Protocol C2321005

A Phase 1, Randomized, Open-label, 3-period, crossover, single-dose, 2-part study in healthy participants to investigate the effect of tablet formulation and food on the relative bioavailability of PF-06821497

Statistical Analysis Plan
(SAP)

Version: 1

Date: 30 Mar 2023

[redacted]

TABLE OF CONTENTS

LIST OF TABLES

APPENDICES

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 Mar 2023	Original 02 Feb 2023	N/A	N/A

2. INTRODUCTION

PF-06821497 is a potent and selective inhibitor of EZH2 as evidenced by its biochemical inhibition of both WT and EZH2 Y641N mutant enzymes. PF-06821497 is currently being proposed for investigation in patients with SCLC, CRPC, DLBCL, and FL.

The purpose of the study is to investigate the relative bioavailability of tablet formulations of PF-06821497 and to characterize the effect of food on a PF-06821497 CCI tablet formulation (Formulation 2). The data generated from this study will be used to support the pivotal study formulation, to inform dose administration instructions for PF-06821497 with regard to dosing with or without food, and to enable the establishment of the API particle size specifications for eventual commercialization.

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study C2321005.

2.1. Modifications to the Analysis Plan Described in the Protocol

None.

2.2. Study Objectives and Endpoints

Objectives	***Endpoints***
Primary:	***Primary:***
• *To estimate the bioavailability of a single CC mg dose of PF-06821497 CC tablet formulation (Formulation 2) relative to a single CC mg dose of PF-06821497 CCI tablet formulation (Formulation 1) under fasted conditions in adult healthy participants*	• *Plasma AUC_{inf} and C_{max} for PF-06821497. (AUC_{last} will be used as the primary estimate if AUC_{inf} cannot be reliably estimated).*
Secondary:	***Secondary:***
• *To estimate the bioavailability of a single CC mg dose of PF-06821497 CC tablet (larger API particle size) formulation (Formulation 3) relative to a single CC mg dose of PF-06821497 CC tablet (Formulation 2) and a single 250 mg dose of the PF-06821497 CCI tablet formulation (Formulation 1) under fasted conditions in adult healthy participants*	• *Plasma AUC_{inf} and C_{max} for PF-06821497 for CC tablet (larger API particle size) (Formulation 3) relative to CC (Formulation 2) and CCI tablet (Formulation 1) formulations. (AUC_{last} will be used as the primary estimate if AUC_{inf} cannot be reliably estimated).*

Objectives	***Endpoints***
• *To estimate the effect of a high-fat, high-calorie meal on the bioavailability of a single* CCI *mg dose of the PF-06821497* CC *tablet formulation (Formulation 2) relative to fasted conditions in adult healthy participants* • *To estimate the effect of a low-fat, low-calorie meal on the bioavailability of a single* CCI *mg dose of the PF-06821497* CC *tablet formulation (Formulation 2) relative to fasted conditions in adult healthy participants*	• *Plasma AUC_{inf} and C_{max} for PF-06821497 under fed (high-fat, high-calorie meal) conditions relative to fasting conditions. (AUC_{last} will be used as the primary estimate if AUC_{inf} cannot be reliably estimated).* • *Plasma AUC_{inf} and C_{max} for PF-06821497 under fed (low-fat, low-calorie meal) conditions relative to fasting conditions. (AUC_{last} will be used as the primary estimate if AUC_{inf} cannot be reliably estimated).*
• *To evaluate the safety and tolerability of PF-06821497 when administered as a tablet formulation to healthy participants*	• *Assessment of TEAEs, clinical laboratory abnormalities, vital signs, physical examinations, and 12-lead ECGs.*
CCI [redacted]	[redacted]
[redacted]	[redacted]

2.3. Study Design

This is a Phase 1, randomized, open-label, 3-period, crossover, single-dose 2-part study in healthy participants to investigate the effect of tablet formulation and food on the bioavailability of PF-06821497.

In each part of the study, each enrolled participant will participate in 3 study periods to receive 3 different treatments according to the sequence determined by randomization with 5-day washouts between PF-06821497 administration:

Part 1 (rBA):

- *Treatment A – Single* CCI *mg dose* CCI [redacted] *tablet formulation (Formulation 1), under fasting conditions (following an overnight fast of at least 10 hours)*
- *Treatment B – Single* CCI *mg dose* CCI [redacted] *of WG tablet formulation (Formulation 2), under fasting conditions (following an overnight fast of at least 10 hours)*
- *Treatment C – Single* CCI *mg dose* CCI [redacted] *tablet formulation (larger API particle size) (Formulation 3), under fasting conditions (following an overnight fast of at least 10 hours)*

Part 2 (Food Effect):

- *Treatment D – Single [redacted] tablet formulation (Formulation 2), under fasting conditions (following an overnight fast of at least 10 hours)*
- *Treatment E – Single [redacted] tablet formulation (Formulation 2), given with a low-fat/low-calorie meal*
- *Treatment F – Single [redacted] tablet formulation (Formulation 2), given with a high-fat/high-calorie meal*

Approximately 18 participants will be enrolled to the study intervention. If there are participants who withdraw or discontinue treatment and are considered to be non-evaluable with respect to the primary PK objective(s), additional participants can be enrolled at the discretion of the investigator upon consulation with the sponsor.

In each part of the study, each enrolled participant will receive 1 of the 3 treatments in each period according to treatment schedule shown in Table 2.

Table 2. Treatment Schedule

Part 1 (rBA):

Sequence	***Period 1***	***Washout: at least [redacted] days between PF-06821497 doses***	***Period 2***	***Washout: at least [redacted] days between PF-06821497 doses***	***Period 3***
1 (6 Participants)	*A*		*B*		*C*
2 (6 Participants)	*B*		*A*		*C*

Treatment A – [redacted] formulation (Formulation 1) [redacted] fasted;
Treatment B – [redacted] formulation (Formulation 2) [redacted] fasted;
Treatment C – [redacted] formulation (Formulation 3) [redacted] larger API particle size) fasted ;

Part 2 (Food effect):

Sequence	***Period 1***	***Washout: at least [redacted] days between PF-06821497 doses***	***Period 2***	***Washout: at least [redacted] days between PF-06821497 doses***	***Period 3***
1 (6 Participants)	*D*		*E*		*F*

Treatment D – [redacted] formulation (Formulation 2) [redacted] fasted;
Treatment E – [redacted] formulation (Formulation 2) [redacted] fed: Low-fat meal;
Treatment F – [redacted] formulation (Formulation 2) [redacted] fed: High-fat meal

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

The primary endpoints are the plasma AUC_{inf} (if data permit, otherwise AUC_{last}) and C_{max} for PF-06821497. The test/reference ratios for AUC_{inf} (if data permit), AUC_{last} and C_{max} will be derived with Treatment B (CCI formulation (Formulation 2) CCI fasted) as the Test treatment and Treatment A (CCI formulation (Formulation 1) CCI fasted) as the Reference treatment.

3.2. Secondary Endpoints

The test/reference ratios for AUC_{inf} (if data permit), AUC_{last} and C_{max} will be derived with Treatment C (CCI formulation (Formulation 3) CCI; larger API particle size) fasted) as the Test treatment and Treatment B (CCI formulation (Formulation 2) CCI (CCI) fasted) and Treatment A (CCI formulation (Formulation 1) CCI mg) fasted) as the Reference treatments.

The test/reference ratios for AUC_{inf} (if data permit), AUC_{last} and C_{max} will be derived with Treatments E and F (CCI formulation (Formulation 2) CCI) fed: low-fat meal and CCI formulation (Formulation 2) CCI) fed: high-fat meal) as the Test treatments and Treatment D (CCI formulation (Formulation 2) CCI) fasted) as the Reference treatment.

Included as secondary endpoints are the safety and tolerability data, discussed in Section 3.5.

3.3. Baseline Variables

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

3.4. Other Endpoints

CCI

Plasma PK parameters of PF-06821497 will be derived (as data permits) from the concentration-time data using standard noncompartmental methods as outlined in Table 3. The PF-06821497 plasma PK parameters will be summarized descriptively by Treatment. Plasma concentrations will be listed and summarized descriptively by Treatment, and nominal PK sampling time. Individual participant and summary profiles (mean and median plots) of the plasma concentration time data will be plotted using actual and nominal times, respectively.

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 3. Plasma PF-06821497 PK Parameters Definitions

Parameter	***Definition***	***Method of Determination***
*AUC_{inf}**	*area under the concentration-time curve from time 0 to infinity*	*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 and k_{el} is the terminal phase rate constant calculated by a linear regression of the loglinear concentration-time curve*
AUC_{last}	*area under the concentration-time curve from 0 to time of last measurable concentration*	*Linear/Log trapezoidal method.*
C_{max}	*maximum observed concentration*	*Observed directly from data*
CC I	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

**If data permits.*

3.5. Safety Endpoints

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

- adverse events (AE)
- laboratory data
- vital signs data
- electrocardiogram (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. 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 participants's baseline test result is within or outside the laboratory reference range for the particular laboratory parameter.

For each period, the baseline measurement is the predose measurement on Day -1.

3.5.3. Vital Signs

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

For each period, the baseline measurement is the predose measurement on Day 1.

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. 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 each period, the baseline measurement is the predose measurement on Day 1.

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. 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, are not considered enrolled, unless otherwise specified by the protocol.*

Participant Analysis Set	***Description***
PK Concentration Population	*The PK concentration population is defined as all participants randomized and treated who have at least 1 PF-06821497 concentration in at least 1 treatment period.*
PK Parameter Population	*The PK parameter analysis population is defined as all participants randomized and treated who have at least 1 of the PF-06821497 PK parameters of primary interest in at least 1 treatment period.*
Safety analysis set	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention. Participants will be analyzed according to the product they actually received.*

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. Pharmacokinetic Data

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 1 of the following cases is true:

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

2. A deviation in sampling time is of sufficient concern or a concentration has been flagged 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.

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 (ie, not calculated). (Note that NC values will not be generated beyond the day that a participant discontinues).

In summary tables, statistics will not be presented for a particular treatment group if more than 50% of the data are NC. For statistical analyses, PK parameters coded as NC will also be set to missing.

If an individual participant has a known biased estimate of a PK parameter (due for example to a dosing error or 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. CC

[redacted]

5.3.2. Safety Data

Missing values in standard summaries of AEs and laboratory data will be imputed according to CaPS.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoints

AUC_{inf} (if data permit), AUC_{last} and C_{max} will be summarized by treatment group and will include the set of summary statistics as specified in Table 4.

For the evaluation of relative bioavailability, *natural log transformed AUC_{inf} (if data permit), AUC_{last} and C_{max} will be analyzed using a mixed effects model with sequence, period and treatment as fixed effects and participant within sequence as a random effect. Estimates of the adjusted mean differences (Test-Reference) and corresponding 90% confidence intervals will be obtained from the model. The adjusted mean differences and 90% confidence intervals for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% confidence intervals for the ratios. Treatment A (CCI formulation (Formulation 1) CCI [redacted] fasted) will be the Reference treatment and Treatment B (CCI formulation (Formulation 2) CCI [redacted]) fasted) will be the Test treatment.*

For AUC_{inf}, AUC_{last} and C_{max}, a listing of the individual participant ratios (Test/Reference) will be provided. Box and whisker plots for AUC_{inf}, AUC_{last} and C_{max}, will be plotted by treatment and overlaid with geometric means.

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 given in the report of the study.

6.2. Secondary Endpoints

For the evaluation of relative bioavailability, *natural log transformed AUC_{inf} (if data permit), AUC_{last} and C_{max} will be analyzed using a mixed effects model with sequence and treatment as fixed effects and participant within sequence as a random effect. Estimates of the adjusted mean differences (Test-Reference) and corresponding 90% confidence intervals will be obtained from the model. The adjusted mean differences and 90% confidence intervals for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% confidence intervals for the ratios. Treatment A (CCI formulation (Formulation 1) CCI [redacted] mg) fasted) will be the Reference treatment and Treatment C (CCI formulation (Formulation 3) CCI [redacted] mg; larger API particle size) fasted) will be the Test treatment. For the second comparison, Treatment B (CCI formulation (Formulation 2) CCI [redacted] mg) fasted) will be the Reference treatment and Treatment C (CCI formulation (Formulation 3) CCI [redacted] mg; larger API particle size) fasted) will be the Test treatment.*

For the evaluation of food effect, *natural log transformed AUC_{inf} (if data permit), AUC_{last} and C_{max} will be analyzed using a mixed effects model with treatment as a fixed effect and participant as a random effect. Estimates of the adjusted mean differences (Test-Reference)*

and corresponding 90% confidence intervals will be obtained from the model. The adjusted mean differences and 90% confidence intervals for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% confidence intervals for the ratios. Treatment D (CCI formulation (Formulation 2) CCI mg) fasted) will be the Reference treatment and Treatments E and F (CCI formulation (Formulation 2) CCI mg) fed: low-fat meal and CCI formulation (Formulation 2) CCI) fed: high-fat meal) will be the Test treatments.

For AUC_{inf}, AUC_{last} and C_{max}, a listing of the individual participant ratios (Test/Reference) will be provided. Box and whisker plots for AUC_{inf}, AUC_{last} and C_{max}, will be plotted by treatment and overlaid with geometric means.

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 given in the report of the study.

Analyses and summaries of safety data are described in Section 6.6.

6.3. Other Endpoints

PK Parameters:

The PK parameters will be listed and summarized descriptively by treatment group in accordance with Pfizer data standards on the PK Parameter Analysis Set, as data permit. Missing values will be handled as detailed in Section 5.3.1. Each PK parameter will be summarized by treatment group 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}, C_{max}, CCI CCI	N, arithmetic mean, median, SD, %CV, minimum, maximum, geometric mean and geometric %CV

Supporting data from the estimation of $t_{½}$ and AUC_{inf} will be listed by analyte and group: 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 Concentrations:

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

Presentations of 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 given 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].

6.4. Subset Analyses

There are no planned subset analyses.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Demographic Summaries

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

6.5.2. 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.

6.5.3. Study Treatment Exposure

Study treatment exposure will be listed.

6.5.4. Concomitant Medications and Nondrug Treatments

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

6.6. 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.

6.6.1. 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.

6.6.2. Laboratory Data

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

6.6.3. Vital Signs

Vital sign data will be databased and available upon request.

6.6.4. Electrocardiograms

ECG data will be databased and available upon request.

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/PD modeling, and/or supporting clinical development.

Final analysis will follow the official database release. As this will be an open-label study, there is no formal unblinding of the randomization code.

APPENDICES

Appendix 1. SAS Code for Analyses

An example of the PROC MIXED code is provided below:

For the primary objective – relative BA:

```
proc mixed data=tab.pk;
        class seq period trt participant;
        model l&var=seq period trt/ ddfm=KR;
        random participant(seq) /subject=participant(seq);
        lsmeans trt;
        estimate 'B vs A' trt -1 1 0 /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;
```

For the secondary objective – relative BA:

```
proc mixed data=tab.pk;
        class seq trt participant;
        model l&var=seq trt/ ddfm=KR;
        random participant(seq) /subject=participant(seq);
        lsmeans trt;
        estimate 'C vs A' trt -1 0 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;

proc mixed data=tab.pk;
        class seq trt participant;
        model l&var=seq trt/ ddfm=KR;
        random participant(seq) /subject=participant(seq);
        lsmeans trt;
        estimate 'C vs B' trt 0 -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;
```

For the secondary objective – food effect:

```
proc mixed data=tab.pk;
        class trt participant;
        model l&var= trt/ ddfm=KR;
        random participant /subject=participant;
        lsmeans trt;
        estimate 'E vs D' trt -1 1 0 /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;

proc mixed data=tab.pk;
        class trt participant;
        model l&var= trt/ ddfm=KR;
        random participant /subject=participant;
        lsmeans trt;
        estimate 'F vs D' trt -1 0 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
Treatment A – CCI formulation (Formulation 1) CCI fasted;
Treatment B – CCI formulation (Formulation 2) CCI fasted;
Treatment C – CCI formulation (Formulation 3) CCI ; larger API particle
size) fasted;
Treatment D – WG formulation (Formulation 2) CCI fasted;
Treatment E – WG formulation (Formulation 2) CCI fed: Low-fat meal;
Treatment F – WG formulation (Formulation 2) CCI fed: High-fat meal  */
```

Appendix 2. List of Abbreviations

Abbreviation	Term
%CV	coefficient of variation
AE	adverse event
API	Active Pharmaceutical Ingredients
AUC_{extrap}%	the percent of AUC_{inf} based on extrapolation
AUC_{inf}	area under the concentration-time curve from time 0 to infinity
AUC_{last}	area under the concentration-time curve from 0 to time of last measurable concentration
BA	bioavailability
BLQ	below the limit of quantitation
BP	blood pressure
CaPS	Clinical Data Interchange Standards Consortium and Pfizer Standards
CI	confidence interval
C_{last}	last quantifiable concentration
CCI	[redacted]
C_{max}	maximum observed concentration
CRPC	castration resistant prostate cancer
CSR	clinical study report
DLBCL	diffuse large B-cell lymphoma
ECG	electrocardiogram
FL	follicular lymphoma
HR	heart rate
k_{el}	terminal phase rate constant
LLQ	lower limit of quantitation
mg	milligram
CCI	[redacted]
N/A	not applicable
NC	not calculated
ND	not done
NS	no sample
PD	pharmacodynamic(s)
PK	pharmacokinetic(s)
PR	pulse rate
PR interval	time from the beginning of the P wave to the beginning of the QRS complex
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
rBA	relative bioequivalence

Abbreviation	Term
RR	the time between the start of one QRS complex and the start of the next QRS complex
SAP	statistical analysis plan
SCLC	small cell lung cancer
SD	single dose; standard deviation
SoA	schedule of activities
[redacted]	[redacted]
TEAE	treatment emergent adverse event
CCI [redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
WT	wild type