DIVISION	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for: A Two Part Study to Assess i) the Relative Bioavailability and Food Effect of a Novel Tablet Formulation of Boosted-GSK2838232 Compared to Capsule and ii) the Safety and Pharmacokinetics of Repeated Once-Daily Doses of Non boosted GSK2838232
Compound Number	:	GSK2838232
Effective Date	:	07-DEC-2017 (Final 1.0)

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 205820.
- This RAP is intended to describe the statistical analyses for safety and pharmacokinetic analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

RAP Authors:

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol:

Revision Chronology:		
2017N322544_00	09-JUN-2017	Original
2017N322544_01	17-JUL-2017	Amendment No.: 1. The protocol was amended to include an assessment of neuropsychiatric adverse events at each AE enquiry as well as a statement to inform FDA of any grade 2 or higher alteration in personality-behavior or in mood or altered mental status within 7 days, per FDA request. Minor typographical errors were also amended in the Schedule of Assessments, the Exclusion Criteria and the Study Assessment and Procedures.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1 Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the amended protocol (dated: 17-JUL-2017).

2.2 Study Objectives and Endpoints

Part 1.

Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To assess the relative bioavailability of a novel GSK2838232 tablet formulations versus the capsule formulation (Part 1A)	• AUC(0-∞) and Cmax
• To assess the effect of food on GSK2838232 exposure of the tablet formulation (Part 1A and Part 1B)	• AUC(0-∞), Cmax, and tmax
Secondary Objectives	**Secondary Endpoints**
• To investigate the safety and tolerability of GSK2838232 following single dose administration as tablets or capsules, with Ritonavir (RTV)	• GSK2838232 safety parameters: adverse events (AEs); absolute values and changes over time of clinical laboratory evaluations (hematology, clinical chemistry, urinalysis), vital signs, and 12-lead electrocardiogram (ECG) parameters from pre-dose values
• To characterize the pharmacokinetics (PK) of GSK2838232 after administration of a novel tablet formulation and capsule formulation with food, and the tablet formulation given without food	• tlag, tmax, t½, tlast, C24, and AUC(0-t)

Part 2.

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the safety of GSK2838232 administered as non-boosted once-daily doses of a tablet formulation for 11 days	• GSK2838232 safety parameters: AEs; absolute values and changes over time of clinical laboratory evaluations (hematology, clinical chemistry, urinalysis), vital signs, and ECG parameters from pre-dose values
• To assess the PK of GSK2838232 administered as non-boosted once-daily doses of a tablet formulation for 11 days	• Day 1 dose: AUC(0-τ), Cmax, Cτ, tmax, tlag • Day 11 dose: AUC(0-τ), AUC(0-∞), Cmax, Cτ, tmax, t½, tlast
Secondary Objectives	**Secondary Endpoints**
• To assess time to steady-state of GSK2838232 when administered as non-boosted once-daily doses of a tablet formulation for 11 days	• Pre-dose concentrations on Days 2 to 11
• To assess accumulation of GSK2838232 when administered as non-boosted once-daily doses of a tablet formulation for 11 days	• Accumulation ratios: Ro[AUC(0-τ)], R(Cmax), R(Cτ)

AUC(0-τ) = Area under the curve (Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval); AUC(0-∞) = Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time; Cmax = Maximum observed concentration; Cτ=Observed concentration at the end of the dosing interval; t½ = Apparent terminal phase half-life; tmax = Time of occurrence of Cmax; tlag = Lag time (time delay between drug administration and first observed concentration above LOQ in plasma); AUC(0-t) = Area under the concentration-time curve from zero up to last quantifiable concentration; tlast = Time of last quantifiable concentration

2.3 Study Design

Overview of Study Design and Key Features

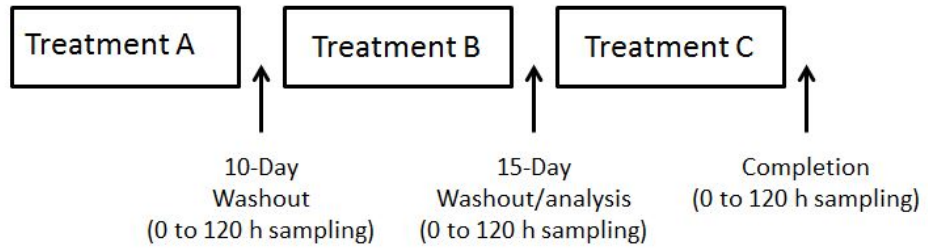
This study is divided into two study parts, Part 1 (Table 1 and Figure 1) and Part 2 (Figure 2).

Table 1 Study Design for Part 1

Sequence	N	Part 1A		Part 1B
		Period 1	Period 2	Period 3
1	6	A	B	C
2	6	B	A	

1. All treatments in Part 1A to be administered with RTV in fed state, following two RTV pre-doses.
2. There will be a washout of at least 10 days between each Period.
3. Treatment A = GSK2838232 200 mg/r (as 4 x 50 mg) capsule formulation, fed, normal fat (i.e., approximately 30%) meal (reference).
4. Treatment B = GSK2838232 200 mg/r (as 2 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal.
5. Treatment C = GSK2838232 200 mg/r (as 2 x 100 mg) tablet, confirmed from Part 1A, fasted.

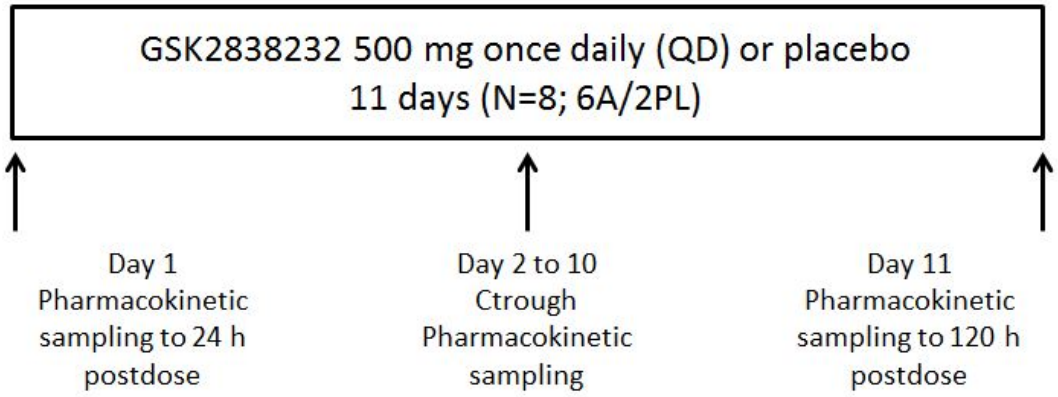
Figure 1 Part 1: Single Dose, Food Effect Study Design Schematic



Treatments A and B will be Capsule and Tablet administered in a randomized crossover design with 100 mg Ritonavir with food (fed state) (Part 1A).
Treatment C will be Tablet assessed in Part 1A, administered with 100 mg Ritonavir without food (fasted state) (Part 1B)

Overview of Study Design and Key Features

Figure 2 Part 2: Single Daily Dose Study Design Schematic



Design Features	Part 1: • Part 1 is a relative bioavailability study (Table 1) that will further subdivide into two parts (Part 1A and Part 1B). • In Part 1A, the safety and PK of a novel tablet formulation of GSK2838232 will be evaluated in open label, randomized, cross over fashion against the capsule formulation as reference. • Each actual treatment dose will be separated by a minimum 10 day washout period. Part 1A will be studied in the fed state using a normal fat (i.e., approximately 30%) meal in all participants. • The safety and PK will be evaluated, and the tablet will be evaluated for suitability, and further clinical assessment in Part 1B, where the tablet will be administered in the fasted state to understand the impact of food on relative bioavailability. • GSK2838232 as tablets or capsules (at a 200 mg dose level) will be administered with 100 mg RTV, after two pre-doses of 100 mg RTV once daily (QD) over 48 h. The use of RTV priming is an aspect of GSK2838232 clinical development (specifically relative bioavailability studies) so far and allows a more accurate assessment of what will ultimately happen in the repeat-dose clinical studies with GSK2838232 when boosted with RTV. In Part 2 of the study, however, GSK2838232 will be administered unboosted and no RTV will be co administered. • Participants will have a screening visit within 30 days prior to first dose, a minimum 10-day washout period between doses, and a follow-up visit 7 to 14 days after the last dose. The maximum duration of study participation will be approximately 9 to 10 weeks. After completion of Part 1A, preliminary PK data will be analyzed, and a decision will be made based on tolerability, relative bioavailability PK criteria, as well as feasibility considerations, as to whether the tablet formulation will be used to conduct Part 1B (fasted) and Part 2. Part 2: • Part 2 will evaluate non-RTV boosted GSK2838232, given as single daily doses

Overview of Study Design and Key Features	
	for 11 days in a separate cohort of participants (N=8; 6A/2P). • The placebo tablet supplied will not be identical to GSK2838232 and as such will be administered by site staff via an opaque card/paper tube to facilitate the single blind (i.e., the Principal Investigator [PI] and the participants themselves will be blinded as to their treatment). • The dose chosen for Part 2 will depend upon the preliminary results of the tablet in Part 1A but is likely to be, but will not exceed, 500 mg (i.e., 5 x 100 mg tablets) QD. • Participants will have a screening visit within 30 days prior to first dose, and a follow-up visit 7 to 14 days after the last dose. The maximum duration of study participation will be approximately 8 to 9 weeks. Details of the assessments and procedures participants will undergo are listed in Section 9 of the Clinical Study Protocol (CSP). The time points and visits are provided in the schedule of assessments, (Table 2 and Table 3 of the CSP for the Schedule of assessments for study Parts 1 and 2 respectively).
Dosing	• The dose for Part 1A and Part 1B of this study will be 200 mg (achieved as either 4 x 50 mg capsules or 2 x 100 mg tablets) administered with 100 mg RTV. • The dose for Part 2 will be confirmed from Part 1A but is likely to be, and will not exceed, 500 mg (as 5 x 100 mg tablets).
Treatment Assignment	• The randomization number will determine the allocation of treatment sequences (ABC or BAC) for Part 1, and of treatment (GSK2838232 without RTV or placebo) for Part 2. • Part 1 treatments: o Treatment A = GSK2838232 200 mg/r (as 4 x 50 mg) capsule formulation, fed, normal fat (i.e., approximately 30%) meal (reference). o Treatment B = GSK2838232 200 mg/r (as 2 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal. o Treatment C = GSK2838232 200 mg/r (as 2 x 100 mg) tablet, formulation confirmed from Part 1A, fasted. • Part 2 treatments: o Treatment D = GSK2838232 500 mg/r (as 5 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal (reference). o Treatment E = Placebo The dose chosen for Part 2 will depend upon the preliminary results of the tablet in Part 1A but is likely to be, but will not exceed, 500 mg (i.e., 5 x 100 mg tablets) QD.
Interim Analysis	• No formal interim analyses are planned for this study; an informal analysis of data from Part 1A of the study will decide the dose and formulation to be administered in Part 1B and Part 2.

2.4 Statistical Hypotheses/Statistical Analysis

No formal statistical hypotheses will be tested. Analysis will be descriptive and exploratory. An estimation approach providing point estimates and corresponding confidence intervals will be used, where appropriate.

Part 1A Relative Bioavailability

Part 1A of this study is designed to estimate the bioavailability of a novel GSK2838232 tablet formulations versus the capsule formulation at 200 mg/r. No formal hypothesis will be tested. The dependent variable will be the log-transformed PK parameters of interest (AUC(0-∞) and Cmax) and the independent variables will include fixed effects for treatment (table or capsule), sequence and period, and participant (sequence) as a random effect. For each primary pharmacokinetic endpoint, point estimates and corresponding 90% confidence intervals will be constructed for the ratio of the geometric mean of the test treatment (GSK2838232 200 mg/r tablet) to the geometric mean of the reference treatment (GSK2838232 200 mg/r capsule), μ(test)/μ(reference).

Part 1A and 1B Food Effect

Part 1A and 1B of this study are designed to evaluate the effect of food on GSK2838232 exposure of the tablet formulation. No formal hypothesis will be tested. The dependent variable will be the log-transformed PK parameters of interest (AUC(0-∞) and Cmax) and the independent variables will include a fixed effect for treatment (with or without food) and participant as a random effect. The estimated difference and confidence interval (CI) obtained on the log scale will be exponentiated to provide an estimate of the fed to fasted ratio and its associated 90% CI.

For the parameter tmax the corresponding non-parametric analysis will be performed on the original scale using CIs for the estimation of the treatment difference based on the Hodges-Lehman estimator.

Part 2 Steady State Assessments

Part 2 of this study is designed to assess time to steady-state of GSK2838232 when administered as non-boosted once-daily doses of a tablet formulation for 11 days. No formal hypothesis will be tested. Mean plasma GSK2838232 pre-dose values between Days 2 through 11 and Cτ of Day 11 will be plotted against time. Achievement of plasma GSK2838232 steady-state will be assessed by calculating the 90% CI of the slope of the linear regression of log (Cτ) versus time. The dependent variable in the linear regression model will be log (Cτ) and the model will include a random intercept effect for participant and a fixed slope effect for study day. Steady state will be reached if the 90% CI for the slope estimate includes zero.

Part 2 Accumulation

Part 2 of this study is designed to assess accumulation of GSK2838232 when administered as non-boosted once-daily doses of a tablet formulation for 11 days. No formal hypothesis will be tested. The extent of accumulation of GSK2838232 will be

evaluated by comparing AUC(0-τ), Cmax and Cτ between Day 11 and Day 1. For each of these comparisons an analysis of variance will be conducted on the log scale. The difference between Day 11 and Day 1 least square (LS) means and a 90% CI will be computed by fitting a mixed effects model with the log-transformed PK parameter as the dependent variable, day as a fixed effect and participant as a random effect. The estimated difference and confidence interval obtained on the log-scale will be exponentiated to provide an estimate of the Day 11 to Day 1 ratio and its associated 90% CI. If the model fails to converge, participants will be fit as a fixed effect.

3. PLANNED ANALYSES

3.1 Interim Analyses

No formal interim analyses are planned for this study. The dose and formulation to be administered in Part 1B and Part 2 will be decided, based on the outcome and results of an informal analysis of preliminary safety and PK data from Part 1A of the study. In addition, and descriptive analysis of preliminary safety and PK data from Part 1 and 2 of the study will be performed.

3.2 Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

- All participants have completed the study as defined in the protocol.
- All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
- All criteria for unblinding the randomisation codes have been met.
- Randomisation codes have been distributed according to PAREXEL procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Study Population
Safety	• The Safety Population will include all participants who received at least 1 dose of the study treatment (including placebo) with at least 1 post-baseline safety assessment. • This population will be based on the treatment the participant received. • The population will be defined separately for Part 1 and Part 2 of the study.	• Safety and Demography

Population	Definition / Criteria	Analyses Evaluated
PK	• All participants in the Safety population who had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values). Pharmacokinetic samples that may be affected by protocol deviations will be reviewed by the study team to determine whether the sample will be excluded. • This population will be based on the treatment the participant received. • The population will be defined separately for Part 1A, Part 1B and Part 2 of the study.	• PK

NOTES :

- Please refer to Appendix 8: List of Data Displays which details the population to be used for each displays being generated.

4.1 Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarised and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP) version final 1.0 dated 22 Aug 2017.

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the Electronic Case Record Form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1 Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions – Part 1			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TFL
C1	GSK2838232 200 mg/r (as 4 x 50 mg) capsule formulation, fed, normal fat (i.e., approximately 30%) meal (reference)	GSK 200 mg/r capsule fed	1
T1	GSK2838232 200 mg/r (as 2 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal	GSK 200 mg/r tablet fed	2
T2	GSK2838232 200 mg/r (as 2 x 100 mg) tablet, confirmed from Part 1A, fasted	GSK 200 mg/r tablet fasted	3

Treatment comparisons will be displayed as follows using the descriptors as specified:

1. GSK 200 mg/r tablet fed vs GSK 200 mg/r capsule fed
2. GSK 200 mg/r tablet fed vs GSK 200 mg/r tablet fasted

Treatment Group Descriptions – Part 2			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TFL
T3	GSK2838232 500 mg/r (as 5 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal (reference).	GSK 500 mg/r tablet fed	2
P	Placebo	Placebo	1

Treatment comparisons will be displayed as follows using the descriptors as specified:

1. GSK 500 mg/r tablet fed vs Placebo

5.2 Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline. In part 1, baseline definitions are applicable to each period.

Parameter	Study Assessments Considered As Baseline				Baseline Used in Data Display
	Screening	Day -2	Day -1	Day 1 (Pre-Dose)	
Safety Data					
Vital Signs	X	X*	X	X	Mean of replicate assessments on Day 1
ECG	X	X*	X	X	Mean of replicate assessments on Day 1
Laboratory tests	X	X*	X		Day -1

* Vital Sign, ECG and laboratory tests are not collected at day -2 for Part 2.

Unless otherwise stated, if baseline data is missing no derivation will be performed and baseline will be set to missing.

5.3 Multicentre Studies

Not applicable.

5.4 Examination of Covariates, Other Strata and Subgroups

Not applicable.

5.5 Multiple Comparisons and Multiplicity

Not applicable.

5.6 Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
14.3	Appendix 3: Assessment Windows
14.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
14.5	Appendix 5: Data Display Standards & Handling Conventions
14.6	Appendix 6: Derived and Transformed Data
14.7	Appendix 7: Reporting Standards for Missing Data

Section	Component
14.8	Appendix 8: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1 Overview of Planned Analyses

The study population analyses will be based on the Safety Population, unless otherwise specified.

Study population analyses including analyses of participant's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 12: List of Data Displays.

6.2 Disposition of Participants

A summary of the number of participants in each of the analysis populations described in Section 4 will be provided and this table will be displayed by treatment/sequence and overall of each part. A listing of participants excluded from analysis populations will also be provided.

A summary of participant status and reason for study withdrawal will be provided. This display will show the number and percentage of participants who withdrew from the study, including primary reasons for study withdrawal.

A summary of study treatment status will be provided. This display will show the number and percentage of participants who have completed the study or have discontinued study treatment and a summary of the primary reasons for discontinuation of study treatment. A listing of study treatment discontinuation will be generated. The listing will include last dose date, and reasons for study treatment discontinuation as well as study part and period, when applicable, of discontinuation.

6.3 Demographic and Baseline Characteristics

The demographic characteristics (e.g., age, ethnicity, sex, height, and body weight) will be summarized and listed by participant. Race will be summarized and listed separately from the other demographic characteristics. Age, height, body mass index (BMI) and weight will be summarized using the mean, standard deviation, minimum, median, and maximum. The count and percentage will be computed for sex, race and ethnicity. The summary table will be displayed by treatment/treatment sequence and overall of each part.

Medical conditions present at screening will be summarized by treatment/treatment sequence and overall of each part, and listed by participant.

Substance use will be listed.

6.4 Concomitant Medications

Concomitant medications will be coded using GSK Drug coding dictionary, summarized by treatment and study part, and listed by participant. The summary of concomitant

medications will show the number and percentage of participants taking concomitant medications by ingredient. Multi-ingredient products will be summarized by their separate ingredients rather than as a combination of ingredients. Anatomical Therapeutic Chemical (ATC) classification Level 1 (Body System) information will be included in the dataset created, however, will not appear on the listing or summary.

In the summary of concomitant medications, each participant is counted once within each unique ingredient. For example, if a participant takes amoxicillin on two separate occasions, the participant is counted only once under the ingredient “amoxicillin”.

In the summary of concomitant medications, the ingredients will be summarized by the base only, using CMBASECD and CMBASE.

6.5 Treatment Compliance and Protocol Deviations

Information of each participant not received the correct treatment during each treatment period, the reason for not receiving the correct treatment, and any other protocol deviations will be summarized by treatment /sequence and overall of each part, and listed by participant and period (treatment). In addition, a listing will be provided including dose administered along with dosing dates and time for the investigational product.

Participants who did not satisfy all inclusion and exclusion criteria and corresponding criteria that were violated will be summarized and listed.

For the food effect of Part 1, a by-participant listing of the meal data will also be generated including start and stop date and time of meal, dosing time, type of meal and whether the totality of the meal was ingested.

6.6 Extent of Exposure

A by-participant summary of treatments administered in each part will be generated, with dose, and dosing start date, dosing end date and number of dose. A by-participant listing of data on participant exposure will be generated including dose date and time, unit, formulation, route and frequency.

7. EFFICACY ANALYSES

Not applicable.

8. SAFETY ANALYSES

The safety analyses will be based on the "Safety Population", unless otherwise specified.

8.1 Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 12: List of Data Displays.

8.2 Adverse Events of Special Interest Analyses

Not applicable.

8.3 Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests, Urinalysis, and liver function tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 12: List of Data Displays.

8.4 Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 12: List of Data Displays.

9. PHARMACOKINETIC ANALYSES

9.1 Primary Pharmacokinetic Analyses

9.1.1 Endpoint / Variables

9.1.1.1 Drug Concentration Measures

Pharmacokinetic data will be presented in graphical and/or tabular form and will be summarized descriptively. Plasma GSK2838232 concentration-time data will be listed by participant, treatment group and time and summarized by treatment group and time for each part of the study. Individual participant profiles for GSK2838232 concentration-time data will be presented on both a linear and semi-log scale. Linear and semi-log figures for mean and median GSK2838232 plasma concentrations versus time will also be generated.

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 14.5.3 Reporting Standards for Pharmacokinetic).

9.1.1.2 Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Part 1:

Parameter	Parameter Description
AUC(0-∞)	Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time will be calculated as: **AUC = AUC(0-last) + C(last) / lambda_z**
Cmax	Maximum observed concentration, determined directly from the concentration-time data
tmax	Time of occurrence of Cmax, determined directly from the concentration-time data

Part 2

Parameter	Parameter Description
AUC(0-τ)	Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval (where τ = 24 h) (Day 1 and Day 11)
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-last) + C(last) / lambda_z**
Cmax	Maximum observed concentration, determined directly from the concentration-time data. (Day 1 and Day 11)
tmax	Time of occurrence of Cmax, determined directly from the concentration-time data (Day 1 and Day 11)
tlag	Lag-time (time delay between drug administration and first observed concentration),

Parameter	Parameter Description
	determined directly from the concentration-time data (Day 1)
tlast	Time of last quantifiable concentration, determined directly from the concentration-time data (Day 11)
t½	Apparent terminal phase half-life, calculated as; t½ = ln2 / lambda_z (Day 11)
Cτ	Observed concentration at the end of the dosing interval, determined directly from the concentration-time data (where τ = 24 h) (Day 1 and Day 11)
Ctrough	Observed pre-dose concentrations on Days 2 to 11, determined directly from the concentration-time data

NOTES:

- C24, Cτ and Ctrough will be extracted from the concentration data by Clinical Statistics group and merged with other calculated PK parameters provided by CPMS.

All the derived parameters described above will be listed. For each of these parameters, except tmax and tlag, the following summary statistics will be calculated for each treatment group: n, arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean with associated 90% CI, standard deviation of logarithmically transformed data, and the between-participant CV (%CVb) based on the geometric mean for the loge-transformed PK parameters. For tmax and tlag, median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

9.1.2 Summary Measure

The measures used for the treatment comparisons are the following:

- For part 1; AUC(0-∞), Cmax, and, for food effect, tmax.
- For part 2; Not applicable.

9.1.3 Population of Interest

The primary pharmacokinetic analyses will be based on the Pharmacokinetic population, unless otherwise specified.

9.1.4 Strategy for Intercurrent (Post-Randomization) Events

Not applicable.

9.1.5 Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 9.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

Statistical Methodology Specification

The following pharmacokinetic statistical analyses will only be performed if sufficient data is available (i.e. if participants have well defined plasma profiles).

Part 1A Relative Bioavailability

Endpoint / Variables
• AUC(0-∞) and Cmax
Model Specification
• AUC(0-∞) and Cmax will be separately analysed using a mixed effects model. The dependent variable will be the log-transformed PK parameters of interest (AUC(0-∞) and Cmax) and the independent variables will include fixed effects for treatment (GSK2838232 200 mg/r tablet or GSK2838232 200 mg/r capsule), sequence and period, and participant (sequence) as a random effect.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data. • The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. • Normality assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. • If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.
Model Results Presentation
• Geometric least-squares means for each treatment (tablet or capsule), point estimates and associated 90% confidence intervals for the ratios for each parameter will be produced in tabular format. Estimates of within-subject variability (%CVw) will also be provided. %CVw represents a pooled measure of within-subject variability across all treatments. • Comparative plots of individual PK parameters will be generated by treatment on linear and semi-logarithmic scales. • Plots of adjusted geometric mean ratio of test to reference treatment together with 90% confidence intervals will be produced. • Listing of individual PK parameter ratios will be generated. • Supportive SAS output from statistical analysis will be generated.
Subgroup Analyses
• Not applicable
Sensitivity and Supportive Analyses
• Not applicable

Part 1 A and 1B Food Effect

Endpoint / Variables
• AUC(0-∞) and Cmax
Model Specification
• AUC(0-∞) and Cmax will be separately analysed using a mixed effects model. The dependent variable will be the log-transformed PK parameters of interest (AUC(0-∞) and Cmax) and the independent variables will include a fixed effect for treatment (with or without food) and participant as a random effect. • To assess the effect of food on GSK2838232 exposure of the tablet formulation (Part 1A and Part 1B)
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data. • The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. • Normality assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.
Model Results Presentation
• The estimated difference and CI obtained on the log scale will be exponentiated to provide an estimate of the fed to fasted ratio and its associated 90% CI. Estimates of within-subject variability (%CVw) will also be provided. %CVw represents a pooled measure of within-subject variability across all treatments. • Comparative plots of individual PK parameters will be generated by treatment on linear and semi-logarithmic scales. • Plots of adjusted geometric mean ratio of test to reference treatment together with 90% confidence intervals will be produced. • Listing of individual PK parameter ratios will be generated. • Supportive SAS output from statistical analysis will be generated.
Subgroup Analyses
• Not applicable
Sensitivity and Supportive Analyses
• Not applicable

Endpoint / Variables
• tmax
Model Specification
• Non-parametric analysis, using PROC NPAR1WAY will be performed on the original scale PK parameters of interest (tmax). The dependent variable will be the original scale PK parameter of interest (tmax) and the independent variables will be treatment (with or without food). • SAS code; PROC NPAR1WAY data= data hl ALPHA=0.1; CLASS treatment; VAR pk; EXACT hl; /* where PK parameter pk = tmax*/ ods select HodgesLehmann; RUN;
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation
• 90% CIs for the estimation of the treatment difference based on the Hodges-Lehman estimator will be produced
Subgroup Analyses
• Not applicable
Sensitivity and Supportive Analyses
• Not applicable

9.2 Secondary Pharmacokinetic Analyses

9.2.1 Endpoint / Variables

9.2.1.1 Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 14.5.3 Reporting Standards for Pharmacokinetic)

9.2.1.2 Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Part 1:

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve from zero up to the last quantifiable concentration will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid
tmax	Time to reach Cmax, determined directly from the concentration-time data.
tlag	Lag-time (time delay between drug administration and first observed concentration)
t½	Apparent terminal half-life will be calculated as: **t½ = ln2 / lambda_z**
tlast	Time of last quantifiable concentration, determined directly from the concentration-time data.
C24	Observed concentration 24 hours post-dose, determined directly from the concentration-time data.

NOTES:

- Additional parameters may be included as required.
- Lambda_z is the terminal phase rate constant.

Part 2

Parameter	Parameter Description
Ctrough	Observed pre-dose concentrations on Days 2 to 11, determined directly from the concentration-time data
Ro[AUC(0-τ)]	Accumulation ratio based on AUC(0-τ), determined by; Day 11 AUC(0-τ) / Day 1 AUC(0-τ)
R(Cmax)	Accumulation ratio based on Cmax, determined by; Day 11 Cmax / Day 1 Cmax
R(Cτ)	Accumulation ratio based on Cτ, determined by; Day 11 Cτ / Day 1 Cτ

NOTES:

- Additional parameters may be included as required.
- Cτ, and Ctrough will be extracted from the concentration data by Clinical Statistics group and merged with other calculated PK parameters provided by CPMS.

All the derived parameters described above will be listed. For each of these parameters, except tmax and tlag, the following summary statistics will be calculated for each treatment group: n, arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean with associated 90% CI, standard deviation of logarithmically transformed data, and the between-participant CV (%CVb) based on the geometric mean for the loge-transformed PK parameters. For tmax and tlag, median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

9.2.2 Summary Measure

The measures used for the treatment comparisons are the followings:

- For part 1; Not applicable.
- For part 2; Accumulation ratios: Ro[AUC(0-τ)], R(Cmax), R(Cτ).

9.2.3 Population of Interest

The secondary pharmacokinetic analyses will be based on the Pharmacokinetic population, unless otherwise specified.

9.2.4 Strategy for Intercurrent (Post-Randomization) Events

Not applicable.

9.2.5 Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 9.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

Statistical Methodology Specification

Part 2 Steady State Assessments

Endpoint / Variables
• GSK2838232 pre-dose values between Days 2 through 11
Model Specification
• Achievement of plasma GSK2838232 steady-state will be assessed by calculating the 90% CI of the slope of the linear regression of $\log_e(C\tau)$ versus time. The dependent variable in the mixed effect model will be $\log_e(C\tau)$ and the model will include a random intercept effect for participant and a fixed slope effect for study day. Day will be treated as a continuous variable in the model.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data. • The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. • An unstructured covariance structure for the R matrix will be used by specifying 'type=UN' on the REPEATED line. • In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. • Normality assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. • If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.

Model Results Presentation
• Steady state will be reached if the pre-dose concentration slope estimate is close to zero or the 90% CI for the slope estimate includes zero. • Mean plasma GSK2838232 pre-dose values between Days 2 through 11 and Cτ of Day 11 will be plotted against time on linear and semi-logarithmic scale..
Subgroup Analyses
• Not applicable
Sensitivity and Supportive Analyses
• Not applicable

Part 2 Accumulation

Endpoint / Variables
• AUC(0-τ), Cmax and Cτ between Day 11 and Day 1
Model Specification
• The extent of accumulation of GSK2838232 will be evaluated by comparing AUC(0-τ), Cmax and Cτ between Day 11 and Day 1. For each of these comparisons an analysis of variance will be conducted on the log scale. The difference between Day 11 and Day 1 least square (LS) means and a 90% CI will be computed by fitting a mixed effects model with the log-transformed PK parameter as the dependent variable, day as a fixed effect and participant as a random effect.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data. • The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. • Normality assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. • If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.
Model Results Presentation
• Geometric least-squares means for each treatment, point estimates and associated 90% confidence intervals for the ratios for each parameter will be produced in tabular format. Estimates of within-subject variability (%CVw) will also be provided. %CVw represents a pooled measure of within-subject variability across all treatments. • Comparative plots of individual Accumulation Ratio will be generated by dose group on linear and semi-logarithmic scales. • The accumulation ratio will be listed and summarized along with other PK parameters. • Supportive SAS output from statistical analysis will be generated.

Subgroup Analyses
• Not applicable
Sensitivity and Supportive Analyses
• Not applicable

9.3 Exploratory Pharmacokinetic Analyses

Not applicable.

10. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

Not applicable.

11. PHARMACODYNAMIC ANALYSES

Not applicable.

12. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

Not applicable.

13. REFERENCES

GlaxoSmithKline documents:

GUI_51487: Non-compartmental Analysis of Pharmacokinetic Data, CPMS Global

Reporting and Analysis Plan (RAP) Template [Phases I to IV] Version 2.0 [Dated: 08-AUG-2017]

14. APPENDICES

14.1 Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

14.2.1 Exclusions from Per Protocol Population

Not applicable.

14.2 Appendix 2: Schedule of Activities

14.2.1 Protocol Defined Schedule of Events

Schedule of Assessments for Part 1A and Part 1B: Single Dose RBA ± Food

Procedure	Screening (within 30 days of Day 1 - carried out over multiple days – except as noted in footnotes)	Periods 1 through 3										Follow-up[1]
		Day -3	Day -2	Day -1	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	7-14 days
						24 h	48 h	72 h	96 h	120 h		
Admission to Unit		X[2]										
Outpatient Visit	X											X
Informed Consent	X											
Medical/medication/ drug/alcohol history (Demographics)	X											
Full Physical Examination	X											
Brief Physical Examination			X				X					X
Height, Weight, BMI	X											
Inclusion/Exclusion	X											
Vital signs[3]	X		X	X	X	X	X	X				X
12 Lead ECG[4]	X		X	X	X	X	X					X
Echocardiogram[5]	X											
Drug/alcohol/cotinine screen	X	X										
HbsAg, HCV, HIV tests	X											
Hem/Chem/Urine tests[6]	X		X	X		X		X				X
Serum FSH (as appropriate)	X											
Troponin I[7]	X			X	X	X		X				
24 h Holter Monitoring[8]	X											
Pregnancy test (women)	X	X										X
Run-in Dosing with RTV			X	X								
Dosing with GSK2838232+RTV					X							

Procedure	**Screening** (within 30 days of Day 1 - carried out over multiple days – except as noted in footnotes)	**Periods 1 through 3**										**Follow-up[1]**
		Day -3	**Day -2**	**Day -1**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**7-14 days**
						24 h	**48 h**	**72 h**	**96 h**	**120 h**		
PK Sampling[9]					X	X	X	X	X	X		
Adverse Event Review[10]				X	X	X	X	X	X	X	X	X
Con Med Review			X	X	X	X	X	X	X	X	X	X
Discharge from Unit[11]						X						
Out Patient Visit							X	X	X	X	X	

BMI = Body Mass Index; ECG = Electrocardiogram; FSH = Follicle Stimulating; HbsAg = Hepatitis B surface Antigen; HCV = Hepatitis C Virus; HIV = Human Immunodeficiency Virus; Hem/Chem = Hematology/Clinical Chemistry; RTV = Ritonavir; PK = Pharmacokinetic(s); Con Med = Concomitant medications.

1. Follow-up Visit to take place after Treatment Period 2.
2. When participants stay in the unit across treatment periods, drug/alcohol/cotinine screen and pregnancy test (women) are not required on Day -3 for later periods.
3. On Day 1, Blood pressure (BP) and Heart rate (HR) will be collected at pre-dose (triplicate) and single assessments at 1, 2, 4, 6, 8, 12, 24, 48, and 72 h post-dose.
4. On Day 1, 12-lead ECG will be collected at pre-dose (triplicate), and single assessments at 1, 2, 4, 6, 8, 12, 24, 48 and 72 h post-dose.
5. Echocardiograms must be within 100 days of Day 1.
6. Samples for Chemistry and Hematology: Blood samples will be obtained after an 8-hour fast.
7. Collect one troponin sample to be analyzed at local laboratory. A second sample will be collected, frozen and stored on site for potential high sensitivity troponin analysis.
8. 24-h Holter monitoring to be performed after confirming negative urine drug screen at screening, and must be within 30 days of Day 1. Holter monitoring on other days only if needed.
9. Plasma PK samples for bioanalysis for GSK2838232 will be collected pre-dose (within 15 minutes prior to dosing) and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 12, 24, 36, 48, 72, 96, and 120 h post-dose. Samples will be acidified with an equal volume of 50 mmol citrate acid buffer pH 4.0.
10. An AE enquiry will be made at each visit, participants will be asked if they have experienced any neuropsychiatric adverse events, including psychosis or altered mental status. (see guidance for grading Altered Mental Status in Appendix 4).
11. Participants may be discharged after all study procedures are completed. Participants will be in house for PK blood samples on Day 3 (48 h), Day 4 (72 h), Day 5 (96 h) and Day 6 (120 h) of both study periods.

Schedule of Assessments for Part 2: Repeated Doses for 11 days:

Measurement	**Screening** (within 30 days of Day 1 - carried out over multiple days - except as noted in footnotes)																		**Follow-up**
		Day –1	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Day 8**	**Day 9**	**Day 10**	**Day 11 0 h**	**Day 12 24 h**	**Day 13 48 h**	**Day 14 72 h**	**Day 15 96 h**	**Day 16 120 h**	**7-14 days after last dose**
Admission to Unit		X																	
Informed Consent	X																		
Medical/medication/ drug/alcohol history (Demographics)	X																		
Full Physical Examination	X													X					
Brief Physical Examination		X																	X
Height, Weight, BMI	X																		
Inclusion/Exclusion	X																		
Medical History	X																		
Vital Signs[1]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			X
12-lead ECG[2]	X	X	X	X	X		X			X			X	X					X
Echocardiogram[3]	X																		
Drug/alcohol/ /cotinine Screen	X	X																	
HbsAg, HCV, HIV Testing	X																		
Hem/Chem tests[4]	X	X		X		X		X		X			X			X			X
Urinalysis	X	X		X		X							X			X			X
Serum FSH (as appropriate)	X																		
Troponin I[5]	X	X	X	X			X			X			X			X			

Measurement	**Screening** (within 30 days of Day 1 - carried out over multiple days - except as noted in footnotes)	**Day –1**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Day 8**	**Day 9**	**Day 10**	**Day 11 0 h**	**Day 12 24 h**	**Day 13 48 h**	**Day 14 72 h**	**Day 15 96 h**	**Day 16 120 h**	**Follow-up 7-14 days after last dose**
24 h Holter Monitoring[6]	X																		
Pregnancy Test (females)	X	X																	X
Dosing of GSK2838232			X	X	X	X	X	X	X	X	X	X	X						
Plasma PK sampling[7]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Event Assessment[8]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Discharge from Unit															X[9]				
Out Patient Visit	X															X	X	X	X

BMI = Body Mass Index; ECG = Electrocardiogram; FSH = Follicle Stimulating Hormone; HbsAg = Hepatitis B surface Antigen; HCV = Hepatitis C Virus; Hem/Chem = Hematology/Clinical Chemistry; HIV = Human Immunodeficiency Virus; IP = Investigational Product; PK = Pharmacokinetic(s).

1. A single blood pressure (BP) and Heart rate (HR) assessment will be collected at screening and Day -1. On Day 1 triplicate BP and HR will be collected at pre-dose and single assessments at 1, 4, 24, 48 and 72 h (Day 4) post-dose, Day 5, Day 6, Day 7, Day 8, Day 9, Day 10, Day 11 at pre-dose (triplicate), and single assessment at 1, 4, 24, 48 and 72 h post-dose, and at follow-up.
2. A single 12-Lead ECG will be collected at screening and Day -1. On Day 1 triplicate 12-Lead ECGs will be collected at pre-dose, and then single 12-Lead ECGs at 1, 4 and 12 h post-dose. Single 12-Lead ECGs will be collected on Days 2, 3, 5, 8. On Day 11 triplicate 12-Lead ECGs will be collected pre-dose, and then single 12-Lead ECGs collected at 1, 4, 12 and 24 h post-dose and at follow-up.
3. Echocardiograms must be within 100 days of Day 1.
4. Samples for Chemistry and Hematology: Blood samples will be obtained after an 8-hour fast.
5. Collect one troponin sample to be analyzed at local laboratory. A second sample will be collected and frozen for potential high sensitivity troponin analysis.
6. 24-h Holter monitoring to be performed after confirming negative urine drug screen at screening, and must be within 30 days of Day 1. Holter monitoring on other days only if needed.

7. Plasma PK samples for GSK2838232 will be collected as follows: Day 1; pre-dose (within 15 minutes prior to dosing) and 0.5,1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 12 and 24 h post-dose (prior to Day 2 dose). Days 3 to 10 pre-dose (within 15 minutes prior to dosing). Day 11; pre-dose (within 15 minutes prior to dosing) and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 12, 24, 36, 48, 72, 96 and 120 h post-dose. Samples will be acidified with an equal volume of 50 mmol citrate acid buffer pH 4.0.
8. An AE enquiry will be made at each visit, participants will be asked if they have experienced any neuropsychiatric adverse events, including psychosis or altered mental status. (see guidance for grading Altered Mental Status in Appendix 4).
9. Participants will be discharged after all study procedures are completed on the morning of Day 13 (after the 48 h post-final dose sample time point) with instructions to return fasted on the mornings of Day 14 for 72 h PK sample, Day 15 for 96 h PK sample, and Day 16 for 120 h PK sample

14.3 Appendix 3: Assessment Windows

14.3.1 Definitions of Assessment Windows for Analyses

Not applicable.

14.4 Appendix 4: Study Phases and Treatment Emergent Adverse Events

14.4.1 Study Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment.

Treatment Phase	Definition
Pre-Treatment	Date/Time < Study Treatment Start Date/Time
On- Treatment	Study Treatment Start Date/Time ≤ Date/Time ≤ Study Treatment Stop Date/Time
Post- Treatment	Date/Time > Study Treatment Stop Date/Time

14.4.4.1 Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before 28 days prior to screening visit
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

14.4.2 Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date is on or after treatment start date & on or before treatment stop date. (plus washout or protocol-specified time limit (e.g. half-life of drug, certain number of days, etc.). • Study Treatment Start Date/Time ≤ AE Start Date/Time. • For studies with greater than one treatment period (e.g., crossover study), if AE onset is during one period and worsens during a later period it would be counted in both periods. For the initial period the logic would be as above. For the later period the logic would use the treatment dates associated with the later period: • Treatment Period Start Date ≤ AE Worsening Date.

NOTES:

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

14.4.3 Adverse Events Assignment to Treatment Period for Part 1

Adverse events (AEs) will be assigned to a treatment period and corresponding treatment received in that treatment period after the imputations defined in RAP section 14.7.3 have been performed.

- Treatment Period 1: all AEs with start date/time at the time of or after IMP administration in Treatment Period 1 and before IMP administration in Treatment Period 2
- Treatment Period 2: all AEs with start date/time at the time of or after IMP administration in Treatment Period 2 and before IMP administration in Treatment Period 3
- Treatment Period 3: all AEs with start date/time at the time of or after IMP administration in Treatment Period 3

Thus, AEs occurring during the 1st washout will be assigned to the treatment received in Treatment Period 1, AEs occurring during the 2th washout will be assigned to the treatment received in Treatment Period 2 and AEs occurring during follow-up will be assigned to the treatment received in Treatment Period 3.

14.4.4 Concomitant Medication Assignment to Treatment Period for Part 1

Concomitant medications (CMs) will be assigned to a treatment period and corresponding treatment received in that treatment period after the imputations defined in RAP section 14.7.3 have been performed.

- Treatment Period 1: all CMs with start date/time at the time of or after IMP administration in Treatment Period 1 and before IMP administration in Treatment Period 2
- Treatment Period 2: all CMs with start date/time at the time of or after IMP administration in Treatment Period 2 and before IMP administration in Treatment Period 3
- Treatment Period 3: all CMs with start date/time at the time of or after IMP administration in Treatment Period 3

Thus, CMs occurring during the 1st washout will be assigned to the treatment received in Treatment Period 1, CMs occurring during the 2th washout will be assigned to the treatment received in Treatment Period 2 and CMs occurring during follow-up will be assigned to the treatment received in Treatment Period 3.

14.5 Appendix 5: Data Display Standards & Handling Conventions

14.5.1 Reporting Process

Software
• The currently supported versions of SAS and WinNonlin software will be used.
Analysis Datasets
• Analysis datasets will be created according to AdaM IG Version 1.1. • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM. • Define XML Version 2.0
Generation of RTF Files
• RTF files will be generated for Tables, Listings, and Figures, one RTF file per item.

14.5.2 Reporting Standards

General
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics • Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings
Formats
• GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of decimal places (DP's).
Planned and Actual Time
• Reporting for tables, figures and formal statistical analyses: • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate. • Reporting for Data Listings: • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). • Unscheduled or unplanned readings will be presented within the participant's listings.
Unscheduled Visits

• Unscheduled visits will not be included in summary tables and/or figures.   • All unscheduled visits will be included in listings.
Descriptive Summary Statistics
Continuous Data: Refer to IDSL Statistical Principle 6.06.1
Categorical Data: N, n, frequency, %
Graphical Displays
• Refer to IDSL Statistical Principals 7.01 to 7.13 • The same symbol and line type will be used across figures to represent a given treatment group. The placebo group will be displayed using symbol type=empty circle and line type= solid line and color=black. • When line plots are presented with treatment groups overlaid, the x-values will be offset (jittered) so the data are not plotted on top of each other. • X-axis variables of time and dose will be plotted as continuous numeric variables..

14.5.3 Reporting Standards for Pharmacokinetic Data

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to Standards for the Transfer and Reporting of PK Data using HARP. Note: Concentration values will be imputed as per GUI_51487
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	The following PK parameters will be derived by the Programmer: C24, Cτ, Ctrough. Ro[AUC(0-τ)], R(Cmax), R(Cτ)
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	No
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.

Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)

Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log_e Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between and or within geometric coefficient of variation (CVb/w (%)) will be reported. [1] Geometric mean = exp(mean log_e-transformed values) [2] CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data) [3] CV_w (%) = $\sqrt{}$ (exp(MSE) - 1) * 100 (MSE = mean square error from mixed effect model of loge-transformed data).
All Parameters	N, n, mean, SD, median, minimum, maximum
Summary Tables	The following PK parameters will not be summarised: %AUCex
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13. • The same symbol and line type will be used across figures to represent a given treatment group. The placebo group will be displayed using symbol type=empty circle and line type= solid line and color=black. • When line plots are presented with treatment groups overlaid, the x-values will be offset (jittered) so the data are not plotted on top of each other. • X-axis variables of time and dose will be plotted as continuous numeric variables.	

14.6 Appendix 6: Derived and Transformed Data

14.6.1 General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window (as per Section 14.3.1) the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean will be taken. • Participants having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from First Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date
  • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

14.6.2 Study Population

Demographics
Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  o Any participant with a missing day will have this imputed as day '15'.
  o Any participant with a missing date and month will have this imputed as '30th June'.
  o The age will be calculated by Data Management and mapped from ClinBase to SDTM dataset DM
• Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**
Treatment Compliance
• Treatment compliance will be calculated based on the formula: **Treatment Compliance = Number of Actual Doses / (Planned Treatment Duration in Days * Frequency)** • Frequency is 2 for BID and 1 for QD. Treatment compliance could be greater than 100% if there are events of overdose. Cumulative compliance (since Day 1) at each visit will be calculated. • Planned Treatment Duration is defined as 1 day for study part 1, and as 11 day for study part 2.
Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1** • Participants who were randomized but did not report a treatment start date will be categorised

Demographics

as having zero days of exposure.

- The cumulative dose will be based on the formula:

  Cumulative Dose = Sum of (Number of Days x Total Daily Dose)

- If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

14.6.3 Efficacy

Not applicable.

14.6.4 Safety

ECG Parameters

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as :

  [1] If QTcB is machine read & QTcF is not provided, then :

$$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$

  [2] If QTcF is machine read and QTcB is not provided, then:

$$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$

- If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.

Corrected QT Intervals

- When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.
- IF RR interval (msec) is provided then missing QTcB and/or QTcF will be derived as :

$$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

- Also QTc interval will be categorized as follows:

ECG Parameter	Potential Clinical Importance Range (PCI)	Units
Absolute QTc Interval	>450 to ≤480	msec
Absolute QTc Interval	>480 to ≤500	msec
Absolute QTc Interval	>500	msec
Increase from Baseline QTc	≤30	msec
Increase from Baseline QTc	>30 to ≤60	msec
Increase from Baseline QTc	>60	msec

Laboratory Parameters
• If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, will be imputed with the value of the number without the sign for the descriptive statistics and the calculation of changes from baseline, e.g., a value of <2.2 will be imputed as 2.2 for the calculations. There will be no imputation in the data listings; all values will be displayed as recorded in the database.

14.6.5 Pharmacokinetic

Calculation of Pharmacokinetic Parameter Values Not Described in Section 9 (refer to GUI_51487 for pharmacokinetic analysis information)
lambda_z (terminal phase rate constant)
• Slope of the line determined by linear regression of logarithmically transformed concentration v. time data
%AUCex (percentage of AUC(0-∞) obtained by extrapolation)
• Calculated as 100 x [AUC(0-∞) – AUC(0-t)] / AUC(0-∞)

14.6.6 Population Pharmacokinetic (PopPK)

Not applicable.

14.6.7 Pharmacodynamic

Not applicable.

14.7 Appendix 7: Reporting Standards for Missing Data

14.7.1 Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as participants who has received the study treatment per the protocol and who has completed all phases of the study including the follow-up visit. • The end of the study is defined as the last participant's last visit. • Withdrawn participants will not be replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Withdrawal visits will be summarised as withdrawal visits.

14.7.2 Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument : o These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

14.7.3 Handling of Missing and Partial Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix : Treatment States and Phases. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates (i.e. no year specified) will remain

Element	Reporting Detail
	missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Element	**Reporting Detail**
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

14.8 Appendix 8: Values of Potential Clinical Importance

14.8.1 Laboratory Values

Division of AIDS (DAIDS, Version 2.0, November 2014) AE grades 2, 3, and 4 of lab abnormalities will be listed by subject, period/treatment, visit, and actual date and time.

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Female		0.54
		Δ from BL	↓0.075	
Hemoglobin	g/L	Male		180
		Female		180
		Δ from BL	↓25	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		30	
Calcium	mmol/L		2	2.75
Creatinine	μmol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Magnesium	mmol/L		0.5	1.23
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Total CO2	mmol/L		18	32

Liver Function			
Test Analyte	**Units**	**Category**	**Potential Clinical Importance Range**
ALT/SGPT	U/L	High	≥ 2x ULN
AST/SGOT	U/L	High	≥ 2x ULN
AlkPhos	U/L	High	≥ 2x ULN
T Bilirubin	µmol/L	High	≥ 1.5xULN
T. Bilirubin + ALT	µmol/L U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT

14.8.2 ECG

ECG Parameter	Units	Potential Clinical Importance Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		> 450
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110
Change from Baseline			
Increase from Baseline QTc	msec		> 60

14.8.3 Vital Signs

Vital Sign Parameter (Absolute)	Units	Potential Clinical Importance Range	
		Lower (<x)	Upper (>x)
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

14.9 Appendix 9: Population Pharmacokinetic (PopPK) Analyses

14.9.1 Population Pharmacokinetic (PopPK) Dataset Specification

Not applicable.

14.9.2 Population Pharmacokinetic (PopPK) Methodology

Not applicable.

14.10 Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

14.10.1 Pharmacokinetic / Pharmacodynamic Dataset Specification

Not applicable.

14.10.2 Pharmacokinetic / Pharmacodynamic Methodology

Not applicable.

14.11 Appendix 11: Abbreviations & Trade Marks

14.11.1 Abbreviations

Abbreviation	Description
A&R	Analysis and Reporting
ADaM	Analysis Data Model
AE	Adverse Event
AlkPhos	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANOVA	Analysis of Variance
AST	Aspartate Aminotransferase
ATC	Anatomical, Therapeutical, Chemical
AUC	Area-under-the-curve
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity
AUC(0-last)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration
AUC(0-t)	Partial area under the concentration-time curve to time
BMI	Body Mass Index
BP	Blood Pressure
C24	Observed concentration 24 hours post-dose, determined directly from the concentration-time data.
CDISC	Clinical Data Interchange Standards Consortium
Chem	Chemistry
CI	Confidence Interval
CL	Clearance
CM	Concomitant Medication
C_{max}	Maximum observed concentration, determined directly from the concentration-time data.
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSP	Clinical Study Protocol
CSR	Clinical Study Report
$C\tau$	Observed concentration at time τ
DLT	Dose-limiting Toxicity
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
FDA	Food and Drug Administration
FSH	Follicle Stimulating Hormone
GSK	GlaxoSmithKline
GUI	Guidance
HBsAG	Hepatitis-B-Virus Surface Antigen
HCV	Hepatitis C virus
Hem	Hematology
HIV	Human Immunodeficiency Virus

Abbreviation	Description
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IP	Investigational Product
Lambda_z	Terminal Phase Rate Constant
LOQ	Limit of Quantification
LS	Least Squares
MedDRA	Medical dictionary for Regulatory Activities
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PI	Principal Investigator
PK	Pharmacokinetics
PopPK	Population Pharmacokinetic
PP	Per Protocol
PT	Preferred Term
QCD	Quantitative Clinical Development
QD	Once daily
QTcB	Bazett's QT Interval Corrected for Heart Rate
QTcF	Frederica's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
Ro	Accumulation ratio
RTV	Ritonavir
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SD	Standard deviation
SDTM	Study Data Tabulation Model
SGOT	Serum GlutamicOxaloacetic Transaminas
SGPT	Serum Glutamic-Pyruvic Transaminase
SOC	System Organ Class
SOP	Standard Operation Procedure
SRT	Safety Review Team
$t_{½}$	Apparent terminal half-life
TA	Therapeutic Area
TFL	Tables, Figures & Listings
tlag	Lag-time (time delay between drug administration and first observed)
tlast	Time of last quantifiable concentration, determined directly from the concentration-time data.
tmax	Time to reach Cmax, determined directly from the concentration-time data.

14.11.2 Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
Not applicable

Trademarks not owned by the GlaxoSmithKline Group of Companies
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14.12 Appendix 12: List of Data Displays

14.12.1 Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.24	Not applicable
Efficacy	Not applicable	Not applicable
Safety	3.1 to 3.46	3.1 to 3.6
Pharmacokinetic	5.1 to 5.18	5.1 to 5.23
Section	**Listings**	
ICH Listings	1 to 67	
Other Listings	68 to 74	

14.12.2 Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 13: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

14.12.3 Deliverable [Priority]

Delivery [Priority] [1]	Description
SAC [1]	Final Statistical Analysis Complete

NOTES:

1. Indicates priority (i.e. order) in which displays will be generated for the reporting effort.

14.12.4 Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Participant Disposition					
1.1.	Safety	ES8	Summary of Participant Status and Reason for Study Withdrawal – Part 1	ICH E3, FDAAA, EudraCT Summarize by treatment /sequence and overall of each part	SAC [1]
1.2.	Safety	ES8	Summary of Participant Status and Reason for Study Withdrawal – Part 2	ICH E3, FDAAA, EudraCT Summarize by treatment /sequence and overall of each part	SAC [1]
1.3.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment – Part 1	ICH E3 Summarize by treatment /sequence and overall of each part	SAC [1]
1.4.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment – Part 2	ICH E3 Summarize by treatment /sequence and overall of each part	SAC [1]
1.5.	Safety	ES4	Summary of Participant Disposition at Each Study Epoch – Part 1	ICH E3	SAC [1]
1.6.	Safety	ES4	Summary of Participant Disposition at Each Study Epoch – Part 2	ICH E3	SAC [1]
1.7.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure – Part 1	Journal Requirements	SAC [1]
1.8.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure – Part 2	Journal Requirements	SAC [1]

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Protocol Deviation					
1.9.	Safety	DV1	Summary of Protocol Deviations – Part 1	ICH E3	SAC [1]
1.10.	Safety	DV1	Summary of Protocol Deviations – Part 2	ICH E3	SAC [1]
Population Analysed					
1.11.	Screened	SP1	Summary of Study Populations – Part 1	By treatment and combined overall	SAC [1]
1.12.	Screened	SP1	Summary of Study Populations – Part 2	By treatment and combined overall	SAC [1]
Demographic and Baseline Characteristics					
1.13.	Safety	DM3	Summary of Demographic Characteristics – Part 1	ICH E3, FDAAA, EudraCT	SAC [1]
1.14.	Safety	DM1	Summary of Demographic Characteristics – Part 2	ICH E3, FDAAA, EudraCT	SAC [1]
1.15.	Safety	DM11	Summary of Age Ranges – Part 1	EudraCT	SAC [1]
1.16.	Safety	DM11	Summary of Age Ranges – Part 2	EudraCT	SAC [1]
1.17.	Safety	DM5	Summary of Race and Racial Combinations – Part 1	ICH E3, FDA, FDAAA, EudraCT	SAC [1]
1.18.	Safety	DM5	Summary of Race and Racial Combinations – Part 2	ICH E3, FDA, FDAAA, EudraCT	SAC [1]
Prior and Concomitant Medications					

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.19.	Safety	MH4	Summary of Medical Conditions – Part 1	ICH E3.	SAC [1]
1.20.	Safety	MH4	Summary of Medical Conditions – Part 2	ICH E3	SAC [1]
1.21.	Safety	CM1	Summary of Concomitant Medications – Part 1	ICH E3.	SAC [1]
1.22.	Safety	CM1	Summary of Concomitant Medications – Part 2	ICH E3	SAC [1]
Exposure and Treatment Compliance					
1.23.	Safety	EX1	Summary of Exposure to Study Treatment – Part 1	ICH E3	SAC [1]
1.24.	Safety	EX1	Summary of Exposure to Study Treatment – Part 2	ICH E3	SAC [1]

14.12.5 Efficacy Tables

Not applicable.

14.12.6 Efficacy Figures

Not applicable.

14.12.7 Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity by System Organ Class and Preferred Term – Part 1	ICH E3 Use AE5A/B (with a Total column across all grades/severities.)	SAC [1]
3.2.	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity by System Organ Class and Preferred Term – Part 2	ICH E3 Use AE5A/B (with a Total column across all grades/severities.)	SAC [1]
3.3.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency – Part 1	ICH E3	SAC [1]
3.4.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency – Part 2	ICH E3	SAC [1]
3.5.	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Intensity – Part 1	ICH E3	SAC [1]
3.6.	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Intensity – Part 2	ICH E3	SAC [1]
3.7.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences) – Part 1	FDAAA, EudraCT	SAC [1]
3.8.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences) – Part 2	FDAAA, EudraCT	SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.9.	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events by Overall Frequency – Part 1	ICH E3	SAC [1]
3.10.	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events by Overall Frequency – Part 2	ICH E3	SAC [1]
3.11.	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency – Part 1	ICH E3	SAC [1]
3.12.	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency – Part 2	ICH E3	SAC [1]
Serious and Other Significant Adverse Events					
3.13.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) – Part 1	FDAAA, EudraCT	SAC [1]
3.14.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) – Part 2	FDAAA, EudraCT	SAC [1]
3.15.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency – Part 1	IDSL	SAC [1]
3.16.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency – Part 2	IDSL	SAC [1]
Laboratory: Chemistry					

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.17.	Safety	LB17	Summary of Worst Case Chemistry Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 1	ICH E3	SAC [1]
3.18.	Safety	LB17	Summary of Worst Case Chemistry Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 2	ICH E3	SAC [1]
3.19.	Safety	LB1	Summary of Chemistry Changes from Baseline – Part 1	ICH E3 Includes Baseline values..	SAC [1]
3.20.	Safety	LB1	Summary of Chemistry Changes from Baseline – Part 2	ICH E3 Includes Baseline values	SAC [1]
Laboratory: Hematology					
3.21.	Safety	LB17	Summary of Worst Case Hematology Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 1	ICH E3	SAC [1]
3.22.	Safety	LB17	Summary of Worst Case Hematology Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 2	ICH E3	SAC [1]
3.23.	Safety	LB1	Summary of Hematology Changes from Baseline – Part 1	ICH E3 Includes Baseline values.	SAC [1]
3.24.	Safety	LB1	Summary of Hematology Changes from Baseline – Part 2	ICH E3 Includes Baseline values.	SAC [1]
Laboratory: Urinalysis					
3.25.	Safety	LB15	Summary of Worst Case Urine Data Results Relative to Normal Range Criteria Post-Baseline Relative to Baseline – Part 1	ICH E3	SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.26.	Safety	LB15	Summary of Worst Case Urine Data Results Relative to Normal Range Criteria Post-Baseline Relative to Baseline – Part 2	ICH E3	SAC [1]
3.27.	Safety	LB1	Summary of Urine Changes from Baseline – Part 1	ICH E3 Includes Baseline values.	SAC [1]
3.28.	Safety	LB1	Summary of Urine Changes from Baseline– Part 2	ICH E3 Includes Baseline values.	SAC [1]
Laboratory: Abnormalities					
3.29.	Safety	LB1	Summary of Grade 1 or Higher Lab Abnormalities– Part 1	Summary of Treatment Emergent Lab toxicity only.	SAC [1]
3.30.	Safety	LB1	Summary of Grade 1 or Higher Lab Abnormalities – Part 2	Summary of Treatment Emergent Lab toxicity only.	SAC [1]
Laboratory: Hepatobiliary (Liver)					
3.31.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 1	IDSL	SAC [1]
3.32.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 1	IDSL	SAC [1]
3.33.	Safety	LIVER10	Summary of Subjects Meeting Emergent Hepatobiliary Laboratory Abnormalities Event Reporting – Part 1	IDSL	SAC [1]
3.34.	Safety	LIVER10	Summary of Subjects Meeting Emergent Hepatobiliary Laboratory Abnormalities Event Reporting – Part 2	IDSL	SAC [1]
ECG					
3.35.	Safety	EG1	Summary of ECG Findings –Part 1	IDSL Use ECG findings categories (and change from baseline categories, if applicable).	SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.36.	Safety	EG1	Summary of ECG Findings –Part 2	IDSL Use ECG findings categories (and change from baseline categories, if applicable).	SAC [1]
3.37.	Safety	EG2	Summary of Change from Baseline in ECG Values–Part 1	IDSL Includes Baseline values.	SAC [1]
3.38.	Safety	EG2	Summary of Change from Baseline in ECG Values–Part 2	IDSL Includes Baseline values.	SAC [1]
3.39.	Safety	EG1	Summary of Category of QTc Data–Part 1	IDSL	SAC [1]
3.40.	Safety	EG1	Summary of Category of QTc Data–Part 2	IDSL	SAC [1]
3.41.	Safety	EG1	Summary of Category of QTc Change from Baseline–Part 1	IDSL Includes Baseline values.	SAC [1]
3.42.	Safety	EG1	Summary of Category of QTc Change from Baseline –Part 2	IDSL Includes Baseline values.	SAC [1]
Vital Signs					
3.43.	Safety	VS1	Summary of Vital Signs – Part 1	ICH E3	SAC [1]
3.44.	Safety	VS1	Summary of Vital Signs – Part 2	ICH E3	SAC [1]
3.45.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 1	ICH E3 Includes Baseline values.	SAC [1]
3.46.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 2	ICH E3 Includes Baseline values.	SAC [1]

14.12.8 Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory Values					
3.1.	Safety	As EG9	Plot of Selected Clinical Lab Tests Mean Change from Baseline by Treatment and Time – Part 1	Only include scheduled visits and for selected lab test (BNP, Tnp1, ALT, AST, Bili) Plots will be presented with treatment groups overlaid	SAC [1]
3.2.	Safety	As EG9	Plot of Selected Clinical Lab Tests Mean Change from Baseline by Treatment and Time – Part 2	Only include scheduled visits and for selected lab test (BNP, Tnp1, ALT, AST, Bili) Plots will be presented with treatment groups overlaid	SAC [1]
ECG					
3.3.	Safety	EG9	Plot of Mean Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 1	Plots will be presented with treatment groups overlaid	SAC [1]
3.4.	Safety	EG9	Plot of Mean Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 2	Plots will be presented with treatment groups overlaid	SAC [1]
Vital Signs					
3.5.	Safety	As EG8	Box Plot of Change from Baseline for Vital Signs by Treatment and Time – Part 1	Plots will be presented with treatment groups overlaid	SAC [1]
3.6.	Safety	As EG8	Box Plot of Change from Baseline for Vital Signs by Treatment and Time – Part 2	Plots will be presented with treatment groups overlaid	SAC [1]

14.12.9 Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic					
5.1.	PK	PK14	Listing of Derived Plasma GSK2838232 PK Parameters – Part 1A	Sort by participant and treatment	SAC [1]
5.2.	PK	PK14	Listing of Derived Plasma GSK2838232 PK Parameters – Part 1B	Sort by participant and treatment	SAC [1]
5.3.	PK	PK13	Listing of Derived Plasma GSK2838232 PK Parameters – Part 2	Sort by participant and treatment	SAC [1]
Bioavailability					
5.4.	PK	PK01	Summary Statistics of Plasma GSK2838232 PK Concentration-Time Data, Bioavailability		SAC [1]
5.5.	PK	PK04	Summary Statistics of Derived Plasma GSK2838232 PK Parameters by Treatment, Bioavailability		SAC [1]
5.6.	PK	PK05	Summary Statistics of Log_e-transformed Derived Plasma GSK2838232 PK Parameters, Bioavailability		SAC [1]
5.7.	PK	Non-Standard1	Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Relative Bioavailability		SAC [1]
5.8.	PK	PK15	Listing of Individual Derived Plasma GSK2838232 PK Parameters Treatment Ratios	PK Parameter: AUC(0-inf), and Cmax Ratio: Tablet/Capsule	SAC [1]
Food Effect					
5.9.	PK	PK01	Summary Statistics of Plasma GSK2838232 PK Concentration-Time Data, Food Effect		SAC [1]
5.10.	PK	PK04	Summary Statistics of Derived Plasma GSK2838232 PK Parameters by Treatment, Food Effect		SAC [1]

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.11.	PK	PK05	Summary Statistics of Log_e-transformed Derived Plasma GSK2838232 PK Parameters, Food Effect		SAC [1]
5.12.	PK	Non-Standard2	Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Food Effect		SAC [1]
5.13.	PK	PK15	Listing of Individual Derived Plasma GSK2838232 PK Parameters Treatment Ratios	PK Parameter: AUC(0-inf), Cmax, and tmax Ratio: Fed/Fasted	SAC [1]
Steady State Assessments and Accumulation					
5.14.	PK	PK04	Summary Statistics of Plasma GSK2838232 PK Parameters by Treatment and by Day – Part 2	Day 1 & Day 11	SAC [1]
5.15.	PK	PK04	Summary Statistics of Derived Plasma GSK2838232 PK Parameters by Treatment and by Day – Part 2	Day 1 & Day 11	SAC [1]
5.16.	PK	PK05	Summary of Log_e-transformed Derived Plasma GSK2838232 PK Parameters by Treatment and by Day – Part 2	Day 1 & Day 11	SAC [1]
5.17.	PK	Non-Standard3	Summary of Results of GSK2838232 PK Parameter Treatment Comparisons -Accumulation Assessments- Part 2	One for each treatment	SAC [1]
5.18.	PK	Non-Standard4	Summary Results of Steady State GSK2838232 Concentrations Assessments- Part 2	One for each treatment	SAC [1]

14.12.10 Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Biovailability					
5.1.	PK	PK16B	Individual Plasma GSK2838232 PK Concentration-Time Plots for Relative Bioavailability	Linear and Semi-Log Scale By participant, overlay all treatments for each participant	SAC [1]
5.2.	PK	PK17	Mean Plasma GSK2838232 PK Concentration for Relative Bioavailability	Linear and Semi-Log Scale Overlay all treatments	SAC [1]
5.3.	PK	PK18	Median Plasma GSK2838232 PK Concentration for Relative Bioavailability	Linear and Semi-Log Scale Overlay all treatments	SAC [1]
5.4.	PK	PK28	Geometric Mean Treatment Ratio and 90% Confidence Interval of GSK2838232 PK Parameter for the Relative Bioavailability		SAC [1]
5.5.	PK	PK25	Comparative Plot of Individual Plasma GSK2838232 PK Parameters for Relative Bioavailability by treatment		SAC [1]
Food Effect					
5.6.	PK	PK16A	Individual Plasma GSK2838232 PK Concentration-Time Plots for Food Effect	Linear and Semi-Log Scale By participant, overlay all treatments for each participant	SAC [1]
5.7.	PK	PK17	Mean Plasma GSK2838232 PK Concentration for Food Effect	Linear and Semi-Log Scale Overlay all treatments	SAC [1]
5.8.	PK	PK18	Median Plasma GSK2838232 PK Concentration for Food Effect	Linear and Semi-Log Scale Overlay all treatments	SAC [1]
5.9.	PK	PK28	Geometric Mean Treatment Ratio and 90% Confidence Interval of GSK2838232 PK Parameter for Food Effect		SAC [1]

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.10.	PK	PK25	Comparative Plot of Individual Plasma GSK2838232 PK Parameters for Food Effect by treatment		SAC [1]
Steady State Assessments and Accumulation					
5.11.	PK	PK16a	Individual Plasma GSK2838232 PK Concentration-Time Plots by Day – Part 2	Linear and Semi-Log Scale By participant, overlay days for each participant	SAC [1]
5.12.	PK	PK17	Mean Plasma GSK2838232 PK Concentration by Day – Part 2	Linear and Semi-Log Scale	SAC [1]
5.13.	PK	PK18	Median Plasma GSK2838232 PK Concentration by Day – Part 2	Linear and Semi-Log Scale	SAC [1]
5.19.	PK	PK16a	Individual Plasma GSK2838232 Predose Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Overlay all individual profile with all days profiles	SAC [1]
5.20.	PK	PK17	Mean Plasma GSK2838232 Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale	SAC [1]
5.21.	PK	PK18	Median Plasma GSK2838232 Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale	SAC [1]
5.22.	PK	PK16a	Individual and Box Plot of Plasma GSK2838232 PK Parameters by Day – Part 2	Include all the PK parameters.	SAC [1]
5.23.	PK	PK25	Comparative Plot of Plasma GSK2838232 PK Parameters for Accumulation	Linear and Log Scale	SAC [1]

14.12.11 Pharmacokinetic Population (PopPK) Tables

Not applicable.

14.12.12 Pharmacokinetic Population (PopPK) Figures

Not applicable.

14.12.13 Pharmacodynamic Tables

Not applicable.

14.12.14 Pharmacodynamic Figures

Not applicable.

14.12.15 Pharmacokinetic / Pharmacodynamic Tables

Not applicable.

14.12.16 Pharmacokinetic / Pharmacodynamic figures

Not applicable.

14.12.17 ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Participant Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure – Part 1	Journal Guidelines	SAC [1]
2.	Screened	ES7	Listing of Reasons for Screen Failure – Part 2	Journal Guidelines	SAC [1]
3.	Safety	ES3	Listing of Reasons for Study Withdrawal – Part 1	ICH E3	SAC [1]
4.	Safety	ES2	Listing of Reasons for Study Withdrawal – Part 2	ICH E3	SAC [1]
5.	Safety	SD3	Listing of Reasons for Study Treatment Discontinuation – Part 1	ICH E3	SAC [1]
6.	Safety	SD2	Listing of Reasons for Study Treatment Discontinuation – Part 2	ICH E3	SAC [1]
7.	Safety	BL1	Listing of Participants for Whom the Treatment Blind was Broken – Part 2	ICH E3	SAC [1]
8.	Safety	CP_RA1x	Listing of Planned and Actual Treatments – Part 1	IDSL	SAC [1]
9.	Safety	CP_RA1p	Listing of Planned and Actual Treatments – Part 2	IDSL	SAC [1]
Protocol Deviations					
10.	Safety	DV2A	Listing of Important Protocol Deviations – Part 1	ICH E3 Listing also includes analysis population exclusions.	SAC [1]
11.	Safety	DV2	Listing of Important Protocol Deviations – Part 2	ICH E3 Listing also includes analysis population exclusions.	SAC [1]
12.	Safety	IE4	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part 1	ICH E3	SAC [1]
13.	Safety	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part 2	ICH E3	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Populations Analysed					
14.	Safety	SP3A	Listing of Participants Excluded from Any Population – Part 1	ICH E3	SAC [1]
15.	Safety	SP3	Listing of Participants Excluded from Any Population – Part 2	ICH E3	SAC [1]
Demographic and Baseline Characteristics					
16.	Safety	DM4	Listing of Demographic Characteristics – Part 1	ICH E3	SAC [1]
17.	Safety	DM2	Listing of Demographic Characteristics – Part 2	ICH E3	SAC [1]
18.	Safety	DM10	Listing of Race – Part 1	ICH E3	SAC [1]
19.	Safety	DM9	Listing of Race – Part 2	ICH E3	SAC [1]
Prior and Concomitant Medications					
20.	Safety	CP_CM4	Listing of Concomitant Medications – Part 1	IDSL	SAC [1]
21.	Safety	CP_CM3	Listing of Concomitant Medications – Part 2	IDSL	SAC [1]
Exposure and Treatment Compliance					
22.	Safety	EX4	Listing of Exposure Data – Part 1	ICH E3	SAC [1]
23.	Safety	EX3	Listing of Exposure Data – Part 2	ICH E3	SAC [1]
Adverse Events					
24.	Safety	CP_AE9	Listing of All Adverse Events – Part 1	ICH E3	SAC [1]
25.	Safety	CP_AE8	Listing of All Adverse Events – Part 2	ICH E3	SAC [1]
26.	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events – Part 1	ICH E3	SAC [1]
27.	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events – Part 2	ICH E3	SAC [1]
28.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part 1	IDSL	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part 2	IDSL	SAC [1]
Serious and Other Significant Adverse Events					
30.	Safety	CP_AE9a	Listing of Fatal Serious Adverse Events – Part 1	ICH E3	SAC [1]
31.	Safety	CP_AE8a	Listing of Fatal Serious Adverse Events – Part 2	ICH E3	SAC [1]
32.	Safety	CP_AE9a	Listing of Non-Fatal Serious Adverse Events – Part 1	ICH E3	SAC [1]
33.	Safety	CP_AE8a	Listing of Non-Fatal Serious Adverse Events – Part 2	ICH E3	SAC [1]
34.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC [1]
35.	Safety	CP_AE9a	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment – Part 1	ICH E3	SAC [1]
36.	Safety	CP_AE8a	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment – Part 2	ICH E3	SAC [1]
37.	Safety	CP_AE9a	Listing of Grade 3 or 4 Adverse Events – Part 1	Division of AIDS Table For Grading	SAC [1]
38.	Safety	CP_AE8a	Listing of Grade 3 or 4 Adverse Events – Part 2	Division of AIDS Table For Grading	SAC [1]
Hepatobiliary (Liver)					
39.	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events – Part 1	IDSL	SAC [1]
40.	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events – Part 2	IDSL	SAC [1]
41.	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events – Part 1	IDSL	SAC [1]
42.	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events – Part 2	IDSL	SAC [1]
All Laboratory					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
43.	Safety	LB13	Listing of Reference Ranges for Clinical Laboratory Tests		SAC [1]
44.	Safety	LB6	Listing of Hematology Data– Part 1	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	SAC [1]
45.	Safety	LB5	Listing of Hematology Data– Part 2	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	SAC [1]
46.	Safety	LB6	Listing of Clinical Chemistry Data– Part 1	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	SAC [1]
47.	Safety	LB5	Listing of Clinical Chemistry Data– Part 2	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	SAC [1]
48.	Safety	LB6	Listing of Urinalysis Data– Part 1	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	SAC [1]
49.	Safety	LB5	Listing of Urinalysis Data– Part 2	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
50.	Safety	LB6	Listing of All Laboratory Data for Participants with Any Value of Potential Clinical Importance– Part 1	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a participant who experienced a value of potential clinical importance.	SAC [1]
51.	Safety	LB5	Listing of All Laboratory Data for Participants with Any Value of Potential Clinical Importance– Part 2	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a participant who experienced a value of potential clinical importance.	SAC [1]
52.	Safety	LB6	Listing of Lab Results Identified as Adverse Events– Part 1	Lab results identified as AEs. Only needed if there are a sufficient number of labs identified as AEs.	SAC [1]
53.	Safety	LB5	Listing of Lab Results Identified as Adverse Events – Part 2	Lab results identified as AEs. Only needed if there are a sufficient number of labs identified as AEs.	SAC [1]
54.	Safety	LB6	Listing of Grade 2 or Higher Lab Abnormalities – Part 1		SAC [1]
55.	Safety	LB5	Listing of Grade 2 or Higher Lab Abnormalities – Part 2		SAC [1]
56.	Safety	LB14	Listing of Laboratory Data with Character Results – Part 1	ICH E3	SAC [1]
57.	Safety	LB14	Listing of Laboratory Data with Character Results – Part 2	ICH E3	SAC [1]
58.	Safety	UR2B	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part 1	ICH E3 Display ALL data for a participant who experienced a value of potential clinical importance.	SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
59.	Safety	UR2A	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part 2	ICH E3 Display ALL data for a participant who experienced a value of potential clinical importance.	SAC [1]
ECG and Holter					
60.	Safety	EG4	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance – Part 1	IDSL	SAC [1]
61.	Safety	EG3	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance – Part 2	IDSL	SAC [1]
62.	Safety	EG6	Listing of All ECG Findings for Participants with an Abnormal ECG Finding – Part 1	IDSL	SAC [1]
63.	Safety	EG5	Listing of All ECG Findings for Participants with an Abnormal ECG Finding – Part 2	IDSL	SAC [1]
64.	Safety	HM8	Listing of Holter Monitoring – Part 1	IDSL	SAC [1]
65.	Safety	HM8	Listing of Holter Monitoring – Part 2	IDSL	SAC [1]
Vital Signs					
66.	Safety	VS5	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance – Part 1	IDSL	SAC [1]
67.	Safety	VS4	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance – Part 2	IDSL	SAC [1]

14.12.18 Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic					
68.	PK	PK08	Listing of Plasma GSK2838232 PK Concentration-Time Data – Part 1A	Sort by participant, treatment, day, and time	SAC [1]
69.	PK	PK08	Listing of Plasma GSK2838232 PK Concentration-Time Data – Part 1B	Sort by participant, treatment, day, and time	SAC [1]
70.	PK	PK07	Listing of Plasma GSK2838232 PK Concentration-Time Data – Part 2	Sort by participant, treatment, day, and time	SAC [1]
PK Statistical Analysis					
71.	PK	SAS output of Table5.6	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons for the Relative Bioavailability – Part 1A		SAC [1]
72.	PK	SAS output of Table 5.10	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons for the Food Effect – Part 1B		SAC [1]
73.	PK	SAS output of Table 5.16	SAS Output of Summary Results of Steady-State GSK2838232 Concentrations Assessment – Part 2		SAC [1]
74.	PK	SAS output of Table 5.17	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons – Accumulation Ratio – Part 2		SAC [1]

14.13 Appendix 13: Example Mock Shells for Data Displays

Example: Non-Standard1

Protocol: XXXXXX
Population: PK Parameter

Table X.XX
Summary Results of Treatment Comparisons for the Relative Bioavailability - Part 1B

PK Parameter	Comparison Test/Ref.	Geometric LSMean A (N=12)	Geometric LSMean G (N=12)	Ratio	90% Confidence Interval	CVw(%)
AUC (0-inf) (h*ng/mL)	G vs A	1029.925	1469.603	1.4269	(1.1962,1.7021)	24.18
AUC (0-t) (h*ng/mL)	G vs A	989.181	1443.028	1.4588	(1.2320,1.7274)	23.14
AUC (0-24) (h*ng/mL)	G vs A	460.663	681.540	1.4795	(1.2479,1.7541)	23.32
Cmax (ng/mL)	G vs A	30.126	47.561	1.5787	(1.3118,1.9000)	25.43
C24 (ng/mL)	G vs A	15.382	21.782	1.4161	(1.2044,1.6649)	22.14
t1/2 (h)	G vs A	19.770	18.779	0.9499	(0.8578,1.0519)	13.85

A: Treatment description
G:Treatment description

Example: Non-Standard2

Protocol: XXXXXX
Population: PK Parameter

Table X.XX
Summary Results of Treatment Comparisons for the Food Effect - Part 1B

PK Parameter	Comparison Test/Ref.	Geometric LSMean G (N=12)	Geometric LSMean F (N=11)	Ratio	90% Confidence Interval	CVw(%)
AUC (0-inf) (h*ng/mL)	F (Fed) Vs G (Fasted)	1469.603	2327.794	1.5840	(1.4120,1.7768)	14.95
AUC (0-t) (h*ng/mL)	F (Fed) Vs G (Fasted)	1443.028	2299.310	1.5934	(1.4185,1.7899)	15.13
AUC (0-24) (h*ng/mL)	F (Fed) Vs G (Fasted)	681.540	1048.089	1.5378	(1.3761,1.7185)	14.50
Cmax (ng/mL)	F (Fed) Vs G (Fasted)	47.561	77.132	1.6217	(1.3762,1.9111)	21.81
C24 (ng/mL)	F (Fed) Vs G (Fasted)	21.782	35.718	1.6398	(1.4417,1.8653)	16.80
t1/2 (h)	F (Fed) Vs G (Fasted)	18.779	18.582	0.9895	(0.9155,1.0695)	10.14

G: GSKXXXXXX Capsule 100mg + XXX
F: GSKXXXXXX Capsule 100mg + Food + XXX

Example: Non-Standard3

Protocol: XXXXXX
Population: PK Parameter

Table X.XX
Summary Results of GSKXXXXXX PK Parameter Treatment Comparisons - Accumulation Ratio - Part 2

	Treatment	Comparison Test/Ref.	Geometric LSmean Ref.	Geometric LSmean Test.	Ratio	90% Confidence Interval	CVb(%)
Accumulation Ratio AUC(0-tau)	RD20mg+RTV	Day 11 vs Day 1	175.060	449.021	2.5650	(1.9931,3.3008)	21.94
	RD50mg+RTV	Day 11 vs Day 1	265.413	1087.465	4.0973	(2.7102,6.1943)	36.68
	CapRD100mg+RTV	Day 11 vs Day 1	635.446	2411.467	3.7949	(2.8185,5.1096)	25.99
	CapRD200mg+RTV	Day 11 vs Day 1	1056.386	4014.085	3.7998	(3.1234,4.6227)	16.97
	CapRDQ12H200mg	Day 11 vs Day 1	267.134	742.180	2.7783	(2.3991,3.2175)	12.67
Accumulation Ratio Cmax	RD20mg+RTV	Day 11 vs Day 1	11.109	25.335	2.2807	(1.6717,3.1114)	27.18
	RD50mg+RTV	Day 11 vs Day 1	17.098	56.614	3.3111	(2.2479,4.8771)	34.23
	CapRD100mg+RTV	Day 11 vs Day 1	46.172	129.785	2.8109	(2.0427,3.8681)	27.97
	CapRD200mg+RTV	Day 11 vs Day 1	75.033	224.886	2.9972	(2.4531,3.6619)	17.35
	CapRDQ12H200mg	Day 11 vs Day 1	51.237	96.085	1.8753	(1.6520,2.1288)	10.93
Accumulation Ratio Ctau	RD20mg+RTV	Day 11 vs Day 1	5.673	14.525	2.5604	(2.0159,3.2521)	20.77
	RD50mg+RTV	Day 11 vs Day 1	8.919	37.403	4.1939	(2.8754,6.1169)	33.31
	CapRD100mg+RTV	Day 11 vs Day 1	20.560	78.196	3.8033	(2.6625,5.4329)	31.39
	CapRD200mg+RTV	Day 11 vs Day 1	36.696	136.681	3.7247	(2.9585,4.6892)	19.99
	CapRDQ12H200mg	Day 11 vs Day 1	18.364	39.144	2.1315	(1.7403,2.6107)	17.56

Example: Non-Standard4

Protocol: XXXXXX
Population: PK Parameter

Table X.XX
Summary Results of Steady-State GSK XXXXXX Concentrations Assessment - Part 2

Included Days	Treatment	Slope	90% Confidence Interval
Days 3-11	RD20mg+RTV	0.023	(0.009,0.037)
	RD50mg+RTV	0.082	(0.065,0.100)
	CapRD100mg+RTV	0.058	(0.044,0.072)
	CapRD200mg+RTV	0.033	(0.018,0.047)
	CapRDQ12H200mg	0.007	(-0.005,0.019)
Days 4-11	RD20mg+RTV	0.006	(-0.009,0.020)
	RD50mg+RTV	0.063	(0.046,0.081)
	CapRD100mg+RTV	0.037	(0.022,0.051)
	CapRD200mg+RTV	0.003	(-0.008,0.015)
	CapRDQ12H200mg	0.004	(-0.010,0.018)
Days 5-11	RD20mg+RTV	-0.012	(-0.029,0.005)
	RD50mg+RTV	0.038	(0.022,0.053)
	CapRD100mg+RTV	0.013	(-0.001,0.027)
	CapRD200mg+RTV	-0.004	(-0.018,0.010)
	CapRDQ12H200mg	0.001	(-0.019,0.020)
Days 6-11	RD20mg+RTV	-0.021	(-0.041,-0.001)
	RD50mg+RTV	0.029	(0.010,0.048)
	CapRD100mg+RTV	0.008	(-0.011,0.028)
	CapRD200mg+RTV	-0.009	(-0.027,0.009)
	CapRDQ12H200mg	0.001	(-0.022,0.025)

STATISTICAL ANALYSIS PLAN ADDENDUM

205820

Reporting and Analysis Plan for: A Two Part Study to Assess i) the Relative Bioavailability and Food Effect of a Novel Tablet Formulation of Boosted-GSK2838232 Compared to Capsule and ii) the Safety and Pharmacokinetics of Repeated Once-Daily Doses of Non boosted GSK2838232

Version: Final 1.0

Date: 16/Apr/2018

REVISION HISTORY

Version	Version Date	Author	Summary of Changes Made
Final 1.0	See Footer	PPD	New Document

SIGNATURE PAGE - GLAXOSMITHKLINE RESEARCH & DEVELOPMENT LIMITED

Declaration

The undersigned has/have reviewed and agree to the statistical analyses and procedures of this clinical study as presented in this document.

PPD

Date (DD Mmm YY)

Principal Biostatistician (PCPS, GSK)

PPD

Date (DD Mmm YY)

Director, Clinical Pharmacology (CPMS, GSK)

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Date (DD Mmm YY)

Principal Clinical Research Scientist (CPSSO, GSK)

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Date (DD Mmm YY)

Sm Executive Medical Director (GSK)

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Principal Programmer (PCPS, GSK)

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Principal Data Manager (CPSSO, GSK)

Date (DD Mmm YY)

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Senior Director, Biostatistics (PCPS, GSK)

Date (DD Mmm YY)

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Manager, Programming (PCPS, GSK)

Date (DD Mmm YY)

SIGNATURE PAGE - PAREXEL

Declaration

The undersigned agree to the statistical analyses and procedures of this clinical study.

If this document has been signed electronically, signature(s) and date(s) are present at the end of the document:

Document prepared and approved by:

PPD

Date (DD Mmm YY)

Sr. Biostatistician

Document prepared and approved by:

PPD

Date (DD Mmm YY)

QCD Senior Scientific

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LIST OF TABLES

ABBREVIATION AND ACRONYM LIST

Abbreviation / Acronym	Definition / Expansion
AUC	Area under the concentration-time curve
$AUC_{(0\text{-inf})}$	AUC from time zero extrapolated to infinity
$AUC_{(0\text{-t})}$	AUC from time zero to the last quantifiable concentration
$AUC_{(0\text{-}\tau),ss}$	AUC over the dosing interval at steady state
BLQ	Below the lower limit of quantification
CI	Confidence interval
C_{last}	Last quantifiable concentration at t_{last}
CL_R	Renal clearance
CL/F	Apparent clearance following oral administration
$CL/F_{,ss}$	Apparent clearance following oral administration at steady state
CSP	Clinical Study Protocol
C_{max}	Maximum observed concentration
C_{min}	Minimum observed concentration in the dosing interval
C_{trough}	Concentration immediately prior to dosing
CV	Coefficient of variation
PK	Pharmacokinetic
R_{ac}	Accumulation ratio
RAP	Report And Analysis Plan
SAP	Statistical Analysis Plan
SD	Standard deviation
SE	Standard error of the mean
$t_{½}$	Apparent terminal elimination half-life
$t_{½,ss}$	Apparent terminal elimination half-life at steady state
t_{last}	Time of last quantifiable concentration
t_{max}	Time corresponding to occurrence of C_{max}
λ_z	Terminal elimination rate constant
$\lambda_{z,ss}$	Terminal elimination rate constant at steady state
$\%AUC_{ex}$	Percentage of $AUC_{(0\text{-inf})}$ obtained by extrapolation

1. STATISTICAL ANALYSIS PLAN ADDENDUM

The Statistical Analysis Plan (SAP) Addendum details the changes and/or additional analyses required that are not currently described in the final RAP Version **1.0** dated 07/Dec/2017.The SAP Addendum describes any deviations from the planned analyses, additional analyses and if applicable, new Tables, Listings and Figures (TLFs) that are to be produced.

As Sponsor (GlaxoSmithKline Research & Development Limited) does not have any template available for RAP Addendum, PAREXEL Template of SAP Addendum is used to document the changes after database lock and finalization of the RAP.

2. OVERVIEW OF CHANGES REQUIRED

2.1 Summary of Changes

- Secondary end point is considered as pre-dose concentration on days 3 to 11 rather than pre-dose concentration on day 2 to 11. This is applicable to final RAP Sections 2.2, 2.4 and 9.2.5
- PK parameter Ctrough is calculated for days 3 to 11 rather than for days 2 to 11. This is applicable to final RAP Sections 9.1.1.2, and 9.2.1.2

  However Ctrough should not be considered as PK Parameter of the study and this should not be included in ADPP dataset and those values can only be used from ADPC dataset directly and use for Steady State Assessment only. No summary statistics will be provided for this PK parameter.
- Part 2 treatments is changed as Treatment R = GSK2838232 500 mg tablet fed rather than D=GSK2838232 500 mg/r tablet fed and Treatment P=Placebo than Treatment E=Placebo. This is applicable to final RAP Section 2.3
- Listing and summary of the protocol deviation should be presented for all Important Protocol Deviation rather than all Protocol Deviation. This is applicable to final RAP section 6.5.
- For each of the PK parameters given in section of RAP, for the summary statistics calculation, geometric mean associated with 95% CI should be calculated for each treatment group; however in RAP geometric mean associated with 90% CI should be calculated for each treatment group for the summary statistics. This is applicable to RAP sections 9.1.1.2 and 9.2.1.2
- In the statistical methodology, analysis for the steady state assessment should only be mentioned as predose concentrations from days 3 to 11, and no Ctrough or Ctau terminology will be considered for this analysis.

There will be no changes to the structure/format of the tables, figures and listings based on this change. The details of these changes are provided from sections 2.2 to 2.9 below. Details of the changes in the Tables, Listings and Figures are mainly due to clarity purpose (added more clarity in title, and programming notes) as well as some Tables and Listings are clubbed for better presentation, and hence due to that number of the tables, listings and figures are changed.

2.2 Study objective and secondary end point

In the final SAP Section **2.2** in the secondary objective section of part 2 is stated that secondary endpoint is pre-dose concentration on days 2 to 11. However, for the final analyses secondary endpoint is considered as pre-dose concentration on day 3 to 11.

2.3 Study Design

In the final SAP Section 2.3 in treatment assignment section it is stated that Part 2 treatment section states as below:

"Part 2 treatments:

Treatment D = GSK2838232 500 mg (as 5 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal (reference).

Treatment E = Placebo

However this should be like this:

"Part 2 treatments:

Treatment R = GSK2838232 500 mg (as 5 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal.

Treatment P = Placebo

2.4 Statistical Hypothesis/Statistical Analysis

For Part 2 study state assessment in the RAP section 2.4 it is stated as below:

Mean plasma GSK2838232 pre-dose values between Days 2 through 11 and $C\tau$ of Day 11 will be plotted against time.

However it should be as below:

Mean plasma GSK2838232 pre-dose values between Days 3 through 11 and $C\tau$ of Day 11 will be plotted against time.

2.5 Study Treatment and Sub-group Display Descriptors

In the RAP Section 5.1 Part 2 treatment group descriptors are given as below:

Treatment Group Descriptions – Part 2			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TFL
T3	GSK2838232 500 mg (as 5 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal (reference).	GSK 500 mg/r tablet fed	2
P	Placebo	Placebo	1

However it should be as follows:

Treatment Group Descriptions – Part 2			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TFL
T3	GSK2838232 500 mg (as 5 x 100 mg) tablet formulation, fed, normal fat (i.e., approximately 30%) meal (reference).	GSK 500 mg tablet fed	2
P	Placebo	Placebo	1

2.6 Concomitant Medications

As per RAP Section 6.4 it is stated that "in the summary of concomitant medications, the ingredients will be summarized by the base only, using CMBASECD and CMBASE". However this is not followed.

2.7 Treatment Compliance and Protocol Deviations

In RAP Section 6.5 it is stated below:

"Information of each participant not received the correct treatment during each treatment period, the reason for not receiving the correct treatment, and any other protocol deviations will be summarized by treatment sequence/group and overall of each part, and listed by participant and period (treatment). In addition, a listing will be provided including dose administered along with dosing dates and time for the investigational product.

However it should be as below:

Information of each participant not received the correct treatment during each treatment period, the reason for not receiving the correct treatment, and any other important protocol deviations will be summarized by treatment and overall of each part if enough important protocol deviations occur, and listed by participant and period (treatment). In addition, a listing will be provided including dose administered along with dosing dates and time for the investigational product.

2.8 Derived Pharmacokinetic Parameters

In final RAP section 9.1.1.2, details of derived pharmacokinetic parameter are given as follows:

Parameter	Parameter Description
AUC(0-τ)	Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval (where τ = 24 h) (Day 1 and Day 11)
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-last) + C(last) / lambda_z**

Parameter	Parameter Description
Cmax	Maximum observed concentration, determined directly from the concentration-time data. (Day 1 and Day 11)
Tmax	Time of occurrence of Cmax, determined directly from the concentration-time data (Day 1 and Day 11)
Tlag	Lag-time (time delay between drug administration and first observed concentration), determined directly from the concentration-time data (Day 1)
Tlast	Time of last quantifiable concentration, determined directly from the concentration-time data (Day 11)
t½	Apparent terminal phase half-life, calculated as; t½ = ln2 / lambda_z (Day 11)
Cτ	Observed concentration at the end of the dosing interval, determined directly from the concentration-time data (where τ = 24 h) (Day 1 and Day 11)
Ctrough	Observed pre-dose concentrations on Days 3 to 11, determined directly from the concentration-time data

NOTES: C24, Cτ and Ctrough will be extracted from the concentration data by Clinical Statistics group and merged with other calculated PK parameters provided by CPMS.

All the derived parameters described above will be listed. For each of these parameters, except tmax and tlag, the following summary statistics will be calculated for each treatment group: n, arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean with associated 90% CI, standard deviation of logarithmically transformed data, and the between-participant CV (%CVb) based on the geometric mean for the loge-transformed PK parameters. For tmax and tlag, N, n, median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

However this should be as below:

Parameter	Parameter Description
AUC(0-τ)	Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval (where τ = 24 h) (Day 1 and Day 11)
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-last) + C(last) / lambda_z**
Cmax	Maximum observed concentration, determined directly from the concentration-time data. (Day 1 and Day 11)
Tmax	Time of occurrence of Cmax, determined directly from the concentration-time data (Day 1 and Day 11)
Tlag	Lag-time (time delay between drug administration and first observed concentration), determined directly from the concentration-time data (Day 1)
Tlast	Time of last quantifiable concentration, determined directly from the concentration-time data (Day 11)
t½	Apparent terminal phase half-life, calculated as; t½ = ln2 / lambda_z (Day 11)
Cτ	Observed concentration at the end of the dosing interval, determined directly from the

Parameter	Parameter Description
	concentration-time data (where τ = 24 h) (Day 1 and Day 11)

NOTES: C24, and Cτ will be extracted from the concentration data by Clinical Statistics group and merged with other calculated PK parameters provided by CPMS.

All the derived parameters described above will be listed. For each of these parameters, except tmax and tlag, the following summary statistics will be calculated for each treatment group: N, n, arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean with associated 95% CI, standard deviation of logarithmically transformed data, and the between-participant CV (%CVb) based on the geometric mean for the loge-transformed PK parameters. For tmax and tlag, N, n, median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

2.9 Statistical Analysis/Method

Part 2

Parameter	Parameter Description
Ctrough	Observed pre-dose concentrations on Days 3 to 11, determined directly from the concentration-time data
Ro[AUC(0-τ)]	Accumulation ratio based on AUC(0-τ), determined by; Day 11 AUC(0-τ) / Day 1 AUC(0-τ)
R(Cmax)	Accumulation ratio based on Cmax, determined by; Day 11 Cmax / Day 1 Cmax
R(Cτ)	Accumulation ratio based on Cτ, determined by; Day 11 Cτ / Day 1 Cτ

NOTES:

- Additional parameters may be included as required.
- Cτ, and Ctrough will be extracted from the concentration data by Clinical Statistics group and merged with other calculated PK parameters provided by CPMS.

All the derived parameters described above will be listed. For each of these parameters, except tmax and tlag, the following summary statistics will be calculated for each treatment group: n, arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean with associated 90% CI, standard deviation of logarithmically transformed data, and the between-participant CV (%CVb) based on the geometric mean for the loge-transformed PK parameters. For tmax and tlag, N, n,median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

However is should be as follows:

Part 2

Parameter	Parameter Description
Ro[AUC(0-τ)]	Accumulation ratio based on AUC(0-τ), determined by; Day 11 AUC(0-τ) / Day 1 AUC(0-τ)

Parameter	Parameter Description
R(Cmax)	Accumulation ratio based on Cmax, determined by; Day 11 Cmax / Day 1 Cmax
R(Cτ)	Accumulation ratio based on Cτ, determined by; Day 11 Cτ / Day 1 Cτ

NOTES:

- Additional parameters may be included as required.
- Cτ will be extracted from the concentration data by Clinical Statistics group and merged with other calculated PK parameters provided by CPMS.

All the derived parameters described above will be listed. For each of these parameters, except tmax and tlag, the following summary statistics will be calculated for each treatment group: N, n, arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean with associated 95% CI, standard deviation of logarithmically transformed data, and the between-participant CV (%CVb) based on the geometric mean for the loge-transformed PK parameters. For tmax and tlag, N, n,median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

As per final RAP Section 9.2.5, statistical methodology section of Part 2 Steady State Assessment, end point or variable is given as GSK2838232 pre-dose values between Days 2 through 11, however it should be GSK2838232 pre-dose values between Days 3 through 11.

3. TABLES/LISTINGS/FIGURES

3.1 Final Tables, Listings and Figures

Final Table, Listings and Figures that are used for the Final SAC deliverables are shown in tables 1 to 7 for Study Population Tables, Safety Tables, Safety Figures, Pharmacokinetic Tables, Pharmacokinetic Figures, ICH Listings and Non-ICH Listings respectively. The last column “Any Change from the RAP” specifies whether there is any change from RAP for respective Table, Listing or Figure.

Overview of changes from the RAP in final Tables, Listings and Figures are given in tables 8 to 14 for Study Population Tables, Safety Figures, Pharmacokinetic Tables, Pharmacokinetic Figures, ICH Listings and Non-ICH Listings respectively.

Tables 8 to 14 contain only the Tables, Listings and Figures which has any changes from the RAP. Column apart from “Changes from RAP” contains the details from the final RAP.

Table 1 Study Population Tables

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
1.1	Safety	ES8A	Summary of Participant Status and Reason for Study Withdrawal – Part 1	ICH E3, FDAAA, EudraCT Summarize by treatment /sequence and overall of each part	No
1.2	Safety	ES8	Summary of Participant Status and Reason for Study Withdrawal – Part 2	ICH E3, FDAAA, EudraCT Summarize by treatment /sequence and overall of each part	No
1.3	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment – Part 1	ICH E3 Summarize by treatment /sequence and overall of each part	No
1.4	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment – Part 2	ICH E3 Summarize by treatment /sequence and overall of each part	No
1.5	Safety	ES4	Summary of Participant Disposition at Each Study Epoch – Part 1	ICH E3	No
1.6	Safety	ES4	Summary of Participant Disposition at Each Study Epoch – Part 2	ICH E3	No
1.7	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure – Part 1	Journal Requirements	No
1.8	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure – Part 2	Journal Requirements	No
1.9	Safety	DV1	Summary of Important Protocol Deviations – Part 1	ICH E3. If important protocol deviation events are less than 15, please produce the summary with wording"not enough	Yes

				important protocol deviation to warren a summary".	
1.10	Safety	DV1	Summary of Important Protocol Deviations – Part 2	ICH E3. If important protocol deviation events are less than 15, please produce the summary with wording"not enough important protocol deviation to warren a summary".	Yes
1.11	Screened	SP1	Summary of Study Populations – Part 1	By treatment and combined overall	No
1.12	Screened	SP1	Summary of Study Populations – Part 2	By treatment and combined overall	No
1.13	Safety	DM3	Summary of Demographic Characteristics – Part 1	ICH E3, FDAAA, EudraCT	No
1.14	Safety	DM1	Summary of Demographic Characteristics – Part 2	ICH E3, FDAAA, EudraCT	No
1.15	Safety	DM11	Summary of Age Ranges – Part 1	EudraCT	No
1.16	Safety	DM11	Summary of Age Ranges – Part 2	EudraCT	No
1.17	Safety	DM5	Summary of Race and Racial Combinations – Part 1	ICH E3, FDA, FDAAA, EudraCT	No
1.18	Safety	DM5	Summary of Race and Racial Combinations – Part 2	ICH E3, FDA, FDAAA, EudraCT	No
1.19	Safety	MH4	Summary of Medical Conditions – Part 1	ICH E3	No
1.20	Safety	MH4	Summary of Medical Conditions – Part 2	ICH E3	No
1.21	Safety	CM8	Summary of Concomitant Medications – Part 1	ICH E3	No
1.22	Safety	CM8	Summary of Concomitant Medications – Part 2	ICH E3	No
1.23	Safety	EX1	Summary of Exposure to Study Treatment – Part 1	ICH E3	No
1.24	Safety	EX1	Summary of Exposure to Study Treatment – Part 2	ICH E3	No

Table 2 Safety Tables

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
3.1	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity by System Organ Class and Preferred Term – Part 1	ICH E3 Use AE5A/B (with a Total column across all grades/severities.)	No
3.2	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity by System Organ Class and Preferred Term – Part 2	ICH E3 Use AE5A/B (with a Total column across all grades/severities.)	No
3.3	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency – Part 1	ICH E3	No
3.4	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency – Part 2	ICH E3	No
3.5	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Intensity – Part 1	ICH E3	No
3.6	Safety	AE5A	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Intensity – Part 2	ICH E3	No
3.7	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences) – Part 1	FDAAA, EudraCT	No
3.8	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and	FDAAA, EudraCT	No

			Occurrences) – Part 2		
3.9	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events by Overall Frequency – Part 1	ICH E3	No
3.10	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events by Overall Frequency – Part 2	ICH E3	No
3.11	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency – Part 1	ICH E3	No
3.12	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency – Part 2	ICH E3	No
3.13	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) – Part 1	FDAAA, EudraCT	No
3.14	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) – Part 2	FDAAA, EudraCT	No
3.15	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency – Part 1	IDSL	No
3.16	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency – Part 2	IDSL	No
3.17	Safety	LB17	Summary of Worst Case Chemistry Results to Potential Clinical	ICH E3	No

			Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 1		
3.18	Safety	LB17	Summary of Worst Case Chemistry Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 2	ICH E3	No
3.19	Safety	LB1	Summary of Chemistry Changes from Baseline – Part 1	ICH E3 Includes Baseline values.	No
3.20	Safety	LB1	Summary of Chemistry Changes from Baseline – Part 2	ICH E3 Includes Baseline values.	No
3.21	Safety	LB17	Summary of Worst Case Hematology Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 1	ICH E3	No
3.22	Safety	LB17	Summary of Worst Case Hematology Results to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 2	ICH E3	No
3.23	Safety	LB1	Summary of Hematology Changes from Baseline – Part 1	ICH E3 Includes Baseline values.	No
3.24	Safety	LB1	Summary of Hematology Changes from Baseline – Part 2	ICH E3 Includes Baseline values.	No
3.25	Safety	LB15	Summary of Worst Case Urine Data Results Relative to Normal Range Criteria Post-Baseline Relative to Baseline – Part 1	ICH E3	No
3.26	Safety	LB15	Summary of Worst Case Urine Data Results Relative to Normal Range Criteria Post-Baseline Relative to Baseline – Part 2	ICH E3	No
3.27	Safety	LB1	Summary of Urine Changes from Baseline – Part 1	ICH E3 Includes Baseline values.	No

3.28	Safety	LB1	Summary of Urine Changes from Baseline– Part 2	ICH E3 Includes Baseline values.	No
3.29	Safety	LB1	Summary of Grade 1 or Higher Lab Abnormalities– Part 1	Summary of Treatment Emergent Lab toxicity only.	No
3.30	Safety	LB1	Summary of Grade 1 or Higher Lab Abnormalities – Part 2	Summary of Treatment Emergent Lab toxicity only.	No
3.31	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 1	IDSL	No
3.32	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 1	IDSL	No
3.33	Safety	LIVER10	Summary of Subjects Meeting Emergent Hepatobiliary Laboratory Abnormalities Event Reporting – Part 1	IDSL	No
3.34	Safety	LIVER10	Summary of Subjects Meeting Emergent Hepatobiliary Laboratory Abnormalities Event Reporting – Part 2	IDSL	No
3.35	Safety	EG1	Summary of ECG Findings –Part 1	IDSL Use ECG findings categories (and change from baseline categories, if applicable).	No
3.36	Safety	EG1	Summary of ECG Findings –Part 2	IDSL Use ECG findings categories (and change from baseline categories, if applicable).	No
3.37	Safety	EG2	Summary of Change from Baseline in ECG Values– Part 1	IDSL Includes Baseline values.	No
3.38	Safety	EG2	Summary of Change from Baseline in ECG Values– Part 2	IDSL Includes Baseline values.	No
3.39	Safety	EG1	Summary of Category of QTc Data–Part 1	IDSL	No
3.40	Safety	EG1	Summary of Category of	IDSL	No

			QTc Data–Part 2		
3.41	Safety	EG1	Summary of Category of QTc Change from Baseline–Part 1	IDSL Includes Baseline values.	No
3.42	Safety	EG1	Summary of Category of QTc Change from Baseline –Part 2	IDSL Includes Baseline values.	No
3.43	Safety	VS1	Summary of Vital Signs – Part 1	ICH E3	No
3.44	Safety	VS1	Summary of Vital Signs – Part 2	ICH E3	No
3.45	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 1	ICH E3 Includes Baseline values.	No
3.46	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 2	ICH E3 Includes Baseline values.	No

Table 3 Safety Figures

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
3.1	Safety	As EG9	Plot of Selected Clinical Lab Tests Mean (95% CI) Change from Baseline by Treatment and Time – Part 1	Only include scheduled visits and for selected lab test (BNP, Tnp1, ALT, AST, Bili) Plots will be presented with treatment groups overlaid	Yes
3.2	Safety	As EG9	Plot of Selected Clinical Lab Tests Mean (95% CI) Change from Baseline by Treatment and Time – Part 2	Only include scheduled visits and for selected lab test (BNP, Tnp1, ALT, AST, Bili) Plots will be presented with treatment groups overlaid	Yes
3.3	Safety	EG9	Plot of Mean (95% CI) Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 1	Plots will be presented with treatment groups overlaid	Yes
3.4	Safety	EG9	Plot of Mean (95% CI) Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 2	Plots will be presented with treatment groups overlaid	Yes
3.5	Safety	As EG8	Box Plot of Change from Baseline for Vital Signs by Treatment and Time – Part 1	Plots will be presented with treatment groups overlaid	No
3.6	Safety	As EG8	Box Plot of Change from Baseline for Vital Signs by Treatment and Time – Part 2	Plots will be presented with treatment groups overlaid	No

Table 4 Pharmacokinetic Tables

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
5.1	PK	PK14	Listing of Derived Plasma GSK2838232 PK Parameters – Part 1	Sort by participant and treatment	Yes
5.2	PK	PK13	Listing of Derived Plasma GSK2838232 PK Parameters – Part 2	Sort by participant and treatment	No
5.3	PK	PK01	Summary Statistics of Plasma GSK2838232 PK Concentration-Time Data, Bioavailability		No
5.4	PK	PK04	Summary Statistics of Derived Plasma GSK2838232 PK Parameters by Treatment, Bioavailability		No
5.5	PK	PK05	Summary Statistics of Log_e-transformed Derived Plasma GSK2838232 PK Parameters, Bioavailability		No
5.6	PK	Non-Standard1	Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Relative Bioavailability	PK Parameter: AUC(0-inf), and Cmax Ratio: Tablet/Capsule	No
5.7	PK	PK15	Listing of Individual Derived Plasma GSK2838232 PK Parameters Treatment Ratios		No
5.8	PK	PK01	Summary Statistics of Plasma GSK2838232 PK Concentration-Time Data, Food Effect		No
5.9	PK	PK04	Summary Statistics of Derived Plasma GSK2838232 PK Parameters by Treatment, Food Effect		No
5.10	PK	PK05	Summary Statistics of Log_e-transformed Derived Plasma GSK2838232 PK		No

			Parameters, Food Effect		
5.11	PK	Non-Standard2	Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Food Effect		No
5.12	PK	Non-Standard 6	Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Food Effect (Non-parametric)	PK Parameter Tmax	Yes
5.13	PK	PK15	Listing of Individual Derived Plasma GSK2838232 PK Parameters Treatment Ratios	PK Parameter: AUC(0-inf), Cmax, and tmax Ratio: Fed/Fasted	No
5.14	PK	PK01	Summary Statistics of Plasma GSK2838232 PK Concentration-Time Data – Part 2	Day 1 & Day 11	No
5.15	PK	PK04	Summary Statistics of Derived Plasma GSK2838232 PK Parameters by Treatment and by Day – Part 2	Day 1 & Day 11	No
5.16	PK	PK05	Summary of Log_e-transformed Derived Plasma GSK2838232 PK Parameters by Treatment and by Day – Part 2	Day 1 & Day 11	No
5.17	PK	Non-Standard3	Summary of Results of GSK2838232 PK Parameter Treatment Comparisons - Accumulation Assessments- Part 2	One for each treatment	No
5.18	PK	Non-Standard4	Summary Results of Steady State GSK2838232 Concentrations Assessments- Part 2	One for each treatment	No

Table 5 Pharmacokinetic Figures

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
5.1	PK	PK16B	Individual Plasma GSK2838232 PK Concentration-Time Plots for Relative Bioavailability	Linear and Semi-Log Scale By participant, overlay all treatments for each participant Include LOQ line in plot	Yes
5.2	PK	PK17	Mean Plasma GSK2838232 PK Concentration for Relative Bioavailability	Linear and Semi-Log Scale Overlay all treatments Include LOQ line in plot	Yes
5.3	PK	PK18	Median Plasma GSK2838232 PK Concentration for Relative Bioavailability	Linear and Semi-Log Scale Overlay all treatments Include LOQ line in plot	Yes
5.4	PK	PK28	Geometric Mean Treatment Ratio and 90% Confidence Interval of GSK2838232 PK Parameter for the Relative Bioavailability		No
5.5	PK	PK25	Comparative Plot of Individual Plasma GSK2838232 PK Parameters for Relative Bioavailability by treatment		No
5.6	PK	PK16A	Individual Plasma GSK2838232 PK Concentration-Time Plots for Food Effect	Linear and Semi-Log Scale By participant, overlay all treatments for each participant Include LOQ line in plot	Yes
5.7	PK	PK17	Mean Plasma GSK2838232 PK Concentration for Food Effect	Linear and Semi-Log Scale Overlay all treatments Include LLQ line in plot	Yes
5.8	PK	PK18	Median Plasma GSK2838232 PK Concentration for Food	Linear and Semi-Log Scale Overlay all treatments	Yes

			Effect	Include LOQ line on plot	
5.9	PK	PK28	Geometric Mean Treatment Ratio and 90% Confidence Interval of GSK2838232 PK Parameter for Food Effect		No
5.10	PK	PK25	Comparative Plot of Individual Plasma GSK2838232 PK Parameters for Food Effect by treatment		No
5.11	PK	PK16a	Individual Plasma GSK2838232 PK Concentration-Time Plots by Day – Part 2	Linear and Semi-Log Scale By participant, overlay days for each participant Include LLQ line on plot	Yes
5.12	PK	PK17	Mean Plasma GSK2838232 PK Concentration by Day – Part 2	Linear and Semi-Log Scale Include LLQ line on plot Plot Day 1 and Day 11 on Separate page	Yes
5.13	PK	PK18	Median Plasma GSK2838232 PK Concentration by Day – Part 2	Linear and Semi-Log Scale Include LLQ line on plot Plot Day 1 and Day 11 on Separate page	Yes
5.14	PK	PK16a	Individual Plasma GSK2838232 Predose Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Overlay all individual profile with all days profiles Day on x-axis, predose concentration on y-axis, join day to day for each subject.	Yes
5.15	PK	PK17	Mean Plasma GSK2838232 Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Days on same plot with x-axis as Days, mean concentration plotted across and joined	Yes
5.16	PK	PK18	Median Plasma GSK2838232 Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Days on same plot with x-axis as Days, median concentration plotted across and joined	Yes

5.17	PK	PK16a	Individual and Box Plot of Plasma GSK2838232 PK Parameters by Day – Part 2	Include all the PK parameters.	Yes
5.18	PK	PK25	Comparative Plot of Plasma GSK2838232 PK Parameters for Accumulation	Linear and Log Scale	Yes

Table 6 ICH Listings

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
1	Screened	ES7	Listing of Reasons for Screen Failure – Part 1		**No**
2	Screened	ES7	Listing of Reasons for Screen Failure – Part 2		No
3	Safety	ES3	Listing of Reasons for Study Withdrawal – Part 1		No
4	Safety	ES2	Listing of Reasons for Study Withdrawal – Part 2		No
5	Safety	SD3	Listing of Reasons for Study Treatment Discontinuation – Part 1		No
6	Safety	SD2	Listing of Reasons for Study Treatment Discontinuation – Part 2		No
7	Safety	BL1	Listing of Participants for Whom the Treatment Blind was Broken – Part 2		No
8	Safety	CP_RA1x	Listing of Planned and Actual Treatments – Part 1		No
9	Safety	CP_RA1p	Listing of Planned and Actual Treatments – Part 2		No
10	Safety	DV2A	Listing of Important Protocol Deviations – Part 1	ICH E3 Listing also includes analysis population exclusions.	No
11	Safety	DV2	Listing of Important Protocol Deviations – Part 2	ICH E3 Listing also includes analysis population exclusions.	No
12	Safety	IE4	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part 1	ICH E3	No
13	Safety	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part 2	ICH E3	No
14	Safety	SP3A	Listing of Participants Excluded from Any Population – Part 1	ICH E3	No

15	Safety	SP3	Listing of Participants Excluded from Any Population – Part 2	ICH E3	No
16	Safety	DM4	Listing of Demographic Characteristics – Part 1	ICH E3	No
17	Safety	DM2	Listing of Demographic Characteristics – Part 2	ICH E3	No
18	Safety	DM10	Listing of Race – Part 1	ICH E3	No
19	Safety	DM9	Listing of Race – Part 2	ICH E3	No
20	Safety	CP_CM4	Listing of Concomitant Medications – Part 1	IDSL	No
21	Safety	CP_CM3	Listing of Concomitant Medications – Part 2	IDSL	No
22	Safety	EX4	Listing of Exposure Data – Part 1	ICH E3	No
23	Safety	EX3	Listing of Exposure Data – Part 2	ICH E3	No
24	Safety	CP_AE9	Listing of All Adverse Events – Part 1	ICH E3	No
25	Safety	CP_AE8	Listing of All Adverse Events – Part 2	ICH E3	No
26	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events – Part 1	ICH E3	No
27	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events – Part 2	ICH E3	No
28	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part 1	IDSL	No
29	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part 2	IDSL	No
30	Safety	CP_AE9a	Listing of Fatal Serious Adverse Events – Part 1	ICH E3	No
31	Safety	CP_AE8a	Listing of Fatal Serious Adverse Events – Part 2	ICH E3	No
32	Safety	CP_AE9a	Listing of Non-Fatal Serious Adverse Events – Part 1	ICH E3	No
33	Safety	CP_AE8a	Listing of Non-Fatal Serious	ICH E3	No

			Adverse Events – Part 2		
34	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	No
35	Safety	CP_AE9a	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment – Part 1	ICH E3	No
36	Safety	CP_AE8a	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment – Part 2	ICH E3	No
37	Safety	CP_AE9a	Listing of Grade 3 or 4 Adverse Events – Part 1	Division of AIDS Table For Grading	No
38	Safety	CP_AE8a	Listing of Grade 3 or 4 Adverse Events – Part 2	Division of AIDS Table For Grading	No
39	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events – Part 1	IDSL	No
40	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events – Part 2	IDSL	No
41	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events – Part 1	IDSL	No
42	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events – Part 2	IDSL	No
43	Safety	LB13	Listing of Reference Ranges for Clinical Laboratory Tests		No
44	Safety	LB6	Listing of Hematology Data– Part 1	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	No
45	Safety	LB5	Listing of Hematology Data– Part 2	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	No
46	Safety	LB6	Listing of Clinical Chemistry	If any laboratory test	No

			Data– Part 1	results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	
47	Safety	LB5	Listing of Clinical Chemistry Data– Part 2	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	No
48	Safety	LB6	Listing of Urinalysis Data– Part 1	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	No
49	Safety	LB5	Listing of Urinalysis Data– Part 2	If any laboratory test results are outside of the reference range, they will be flagged with high/low and/or toxicity grade in the listing	No
50	Safety	LB6	Listing of All Laboratory Data for Participants with Any Value of Potential Clinical Importance– Part 1	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a participant who experienced a value of potential clinical importance.	No
51	Safety	LB5	Listing of All Laboratory Data for Participants with Any Value of Potential Clinical Importance– Part 2	ICH E3 May be split into separate listings by chemistry, hematology, etc. Display ALL labs for a participant who experienced a value of potential clinical importance.	No
52	Safety	LB6	Listing of Lab Results Identified as Adverse Events–	Lab results identified as AEs. Only needed	No

			Part 1	if there are a sufficient number of labs identified as AEs.	
53	Safety	LB5	Listing of Lab Results Identified as Adverse Events – Part 2	Lab results identified as AEs. Only needed if there are a sufficient number of labs identified as AEs.	No
54	Safety	LB6	Listing of Grade 2 or Higher Lab Abnormalities – Part 1		No
55	Safety	LB5	Listing of Grade 2 or Higher Lab Abnormalities – Part 2		No
56	Safety	LB14	Listing of Laboratory Data with Character Results – Part 1	ICH E3	No
57	Safety	LB14	Listing of Laboratory Data with Character Results – Part 2	ICH E3	No
58	Safety	UR2B	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part 1	ICH E3 Display ALL data for a participant who experienced a value of potential clinical importance.	No
59	Safety	UR2A	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part 2	ICH E3 Display ALL data for a participant who experienced a value of potential clinical importance.	No
60	Safety	EG4	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance – Part 1	IDSL	No
61	Safety	EG3	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance – Part 2	IDSL	No
62	Safety	EG6	Listing of All ECG Findings for Participants with an Abnormal ECG Finding – Part 1	IDSL	No
63	Safety	EG5	Listing of All ECG Findings for Participants with an Abnormal ECG Finding – Part 2	IDSL	No
64	Safety	HM8	Listing of Holter Monitoring – Part 1	IDSL	No

65	Safety	HM8	Listing of Holter Monitoring – Part 2	IDSL	No
66	Safety	VS5	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance – Part 1	IDSL	No
67	Safety	VS4	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance – Part 2	IDSL	No
68	Safety	Non-Standard 5	Listing of Meal- Part 1		Yes

Table 7 Non-ICH Lisitngs

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Any Changes in existing RAP
69	PK	PK08	Listing of Plasma GSK2838232 PK Concentration-Time Data –Part 1	Sort by participant, treatment, day, and time	Yes
70	PK	PK07	Listing of Plasma GSK2838232 PK Concentration-Time Data –Part 2	Sort by participant, treatment, day, and time	Yes
71	PK	SAS output of Table 5.6	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons for the Relative Bioavailability – Part 1A		Yes
72	PK	SAS output of Table 5.10	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons for the Food Effect – Part 1B		Yes
73	PK	SAS output of Table 5.12	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons for the Food Effect (Non-parametric) – Part 1B		Yes
74	PK	SAS output of Table 5.16	SAS Output of Summary Results of Steady-State GSK2838232 Concentrations Assessment – Part 2		Yes
75	PK	SAS output of Table 5.17	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons – Accumulation Ratio – Part 2		Yes

Table 8 Study Population Tables (Changes from RAP)

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Changes done from the RAP
1.9	Safety	DV1	Summary of Protocol Deviations – Part 1	ICH E3 .	1. Title has been changed from "Summary of Protocol Deviations – Part 1" to "Summary of Important Protocol Deviations – Part 1" 2. Programming note has been appended with following texts: "If important protocol deviation events are less than 15, please produce the summary with wordings"not enough important protocol deviation to warren a summary".
1.10	Safety	DV1	Summary of Protocol Deviations – Part 2	ICH E3	1. Title has been changed from "Summary of Protocol Deviations – Part 2" to "Summary of Important Protocol Deviations – Part 2" 2. Programming note has been appended with following texts: "If important protocol deviation events are less than 15, please produce the summary with wordings "not enough important protocol deviation to warren a summary".

Table 9 Safety Figures (Changes from RAP)

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Changes from RAP
3.1	Safety	As EG9	Plot of Selected Clinical Lab Tests Mean Change from Baseline by Treatment and Time – Part 1	Only include scheduled visits and for selected lab test (BNP, Tnp1, ALT, AST, Bili) Plots will be presented with treatment groups overlaid	Title has been changed to "Plot of Selected Clinical Lab Tests Mean (95% CI) Change from Baseline by Treatment and Time – Part 1"
3.2	Safety	As EG9	Plot of Selected Clinical Lab Tests Mean Change from Baseline by Treatment and Time – Part 2	Only include scheduled visits and for selected lab test (BNP, Tnp1, ALT, AST, Bili) Plots will be presented with treatment groups overlaid	Title has been changed to "Plot of Selected Clinical Lab Tests Mean (95% CI) Change from Baseline by Treatment and Time – Part 2"
3.3	Safety	EG9	Plot of Mean Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 1	Plots will be presented with treatment groups overlaid	Title has been changed to "Plot of Mean (95% CI) Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 1"
3.4	Safety	EG9	Plot of Mean Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 2	Plots will be presented with treatment groups overlaid	Title has been changed to "Plot of Mean (95% CI) Change from Baseline QTcB and QTcF Data by Treatment and Time – Part 2"

Table 10 Pharmacokinetic Tables (Changes from RAP)

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Changes from RAP
5.1	PK	PK14	Listing of Derived Plasma GSK2838232 PK Parameters – Part 1A	Sort by participant and treatment	This table is clubbed with table 5.2 Title has been changed to "Listing of Derived Plasma GSK2838232 PK Parameters – Part 1"
5.2	PK	PK14	Listing of Derived Plasma GSK2838232 PK Parameters – Part 1B	Sort by participant and treatment	This table has been removed.
5.3	PK	PK13	Listing of Derived Plasma GSK2838232 PK Parameters – Part 2	Sort by participant and treatment	Table no is changed to 5.2
x.xx	PK	Non-Standard 6	Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Food Effect (Non-parametric)	PK Parameter Tmax	Newly added, with Table no 5.12
5.14	PK	PK04	Summary Statistics of Plasma GSK2838232 PK Parameters by Treatment and by Day – Part 2	Day 1 & Day 11	Title has been changed to "Summary Statistics of Plasma GSK2838232 PK Concentration time data by Treatment and by Day – Part 2

Table 11 Pharmacokinetic Figures (Changes from RAP)

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Changes from RAP
5.1	PK	PK16B	Individual Plasma GSK2838232 PK Concentration-Time Plots for Relative Bioavailability	Linear and Semi-Log Scale By participant, overlay all treatments for each participant Include LOQ line in plot	In programming note "Include LOQ line in plot" is added
5.2	PK	PK17	Mean Plasma GSK2838232 PK Concentration for Relative Bioavailability	Linear and Semi-Log Scale Overlay all treatments Include LOQ line in plot	In programming note "Include LOQ line in plot" is added
5.3	PK	PK18	Median Plasma GSK2838232 PK Concentration for Relative Bioavailability	Linear and Semi-Log Scale Overlay all treatments Include LOQ line in plot	In programming note "Include LOQ line in plot" is added
5.6	PK	PK16A	Individual Plasma GSK2838232 PK Concentration-Time Plots for Food Effect	Linear and Semi-Log Scale By participant, overlay all treatments for each participant Include LOQ line in plot	In programming note "Include LOQ line in plot" is added
5.7	PK	PK17	Mean Plasma GSK2838232 PK Concentration for Food Effect	Linear and Semi-Log Scale Overlay all treatments Include LLQ line in plot	In programming note "Include LOQ line in plot" is added
5.8	PK	PK18	Median Plasma GSK2838232 PK Concentration for Food Effect	Linear and Semi-Log Scale Overlay all treatments Include LOQ	In programming note "Include LOQ line in plot" is added

				line on plot	
5.11	PK	PK16a	Individual Plasma GSK2838232 PK Concentration-Time Plots by Day – Part 2	Linear and Semi-Log Scale By participant, overlay days for each participant Include LLQ line on plot	In programming note "Include LOQ line in plot" is added
5.12	PK	PK17	Mean Plasma GSK2838232 PK Concentration by Day – Part 2	Linear and Semi-Log Scale Include LLQ line on plot Plot Day 1 and Day 11 on Separate page	In programming note Include LLQ line on plot Plot Day 1 and Day 11 on Separate page are added.
5.13	PK	PK18	Median Plasma GSK2838232 PK Concentration by Day – Part 2	Linear and Semi-Log Scale Include LLQ line on plot Plot Day 1 and Day 11 on Separate page	In programming note Include LLQ line on plot Plot Day 1 and Day 11 on Separate page are added.
5.19	PK	PK16a	Individual Plasma GSK2838232 Predose Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Overlay all individual profile with all days profiles Day on x-axis, predose concentration on y-axis, join day to day for each subject.	In programming note Day on x-axis, predose concentration on y-axis, and join day to day for each subject is added. Figure no change to 5.14
5.20	PK	PK17	Mean Plasma GSK2838232 Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Days on same plot with x-axis as Days, mean concentration plotted across and joined	In programming note Days on same plot with x-axis as Days, mean concentration plotted across and joined, is added. Figure no change 5.15
5.21	PK	PK18	Median Plasma GSK2838232 Concentration-Time Plots for Steady State Assessment – Part 2	Linear and Semi-Log Scale Days on same plot with x-axis as Days, median concentration	In programming note Days on same plot with x-axis as Days, median concentration plotted across and joined, is added.

				plotted across and joined	Figure no changed to 5.16
5.22	PK	PK16a	Individual and Box Plot of Plasma GSK2838232 PK Parameters by Day – Part 2	Include all the PK parameters.	Figure no change to 5.17
5.23	PK	PK25	Comparative Plot of Plasma GSK2838232 PK Parameters for Accumulation	Linear and Log Scale	Figure no change to 5.18

Table 12 ICH Listing (Changes from RAP)

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Changes from RAP
xx	Safety	Non-Standard 5	Listing of Meal Data - Part 1	Part 1 only	Newly Added with listing no 68

Table 13 Non-ICH Listings (Change from RAP)

No	Population	IDSL Shell/TST ID /Example shell	Title	Programming Note	Changes from RAP
68	PK	PK08	Listing of Plasma GSK2838232 PK Concentration-Time Data –Part 1A	Sort by participant, treatment, day, and time	This listing has been combined with listing number 69. Title of this listing is changed to "Listing of Plasma GSK2838232 PK Concentration-Time Data –Part 1" This listing number has been changed to 69.
69	PK	PK08	Listing of Plasma GSK2838232 PK Concentration-Time Data –Part 1B	Sort by participant, treatment, day, and time	This listing has been removed
xx	PK	SAS output of Table 5.12	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons for the Food Effect (Non-parametric) – Part 1B		This is newly added
73	PK	SAS output of Table 5.16	SAS Output of Summary Results of Steady-State GSK2838232 Concentrations Assessment – Part 2		This listing number is changed to 74
74	PK	SAS output of Table 5.17	SAS Output of Summary Results of GSK2838232 PK Parameter Treatment Comparisons – Accumulation Ratio – Part 2		This listing no is changed to 75

4. SHELLS

Example: Non-Standard 5

Protocol: AAA111111 Page 1 of xx
Population: Safety

Listing x
Listing of Meal Data (Safety Population)

{Inv./} Subj.	{Age(y)/ Sex/ Race}	Trt.	Visit/Pl. Time	Start Date/Start Time of Meal	Stop Date/Stop Time of Meal	Start Date/Start Time of Dosing	Meal Type	Totality of the Meal been Ingested ?	Proportional of the Meal Consumed ?
PPD	36/ M/ Mixed Race	A	PART1 P1D1/PREDOSE	PPD /09:00	9/09:10	/09:30	High Fat Meal	No	76-100%

Example: Non-Standard 6

Protocol: AAA111111 Page 1 of xx
Population: Pharmacokinetic

Table x
Summary of Result of Plasma GSK2838232 PK Parameter Treatment Comparisons for Food Effect (Non-Parametric)

		Median				
PK Parameter	Comparison Test/Ref.	GSK 200 mg/r tablet fasted (N=xx)	GSK 200 mg/r tablet fed (N=xx)	Difference	90% Confidence Interval	p-value
Tmax(h)	GSK 200 mg/r tablet fed vs GSK 200 mg/r tablet fasted	xx.xx	xx.xx		(xx.xx,xx.xx)	x.xxxx

5. REFERENCES

1. SAS® Version 9.3 of the SAS System for Personal Computers. Copyright © 2002-2003. SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.
2. WinNonlin Professional Software Version 5.2. http://www.pharsight.com