Statistical Analysis Plan

A Four-way Crossover Food Effect and Bioequivalence Pharmacokinetic Study of Simufilam in Healthy Volunteers

Protocol Number: PTI-125-05

Protocol Version: 1.0 / 5 Mar 2021

SAP Version 1.0

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Previous SAP Versions

Not Applicable (First Version)

SAP Amendments before database lock

Version	Issue Date	Section	Revision / Addition	Rationale
-	-	-	-	-

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1 INTRODUCTION

This document details the planned statistical analyses for *Cassava Sciences, Inc.*, protocol "PTl-125-05" study titled "A Four-way Crossover Food Effect and Bioequivalence Pharmacokinetic Study of Simufilam in Healthy Volunteers".

The proposed analyses are based on the contents of the final version of the protocol (dated 05-MAR-2021)

2 STUDY OBJECTIVES

The objectives of this study are

1. to assess the effect of food on the rate and extent of absorption of simufilam
2. to compare the pharmacokinetic profile of the Phase 3 formulation of simufilam to that of the earlier Phase 2 formulation.

3 ENDPOINTS

3.1 Primary Endpoints

- C_{max} - The maximum concentration determined directly from individual
- T_{max} - Time to reach maximum concentration
- AUC_{last} - Area under the curve to the time of the last quantifiable concentration, calculated using the linear trapezoidal method
- AUC_{inf} - Area under the curve extrapolated to infinity
- C_{last} - The last quantifiable concentration determined directly from individual concentration-time data
- T_{last} - Time of the last quantifiable concentration
- λ_z - The observed elimination rate constant; estimated by linear regression through at least three data points in the terminal phase of the log concentration-time profile
- $T_{1/2}$ - The observed terminal elimination half-life

4 SAMPLE SIZE

Twenty-four (24) subjects (12 male and 12 female) will be enrolled in this study. Sample size was determined by estimating the intrasubject variability for log-transformed data from previous studies of simufilam. A sample size of twenty-four subjects is expected to provide 80% power to obtain 90% confidence intervals for the geometric mean ratios of Cmax and the AUCs.

5 RANDOMIZATION

Subjects will be randomly assigned to one of four treatment sequences (6 subjects/sequence) to receive a single oral dose of simufilam in each treatment period either under fasted condition or low fat fed condition or high fat fed condition or phase 2 tablet as shown in Table 1.

The administration of each dose of study drug will be separated by a 48-hour washout period. PK blood samples will be obtained prior to dosing and at specified intervals during the study (0-48 h post-dose for Treatment Periods 1 - 4). The observation period for safety will continue through the incarceration period.

Table 1 Treatment Sequences by Period

Sequence	Treatment Period -1				Treatment Period -2				Treatment Period -3				Treatment Period -4			
	Fasted	High	Low	Phase 2 Tablet	Fasted	High	Low	Phase 2 Tablet	Fasted	High	Low	Phase 2 Tablet	Fasted	High	Low	Phase 2 Tablet
Sequence A (n = 6)				X			X		X					X		
Sequence B (n = 6)	X							X		X					X	
Sequence C (n = 6)		X			X						X					X
Sequence D (n = 6)			X			X						X	X			

6 PLANNED ANALYSES

No statistical analysis plan (SAP) prepared in advance of the data can be absolutely definitive and the final Clinical Study Report (CSR) may contain additional tables or statistical tests if warranted by the data obtained. The justification for any such additional analyses will be fully documented in the final CSR.

6.1 Analysis Sets

Subjects excluded from the analysis sets and the reason for their exclusion will be listed in Appendix 16.2 of the CSR.

6.1.1 Randomized Population

The Randomized Population is defined as all subjects who were randomized irrespective of receiving study drug.

6.1.2 Safety Analysis Set

The Safety Population is defined as all subjects who receive one dose of study medication.

6.1.3 Pharmacokinetic (PK) Population

The PK Population will include all evaluable subjects that complete all 4 periods of the study. Concentrations from subjects who drop out early will be analyzed and reported in the concentration-time listing only.

6.2 Derived Data

This section describes the derivations required for statistical analysis. Unless otherwise stated, variables derived in the source data will not be re-calculated.

6.2.1 Treatment Period / Visits

Each visit as per study schedule will be mapped to treatment period and analysis visit for summary tables as given below. Listings will reflect actual period and visit as defined in protocol.

Collected visit	Treatment Period	Analysis visit
Screening	-	Screening
DAY 0 Check-in	-	Check-in
DAY 1	Period 1	Day 1
DAY 2	Period 1	Day 2
DAY 3	Period 2	Day 3
DAY 4	Period 2	Day 4
DAY 5	Period 3	Day 5
DAY 6	Period 3	Day 6
DAY 7	Period 4	Day 7
DAY 8	Period 4	EOS / ET
Early Termination	Subject's last treatment period	EOS / ET

6.2.2 Race

Where more than one race category has been selected for a subject, these race categories will be combined into a single category labeled "Multiple Race" in the summary tables. The listings will reflect the original selected categories.

6.2.3 Baseline

Baseline is defined as the last non-missing value (either scheduled, unscheduled or repeat) before the subject receives the first dose of study drug.

For variables that will be summarized by treatment, the baseline for each period is defined as the last non-missing value (either scheduled, unscheduled or repeat) that is collected before dosing of respective period.

6.2.4 Duration / Study Day / Time

Study day will be calculated as the number of days from first dose of *study drug*.

- date of event – date of first dose of study drug + 1, for events on or after first dose
- date of event – date of first dose of study drug, for events before first dose

6.2.5 Adverse Event

A treatment emergent adverse event (TEAE) is defined as an AE that emerges during treatment, having been absent pretreatment, or worsens relative to the pretreatment state. The following rules will be used to assign a TEAE to a treatment group:

- A TEAE will be assigned to the treatment received immediately before onset.
- Any TEAE reported within the washout period between doses will be attributed to the previous treatment.
- If a TEAE started in one treatment period and continued to subsequent periods, the event will be counted in period which AE started.

If a TEAE is missing relationship, it is assumed to be 'probably related' to the study drug for analysis purposes. Maximum severity will be assumed for an AE with missing severity. Adverse events that are reported as 'possibly' or 'probably' related will be considered as Related and events that are 'unlikely' related will be considered as Not Related.

If a subject has multiple occurrences of same SOC and PT within a treatment period, then maximum severity and closest relationship will be separately flagged.

6.2.6 Conventions for Missing and Partial Dates

It is not expected that there will be any missing dates, however in the rare case that an Adverse Event (AE) start date or time is missing and it is unclear whether the AE is treatment emergent or not then a conservative approach will be taken and it will be assumed that the AE occurred after first dosing.

All dates presented in the individual subject listings will be as recorded on the Electronic Case Report Form (eCRF).

6.2.7 Inexact Values

In the case where a safety laboratory variable is recorded as "> x", "≥ x", "< x" or "≤ x", a value of x will be taken for analysis purposes.

6.2.8 Not Done/Missing

For safety assessments where shift summaries are required, records will be imputed for all subjects who received IMP in the respective period in all scheduled visits and marked as 'Not Done/Missing' if either the subjects did not attend the visit, or discontinued or had missing assessment at the respective visit

6.2.9 Unscheduled Visits

Only scheduled post-baseline laboratory and vital signs values will be tabulated. Post-baseline repeat / unscheduled assessments will be disregarded, although these post-baseline assessments will be listed in the relevant appendices to the CSR.

6.2.10 PK Parameters

Concentration-time data for simufilam will be analyzed using noncompartmental methods in Phoenix™ WinNonlin® (Version 8.1 or higher, Certara, L.P.) in conjunction with the internet-accessible implementation of Pharsight® Knowledgebase Server™ (PKSO; Version 4.0.4, Certara, L.P.). Concentrations that are below the limit of quantification (BLQ) will be treated as zero in the data summarization and descriptive statistics.

Blood samples for PK samples for the determination of simufilam will be collected at pre-dose (0), and at 0.333 (20 min), 0.667 (40 min), 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10, 12, and 24 hours post-dose, for each treatment period.

Mean plasma concentration-time data will be presented graphically on both linear and semi-log scales using nominal time. Spaghetti plots and individual plots will be presented on both linear and semi-log scales using actual time. The following plots will be created:

1) Mean plot: Phase 3 Simufilam Tablet Fasted, Low-fat, and High-fat
2) Mean plot: Phase 2 Simufilam Tablet Fasted, Phase 3 Simufilam Fasted
3) All Subject plot: All subjects in one plot per Treatment
4) Individual Subject plot: Phase 3 Simufilam Tablet Fasted, Low-fat, and High-fat plotted together for each subject
5) Individual Subject plot: Phase 2 Simufilam Tablet Fasted, Phase 3 Simufilam Fasted plotted together for each subject

Individual plasma concentrations from subjects that were excluded from the PK Analysis Population will be listed in Concentration Listings.

Concentration-time data for simufilam in plasma will be analyzed using non-compartmental methods. The following descriptive statistics will be presented by treatment and nominal time: sample size (N), arithmetic mean, standard deviation (SD), coefficient of variation (CV%), minimum, median, and maximum.

In the PK analysis, BLQ concentrations will be treated as zero from time-zero up to the time at which the first quantifiable concentration is observed; embedded and terminal BLQ concentrations will be treated as "missing". Actual time relative to dosing will be used in the PK analysis.

The following PK parameters will be calculated for simufilam for each treatment:

C_{max}	Maximum plasma concentration determined directly from individual concentration-time data
T_{max}	Time to reach maximum plasma concentration
AUC_{last}	Area under the plasma concentration versus time curve, from time 0 to the last quantifiable concentration (C_{last}), as calculated by the linear trapezoidal rule

C_{last}	Last quantifiable concentration determined directly from individual concentration-time data
T_{last}	Time of the last quantifiable concentration
AUC_{inf}	AUC from the time of dosing extrapolated to infinity, calculated as: $AUC_{inf} = AUC_{last} + C_{last}/\lambda z$
AUC_{Extrap}	The percentage of $AUC_{0\text{-}inf}$ obtained by extrapolation, calculated as: $AUC_{extrap} = [(AUC_{inf} - AUC_{last})/AUC_{0\text{-}inf}]*100$
λ_Z	Apparent terminal elimination rate constant calculated by linear regression using the terminal log-linear phase of the logarithmic (log) transformed concentration vs. time data
$T_{1/2}$	The observed terminal elimination half-life, calculated as: $T_{1/2} = \ln(2)/\lambda_z$

λ_Z Criteria

The following criteria will be used to report λ_Z:

- At least three quantifiable concentrations will be used in the regression
- C_{max} or data prior to C_{max} will not be included in the regression.
- The adjusted regression coefficient (R^2 adj) should be ≥ 0.80.

If these acceptance criteria are not met, λ_Z and descriptive parameters (λ_Z time range, Adj R^2, etc.) will be retained in a PK parameter table for informational purposes; λ_Z will be flagged and excluded from summary statistics. Parameters calculated using λ_Z ($T_{1/2}$) will be reported as ND (not determinable).

If λ_Z acceptance criteria are met and AUC_{inf} is estimable, the following criteria are used to report AUC_{inf}:

- The percentage of AUC_{inf} based on extrapolation should be <30.0%.

If the percentage of AUC_{inf} based on extrapolation is 30.0% or greater, AUC_{inf} and AUC_{extrap} will be excluded from summary statistics, subsequent PK calculations and statistical analysis (e.g. ANOVA).

6.3 Conventions

All clinical data listings, summaries, figures and statistical analyses will be generated using SAS (Version 9.4 or higher)[1].

Summaries of the clinical data will be presented by treatment group / sequence or overall.

PK data listings, tables, figures, and statistical analyses will be generated using Phoenix® WinNonlin® (Version 8.1 or higher, Certara, L.P.)[2] or SAS® (Version 9.4 or higher, SAS Institute Inc.)[1]. PK concentration-time data will be summarized by the number of non-missing observations (n), arithmetic mean (mean), standard deviation (SD), median, minimum (min), maximum (max), and coefficient of variation (CV%). PK parameter data will be summarized by n, mean, SD, median, min, max, CV%, geometric mean, and geometric CV%. Summary statistics that are not calculable due to lack of quantifiable data will be presented as NC in the descriptive statistic tables.

Treatment labels will be displayed as follows:

Fasted Simufilam	**Low fat fed Simufilam**	**High fat fed Simufilam**	**Phase 2 Simufilam**

Sequence group labels will be displayed as follows:

Sequence A	**Sequence B**	**Sequence C**	**Sequence D**

Note: Footnotes will be added in all TLFs to clarify each sequence.

Listings will be sorted in the following order subject, period, visit / date and parameter unless otherwise stated. All data will be listed, subjects who were not randomized will be displayed after the randomized treatment / sequence groups.

Safety parameters (continuous variables) will be summarized by the number of non-missing observations, mean, median, standard deviation, and minimum and maximum.

Categorical variables will be summarized by presenting the frequency and percent. Percentages will be based on the number of non-missing observations or the subject population unless otherwise specified. For each variable, all categories will be shown. Zero frequencies (but not the percent) within a category will be presented.

6.3.1 Decimal Places

Derived data, where it is known in advance that the result will be an integer, such as age, will be presented with zero decimal places.

Mean and median will be displayed to one more decimal place than the data**,** standard deviation will have two more decimal places, and the minimum and maximum will be displayed to the same

number of decimal places as reported in the raw data. Percentages will be displayed with one decimal place.

For PK data, individual concentrations and PK parameters will be reported to 3 significant figures. Time (hour) will also be presented in 3 significant figures For summary statistics, n will be reported as a whole number; mean, SD, median, min, max, CV%, geometric mean, and geometric mean CV% will be reported to the same precision as for individual data (3 significant figures). For ANOVA results, geometric means, least squares means, and the difference in least squares means will be reported to 3 significant figures. Percent ratios of the geometric least squares means and associated 90% confidence intervals will be reported to 2 decimal places. CV% (intra-subject variability) will be presented to 2 decimal places.

6.4 Subject Disposition

Subject disposition will be summarized as follows:

- The number of subjects included in Randomized Population; number and percentage of subjects included in the Safety and PK Populations will be summarized. Within the Safety Population, the number and percentage of subjects within each period and treatment will be summarized.
- The number and percentage of subjects who completed the study and who terminated early, along with subject's last period and treatment and reasons for early termination, will be summarized based on the Safety Population.

The Randomized Population will be based on planned treatment, and the Safety / PK Populations will be based on actual treatment received. Percentages for the Safety Population will be based on the Randomized Population; Percentages for all other categories will be based on Safety Population. Percentages for sub-categories will be based on main categories.

All subjects Disposition details, Treatment sequence and Population flags will be listed.

In Mock Shells: Table 14.1.1.1, Listing 16.2.1.1, Listing 16.2.3.1.

6.5 Protocol Deviations

A listing of protocol deviations will be provided.

In Mock Shells: Listing 16.2.2.1.

6.6 Demographic and Baseline Characteristics

Subject demographics will be summarized by Treatment sequence. Categorical and continuous variables will be provided in the same table. The following variables will be presented: age (years), sex, ethnicity, race, height (cm), weight (kg), BMI (kg/m^2). Percentages will be based on the respective population.

The summaries will be repeated for all Randomized, Safety, PK Populations (as per ICH E3 Guidelines). If the populations are the same, then demographic summary for Randomized Populations will be removed.

In Mock Shells: Table 14.1.2.1 to 14.1.2.3, Listing 16.2.4.1

6.7 Medical History

Previous and ongoing conditions at screening will be listed for the Safety Population. Conditions will be coded using the Medical Dictionary of Regulated Activities (MedDRA, version 24.0 or higher) and primary SOC and PT will be presented in listings.

In Mock Shells: Listing 16.2.4.2.

6.8 Prior and Concomitant Medications

Prior and concomitant medications will be listed for the Safety Population. Medications will be coded using the WHO Drug Dictionary (version Mar 2021 or later) and ATC levels will be presented in listings. Prior medications are defined as all medications that ended before the date of first dose of study drug. Concomitant medications are defined as medications ongoing on or after the date of first dose of study drug.

In Mock Shells: Listing 16.2.4.3.

6.9 Exposure to Study Drug

All dosing and meal consumption information will be listed for the Safety Population.

In Mock Shells: Listing 16.2.5.1.

6.10 Statistical Analysis of PK Data

Natural log transformed AUC_{inf} (if data permit), AUC_{last}, and C_{max}, will be analyzed using a mixed effect model with sequence, period, and treatment as fixed effects and subject within sequence as a random effect. Estimates of the adjusted mean differences (Test-Reference) and corresponding 90% confidence intervals (CIs) will be obtained from the model. The adjusted

mean differences and 90% CIs for the differences will be exponentiated to provide estimates of the ratio of adjusted geometric means (Test/Reference) and 90% CIs for the ratios.

For the food effect assessment, simufilam in the fasted state will be the intended reference treatment. The following comparisons will be made:

- High-fat (Test) vs. Fasted (Reference)
- Low-fat (Test) vs. Fasted. (Reference)
- Phase 2 tablet formulation (Test) vs. current tablet formulation (Reference; both Fasted).

6.11 Safety Analyses

The safety analyses will be presented by the treatment received for the Safety Analysis Set.

6.11.1 Adverse Events

All AEs will be coded by system organ class (SOC) and preferred term (PT) using the latest version of the Medical Dictionary for Regulatory Activities (MedDRA, version 24.0 or higher) and summarized by treatment and total.

The following tables/Listings will be presented for TEAEs:

- Overall incidence and the number of TEAEs, Treatment Related TEAEs, Serious TEAEs and Serious Related TEAEs. TEAEs will also be presented by Severity and Relationship
- TEAE by system organ class and preferred term, incidence and number of events.
- Treatment related TEAE by system organ class and preferred term, incidence and number of events.
- Serious TEAE by system organ class and preferred term, incidence and number of events.
- TEAEs leading to early withdrawal by system organ class and preferred term, incidence and number of events.
- TEAE by system organ class, preferred term and maximum severity, incidence. If a subject had multiple occurrences of the same PT within a treatment period, it is counted once with maximum severity under the PT; if a subject had multiple PTs within the SOC with different grades of maximum severity, it is counted once within each applicable severity grade within the SOC and Any TEAE categories.

- TEAE by system organ class, preferred term and closest relationship, incidence. If a subject had multiple occurrences of the same PT within a treatment period, it is counted once with closest relationship under the PT; if a subject had multiple PTs within the SOC with different grades of closest relationship, it is counted once within each applicable relationship category within the SOC and Any TEAE categories.
- Listing of Serious TEAEs (presented in the Table section of the appendices).
- Listing of Deaths (presented in the Table section of the appendices).

All AEs will be separately listed.

In Mock Shells: Tables 14.3.1.1 to 14.3.1.7, Tables 14.3.2.1 to 14.3.2.2, Listing 16.2.7.1

6.11.2 Laboratory Data

6.11.2.1 Descriptive Summaries

Hematology, Serum Chemistry and Urinalysis assessment at Baseline and EOS/ET will be summarized. Descriptive statistics of the observed values and change from baseline will be presented by visit for each Hematology, Serum Chemistry and Urinalysis listed below for Safety Population. Only total column will be presented. For Urinalysis, categorical results will be presented in the same table and percentages will be based on number of subjects with non-missing assessments within each visit.

All laboratory parameters will be listed in the order given below and in units in compliance with CDISC Controlled Terminology version 2020-11-06 or later.

Hematology: White blood cell (WBC) count with differential, red blood cell (RBC) count, hemoglobin, hematocrit, platelet count

Serum Chemistry: glucose, sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), creatinine, uric acid, phosphorus, calcium, total protein, albumin, globulin, alkaline phosphatase, alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin, lactose dehydrogenase (LDH)

Urinalysis: color, specific gravity, pH, protein, sugar, ketones, occult blood

In Mock Shells: Tables 14.3.4.1 and 14.3.4.3

6.11.2.2 Shift Summary

Shift summaries of the Normal range indicator (Low/Normal/High) will be presented at EOS/ET visit for Safety Population.

All laboratory data including Pregnancy tests, FSH tests, Urine Drug, Alcohol, and Cotinine Screens and Serology will be listed. Out of normal range laboratory results will be separately listed.

In Mock Shells: Tables 14.3.4.4 and 14.3.4.6, 14.3.4.7, Listing 16.2.8.1 to 16.2.8.6

6.11.3 Vital Signs

Vital signs will be measured once in Screening and Day 8 (discharge); on Day 1, Day 3, Day 5, and Day 7 at following timepoints: predose (1 hour), postdose 30 and 90 min, and 4, 8, 12 hours post-dose (within 15 min of nominal time); on Day 2, Day 4 and Day 6 at timepoints 4 h and 12 h, and at any other time deemed medically necessary. Vital signs will be measured after a 3-minute sitting period.

Vital Signs results at Baseline and all post-baseline timepoints will be summarized. Descriptive statistics for observed values and changes from Baseline in the following vital signs parameters will be presented by treatment at each visit/timepoint for Safety Population. Screening, results will only be listed. All parameters will be listed in the order given below and in units collected.

- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Heart rate (beats/min)
- Respiration rate (breath/min)
- Temperature (^{o}C)

All vital signs data will be listed.

In Mock Shells: Tables 14.3.5.1, Listing 16.2.8.7

6.11.4 Electrocardiogram Data

A 12 Lead ECG will be collected in Screening and at Day 8 before discharge.

6.11.4.1 Descriptive Summaries

ECG results at Baseline and EOS/ET will be summarized. Descriptive statistics for observed values and changes from Baseline in the following ECG variables will be tabulated at each visit, only total column will be presented.

- PR Duration(ms)
- QRS Duration(ms)
- QT interval (ms)
- QTc interval (ms)
- QTc interval (ms) [Fridericia's formula - QTcF]
- QTc interval (ms) [Bazett's formula - QTcB]
- Ventricular rate (bpm)
- RR interval (ms)

In Mock Shells: Tables 14.3.6.1, Listing 16.2.8.8

6.11.4.2 Interpretations

Shift summaries of the Normal range indicator (Normal/Abnormal CS/Abnormal NCS) will be presented at EOS/ET visit for Safety Population.

In Mock Shells: Tables 14.3.6.2

6.11.5 Physical Examination

Physical examination collected in Screening and Day 8 before discharge. All physical and oral examination results will be listed including Examination results and Clinically Significant findings.

In Mock Shells: Listing 16.2.8.9

7 CHANGES TO PLANNED PROTOCOL ANALYSIS

No changes to planned protocol analysis.

8 REFERENCES

1. SAS Institute Inc., Cary, NC, 27513, USA
2. Phoenix™ WinNonlin® (Version 8.1, Certara L.P.)

9 LIST OF TABLES, FIGURES AND LISTINGS

The following table includes details of the tables, figures and listings to be included within each section of the electronic common technical document (eCTD). The eCTD section is shown in bold. The following validation methods maybe used:

- Independent programming of numbers and manual review of format (IP)
- Independent programming by statistician of numbers and manual review of format (Stat IP)
- Manual review (MR)
- Code review (CR)

Table Number	Table Title	Validation Method	Shell Number (if repeat)
Items in bold are not table titles but references to the section headings within eCTD.			
14.1	**Demographics Data**		
14.1.1	**Disposition**		
14.1.1.1	Subject Disposition, Analysis Populations - All Subjects	IP	-
14.1.2	**Demographics**		
14.1.2.1	Subject Demographics – Safety Population	IP	-
14.1.2.2	Subject Demographics – PK Population	IP	14.1.2.1
14.1.2.3	Subject Demographics – Randomized Population	IP	14.1.2.1
14.2	**Efficacy Data**		
	Not Applicable	-	-
14.3	**Safety Data**		
14.3.1	**Displays of Adverse Events**		
14.3.1.1	Adverse Events, Overall Summary of TEAEs - Safety Population	IP	-
14.3.1.2	Adverse Events, Treatment Emergent Adverse Events by SOC and PT - Safety Population	IP	-
14.3.1.3	Adverse Events, Related Treatment Emergent Adverse Events by SOC and PT - Safety Population	IP	14.3.1.2

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.1.4	Adverse Events, Serious Treatment Emergent Adverse Events by SOC and PT - Safety Population	IP	14.3.1.2
14.3.1.5	Adverse Events, Treatment Emergent Adverse Events leading to Early Withdrawal by SOC and PT - Safety Population	IP	14.3.1.2
14.3.1.6	Adverse Events, Treatment Emergent Adverse Events by SOC, PT and Maximum Severity - Safety Population	IP	-
14.3.1.7	Adverse Events, Treatment Emergent Adverse Events by SOC, PT and Closest Relationship - Safety Population	IP	-
14.3.2	**Listings of Deaths, Other Serious and Significant Adverse Events**		
14.3.2.1	Adverse Event Leading to Death – Safety Population	IP	16.2.7.1
14.3.2.2	Serious Adverse Event Data – Safety Population	IP	16.2.7.1
14.3.3	**Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events**		
14.3.4	**Abnormal Laboratory Values**		
14.3.4.1	Hematology Data, Descriptive Statistics - Safety Population	IP	-
14.3.4.2	Clinical Chemistry Data, Descriptive Statistics - Safety Population	IP	14.3.4.1
14.3.4.3	Urinalysis Data, Descriptive Statistics - Safety Population	IP	-
14.3.4.4	Hematology Data, Shift Summary - Safety Population	IP	-
14.3.4.5	Clinical Chemistry Data, Shift Summary - Safety Population	IP	14.3.4.4
14.3.4.6	Urinalysis Data, Shift Summary - Safety Population	IP	14.3.4.4
14.3.4.7	Out of Range Laboratory Data – Safety Population	IP	16.2.8.1
14.3.5	**Vital Signs**		
14.3.5.1	Vital Signs Data, Descriptive Statistics - Safety Population	IP	-
14.3.6	**Other Safety**		
14.3.6.1	12 Lead ECG, Descriptive Statistics - Safety Population	IP	-

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.6.2	12 Lead ECG, Shift Summary - Safety Population	IP	-
14.4	**PK Tables**		
14.4.1	Descriptive Statistics of Simufilam Plasma Concentration-Time Data after Administration of Phase 3 Simufilam 100 mg Tablet under Fasted Conditions, with a Low-fat Breakfast, with a High-fat Breakfast, and after Administration of Phase 2 Simufilam 100 mg Tablet under Fasted Conditions– PK Population	IP	-
14.4.2	Pharmacokinetic Parameters of Simufilam in Plasma after Administration of Phase 3 Simufilam 100 mg Tablet under Fasted Conditions, with a Low-fat Breakfast, with a High-fat Breakfast, and after Administration of Phase 2 Simufilam 100 mg Tablet under Fasted Conditions– PK Population	IP	-
14.4.3	Statistical Analysis of the Natural Log-Transformed Systemic Exposure Parameters of Simufilam Comparing Phase 3 Simufilam 100 mg Tablet Administered with a Low-fat Breakfast (Test) or a High-fat Breakfast (Test) to Phase 3 Simufilam 100 mg Tablet Administered under Fasted Conditions (Reference)– PK Population	IP	-
14.4.4	Statistical Analysis of the Natural Log-Transformed Systemic Exposure Parameters of Simufilam Comparing Phase 2 Simufilam 100 mg Tablet (Test) and Phase 3 Simufilam 100 mg Tablet (Reference)– PK Population	IP	-
14.6	**Other Data**		
	Not Applicable	-	-

Figure Number	Figure Title	Validation Method
14.4.1	Mean Plasma Simufilam Concentration-Time Data after Administrations of Phase 3 Simufilam 100 mg Tablet under Fasted Conditions, with a Low-fat Breakfast, and with a High-fat Breakfast on Linear and Semi-logarithmic Scales– PK Population	IP
14.4.2	Mean Plasma Simufilam Concentration-Time Data after Administrations of Phase 2 Simufilam 100 mg Tablet and Phase 3 Simufilam 100 mg Tablet on Linear and Semi-logarithmic Scales– PK Population	IP
14.4.3	Plasma Simufilam Concentration-time Profiles for All Subjects after Administrations of Phase 3 Simufilam 100 mg Tablet under Fasted Conditions, with a Low-fat Breakfast, with a High-fat Breakfast, and after Administration of Phase 2 Simufilam 100 mg Tablet under Fasted Conditions on Linear and Semi-logarithmic Scales – PK Population	IP
14.4.4	Plasma Simufilam Concentration-time Profiles for Individual Subjects after Administrations of Phase 3 Simufilam 100 mg Tablet under Fasted Conditions, with a Low-fat Breakfast, and with a High-fat Breakfast on Linear and Semi-logarithmic Scales – PK Population	IP
14.4.5	Plasma Simufilam Concentration-time Profiles for Individual Subjects after Administrations of Phase 2 Simufilam 100 mg Tablet and Phase 3 Simufilam 100 mg Tablet on Linear and Semi-logarithmic Scales – PK Population	IP
14.4.6	Plasma Simufilam Concentration-time Profiles with Linear Regression for Estimating the Terminal Elimination Rate – PK Population	IP

Listing Number	Listing Title	Validation Method	Shell Number (if repeat)
16.2	**Subject Data Listings**		
16.2.1	**Discontinued Subjects**		
16.2.1.1	Subject Disposition – Randomized Population	IP	-
16.2.2	**Protocol Deviations**		
16.2.2.1	Protocol Deviations – Safety Population	IP	-
16.2.3	**Subjects Excluded from the Pharmacokinetic Analyses**		
16.2.3.1	Analysis Populations – Randomized Population	IP	-
16.2.4	**Demographic Data**		
16.2.4.1	Demographic Data – Safety Population	IP	-
16.2.4.2	Medical History – Safety Population	IP	-
16.2.4.3	Prior and Concomitant Medications – Safety Population	IP	-
16.2.5	**Compliance and / or Drug Concentration Data**		
16.2.5.1	Exposure and Meal Data – Safety Population	IP	-
16.2.6	**Individual Efficacy Response Data**		
16.2.6.1	Plasma Simufilam Concentration-Time Data Listing by Subject - Safety Population		
16.2.6.2	Plasma Terminal Elimination Rate of Simufilam for Individual Subjects - PK Population		
16.2.6.3	PK Output Text (WinNonlin Text File)		
16.2.6.4	SAS Output Text		
16.2.7	**Adverse Event Listings**		
16.2.7.1	Adverse Event Data – Safety Population	IP	-
16.2.8	**Individual Laboratory Measurements and Other Safety**		
16.2.8.1	Hematology Data – Safety Population		
16.2.8.2	Serum Chemistry Data – Safety Population	IP	16.2.8.1
16.2.8.3	Urinalysis Data – Safety Population	IP	16.2.8.1
16.2.8.4	Drug, Alcohol and Cotinine Screen – Safety Population	IP	-
16.2.8.5	Serology Data – Safety Population	IP	16.2.8.1

Listing Number	Listing Title	Validation Method	Shell Number (if repeat)
16.2.8.6	Pregnancy Test Data – Safety Population	IP	-
16.2.8.7	Vital Signs Data – Safety Population	IP	-
16.2.8.8	ECG Data – Safety Population	IP	-
16.2.8.9	Physical Examination Data – Safety Population	IP	-