

Statistical Analysis Plan J2G-OX-JZJS (1.0)

An Open-Label, Fixed-Sequence Study to Evaluate the Effect of Multiple Doses of LOXO-292 on the Single Dose Pharmacokinetics of Repaglinide in Healthy Adult Subjects

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Statistical Analysis Plan

An Open-Label, Fixed-Sequence Study to Evaluate the Effect of Multiple Doses of LOXO-292 on the Single Dose Pharmacokinetics of Repaglinide 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-18026. 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

Primary:

To investigate the effect of multiple-dose LOXO-292 on the single-dose pharmacokinetics (PK) of repaglinide, a sensitive cytochrome P450 (CYP) 2C8 (CYP2C8) substrate, in healthy adult subjects.

Secondary:

1. To evaluate the single-dose PK of LOXO-292 administered alone and the multiple-dose PK of LOXO-292 with coadministration of repaglinide in healthy adult subjects.
2. To determine the safety and tolerability of multiple-dose LOXO-292 with and without coadministration of repaglinide in healthy adult subjects.

2.2 Endpoints

Pharmacokinetics:

The following PK parameters will be calculated for repaglinide in plasma in Period 1, **CCI** and Period 2, **CCI**: AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, t_{1/2}, CL/F, and Vz/F.

The following PK parameters will be calculated for LOXO-292 in plasma in Period 2, on Day 1 (following morning dosing): AUC0-12, AUC0-t, Cmax, and Tmax; and on Day 10 (following morning dosing): AU τ , Cmax,ss, Tmax,ss, and CL,ss/F. Additionally, C_{trough} values will be assessed following the 2nd dose on **CCI**

CCI



Safety:

Safety endpoints will include 12-lead ECGs, physical examinations, vital signs, glucose monitoring, clinical laboratory tests, and AEs.

3. STUDY DESIGN

This is an open label, 2-period, fixed-sequence study.

Sixteen (16), healthy, adult male and female (women of non-childbearing potential only) subjects will be enrolled. Every attempt will be made to enroll at least 3 subjects of each sex.

Screening of subjects will occur within 28 days prior to the first dosing (i.e., repaglinide).

In Period 1, Day 1, a single oral dose of repaglinide will be administered. PK samples for repaglinide will be collected predose and for 16 hours postdose.

In Period 2, oral doses of LOXO-292 will be administered twice daily (BID) for 10 consecutive days (Days 1 to 10). The single dose of repaglinide will be coadministered with the single dose of LOXO-292 on the morning of Day 10. PK sampling for repaglinide will be collected predose and for 16 hours following repaglinide dosing on Day 10. PK sampling in plasma for LOXO-292 will be collected CCI



In both periods, glucose will be administered immediately following repaglinide dosing on Day 1 of Period 1 and Day 10 of Period 2 and additionally, at approximately 1 hour postdose on Day 10 of Period 2.

There will be a washout period of 24 hours between the repaglinide dose in Period 1 and the first LOXO-292 dose in Period 2.

Safety and tolerability will be assessed through End of Treatment (EOT) or early termination (ET) by monitoring AEs, performing physical examinations, glucose monitoring, and clinical laboratory tests, measuring vital signs, and recording ECGs.

Subjects will be permitted to be replaced at the discretion of the Sponsor.

Subjects will be housed through EOT or ET beginning in Period 1, Day -1, at the time indicated by the clinical research unit (CRU), until after completion of study procedures in Period 2, Day 11 (EOT) or ET study procedures.

The CRU will contact all subjects who received at least one dose of study drug (including subjects who terminated the study early [ET]) at the End of Study (EOS) by a follow up (FU) phone call. The EOS/FU phone call will be performed 7 ± 2 days after the EOT visit or ET visit to determine if any SAE or study drug related AE has occurred since the EOT or ET visit.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety Population

All subjects who received at least one dose of either of the study drugs 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 repaglinide and LOXO-292 may 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 criterion, deviate significantly from the protocol, or have unavailable or incomplete data that 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 is planned for this study.

5. TREATMENT DESCRIPTIONS

LOXO-292 will be supplied as 80 mg capsules.

Repaglinide will be supplied as 0.5 mg tablets.

Glucose will be provided as 4 g chewable tablets.

Each dose of LOXO-292 and repaglinide will be administered orally with 240 mL of room temperature water. When LOXO-292 and repaglinide are administered concurrently, only 240 mL of room temperature water will be administered for both drugs. The dose of repaglinide on Day 1 of Period 1 and the coadministered morning doses of LOXO-292 and repaglinide on Day 10 of Period 2 will be preceded by an overnight fast of at least 10 hours. All other doses will be preceded by a 2-hour fast and followed by a 1 hour postdose fast.

On Day 1 of Period 1, immediately following administration of repaglinide, subjects will be provided with 12 g of glucose (3 x 4 g chewable tablets). On Day 10 of Period 2, immediately following administration of repaglinide and at approximately 1 hour after administration of repaglinide, subjects will be provided with 16 g of glucose (4 x 4 g chewable tablets). An additional 100 mL of room temperature water may be taken if required.

Subjects will be instructed not to crush, split, or chew LOXO-292 capsules or repaglinide tablets, and will be instructed to chew the glucose tablets.

All Subjects (n = 16)

Table 5.1 Treatment Description

Treatment	Short Description (text, tables headers, figures, listings, SAS output)	Description
A (Period 1)	0.5 mg repaglinide	A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
B* (Period 2)	0.5 mg repaglinide + MD 160 mg LOXO-292	Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10
B1	MD 160 mg LOXO-292 Alone	Multiple doses of 160 mg LOXO-292 BID from Day 1 to Day 9

B2	0.5 mg repaglinide + MD 160 mg LOXO-292	Multiple doses of 160 mg LOXO-292 BID on Day 10 with a single dose of 0.5 mg repaglinide coadministered on the morning of Day 10
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* For AEs, Treatment B will be divided into two segments as B1 and B2.
MD = multiple dose

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

Blood samples for PK assessment of repaglinide will be taken at the following time points on Day CCI [REDACTED]

Blood samples for PK assessment of LOXO-292 will be taken at the following time points after the morning dose on Days CCI [REDACTED]

[REDACTED] . Trough samples will be taken following the CCI [REDACTED]

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

6.2.1 Repaglinide

Plasma concentrations of repaglinide 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 repaglinide in plasma is 0.02 – 20 ng/mL.

6.2.2 LOXO-292

Plasma concentrations of LOXO-292 will be determined using LC-MS/MS method validated with respect to accuracy, precision, linearity, sensitivity, and specificity at

Alturas Analytics, Inc. (Moscow, Idaho, USA). The analytical range (LLOQ – ULOQ) for LOXO-292 in plasma 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

6.3.1 Repaglinide

Repaglinide was supplied as repaglinide 0.5 mg tablets, each 0.5 mg contained 0.5 mg of repaglinide (freebase).

6.3.2 LOXO-292

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

6.4 Pharmacokinetic Concentrations

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

6.5 Noncompartmental Pharmacokinetic Analysis and Parameter Calculation for Repaglinide and LOXO-292

The appropriate noncompartmental PK parameters will be calculated from the plasma repaglinide and LOXO-292 concentration-time data using Phoenix® WinNonlin® Version 7.0 or higher. Actual sample collection times will be used in the calculations of the PK parameters. The calculation of the actual time for repaglinide will be in respect to the dose administration time of repaglinide on Day 1 of Period 1 and Day 10 of Period 2. The calculation of the actual time for LOXO-292 will be in respect to the administration time of the morning LOXO-292 dose on Days 1 and 10 in Period 2. All PK parameters included in the protocol are listed in Tables 6.1, 6.2, and 6.3 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated for Repaglinide

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
AUC%extrap	Percent of AUC0-inf extrapolated	Calculated as (1- AUC0-t/AUC0-inf)*100
Cmax	Maximum observed concentration	Taken directly from bioanalytical data
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.
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 during the terminal elimination phase
t½	Apparent first-order terminal elimination half-life	Calculated as 0.693/Kel
CL/F	Apparent total plasma clearance after oral (extravascular) administration	Calculated as Dose/(AUC0-inf)
Vz/F	The apparent volume of distribution during the terminal elimination phase after extravascular administration	Calculated as Dose/(AUC0-inf x Kel)

Table 6.2. Single-dose Noncompartmental Pharmacokinetic Parameters to be Calculated for LOXO-292 on Day 1

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC0-12	Area under the concentration-time curve from time 0 to 12 hours	Calculated using the Linear Trapezoidal with Linear Interpolation Method
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
Cmax	Maximum observed concentration	Taken directly from bioanalytical data
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.

Table 6.3. Multiple-dose Noncompartmental Pharmacokinetic Parameters to be Calculated for LOXO-292 on Day 10

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUCtau	Area under the concentration-time curve during a dosing interval, tau, at steady state Will be calculated after the morning dose, where tau is defined as 12 hours	Calculated using the Linear Trapezoidal with Linear Interpolation Method
Cmax,ss	The maximum observed concentration at steady state, following the morning dose	Taken directly from bioanalytical data
Ctrough*	Concentration observed at the end of a dosing interval Dosing interval is defined as 12 hours following the 2 nd dose on Days 1, 2, 3, 4, 5, 6, 7, 8, and 9 (corresponding to pre-morning dose samples collected on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10)	Taken directly from bioanalytical data at any given time point

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
Tmax,ss	The time to reach Cmax at steady state, following the morning dose	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,ss/F	Apparent total body clearance estimated at steady state after oral/extravascular administration	Calculated as Dose/AUC _{tau,ss}

CCI

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 all statistical analysis.

For the calculation of the PK parameters on Day 1 and Day 10, plasma concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration of a PK profile will be set to 0 and plasma concentrations BLQ after the first quantifiable concentration of a PK profile 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 $t_{1/2}$, AUC_{0-inf}, AUC%extrap, CL/F, CL,ss/F, and Vz/F, as appropriate, are considered not calculable and will not be reported. Wherever the resulting $t_{1/2}$ is more than half as long as the sampling interval, the Kel values and associated parameters ($t_{1/2}$, AUC_{0-inf}, AUC%extrap, CL/F, CL,ss/F, and Vz/F) may not be presented as judged appropriate and in accordance with Celerion SOPs.

6.6 Data Summarization and Presentation

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

The plasma concentrations of repaglinide will be listed and summarized by treatment and time point for all subjects in the PK Population. The plasma concentrations of LOXO-292 will be listed and summarized by Study Day and time point for all subjects in the PK Population. Plasma concentrations of repaglinide and 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 repaglinide PK parameters will be listed and summarized by treatment for all subjects in the PK Population. Plasma LOXO-292 PK parameters will be listed and summarized by Study Day for all subjects in the PK Population. PK parameters will be reported to 3 significant figures for individual parameters, with the exception of Tmax and t½, 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 repaglinide and 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/Geom Mean in one more level of precision than minimum/maximum,
- SD/SEM in one more level of precision than mean/median/Geom Mean,
- n will be presented as an integer, and
- CV%/ Geom CV% will be presented to the nearest tenth.

6.7 Statistical Analysis of PK

6.7.1 Analysis of Variance of PK Parameters

PK parameters (AUC0-t, AUC0-inf, and Cmax) of repaglinide will be natural log (ln)-transformed and analyzed by an analysis of variance (ANOVA) to evaluate the effects of multiple-dose administration of LOXO-292 on repaglinide (Treatment B Versus Treatment A) using PROC MIXED in SAS®. The ANOVA model will include treatment as a fixed-effect and subject as a random-effect. The Kenward and

Roger adjustment will be used to calculate the denominator degrees of freedom for the fixed-effects (DDFM=KR). Each ANOVA will include calculation of least-squares means (LSMs), the difference between treatment LSMs, the standard error and 90% confidence intervals (CIs) associated with this difference. The ANOVA analysis will be performed using the following SAS® code:

CCI



Ratios of LSMs and associated 90% CIs of ratios will be calculated by exponentiation of the difference between two treatment LSMs and the corresponding CIs from the ANOVA analyses on the ln-transformed repaglinide AUC0-t, AUC0-inf, and Cmax when repaglinide is coadministered with LOXO-292 (Treatment B) versus when administered alone (Treatment A). These ratios and CIs will be expressed as a percentage relative to the reference treatment (Treatment A). Geometric LSMs, GMRs, and 90% CIs will be presented.

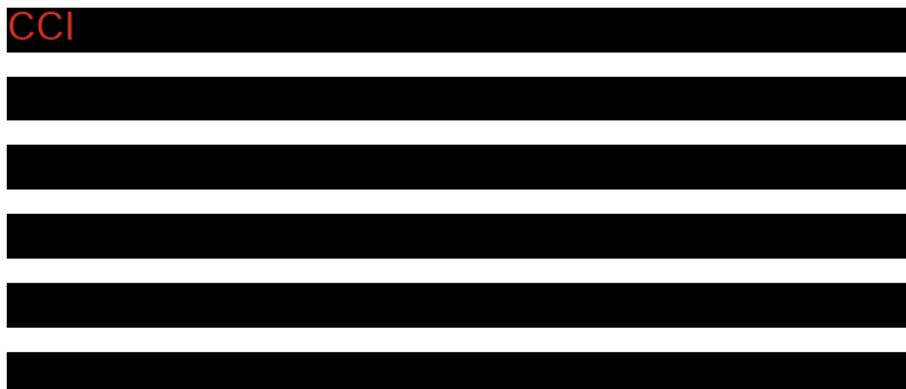
6.7.2 Steady-State Analysis of LOXO-292

A steady-state analysis will be performed on the ln-transformed Ctrough concentrations for LOXO-292, on Days CCI

using Helmert contrasts. Additional Ctrough concentrations CCI may be used, if warranted, for the steady-state analysis to gather more information on steady-state attainment.

Helmert contrasts are constructed such that each time point is compared to the mean of the subsequent time points. Steady state will be concluded at the time point where no more statistical difference (alpha=5%) can be observed. The contrasts will be:

CCI



CCI



The steady-state analysis will be conducted using PROC MIXED of SAS®. The following SAS® code will be used.

CCI



The variance-covariance matrices &TYPE: UN, CS, CSH, AR(1), VC, ARH(1), ARMA(1,1) will be tried. The one with the smallest AICC will be chosen.

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, 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. 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 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 at Period 1. Frequency counts will be provided for categorical variables (race, ethnicity, and sex) for overall. A by-subject listing will also be provided.

7.3 Adverse Events

All AEs occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 21.1.

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. Therefore, some AEs are listed within the CTCAE with fewer than 5 options for grade selection.

The following clinical descriptions of severity for each AE are based on the following general guideline [[CTCAE Nov2017](#)]:

Table 7.3: Adverse Event Severity 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 activities of daily living (ADL)*.

Grade	Description
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 Repaglinide.

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. 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. For an AE with multiple changes in severity, a new record with severity less or equal to its maximum severity will not be considered as a new event in the summary tables.

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. Treatment B will be divided into two segments as B1 (Multiple doses of 160 mg LOXO-292 BID from Day 1 to Day 9) and B2 (Multiple doses of 160 mg LOXO-292 BID on Day 10 with a single dose of 0.5 mg repaglinide coadministered on the morning of Day 10) (see [Table 5.1](#)). Tables will also be presented by severity grade and relationship to study drugs. If a subject experienced the same TEAE at 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 at 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

Period	Period Day
Screen	Screening*
1	Day -1 (check-in)*
2	Day 1**
2	Day 3***
2	Day 6**
2	Day 10**
2	Day 11***

* performed following a fast of at least 12 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.

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. Change from baseline in Treatment B (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 urinalysis tests, the categories are normal and outside normal.

Baseline is Day -1 of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2), and is the last non-missing predose measurement prior to dosing of LOXO-292, including rechecks and unscheduled assessments.

7.5 **Blood Glucose Monitoring**

Blood glucose monitoring will be performed at the following time points:

Table 7.5 Glucose Monitoring Time Points

Period	Period Day	Study Hour
1	Day 1	0*
1	Day 1	1
1	Day 1	2
1	Day 1	4
1	Day 1	6
1	Day 1	9
2	Day 10	0*
2	Day 10	0.5
2	Day 10	1
2	Day 10	1.5
2	Day 10	2
2	Day 10	3
2	Day 10	4
2	Day 10	6
2	Day 10	9
* performed prior dosing		

Descriptive statistics will be reported for blood glucose determinations and change from baseline by treatment and time point. Baseline is Day 1 predose of Treatment A (Period 1) and Day 10 predose of Treatment B (Period 2) and is the last non-missing predose measurement prior to dosing of repaglinide including rechecks and unscheduled assessments. Postdose rechecks, unscheduled assessments, and ET results will not be used for calculation of descriptive statistics. All blood glucose results will be listed by subject.

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

Vital signs will be performed at the following time points:

Table 7.6 Vital Signs Time Points

Period	Period Day	Study Hour	Assessment
Screen	Screening		HR, BP, RR, T
1	Day -1	Check-in*	HR, BP, RR
1	Day 1	0**	HR, BP, RR, T
1	Day 1	0.75	HR, BP, RR
1	Day 1	2	HR, BP, RR
1	Day 1	4	HR, BP, RR
2	Day 1	0**	HR, BP, RR

Period	Period Day	Study Hour	Assessment
2	Day 1	0.75	HR, BP, RR
2	Day 1	2	HR, BP, RR
2	Day 1	4	HR, BP, RR
2	Day 2	0**	HR, BP, RR
2	Day 3	0**	HR, BP, RR
2	Day 4	0**	HR, BP, RR
2	Day 5	0**	HR, BP, RR
2	Day 6	0**	HR, BP, RR
2	Day 7	0**	HR, BP, RR
2	Day 8	0**	HR, BP, RR
2	Day 9	0**	HR, BP, RR
2	Day 10	0**	HR, BP, RR
2	Day 10	0.75	HR, BP, RR
2	Day 10	2	HR, BP, RR
2	Day 10	4	HR, BP, RR
2	Day 11	24***	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. Baseline is Day 1 predose of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2) and is the last non-missing predose measurement prior to dosing of repaglinide (Treatment A) or LOXO-292 (Treatment B), including rechecks and unscheduled assessments. Postdose rechecks, unscheduled assessments, and ET results will not be used for calculation of descriptive statistics. All vital signs results will be listed by subject.

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

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

Table 7.7: ECG Time Points

Period	Period Day	Study Hour
Screen	Screening	
1	Day -1	Check-in*
1	Day 1	0**
1	Day 1	2
2	Day 1	0**
2	Day 1	2

Period	Period Day	Study Hour
2	Day 2	0**
2	Day 3	0**
2	Day 4	0**
2	Day 5	0**
2	Day 6	0**
2	Day 7	0**
2	Day 8	0**
2	Day 9	0**
2	Day 10	0**
2	Day 10	2
2	Day 11	24***

* 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. Baseline is Day 1 predose of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2) and is the last non-missing predose measurement prior to dosing of repaglinide (Treatment A) or LOXO-292 (Treatment B), including rechecks and unscheduled assessments. Postdose rechecks, unscheduled assessments, 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 with QTcF > 450 msec and change from baseline > 30 msec flagged.

7.8 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary, Version 01-Sep-2018 and listed.

7.9 Physical Examination

A full physical examination will be performed at screening. An abbreviated physical examination will be performed at check-in for Period 1, and Day 1 predose of Period 2. 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 Harmonization (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 (Safety Population)

Section 11:

Table 11-1 Demographic Summary (Safety Population)

Table 11-2 Summary of Plasma Repaglinide Pharmacokinetic Parameters Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)

Table 11-3 Summary of Statistical Comparisons of Plasma Repaglinide Pharmacokinetic Parameters Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) Versus Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) (Pharmacokinetic Population)

Table 11-4 Summary of Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Day 1) and Multiple Twice Daily Doses of 160 mg LOXO-292 Coadministered with a Single Dose of 0.5 mg Repaglinide (Day 10) (Treatment B) (Pharmacokinetic Population)

Table 11-5 Steady-State Assessment of Plasma LOXO-292 Ctroughs on Days █ (Pharmacokinetic Population)

Figure 11-1 Arithmetic Mean Plasma Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)

Figure 11-2 Arithmetic Mean Plasma LOXO-292 Concentration-Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292

Alone (Day 1) and Multiple Twice Daily Doses of 160 mg LOXO-292
Coadministered with a Single Dose of 0.5 mg Repaglinide (Day 10)
(Treatment B) (Pharmacokinetic Population)

Figure 11-3 Arithmetic Mean Plasma LOXO-292 Trough Concentrations
Following Administration of Multiple Twice Daily Doses of 160 mg
LOXO-292 on Days CCI (Treatment B) (Linear
Scale) (Pharmacokinetic Population)

Section 12:

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

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 (Safety Population)
- Table 14.1.1.2 Disposition of Subjects (Safety Population)
- Table 14.1.1.3 Demographic Summary (Safety Population)

14.2 Pharmacokinetic Data Summary Tables and Figures

14.2.1 Repaglinide

14.2.1.1 Plasma Repaglinide Tables

- Table 14.2.1.1.1 Plasma Repaglinide Concentrations (ng/mL) Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) (Pharmacokinetic Population)
- Table 14.2.1.1.2 Plasma Repaglinide Concentrations (ng/mL) Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)
- Table 14.2.1.1.3 Plasma Repaglinide Pharmacokinetic Parameters Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) (Pharmacokinetic Population)

Table 14.2.1.1.4 Plasma Repaglinide Pharmacokinetic Parameters Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)

Table 14.2.1.1.5 Intervals (Hours) Used for Determination of Plasma Repaglinide Kel Values Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)

Table 14.2.1.1.6 Statistical Comparisons of Plasma Repaglinide Pharmacokinetic Parameters Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) Versus Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) (Pharmacokinetic Population)

14.2.1.2 Plasma Repaglinide Figures

Figure 14.2.1.2.1 Mean (SD) Plasma Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.1.2.2 Mean Plasma Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.1.2.3 Mean Plasma Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Semi-Log Scale) (Pharmacokinetic Population)

14.2.2 LOXO-292

14.2.2.1 Plasma LOXO-292 Tables

Table 14.2.2.1.1 Plasma LOXO-292 Concentrations (ng/mL) Following Administration of a Single Dose of 160 mg LOXO-292 on Day 1 (Treatment B) (Pharmacokinetic Population)

Table 14.2.2.1.2 Plasma LOXO-292 Trough Concentrations (ng/mL) Following Administration of Multiple Twice Daily Doses of 160 mg LOXO-292 on CCI [REDACTED] (Treatment B) (Pharmacokinetic Population)

Table 14.2.2.1.3 Plasma LOXO-292 Concentrations (ng/mL) Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 on Day 10 (Treatment B) (Pharmacokinetic Population)

Table 14.2.2.1.4 Plasma LOXO-292 Pharmacokinetic Parameters Following Administration of a Single Dose of 160 mg LOXO-292 on Day 1 (Treatment B) (Pharmacokinetic Population)

Table 14.2.2.1.5 Plasma LOXO-292 Pharmacokinetic Parameters Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 on Day 10 (Treatment B) (Pharmacokinetic Population)

Table 14.2.2.1.6 Steady-State Assessment of Plasma LOXO-292 Ctroughs on Days 1 Through 9 (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 (Day 1) and Multiple Twice Daily Doses of 160 mg LOXO-292 Coadministered with a Single Dose of 0.5 mg Repaglinide (Day 10) (Treatment B) (Linear Scale) (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 (Day 1) and Multiple Twice Daily Doses of 160 mg LOXO-292 Coadministered with a Single Dose of 0.5 mg Repaglinide (Day 10) (Treatment B) (Linear Scale) (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 (Day 1) and Multiple Twice Daily Doses of 160 mg LOXO-292 Coadministered with a Single Dose of 0.5 mg Repaglinide (Day 10) (Treatment B) (Semi-Log Scale) (Pharmacokinetic Population)

Figure 14.2.2.2.4 Mean (SD) Plasma LOXO-292 Trough Concentrations Following Administration of Multiple Twice Daily Doses of 160 mg LOXO-292 on Days CCI [REDACTED] (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.2.2.5 Mean Plasma LOXO-292 Trough Concentration Following Administration of Multiple Twice Daily Doses of 160 mg

LOXO-292 on Days **CCI** (Treatment B) (Linear Scale) (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) (Safety Population)

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by
Treatment, Severity Grade, and Relationship to Study Drugs
- Number of Subjects Reporting Events (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Population)

<If no serious adverse event occurred, a statement ‘There was no serious
adverse event recorded during the study.’ 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 (Safety Population)

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology
and Coagulation

Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis

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

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

Table 14.3.5.3 Clinical Laboratory Summary and Change from Baseline –
Hematology and Coagulation (Safety Population)

Table 14.3.5.4 Clinical Laboratory Shift from Baseline – Hematology and
Coagulation (Safety Population)

Table 14.3.5.5 Clinical Laboratory Summary and Change from Baseline –
Urinalysis (Safety Population)

- Table 14.3.5.6 Clinical Laboratory Shift from Baseline – Urinalysis (Safety Population)
- Table 14.3.5.7 Fingerstick Blood Glucose Summary and Change from Baseline (Safety Population)
- Table 14.3.5.8 Vital Sign Summary and Change from Baseline (Safety Population)
- Table 14.3.5.9 12-Lead Electrocardiogram Summary and Change from Baseline (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 (Safety Population)

16.2.2. Protocol Deviations

Appendix 16.2.2 Protocol Deviations

Note: Protocol deviations will be provided by the clinical study manager as Microsoft Excel file and read into the SDTM to generate the data listing.

16.2.3. Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3 Subjects Excluded from Pharmacokinetic Analysis

Note: Appendix 16.2.3 is generated in MS Word for inclusion in the CSR.

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Safety Population)

- Appendix 16.2.4.2 Updated Informed Consent (Safety Population)
- Appendix 16.2.4.3 Physical Examination (Safety Population)
- Appendix 16.2.4.4 Medical and Surgical History (Safety Population)
- Appendix 16.2.4.5 Nicotine Use (Safety Population)

16.2.5. Compliance and Drug Concentration Data

- Appendix 16.2.5.1.1 Inclusion Criteria
- Appendix 16.2.5.1.2 Exclusion Criteria
- Appendix 16.2.5.2 Subject Eligibility (Safety Population)
- Appendix 16.2.5.3.1 Check-in and Return Criteria
- Appendix 16.2.5.3.2 Check-in and Return Responses (Safety Population)
- Appendix 16.2.5.4.1 Test Compound Description
- Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)
- Appendix 16.2.5.4.3 Glucose Administration Times (Safety Population)
- Appendix 16.2.5.5 PK Blood Draw Times (Safety Population)
- Appendix 16.2.5.6 Meal Times (Safety Population)
- Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic Response Data

- Appendix 16.2.6.1 Individual Plasma Repaglinide Concentration Versus Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) for Subject X (Linear and Semi-Log Scales)
- Appendix 16.2.6.2 Individual Plasma LOXO-292 Concentration Versus Time Profiles Following Administration of a Single Dose of 160 mg LOXO-292 Alone (Day 1) and Multiple Twice Daily Doses of 160 mg LOXO-292 Coadministered with a Single Dose of 0.5 mg Repaglinide (Day 10) (Treatment B) for Subject X (Linear and Semi-Log Scale)
- Appendix 16.2.6.3 Individual Plasma LOXO-292 Ctroughs Versus Ctrough Day Following Administration of Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) for Subject X

16.2.7 Adverse Events Listings

- Appendix 16.2.7.1 Adverse Events (I of II) (Safety Population)
- Appendix 16.2.7.2 Adverse Events (II of II) (Safety Population)
- Appendix 16.2.7.3 Adverse Event Non-Drug Therapy (Safety Population)
- Appendix 16.2.7.4 Adverse Event Preferred Term Classification (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

- Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)
- Appendix 16.2.8.1.2 Clinical Laboratory Report - Hematology and Coagulation (Safety Population)
- Appendix 16.2.8.1.3 Clinical Laboratory Report - Urinalysis (Safety Population)
- Appendix 16.2.8.1.4 Clinical Laboratory Report - Urine Drug Screening (Safety Population)
- Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Safety Population)
- Appendix 16.2.8.2 Fingerstick Blood Glucose Monitoring (Safety Population)
- Appendix 16.2.8.3 Vital Signs (Safety Population)
- Appendix 16.2.8.4 12-Lead Electrocardiogram (Safety Population)
- Appendix 16.2.8.5 Phone Call (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 size font 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 (Safety Population)

Disposition	Treatment		Overall
	A	B	
Enrolled	XX (100%)	XX (100%)	XX (100%)
Completed Study	XX (XX%)	XX (XX%)	XX (XX%)
Discontinued Early	XX (XX%)	XX (XX%)	XX (XX%)
<Reason1>	XX (XX%)	XX (XX%)	XX (XX%)
<Reason2>	XX (XX%)	XX (XX%)	XX (XX%)

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

Source: Table 14.1.1.1
Program: /CAXXXXX/sas_prg/stsas/intext/t_disp.sas DDMMYY YYYY HH:MM

Table 11-1 Demographic Summary (Safety Population)

Trait		Study Overall
Sex	Male	XX (XX%)
	Female	XX (XX%)
Race	Asian	XX (XX%)
	Black or African American	XX (XX%)
	White	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)
	Not Hispanic or Latino	XX (XX%)
Age* (yr)	n	XX
	Mean	XX.XX
	SD	XX.XXX
	Minimum	XX.XX
Height (cm)	Median	XX.X
	Maximum	XX.XX
	n	XX
	Mean	XXX.X
	SD	X.XX
	Minimum	XXX
	Median	XXX.X
	Maximum	XXX
* 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/m²) 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 Repaglinide Pharmacokinetic Parameters Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)

Pharmacokinetic Parameters	Treatment A	Treatment B
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]

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

AUC and Cmax values are presented as geometric mean (geometric CV%).
Tmax values are presented as median (min, max).
Other parameters are presented as arithmetic mean (\pm 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:
 - Table 11-2 (Repaglinide): AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, t_{1/2}, CL/F, and Vz/F
 - Table 11-4 (LOXO-292): 2 columns for Treatment B will be presented: SD LOXO-292 Alone and MD LOXO-292 Coadministered with Repaglinide
 - SD LOXO-292 Alone: AUC0-12, AUC0-t, Cmax, Tmax
 - MD LOXO-292 Coadministered with Repaglinide: AU_{Ctau}, Cmax,ss, Tmax,ss, and CL,ss/F
- n will be presented as an integer (with no decimal);
- Summary statistics will be presented with same precision as defined in post-text shells

Program: /CAXXXX/sas_prg/pksas/intext-pk-tables.sas
Program: /CAXXXX/sas_prg/pksas/adam_intext_pkparam.sas

DDMMYYYY HH:MM
DDMMYYYY HH:MM

In-text Table 11-3 will be in the following format:

Table 11-3 Summary of Statistical Comparisons of Plasma Repaglinide Pharmacokinetic Parameters Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) Versus Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) (Pharmacokinetic Population)

Parameter	Treatment B (Test)		Treatment A (Reference)		GMR (%)	90% Confidence Interval	Intra-subject CV%
	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

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
 Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10
 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: AUC0-t, AUC0-inf, and Cmax
- n will be presented as an integer (with no decimal);
- All statistics will be presented with same precision as defined in post-text shells

Program: /CAXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMYYYY HH:MM
 Program: /CAXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMYYYY HH:MM

In-text Table 11-5 will be in the following format:

Table 11-5 Steady-State Assessment of Plasma LOXO-292 Ctroughs on Days 1 Through 9 (Pharmacokinetic Population)

Treatment	Ctrough Day	Geometric LSM	p-value	Ratio
Treatment B	DAY X	X.XXX	X.XXXX	X.XXXX
	DAY X	X.XXX	X.XXXX	X.XXXX
	DAY X	X.XXX	X.XXXX	X.XXXX

Ctroughs were ln-transformed prior to analysis.

Geometric least-squares means (LSMs) were obtained by taking exponential of the LSMs from ANOVA.

P-value corresponds to the Helmert contrast, i.e., the comparison of that day versus the average of the remaining days.

Source: Table 14.2.2.1.6

Notes for Generating the Actual Table:

Presentation of Data:

- Geometric LSM will be presented to precision as in the bioanalytical data +1 decimal place precision
- p-value will be presented to 4 decimals
- Ratio will be presented to 4 decimals
- Add footnotes:
 - Ctrough Day refers to the LOXO-292 dosing day that the postdose trough samples were taken (corresponding to predose samples collected on Days 2 through 10)
 - Ratio is calculated by exponentiating the difference of each Ctrough day minus the mean of subsequent Ctrough days

Please use CPSS1 internal template

Program: DM_PX:[HLXXXXX.PKSAS]STEADYSTATE-HELMERT.SAS
XXAPRXXXX HH:MM

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

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

* Adverse events are coded using MedDRA® Version 21.1 by System Organ Class and Preferred Term.
 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: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
 Treatment B1: Multiple doses of 160 mg LOXO-292 BID from Day CCI
 Treatment B2: Multiple doses of 160 mg LOXO-292 BID on Day 10 with a single dose of 0.5 mg repaglinide coadministered on the morning of Day 10

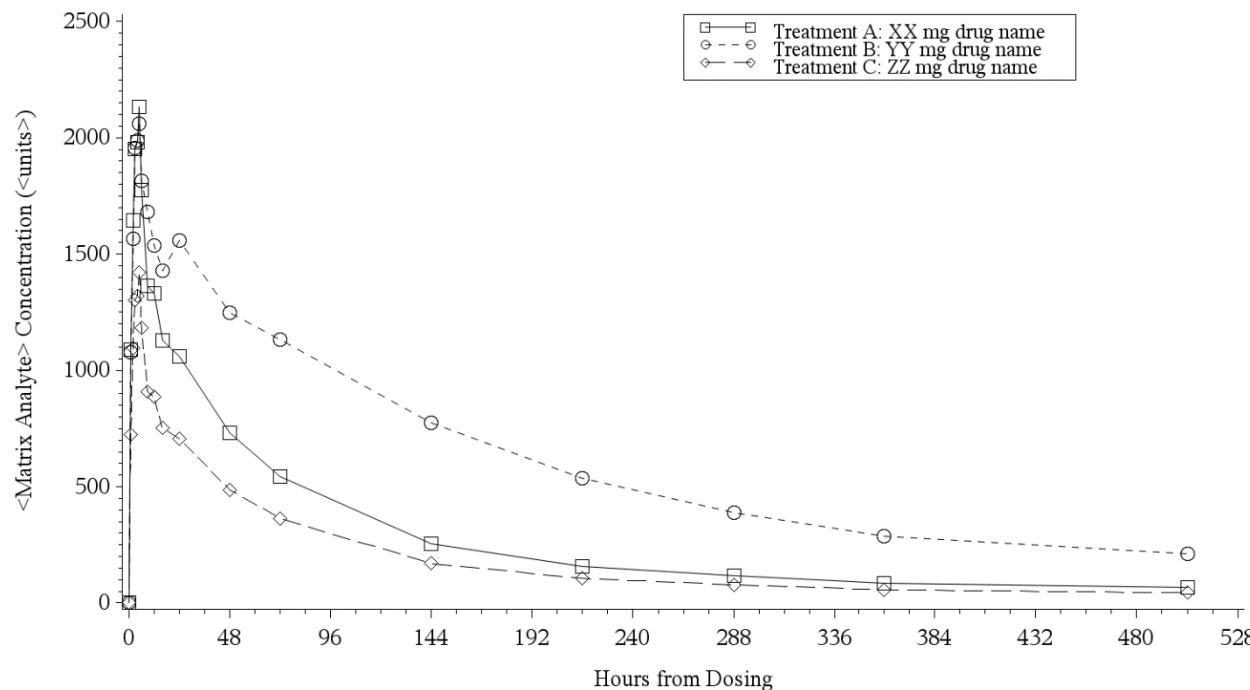
Source: Table 14.3.1.1
 Program: /CAXXXXX/sas_prg/stsas/intexttest/t ae.sas DDMMYY YYYY HH:MM

Programmer Note: Sort by decreasing frequency of system organ class and by preferred term within a system organ class of Overall column.

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 Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population)



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

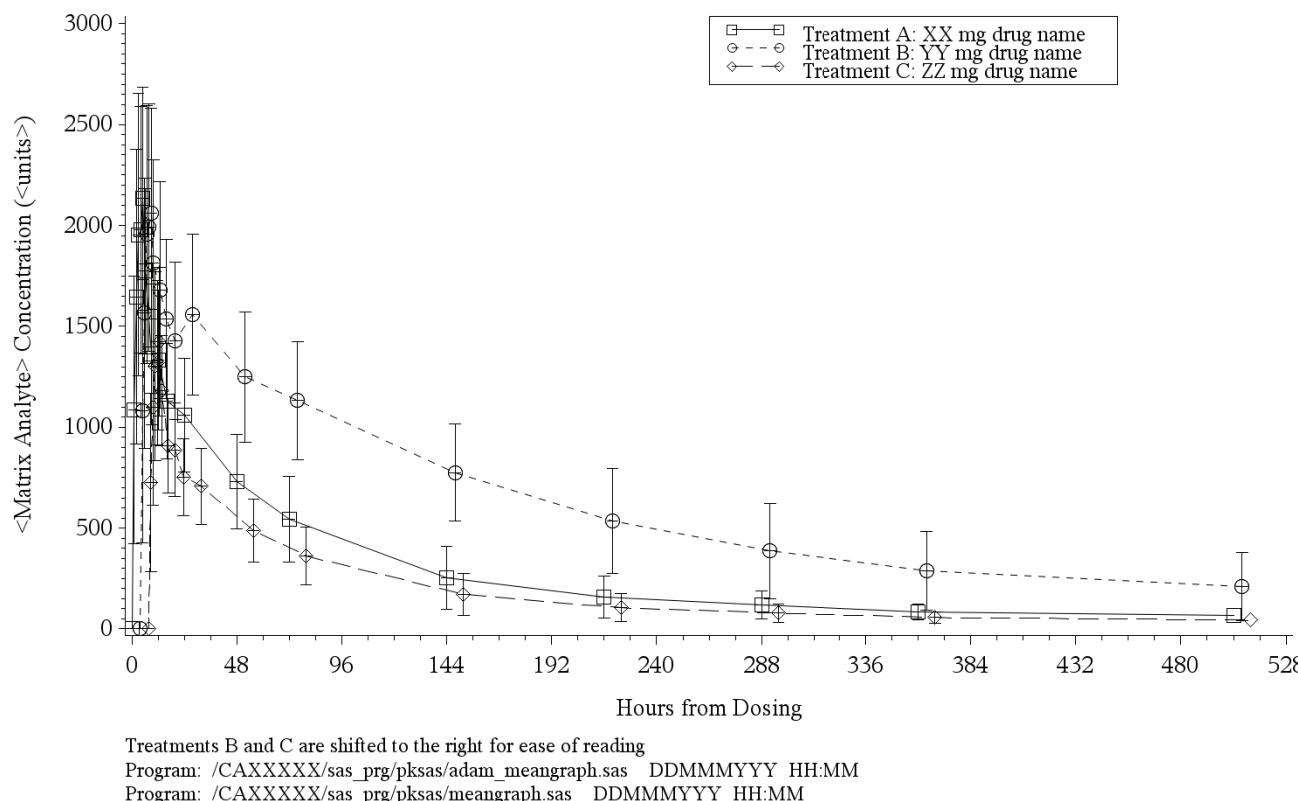
Notes for Generating the Actual Mean Figure:

- Figures 11-1 and 14.2.1.2.2:
 - Legend will be:
 - Treatment A: 0.5 mg Repaglinide Alone
 - Treatment B: 0.5 mg Repaglinide + Multiple BID 160 mg LOXO-292
 - Y-axis label will be “Plasma Repaglinide Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from Repaglinide Dose”
 - Add in footnote: LLOQ value for repaglinide is 0.02 ng/mL
- Figures 11-2 and 14.2.2.2.2:
 - Legend will be:
 - 160 mg LOXO-292 on Day 1
 - Multiple BID Doses of 160 mg LOXO-292 + 0.5 mg Repaglinide on Day 10
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from LOXO-292 Morning Dose”
 - Add in footnote: LLOQ value for LOXO-292 is 1.00 ng/mL.
- Figure 11-3 and Figure 14.2.2.2.5:
 - Legend will be:
 - Multiple BID Doses of 160 mg LOXO-292
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “LOXO-292 Ctrough Day”
 - Add footnote: Ctrough Days 1 through 9 are the predose samples on dosing Days 2 through 10.

Program: /CAXXXX/sas_prg/pksas/meangraph.sas DDMMYYYY HH:MM
Program: /CAXXXX/sas_prg/pksas/adam_meangraph.sas DDMMYYYY 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 Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Linear Scale) (Pharmacokinetic Population)



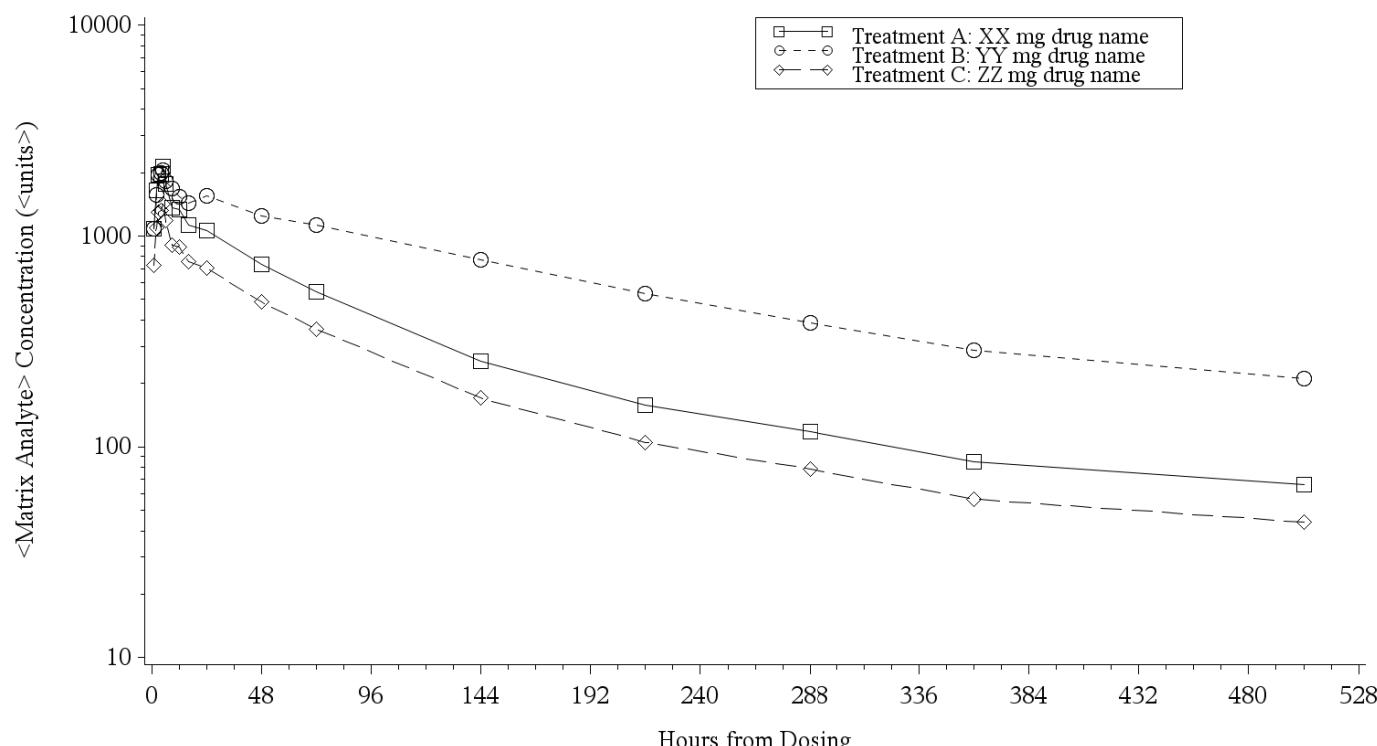
Notes for Generating the Actual Mean Figure:

- Figure 14.2.1.2.1:
 - Legend will be:
 - Treatment A: 0.5 mg Repaglinide Alone
 - Treatment B: 0.5 mg Repaglinide + Multiple BID 160 mg LOXO-292
 - Y-axis label will be “Plasma Repaglinide Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from Repaglinide Dose”
 - Add in footnote: LLOQ value for repaglinide is 0.02 ng/mL.
- Figure 14.2.2.2.1:
 - Legend will be:
 - 160 mg LOXO-292 on Day 1
 - Multiple BID Doses of 160 mg LOXO-292 + 0.5 mg Repaglinide on Day 10
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from LOXO-292 Morning Dose”
 - Add in footnote: LLOQ value for LOXO-292 is 1.00 ng/mL.
- Figure 14.2.2.2.4:
 - Legend will be:
 - Multiple BID Doses of 160 mg LOXO-292
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “LOXO-292 Ctrough Day”
 - Add footnote: Ctrough Days 1 through 9 are the predose samples on dosing Days 2 through 10.

Program: /CAXXXX/sas_prg/pksas/meangraph.sas DDMMYYYY HH:MM
Program: /CAXXXX/sas_prg/pksas/adam_meangraph.sas DDMMYYYY HH:MM

Figures 14.2.1.2.3 and 14.2.2.2.3 will be in the following format:

Figure 14.2.1.2.3 Mean Plasma Repaglinide Concentration-Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Semi-Log Scale) (Pharmacokinetic Population)



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

Notes for Generating the Actual Mean Figure:

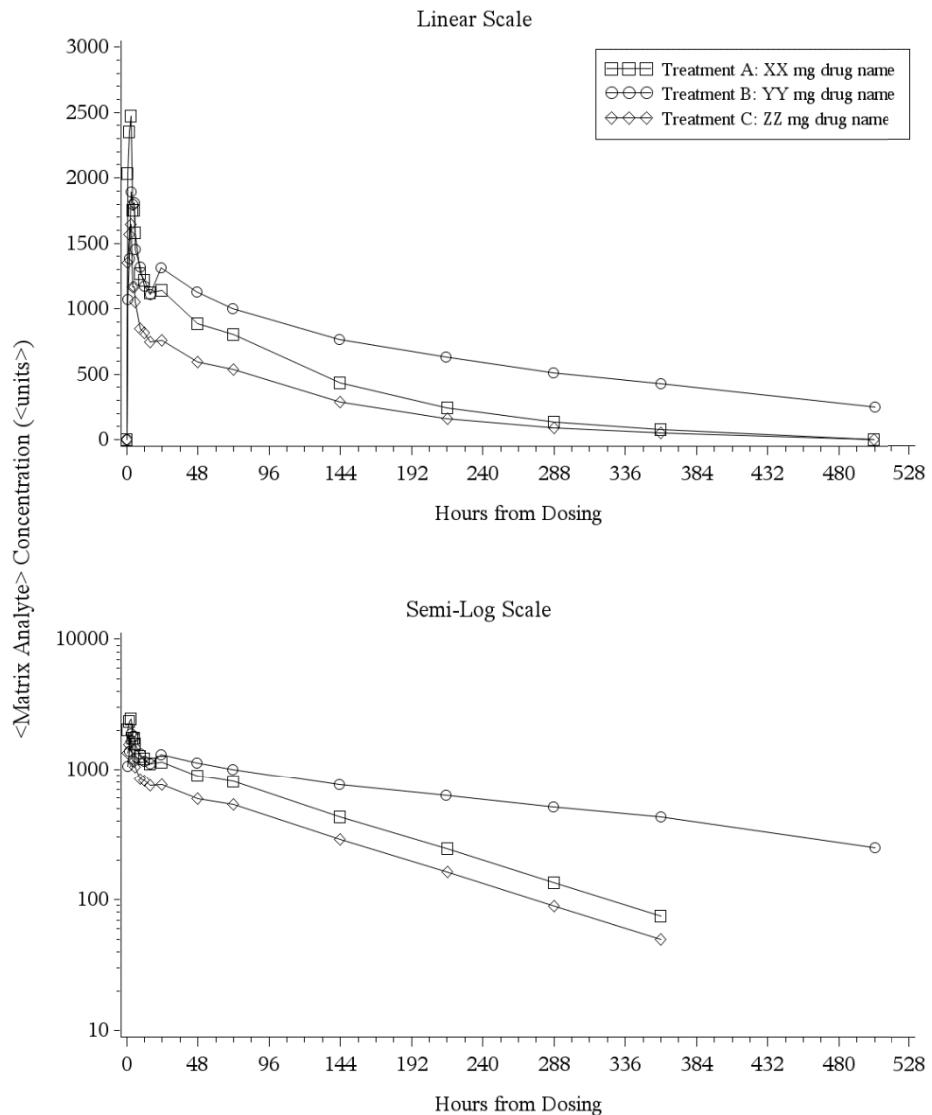
- Figure 14.2.1.2.3:
 - Legend will be:
 - Treatment A: 0.5 mg Repaglinide Alone
 - Treatment B: 0.5 mg Repaglinide + Multiple BID 160 mg LOXO-292
 - Y-axis label will be “Plasma Repaglinide Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from Repaglinide Dose”
 - Add in footnote: LLOQ value for repaglinide is 0.02 ng/mL
- Figure 14.2.2.2.3:
 - Legend will be:
 - 160 mg LOXO-292 on Day 1
 - Multiple BID Doses of 160 mg LOXO-292 + 0.5 mg Repaglinide on Day 10
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from LOXO-292 Morning Dose”
 - Add in footnote: LLOQ value for LOXO-292 is 1.00 ng/mL.

Program: /CAXXXX/sas_prg/pksas/meangraph.sas DDMMYYYY HH:MM
Program: /CAXXXX/sas_prg/pksas/adam_meangraph.sas DDMMYYYY HH:MM

Appendix 16.2.6.1 and 16.2.6.2 will be in the following format:

Appendix 16.2.6.1

Individual Plasma Repaglinide Concentration Versus Time Profiles Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) for Subject X (Linear and Semi-Log Scale)



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

Notes for Generating the Actual Individual Figure:

- Appendix 16.2.6.1:
 - Legend will be:
 - Treatment A: 0.5 mg Repaglinide Alone
 - Treatment B: 0.5 mg Repaglinide + Multiple BID 160 mg LOXO-292
 - Y-axis label will be “Plasma Repaglinide Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from Repaglinide Dose”
 - Add in footnote: LLOQ value for repaglinide is 0.02 ng/mL
- Appendix 16.2.6.2:
 - Legend will be:
 - 160 mg LOXO-292 on Day 1
 - Multiple BID Doses of 160 mg LOXO-292 + 0.5 mg Repaglinide on Day 10
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “Hours Postdose (hr) from LOXO-292 Morning Dose”
 - Add in footnote: LLOQ value for LOXO-292 is 1.00 ng/mL.
- Appendix 16.2.6.3:
 - Legend will be:
 - Multiple BID Doses of 160 mg LOXO-292
 - Y-axis label will be “Plasma LOXO-292 Concentration (ng/mL)”
 - X-axis label will be “LOXO-292 Ctrough Day”
 - Add footnote: Ctrough Days 1 through 9 are the predose samples on dosing Days 2 through 10.

Program: /CAXXXX/sas_prg/pksas/indgraph-all.sas
Program: /CAXXXX/sas_prg/pksas/adam_indgraph.sas

DDMMYYYY HH:MM
DDMMYYYY HH:MM

10.3 Post-text Table Shells

Table 14.1.1.1 Summary of Disposition (Safety Population)

Page X of X

Disposition	Treatment		
	A	B	Overall
Enrolled	XX	XX	XX
Completed	XX	XX	XX
Discontinued Early	XX	XX	XX
Reason 1	XX	XX	XX
Reason 2	XX	XX	XX
Reason 3	XX	XX	XX
etc.			

Note: Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide (coadministered on the morning of Day 10)

Program: /CAXXXX/sas_prg/stsas/tbl_PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.1.1.2 Disposition of Subjects (Safety Population)

Subject Number	Treatment Sequence	Dosed Period		Completed Period		Study Completion	
		1	2	1	2	Status	Date
XXX-XXX	AB	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
XXX-XXX	AB	Yes	Yes	Yes	No	Terminated Study Prematurely	DDMMYYYY

Note: Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide (coadministered on the morning of Day 10)

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.1.1.3 Demographic Summary (Safety Population)

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

Programmer Note: Also include weight (kg) and BMI (kg/m²)

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

BMI = Body mass index

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

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

Table 14.2.1.1.1 Plasma Repaglinide Concentrations (ng/mL) Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A)
(Pharmacokinetic Population)

Subject Number	Treatment Sequence	Study Period	Predose	Sample Times (hr)								-
				XX	XX	XX	XX	XX	XX	XX	XX	
XXX-XXX	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX	XX
XXX-XXX	XXX	X	BLQ	XX	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							
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:

- Present the subject number in the following format: XXX-XXX
- Concentrations will be presented to same precision as in the bioanalytical data.
- Summary statistics presentation with respect to the precision of the bioanalytical 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:
 - Tables 14.2.1.1.1 and 14.2.1.1.2: CCI
 - Table 14.2.2.1.1: CCI
 - Table 14.2.2.1.2: CCI
 - Table 14.2.2.1.3: CCI

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

1. Please remove the “Treatment Sequence” column

Program: /CAXXXX/sas_prg/pksas/pk-conc-tables.sas	DDMMYYYY HH:MM
Program: /CAXXXX/sas_prg/pksas/pk-conc-tables-sig.sas	DDMMYYYY HH:MM
Program: /CAXXXX/sas_prg/pksas/adam_conc.sas	DDMMYYYY HH:MM

Tables 14.2.1.1.3, 14.2.1.1.4, and 14.2.2.1.4 and 14.2.2.1.5 will be in the following format:

Table 14.2.1.1.3 Plasma Repaglinide Pharmacokinetic Parameters Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A)
 (Pharmacokinetic Population)

Subject Number	Treatment Sequence	Study Period	Parameters					
			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	XX.X	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:

- Present the subject number in the following format: XXX-XXX
- The following PK parameters will be presented in the following order:
 - Table 14.2.1.1.3 and 14.2.1.1.4: AUC0-t, AUC0-inf, AUC%extrap, Cmax, Tmax, Kel, t½, CL/F, and Vz/F
 - Table 14.2.2.1.4: AUC0-12, AUC0-t, Cmax, Tmax
 - Table 14.2.2.1.5: AUCtau, Cmax,ss, Tmax,ss, and CL,ss/F
- n will be presented as an integer (with no decimal);
- Parameter values for exposure-based parameters (i.e. AUCs, AUC%extrap, Cmax, CL/F, and Vz/F) will be presented with, at maximum, the precision of the bioanalytical data, and, at minimum, 3 significant figures (to be determined by the PKist once the bioanalytical 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 with respect to the number of significant figures.
- 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 with respect to the number of decimals.
- 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 with respect to the number of significant figures.
- CV% and Geom CV% for all parameters will be presented with 1 decimal
- Remove 'Treatment Sequence'

Program: /CAXXXX/sas_prg/pksas/pk-tables.sas
Program: /CAXXXX/sas_prg/pksas/adam_pkparam.sas

DDMMYYYY HH:MM
DDMMYYYY HH:MM

Table 14.2.1.1.5 will be in the following format:

Table 14.2.1.1.5 Intervals (Hours) Used for Determination of Plasma Repaglinide Kel Values Following Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) and Coadministered with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) (Pharmacokinetic Population) (Pharmacokinetic Population)

Subject Number	Treatment Sequence	Treatment A			Treatment B		
		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
XXX-XXX	XX	XX.X - XX.X	X.XXX	X	XX.X - XX.X	X.XXX	X

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

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:

- Present the subject number in the following format: XXX-XXX
- Interval start and stop times will be presented to 1 decimal or 3 significant figures minimum;
- 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. Remove treatment sequence.

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

DDMMYYYY HH:MM
DDMMYYYY HH:MM

Table 14.2.1.1.6 will be in the following format:

Table 14.2.1.1.6 Statistical Comparisons of Plasma Repaglinide Pharmacokinetic Parameters Following Coadministration of a Single Dose of 0.5 mg Repaglinide with Multiple Twice Daily Doses of 160 mg LOXO-292 (Treatment B) Versus Administration of a Single Dose of 0.5 mg Repaglinide Alone (Treatment A) (Pharmacokinetic Population)

Parameter	(unit)	Treatment				Geometric Mean Ratio	90% Confidence Intervals	Intra-subject CV%
		Geometric LSMs		A	n			
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: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

Parameters were ln-transformed prior to analysis.

Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANOVA.

Geometric Mean Ratio (B/A) is calculated by exponentiating the LSM difference (B - A) and multiplying by 100.

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 the same precision as the Mean in the PK parameter table,
- Geometric Mean Ratio, 90% CI and intra-subject CV% will be presented to 2 decimal places,
- PK parameters to be presented are AUC0-t, AUC0-inf, and Cmax

Program: /CAXXXX/sas_prg/pksas/stats-tables-mixed.sas
 Program: /CAXXXX/sas_prg/pksas/adam_statsmixed.sas

DDMMYY YYYY HH:MM
 DDMMYY YYYY HH:MM

Table 14.2.2.1.6 will be presented in the following format:

Table 14.2.2.1.6 Steady-State Assessment of Plasma LOXO-292 Ctroughs on Days 1 Through 9 (Pharmacokinetic Population)

Treatment	Ctrough Day*	Geometric LSM	p-value	Ratio
Treatment B	DAY X	X.XXX	X.XXXX	X.XXXX
	DAY X	X.XXX	X.XXXX	X.XXXX
	DAY X	X.XXX	X.XXXX	X.XXXX
	DAY X	X.XXX	X.XXXX	X.XXXX
	DAY X	X.XXX	X.XXXX	X.XXXX

Ctroughs were ln-transformed prior to analysis.

*Ctrough Day refers to the LOXO-292 dosing day that the postdose trough samples were taken (corresponding to predose samples collected on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10).

Geometric least-squares means (LSMs) were obtained by taking exponential of the LSMs from ANOVA.

P-value corresponds to the Helmert contrast, i.e., the comparison of that day versus the average of the remaining days.

Ratio is calculated by exponentiating the difference of each Ctrough day minus the mean of subsequent Ctrough days.

. = Value not reportable

Notes for Generating the Actual Table:

Presentation of Data:

- Geometric LSM will be presented to the same precision as the bioanalytical data +1 decimal place precision
- p-value will be presented to 4 decimals
- Ratio will be presented to 4 decimals

Programmer Note: Please use Table CPSS1 internal template

Notes for preparation of standard programs (to be deleted after standard programs are updated):

Update standard program name to include CPSS1 shell name

Program: DM_PX:[HLXXXXX.PKSAS]STEADYSTATE-HELMERT.SAS XXAPRXXXX HH:MM

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

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

Note: * Adverse events are classified according to the MedDRA Version 21.1 by System Organ Class and Preferred Term.

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: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B1: Multiple doses of 160 mg LOXO-292 BID from Day 1 to Day 9

Treatment B2: Multiple doses of 160 mg LOXO-292 BID on Day 10 with a single dose of 0.5 mg repaglinide coadministered on the morning of Day 10

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMYY YYYY HH:MM

Programmer Note: Sort by decreasing frequency of system organ class and by preferred term within a system organ class of Overall column. 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". Won't repeat this comment again.

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment, Severity Grade, and Relationship to Study Drugs - Number of Subjects Reporting Events (Safety Population)

TE Adverse Event*	Treatment	Number of Subjects with Adverse Events	Severity Grade					Relationship to LOXO-292		Relationship to Repaglinide	
			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	X
Treatment B1	XX	X	X	X	X	X	X	X	X	X	X
Treatment B2	XX	X	X	X	X	X	X	X	X	X	X
Overall	XX	X	X	X	X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 21.1 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 in 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 A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B1: Multiple doses of 160 mg LOXO-292 BID from Day 1 to Day 9

Treatment B2: Multiple doses of 160 mg LOXO-292 BID on Day 10 with a single dose of 0.5 mg repaglinide coadministered on the morning of Day 10

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Subject Number	Treatment	TE?^	Adverse Event	PT*/ SOC	Onset/Resolution				Severity Grade	Ser*	Outcome	Action for LOXO-292/ Repaglinide	Relationship to LOXO-292/ Repaglinide
					Day	Date	Time	Freq*					
XXX-XXX	X	Yes	XXXXXXX	XXXXXXX/XXXXXXX	XX/XX	DDMMYYYY/DDMMYYYY	XX:XX/XX:XX	Inter.	X	NS	Resolved	XXXXXXXXXX/XXXXXXX	XXXXXXXXXX/XXXXXXX

Note: * Adverse events are classified according to MedDRA Version 21.1 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/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.

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B1: Multiple doses of 160 mg LOXO-292 BID from Day 1 to Day 9

Treatment B2: Multiple doses of 160 mg LOXO-292 BID on Day 10 with a single dose of 0.5 mg repaglinide coadministered on the morning of Day 10

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMYYYY 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."

Tables 14.3.4.2-14.3.4.3 will have the following format.

Page 1 of X

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

Subject Number	Age\$/ Sex	Study Period	Day	Hour	Date	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5
						< Range> (Unit)				
XXX-XXX	XX/M	Screen			DDMMYYYY	XX HN	XX	XX	XX	XX HN
			1	-X	DDMMYYYY	XX	XX	XX	XX	XX
			2	X	DDMMYYYY	XX	XX	XX	XX HN	XX
				0	DDMMYYYY	XX	XX	XX	XX	XX
				X	DDMMYYYY	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 DDMMYYYY HH:MM

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

Subject Number	Age\$/ Sex	Study Period	Day	Hour	Date	Time	Department	Test	Result	Reference Range	Unit
XXX-XXX	XX/X	X	X	X.XX	DDMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	X - X	mg/dL
			X	XX.XX	DDMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	mg/dL
			X	XX.XX	DDMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HY-	mg/dL
			X	XX.XX	DDMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HN	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

Flag starting with "G" is graded according to NCI CTCAE grading.

Program : /CAXXXX/ECR/sas_prg/stsas/tab/PROGRAMNAME.sas DDMMYYYY HH:MM

Tables 14.3.5.1, 14.3.5.3, and 14.3.5.5 will have the following format.

Page 1 of X

Table 14.3.5.1 Clinical Laboratory Summary and Change from Baseline - Serum Chemistry (Safety Population)

Laboratory Test (unit)	Normal Range#	Time Point	Statistic	Treatment		Change From Baseline	
				A	B	A	B
Parameter1 (unit)	XX - XX	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 3	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 6	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 laboratory tests. Also need to add Days 10 and 11 time points of Period 2 (Treatment B). 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 -1 for Treatment A (Period 1) and Day 1 for Treatment B (Period 2)

Baseline is Day 1 predose of Period 2 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: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.5.2, 14.3.5.4, and 14.3.5.6 will have the following format.

Page 1 of X

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

Laboratory Test (units)	Treatment	Time Point	Baseline L			Baseline N			Baseline H		
			Postdose			Postdose			Postdose		
			L	N	H	L	N	H	L	N	H
Testname(unit)	B	Day 3	X	XX	X	X	XX	X	X	XX	X
		Day 6	X	XX	X	X	XX	X	X	XX	X
		Day 9	X	XX	X	X	XX	X	X	XX	X
		Day 11	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 predose of Period 2 and is the last non-missing predose measurement prior to dosing of LOXO-292, including Rechecks and unscheduled assessments.

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

Program: /CAXXXX/sas_prg/stsas/tab_programname.sas DDMMYYYY HH:MM

Table 14.3.5.7 Fingerstick Blood Glucose Summary and Change from Baseline (Safety Population)

Parameter (unit)	Statistic	Treatment A			Treatment B		
		Time Point	Measured Value	Change From Baseline	Time Point	Measured Value	Change From Baseline
Blood Glucose (units)	n	CCI	XX		CCI	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	
	n	CCI	XX	XX	CCI	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
	n	CCI	XX	XX	CCI	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

CCI

Note: Baseline is Day 1 predose of Treatment A (Period 1) and Day 10 predose of Treatment B (Period 2) and is the last non-missing predose measurement prior to dosing of repaglinide, including rechecks and unscheduled assessments.

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.3.5.8 Vital Sign Summary and Change from Baseline (Safety Population)

Vital Sign Parameter (unit)	Statistic	Treatment A			Treatment B		
		Time Point	Measured Value	Change From Baseline	Time Point	Measured Value	Change From Baseline
Parameter1 (unit)	n	Day 1 Predose	XX		Day 1 Hour 0	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	
	n	Day 1 Hour 0.75	XX	XX	Day 1 Hour 0.75	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
	n	Day 1 Hour 2	XX	XX	Day 1 Hour 2	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
	n	Day 1 Hour 4	XX	XX	Day 1 Hour 4	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

CCI

Note: Baseline is Day -1 of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2) and is the last non-missing predose measurement prior to dosing of repaglinide (Treatment A) or LOXO-292 (Treatment B), including rechecks and unscheduled assessments.>

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

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

Table 14.3.5.9 12-Lead Electrocardiogram Summary and Change from Baseline (Safety Population)

ECG Parameter (unit)	Statistic	Treatment A			Treatment B		
		Time Point	Measured Value	Change From Baseline	Time Point	Measured Value	Change From Baseline
Parameter1 (unit)	n	Day Predose	XX		Day 1 Hour 0	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	
	n	Day 1 Hour 2	XX	XX	Day 1 Hour 2	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 2 Hour 0	XX	XX	
					XX.XX	XX.XX	
					X.XXX	X.XXX	
					XX.X	XX.X	
					XX.XX	XX.XX	
					XX.X	XX.X	

CCI

Note: Baseline is Day -1 of Treatment A (Period 1) and Day 1 predose of Treatment B (Period 2) and is the last non-missing predose measurement prior to dosing of Repaglinide (Treatment A) or LOXO-292 (Treatment B), including rechecks and unscheduled assessments.

Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1

Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMYYYY 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

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: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.1 Subject Discontinuation (Safety Population)

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

Note: Treatment A: A single dose of 0.5 mg repaglinide administered at Hour 0 on Day 1
Treatment B: Multiple doses of 160 mg LOXO-292 (2 x 80 mg capsules) administered BID, approximately every 12 hours, for 10 consecutive days with 0.5 mg repaglinide coadministered on the morning of Day 10

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

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
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY
XXX-XXX	DDMMYYYY	XX	AAAAAA	AAAAAAA	AAAAAAAAA	XXX	XX.XX	XX.XX	DDMMYYYY	DDMMYYYY

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.2 Updated Informed Consent (Safety Population)

Subject Number	Date Subject Signed Informed Re-Consent	Informed Re-Consent Version Date	Reason for Re-Consent
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX
XXX-XXX	DDMMYYYY	DDMMYYYY	XXXXXXXXXXXXXX

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.3 Physical Examination (Safety Population)

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

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.4 Medical and Surgical History (Safety Population)

Subject Number	Any History?	Study Period	Category	Body system	Date			Condition or Events
					Start	End	Ongoing?	
XXX-XXX	XXX	Screen	Medical Surgical	XXXXXXXXXXXX	DDMMYYYY DDMMYYYY	DDMMYYYY DDMMYYYY	YES	XXXXXX XXXXX XXXXXXXX
XXX-XXX	XXX	Screen	Medical	XXXXXXXXXXXX	DDMMYYYY	DDMMYYYY	NO	

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.5 Nicotine Use (Safety Population)

Subject Number	Study Period	Substance	Description of Use	Start Date	End Date
XXX-XXX	Screen	XXXXXXXX XXX	XXXXX XXXXXXXX XXXXX	DDMMYYYY	DDMMYYYY

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.1.1 Inclusion Criteria

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

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

Appendix 16.2.5.1.2 Exclusion Criteria

1. Is mentally or 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: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.3.1 Check-in Criteria

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: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3.2 Check-in Responses (Safety Population)

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

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.4.1 Test Compound Description

Compound	Form	Route
XXXXXXXXXXXXXX	< >	XXXX
XXXXXXXXXXXXXX	< >	XXXX

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

Appendix 16.2.5.4.2 and 16.2.5.4.3 will be in the following format:

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Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)

Subject Number	Study Period	Treatment	Day	Hour	Start Date	Start Time	Compound	Dosage	Comments
XXX-XXX	1	X	X	0	DDMMYYYY	HH:MM:SS	XXXXXXXXXX	< >	<Only populate if there are comments present in the data>
	2	X	X	0	DDMMYYYY	HH:MM:SS	XXXXXXXXXX	< >	

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Loxo Oncology, Inc.
LOXO-292, LOXO-RET-18026
Celerion, Clinical Study Report No. CA26434

Appendix 16.2.5.5 will be in the following format:

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Appendix 16.2.5.5 PK Blood Draw Times (Safety Population)

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

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

Program: /CAXXXX/sas_prg/stsas/lis PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.6 Meal Times (Safety Population)

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

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

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

Note: * Concomitant medications are coded with WHO Dictionary Version 01SEP2018.

^ 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.

Treatment A: <description>

Treatment B1: <description>

Treatment B2: <description>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (I of II) (Safety Population)

Subject Number	Treatment	TE?^	Adverse Event/ Preferred Term*	Time from Last Dose (DD:HH:MM)	Onset			Resolved			Duration (DD:HH:MM)
					Day	Date	Time	Day	Date	Time	
XXX-XXX			None								
XXX-XXX	X	Yes	XXXXXXXXXXXXXX/ XXXXXXXXXXXX	XX:XX:XX	XX	DDMMYYYY	X:XX	XX	DDMMYYYY	X:XX	XX:XX:XX
			No	XXXXXXXXXXXXXX/ XXXXXXXXXXXX	XX:XX:XX	XX	DDMMYYYY	X:XX	XX	DDMMYYYY	X:XX

Note: * Adverse events are classified according to MedDRA Version 21.1 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>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Events (II of II) (Safety Population)

Subject Number	Treatment	Adverse Event	Onset			Freq*	Severity Ser*	Outcome	Action for		Other Action Taken	Relationship to		
			Day	Date	Time				LOXO-292	Repaglinide		LOXO-292	Repaglinide	
XXX-XXX		None												
XXX-XXX	X	XXXXXXX XX DDMMYYYY XX:XX				Inter.	Grade 1	NO	Resolved	Dose Not Changed	Dose Not Changed	None	Not Related to LOXO-292	Not Related to Repaglinide

Note: Ser* = Serious; Freq* represents Frequency: SI = Single Episode, Inter. = Intermittent, Cont. = Continuous 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 in the CTCAE with fewer than 5 options for grade selection.
Treatment A: <description>
Treatment B1: <description>
Treatment B2: <description>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

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

Subject Number	Treatment	Adverse Event	Onset			Resolved			Therapy		
			Day	Date	Time	Day	Date	Time	Date	Time	Description
XXX-XXX	X	DRY LIPS	XX	DDMMYYYY	X:XX	XX	DDMMYYYY	X:XX	DDMMYYYY	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>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.4 Adverse Event Preferred Term Classification (Safety Population)

Subject Number	Treatment	Adverse Event	Preferred Term*	Body System	Onset		
					Day	Date	Time
XXX-XXX	X	XXXXXX XXXX XXXX XXXX	XXXXXXXXXXXX XXXXXX	XXXXXXXXXXXXXXXXXXXX	XX	DDMMYYYY	X:XX

Note: * Adverse events are classified to MedDRA Version 21.1 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>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY 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 (Safety Population)

Subject Number	Age\$/ Sex	Study Period	Day	Hour	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)
XXX-XXX	XX/M	Screen			DDMMYYYY	XX HN	XX	XX	XX	XX HN
		1	-X	Check-in	DDMMYYYY	XX	XX	XX	XX	XX
		2	X	0	DDMMYYYY	XX	XX	XX	XX HN	XX
			X	0	DDMMYYYY	XX	XX	XX	XX	XX
			X	0	DDMMYYYY	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: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Safety Population)

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

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.2 Fingerstick Blood Glucose Monitoring (Safety Population)

Subject Number	Study Period	Day	Hour	Date	Time	Blood Glucose Level (mg/dL)	Glucometer (CC-GLUC-#)	Comment
XXX-XXX	X	X	-X.X	DDMMYYYY	HH:MM	XXX.X	XXXXXX	(Only populate if there are comments)

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.3 Vital Signs (Safety Population)

Subject Number	Study Period	Treatment	Day	Hour	Blood Pressure (mmHg)			Pulse (bpm)	Respir- ation (rpm)	Temper- ature (°C)	Oxygen (%)	Weight (kg)	Comments	
					Date	Time	Test	Arm	Sys/Dia					
XXX-XXX	Screen				DDMMYYYY	X:XX:XX								XXX.X
X	X	-X	Check-in		DDMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX	XX	XX.X		XXX.X
					DDMMYYYY	XX:XX:XX								
X	X.X				DDMMYYYY	XX:XX:XX	SUPX	Right	XXX/ XX	XX	XX			XX
	X.X				DDMMYYYY	XX:XX:XX	SUPX	Right						XX
X.X					DDMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX	XX			XX
X.X					DDMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX	XX			XX
X.X					DDMMYYYY	X:XX:XX	SUPX	Right	XXX/ XX	XX	XX			XX
R					DDMMYYYY	XX:XX:XX	SUPX	Right	XXX/ XX	XX	XX			
X.X					DDMMYYYY	XX:XX:XX	SUPX	Right						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: SUPX = X-minute supine, R = Recheck Value, Sys/Dia = Systolic/Diastolic
 Treatment A: <description>
 Treatment B: <description>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.4 12-Lead Electrocardiogram (Safety Population)

Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Result	Heart					Comments	
								Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcF*		
XXX-XXX	Screen	X	.	-1	Check-in	DDMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
						X.XX	DDMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X
	2	X	X	X.XX	X.XX	DDMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	
						X.XX	DDMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X
				X	X.XX	DDMMYYYY	X:XX:XX	NORMAL	XX	XXX.X	XX.X	XXX.X	XXX.X	#
						X	DDMMYYYY	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: NCS = Abnormal, Not Clinically Significant
 QTcF* = QT corrected for heart rate using Fridericia's correction.
 # = QTcF > 450, @ = QTcF change from baseline greater than 30 msec
 Treatment A: <description>
 Treatment B: <description>

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.5 Phone Call (Safety Population)

Subject Number	Study Period	Day	Phone Call Completed?	Date	Time	If no, reason
XXX-XXX	X	X	Yes/No	DDMMYYYY	HH:MM	Wrong number

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM