-07817883 in healthy participants in the absence and presence of multiple doses of itraconazole* • *To characterize additional PK parameters of PF-07817883 when administered alone or with itraconazole in healthy participants*	• *Assessment of TEAEs, clinical laboratory abnormalities, vital signs, physical exams, and 12-lead ECGs* • *PF-07817883 plasma PK parameters: T_{max}, and if data permits, $t_{½}$, CL/F, V_z/F, with and without coadministration of itraconazole*
Tertiary/Exploratory:	***Tertiary/Exploratory:***
• *To assess the similarity of PK in blood by microsampling technique(s) with those in plasma by venipuncture* • *To characterize additional PK parameters of PF-07817883 following a single oral dose of PF-07817883 with and without itraconazole by renal function* • *To evaluate the drug-product acceptability of PF-07817883*	• *Concentration of PF-07817883 in blood and plasma as well as PF-07817883 plasma PK parameters: AUC_{12}, C_{max}* • *Concentration of PF-07817883 in urine and urine PF-07817883 PK parameters: Ae_{24}, CL_R, if applicable and as data permits* • *Score on a 14-item drug-product acceptability questionnaire*

2.3. Study Design

This is a Phase 1, open label, 2-period, fixed sequence study to estimate the effect of the strong CYP3A4 inhibitor, itraconazole, on the plasma and urine (if applicable) PK of PF-07817883 in healthy adult participants. The study will consist of 2 treatments: a single oral dose of PF 07817883 300 mg alone and a single oral dose of PF-07817883 300 mg in combination with multiple doses of itraconazole 200 mg QD. A total of approximately 12 healthy adults will be enrolled into the study to ensure at least 10 participants complete the study. The treatment will consist of a single fixed sequence. Participants who discontinue from the study for non-safety reasons may be replaced at the sponsor's discretion in collaboration with the investigator.

Figure 1. Study Schema



3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

The primary endpoints of the study are plasma C_{max} and AUC_{inf} (if data permits, otherwise AUC_{last}) of PF-07817883 following a single dose administration of PF-07817883 (alone) and coadministered with multiple doses of itraconazole. Adjusted geometric mean ratios of C_{max}, AUC_{inf} and AUC_{last} will be derived.

PK parameters of PF-07817883 will be derived (as data permits) from the concentration-time data using standard noncompartmental methods as outlined in Table 2. Actual PK sampling times will be used in the derivation of PK parameters. In the case that actual PK sampling times are not available, nominal PK sampling time will be used in the derivation of PK parameters.

Table 2. Plasma PF-07817883 PK Parameter Definitions

Parameter	***Definition***	***Method of Determination***
C_{max}	*Maximum observed concentration*	*Observed directly from data*
AUC_{inf}*	*Area under the plasma concentration time curve from time 0 extrapolated to infinite time*	$AUC_{last} + (C_{last}*/k_{el})$, *where* C_{last}* *is the predicted plasma concentration at the last quantifiable time point from the log-linear regression analysis*
AUC_{last}	*Area under the plasma concentration-time profile from time zero to the time of the last quantifiable concentration* (C_{last}).	*Linear/Log trapezoidal method.*
AUC_{12}	*Area under the plasma concentration-time profile from time zero to 12 hours*	*Linear/Log trapezoidal method.*
AUC_{24}	*Area under the plasma concentration-time profile from time zero to 24 hours*	*Linear/Log trapezoidal method.*
T_{max}	*Time for* C_{max}	*Observed directly from data as time of first occurrence*
$t_{½}$*	*Terminal half-life*	$Log_e(2)/k_{el}$, *where* k_{el} *is the terminal phase rate constant calculated by a linear regression of the loglinear concentration-time curve. Only those data points judged to describe the terminal loglinear decline will be used in the regression.*
CL/F*	*Apparent clearance*	$Dose/AUC_{inf}$
V_z/F*	*Apparent volume of distribution*	$Dose/(AUC_{inf} \bullet k_{el})$

** If data permits.*

3.2. Secondary Endpoints

The secondary endpoints include the overall safety profile of a single dose of PF-07817883 alone and with multiple doses of itraconazole, as characterized by adverse events, laboratory tests, vital signs, physical exams, and 12-lead ECGs (discussed in Section 3.5).

Other secondary endpoints are additional plasma PK parameters (including T_{max}, $t_{1/2}$, CL/F and V_z/F, defined in Table 2) of PF-07817883 (following a single dose administration of PF-07817883 alone and with multiple doses of itraconazole).

3.3. Other Endpoints

3.3.1. Exploratory PK Endpoints

Blood (by microsampling using the Tasso® M20 device) and urine samples for urine PK analysis of PF-07817883 will be taken according to the SoA given in the protocol. For each individual, a blood to plasma (B/P) ratio will be calculated by dividing concurrent (i.e. Day 1, 1 hour post-dose) whole blood PF-07817883 concentration with the plasma PF-07817883 concentration. A geometric mean and CV% of the B/P ratio from all individuals will also 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 from all individuals. AUC_{12} and C_{max} will be derived from blood samples collected using the Tasso® M20 device, and then adjusted for B/P ratio. Concentration of PF-07817883 in urine will be analyzed and additional urine PK parameters defined in Table 3 will be derived.

Table 3. Urine PF-07817883 PK parameter definitions

Parameter	***Definition***	***Method of Determination***
Ae_{24}	*Total amount of unchanged drug excreted in the urine over 24 hours*	*Sum of amount excreted for each collection period.*
$Ae_{24\%}$	*Total amount of unchanged drug excreted in the urine over 24 hours, expressed as percent of dose*	$100 \times (Ae_{24}/Dose)$
CL_R	*Renal clearance*	Ae_{24}/AUC_{24}

3.3.2. Drug-Product Acceptability

Drug product acceptability will be assessed based on participants' responses to a sponsor-provided 14-item questionnaire. Each item will be evaluated on a Likert scale with numeric categories to capture the level of agreement or disagreement with a statement about drug-product appearance, palatability, swallowability, or overall impression of taking the drug product (1=strongly agree, 5=strongly disagree).

3.4. Baseline Variables

Baseline characteristics will be collected according to the schedule of activities (SoA) as specified in the protocol.

3.5. Safety Endpoints

The following data will be considered in standard safety summaries (see protocol for collection days, baseline assessment, and list of parameters):

- Adverse events (AE)
- Laboratory data
- Vital signs data
- ECG results

3.5.1. Adverse Events

Any adverse events occurring following start of treatment will be considered as treatment emergent adverse event (TEAE). Events that occur during follow-up within the lag time of up to 35 days after the last dose of study intervention will be counted as treatment emergent and attributed to the last treatment taken. Events that occur during the washout period between study periods will be counted as treatment emergent and attributed to the previous treatment taken. The time period for collecting AEs ("active collection period") for each participant begins from the time the participant provides informed consent.

3.5.2. Laboratory Data

Safety laboratory tests will be performed as described in the protocol. To determine if there are any clinically significant laboratory abnormalities, the haematological, clinical chemistry (serum) and urinalysis safety tests will be assessed against the criteria specified in the sponsor reporting standards. The assessment will not take into account whether each participant's baseline test result is within or outside the laboratory reference range for the particular laboratory parameter.

For both periods, the baseline measurement is the last predose measurement prior to administration of PF-07817883 in each study period. Changes from baseline will be defined as the change between the postdose and baseline measurements.

3.5.3. Vital Signs

Supine blood pressure (BP), pulse rate (PR) and respiratory rate will be measured at times specified in the SoA given in the protocol.

For both periods, the baseline measurement is the last predose measurement prior to administration of PF-07817883 in each study period. Changes from baseline will be defined as the change between the postdose and baseline measurements.

3.5.4. Electrocardiograms

QT interval, QTcF, PR interval, QRS and heart rate (HR) will be recorded at each assessment time indicated in the SoA given in the protocol. If not supplied, QTcF will be derived using Fridericia's heart rate correction formula:

$$QTcF = QT / (RR)^{(1/3)} \text{ where } RR = 60/HR \text{ (if not provided)}$$

For both periods, the baseline measurement is the last predose measurement prior to administration of PF-07817883 in Period 1. Changes from baseline will be defined as the change between the postdose ECG measurement and the baseline ECG.

The maximum absolute value (postdose) and the maximum increase from baseline for QTcF, PR interval and QRS, over all measurements taken postdose, will be determined.

The maximum increase from baseline will be calculated by first subtracting the baseline value from each postdose measurement to give the change from baseline. The maximum of these values over the respective period will then be selected, except in the case where a participant does not show an increase. In such an instance, the minimum decrease should be taken.

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 releasing the database and classifications will be documented per standard operating procedures.

Participant Analysis Set	***Description***
Enrolled	*"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 assignment to study intervention. Potential participants who are screened for the purpose of determining eligibility for the study, but do not participate in the study, are not considered enrolled, unless otherwise specified by the protocol. A participant will be considered enrolled if the informed consent is not withdrawn prior to participating in any study activity.*
Safety Analysis Set	*All participants enrolled and who take at least 1 dose of study intervention.*
PK Concentration Set	*All participants who take at least 1 dose of study intervention and in whom at least 1 concentration value is reported.*
PK Parameter Set	*All participants who take at least 1 dose of study intervention and in whom at least 1 of the PK parameters of primary interest are reported.*

5. GENERAL METHODOLOGY AND CONVENTIONS

Final analysis will be performed after study participant data set release following last participant last visit.

5.1. Hypotheses and Decision Rules

No statistical hypothesis will be tested in this study.

5.2. General Methods

5.2.1. Analyses for Binary/Categorical Endpoints

For binary or categorical variables, number of participants, numbers and percentages of participants meeting the categorical criteria will be presented in accordance with the Clinical Data Interchange Standards Consortium and Pfizer Standards (CaPS).

5.2.2. Analyses for Continuous Endpoints

For continuous variables, the data will be summarized using the number of participants, mean, median, standard deviation (SD), minimum, and maximum in accordance with the CaPS. For appropriate PK parameters, geometric mean and geometric coefficient of variation (%CV) will also be summarized.

5.3. Methods to Manage Missing Data

5.3.1. PK Concentrations

Methods to handle missing PK data are described below.

Concentrations Below the Limit of Quantification:

In all data presentations (except listings), concentrations below the limit of quantification (BLQ) will be set to zero. (In listings BLQ values will be reported as "<LLQ" where LLQ will be replaced with the value for the lower limit of quantification.).

Deviations, Missing Concentrations and Anomalous Values:

In summary tables and plots of median profiles, statistics will be calculated having set concentrations to missing if one of the following cases is true:

1. A concentration has been collected as ND (i.e., not done) or NS (i.e., no sample).

2. A deviation in sampling time (time deviation > 20%) is of sufficient concern or a concentration has been flagged as anomalous by the pharmacokineticist.

Note that summary statistics will not be presented at a particular time point if more than 50% of the data are missing.

An anomalous concentration value is one that, after verification of bioanalytical validity, is grossly inconsistent with other concentration data from the same individual or from other participants. For example, a BLQ concentration that is between quantifiable values from the same dose is considered as anomalous. Anomalous concentration values may be excluded from PK analysis at the discretion of the PK analyst or pharmacokineticist.

5.3.2. PK Parameters

Actual PK sampling times will be used in the derivation of PK parameters. If a PK parameter cannot be derived from a participant's concentration data, the parameter will be coded as NC (i.e., not calculated). (Note that NC values will not be generated beyond the day that a participant discontinues). In summary tables, statistics will be calculated by setting NC values to missing; and statistics will be presented for a particular treatment with ≥3 evaluable measurements. PK parameter analyses will not be performed for a particular parameter if more than 50% of the data are NC.

If an individual participant has a known biased estimate of a PK parameter (due for example to an unexpected event such as vomiting before all the compound is adequately absorbed from the gastrointestinal tract), this will be footnoted in summary tables and will not be included in the calculation of summary statistics or statistical analyses.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoints

The primary endpoints C_{max} and AUC_{inf} (if data permits, otherwise AUC_{last}) will be summarized descriptively by treatment and will include the set of summary statistics as specified in Table 4. Box and whisker plots for individual participant parameters (C_{max}, AUC_{inf} and AUC_{last}) will be plotted by treatment and overlaid with geometric means.

Natural log transformed parameters C_{max} and AUC_{inf} (if data permits, otherwise AUC_{last}) of PF-07817883 will be analyzed using a mixed effect model with treatment as fixed effect and participant as a random effect. Estimates of the adjusted means, adjusted mean differences (Test-Reference) and corresponding 90% CIs will be obtained from the model. The adjusted mean differences and 90% CIs for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% CI for the ratios. PF-07817883 administered alone will be the Reference treatment and PF-07817883 co-administered with itraconazole will be the Test treatment.

For C_{max}, AUC_{inf} and AUC_{last}, a listing of the individual participant ratios (Test/Reference) will be provided.

Residuals from the model will be examined for normality and the presence of outliers via visual inspection of plots of residuals vs predicted values and normal probability plots of residuals but these will not be included in the CSR. If there are major deviations from normality or outliers then the effect of these on the conclusions will be investigated through alternative transformations and/or analyses excluding outliers. Justification for any alternative to the planned analysis will be provided in the clinical study report.

6.2. Secondary Endpoints

6.2.1. Safety data

Safety data will be analyzed in accordance with the CaPS (described in Section 6.5).

6.2.2. Other PK parameters

T_{max}, $t_{1/2}$, CL/F and V_z/F will be summarized descriptively by treatment and will include the set of summary statistics as specified in Table 4.

PK parameter summaries:

The PF-07817883 PK parameters will be summarized descriptively by treatment in accordance with Pfizer data standards for the PK Parameter Set, as data permit. Missing values will be handled as detailed in Section 5.3.2. Each PF-07817883 PK parameter will be summarized by treatment and will include the set of summary statistics as specified in Table 4.

Table 4. PK Parameters to be Summarized Descriptively by Treatment

Parameter	Summary Statistics
AUC_{inf}, AUC_{last}, AUC_{12}, AUC_{24}, C_{max}, CL/F, V_z/F, Ae_{24}, $Ae_{24\%}$, CL_R	N, arithmetic mean, median, SD, %CV, minimum, maximum, geometric mean and geometric %CV
T_{max}	N, median, minimum, maximum
$t_{½}$	N, arithmetic mean, median, SD, %CV, minimum, maximum

N: Number of participants contributing to the summary statitics

Supporting data from the estimation of $t_{½}$ and AUC_{inf} will be listed by treatment: terminal phase rate constant (k_{el}); goodness of fit statistic from the log-linear regression (r^2); the percent of AUC_{inf} based on extrapolation (AUC_{extrap}%); and the first, last, and number of time points used in the estimation of k_{el}. This data may be included in the clinical study report.

PK concentration summaries:

The plasma concentrations of PF-07817883 will be listed and descriptively summarized by nominal PK sampling time and treatment for the PK Concentration Set. Individual participant and summary profiles (mean and median plots) of the plasma concentration-time data will be plotted by treatment using actual and nominal times, respectively. Mean and median PF-07817883 plasma concentration profiles will be presented on both linear and semi-log scales.

Presentations for PF-07817883 plasma concentrations will include:

- A listing of all concentrations sorted by participant ID, treatment and nominal time postdose. The concentration listing will also include the actual times. Deviations from the nominal time will be provided in a separate listing.

- A summary of concentrations by treatment and nominal time postdose, where the set of statistics will include n, mean, median, SD, %CV, minimum, maximum and the number of concentrations above the LLQ.

- Median concentrations time plots (on both linear and semi-log scales) against nominal time postdose by treatment (all treatments on the same plot per scale, based on the summary of concentrations by treatment and time postdose).

- Mean concentrations time plots (on both linear and semi-log scales) against nominal time postdose by treatment (all treatments on the same plot per scale, based on the summary of concentrations by treatment and time postdose).

- Individual concentration time plots by treatment (on both linear and semi-log scales) against actual time postdose (there will be separate spaghetti plots for each treatment per scale).

- Individual concentration time plots by participant (on both linear and semi-log scales) against actual time postdose [there will be separate plots for each participant (containing all treatments) per scale].

6.2.3. Other Endpoints – Exploratory PK Endpoints

AUC_{12} and C_{max} derived from blood samples collected using the Tasso® M20 device adjusted for B/P ratio will be summarized for PF-07817883 (administered alone in Period 1) and will include the set of summary statistics as specified in Table 4. Summary statistics 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 will be calculated.

Furthermore, to determine correlation in concentrations derived from time matched Tasso® M20 microsampling (calculated using individual or population) and traditional venous plasma sampling, Bland-Altman plot 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.

In addition, Ae_{24}, $Ae_{24\%}$ and CL_R, derived from PF-07817883 concentrations measured from urine samples collected (if analyzed) will be summarized by treatment and will include the set of summary statistics as specified in Table 4.

6.2.4. Drug-Product Acceptability

For each item in the Drug-Product Acceptability Questionnaire, summary statistics will include number and percent with each numeric score (1,2,3,4,5) and negative (1, 2), neutral (3) and positive (4, 5) scores and will be presented by item and domain (Appearance, Mouthfeel, Taste, Swallowability and Overall assessment).

6.3. Subset Analyses

There are no planned subset analyses.

6.4. Baseline and Other Summaries and Analyses

6.4.1. Demographic Summaries

Demographic characteristics will be summarized for enrolled population in accordance with the CaPS.

6.4.2. Study Conduct and Participant Disposition

Participants evaluation groups will show end of study participant disposition. Frequency counts will be supplied for participant discontinuation(s) by treatment. Data will be reported in accordance with the CaPS.

6.4.3. Study Treatment Exposure

Study treatment exposure will be listed.

6.4.4. Concomitant Medications and Nondrug Treatments

All concomitant medication(s) as well as non-drug treatment(s) will be reported in the listings.

6.5. Safety Summaries and Analyses

All safety analyses will be performed on the Safety Analysis Set.

Safety data will be presented in tabular and/or graphical format and summarized descriptively, where appropriate.

Safety data will be summarized for three (3) separately defined treatments: (i) PF-07817883 300 mg SD (from Period 1 Day 1 up to just before the first dose of itraconazole administered alone in Period 2 Day 1), (ii) itraconazole 200 mg QD alone (from first dose of itraconazole administered alone in Period 2 Day 1 up to just before coadministration of PF-07817883 in Period 2 Day 4), and (iii) itraconazole 200 mg QD with PF-07817883 300 mg SD (from coadministration of PF-07817883 with itraconazole in Period 2 Day 4 through the end of the study).

A set of summary tables split by these 3 treatments will be produced to evaluate any potential risk associated with the safety and tolerability of administering PF-07817883 300 mg SD alone, itraconazole 200 mg QD alone, and PF-07817883 300 mg SD in the presence of itraconazole 200 mg QD.

6.5.1. Adverse Events

Adverse events will be reported in accordance with the CaPS.

Participant discontinuations due to adverse events will be detailed by treatment. Data will be reported in accordance with the CaPS.

6.5.2. Laboratory Data

Laboratory data will be listed and summarized by treatment in accordance with the CaPS.

6.5.3. Vital Signs

Vital signs data will be listed and summarized by treatment in accordance with the CaPS.

6.5.4. Electrocardiograms

ECG data will be listed and summarized by treatment in accordance with the CaPS.

7. INTERIM ANALYSES

No formal interim analysis will be conducted for this study. As this is an open-label study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment, facilitating PK modeling, and/or supporting clinical development.

7.1. Introduction

Not applicable.

7.2. Interim Analyses and Summaries

Available safety and PK data may be reviewed.

APPENDICES

Appendix 1. Summary of Analyses

Endpoint	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Method
Ratio of PF-07817883 C_{max}, AUC_{inf} and AUC_{last}	PK Parameter Set	Observed data	Mixed effect ANOVA model
PF-07817883 PK parameters	PK Parameter Set	Observed data and imputed (Section 5.3.2) data	Descriptive statistics
PF-07817883 concentrations	PK Concentration Set	Observed and imputed (Section 5.3.1) data	Descriptive statistics
Safety data	Safety Analysis Set	Observed data	Descriptive statistics
Drug-product acceptability data	Safety Analysis Set	Observed data	Descriptive statistics

Appendix 2. SAS Code for Analyses

An example of the PROC MIXED code is provided below:

For the primary objective:

```
proc mixed data=tab.pk;
        class trt participant;
        model log&var=trt / ddfm=KR;
        random participant / subject=participant;
        lsmeans trt;
        estimate 'B vs A' trt  -1  1  /cl alpha=0.1;

        ods 'Estimates' out=est&var;
        ods 'lsmeans' out=ls&var;
        ods 'covparms' out=cov&var;
        ods 'tests3' out=tst&var;
run;

/* Letter assignments for treatments (trt) within the estimate statement above are as follows
A: single dose of PF-07817883 300 mg (reference)
B: multiple doses of itraconazole 200 mg QD + single dose of PF-07817883 300 mg (test)
*/
```

Appendix 3. List of Abbreviations

Abbreviation	Term
%CV	coefficient of variation
AE	adverse event
Ae_{24}	cumulative total amount of drug recovered unchanged in the urine, from time 0 to 24 hours
$Ae_{24\%}$	cumulative total amount of drug recovered unchanged in the urine, from time 0 to 24 hours, expressed as percent of dose
ANOVA	analysis of variance
AUC_{12}	area under the plasma concentration-time curve from time 0 to the time 12 hours
AUC_{24}	area under the plasma concentration-time curve from time 0 to the time 24 hours
$AUC_{extrap}\%$	the percent of AUC_{inf} based on extrapolation
AUC_{inf}	area under the plasma concentration-time profile from time zero extrapolated to infinite time
AUC_{last}	area under the plasma concentration-time profile from time zero to the time of the last quantifiable concentration
BLQ	below the limit of quantitation
B/P	blood to plasma
BP	blood pressure
CaPS	Clinical Data Interchange Standards Consortium and Pfizer Standards
CI	confidence interval
CL/F	apparent clearance
C_{last}	predicted plasma concentration at the last quantifiable time point from the log-linear regression analysis
CL_R	renal clearance
C_{max}	maximum plasma concentration
COVID-19	coronavirus disease 2019
CSR	clinical study report
CYP3A	cytochrome P450, family 3, subfamily A
ECG	electrocardiogram
HR	heart rate
k_{el}	elimination rate constant estimated from the log-linear regression analysis
LLQ	lower limit of quantitation
M^{pro}	main protease
ms	milliseconds
N/A	not applicable
NC	not calculated
ND	not done
NS	no sample

Abbreviation	Term
PK	pharmacokinetic(s)
PR	pulse rate
PR interval	time from the beginning of the P wave to the beginning of the QRS complex
QD	once a day
QRS	Combination of Q-, R- and S- wave on an electrocardiogram representing ventricular depolarization
QTc	corrected QT
QTcF	corrected QT (Fridericia method)
r^2	goodness of fit statistic from the log-linear regression
RR interval	the time between the start of one QRS complex and the start of the next QRS complex
SAP	statistical analysis plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	standard deviation; single dose
SoA	schedule of activities
$t_{1/2}$	terminal plasma elimination half-life
TEAE	treatment emergent adverse event
T_{max}	time for C_{max}
V_z/F	apparent volume of distribution after oral dose