Statistical Analysis Plan Version 2 -J2G-OX-JZJP

A 2-Part, Open-Label, Fixed-Sequence Study to Evaluate the Effects of Multiple Doses of Itraconazole and Rifampin on the Single-Dose Pharmacokinetics of LOXO-292 in Healthy Adult Subjects

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16.1.9 Documentation of Statistical Methods

16.1.9.1 Statistical Analysis Plan

Statistical Analysis Plan

A 2-Part, Open-Label, Fixed-Sequence Study to Evaluate the Effects of Multiple Doses of Itraconazole and Rifampin on the Single-Dose Pharmacokinetics of LOXO-292 in Healthy Adult Subjects

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Compound Name: LOXO-292

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Statistical Analysis Plan Signature Page

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from study LOXO-RET-18014. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within the protocol or after the locking of the database will be documented in the clinical study report (CSR). The section referred to as Table Shells within this SAP describes the traceability of the tables, figures, and listings (TFLs) back to the data. Note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this SAP and/or driven by the data, or requested by Loxo Oncology, Inc., will be considered out of scope and will be described in the CSR as needed.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

Part 1 (Itraconazole):

Primary:

To investigate the effect of multiple-dose itraconazole, a strong Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitor, on the single dose pharmacokinetics (PK) of LOXO-292 in healthy adult subjects.

Secondary:

To determine the safety and tolerability of a single dose of LOXO-292 alone and coadministered with multiple doses of itraconazole in healthy adult subjects.

Part 2 (Rifampin):

Primary:

To investigate the effect of single-dose rifampin, a P-gp inhibitor, and multiple-dose rifampin, a strong CYP3A4 and P-gp inducer, on the single dose PK of LOXO-292 in healthy adult subjects.

Secondary:

To determine the safety and tolerability of a single dose of LOXO-292 alone and coadministered with single and multiple doses of rifampin in healthy adult subjects.

2.2 Endpoints

Pharmacokinetics:

Part 1 (Itraconazole):

The PK endpoints will include AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, CL/F, and t½ for LOXO-292 administered with and without interacting drug itraconazole.

Part 2 (Rifampin):

The PK endpoints will include AUC0-t, AUC0-24 (Day 1 PK only), AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, CL/F, and t½ for LOXO-292 administered with and without interacting drug rifampin.

Safety:

Parts 1 and 2:

Safety endpoints will include 12-lead electrocardiograms (ECGs), physical examinations, vital signs, clinical laboratory tests, and adverse events (AEs) for both parts.

3. STUDY DESIGN

This was a 2-part study. Each part was conducted as an open label, 2-period, fixed-sequence study. Study parts were conducted sequentially. Subjects participated in one study part.

CCI healthy, adult male and female (women of non-childbearing potential only) subjects were enrolled in total; CCI to each study part (Parts 1 and 2). Every attempt was made to enroll at least 4 subjects of each sex in each study part.

Screening of subjects occurred within 28 days prior to the first dosing.

In both study parts, subjects were permitted to be replaced at the discretion of the Sponsor, however no subjects were replaced in this study.

Part 1 (Itraconazole):

On Day 1 of Period 1, a single oral dose of LOXO-292 was administered followed by PK sampling for 168 hours.

In Period 2, an oral dose of itraconazole was administered once daily (QD) for 11 consecutive days (Day -4 to Day 7) with a single oral dose of LOXO-292

coadministered on Day 1. Pharmacokinetic sampling for LOXO-292 was taken for 168 hours following LOXO-292 dosing on Day 1.

A sentinel group of 3 subjects initiated Part 1; all subjects received a single dose of LOXO-292 on Day 1 of both periods. Following collection of the last PK sample in Period 2, the principal investigator (PI), in consultation with the Sponsor, reviewed all pertinent safety and tolerability data before proceeding to dose the remaining subjects.

There was a washout period of at least 7 days between the dose in Period 1 and the first dose (i.e., itraconazole) in Period 2.

Subjects were housed on Day -1 of Period 1, at the time indicated by the clinical research unit (CRU) until after the last PK blood draw and/or study procedures scheduled on Day 8 of Period 2.

Safety was monitored throughout the study.

Part 2 (Rifampin):

On Day 1 of Period 1, a single oral dose of LOXO-292 was administered followed by PK sampling for 168 hours.

In Period 2, an oral dose of rifampin was administered QD for 16 consecutive days (Days 1 to 16) with a single oral dose of LOXO-292 coadministered on Day 1 and Day 10.

Pharmacokinetic sampling for LOXO-292 was taken for 24 hours following LOXO-292 dosing on Day 1 and for 168 hours following LOXO-292 dosing on Day 10.

Morning urine was collected on Days 1, 4, 8, and 10 of Period 2 (and was stored for future potential assessment of 6β-hydroxycortisol and free cortisol concentrations to evaluate the level of CYP3A enzyme induction).

There was a washout period of at least 7 days between the dose in Period 1 and the first dosing (i.e., rifampin and LOXO-292) in Period 2.

Subjects were housed on Day -1 of Period 1, at the time indicated by the CRU, until after the last PK blood draw and/or study procedures scheduled on Day 17 of Period 2.

Safety was monitored throughout the study.

Parts 1 and 2

Subjects were confined throughout the washout period.

At all times, a subject may have been required to remain at the CRU for longer at the discretion of the PI or designee.

The CRU made every attempt to contact all subjects who received at least one dose of study drug (including subjects who terminate the study early) using their standard procedures (i.e., phone call or other method of contract) approximately 7 days after the last study drug administration to determine if any AE had occurred since the last study visit.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety Population

All subjects who received at least one dose of LOXO-292 will be included in the safety evaluations.

Pharmacokinetic Population

Samples from all subjects will be assayed even if the subjects do not complete the study. All subjects who comply sufficiently with the protocol and display an evaluable PK profile (e.g., exposure to treatment, availability of measurements and absence of major protocol violations) will be included in the statistical analyses.

Data for each subject will be included in the summary statistics and statistical comparisons of PK parameters with the exceptions described as follows:

- Data from subjects who experience emesis at or before 2 times median Tmax for the given treatment during the PK sampling period time course of the study for LOXO-292 will be excluded from the summary statistics for the given treatment and from the statistical comparison of PK parameters.
- Data from subjects who significantly violate a protocol inclusion or exclusion criteria, deviate significantly from the protocol, or have unavailable or incomplete data which may influence the PK analysis will be excluded from the PK Population.

Any subject or data excluded from the analysis will be identified, along with their reason for exclusion, in the CSR.

4.2 Preliminary Data and Interim Analysis

No interim analysis was planned for this study.

5. TREATMENT DESCRIPTIONS

LOXO-292 was supplied as a 20 mg or 80 mg capsules. However, only the 80 mg capsules were used in this study.

Itraconazole was supplied as 100 mg capsules.

Rifampin was supplied as 300 mg capsules.

All study drugs were administered orally under fasting conditions, with approximately 240 mL of water.

Subjects were instructed not to crush, split, or chew the study drugs.

Part 1:

All Subjects (CCI [redacted]

Table 5.1 Treatment Description (Part 1)

Treatment	Short Description (text, tables headers, figures, listings, SAS output)	Abbreviated Description
A	160 mg LOXO-292 (Part 1)	Single dose of 160 mg LOXO-292
B	MD 200 mg Itraconazole + 160 mg LOXO-292 (Part 1)	Multiple doses of 200 mg itraconazole QD from Day -4 to Day 7 with a single dose of 160 mg LOXO-292 on Day 1
B1	MD 200 mg Itraconazole Alone	Multiple doses of 200 mg itraconazole QD from Day -4 to Day -1
B2	MD 200 mg Itraconazole + 160 mg LOXO-292	Multiple doses of 200 mg itraconazole QD from Day1 to Day 7 with a single dose of 160 mg LOXO-292 on Day 1

* The 160 mg LOXO-292 dose was administered as 80 mg capsules (2 x 80 mg). If the study drugs could not all be swallowed at the same time, the drug administration was permitted to be divided; however, dosing was to be completed within 10 minutes. Additional water, up to a maximum of 50 mL was permitted to be administered as required by the subject. Treatment B will be divided into two categories as B1 and B2 for AE summary.

MD = multiple dose

On Day 1 of both Periods 1 and 2, study drug(s) were administered following an overnight fast. On all other dosing days in Period 2, itraconazole was administered approximately 30 minutes after the start of a standard breakfast.

Part 2:

All Subjects CCI

Table 5.2 Treatment Description (Part 2)

Treatment	Short Description (text, tables headers, figures, listings, SAS output)	Abbreviated Description
C	160 mg LOXO-292 (Part 2)	Single dose of 160 mg LOXO-292
D	MD 600 mg Rifampin + 160 mg LOXO-292 (Part 2)	Multiple doses of 600 mg rifampin QD from Day 1 to Day 16 with a single dose of 160 mg LOXO-292 on Day 1 and Day 10

* The 160 mg LOXO-292 dose was administered as 80 mg capsules (2 x 80 mg). If the study drugs could not all be swallowed at the same time, the drug administration was permitted to be divided; however, dosing was to be completed within 10 minutes. Additional water, up to a maximum of 50 mL was permitted to be administered as required by the subject.

MD = multiple dose

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

Part 1:

Blood samples for PK assessment of LOXO-292 were taken at the following time points on Day 1 of each period: at predose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours postdose.

Part 2:

Blood samples for PK assessment of LOXO-292 were taken at the following time points on Day 1 of Period 1 and Day 10 of Period 2: at predose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours postdose.

Blood samples for PK assessment of LOXO-292 were taken at the following time point on Day 1 of Period 2: at predose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, and 24 hours postdose.

All concentration data will be included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there are any significant deviations from nominal sample times, some concentration data may be excluded from mean concentration-time plots and/or additional concentration-time plots of the mean data may be provided. All deviations and excluded data will be provided and discussed in the CSR.

6.2 Bioanalytical Method for LOXO-292

Plasma concentrations of LOXO-292 will be determined using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Alturas Analytics, Inc. (Moscow, Idaho, USA). The analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for LOXO-292 is 1 – 1000 ng/mL. Samples that contain concentrations greater than 1000 ng/mL may be diluted up to 51-fold, if necessary, to be within the quantification range.

6.3 Investigational Product and PK Analyte Information of LOXO-292

LOXO-292 has a molecular weight of approximately 500 g/mol. LOXO-292 was supplied as a powder-in-capsule containing 20 mg or 80 mg of drug substance (freebase) and as a simple blend with excipients in a hard gelatin capsule.

6.4 Pharmacokinetic Concentrations

Plasma concentrations of LOXO-292 as determined at the collection times and per the bioanalytical method described in Section 6.1 and Section 6.2, respectively, will be used for the calculation of the plasma LOXO-292 PK parameters.

6.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation for LOXO-292

The appropriate noncompartmental PK parameters will be calculated from the plasma LOXO-292 concentration-time data using Phoenix® WinNonlin® Version 7.0 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual time for LOXO-292 will be in respect to the dose administration time of LOXO-292 on Day 1 of Period 1 (Parts 1 and 2), Day 1 of Period 2 (Parts 1 and 2), and Day 10 of Period 2 (Part 2). All PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated for LOXO-292

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC0-t	Area under the concentration-time curve from time 0 to the time of the last observed non-zero concentration	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-inf	Area under the concentration-time curve from time 0 extrapolated to infinity	Calculated as AUC0-t + (Clast/kel) where Clast is the last observed/measured concentration
AUC0-24	Area under the concentration-time curve from time 0 to 24 hours postdose Day 1 (for Part 2, Day 1 PK only)	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC%extrap	Percent of AUC0-inf extrapolated	Calculated as (1-AUC0-t/AUC0-inf)*100
Cmax	Maximum observed concentration	Taken directly from bioanalytical data

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
Tmax	The time to reach Cmax. If the maximum value occurs at more than one time point, Tmax is defined as the first time point with this value	Taken from clinical database as the difference in the time of administration and the time of the blood draw which is associated with the Cmax.
CL/F	Apparent total plasma clearance after oral (extravascular) administration	Calculated as Dose/(AUC0-inf)
Kel	Apparent terminal elimination rate constant; represents the fraction of drug eliminated per unit time	Calculated as the negative of the slope of a linear regression of the log(concentration)-time for all concentrations > LLOQ
t½	Apparent first-order terminal elimination half-life	Calculated as 0.693/Kel

Pharmacokinetic parameters will not be calculated for subjects with fewer than 3 consecutive postdose time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the statistical analysis.

For the calculation of the PK parameters, plasma concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration will be set to 0 and plasma concentrations BLQ after the first quantifiable concentration will be treated as missing.

The Kel will be determined using linear regressions composed of least 3 data points. The Kel will not be assigned if 1) the terminal elimination phase is not apparent, 2) if Tmax is one of the 3 last data points, or 3) if the R^2 value is less than 0.75. In cases where the Kel interval is not assigned, the values of t½, AUC0-inf, and CL/F are considered not calculable and will not be reported. Wherever the resulting t½ is more than half as long as the sampling interval, the Kel values and associated parameters (t½, AUC0-inf, and CL/F) may not be presented as judged appropriate and in accordance with Celerion SOPs.

If predose concentrations were to occur, the following procedure will be used: if the predose concentration is less than or equal to 5% of Cmax for that subject period, the subject's data will be included in all PK measurements and calculations without any adjustments. If the predose value is greater than 5% of Cmax, the subject will be excluded from the PK analysis for that period only.

6.6 Data Summarization and Presentation

All LOXO-292 PK concentrations and PK parameters descriptive statistics will be generated using SAS® Version 9.3 or higher.

The plasma concentrations of LOXO-292 will be listed and summarized by treatment, study day (for Part 2), and time point for all subjects in the PK Population. Plasma concentrations of LOXO-292 will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for all nominal concentration time points. Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration listings and footnoted accordingly.

Mean and individual concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD.

Plasma LOXO-292 PK parameters will be listed and summarized by treatment for all subjects in the PK Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of Tmax, which will be presented with 2 decimal places. Summary statistics (n, Mean, SD, CV%, SEM, minimum, median, maximum, geometric mean [Geom Mean] and geometric CV% [Geom CV%]) will be calculated for plasma LOXO-292 PK parameters. Excluded subjects will be listed in the PK parameter tables, but will be excluded from the summary statistics and noted as such in the tables.

The level of precision for each concentration and PK parameter statistic will be presented as follows:

- minimum/maximum in same precision as in bioanalytical data and parameter output,
- mean/median in one more level of precision than minimum/maximum,
- SD/SEM in one more level of precision than mean/median,
- n will be presented as an integer, and
- CV% will be presented to the nearest tenth.

6.7 Statistical Analysis of PK Parameters

A comparison of ln-transformed PK parameters (AUC0-24, AUC0-t, AUC0-inf, and Cmax, as appropriate) will be made to evaluate the effect of:

Part 1: multiple-dose administrations of itraconazole on the single-dose administration of LOXO-292 (Treatment B Versus Treatment A);

Part 2: single-dose rifampin on the single-dose administration of LOXO-292 (Treatment D on Day 1 Versus Treatment C) and the effect of multiple-dose rifampin on the single-dose administration of LOXO-292 (Treatment D on Day 10 Versus Treatment C)

by performing an analysis of variance (ANOVA) model using PROC MIXED in SAS®.

/* Programmer note: for Part 2, use the PK parameter data of Day 1 of Period 1 (LOXO-292 Alone), Day 1 of Period 2 (LOXO-292 + SD Rifampin) to compare Treatment D on Day 1 Versus Treatment C, and use the PK parameter data of Day 1 of Period 1 (LOXO-292 Alone), Day 10 (LOXO-292 + MD Rifampin) to compare Treatment D on Day 10 Versus Treatment C (Adjust coefficients in the ESTIMATE statement accordingly) */

7. SAFETY

No inferential statistics are to be performed for the safety analysis.

All clinical safety and tolerability data will be listed by subject and assessment time points, including rechecks, unscheduled assessments, and early termination (ET), chronologically.

Continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum. Frequency counts will be reported for categorical data when appropriate.

The level of precision will be presented as follows: "n" as an integer, minimum/maximum in same precision as in the database, mean/median in one more precision level than minimum/maximum, and SD in one more precision level than mean/median.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

When change from baseline is calculated, baseline is the last scheduled assessment before dosing at Period 1, including rechecks and unscheduled assessments, whichever is later, unless otherwise specified in the sections below. Rechecks, unscheduled assessments and ET measurements taken after first dosing will not be used in the summarization.

7.1 Subject Discontinuation

Subjects will be summarized by the number of subjects enrolled, completed, and discontinued from the study with discontinuation reasons by treatment and overall for each part. Discontinuation data will be listed by-subject.

7.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index) for each part and study overall. Weight, height and body mass index are summarized at screening. Age will be derived from the date of birth to the date of first dosing. Frequency counts will be provided for categorical variables (race, ethnicity, and sex) for each part and overall. A by-subject listing will also be provided.

7.3 Adverse Events

All adverse events (AEs) occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 21.0.

Each AE will be graded, by the clinical site, on the National Institution of Health's Common Terminology Criteria for Adverse Events (CTCAE, version 5.0) 5-point severity scale (Grade 1, 2, 3, 4 and 5). Not all grades are appropriate for all AEs. The following definitions for clinical descriptions of severity grade for each AE are based on the following general guideline [CTCAE Nov2017]:

Table 7.3: Adverse Event Severity Grade Level and Description

Grade	Description
Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**.
Grade 4	Life-threatening consequences; urgent intervention indicated.
Grade 5	Death related to AE.
* Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc. ** Self care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications and not bedridden.□	

Similarly, the causal relationship of the study drugs to the AE will be described as Related or Unrelated to study drugs LOXO-292, and/or itraconazole and/or rifampin.

All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, treatment group, severity grade, relationship to study drugs, and action; however, only treatment-emergent AEs (TEAEs) will be summarized.

A TEAE is defined as an undesirable event not present prior to medical treatment, or an already present event that worsens either in intensity or frequency following the treatment. Each TEAE will be attributed to a treatment based on Investigator (or designee) judgment as well as on its onset date and time. An AE that occurs during the washout period between treatments will be considered treatment-emergent to the last treatment given. If an AE has a change in severity grade, the original AE will be given a resolution date and time of the time of severity grade increase or decrease and a new AE record will be initiated with the new severity grade, and the new AE record will use the resolved date/time of the previous record as the onset date/time. If an AE decreases in severity grade, the new AE record with less severity will be considered and counted as the same AE event of the previous record with worse severity under the same treatment group and period in the analysis and summary tables. If the

severity grade of an AE remains the same, the AE will be kept open through to resolution.

If the onset time of an AE is missing and the onset date is the same as the treatment dosing date, then the AE will be considered treatment-emergent in both the prior and current treatment. If the onset time of an AE is missing and the onset date does not fall on a dosing date, then the AE will be considered treatment-emergent for the last treatment administered. If the onset date of an AE is missing, then the AE will be considered treatment-emergent and attributed to the first treatment group on the study, unless the onset date is known to have occurred within or between specific treatment periods.

TEAEs will be tabulated by system organ class and preferred term. Summary tables will include the number of subjects reporting the AE and as a percent of the number of subjects dosed by treatment and overall for each part. Treatment B will be divided into two categories as B1 and B2 (see Table 5.1). In addition, the number of AEs will be summarized. Tables will also be presented by severity grade and relationship to study drugs. If a subject experienced the same TEAE more than once with different level of severity grade for a given treatment, only the most severe one will be counted. Similarly, if a subject experienced the same TEAE more than once with different level of drug relationship for a given treatment, only the one most closely related to the study drug will be counted.

Should any serious adverse events (SAEs) occur during the study, the SAEs will be displayed in a table and a narrative included in the Clinical Study Report.

7.4 Clinical Laboratory Tests (Serum Chemistry, Hematology, Coagulation, and Urinalysis)

All clinical laboratory test results will be presented in by-subject data listings, however, only serum chemistry, hematology, coagulation and urinalysis values will be summarized.

Hematology, coagulation, serum chemistry and urinalysis tests will be conducted at the following time points:

Table 7.4 Lab Test Time Points

Study Part	Period	Period Day
1	Screen	Screening
	1	Day -1*
	1	Day 4*
	1	Day 7*
	2	Day -1*
	2	Day 4**

	2	Day 8***
2	Screen	Screening
	1	Day -1*
	1	Day 4*
	1	Day 7*
	2	Day 4**
	2	Day 9**
	2	Day 13**
	2	Day 17***
* performed following a fast of at least 8 hours ** performed prior dosing *** performed at the end of Period 2 or prior to ET		

Out-of-normal range (OOR) flags will be recorded as follows: high (H) and low (L) for numerical results and did-not-match (*) for categorical results. If a value fails the reference range, it will automatically be compared to a computer clinically significant (CS) range suggested by the PI (Celerion SOP GSOP.10.1028). If the value falls within the computer CS range, it will be noted as “N” for not clinically significant. If the value fails (i.e. falls outside of the CS range) the computer CS range, it will be flagged with a “Y” which prompts the PI to determine how the OOR value should be followed using 4 Investigator flags: "N", not clinically significant, "R", requesting a recheck, "^", checking at the next scheduled visit, or "Y", clinically significant. To distinguish the PI flag from the CS range flags, the PI flags “N” and “Y” will be presented as “-” and “+” in the data listings, respectively. Additionally, a derived flag based on a search of the PI comments for a comment of “CS” or “Clinically Significant” will be used. The derived flag will be populated with “+” if the positive clinically significant determination is found in the comments for cases when the PI flag is populated with a “^” or an “R”. In addition, CTCAE, version 5.0 grading (found in NCI CTCAE guidance) will be applied to all out of range lab values deemed clinically significant by the Investigator (or designee) which are recorded as AEs. The resulting flag, e.g., G1, will be placed along with the Celerion flags (see shell of Table 14.3.4.4).

Out-of-range values and corresponding recheck results will be listed. Other lab results within this panel and time point will also be listed for this subject. Results that are indicated as CS by the PI (either in the PI flag or in PI comments) will be listed in the table. Out-of-range values laboratory value results which are indicated as CS by PI will be reported as AEs.

For all laboratory values that are numeric, descriptive statistics (n, mean, SD, minimum, median, and maximum) will be presented for each laboratory test by treatment and time point for each part, respectively. Change from baseline (defined below) will also be summarized. Postdose unscheduled events or rechecks will not be summarized. Similarly, ET results will not be included in summaries.

For each laboratory test, a shift table will be developed comparing the frequency of the results at baseline (above normal, normal, or below normal) to postdose results for each part, respectively. For urinalysis tests, the categories are normal and outside normal.

For Parts 1 and 2, baseline is Day -1 of each period and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments. For Part 2, Day 7 of Period 1 is Day -1 of Period 2 so Day 7 of Period 1 is used as the baseline for Period 2.

7.5 Vital Signs (Blood Pressure, Pulse Rate, Respiration Rate, and Temperature)

Vital signs were performed at the following time points:

Table 7.5 Vital Signs Time Points

Study Part	Period	Period Day	Study Hour	Parameter
1	Screen	Screening		HR, BP, RR, T
	1	Day -1	0*	HR, BP, RR
	1	Day 1	2	HR, BP, RR
	1	Day 4	72	HR, BP, RR
	2	Day -4	0**	HR, BP, RR
	2	Day 1	0**	HR, BP, RR
	2	Day 1	2	HR, BP, RR
	2	Day 4	72**	HR, BP, RR
	2	Day 5	96**	HR, BP, RR
	2	Day 8	168***	HR, BP, RR, T
2	Screen	Screening		HR, BP, RR, T
	1	Day -1	0*	HR, BP, RR
	1	Day 1	2	HR, BP, RR
	1	Day 4	72	HR, BP, RR
	2	Day 1	0**	HR, BP, RR
	2	Day 1	2	HR, BP, RR
	2	Day 10	0**	HR, BP, RR
	2	Day 10	2	HR, BP, RR
	2	Day 13	72**	HR, BP, RR
	2	Day 17	168***	HR, BP, RR, T

* performed within 24 hours prior dosing
** performed prior dosing
*** performed at the end of Period 2 or prior to ET

Descriptive statistics will be reported for vital sign measurements (blood pressure, pulse, and respiration rate) and change from baseline by treatment and time point for each part, respectively. For Part 1, baseline is Day -1 for Treatment A (Period 1) and

Day 1 predose for Treatment B (Period 2) which is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments. For Part 2, baseline is Day -1 for Treatment C (Period 1) and Day 1 predose for Treatment D (Period 2) which is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments. Postdose recheck values and ET results will not be used for calculation of descriptive statistics. All vital signs results will be listed by subject.

7.6 ECG (Heart Rate, PR, QRS, QT, and QTcF [QT with Fridericia correction])

Single 12-lead ECGs were performed at the following time points:

Table 7.6: ECG Time Points

Study Part	Period	Period Day	Study Hour
1	Screen	Screening	
	1	Day -1	0*
	1	Day 1	2
	1	Day 4	72
	2	Day -4	0**
	2	Day 1	0**
	2	Day 1	2
	2	Day 4	72**
	2	Day 5	96**
	2	Day 8	168***
2	Screen	Screening	
	1	Day -1	0*
	1	Day 1	2
	1	Day 4	72
	2	Day 1	0**
	2	Day 1	2
	2	Day 10	0**
	2	Day 10	2
	2	Day 13	72**
	2	Day 17	168***

* performed within 24 hours prior dosing
** performed prior dosing
*** performed at the end of Period 2 or prior to ET

Descriptive statistics will be reported for ECG parameters and change from baseline by treatment and time point for each part, respectively. For Part 1, baseline is Day -1 for Treatment A (Period 1) and Day 1 predose for Treatment B (Period 2) which is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments. For Part 2, baseline is Day -1 for Treatment C

(Period 1) and Day 1 predose for Treatment D (Period 2) which is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments. Postdose recheck values and ET results will not be used for calculation of descriptive statistics. All ECG interval parameters will be listed by subject and time point of collection.

7.7 Prior and Concomitant Medications

All prior and concomitant medications recorded during the study will be coded with the WHO Dictionary, Version Mar2017 B3 and listed. Prior medication is medication taken prior to study drug administration.

7.8 Physical Examination

Physical examinations will be performed at screening. Abbreviated physical examinations may be performed at check-in (Day -1) of the first period. Abnormal findings will be reported as medical history or adverse events by the clinical site. Physical examination results will be listed by subject and time point.

8. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol.

9. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Council for Harmonisation (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all summary tables and figures will be generated using SAS® Version 9.3 or higher.

9.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Summary of Disposition (Part 1 and 2) (Safety Population)

Section 11:

Table 11-1 Demographic Summary (Part 1 and 2) (Safety Population)

Part 1

9.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

14.1.1 Demographic Tables

Table 14.1.1.1 Summary of Disposition (Part 1 and 2) (Safety Population)

Table 14.1.1.2 Disposition of Subjects (Part 1 and 2) (Safety Population)

Table 14.1.1.3 Demographic Summary (Part 1 and 2) (Safety Population)

14.2 Pharmacokinetic Data Summary Tables and Figures

14.2.1 Part 1

14.2.1.1 Plasma LOXO-292 Tables

Table 14.2.1.1.1 Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) (Part 1) (Pharmacokinetic Population)

Table 14.2.1.1.2 Plasma LOXO-292 Concentrations (ng/mL) Following Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) (Part 1) (Pharmacokinetic Population)

Table 14.2.1.1.3 Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) (Part 1) (Pharmacokinetic Population)

14.2.2.2 Plasma LOXO-292 Figures

Figure 14.2.2.2.1 Mean (SD) Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with a Single Dose of 600 mg Rifampin on Day 1 (Treatment D) (Linear Scale) (Part 2) (Pharmacokinetic Population)

Figure 14.2.2.2.2 Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with a Single Dose of 600 mg Rifampin on Day 1 (Treatment D) (Linear Scale) (Part 2) (Pharmacokinetic Population)

Figure 14.2.2.2.3 Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with a Single Dose of 600 mg Rifampin on Day 1 (Treatment D) (Semi-Log Scale) (Part 2) (Pharmacokinetic Population)

Figure 14.2.2.2.4 Mean (SD) Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 600 mg Rifampin on Day 10 (Treatment D) (Linear Scale) (Part 2) (Pharmacokinetic Population)

Figure 14.2.2.2.5 Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 600 mg Rifampin on Day 10 (Treatment D) (Linear Scale) (Part 2) (Pharmacokinetic Population)

Figure 14.2.2.2.6 Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 600 mg Rifampin on Day 10 (Treatment D) (Semi-Log Scale) (Part 2) (Pharmacokinetic Population)

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1 Treatment-emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting Events (% of Subject Dosed) (Part 1 and 2) (Safety Population)

Table 14.3.1.2 Treatment-emergent Adverse Event Frequency by Treatment – Number of Adverse Events (% of Total Adverse Events) (Part 1 and 2) (Safety Population)

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs - Number of Subjects Reporting Events (Part 1) (Safety Population)

Table 14.3.1.4 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs - Number of Adverse Events (Part 1) (Safety Population)

Table 14.3.1.5 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs - Number of Subjects Reporting Events (Part 2) (Safety Population)

Table 14.3.1.6 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs - Number of Adverse Events (Part 2) (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Part 1) (Safety Population)

Table 14.3.2.2 Serious Adverse Events (Part 2) (Safety Population)

<if no serious adverse event occurred, a statement ‘There was no serious adverse event recorded during the study for Part 1 and 2.” will be added>

14.3.3. Narratives of Deaths, other Serious and Certain other Significant Adverse Events

14.3.4. Abnormal Laboratory Value Listing (each patient)

Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry (Part 1 and 2) (Safety Population)

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology and Coagulation (Part 1 and 2) (Safety Population)

Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis (Part 1 and 2) (Safety Population)

Table 14.3.4.4 Clinically Significant Laboratory and Corresponding Results (Part 1 and 2) (Safety Population)

14.3.5. Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

Table 14.3.5.1 Clinical Laboratory Summary and Change from Baseline – Serum Chemistry (Part 1) (Safety Population)

Table 14.3.5.2 Clinical Laboratory Shift from Baseline – Serum Chemistry (Part 1) (Safety Population)

Table 14.3.5.3 Clinical Laboratory Summary and Change from Baseline – Serum Chemistry (Part 2) (Safety Population)

Table 14.3.5.4 Clinical Laboratory Shift from Baseline – Serum Chemistry (Part 2) (Safety Population)

Table 14.3.5.5 Clinical Laboratory Summary and Change from Baseline – Hematology and Coagulation (Part 1) (Safety Population)

Table 14.3.5.6 Clinical Laboratory Shift from Baseline – Hematology and Coagulation (Part 1) (Safety Population)

Table 14.3.5.7 Clinical Laboratory Summary and Change from Baseline – Hematology and Coagulation (Part 2) (Safety Population)

Table 14.3.5.8 Clinical Laboratory Shift from Baseline – Hematology and Coagulation (Part 2) (Safety Population)

Table 14.3.5.9 Clinical Laboratory Summary and Change from Baseline – Urinalysis (Part 1) (Safety Population)

Table 14.3.5.10 Clinical Laboratory Shift from Baseline – Urinalysis (Part 1) (Safety Population)

Table 14.3.5.11 Clinical Laboratory Summary and Change from Baseline – Urinalysis (Part 2) (Safety Population)

Table 14.3.5.12 Clinical Laboratory Shift from Baseline – Urinalysis (Part 2) (Safety Population)

Table 14.3.5.13 Vital Sign Summary and Change from Baseline (Part 1) (Safety Population)

Table 14.3.5.14 Vital Sign Summary and Change from Baseline (Part 2) (Safety Population)

Table 14.3.5.15 12-Lead Electrocardiogram Summary and Change from Baseline (Part 1) (Safety Population)

Table 14.3.5.16 12-Lead Electrocardiogram Summary and Change from Baseline (Part 2) (Safety Population)

9.3 Section 16 Data Listings

Note: Virology test results (Hepatitis and HIV) that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in the database transfer.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2. Subject Data Listings

16.2.1. Subject Discontinuation

Appendix 16.2.1 Subject Discontinuation (Part 1 and 2) (Safety Population)

16.2.2. Protocol Deviations

Appendix 16.2.2 Protocol Deviations (Part 1 and 2)

16.2.3. Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3 Subjects Excluded from Pharmacokinetic Analysis (Part 1 and 2)

Note: Appendices 16.2.2 and 16.2.3 are generated in MS Word for inclusion in the CSR.

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Part 1 and 2) (Safety Population)
Appendix 16.2.4.2 Updated Informed Consent (Part 1 and 2) (Safety Population)
Appendix 16.2.4.3 Physical Examination (Part 1 and 2) (Safety Population)
Appendix 16.2.4.4 Medical and Surgical History (Part 1 and 2) (Safety Population)
Appendix 16.2.4.5 Nicotine Use (Part 1 and 2) (Safety Population)

16.2.5. Compliance and Drug Concentration Data

Appendix 16.2.5.1.1 Inclusion Criteria (Part 1 and 2)
Appendix 16.2.5.1.2 Exclusion Criteria (Part 1 and 2)
Appendix 16.2.5.2 Subject Eligibility (Part 1 and 2) (Safety Population)
Appendix 16.2.5.3.1 Check-in and Return Criteria (Part 1 and 2)
Appendix 16.2.5.3.2 Check-in and Return Responses (Part 1 and 2) (Safety Population)
Appendix 16.2.5.4.1 Test Compound Description (Part 1 and 2)

Appendix 16.2.5.4.2 Test Compound Administration Times (Part 1 and 2) (Safety Population)

Appendix 16.2.5.5 PK Blood Draw Times (Part 1 and 2) (Safety Population)

Appendix 16.2.5.6 Urine Collection Times (Part 2 Period 2 Only) (Safety Population)

Appendix 16.2.5.7 Phone Call (Part 1 and 2) (Safety Population)

Appendix 16.2.5.8 Meal Times (Part 1 and 2) (Safety Population)

Appendix 16.2.5.9 Prior and Concomitant Medications (Part 1 and 2) (Safety Population)

16.2.6 Individual Pharmacokinetic Response Data

Appendix 16.2.6.1 Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) for Subject X (Part 1) (Linear and Semi-Log Scale)

Appendix 16.2.6.2 Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with a Single Dose of 600 mg Rifampin on Day 1 (Treatment D) for Subject X (Part 2) (Linear and Semi-Log Scale)

Appendix 16.2.6.3 Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment C) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 600 mg Rifampin on Day 10 (Treatment D) for Subject X (Part 2) (Linear and Semi-Log Scale)

16.2.7 Adverse Events Listings

Appendix 16.2.7.1 Adverse Events (I of II) (Part 1 and 2) (Safety Population)

Appendix 16.2.7.2.1 Adverse Events (II of II, Part 1) (Safety Population)

Appendix 16.2.7.2.2 Adverse Events (II of II, Part 2) (Safety Population)

Appendix 16.2.7.3 Adverse Event Non-Drug Therapy (Safety Population)

10. TABLE AND FIGURE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables and figures that will be presented and included in the final CSR. Unless otherwise noted, all in-text tables will be presented in Times New Roman font size 8 and post-text tables in Courier New font size 9. These tables will be generated according to the ADaM Model 2.1 and ADaM implementation guide 1.1.

10.1 In-text Table Shells

Table 10-1 Summary of Disposition (Part 1 and 2) (Safety Population)

	Part 1			Part 2		
Disposition	**Treatment**		**Overall**	**Treatment**		**Overall**
	A	**B**		**C**	**D**	
Enrolled	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Discontinued Early	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
<Reason1>	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
<Reason2>	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple dose of 200 mg itraconazole QD from Day -4 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10
Source: Table 14.1.1.1
Program: /CAXXXXX/sas_prg/stsas/intext/t_disp.sas DDMMMYYYY HH:MM

Table 11-1 Demographic Summary (Part 1 and 2) (Safety Population)

		Treatment Sequence		
Trait		**AB (Part 1)**	**CD (Part 2)**	**Study Overall**
Sex	Male	XX (XX%)	XX (XX%)	XX (XX%)
	Female	XX (XX%)	XX (XX%)	XX (XX%)
Race	Asian	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)
Age* (yrs)	n	XX	XX	XX
	Mean	XX.XX	XX.XX	XX.XX
	SD	XX.XXX	XX.XXX	XX.XXX
	Minimum	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X
	Maximum	XX.XX	XX.XX	XX.XX
Height (cm)	n	XX	XX	XX
	Mean	XXX.X	XXX.X	XXX.X
	SD	X.XX	X.XX	X.XX
	Minimum	XXX	XXX	XXX
	Median	XXX.X	XXX.X	XXX.X
	Maximum	XXX	XXX	XXX

Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple dose of 200 mg itraconazole QD from Day -4 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10
* Age is calculated from the date of first dosing.
BMI = Body mass index
Source: Table 14.1.1.3
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_dem.sas DDMMMYYYY HH:MM

Programmer Note: Weight (kg) and BMI (kg/m^2) will also be summarized in the table above.

In-text Tables 11-2 and 11-4 will be in the following format:

Table 11-2 Summary of Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) (Part 1) (Pharmacokinetic Population)

Pharmacokinetic Parameters	160 mg LOXO-292 (Part 1)	MD 200 mg Itraconazole + 160 mg LOXO-292
Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param4 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]

160 mg LOXO-292 (Part 1): Single dose of 160 mg LOXO-292 (Treatment A)
MD 200 mg Itraconazole + 160 mg LOXO-292 (Part 1): Multiple doses of 200 mg itraconazole QD from Day1 to Day 7 with a single dose of 160 mg LOXO-292 on Day 1 (Treatment B)
AUCs and Cmax values are presented as geometric mean and geometric CV%.
Tmax values are presented as median (min, max).
Other parameters are presented as arithmetic mean (± SD).
Source: Tables 14.2.1.1.3 and 14.2.1.1.4

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order and with following units: AUC0-t <unit>, AUC0-inf <unit>, AUC%extrap <unit>, Cmax <unit>, Tmax <unit>, Kel <unit>, t½ <unit>, and CL/F <unit> for Table 11-2
- The following PK parameters will be presented in the following order and with following units: AUC0-t <unit>, AUC0-inf <unit>, AUC0-24 <unit> (only for Treatment C and D), AUC%extrap <unit>, Cmax <unit>, Tmax <unit>, Kel <unit>, t½ <unit>, and CL/F <unit> for Table 11-4
- n will be presented as an integer (with no decimal);
- Summary statistics will be presented with same precision as defined in post-text shells

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell:

1. Please add a third treatment column for Table 11-4 and label all headers according to Table 5.2 in Section 5
2. Please adjust treatment descriptions table footers for Table 11-4 according to Table 5.2 in Section 5

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

In-text Tables 11-3, 11-5, and 11-6 will be in the following format:

Table 11-3 Summary of Statistical Comparisons of Plasma LOXO-292 Pharmacokinetic Parameters Following Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) Versus Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) (Part 1) (Pharmacokinetic Population)

	MD 200 mg Itraconazole + 160 mg LOXO-292 (Part 1)		160 mg LOXO-292 (Part 1)		GMR (%)	90% Confidence Interval	Intra-subject CV%
Parameter	Geometric LSMs	n	Geometric LSMs	n			
param1 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX	X.XX
param2 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX	X.XX
param3 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX	X.XX

160 mg LOXO-292 (Part 1): Single dose of 160 mg LOXO-292 (Treatment A)
MD 200 mg Itraconazole + 160 mg LOXO-292 (Part 1): Multiple doses of 200 mg itraconazole QD from Day 1 to Day 7 with a single dose of 160 mg LOXO-292 on Day 1 (Treatment B)
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs derived from the ANOVA.
Geometric Mean Ratio (GMR) = 100*(test/reference)
Intra-subject CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
Source: Table 14.2.1.1.6

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order and with following units: AUC0-t <unit>, AUC0-inf <unit>, and Cmax <unit> for Table 11-3 and 11-6
- The following PK parameters will be presented in the following order and with following units: AUC0-t <unit>, AUC0-24 <unit>, AUC0-inf <unit>, and Cmax <unit> for Table 11-5
- n will be presented as an integer (with no decimal);
- All statistics will be presented with same precision as defined in post-text shells

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell:

1. Please adjust treatment descriptions in column headers and table footers according to Table 5.2 in Section 5 for Tables 11-5 and 11-6.

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

Table 12-1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Part 1 and 2) (Safety Population)

Adverse Events*	Part 1				Part 2			Part 1+2
	Treatment			Overall	Treatment		Overall	Overall
	A	B1	B2		C	D		
Number of Subjects Dosed	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Number of Subjects With TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
System Organ Class 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

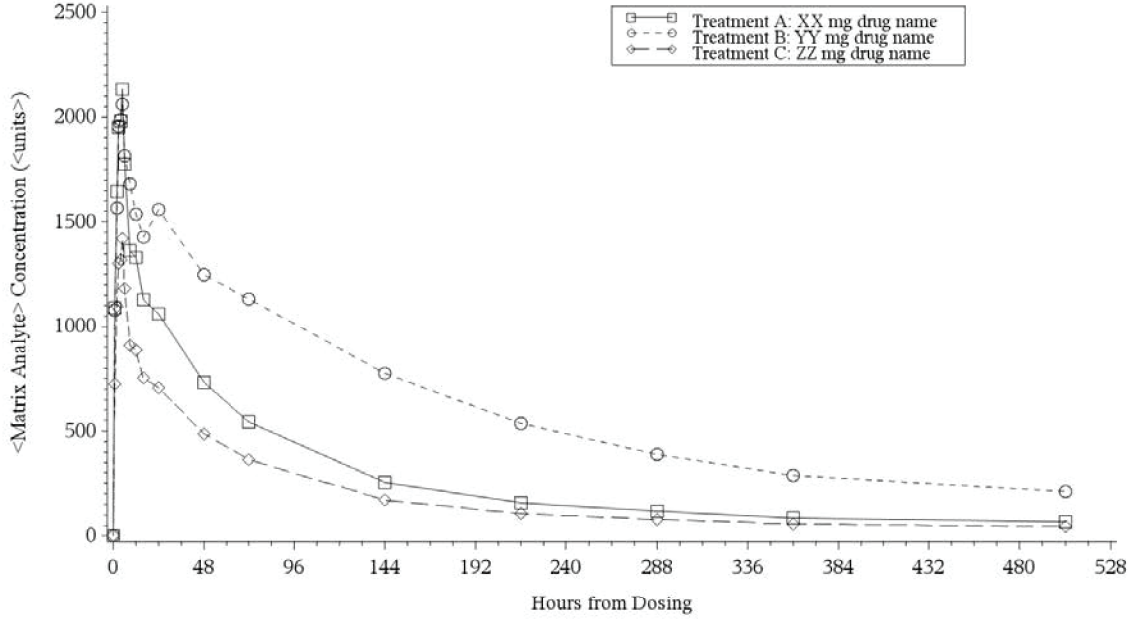
*Adverse events are coded using MedDRA® Version 21.0.
TEAE = Treatment-emergent Adverse event
Although a subject may have had 2 or more clinical adverse experiences, the subject is counted only once within a category. The same subject may appear in different categories.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity under the same treatment group.
Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B1: Multiple dose of 200 mg itraconazole QD from Day -4 to Day -1
Treatment B2: Multiple dose of 200 mg itraconazole QD from Day 1 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10

Source: Table 14.3.1.1
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_ae.sas DDMMMYYYY HH:MM

10.2 Figures Shells

In-text Figures 11-1 through 11-3 and Figures 14.2.1.2.2, 14.2.2.2.2, and 14.2.2.2.5 will be in the following format:

Figure 11-1 Arithmetic Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) (Part 1) (Pharmacokinetic Population)



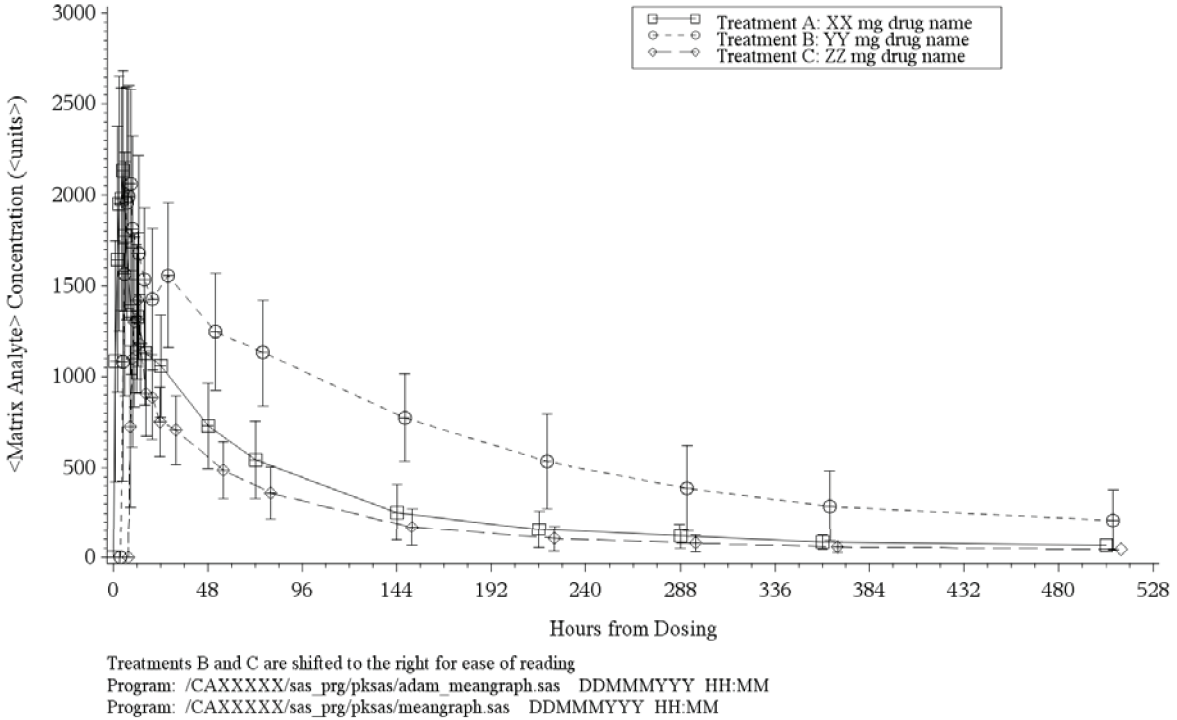
Notes for Generating the Actual Mean Figure:

- Legend will be "160 mg LOXO-292 (Part 1)" and "200 mg Itraconazole + 160 mg LOXO-292 (Part 1)" for Figures 11-1 and 14.2.1.2.2
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 1) (Part 2)" for Figures 11-2 and 14.2.2.2.2
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 10) (Part 2)" for Figures 11-3 and 14.2.2.2.5
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)" for all figures
- X axis label will be "Hours post LOXO-292 dose (hr)" for all figures
- Add footnote: LLOQ value for LOXO-292 is 1 ng/mL

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Figures 14.2.1.2.1, 14.2.2.2.1, and 14.2.2.2.4 will be in the following format:

Figure 14.2.1.2.1 Mean (SD) Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) (Linear Scale) (Part 1) (Pharmacokinetic Population)



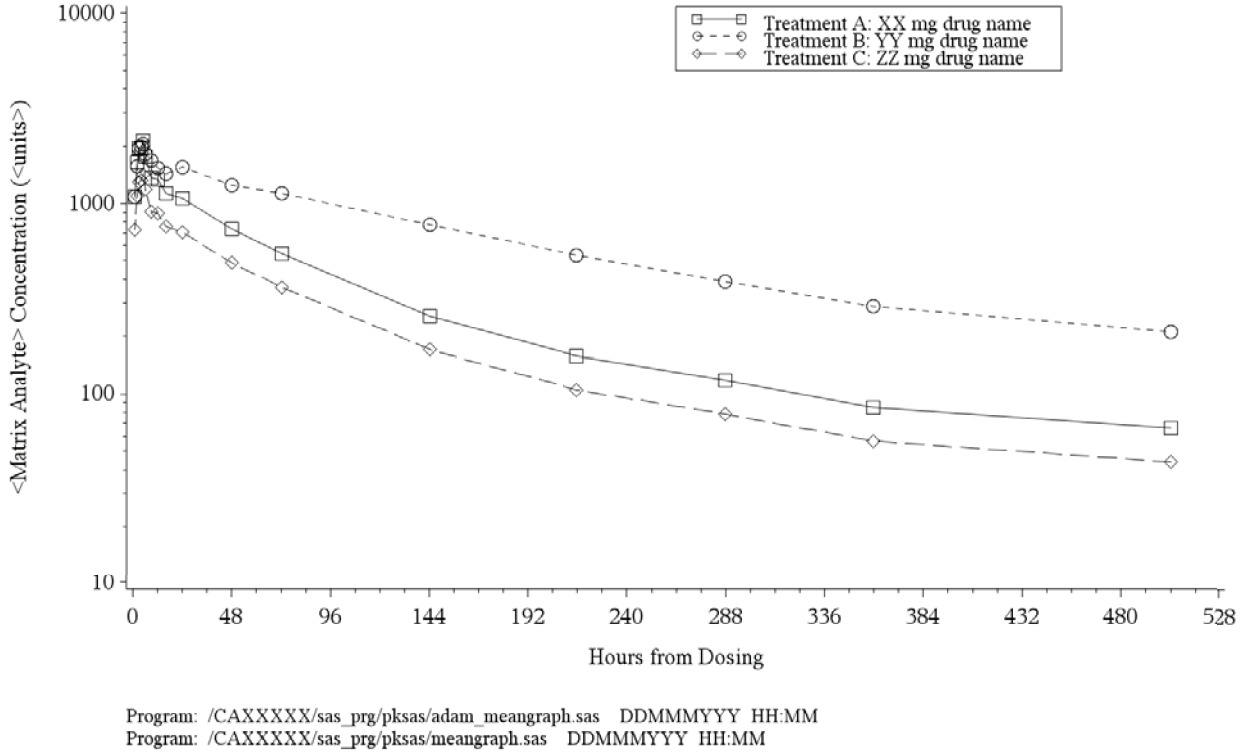
Notes for Generating the Actual Mean Figure:

- Legend will be "160 mg LOXO-292 (Part 1)" and "200 mg Itraconazole + 160 mg LOXO-292 (Part 1)" for Figures 14.2.1.2.1
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 1) (Part 2)" for Figures 14.2.2.2.1
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 10) (Part 2)" for Figures 14.2.2.2.4
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)" for all figures
- X axis label will be "Hours post LOXO-292 dose (hr)" for all figures
- Add footnote: LLOQ value for LOXO-292 is 1 ng/mL

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Figures 14.2.1.2.3, 14.2.2.2.3, and 14.2.2.2.6 will be in the following format:

Figure 14.2.1.2.3 Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) (Semi-Log Scale) (Part 1) (Pharmacokinetic Population)



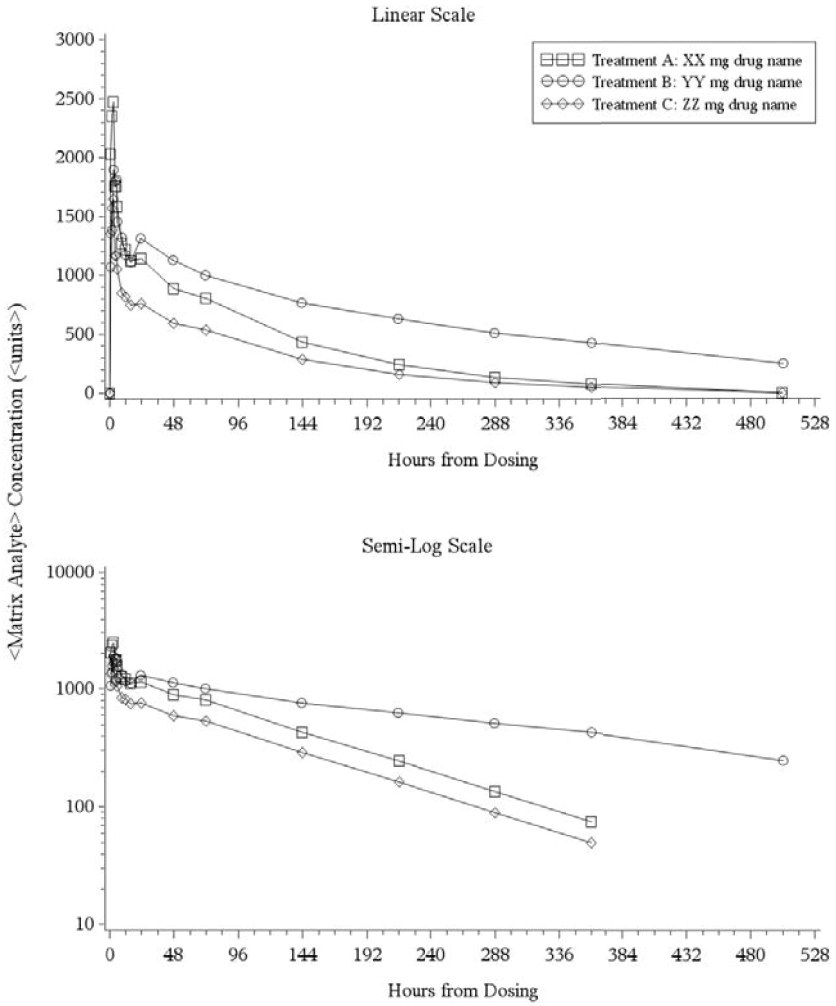
Notes for Generating the Actual Mean Figure:

- Legend will be "160 mg LOXO-292 (Part 1)" and "200 mg Itraconazole + 160 mg LOXO-292 (Part 1)" for Figures 14.2.1.2.3
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 1) (Part 2)" for Figures 14.2.2.2.3
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 10) (Part 2)" for Figures 14.2.2.2.6
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)" for all figures
- X axis label will be "Hours post LOXO-292 dose (hr)" for all figures
- Add footnote: LLOQ value for LOXO-292 is 1 ng/mL

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Appendix 16.2.6.1 through 16.2.6.3 will be in the following format:

Appendix 16.2.6.1
Individual Plasma LOXO-292 Concentrations Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) for Subject X (Part 1) (Linear and Semi-Log Scale)



Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYY HH:MM

Notes for Generating the Actual Individual Figure:

- Legend will be "160 mg LOXO-292 (Part 1)" and "200 mg Itraconazole + 160 mg LOXO-292 (Part 1)" for Appendix 16.2.6.1
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 1) (Part 2)" for Appendix 16.2.6.2
- Legend will be "160 mg LOXO-292 (Part 2)" and "600 mg Rifampin + 160 mg LOXO-292 (Day 10) (Part 2)" for Appendix 16.2.6.3
- Y axis label will be "Plasma LOXO-292 Concentration (ng/mL)" for all figures
- X axis label will be "Hours post LOXO-292 dose (hr)" for all figures
- Add footnote: LLOQ value for LOXO-292 is 1 ng/mL

Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYYY HH:MM

10.3 Post-text Table Shells

Page X of X

Table 14.1.1.1 Summary of Disposition (Part 1 and 2) (Safety Population)

	Part 1			Part 2		
Disposition	A	B	Overall	C	D	Overall
Enrolled	XX	XX	XX	XX	XX	XX
Completed	XX	XX	XX	XX	XX	XX
Discontinued Early	XX	XX	XX	XX	XX	XX
Reason 1	XX	XX	XX	XX	XX	XX
Reason 2	XX	XX	XX	XX	XX	XX
Reason 3	XX	XX	XX	XX	XX	XX
etc.						

Note: Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple dose of 200 mg itraconazole QD from Day -4 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.1.1.2 Disposition of Subjects (Part 1 and 2) (Safety Population)

Subject Number	Study Part	Treatment Sequence	Dosed Period*		Completed Period		Study Completion	
			1	2	1	2	Status	Date
X	1	AB	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
X	2	CD	Yes	Yes	No	Yes	Terminated Study Prematurely	DDMMYYYY

Note: * Period: If Study Part = 1, then 1 = Treatment A and 2 = B; If Study Part = 2, then 1 = C and 2 = D
Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple dose of 200 mg itraconazole QD from Day -4 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.1.1.3 Demographic Summary (Part 1 and 2) (Safety Population)

Trait		Part 1 (AB)	Part 2 (CD)	Study Overall
Sex	Male	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)
Race	Asian	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)
Age*(yrs)	n	XX	XX	XX
	Mean	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX
	Median	XX.X	XX.X	XX.X
	Minimum	XX	XX	XX
	Maximum	XX	XX	XX
Height (cm)	n	XX	XX	XX
	Mean	XX.XX	XX.XX	XX.XX
	SD	XX.XXX	XX.XXX	XX.XXX
	Median	XX.XX	XX.XX	XX.XX
	Minimum	XX.X	XX.X	XX.X
	Maximum	XX.X	XX.X	XX.X

Programmer Note: Also include weight (kg) and BMI (kg/m^2)

Note: * Age is calculated from the date of first dosing.
BMI = Body mass index
Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple dose of 200 mg itraconazole QD from Day -4 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.2.1.1.1, 14.2.1.1.2, 14.2.2.1.1 through 14.2.2.1.3 will be in the following format:

Table 14.2.1.1.1 Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) (Part 1) (Pharmacokinetic Population)

Subject Number	Treatment Sequence	Study Period	Sample Times (hr)							
			Predose	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n			XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX	XX	XX	XX	XX	XX	XX	XX	XX
Median			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum			XX	XX	XX	XX	XX	XX	XX	XX	XX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 1 ng/mL are treated as 0 before the first quantifiable concentration and as missing elsewhere.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:
Concentrations will be presented to same precision as in bio data.
Summary statistics presentation with respect to the precision of the bio data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal

Programmer Note:

- PK Time points are: predose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours postdose for Tables 14.2.1.1.1, 14.2.1.1.2, 14.2.2.1.1, and 14.2.2.1.3
- PK Time points are: predose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, and 24 hours postdose for Table 14.2.2.1.2

Per study design needs, the following changes are made to this table relative to Celerion standard:

1. Please remove the "Treatment Sequence" and "Study Period" columns

Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables-sig.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_conc.sas DDMMMYYYY HH:MM

Tables 14.2.1.1.3, 14.2.1.1.4, 14.2.2.1.4 through 14.2.2.1.6 will be in the following format:

Table 14.2.1.1.3 Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) (Part 1) (Pharmacokinetic Population)

			Parameters					
Subject Number	Treatment Sequence	Study Period	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
XXX-XXX	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
XXX-XXX	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n			XX	XX	XX	XX	XX	XX
Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median			XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum			XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Subject Number to be presented as follow: XXX-XXX
- PK Parameters will be presented in the following order and with following units: AUC0-t <unit>, AUC0-inf <unit>, AUC%extrap <unit>, Cmax <unit>, Tmax <unit>, Kel <unit>, t½ <unit>, and CL/F <unit> for Tables 14.2.1.1.3, 14.2.1.1.4, and 14.2.2.1.6
- PK Parameters will be presented in the following order and with following units: AUC0-t <unit>, AUC0-inf <unit>, AUC0-24 <unit>, AUC%extrap <unit>, Cmax <unit>, Tmax <unit>, Kel <unit>, t½ <unit>, and CL/F <unit> for Tables 14.2.2.1.4 and 14.2.2.1.5
- n will be presented as an integer (with no decimal);
- Parameter values for exposure based parameters (i.e. AUCs, Cmax, and CL/F) will be presented with, at maximum, the precision of the bio data, and, at minimum, 3 significant figures (to be determined by the PKist once bio data are received). Summary statistics for exposure parameters will be presented as: Mean, Median, and Geom Mean+1; SD and SEM +2, Min and Max +0.
- Values for time-based parameters (i.e. Tmax, and t1/2) will be presented with 2 decimals. Summary statistics for time-based parameters will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0.
- Values for rate constants (i.e. Kel) will be presented with 3 significant figures. Summary statistics for Kel will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0.
- CV% and Geom CV% for all parameters will be presented with 1 decimal

Per study design needs, the following changes are made to this table relative to Celerion standard:

1. Please remove the "Treatment Sequence" and "Study Period" columns from all tables

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Tables 14.2.1.1.5 and 14.2.2.1.7 will be in the following format:

Table 14.2.1.1.5 Intervals (Hours) Used for Determination of Plasma LOXO-292 Kel Values Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) and Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) (Part 1)(Pharmacokinetic Population)

Subject	Treatment	160 mg LOXO-292 (Part 1)			MD 200 mg Itraconazole + 160 mg LOXO-292 (Part 1)		
Number	Sequence	Interval	R2	n	Interval	R2	n
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X

160 mg LOXO-292 (Part 1): Single dose of 160 mg LOXO-292 (Treatment A)
MD 200 mg Itraconazole + 160 mg LOXO-292 (Part 1): Multiple doses of 200 mg itraconazole QD from Day 1 to Day 7 with a single dose of 160 mg LOXO-292 on Day 1 (Treatment B)
R2 = Coefficient of determination
n = Number of points used in Kel calculation
. = Kel value not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Subject Number to be presented as follow: XXX-XXX
- Interval start and stop times will be presented to 1 decimal or 3 sig figures min;
- R2 will be presented to 3 decimals;
- n will be presented as an integer (with no decimal)

Per study design needs, the following changes are made to this table relative to Celerion standard:

1. Please add a third column for Table 14.2.2.1.7 and label each column header according to Table 5.2. Adjust table footer accordingly.
2. Please remove the treatment sequence column for both tables

Program: /CAXXXXX/sas_prg/pksas/kel-tables-xover.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM

Tables 14.2.1.1.6, 14.2.2.1.8, and 14.2.2.1.9 will be in the following format:

Table 14.2.1.1.6 Statistical Comparisons of Plasma LOXO-292 Pharmacokinetic Parameters Following Coadministration of a Single Dose of 160 mg LOXO-292 with Multiple Doses of 200 mg Itraconazole (Treatment B) Versus Administration of a Single Dose of 160 mg LOXO-292 Alone (Treatment A) (Part 1)
(Pharmacokinetic Population)

		Treatment				Geometric		
		------- Geometric LSMs -------				Mean	90%	Intra-subject
Parameter	(unit)	B	(n)	A	(n)	Ratio	Confidence Intervals	CV%
Param1	(unit)	X.XX	(n)	X.XX	(n)	X.XX	XX.XX - XXX.XX	X.XX
Param2	(unit)	X.XX	(n)	X.XX	(n)	X.XX	XX.XX - XXX.XX	X.XX
Param3	(unit)	X.XX	(n)	X.XX	(n)	X.XX	XX.XX - XXX.XX	X.XX

Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple doses of 200 mg itraconazole QD from Day -4 to Day 7 with a single dose of 160 mg LOXO-292 on Day 1
Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio = 100*(B/A)
Intra-subject CV% = 100 x (square root (exp[MSE]-1), where MSE = Residual variance from ANOVA.

Notes for Generating the Actual Table:

Presentation of Data:

- Geometric LSMs will be presented to same precision as Mean in the PK parameter table CPPar1,
- Geometric Mean Ratio, 90% CI and intra-subject/inter-subject CV% will be presented to 2 decimal places,
- For optional summaries: p-value (for treatment effect) will be presented to 4 decimals; power will be presented to 2 decimals.
- PK parameters are AUC0-t, AUC0-inf, and Cmax for Tables 14.2.1.1.6 and 14.2.2.1.9
- PK parameters are AUC0-t, AUC0-inf, AUC0-24, and Cmax for Table 14.2.2.1.8

Per study design needs, the following changes are made to this table relative to Celerion standard:

1. Please label each column header and table footer according to Table 5.2 in Section 5 for Tables 14.2.2.1.8 and 14.2.2.1.9.

Program: /CAXXXXX/sas_prg/pksas/stats-tables-mixed.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_statsmixed.sas DDMMMYYYY HH:MM

Table 14.3.1.1 Treatment-emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting Events (% of Subject Dosed) (Part 1 and 2) (Safety Population)

	Part 1				Part 2			Part 1+2
TE Adverse Event*	A	B1	B2	Overall	C	D	Overall	Overall
Number of Subjects Dosed	X (100%)	X (100%)	X(100%)	X(100%)	X (100%)	X (100%)	X(100%)	X(100%)
Number of Subjects with TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects without TE Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
General disorders and administration site conditions	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Fatigue	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Thirst	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
etc.								

Note: * Adverse events are classified according to the MedDRA Version 21.0.
TE = Treatment-emergent
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity under the same treatment group.
Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B1: Multiple dose of 200 mg itraconazole QD from Day -4 to Day -1
Treatment B2: Multiple dose of 200 mg itraconazole QD from Day 1 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer Note: For each subject, please sort the AEs with same verbatim and preferred term by onset date/time. For any pair (e.g., AE_S1, AE_S2) of these AEs (for same subject, same verbatim and preferred term), if the onset date/time of AE_S2 = resolved date/time of AE_S1 and the grade of AE_S2 < the grade level of AE_S1, then mark the AE_S2 with a flag like EVAUL_FLG ="N". Then, for AE analysis (summary tables), please exclude the ones with EVAUL_FLG ="N".

Table 14.3.1.2 Treatment-emergent Adverse Event Frequency by Treatment - Number of Adverse Events (% of Total Adverse Events) (Part 1 and 2) (Safety Population)

	Part 1				Part 2			Part 1+2
TE Adverse Event*	A	B1	B2	Overall	C	D	Overall	Overall
Number of TE Adverse Events	X (100%)	X (100%)	X(100%)	X(100%)	X (100%)	X (100%)	X(100%)	X(100%)
Nervous system disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dizziness	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Headache	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Presyncope	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Respiratory, thoracic and mediastinal disorders	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Dry throat	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Oropharyngeal pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sinus congestion	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Sneezing	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
General disorders and administration site conditions	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Fatigue	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Thirst	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
etc.								

Note: * Adverse events are classified according to theMedDRA Version 21.0 by System Organ Class and Preferred Term.
TE = Treatment-emergent, TEAE = Treatment-emergent adverse event
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity under the same treatment group.
Treatment X: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.1.3 and 14.3.1.5 will have the following format.

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs – Number of Subjects Reporting Events (Part 1) (Safety Population)

TE Adverse Event*	Treatment	Number of Subjects with Adverse Events	Severity Grade					Relationship to LOXO-292		Relationship to Itraconazole	
			1	2	3	4	5	Related	Not Related	Related	Not Related
Dizziness	A	X	X	X	X	X	X	X	X	X	X
Dry eye	B1	X	X	X	X	X	X	X	X	X	X
Dry mouth	A	X	X	X	X	X	X	X	X	X	X
	B1	X	X	X	X	X	X	X	X	X	X
Dry throat	B1	X	X	X	X	X	X	X	X	X	X
Ear pain	A	X	X	X	X	X	X	X	X	X	X
Fatigue	B2	X	X	X	X	X	X	X	X	X	X
Treatment A		XX	X	X	X	X	X	X	X	X	X
Treatment B1		XX	X	X	X	X	X	X	X	X	X
Treatment B2		XX	X	X	X	X	X	X	X	X	X
Overall (Part 1)		XX	X	X	X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 21.0 by System Organ Class and Preferred Term.
TE = Treatment-emergent; AE = Adverse event
Severity Grade: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed within the CTCAE with fewer than 5 options for grade selection.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity under the same treatment group.
When a subject experienced the same TEAE at more than one level of severity during a treatment period, only the most severe one was counted.
When a subject experienced the same TEAE at more than one level of drug relationship during a treatment period, only the one related to study drugs was counted.
Treatment X: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.1.4 and 14.3.1.6 will have the following format.

Table 14.3.1.4 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs - Number of Adverse Events (Part 1) (Safety Population)

TE Adverse Event*	Treat-ment	Number of Adverse Events	Severity Grade					Relationship to LOXO-292		Relationship to Itraconazole	
			1	2	3	4	5	Related	Not Related	Related	Not Related
Dizziness	A	X	X	X	X	X	X	X	X	X	X
Dry eye	B1	X	X	X	X	X	X	X	X	X	X
Dry mouth	A	X	X	X	X	X	X	X	X	X	X
	B1	X	X	X	X	X	X	X	X	X	X
Dry throat	B1	X	X	X	X	X	X	X	X	X	X
Ear pain	A	X	X	X	X	X	X	X	X	X	X
Fatigue	B2	X	X	X	X	X	X	X	X	X	X
Treatment A		XX	X	X	X	X	X	X	X	X	X
Treatment B1		XX	X	X	X	X	X	X	X	X	X
Treatment B2		XX	X	X	X	X	X	X	X	X	X
Overall (Part 1)		XX	X	X	X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 21.0 by System Organ Class and Preferred Term.
TE = Treatment-emergent; AE = Adverse event
Severity Grade: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed within the CTCAE with fewer than 5 options for grade selection.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity under the same treatment group.
Treatment X: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.2.1 and 14.3.2.2 will have the following format.

Table 14.3.2.1 Serious Adverse Events (Part 1) (Safety Population)

Subject Number	Treat-ment	TE?^	Adverse Event	PT*/ SOC	Onset				Severity Grade	Ser*	Outcome	Action for LOXO-292/ Itraconazole	Relationship to LOXO-292/ Itraconazole
					Day	Date	Time	Freq*					
XXX-XXX	X	Yes	XXXXXXXXXX	XXXXXXX/ XXXXXXXX	XX	DDMMMYYYY	X:XX	Inter.	X	NS	Resolved	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX

Note: * Adverse events are classified according to MedDRA Version 21.0 by System Organ Class and Preferred Term.
TE = Treatment-emergent; PT = Preferred Term; SOC = System Organ Class, Onset day is relative to Period 1 Day 1.
Freq* represents Frequency: SI = Single Episode, Inter. = Intermittent, Cont. = Continuous
Ser* represents Serious: NS = Not Serious
Severity Grade: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed within the CTCAE with fewer than 5 options for grade selection.
If a TEAE decreased in severity grade, the new TEAE record with less severity was counted as the same TEAE event of the previous record with worse severity under the same treatment group.
Treatment X: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer Note: if there are no serious adverse events reported, there will be just one table (Table 14.3.2.1) with the statement "There was no serious adverse event recorded during the study for Parts 1 and 2."

Tables 14.3.4.2-14.3.4.3 will have the following format.

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Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Age$/ Sex	Study Period	Day	Hour	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
1	XXX-XXX	XX/M	Screen		.	DDMMMYYYY	XX HN G1	XX	XX	XX	XX HN
			1	-X	-XX.XX	DDMMMYYYY	XX	XX	XX	XX	XX
			2	-X	-XX.XX	DDMMMYYYY	XX	XX	XX	XX HN	XX
				-X	-XX.XX	DDMMMYYYY	XX	XX	XX	XX	XX
				X	XX.XX	DDMMMYYYY	XX LY-	XX LN	XX	XX LY-	XX

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.
Arrange alphabetically by lab test name.

Note: $ Age is calculated from the date of first dosing
Abnormal flag: H = Above Reference Range, L = Below Reference Range
Computer Clinical significance: N = Not Clinically Significant, Y = Clinically Significant
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.4.4 Clinically Significant Laboratory and Corresponding Results (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Age$/ Sex	Study Period	Day	Hour	Date	Time	Department	Test	Result	Reference Range	Unit
X	XXX-XXX	XX/X	X	1	-X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	X - X	mg/dL
				2	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HYR+G3	X - X	mg/dL
				3	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HY- G2	X - X	mg/dL
				4	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX HN G1	X - X	mg/dL

Programmer Note: All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table. If there were no CS values as deemed by PI (i.e., no "CS" or "Clinically Significant" in the PI flag or comment field in the laboratory dataset), then this table will contain only the statement: "There were no laboratory values deemed clinically significant by the PI in the study."

Note: $ Age is calculated from the date of first dosing
H = Above Reference Range, L = Below Reference Range
Computer: N = Not Clinically Significant, Y = Clinically Significant
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Program : /CAXXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.5.1, 14.3.5.5, and 14.3.5.9 will have the following format.

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Table 14.3.5.1 Clinical Laboratory Summary and Change from Baseline – Serum Chemistry (Part 1) (Safety Population)

Laboratory Test (unit)	Normal Range#	Time Point	Statistic	Treatment A	Treatment B	Change From Baseline A	Change From Baseline B
Parameter1 (unit)	XX – XX	Day -1	n	XX	XX		
			Mean	XX.XX	XX.XX		
			SD	X.XXX	X.XXX		
			Minimum	XX.X	XX.X		
			Median	XX.XX	XX.XX		
			Maximum	XX.X	XX.X		
		Day 4	n	XX	XX	XX	XX
			Mean	XX.XX	XX.XX	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X
		Day 7/8$	n	XX	XX	XX	XX
			Mean	XX.XX	XX.XX	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining laboratory tests. Sort alphabetically by lab test name.>

Note: # Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
$ Day 7 for Treatment A (Period 1) and Day 8 for Treatment B (Period 2)
Baseline is Day -1 of each period and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
Treatment A: <description>
Treatment B: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.5.2, 14.3.5.6, and 14.3.5.10 will have the following format.

Table 14.3.5.2 Clinical Laboratory Shift from Baseline - Serum Chemistry (Part 1) (Safety Population)

Laboratory Test (units)	Treatment	Time Point	Baseline L: Postdose L	Baseline L: Postdose N	Baseline L: Postdose H	Baseline N: Postdose L	Baseline N: Postdose N	Baseline N: Postdose H	Baseline H: Postdose L	Baseline H: Postdose N	Baseline H: Postdose H
Testname(unit)	A	Day 4	X	XX	X	X	XX	X	X	XX	X
		Day 7	X	XX	X	X	XX	X	X	XX	X
	B	Day 4	X	XX	X	X	XX	X	X	XX	X
		Day 8	X	XX	X	X	XX	X	X	XX	X

<Programmer note: Similar for remaining laboratory tests. Use N = Within Normal Range, O = Outside Normal Range for urinalysis shift table.>

Note: N = Within Normal Range, L = Below Normal Range, H= Above Normal Range.
Baseline is Day -1 of each period and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
Treatment A: <description>
Treatment B: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_programname.sas DDMMMYYYY HH:MM

Tables 14.3.5.3, 14.3.5.7, and 14.3.5.11 will have the following format.

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Table 14.3.5.3 Clinical Laboratory Summary and Change from Baseline - Serum Chemistry (Part 2) (Safety Population)

Laboratory Test (unit)	Normal Range#	Time Point	Statistic	Treatment C	Treatment D	Change From Baseline C	Change From Baseline D
Parameter1 (unit)	XX - XX	Day -1	n	XX	XX		
			Mean	XX.XX	XX.XX		
			SD	X.XXX	X.XXX		
			Minimum	XX.X	XX.X		
			Median	XX.XX	XX.XX		
			Maximum	XX.X	XX.X		
		Day 4	n	XX	XX	XX	XX
			Mean	XX.XX	XX.XX	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X
		Day 7/9$	n	XX	XX	XX	XX
			Mean	XX.XX	XX.XX	XX.XX	XX.XX
			SD	X.XXX	X.XXX	X.XXX	X.XXX
			Minimum	XX.X	XX.X	XX.X	XX.X
			Median	XX.XX	XX.XX	XX.XX	XX.XX
			Maximum	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining laboratory tests. Also need to add Days 13 and 17 (only applicable to Treatment D. Day 7 of Period 1 is Day -1 of Period 2 (Day 7 of Period 1 is also used as baseline for Period 2).>

Note: # Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
$ Day 7 for Treatment C (Period 1) and Day 9 for Treatment D (Period 2)
Baseline is Day -1 of each period and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments. Day 7 of Period 1 is Day -1 of Period 2 (Day 7 of Period 1 is used as baseline for Period 2).
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.5.4, 14.3.5.8, and 14.3.5.12 will have the following format.

Table 14.3.5.4 Clinical Laboratory Shift from Baseline - Serum Chemistry (Part 2) (Safety Population)

Laboratory Test (units)	Treatment	Time Point	Baseline L: Postdose L	Baseline L: Postdose N	Baseline L: Postdose H	Baseline N: Postdose L	Baseline N: Postdose N	Baseline N: Postdose H	Baseline H: Postdose L	Baseline H: Postdose N	Baseline H: Postdose H
Testname(unit)	C	Day 4	X	XX	X	X	XX	X	X	XX	X
		Day 7	X	XX	X	X	XX	X	X	XX	X
	D	Day 4	X	XX	X	X	XX	X	X	XX	X
		Day 9	X	XX	X	X	XX	X	X	XX	X
		Day 13	X	XX	X	X	XX	X	X	XX	X
		Day 17	X	XX	X	X	XX	X	X	XX	X

<Programmer note: Similar for remaining laboratory tests. Use N = Within Normal Range, O = Outside Normal Range for urinalysis shift table.>

Note: N = Within Normal Range, L = Below Normal Range, H= Above Normal Range.
Baseline is Day -1 of each period and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_programname.sas DDMMMYYYY HH:MM

Table 14.3.5.13 Vital Sign Summary and Change from Baseline (Part 1) (Safety Population)

Vital Sign Parameter (unit)	Time Point	Statistic	Treatment A	Treatment B	Change From Baseline A	Change From Baseline B
Parameter1 (unit)	Day -4	n		XX		
		Mean		XX.XX		
		SD		X.XXX		
		Minimum		XX.X		
		Median		XX.XX		
		Maximum		XX.X		
	Day -1/1$	n	XX	XX		
		Mean	XX.XX	XX.XX		
		SD	X.XXX	X.XXX		
		Minimum	XX.X	XX.X		
		Median	XX.XX	XX.XX		
		Maximum	XX.X	XX.X		
	Postdose Hour 2	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X
	Postdose Hour 72	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining vital sign parameters. Also need to add Days 5 and 8 (Days 5 and 8 only applicable to Treatment B).>
Note: $ Day -1 for Treatment A (Period 1) and Day 1 predose for Treatment B (Period 2)
Baseline is Day -1 of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2) which is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
Treatment A: <description>
Treatment B: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.5.14 Vital Sign Summary and Change from Baseline (Part 2) (Safety Population)

Vital Sign Parameter (unit)	Time Point	Statistic	Treatment		Change From Baseline	
			C	D	C	D
Parameter1 (unit)	Day -1/1$	n	XX	XX		
		Mean	XX.XX	XX.XX		
		SD	X.XXX	X.XXX		
		Minimum	XX.X	XX.X		
		Median	XX.XX	XX.XX		
		Maximum	XX.X	XX.X		
	Day 1 Postdose Hour 2	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X
	Day 1 Postdose Hour 72	n	XX		XX	
		Mean	XX.XX		XX.XX	
		SD	X.XXX		X.XXX	
		Minimum	XX.X		XX.X	
		Median	XX.XX		XX.XX	
		Maximum	XX.X		XX.X	
	Day 10 Predose	n		XX		XX
		Mean		XX.XX		XX.XX
		SD		X.XXX		X.XXX
		Minimum		XX.X		XX.X
		Median		XX.XX		XX.XX
		Maximum		XX.X		XX.X
	Day 10 Postdose Hour 2	n		XX		XX
		Mean		XX.XX		XX.XX
		SD		X.XXX		X.XXX
		Minimum		XX.X		XX.X
		Median		XX.XX		XX.XX
		Maximum		XX.X		XX.X

<Programmer note: Similar for remaining vital sign parameters. Also need to add Days 13 and 17 (Days 13 and 17 only applicable to Treatment D).>

```
Note:  $ Day -1 for Treatment C (Period 1) and Day 1 predose for Treatment D (Period 2)
       Baseline is Day -1 of Treatment C (Period 1) and Day 1 predose for Treatment D (Period 2) which is the last non-missing predose
       measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
       Treatment C:  <description>
       Treatment D:  <description>

Program:  /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas  DDMMMYYYY  HH:MM
```

Table 14.3.5.15 12-Lead Electrocardiogram Summary and Change from Baseline (Part 1) (Safety Population)

ECG Parameter (unit)	Time Point	Statistic	Treatment		Change From Baseline	
			A	B	A	B
Parameter1 (unit)	Day -4	n		XX		
		Mean		XX.XX		
		SD		X.XXX		
		Minimum		XX.X		
		Median		XX.XX		
		Maximum		XX.X		
	Day -1/1$	n	XX	XX		
		Mean	XX.XX	XX.XX		
		SD	X.XXX	X.XXX		
		Minimum	XX.X	XX.X		
		Median	XX.XX	XX.XX		
		Maximum	XX.X	XX.X		
	Postdose Hour 2	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X
	Postdose Hour 72	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X

<Programmer note: Similar for remaining ECG parameters. Also need to add Days 5 and 8 (Days 5 and 8 only applicable to Treatment B).>
Note: $ Day -1 for Treatment A (Period 1) and Day 1 predose for Treatment B (Period 2)
Baseline is Day -1 of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2) which is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
Treatment A: <description>
Treatment B: <description>

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.5.16 12-Lead Electrocardiogram Summary and Change from Baseline (Part 2) (Safety Population)

ECG Parameter (unit)	Time Point	Statistic	Treatment		Change From Baseline	
			C	D	C	D
Parameter1 (unit)	Day -1/1$	n	XX	XX		
		Mean	XX.XX	XX.XX		
		SD	X.XXX	X.XXX		
		Minimum	XX.X	XX.X		
		Median	XX.XX	XX.XX		
		Maximum	XX.X	XX.X		
	Day 1 Postdose Hour 2	n	XX	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X
	Day 1 Postdose Hour 72	n	XX		XX	
		Mean	XX.XX		XX.XX	
		SD	X.XXX		X.XXX	
		Minimum	XX.X		XX.X	
		Median	XX.XX		XX.XX	
		Maximum	XX.X		XX.X	
	Day 10 Predose	n		XX		XX
		Mean		XX.XX		XX.XX
		SD		X.XXX		X.XXX
		Minimum		XX.X		XX.X
		Median		XX.XX		XX.XX
		Maximum		XX.X		XX.X
	Day 10 Postdose Hour 2	n		XX		XX
		Mean		XX.XX		XX.XX
		SD		X.XXX		X.XXX
		Minimum		XX.X		XX.X
		Median		XX.XX		XX.XX
		Maximum		XX.X		XX.X

<Programmer note: Similar for remaining vital sign parameters. Also need to add Days 13 and 17 (Days 13 and 17 only applicable to Treatment D).>

```
Note:  $ Day -1 for Treatment C (Period 1) and Day 1 predose for Treatment D (Period 2)
       Baseline is Day -1 of Treatment C (Period 1) and Day 1 predose for Treatment D (Period 2) which is the last non-missing predose
       measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.
       Treatment C:  <description>
       Treatment D:  <description>
Program:  /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas  DDMMMYYYY  HH:MM
```

11. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final CSR. These listings will be generated off of the Celerion SDTM Tabulation Model 1.4 mapped in accordance with SDTM Implementation Guide 3.2. All listings will be presented in Courier New size font 9.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges (Part 1 and 2)

Laboratory Group	Test Name	Sex	Age Category	Normal Range	Unit
Serum Chemistry	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
Hematology	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units

<Programmer note: Sort alphabetically by lab test name within each lab group.>

<similar for remaining Laboratory Groups and Test Names>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.1 Subject Discontinuation (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Treatment Sequence	Study Period	Date	Completed Study?	Primary Discontinuation Reason
X	XXX-XXX	XX	Post	DDMMMYYYY	YES	
X	XXX-XXX	XX	Post	DDMMMYYYY	YES	
X	XXX-XXX	XX	Post	DDMMMYYYY	NO	Adverse Event
X	XXX-XXX	XX	Post	DDMMMYYYY	YES	

Note: Treatment A: Single dose of 160 mg LOXO-292 (Part 1)
Treatment B: Multiple dose of 200 mg itraconazole QD from Day -4 to Day 7 with a single 160 mg LOXO-292 on Day 1
Treatment C: Single dose of 160 mg LOXO-292 (Part 2)
Treatment D: Multiple dose of 600 mg rifampin QD from Day 1 to Day 16 with a single 160 mg LOXO-292 on Day 1 and Day 10

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Date of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m^2)	Informed Consent Date	Informed Consent Version Date
X	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
X	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
X	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY
X	XXX-XXX	DDMMMYYYY	XX	AAAAAA	AAAAAAAA	AAAAAAAAAA	XXX	XX.XX	XX.XX	DDMMMYYYY	DDMMMYYYY

Note: * Age is calculated form the date of first dosing.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2 Updated Informed Consent (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Date Subject Signed Informed Re-Consent	Informed Re-Consent Version Date	Reason for Re-Consent
X	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
X	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
X	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX
X	XXX-XXX	DDMMMYYYY	DDMMMYYYY	XXXXXXXXXXXX

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3 Physical Examination (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Treatment Sequence	Period	Day Hour	Date	Body System	Answer or Result	Comment
1	XXX-XXX	AB	Screen		DDMMMYYYY	Was PE performed?	Yes	
						General	Normal	
						HEENT	Normal	
						< >	< >	
			1	-1 Check-in	DDMMMYYYY	Was PE performed?	Yes	
						HEENT	Unchanged	
						< >	< >	

Note: Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Medical and Surgical History (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Any History?	Study Period	Category	Body system	Date		Ongoing?	Condition or Events
						Start	End		
1	XXX-XXX	XXX	Screen	Medical Surgical	XXXXXXXXXX	DDMMMYYYY DDMMMYYYY	DDMMMYYYY DDMMMYYYY	YES	XXXXXXX XXXXXX XXXXXXXX
2	XXX-XXX	XXX	Screen	Medical	XXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	NO	

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.5 Nicotine Use (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Substance	Description of Use	Start Date	End Date
1	XXX-XXX	Screen	XXXXXXXX XXX	XXXXX XXXXXXX XXXXXX	DDMMMYYYY	DDMMMYYYY

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.1 Inclusion Criteria (Part 1 and 2)

1. Healthy, adult, male or female (of non-childbearing potential only), 18-55 years of age, inclusive, at screening.
2. < >
3. < >
4. < >
5. < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.2 Exclusion Criteria (Part 1 and 2)

1. Is mentally of legally incapacitated or has significant emotional problems at the time of the screening visit or expected during the conduct of the study.
2. < >
3. < >
4. < >
5. < >
6. < >
7. < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.2 Subject Eligibility (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Did subject meet all eligibility criteria?	Specify
1	XXX-XXX	Screen	YES	
2	XXX-XXX	Screen	NO	<this column is only presented if data is present>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3.1 Check-in Criteria (Part 1 and 2)

1. Did the Subject report any study restriction violations since the last study visit?
2. IF YES TO ANY QUESTION, WAS SUBJECT APPROVED FOR STUDY?

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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Appendix 16.2.5.3.2 Check-in Responses (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Treatment Sequence	Study Period	Day	Hour	Date	Time	Check-in Criteria X	Check-in Criteria X	Specify
1	XXX-XXX	AB	1	X	Check-in	DDMMMYYYY	hh:mm	YES	YES	<this column prints only if data is present>

Note: Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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Appendix 16.2.5.4.1 Test Compound Description (Part 1 and 2)

Compound	Form	Route
XXXXXXXXXXXXX	< >	XXXX
XXXXXXXXXXXXX	< >	XXXX

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.2 Test Compound Administration Times (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Treatment	Day	Hour	Date	Actual Time	Compound	Dosage	Comments
1	XXX-XXX	1	X	X	0	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	<This column prints only
		2	X	X	0	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	if data is present>

Note: Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5 PK Blood Draw Times (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Treatment	Day	Hour	Date	Actual Time	Bioassay	Comments
1	XXX-XXX	1	X	1	-X.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				2	XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	
					XX.XX	DDMMMYYYY	XX:XX:XX	XXXXXXXXXX	
				3	XX.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXXX	

Note: Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.6 Urine Collection Times (Part 2 Period 2 Only) (Safety Population)

						Urine Collection					
						Start		Stop			
Study Part	Subject Number	Study Period	Treat-ment	End Day	Interval	Date	Time	Date	Time	Measurement Type	Result & Unit or Comments
X	XXX-XXX	X	D	X	X	DDMMMYYYY	XX:XX:XX	DDMMMYYYY	XX:XX:XX	Total Volume (mL)	XXX
					X	DDMMMYYYY	XX:XX:XX	DDMMMYYYY	XX:XX:XX	Overall Comment	XXXXXXXXXXXXXXX

Note: Treatment D: <description>

Program: /AAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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Appendix 16.2.5.7 Phone Call (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Was a Telephone Call Performed? (Yes/No)	Day	Date	Time	If No, Reason*
1	XXX-XXX	1	YES	XX	DDMMMYYYY	HH:MM	XXXXXXXXXXXXX

Note: * Reason options: 3 call attempts with no subject return call; Phone Disconnected; Wrong Number

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.8 Meal Times (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Treatment	Day	Hour	Event	Date	Start Time	Stop Time	Comments
1	XXX-XXX	1	A	-X	-XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					-XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					-XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				X	XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				X	XX.XX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
		2	B	-X	-XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					-XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					-XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				X	XX.XX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				X	XX.XX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	

Note: Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.9 Prior and Concomitant Medications (Part 1 and 2) (Safety Population)

Study Part/ Subject Number	Any Med^?	Prior to Study?	Medication (WHO* Term)	Dosage	Route	Frequency	Start Day/Date/Time	Stop Day/Date/Time	Indi-cation	AE No (If Due to AE)	Continuing Medication?
X/XXX-XXX	No		None								
X/XXX-XXX	Yes	Yes	ACETAMINOPHEN (ACETAMINOPHEN)	620 mg	BY MOUTH	AS NEEDED	XX/DDMMMYYYY/ HH:MM	XX/DDMMMYYYY/ HH:MM	XXXXX	XXX	YES

Note: * Concomitant medications are coded with WHO Dictionary Version Mar2017 B3.
^ Med = Medication; UNK = Unknown
Prior medication was medication taken prior to study drug administration.
Start and stop day is relative to Period 1 Day 1.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (I of II) (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Treatment	TE?^	Adverse Event/ Preferred Term*	Time from Last Dose (DD:HH:MM)	Onset Day	Onset Date	Onset Time	Resolved Day	Resolved Date	Resolved Time	Duration (DD:HH:MM)
1	XXX-XXX		None									
	XXX-XXX	X	Yes	XXXXXXXXXXXXX/ XXXXXXXXXX	XX:XX:XX	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	XX:XX:XX
			No	XXXXXXXXXXXXX/ XXXXXXXXXX	XX:XX:XX	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	XX:XX:XX

Note: * Adverse events are classified according to MedDRA Version 21.0 by System Organ Class and Preferred Term.
^ TE = Treatment-emergent, Onset and resolved day is relative to Period 1 Day 1.
Treatment A: <description>
Treatment B1: <description>
Treatment B2: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.2.1 Adverse Events (II of II, Part 1 Only) (Safety Population)

Study Part/ Subject Number	Treat-ment	Adverse Event	Onset Day	Onset Date	Onset Time	Freq*	Severity	Ser*	Outcome	Action for LOXO-292/ Itraconazole	Other Action Taken	Relationship to LOXO-292/ Itraconazole
X/XXX-XXX		None										
X/XXX-XXX	X	XXXXXXX	XX	DDMMMYYYY	X:XX	Inter.	Grade 1	NS	Resolved	Dose Not Changed/ Dose Not Changed	XXXXXXXX	Not Related to LOXO-292/ Not Related to Itraconazole

Note: Ser* represents Serious: NS = Not Serious
Freq* represents Frequency: SI = Single Episode, Inter. = Intermittent, Cont. = Continuous
Onset day is relative to Period 1 Day 1.
Severity/Intensity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed within the CTCAE with fewer than 5 options for grade selection.
Treatment A: <description>
Treatment B1: <description>
Treatment B2: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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Appendix 16.2.7.2.2 Adverse Events (II of II, Part 2 Only) (Safety Population)

Study Part/ Subject Number	Treat-ment	Adverse Event	Onset Day	Onset Date	Onset Time	Freq*	Severity	Ser*	Outcome	Action for LOXO-292/ Rifampin	Other Action Taken	Relationship to LOXO-292/ Rifampin
X/XXX-XXX		None										
X/XXX-XXX	X	XXXXXXX	XX	DDMMMYYYY	X:XX	Inter.	Grade 1	NS	Resolved	Dose Not Changed/ Dose Not Changed	XXXXXXXX	Not Related to LOXO-292/ Not Related to Rifampin

Note: Ser* represents Serious: NS = Not Serious
Freq* represents Frequency: SI = Single Episode, Inter. = Intermittent, Cont. = Continuous
Onset day is relative to Period 1 Day 1.
Severity/Intensity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe or medically significant but not immediately life-threatening; Grade 4 = Life-threatening consequences; Grade 5 = Death related to AE
Not all grades are appropriate for all AEs, therefore some AEs are listed within the CTCAE with fewer than 5 options for grade selection.
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.3 Adverse Event Non-Drug Therapy (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Treatment	Adverse Event	Onset Day	Onset Date	Onset Time	Resolved Day	Resolved Date	Resolved Time	Therapy Date	Therapy Time	Therapy Description
1	XXX-XXX	X	DRY LIPS	XX	DDMMMYYYY	X:XX	XX	DDMMMYYYY	X:XX	DDMMMYYYY	XX:XX	PETROLEUM JELLY

Note: Onset and resolved day is relative to Period 1 Day 1.
Treatment A: <description>
Treatment B1: <description>
Treatment B2: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.4 Adverse Event Preferred Term Classification (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Treatment	Adverse Event	Preferred Term*	Body System	Onset Day	Onset Date	Onset Time
1	XXX-XXX	X	XXXXXXX XXXXX XXXX XXXXXX	XXXXXXXXXX XXXXXXX	XXXXXXXXXXXXXXXXXXXX	XX	DDMMMYYYY	X:XX

Note: * Adverse events are classified to MedDRA Version 21.0 by System Organ Class and Preferred Term.
Onset day is relative to Period 1 Day 1.
Treatment A: <description>
Treatment B1: <description>
Treatment B2: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendices 16.2.8.1.2-16.2.8.1.4 will have the following format.

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Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Age$/ Sex	Study Period	Day	Hour	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
1	XXX-XXX	XX/M	Screen		.	DDMMMYYYY	XX HN	XX	XX	XX	XX HN
			1	-X	-XX.XX	DDMMMYYYY	XX	XX	XX	XX	XX
			2	-X	-XX.XX	DDMMMYYYY	XX	XX	XX	XX HN	XX
				-X	-XX.XX	DDMMMYYYY	XX	XX	XX	XX	XX
				X	XX.XX	DDMMMYYYY	XX LY-	XX LN	XX	XX LY-	XX

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for. Arrange alphabetically by lab test name.

Note: $ Age is calculated from the date of first dosing.
H = Above Reference Range, L = Below Reference Range
Computer Clinical Significance: N = Not Clinically Significant, Y = Clinically Significant
PI Interpretation: - = Not Clinically Significant, R = To be Rechecked, ^ = Will be Retested at a Later Event

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Day	Hour	Date	Department	Test	Result	Unit	Comment
1	XXX-XXX	X	X	-X.X	DDMMMYYYY	Other Tests	Fibrinogen	XXX	mg/dL	Not significant in the context of this study.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.2 Vital Signs (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Test	Arm	Blood Pressure (mmHg) Systolic/Diastolic	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)	Comments
1	XXX-XXX	Screen		.	.	DDMMMYYYY	X:XX:XX							XXX.X	
				.	.	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX	XX.X		
		1	X	-X	-XX.X	DDMMMYYYY	XX:XX:XX							XXX.X	
				X	-X.X	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX			
					X.X	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX			
		2	X	X	-X.X	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX			
					X.X	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX			
					R	DDMMMYYYY	XX:XX:XX	SITX	Right	XXX/ XX	XX	XX			
				X	-X.X	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX			
					X.X	DDMMMYYYY	X:XX:XX	SITX	Right	XXX/ XX	XX	XX			
				X	XX.X	DDMMMYYYY	XX:XX:XX	SITX	Right	XXX/ XX	XX	XX			

Programmer note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Note: SITX = X-minute sitting, R = Recheck Value.
Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.3 12-Lead Electrocardiogram (Part 1 and 2) (Safety Population)

Study Part	Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Result	Heart Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcF* (msec)	Comments
1	XXX-XXX	Screen		.		DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	
		1	X	X	-X.XX	DDMMMYYYY	X:XX:XX	ANCS	XX	XXX.X	XX.X	XXX.X	XXX.X	
					X.XX	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	
		2	X	X	-X.XX	DDMMMYYYY	X:XX:XX	ANCS	XX	XXX.X	XX.X	XXX.X	XXX.X	
					X.XX	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	
				X	-X.XX	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	#
					X.XX	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	
				X	X.XX	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	@

Programmer note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Note: ANCS = Abnormal, Not Clinically Significant
QTcF* = QT corrected for heart rate using Fridericia's correction.
= QTc > 450, @ = QTc change from baseline greater than 30 msec
Treatment A: <description>
Treatment B: <description>
Treatment C: <description>
Treatment D: <description>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

16.1.9.2 Statistical Outputs


CCI


CCI


CCI


CCI


CCI


CCI


CCI


CCI


CCI


CCI


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