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

Title	:	Reporting and Analysis Plan for A Three-Part FTIH Study to Evaluate Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Repeat Oral Doses of GSK3439171A, in a Randomized, Double-Blind (sponsor unblinded), Placebo- Controlled, Dose Escalation study and to Evaluate the Effect of Food on a Single Oral Dose of GSK3439171A in Healthy Adult Participants
Compound Number	:	GSK3439171
Effective Date	:	09-Oct-2019

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 209275.
- This RAP is intended to describe the safety, tolerability, pharmacokinetic and pharmacodynamic analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the reporting efforts, specifically Statistical Analysis Complete (SAC).

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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 209275:

Revision Chronology:		
2018N361438_00	03-JUL-2018	Original
2018N361438_01	27-AUG-2018	Updates to the PK exposure limits for Parts A and B, stopping criteria, and safety review language have been modified based on FDA recommendations. Day -2 has also been removed from Part C of the SoA as it is not necessary. Information around Holter Monitoring has been altered to reflect the intent of collecting but not analyzing Holter Monitoring data in this study.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

- **Detail to Include**: Outline & fully justify (where applicable) changes to the planned protocol analysis.
    - If there are no changes or deviations from the protocol, then specify within this section.

Changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	**Reporting & Analysis Plan**	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Analysis population: Enrolled population has been removed from the population definitions.	• Analysis population: Screened population definition has been added to the population definitions.	• More specific definition according to the new RAP template
• Analysis population: Evaluable population has been removed from the population definitions.	•	• This population will be equivalent to the PK/PD population which are already included

2.2. Study Objective(s) and Endpoint(s)

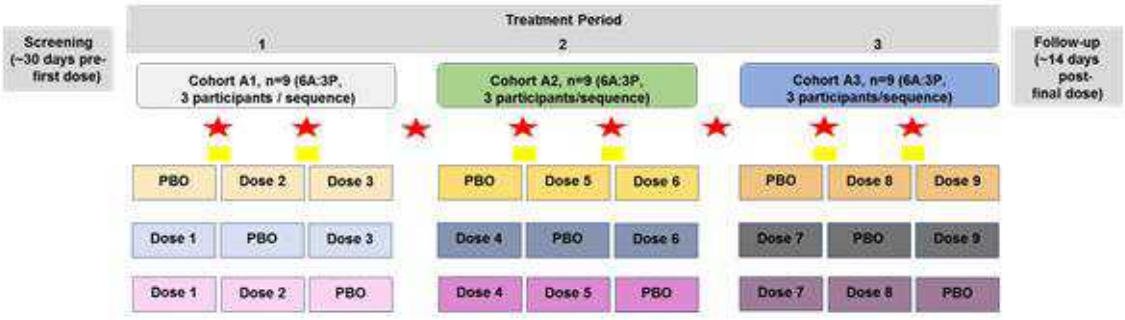
Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
To assess the safety and tolerability of GSK3439171A following single and repeat doses in healthy participants	Adverse events (AE), Serious Adverse Events (SAE), clinical laboratory values, vital signs, and electrocardiograms (ECG)
To characterize the PK of GSK3439171A, following single and repeat doses in healthy participants	Derived PK parameters for GSK3439171A including area under the plasma drug concentration versus time curve (AUC(0-t), AUC(0-inf), maximum observed plasma drug concentration (Cmax), time to maximum observed plasma drug concentration (tmax), and apparent terminal half-life (t1/2) as appropriate
Secondary Objectives	**Secondary Endpoints**
To assess the effect of food on the PK of GSK3439171A following an oral dose in healthy participants	Derived PK parameters for GSK3439171A including area under the plasma drug concentration versus time curve (AUC(0-t), AUC(0-inf), maximum observed plasma drug concentration (Cmax), time to maximum observed plasma drug concentration (tmax), and apparent terminal half-life (t1/2) as appropriate
To assess preliminary dose proportionality of GSK3439171A following single and repeat oral doses, as data permit	AUC(0-t), AUC(0-inf), and Cmax following single dose and AUC(0-τ) and Cmax following repeat dose for the assessment of dose proportionality
To examine the extent of accumulation and achievement of steady-state following repeat oral doses of GSK3439171A, as data permits	• Determine observed accumulation based on AUC(Ro) and Cmax (RCmax) and determine the steadystate ratio (Rss) • Trough plasma concentrations at the end of the dosing interval (Cτ) collected pre-dose for repeat doses 12, 13 and 14* to assess the achievement of steady-state of GSK3439171A
Exploratory Objectives	**Exploratory Endpoints**
To evaluate the PD properties of GSK3439171A	Levels of mediators on prostaglandin and/or inflammatory metabolic pathways such as, but not limited to, PGD2, and PGE2.
To assess the effect of GSK3439171A on QTc in healthy adult volunteers	Holter monitor data collection and storage for evaluation of the correlation between plasma levels of GSK3439171A and changes in the QTc interval in the future, if appropriate
To evaluate additional biomarkers of GSK3439171A target	Levels of change in novel biomarkers in blood, muscle, or urine, such as, but not limited to, urine

Objectives	Endpoints
engagement after single and repeat doses.	tetranor PGDM and PGEM (tPGDM, tPGEM), PGD2, and PGE2
To investigate the plasma, urinary and biliary (Part B) metabolic pathways of GSK3439171A in healthy subjects	GSK3439171-related material in plasma, urine and bile
* 12, 13 and 14 changed to 6,7,9,10, 11, 15,16, and 17	

2.3. Study Design

Overview of Study Design and Key Features

Part A: Single Ascending Dose



Within a cohort, participants will be randomized to one of 3 treatment sequences such that each participant receives 2 active doses and 1 placebo dose resulting in each active dose being administered to 6 participants and placebo to 3 participants

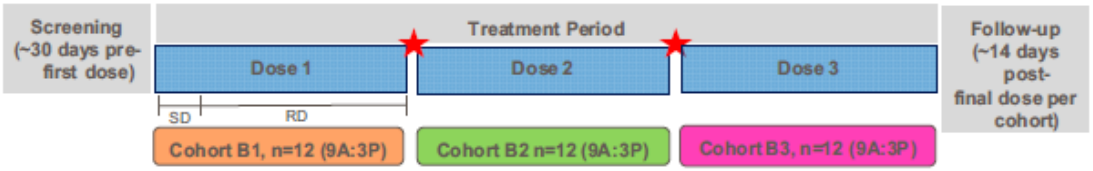
- Starting dose (Dose 1) = 5 mg
- Subsequent dose escalations will be determined based on safety and PK data
- Maximum predicted dose = 500 mg (Genotoxic Risk Assessment Limit= 3000mg)
- Washout= 7 days or 5 half-lives, whichever is longer

= Dose escalation meeting

PBO= Placebo

*Note: dosing strategy is for illustrative purposes and does not represent the randomization strategy

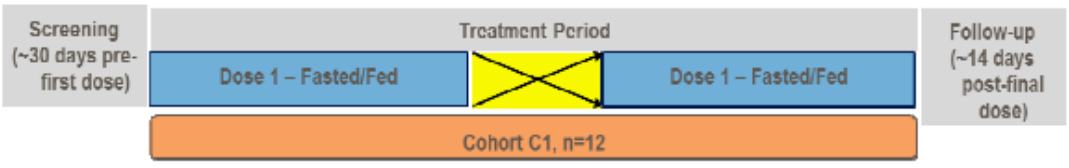
Part B: Single and Repeat Dose 14-day dose-rising



Doses will be selected based on safety, tolerability and PK data from Part A

★ = Dose escalation meeting

Part C: Food Effect



- 7-day or 5 half-lives (whichever is longer) washout period/ participant crossover to fasted/fed arm

Overview of Study Design and Key Features	
Design Features	• Part A is a randomized, double blind, placebo-controlled, crossover, single dose escalation study in healthy participants. Participants will be randomized to placebo or active study intervention groups after screening. • Part B is a randomized, double blind, placebo-controlled, parallel group, repeat dose escalation study in healthy participants. Participants will be randomized to placebo or active study intervention groups after screening. • Part C is a randomized, open label, crossover, food effect study in healthy participants. Participants will be randomized to fed or fasted groups after screening.
Dosing	• Part A: Each participant will participate in 3 dosing periods and will receive 2 doses of GSK3439171A and 1 dose of placebo in a randomized fashion. There will be an approximately 7 day (or 5 half-lives, whichever is longer) washout period between dosing in each session. Each active dose level will be administered initially to a smaller group of participants (1on active and 1 on placebo) and will be followed clinically for 48 hr (or 5 half-lives, whichever is longer) to allow for adequate observation of safety. If no acute safety issues are observed in this smaller group of sentinel participants, then the remaining participants (approximately 5 participants on active and 2 participants on placebo) will receive the dose. • Part B: In each cohort of Part B of the study, approximately twelve participants will be randomized to either one dose level of GSK3439171A or placebo according to a randomization schedule prepared prior to the start of the study. The study will be conducted sequentially starting with Dose 1 Cohort B1. Participants will receive a single dose followed by a 48 hr assessment period and then will receive daily repeat doses until the end of the study. • Part C: In this crossover design, approximately 12 participants will take part in two periods with dosing in each period separated by approximately 7 days (or 5 half-lives of the study intervention, whichever is longer). In each study session, participants will be admitted to the clinical unit and receive a single dose of GSK3439171A either in the fasted state or after a high fat meal.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	Participants will be randomized to receive study intervention. Randomization schedule generated using RandAll NG prior to the study by the Clinical Statistics Department at GSK will be sent to the site and the site pharmacist randomizes the participants according to the randomization schedule. Investigators and all site staff with the exception of the pharmacy staff will remain blinded to each participant's assigned study intervention throughout the course of the study. • Part A: approximately 9 participants in each cohort will be randomized to one of 3 treatment sequences for 3 cohorts. Within each period, allocation of active (A) to placebo (P) treatment will be 2:1. Within a cohort, an increasing dose of GSK3439171A will be administered in each period. • Part B: In each cohort of, approximately 12 participants will be randomized to receive either GSK3439171A or placebo in a parallel design using a 3:1 allocation ratio. • Part C: Approximately 12 participants will be randomized 1:1 to receive

Overview of Study Design and Key Features	
	GSK3439171A in one of two treatment sequences (Fed then Fasted or Fasted then Fed).
Interim Analysis	There will be no formal statistical interim analysis. However, preliminary safety, PK, and PD/biomarker data will be reviewed in-stream by the GSK study team members prior to each dose escalation. Data for these reviews will be cumulative and can include individual participant data, summaries by treatment group and graphical displays. This is a sponsor unblinded trial and GSK staff will be unblinded for these reviews.

2.4. Statistical Hypotheses / Statistical Analyses

The primary objectives of this study are to evaluate safety and tolerability of single and repeat doses of GSK3439171A and to characterize the PK of GSK3439171A. No formal statistical hypotheses will be tested. Descriptive statistics will be used to assess safety and tolerability objectives. Treatment comparisons with placebo will be based on review of descriptive statistics and individual participant data. An estimation approach will be used to address the PK objectives where point estimates and corresponding 90% confidence intervals (CIs) will be constructed as appropriate for the assessment of dose proportionality, steady-state, time invariance and food effect.

3. PLANNED ANALYSES

3.1. Interim Analyses

There will be no formal statistical interim analysis. However, preliminary safety, PK, and PD/biomarker data will be reviewed in-stream by the GSK study team members and investigational site (PAREXEL) team prior to each dose escalation. This data review is conducted in two steps: First GSK staff will review the unblinded data, as this is a sponsor unblinded trial and then the blinded data will be presented to investigational site team in another meeting. Data for these reviews will be cumulative and can include individual participant data, summaries by treatment group and graphical displays.

Preliminary results from available safety data may be reported prior to database freeze for the purposes of safety review by GSK, and where required by regulatory bodies. Other selected preliminary data may be unblinded and reported prior to database freeze for internal decision making. In each case described above, the study will not be officially unblinded and access to the randomization will be restricted.

After completing Part A and cohort 1&2 for Part B there was a safety review of the unblinded data to decide if higher dose can be administered for cohort 3 in Part B. Summaries and figures for Clinical chemistry, Hematology and Hormone level were created for the safety review (The displays that were created are indicated in list of data displays). Unblinded results were produced for an IB update, which was a subset of Study population, Safety and PK concentration displays, more details of the results submitted will be documented in IB update documentation.

Summaries and graphical displays for in-stream reviews will not be provided by Statistics and Programming and as such, no details on these summaries are provided in the RAP.

3.2. Final Analyses

Final analyses will be reported when all subjects in all cohorts have completed their final scheduled visits and the following sequential steps have occurred:

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	All participants who were screened for eligibility	Screen Failures
Randomized	All participants who were randomized	Study Population
Safety	All participants who take at least 1 dose of study intervention. Participants will be analyzed according to the intervention they actually received.	Study Population Safety
PK	Participants in the Safety population for whom a PK sample was taken and analyzed for GSK3439171A and result reported	PK
PD	Participants in the Safety population with at least one PD measure.	PD/Biomarker

Refer to Appendix 12: List of Data Displays which details the population used for each display.
Metabolite ID work will be reported in a separate GSK report

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient 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.

- 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 ClinBase.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

- There are no planned adjustments made for multiple centres in this study.
- There are no planned adjustments for multiple comparisons or multiplicity.

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TLF
Part A			
D1	GSK3439171A Dose 1	5 mg	2
D2	GSK3439171A Dose 2	10 mg	3
D3	GSK3439171A Dose 3	30 mg	4
D4	GSK3439171A Dose 4	60 mg	5
D5	GSK3439171A Dose 5	120 mg	6
D6	GSK3439171A Dose 6	180 mg	7
PA	Placebo Part A	Placebo	1
Part B			
DD1	GSK3439171A R1 mg QD or BID	5 mg	10
DD2	GSK3439171A R2 mg QD or BID	11 mg	11
DD3	GSK3439171A R3 mg QD or BID	40 mg	12
PB	Placebo Part B	Placebo	8
PB3	Placebo Part B Cohort 3	Placebo Cohort 3	9

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TLF
Part C			
C1	GSK3439171A fasted	60 mg Fasted	13
C2	GSK3439171A fed	60 mg Fed	14

Note: If additional dose levels are explored in either Part A or B, then they will follow in a sequential order in the table
Treatment comparisons will be displayed as follows using the descriptors as specified:

1. Day 17 vs Day 1 (e.g.; Ro, RCmax and Rss)
2. Dose X.X mg vs Placebo
3. Repeat Dose X.X mg vs Placebo
4. Fasted vs Fed

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. For the parameters having multiple assessments, mean value of the assessments will be considered as baseline value.

Baseline Definitions – Part A

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Screening	Day -2	Day -1	Day 1 (Pre-Dose)	
Safety Assessments					
Lab results, 12-lead Electrocardiogram (ECG) & Vital Signs	X	X		X	Day 1
Routine Urinalysis	X			X	Day 1
Telemetry				X	Day 1 30 min (±10 min)
Pharmacodynamics parameters			X	X	Day -1 #

Postdose value will be collected on intervals 0-2, 2-4, 4-6, 6-8, 8-12 and 12-24 hr. Time matched predose value for each of these intervals (24-22, 22-20, 20-18, 18-16, 16-12 and 12-0 respectively), predose aggregate value of 24-12hr (for post dose aggregate of 0-12 hrs) and predose aggregate value of 12-0 hr (for post dose aggregate of 12-24 hrs) will be considered as baseline for different pharmacodynamic parameters

Baseline Definitions – Part B

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Screening	Day -2	Day -1	Day 1 (Pre-Dose)	
Safety Assessments					
Lab results	X	X	X	X	Day 1
Hormone monitoring			X		Day -1†
Routine Urinalysis, 12-lead Electrocardiogram (ECG) & Vital Signs	X	X		X	Day 1
Telemetry				X	Day 1 30 min (±10 min)
Pharmacodynamics parameters			X	X	Day -1 #
Blood sampling for metabolite profiling				X	Day 1 (pre-dose)
Muscle Biopsy			X		Day -1

† There will be 2 individual baseline values (samples from midnight and 9am) for ACTH and Cortisol hormones. Both values may be used to calculate change from baseline for post dose measurements.

Postdose value will be collected on intervals 0-2, 2-4, 4-6, 6-8, 8-12 and 12-24hr. Time matched predose value for each of these intervals (24-22, 22-20, 20-18, 18-16, 16-12 and 12-0 respectively), predose aggregate value of 24-12hr (for post dose aggregate of 0-12 hrs) and predose aggregate value of 12-0 hr (for post dose aggregate of 12-24 hrs) will be considered as baseline for different pharmacodynamic parameters

Baseline Definitions – Part C

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety Assessments				
Lab results, 12-lead Electrocardiogram (ECG) & Vital Signs	X		X	Day 1
Routine Urinalysis	X		X	Day 1
Telemetry			X	Day 1 30 min (±10 min)

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

5.3. 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
13.3	Appendix 3: Assessment Windows
13.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
13.5	Appendix 5: Data Display Standards & Handling Conventions
13.6	Appendix 6: Derived and Transformed Data
13.7	Appendix 7: Reporting Standards for Missing Data
13.8	Appendix 8: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

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

Study population analyses including analyses of subject'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.

7. SAFETY ANALYSES

The safety analyses will be based on the safety population, unless otherwise specified.

Descriptive statistics will be used to assess safety and tolerability objectives. No formal statistical analyses of safety data are planned. Data will be summarized according to GSK Integrated Data Standards Library (IDSL) standards for Part A, Part B and Part C separately. In addition, individual participant data will be reviewed. Treatment comparisons with placebo will be based on review of descriptive statistics and individual participant data.

7.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious adverse events (SAEs) and other significant AEs will be based on GSK Core Data Standards.

7.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests, Urinalysis, Liver chemistries and Hormone assessment tests will be based on GSK Core Data Standards. Hormone assessment tests will be done in Part B only and all the other laboratory evaluations will be done for all the 3 parts (A, B & C) of the study.

7.3. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs vital signs and Telemetry will be based on GSK Core Data Standards, unless otherwise specified.

8. PHARMACOKINETIC ANALYSES

8.1. Primary Pharmacokinetic Analyses

8.1.1. Endpoint / Variables

Pharmacokinetic parameters will be determined from the plasma concentration-time data, as data permits.

PK parameters: Maximum observed blood concentration (Cmax), time to Cmax (tmax), area under the plasma concentration-time curve [AUC(0-t), AUC(0-24), AUC(0-inf) and AUC(0-τ)], Pre-dose observed concentration (Cτ), apparent terminal phase half-life (t1/2) will be determined, as data permit.

8.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3. Reporting Standards for Pharmacokinetic)

8.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix 64. 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.

Table 2 Derived Pharmacokinetic Parameters (Primary end points)

Parameter	Parameter Description	Part A	Part B	Part C
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) which will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.	X	X[1]	X
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity calculated as AUC(0-∞)= AUC(0-t) + C(t)/lambda_z	X	X[1]	X
AUC(0-24)	Area under the concentration-time curve from time zero to 24 hours post-dose which will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.	X	X[1,2]	

Parameter	Parameter Description	Part A	Part B	Part C
tmax	Time to reach Cmax, determined directly from the concentration-time data.	X	X[1,2]	X
t1/2	Apparent terminal half-life will be calculated as: t½ = ln2 / lambda_z	X	X[1,2]	X
Ae	Urinary excretion of unchanged drug		X[1,2]	
Clr	Renal clearance		X[1,2]	
Fe	Fraction of the dose excreted in the urine		X[1,2]	
Cmax	Maximum observed concentration, determined directly from the concentration-time data.	X	X[1,2]	X
Cτ	Pre-dose observed concentration (trough) for repeat doses on Days 6,7,9,10, 11, 15,16, and 17 (6, 7, 9 & 10 for 7 day repeat dosing) which will be obtained directly from the concentration-time data.		X[1,2]	

Additional parameters may be calculated as required.
Lambda_z is the terminal phase rate constant.
[1]Determined for dose 1
[2]Determined at SS (following 14 days of consecutive dosing)

8.1.2. Summary Measure

Pharmacokinetic data will be presented in graphical and/or tabular form and will be summarized descriptively by dose group for each study part separately.
Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3**.** Reporting Standards for Pharmacokinetic)

Pharmacokinetic analysis will be the responsibility of the Clinical Pharmacology Modelling and Simulation Department, CPMS, GlaxoSmithKline and Statistical analyses of the pharmacokinetic parameter data will be the responsibility of Clinical Statistics & Programming, GlaxoSmithKline.

8.1.3. Population of Interest

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

8.2. Secondary Pharmacokinetic Analyses

8.2.1. Endpoint / Variables

Observed accumulation ratio AUC(Ro), predicted accumulation ratio AUC(Rp), observed accumulation ratio for Cmax (RCmax) and steady state ratio (Rss).

8.2.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3 Reporting Standards for Pharmacokinetic)

8.2.1.2. Derived Pharmacokinetic Parameters

Table 3 Derived Pharmacokinetic Parameters (Secondary end points)

Parameter	Parameter Description	Part A	Part B	Part C
% AUCex	The percentage of AUC (0-∞) obtained by extrapolation (%AUCex) will be calculated as: AUC(0-∞)- AUC(0-t)/AUC(0- ∞) x 100	X	X	X
AUC(Ro)	Observed accumulation ratio (Ro) for AUC will be calculated as follows: Day 17 AUC(0- τ)/Day 1 AUC(0- τ)		X[1]	
AUC(Rp)	Predicted accumulation ratio will be calculated as follows: Day 1 AUC(0- ∞)/Day 1 AUC(0- 24)	X	X[1]	X
Rss	Steady state accumulation ratio (Rss) will be calculated as follows: Day 17 AUC(0- τ)/Day 1 AUC(0-∞)		X[1]	
RCmax	Observed accumulation ratio for Cmax (Rcmax) will be calculated as follows: Day 17 Cmax/Day 1 Cmax		X[1]	

[1]Day 10 AUC will be considered instead of Day 17 for the reduced treatment period cohort (Part B cohort3).

8.2.2. Summary Measure

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.2. Reporting Standards for Pharmacokinetic)

8.2.3. Population of Interest

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

8.2.4. 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 8.2.1.2 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

8.2.4.1. Statistical Methodology Specification

8.2.4.1.1. Statistical Methodology Specification for Part A (Single Dose)

Pharmacokinetic Statistical Analyses – ANOVA – Single Dose (Part A)
Endpoint / Variables
AUC(0-t), AUC(0-24), AUC(0-∞), Cmax, Cτ, t1/2, AUC(Rp)
Model Specification
Actual value of t1/2 and loge-transformed values of rest of the endpoints will be statistically analyzed using Mixed Model (MM) ANOVA. • Fixed effect: dose • Random effect: Subject An unstructured covariance structure for the G matrix will be used. • If this model fails to converge, alternative covariance structures may be considered. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. Analyses will be done with the MIXED Procedure in SAS, using the Kenward-Roger option to estimate denominator degrees of freedom and standard errors
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
LSmeans and 90% CI are estimated for each dose as well as overall estimate of within-subject CV

Note: AUC(0-t) is only reported when AUC(0-∞) is not reportable

Pharmacokinetic Statistical Analyses - Dose Proportionality (Power Model) – Single Dose (Part A)
Endpoint / Variables
Single Dose: AUC(0-t), AUC(0-∞) and Cmax
Model Specification
Will be statistically analyzed using the power model $y = \alpha^* dose^{\beta}$

Where y =PK parameter being analyzed and α= subject Loge transformed data will be analyzed by fitting the following terms in the mixed effect model: • Fixed effect: loge (dose) • Random effect: Subject (Intercept only)
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
Estimates of the mean slopes of $\log_e$ (dose) will be reported along with corresponding 90% confidence intervals (slope≈1 implies dose proportionality)

Note: AUC(0-t) is only reported when AUC(0-∞) is not reportable

8.2.4.1.2. Statistical Methodology Specification for Part B

Pharmacokinetic Statistical Analyses – ANOVA (Accumulation & Time Invariance) – Repeat Dose (Part B)
Endpoint / Variables
AUC(0- τ), AUC(0-∞), Cmax, Cτ, AUC Rss, t1/2, AUC (Ro), RCmax
Model Specification
Actual value of t1/2 and loge-transformed values of all other will be statistically analyzed using Mixed Model (MM) ANOVA. • Fixed effect: day, dose, day*dose • Random effect: Subject An unstructured covariance structure for the G matrix will be used. • If this model fails to converge, alternative covariance structures may be considered. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. Analyses will be done with the MIXED Procedure in SAS, using the Kenward-Roger option to estimate denominator degrees of freedom and standard errors

Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
LSmeans and 90% CI are estimated for each dose as well as overall estimate of within-subject CV. For AUC(0- τ), Cmax and AUC-Rss, estimates of ratio of Day 17to Day 1 will be evaluated for each dose by exponentiating the difference in least squares means (Day 17– Day 1) and the associated 90% CI. Such that ratios of Day 17 to Day 1 for AUC(0- τ), Cmax and AUC-Rss provide estimates of Ro, RCmax and Rss, respectively Note: For AUC-Rss, Day 17 AUC(0- τ) and Day 1 AUC(0-∞) should be considered. Note: Day 10 values will be considered instead of Day 17 for the reduced treatment period cohort (cohort 3)
Pharmacokinetic Statistical Analyses - Dose Proportionality (Power Model) – Repeat Dose (Part B)
Endpoint / Variables
Repeat Dose: AUC(0-τ) and Cmax
Model Specification
Will be statistically analyzed using the power model $y = \alpha * dose^{\beta}$ Where y =PK parameter being analyzed and α= subject Log_e transformed data will be analyzed by fitting the following terms in the mixed effect model: • Fixed effect: log_e (dose) • Random effect: Subject (Intercept only)
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored.

• Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
Estimates of the mean slopes of $\log_e$ (dose) will be reported along with corresponding 90% confidence intervals (slope≈1 implies dose proportionality)
Pharmacokinetic Statistical Analyses - Achievement of Steady State – Repeat Dose (Part B)
Endpoint / Variables
Trough plasma concentrations at the end of the dosing interval ($C\tau$) for repeat doses Days 6,7,9,10, 11, 15,16, and 17 (6, 7, 9 & 10 for reduced treatment period cohort)
Model Specification
Log_e-transformed values of the endpoint will be statistically analyzed separately by dose using Mixed Model (MM) ANOVA. • Fixed effect: day as continuous variable, dose, day*dose • Random effect: Subject An unstructured covariance structure for the G matrix will be used. • In the event that this model fails to converge, alternative covariance structures may be considered. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. Analyses will be done with the MIXED Procedure in SAS, using the Kenward-Roger option to estimate denominator degrees of freedom and standard errors
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
The coefficient for the slope of the day effect on the log-scale will be used to evaluate steady state for each dose. The 90% confidence intervals for the slope will be calculated. Steady-state will be assessed visually by plotting trough concentration levels, C_T, collected pre-morning dose versus collection day by dose.

8.2.4.1.3. Statistical Methodology Specification for Part C

Pharmacokinetic Statistical Analyses - Food Effect -Single Dose (Part C)
Endpoint / Variables
AUC(0-t), AUC(0-∞), Cmax and t1/2
Model Specification
Log_e-transformed values of AUC(0-t) and AUC(0-∞) and actual value of t1/2 will be statistically analyzed using Mixed Model (MM) ANOVA. • Fixed effect: period, treatment(fed/fasted) • Random effect: Subject An unstructured covariance structure for the G matrix will be used. • If this model fails to converge, alternative covariance structures may be considered. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. Analyses will be done with the MIXED Procedure in SAS, using the Kenward-Roger option to estimate denominator degrees of freedom and standard errors
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
Point estimates for the differences in means (GSK3439171A fed – GSK3439171A fasted) and corresponding 90% CIs will be constructed from the least squares means, using the residual variance. These will then be back-transformed to provide point estimates and corresponding 90% CIs for the ratio of geometric means fed:fasted.
Endpoint(s)
Tmax Note: This endpoint will not be log transformed for analysis
Model Specification
Wilcoxon matched pair test
Model Results Presentation
Point estimate and 90% confidence interval for the median difference (fed – fasted)

Note: AUC(0-t) is only reported when AUC(0-∞) is not reportable Population

8.3. Exploratory Pharmacokinetic Analyses

If data permits, PK data of metabolites will be analyzed in the similar way as for drug substance and similar output will be generated.

9. PHARMACOKINETIC (POPPK) ANALYSES

PopPK will be performed under a separate RAP and will be reported separately.

10. PHARMACODYNAMIC (AND / OR BIOMARKER) ANALYSES

10.1. Exploratory Pharmacodynamic and Biomarker Analyses

10.1.1. Endpoint / Variables

Following table describes the pharmacodynamic/biomarker end points:

Parameter	Parameter Description/Derivation	Part A	Part B
PGD2			X
PGE2			X
Creatinine #		X	X
tPGDM #		X	X
tPGEM #		X	X
6-keto-PGF1A			X
PGF2A			X
TXB2			X
Creatinine corrected data for tPGDM and tPGEM #	Three versions of data to be considered: 1.Raw data(mass) 2. Aggregated data 0-12hrs 3. Aggregated data 12-24hr 4. Aggregated data 24-48hrs Each version of data(mass) divided by time matched creatinine(mass)	X	X
Baseline corrected urinary tetranor data for tPGDM and tPGEM #	Post dose data divided by time matched baseline data Three versions of data to be considered: 1.Creatinine corrected raw data 2. Creatinine corrected aggregated data 0-12hrs 3. Creatinine corrected aggregated data 12-24hrs	X	X
Baseline corrected urinary tetranor data for creatinine #	Post dose data divided by time matched baseline data Three versions of data to be considered: 1.Raw data 2. Aggregated data 0-12hrs 3. Aggregated data 12-24hrs	X	X

Parameter	Parameter Description/Derivation	Part A	Part B
Placebo corrected data for tPGDM and tPGEM #	Creatinine corrected data from active dose divided by time matched placebo data and then find ratio to baseline. Three versions of data to be considered: 1.Creatinine corrected raw data 2. Creatinine corrected aggregated data 0-12hrs 3. Creatinine corrected aggregated data 12-24hrs	X	
Placebo corrected data for creatinine #	Data from active dose divided by time matched placebo data and then find ratio to baseline. Three versions of data to be considered: 1.Raw data 2. Aggregated data 0-12hrs 3. Aggregated data 12-24hrs	X	
Time matched PK Concentration for urinary tetranor data for tPGDM and tPGEM	For each PD marker interval, use the upper bound as target time; e.g. for 0-2hr interval, 2hr is the target time Identify PK concentration with nominal time at the target time; If there is no PK sample taken at target time, use the PK concentration data with nominal time before but closest to target time; Use 0 PK concentration for placebo	X	X
Ratio of tPGDM/tPGEM #	Time matched ratio for tPGDM/tPGEM Three versions of data to be considered: 1.Creatinine corrected raw data 2. Creatinine corrected aggregated data 0-12hrs 3. Creatinine corrected aggregated data 12-24hrs 4. Aggregated data 24-48hrs	X	X

Urine tetranor and urine creatinine data should be considered as mass (Mass=Concentration*Volume).

Raw data – Mass data for each of the intervals 0-2, 2-4, 4-6, 6-8, 8-12 &12-24. (predose and postdose)

Aggregated data 0-12hrs - Add the mass from each interval till 12 hrs (predose and postdose)

Aggregated data 12-24hrs - Mass from 12-24hr interval (predose and postdose)

Aggregated data 124-48hrs - Mass from 24-48hr interval (postdose)

10.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions

10.1.2. Summary Measure

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 13.5.3. Reporting Standards for Pharmacokinetic)

10.1.3. Population of Interest

The exploratory pharmacodynamics (and / or biomarker) analyses will be based on the PD population, unless otherwise specified.

10.1.4. 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 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10.1.4.1. Statistical Methodology Specification

10.1.4.1.1. Statistical Methodology Specification for Part A (Single Dose)

Pharmacodynamic Statistical Analyses – Mixed Effect Model – Single Dose (Part A)
Endpoint / Variables
tPGDM, tPGEM, Creatinine, Creatinine corrected tPGDM and Creatinine corrected tPGEM (Aggregated values for predose 24-12hr & 12-0hr and postdose 0-12 hr, 12-24 hr & 24-48 hr)
Model Specification
Log_e transformed values of the endpoints will be statistically analyzed using Mixed Model (MM). • Fixed effect: dose, timepoint, dose*timepoint • Random effect: Subject An unstructured covariance structure for the G matrix will be used. • If this model fails to converge, alternative covariance structures may be considered. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. Analyses will be done with the MIXED Procedure in SAS, using the Kenward-Roger option to estimate denominator degrees of freedom and standard errors
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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

Pharmacodynamic Statistical Analyses – Mixed Effect Model – Single Dose (Part A)
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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
LS Geometric means and 90% CI are estimated for each dose as well as the estimate (90% CI) of change from baseline for each timepoint, using the time matched baseline. Note: For post dose 24-48hrs baseline (predse) is not available

10.1.4.1.2. Statistical Methodology Specification for Part B (Repeat Dose)

Pharmacodynamic Statistical Analyses – Mixed Effect Model – Repeat Dose (Part B)
Endpoint / Variables
tPGDM, tPGEM, Creatinine, Creatinine corrected tPGDM and Creatinine corrected tPGEM (Aggregated values for predose 24-12hr & 12-0hr and postdose 0-12 hr, 12-24 hr & 24-48 hr)
Model Specification
Log_e transformed values of the endpoints will be statistically analyzed using Mixed Model (MM). • Fixed effect: timepoint, dose, timepoint*dose • Random effect: Subject An unstructured covariance structure for the G matrix will be used. • If this model fails to converge, alternative covariance structures may be considered. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure. Analyses will be done with the MIXED Procedure in SAS, using the Kenward-Roger option to estimate denominator degrees of freedom and standard errors
Model Checking & Diagnostics
• For the Mixed Model, model assumptions will be checked, and appropriate adjustments may be applied based on the data. • Distributional 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 transformations, such as data squared or square root of data, will be explored. • Non-parametric analyses will be conducted if the normality assumption does not hold.
Model Results Presentation
LS Geometric means and 90% CI are estimated for each dose as well as the estimate (90% CI) of change from baseline for each timepoint, using the time matched baseline. Note: For post dose 24-48hrs baseline (predose) is not available Consider Day -1(predose), Day1, Day 7, Day 10, Day 17

11. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

A detailed population PK/PD data analysis plan will be prepared in a separate RAP.

12. REFERENCES

GlaxoSmithKline Document Number 2018N361438_03: Study Protocol of 209275, A Three-Part FTIH Study to Evaluate Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Repeat Oral Doses of GSK3439171A, in a Randomized, Double-Blind (sponsor unblinded), Placebo Controlled, Dose Escalation study and to Evaluate the Effect of Food on a Single Oral Dose of GSK3439171A in Healthy Adult Participants

13. APPENDICES

13.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

As Per Protocol Population is not defined, this section is not applicable.

13.2. Appendix 2: Schedule of Activities

13.2.1. Protocol Defined Schedule of Events

SoA – Part A

	Part A- Single Dose									
Procedure	Screening (up to 30 days before Day 1)	Treatment Period [Days] (for each dosing period)						E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	-1	1	2	3	4			
Informed consent	X									
Inclusion and exclusion criteria (including drug screens)	X			X						Recheck clinical status before randomization and/or 1st dose of study medication.
Demography	X									
Physical examination including height and weight	F	B					B	(B)	F	F: Full exam; B: Brief Exam; height is only taken once at screening

	Part A- Single Dose									
Procedure	Screening (up to 30 days before Day 1)	Treatment Period [Days] (for each dosing period)						E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	-1	1	2	3	4			
Medical history (includes substance usage and family history of premature cardiovascular (CV) disease and any changes in health status occurring between screening and admission to the unit)	X	X								Substances: Drugs, Alcohol, tobacco, and caffeine
Past and current medical conditions	X	X								
Human Immunodeficiency Virus (HIV), Hepatitis B and C screening	X									If test otherwise performed within 3 months prior to first dose of study intervention, testing at screening is not required
Admission to Clinical Unit		X								
Safety Laboratory assessments (include liver chemistries)	X	X		X	X	X	X	(X)	X	Predose; 8 hr, 24 hr, and, 48 hr, and 72 hr post-dose and at follow-up visit
Routine Urinalysis	X			X	X	X	X	(X)	X	Predose; 8 hr, 24 hr, 48 hr, and 72 hr post-dose and at follow-up visit

	Part A- Single Dose									
Procedure	Screening (up to 30 days before Day 1)	Treatment Period [Days] (for each dosing period)						E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	-1	1	2	3	4			
12-lead Electrocardiogram (ECG)	X	X		←==========X==========→				(X)	X	ECGs assessed at screening (triplicate) and admission (single). During treatment period ECGs assessed predose (triplicate at least 5 minutes (min) intervals) and single measurements postdose every 30 min for 1 hr, hourly up to 6 hr, and at 12 hr, 24 hr, 36 hr and 48 hr and 72 hr post-dose
Vital signs (pulse rate, blood pressure (bp), respiratory rate, and oral temperature)	X	X		←==========X==========→				(X)	X	Vitals assessed at screening (triplicate measurements for pulse and (bp)) (and admission (single measurements). During treatment period vitals assessed predose (triplicate measurements for pulse and bp) and postdose (single measurements) every 15 min for 1 hr, hourly up to 6 hr, then at 12 hr, 24 hr, 36 hr, 48 hr, and 72 hr post-dose. See Section 8.2.2 for further information
Randomization				X						Randomization will occur before first dose in period 1.

	Part A- Single Dose									
Procedure	Screening (up to 30 days before Day 1)	Treatment Period [Days] (for each dosing period)						E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	-1	1	2	3	4			
Genetic sample				X						Any time predose on Day 1. This research may be described in a separate Informed Consent Form (ICF) or as part of a combined ICF. A separate signature is required where participant participation is optional
Study intervention				X						
Telemetry				X						Telemetry performed starting 30 min (±10 min) pre-dose to 12 hr (±20 min) post-dose
Adverse Event (AE) review		←==========X==========→						(X)	X	
Serious Adverse Event (SAE) review	X	←==========X==========→						(X)	X	
Concomitant medication review	X	←==========X==========→						(X)	X	

	Part A- Single Dose									
Procedure	Screening (up to 30 days before Day 1)	Treatment Period [Days] (for each dosing period)						E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	-1	1	2	3	4			
24hr urine sampling for Pharmacodynamics (PD)			X[1]	X[2]	X[3]	X[3]		(X)		[1]combined void for windows of 24-22 hr, 22-20 hr, 20-18 hr, 18-16 hr, 16-12 hr, and 12-0 hr predose. [2] combined void for windows of 0-2 hr, 2-4 hr, 4-6 hr, 6-8 hr 8-12 hr, and 12-24 hr post-dose [3]combined void for 24 hr
Blood sampling for Pharmacokinetics (PK)				←==========X==========→				(X)		Predose, 5min, 30min, 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, and 48 hr, 60 hr, and 72 hr post-dose
24 hr Holter Monitoring				X						Predose through 24 hr post-dose
Discharge from Clinical Unit							X	(X)		

The timing and number of planned study assessments, including safety, PK, PD/biomarker or other assessments may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.

Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic/pharmacodynamic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol amendment. The Competent Authority (CA) and ethics committee (EC) will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the ICF. The changes will be approved by the CA and the EC before implementation.

SoA – Part B

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Informed consent	X																				
Inclusion and exclusion criteria (including drug screens)	X	X																			Recheck clinical status before randomization and prior to muscle biopsy/or 1st dose of study medication.
Demography	X																				
Full physical examination including height and weight	F	B																B	(B)	F	F: Full exam; B: Brief exam; height is only taken once at screening
Medical history (includes substance usage and family history of premature CV disease and any changes in health status occurring between screening and admission to the unit)	X	X																			Substances: Drugs, Alcohol, tobacco, and caffeine

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Past and current medical conditions	X	X																			
HIV, Hepatitis B and C screening	X																				If test otherwise performed within 3 months prior to first dose of study intervention, testing at screening is not required
Admission to Clinical Unit		X																			
Safety Laboratory assessments (include liver chemistries)	X	X		X				X[1]		X[1]					X[1]			X	(X)	X[1]	Pre-randomization assessments for eligibility must be performed PRIOR to predose muscle biopsy Predose, 24 hr, and 48, and 72 hr post-Day 1 dose; additional timepoints may be added based on findings in Part A [1]Days 7, 11, 17, 20, and follow-up

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Routine urinalysis	X	X		X				X[2]		X[2]					X[2]			X[2]	(X)	X[2]	Predose, 24 hr, 48 hr, and 72 hr post-Day 1 dose; additional timepoints may be added based on findings in Part A [2]Days 7, 11,17, 20, and follow-up

Part B – Repeat Dose																				
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Hormone monitoring			X												X				(X)		Samples to be taken at midnight and 9am (±10 min) on Days -1 and 17 Samples taken at midnight will be analysed for adrenocorticotropic hormone (ACTH) and cortisol Samples taken at 9am will be analysed for ACTH, cortisol, luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), total testosterone, dihydrotestosterone (DHT), triiodothyronine (T3), and free thyroxine (free T4) See Section 8.2.7. in Protocol for information regarding monitoring of abnormal hormone results

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																		E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
12-lead ECG	X	X		←=====X[5]=====→				X[5]		X[5]			X[5]		X[5]			X[5]	(X)	X	ECGs assessed at screening (triplicate measure) and admission (single measure). During treatment period ECGs assessed predose (triplicate measure at at least 5 min intervals) and post-dose (single measure) every 30 min for 1 hr, hourly up to 6 hr, at 12 hr post-dose then at 24 hr, 36 hr, 48 hr, and 72 hr post-dose [5] Days 7,11, 15, and 17, and 20 Post-dose at Cmax based on observed Cmax in Part A (currently estimated to occur at ~2 hr post dose), except for Day 20. Day 20 ECG to occur any time before Discharge

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Vital signs (pulse rate, bp, respiratory rate, and oral temperature)	X	X		X[6]				X[7]							X[6]				(X)	X	[6]Vitals assessed at screening (triplicate measurements for pulse and bp) and admission (single measurements). During treatment period vitals assessed predose (triplicate measurements for pulse and bp) and postdose (single measurements) every 15 min for 1 hr, hourly up to 6 hr, and at 12 hr, 24 hr, 36 hr, 48 hr, and 72 hr post-dose [7]Vitals assessed once every 24 hr See Section 8.2.2. in Protocol for further information
Randomization				X																	

Part B – Repeat Dose																				
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Genetic sample				X																	Any time predose on Day 1 This research may be described in a separate ICF or as part of a combined ICF. A separate signature is required where participant participation is optional
Study intervention				X			←==========X==========→														
Telemetry				X																	Telemetry performed starting 30 (±10 min) pre-dose to 12 hr (±20 min) post-dose
AE review							←==========X==========→														
SAE review				←==========X==========→																	
Concomitant medication review				←==========X==========→																	

Part B – Repeat Dose																				
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Urine sampling PD			X[8]	X[9]	X[9]					X[9, 10]					X[9]				(X)		[8]combined void for windows of 24-22 hr, 22-20 hr, 20-18 hr, 18-16 hr, 16-12 hr, and 12-0 hr predose. [9]combined void for windows of 0-2 hr, 2-4 hr, 4-6 hr, 6-8 hr, 8-12 hr, and 12-24 hr post-dose [10] Day 10 only Aliquots will be removed prior to pooling for urine PK. Total urine volume will be recorded before aliquots for PD are removed.

Part B – Repeat Dose																				
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
24h urine sampling for PK and metabolite profiling			X	X	X										X				(X)		Voids from urine pharmacodynamic (PD) sampling windows will be combined into 0-24 hr pools on Day -1,1, and 17 after aliquoting for PD. These voids will be combined for PK/metabolite analysis only after aliquots for urine PD are removed See study reference manual (SRM) for details on samples and processing

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																		E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Blood sampling for PK				X[11]				X[12]		X[12]			X[12]		X[11]					(X)		[11]Day 1 and Day 17: Predose, 5 min, 30 min, 1 hr, 1. 5hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, 48 hr, 60 hr, and 72 hr post-dose [12]pre-dose samples collected on days 6,7, 9-11 and 15-16
Blood sampling for metabolite profiling				X											X							Day 1 and Day 17: Predose, 5 min, 30 min, 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, 48 hr, 60 hr, and 72 hr post-dose
Blood sampling for Pharmacodynamics and biomarkers				X[13]	X[13]					X[14]					X[14]					(X)		[13]Predose and 24 hr post-dose on Day 1 [14]Predose Days 10 and 17

Part B – Repeat Dose																				
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Muscle Biopsy			X[15]												X[16]				(X)		Muscle biopsies must be performed AFTER clinical safety assessments on the corresponding days [15]Day -1 muscle biopsy to occur 1-6 hr after estimated timing of initial dose on Day 1. Time of sample collection to be recorded [16]Muscle Biopsy performed any time during pre-dose period; Day 17 muscle biopsy to occur within 1-6 hr after last dose administered Time of sample collection to be recorded. Muscle biopsy can be performed at any time during pre-dose period.

Part B – Repeat Dose																					
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)																	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5-7	8	9-11	12	13-14	15	16	17	18	19	20			
Enterotest (bile sample collection)															X						For second or third dose-level only (depending on PK results in Part A) Enterotest capsule to be swallowed ~2 hr after dosing and removed ~7 hr after dosing (~1 hr after food cue)
Enterotest food cue															X						For second or third dose-level only (depending on PK results in Part A) Food cue will be given 6 hr post-dose
Discharge from Clinical Unit																		X	(X)		

- The time to start the second dose in Part B can be modified based on the estimates of half-life from Part A.
- Duration of dosing in Part B can be modified based on the estimates of half-life from Part A.

- The timing and number of planned study assessments, including safety, PK, PD/biomarker or other assessments may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.

Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic/pharmacodynamic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol amendment. The CA and EC will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the ICF. The changes will be approved by the CA and the EC before implementation.

Part B .2– 7 Day Repeat Dose																			
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Informed consent	X																		
Inclusion and exclusion criteria (including drug screens)	X	X																	Recheck clinical status before randomization and prior to muscle biopsy/or 1st dose of study medication.
Demography	X																		
Full physical examination including height and weight	F	B														B	(B)	F	F: Full exam; B: Brief exam; height is only taken once at screening
Medical history (includes substance usage and family history of premature CV disease and any changes in health status occurring between screening and admission to the unit)	X	X																	Substances: Drugs, Alcohol, tobacco, and caffeine

Part B .2– 7 Day Repeat Dose																			
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Past and current medical conditions	X	X																	
HIV, Hepatitis B and C screening	X																		If test otherwise performed within 3 months prior to first dose of study intervention, testing at screening is not required
Admission to Clinical Unit		X																	
Safety Laboratory assessments (include liver chemistries)	X	X		X						X[1]			X[1]			X[1]	(X)	X[1]	Pre-randomization assessments for eligibility must be performed PRIOR to predose muscle biopsy Predose, 24 hr, and 48, and 72 hr post-Day 1 dose; additional timepoints may be added based on findings in Part A [1]Days 7, 10, 13, and follow-up

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)														E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13		
Routine urinalysis	X	X		X						X[2]			X[2]			X[2]	(X)	X[2]	Predose, 24 hr, 48 hr, and 72 hr post-Day 1 dose; additional timepoints may be added based on findings in Part A [2]Days 7, 10, 13, and follow-up

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Hormone monitoring			X										X						Samples to be taken at midnight and 9am (±10 min) on Days -1 and 10 Samples taken at midnight will be analysed for adrenocorticotropic hormone (ACTH) and cortisol Samples taken at 9am will be analysed for ACTH, cortisol, luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), total testosterone, dihydrotestosterone (DHT), triiodothyronine (T3), and free thyroxine (free T4) See Section 8.2.7. in Protocol for information regarding monitoring of abnormal hormone results

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)														E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13		
12-lead ECG	X	X		←=====X=====→						X[5]			X[5]			X[5]	(X)	X[5]	ECGs assessed at screening (triplicate measure) and admission (single measure). During treatment period ECGs assessed predose (triplicate measure at at least 5 min intervals) and post-dose (single measure) every 30 min for 1 hr, hourly up to 6 hr, at 12 hr post-dose then at 24 hr, 36 hr, 48 hr, and 72 hr post-dose [5] Days 7,10, 13, and Follow-up Post-dose at Cmax based on observed Cmax in Part A (currently estimated to occur at ~2 hr post dose), except for Day 13 . Day 13 ECG to occur any time before Discharge

Part B .2– 7 Day Repeat Dose																			
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Vital signs (pulse rate, bp, respiratory rate, and oral temperature)	X	X		X[6]				X[7]								X[6]	(X)	X	[6]Vitals assessed at screening (triplicate measurements for pulse and bp) and admission (single measurements). During treatment period vitals assessed predose (triplicate measurements for pulse and bp) and postdose (single measurements) every 15 min for 1 hr, hourly up to 6 hr, and at 12 hr, 24 hr, 36 hr, 48 hr, and 72 hr post-dose [7]Vitals assessed once every 24 hr See Section 8.2.2. in Protocol for further information
Randomization				X															

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13	E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
Genetic sample				X															Any time predose on Day 1 This research may be described in a separate ICF or as part of a combined ICF. A separate signature is required where participant participation is optional
Study intervention				X			←==========X==========→												
Telemetry				X															Telemetry performed starting 30 (±10 min) pre-dose to 12 hr (±20 min) post-dose
AE review				←==========X==========→															
SAE review	←==========X==========→																		
Concomitant medication review	←==========X==========→																		

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)														E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Urine sampling PD			X[8]	X[9]						X[9]			X[9]				(X)		[8]combined void for windows of 24-22 hr, 22-20 hr, 20-18 hr, 18-16 hr, 16-12 hr, and 12-0 hr predose. [9]combined void for windows of 0-2 hr, 2-4 hr, 4-6 hr, 6-8 hr, 8-12 hr, and 12-24 hr post-dose Aliquots will be removed prior to pooling for urine PK. Total urine volume will be recorded before aliquots for PD are removed.

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
24h urine sampling for PK and metabolite profiling			X	X									X				(X)		Voids from urine pharmacodynamic (PD) sampling windows will be combined into 0-24 hr pools on Day -1,1, and 10 after aliquoting for PD. These voids will be combined for PK/metabolite analysis only after aliquots for urine PD are removed See study reference manual (SRM) for details on samples and processing

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Blood sampling for PK				X[10]					X[11]	X[11]		X[11]	X[10]				(X)		[10]Day 1 and Day 10: Predose, 5 min, 30 min, 1 hr, 1. 5hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, 48 hr, 60 hr, and 72 hr post-dose [11]pre-dose samples collected on days 6, 7, and 9
Blood sampling for metabolite profiling				X									X						Day 1 and Day 10 Predose, 5 min, 30 min, 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, 48 hr, 60 hr, and 72 hr post-dose
Blood sampling for Pharmacodynamics and biomarkers				X[12]	X[12]					X[13]			X[13]				(X)		[12]Predose and 24 hr post-dose on Day 1 [13]Predose Days 7 and 10

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Muscle Biopsy			X[14]										X[15]				(X)		Muscle biopsies must be performed AFTER clinical safety assessments on the corresponding days [14]Day -1 muscle biopsy to occur 1-6 hr after estimated timing of initial dose on Day 1. Time of sample collection to be recorded [15]Day 10 muscle biopsy to occur within 1-6 hr after last dose administered Time of sample collection to be recorded. Muscle biopsy can be performed at any time during pre-dose period.

Part B .2– 7 Day Repeat Dose																		
Procedure	Screening (up to 30 days before Day 1)	Intervention Period [Days] (for each dosing cohort)															E.D	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–2	–1	1	2	3	4	5	6	7	8	9	10	11	12	13			
Discharge from Clinical Unit																X	(X)		

- The time to start the second dose in Part B can be modified based on the estimates of half-life from Part A.
- Duration of dosing in Part B can be modified based on the estimates of half-life from Part A.
- The timing and number of planned study assessments, including safety, PK, PD/biomarker or other assessments may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.
- Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic/pharmacodynamic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol amendment. The CA and EC will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the ICF. The changes will be approved by the CA and the EC before implementation.

Part C- Food Effect									
	Screening (up to 30 days before Day 1)	Treatment Period [Days] (with or without food)					E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–1	1	2	3	4			
Informed consent	X								
Inclusion and exclusion criteria (including drug screens)	X		X						Recheck clinical status before randomization and/or 1st dose of study medication.
Demography	X								
Physical examination including height and weight	F	B				B	(B)	F	F: Full exam; B: Brief Exam; height is only taken once at screening

Part C- Food Effect									
	Screening (up to 30 days before Day 1)	Treatment Period [Days] (with or without food)					E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–1	1	2	3	4			
Medical history (includes substance usage and family history of premature CV disease and any changes in health status occurring between screening and admission to the unit)	X	X							Substances: Drugs, Alcohol, tobacco, and caffeine
Past and current medical conditions	X	X							
HIV, Hepatitis B and C screening	X								If test otherwise performed within 3 months prior to first dose of study intervention, testing at screening is not required
Admission to Clinical Unit		X							

Part C- Food Effect									
	Screening (up to 30 days before Day 1)	Treatment Period [Days] (with or without food)					E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–1	1	2	3	4			
Safety Laboratory assessments (including liver chemistries)	X	X	X	X	X	X	(X)	X	Predose; 8 hr, 24 hr, 48 hr, and 72 hr post-dose and at follow-up visit
Routine Urinalysis	X		X	X	X	X	(X)	X	Predose; 8 hr, 24 hr, 48 hr, and 72hr post-dose and at follow-up visit
12-lead ECG	X	X	←==========X==========→				(X)	X	ECGs assessed at screening (triplicate) and admission (single). During treatment period ECGs assessed predose (triplicate at least 5 min intervals) and single measurements postdose every 30 min for 1 hr, hourly up to 6 hr, and at 12 hr, 24 hr, 36 hr, 48 hr, and 72 hr post-dose

Part C- Food Effect									
	Screening (up to 30 days before Day 1)	Treatment Period [Days] (with or without food)					E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–1	1	2	3	4			
Vital signs (pulse rate, bp, respiratory rate, and oral temperature)	X	X	←==========X==========→				(X)	X	Vitals assessed at screening (triplicate measurements for pulse and bp) and admission (single measurements). During treatment period vitals assessed predose (triplicate measurements for pulse and bp) and postdose (single measurements) every 15 min for 1 hr, hourly up to 6 hr, and at 12 hr, 24 hr, 36 hr, 48 hr, and 72 hr post-dose See Section 8.2.2. in Protocol for further information
Randomization			X						

Part C- Food Effect									
	Screening (up to 30 days before Day 1)	Treatment Period [Days] (with or without food)					E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–1	1	2	3	4			
Genetic sample			X						Sample can be obtained at any point during dosing. This research may be described in a separate ICF or as part of a combined ICF. A separate signature is required where participant participation is optional
Test Meal			X						Fed Arm only. See Section 5.3.1. in Protocol for timings regarding meals, fasting, and treatment administration
Study intervention			X						
Telemetry			X						Telemetry performed starting 30 min (±10 min) pre-dose to 12hrs (±20 min) post-dose
AE review			←==========X==========→				(X)	X	
SAE review	X	←==========X==========→						(X)	

Part C- Food Effect									
	Screening (up to 30 days before Day 1)	Treatment Period [Days] (with or without food)					E.D.	Follow-up (~14±1 days post last dose)	Notes E.D = early discontinuation/withdrawal
		–1	1	2	3	4			
Concomitant medication review	X	←==========X==========→					(X)	X	
Blood sampling for PK			←==========X==========→				(X)		[3]Predose, 5 min, 30 min, 1 hr, 1.5 hr, 2 hr, 3 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, and 48 hr, 60 hr, and 72 hr post-dose
Discharge from Clinical Unit						X	(X)		

- Duration of dosing in Part C can be modified based on the estimates of half-life from Part A.
- The timing and number of planned study assessments, including safety, PK, PD/biomarker or other assessments may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.

Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic/pharmacodynamic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol amendment. The CA and EC will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the ICF. The changes will be approved by the CA and the EC before implementation.

13.3. Appendix 3: Assessment Windows

Nominal time will be used for all analysis except PK analysis where planned and actual time will be used.

13.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

13.4.1. Study Phases

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

Study Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date + 3 days
Post-Treatment	Date > Study Treatment Stop Date + 3 days

Note: Estimated half-life of GSK3439171 is approx. 13 hours. The maximum of (5 halflives ~ 65 hours ~ 3days) and after the Study Treatment End Date, lag time have been considered to be 3 days to define the end of treatment phase.

13.4.1.1. 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.

13.5. Appendix 5: Data Display Standards & Handling Conventions

13.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: us1salx00259
HARP Compound	: /arenv/arprod/gsk3439171/mid209275/final_01
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.0	
Generation of RTF Files	
• RTF files will be generated for SAC.	

13.5.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject 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, unless otherwise stated. • 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 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 subject's listings.

Unscheduled Visits
• Unscheduled visits will not be included in summary tables and/or figures. However, for baseline consideration if the latest predose is an unscheduled visit, then as per the baseline definition, this will be considered as baseline. And unscheduled visits will be taken into consideration for calculating worst-case post baseline value in ECG displays as well. • 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.

13.5.3. Reporting Standards for 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)
Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 90% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation (CVb (%)) will be reported.

	CVb (%) = √ (exp(SD2) - 1) * 100 [NOTE: SD = SD of loge transformed data] Following steps can be used to calculate 90% CI for PK parameters: Standard Error = [(Geometric Stdev-1)/Sqrt(N)], Margin of Error = [Standard Error * 1.645], and CI = [Geometric Mean ± Margin of Error]
Parameters Not Being Log Transformed	tmax, t½
Summary Tables	Cmax, tmax, AUC(0-τ), AUC(0-t), AUC (0-∞), AUC (Ro), Rcmax, Cτ, t1/2, Rss, Ae, fe, CLr, as data permit
Listings	Include PK Parameters Cmax, tmax, AUC(0-τ), AUC(0-t), AUC (0-∞), AUC (Ro), Rcmax, Cτ, t1/2, Rss, Ae, fe, CLr, as data Permit
Graphical Displays	
Refer to IDSL Statistical Principles 7.01 to 7.13 and Standards for the Transfer and Reporting of PK Data using HARP.	

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the noncompartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to [Insert document name]. 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: [Insert PK parameters, e.g. C24, C12, AUC/Dose]
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.

13.6. Appendix 6: Derived and Transformed Data

13.6.1. General

Multiple Measurements at One Analysis 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 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 visit 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 and Period Study Day
In **PART A and C**, Period Study day is calculated as the number of days from first Dose Date in the period for each subject as follows: • Ref Date = Missing → Period Study Day = Missing • Ref Date < First Dose Date in the period → Period Study Day = Ref Date – First Dose Date in the period • Ref Data ≥ First Dose Date in the period→ Period Study Day = Ref Date – First Dose Date in the period + 1 In **Part A, B & C**: Study day is calculated as the number of days from First Dose Date in each Cohort for each subject as: • 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
Change from baseline and Percentage change from baseline definition
Change from Baseline = Post-Dose Visit Value – Baseline (For Part A & C, corresponding period baseline should be considered as baseline) Percentage Change from Baseline = ((Post-Dose Visit Value – Baseline)/Baseline)*100 (For Part A & C, corresponding period baseline should be considered as baseline) • Unless otherwise specified, the baseline definitions specified in Section 5.2 Baseline Definition will be used for derivations for endpoints / parameters and indicated on summaries and listings • Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing
Displays

- Compound ID should be used as GSK3439171 for the displays
- Listings: Since it is single site study, site id and investigator id will be included in 'Listing of Planned and Actual Treatment' and will be excluded from other Listings.
- Safety summaries and figures:
    - Part A and B, 'All treatment' total (Subjects on treatment except placebo) should be included and footnote to indicate this. Part C overall 'Total' should be included.
    - Part A and C, in Lab, Vitals and ECG displays, Day -2 and -1(if available) should be included for absolute value displays.
    - Part B in Lab, Vitals and ECG displays, Day -2 and -1(if available) should be included for absolute value displays along with screening and follow up data. And for change from baseline and percentage change from baseline displays follow up data should be included

13.6.2. Study Population

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.

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 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.

13.6.3. Safety

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, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value. o Example 1: 2 Significant Digits = '< x ' becomes x – 0.01 o Example 2: 1 Significant Digit = '> x' becomes x + 0.1 o Example 3: 0 Significant Digits = '< x' becomes x – 1

ECG Parameters
RR Interval
• If RR interval (msec) is not provided directly, then RR can be derived as: [1] If QTcF is machine read, 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 ClinBase, corrected QT intervals by Fredericia's (QTcF) formula will be calculated in msec, depending on the availability of other measurements. • IF RR interval (msec) is provided then missing QTcF will be derived as: $$QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

13.6.4. Pharmacokinetic

PK Parameters
The PK Population will include all subjects who undergo PK sampling and have evaluable PK assay results. • See Table 2. Derived Pharmacokinetic Parameters (Primary end points) and Table 3. Derive d Pharmacokinetic Parameters (Secondary end points) for derived Pharmacokinetic parameters

13.7. Appendix 7: Reporting Standards for Missing Data

13.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as 'A participant is considered to have completed the study if he/she has completed all phases of the study including or the last scheduled procedure shown in the SoA.' • Withdrawn subjects may 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.

13.7.2. 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: ○ These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ 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.

13.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The Clinbase 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: ○ 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 4: Study Phases ○ 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 will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day

Element	Reporting Detail
	(dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings. • For each period in crossover design: o If start date is completely missing, then we assume the medication has been taken from the beginning of the study o If stop date is completely missing, then we assume the medication has been taken until the end of the study

13.7.2.2. Handling of PK Concentration Data

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

13.7.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
Imputation	o No imputation will be performed for missing data

13.8. Appendix 8: Values of Potential Clinical Importance

13.8.1. Laboratory Values

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	
Haemoglobin	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	umol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Magnesium	mmol/L		.5	1.23
Phosphorus	mmol/L		.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Creatine Kinase (CK)				>500 U/l
Liver Function				
Test Analyte	**Units**	**Category**	**Clinical Concern 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	≥ 1.5x ULN	
T. Bilirubin + ALT	µmol/L U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT	

13.8.2. ECG

ECG Parameter	Units	Clinical Concern 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

13.8.3. Vital Signs

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

13.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

PopPK will be performed under a separate RAP and will be reported separately

13.10. Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

A detailed population PK/PD data analysis plan will be prepared in a separate RAP.

13.11. Appendix 11: Abbreviations & Trade Marks

13.11.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PopPK	Population PK
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan

Abbreviation	Description
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
SR	Safety Review

13.11.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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13.12. Appendix 12: List of Data Displays

- **PROGRAMMING NOTES:** Where applicable, programming notes can be included to supplement and/or highlight specific information to aid with display generation.
    - Consideration should be given to any changes to the standard GSK IDSL displays or inclusion of optional columns for safety reporting.
    - If applicable, provide additional information to aid generation of graphical displays (e.g. if a multiple panel plot is being generated then details such as the number of rows / columns, panel by variable, legend variable etc may be included).
    - Consideration should be given for additional level of instructions for any outsourced studies, so as to ensure clarity for generating each display to the expected specifications.
    - Note: Small studies (e.g. early phase studies) or where sample sizes or event rates are small, study teams may choose to omit certain summary tables where a listing of the data would be sufficient (See IDSL Principle 4.21 Minimal Analysis). The lead RAP author / RAP Team should consult and get agreement from medical writing / CSR writer that listings would be sufficient for the study.

13.12.1. Data Display Numbering

- **NOTE:** The numbering of data displays is now driven by best practices outlined for the development of the Clinical Study Report but the numbering scheme should be utilised for all reporting efforts. For listings utilise sequential numbering for ICH and Other Listings.
- **Automation:** Numbering of data displays is automated within tables. If rows are added or deleted, the numbering of displays will be automatically updated. Therefore, when updating sections based on the order of objectives / endpoints in the protocol, rename section headings rather than rearranging sections using cut and paste options.

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.33	-
Safety	3.1 to 3.67	3.1 to 3.28
Pharmacokinetic	4.1 to 4.26	4.1 to 4.15
Pharmacodynamic and / or Biomarker	6.1 to 6.9	6.1 to 6.16
Section	**Listings**	
ICH Listings	1 to 110	
Non-ICH Listings	111 to 134	
Other Listings	135	

13.12.2. Mock Example Shell Referencing

- **Mock Example Shells:** Only to be provided if not covered by GSK IDSL, or if there are major changes to the standard data displays.

- Alternately, provide an appropriate GSK IDSL data standard reference and include details in the programming notes column for the display to be generated.

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Section 13.13: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic / Biomarker	PD_Fn	PD_Tn	PD_Ln

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

13.12.3. Deliverables

- **Delivery Priority:** If applicable, can provide information on whether specific outputs are required at times other than statistical analysis complete (SAC) or to provide an order of displays to be generated so as to facilitate and manage reporting.

- Example where the deliverable priority may be used are:

  - **Decision Critical Data Reporting:** For example, this may include endpoints reported prior to SAC that are required for making critical decisions for the compound.

  - **Partial Data Reporting:** For example, this may include a study conducted in multiple parts where there will be unblinding and reporting of one or more parts of the study prior to database freeze.

  - **Exploratory Data Reporting:** For example, this may include endpoints that are potentially analysed post SAC (e.g. TAQMAN data). These may not be intended for the CPSR report and as such would not need to have a table or figure number.

  - **Output for Presentation Purposes Only:** For example, this may include combining output with data from other sources for presentation purposes. These would not be intended for the CPSR report and as such would not need to have a display number.

Delivery [Priority] [1]	Description
SR	Safety Review (after completing Part A and Part B cohort 1& 2)
SAC	Final Statistical Analysis Complete

NOTES:

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

13.12.4. Study Population Tables

- The requirements for each display (i.e. IDSL, ICH etc.) specified in the programming notes may be retained, all other red reference notes should be deleted.
- Select appropriate standard based on study design (i.e. parallel vs cross-over), when applicable.
- The ADaM datasets for the Core Study Population/Safety displays can be found in the IDSL Library under Reference →Statistical Displays →ADaM Datasets for Core RAP Displays

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	CP_ES1	Summary of Subject Status and Reason for Study Withdrawal - Part A	by Cohort	SAC
1.2.	Safety	CP_ES1	Summary of Subject Status and Reason for Study Withdrawal - Part B	by Cohort	SAC
1.3.	Safety	CP_ES1	Summary of Subject Status and Reason for Study Withdrawal - Part C	By Cohort- since only one cohort, 'Total' column	SAC
1.4. \	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment – Part B	By Dose	SAC
1.5.	Safety	ES4	Summary of Participant Disposition at Each Study Epoch - Part A	By Cohort	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.6.	Safety	ES4	Summary of Participant Disposition at Each Study Epoch - Part C	By Cohort	SAC
1.7.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure - Part A	by Cohort	SAC
1.8.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure - Part B	by Cohort	SAC
1.9.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure - Part C	By Cohort- since only one cohort, 'Total' column	SAC
Protocol Deviation					
1.10.	Safety	DV1	Summary of Important Protocol Deviations - Part A	By dose	SAC
1.11.	Safety	DV1	Summary of Important Protocol Deviations - Part B	By Dose	SAC
1.12.	Safety	DV1	Summary of Important Protocol Deviations - Part C	By Dose	SAC
Population Analysed					
1.13.	Screened	SP1	Summary of Study Populations by Dose- Part A	By Dose and 'All Treatment' column (Subjects on treatment except placebo) should be included instead of 'Total' column	SAC
1.14.	Screened	SP1	Summary of Study Populations by Cohort- Part A	By Cohort	SAC
1.15.	Screened	SP1	Summary of Study Populations by Dose- Part B	By Dose and 'All Treatment' column (Subjects on treatment except placebo) should be included instead of 'Total' column	SAC
1.16.	Screened	SP1	Summary of Study Populations by Cohort- Part B	By Cohort	SAC
1.17.	Screened	SP1	Summary of Study Populations - Part C	By Dose and 'Total' column	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
1.18.	Safety	DM3	Summary of Demographic Characteristics - Part A	By cohort	SAC
1.19.	Safety	DM1	Summary of Demographic Characteristics - Part B	By cohort	SAC
1.20.	Safety	DM3	Summary of Demographic Characteristics - Part C		SAC
1.21.	Randomized	DM11	Summary of Age Ranges – Part A	EudraCT, Disclosure display	SAC
1.22.	Randomized	DM11	Summary of Age Ranges – Part B	EudraCT, Disclosure display	SAC
1.23.	Randomized	DM11	Summary of Age Ranges – Part C	EudraCT, Disclosure display Add 'Total' column	SAC
1.24.	Safety	DM5	Summary of Race and Racial Combinations - Part A	ICH E3, FDA, FDAAA, EudraCT, Disclosure display Add 'Total' column	SAC
1.25.	Safety	DM5	Summary of Race and Racial Combinations - Part B	ICH E3, FDA, FDAAA, EudraCT, Disclosure display	SAC
1.26.	Safety	DM5	Summary of Race and Racial Combinations - Part C	ICH E3, FDA, FDAAA, EudraCT, Disclosure display Add 'Total' column	SAC
Prior and Concomitant Medications					
1.27.	Safety	MH1	Summary of Current/Past Medical Conditions - Part A	by Cohort	SAC
1.28.	Safety	MH1	Summary of Current/Past Medical Conditions - Part B	by Cohort	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.29.	Safety	MH1	Summary of Current/Past Medical Conditions - Part C	By Cohort- since only one cohort, 'Total' column	SAC
1.30.	Safety	CP_CM1	Summary of Concomitant Medications - Part A	by Cohort	SAC
1.31.	Safety	CP_CM1	Summary of Concomitant Medications - Part B	by Cohort	SAC
1.32.	Safety	CP_CM1	Summary of Concomitant Medications - Part C	By Cohort- since only one cohort, 'Total' column	SAC
Exposure and Treatment Compliance					
1.33.	Safety	EX1	Summary of Exposure to Study Treatment - Part B	ICH E3 Dose and/or time on treatment, as applicable. Many possible considerations; defer to therapy area standards where available. For ClinPharm, a listing often substitutes for a table.	SAC

13.12.5. Safety Tables

- The requirements for each display (i.e. IDSL, ICH, FDAAA etc) specified in the programming notes may be retained, all other red reference notes should be deleted.
- Select appropriate standard based on study design (i.e. parallel vs cross-over), when applicable.
- Suggested IDSL shells are noted in the third column, but other IDSL shells may be used, as appropriate

- The ADaM datasets for the Core Study Population/Safety displays can be found in the IDSL Library under Reference →Statistical Displays →ADaM Datasets for Core RAP Displays

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	CP_AE1x	Summary of All Adverse Events by System Organ Class and Preferred Term - Part A		SAC
3.2.	Safety	CP_AE1p	Summary of All Adverse Events by System Organ Class and Preferred Term - Part B		SAC
3.3.	Safety	CP_AE1p	Summary of All Adverse Events by System Organ Class and Preferred Term by Study Phase - Part B		SAC
3.4.	Safety	CP_AE1x	Summary of All Adverse Events by System Organ Class and Preferred Term - Part C		SAC
3.5.	Safety	AE5B	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term – Part A		SAC
3.6.	Safety	AE5B	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term – Part B		SAC
3.7.	Safety	AE5B	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term – Part C		SAC
3.8.	Safety	CP_AE1x	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term- Part A		SAC
3.9.	Safety	CP_AE1p	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term - Part B	As 3.1 notes.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	Safety	CP_AE1x	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term - Part C	As 3.1 notes.	SAC
3.11.	Safety	AE15	Summary of Common (>=10%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences) – Part A	FDAAA, EudraCT Disclosure display Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	SAC
3.12.	Safety	AE15	Summary of Common (>=10%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences) – Part B	FDAAA, EudraCT Disclosure display 'Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	Safety	AE15	Summary of Common (>=10%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences) – Part C	FDAAA, EudraCT Disclosure display 'Common' to be defined by study/project team. For studies with very few events/participants, listing is sufficient: discuss this option with your disclosure representative.	SAC
Serious and Other Significant Adverse Events					
3.14.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) - Part A	FDAAA, EudraCT By dose For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative.	SAC
3.15.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) - Part B	FDAAA, EudraCT For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.16.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) - Part C	FDAAA, EudraCT For studies with few events/participants listing is sufficient: discuss this option with your disclosure representative.	SAC
Laboratory: Chemistry					
3.17.	Safety	LB1	Summary of Clinical Chemistry Values – Part A	By dose Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SR, SAC
3.18.	Safety	LB1	Summary of Clinical Chemistry Values – Part B	By dose Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SR, SAC
3.19.	Safety	LB1	Summary of Clinical Chemistry Values – Part C	By treatment group (fed/fasted) Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SAC
3.20.	Safety	LB1	Summary of Chemistry Changes from Baseline - Part A	By dose and 'All Treatment' for all parameters mentioned in the protocol Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SR, SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.21.	Safety	LB1	Summary of Chemistry Changes from Baseline - Part B	By dose for all parameters mentioned in the protocol Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SR, SAC
3.22.	Safety	LB1	Summary of Chemistry Changes from Baseline - Part C	By treatment group (fed/fasted) and 'Total' for all parameters mentioned in the protocol Includes Baseline values. Includes pre-specified parameters repeated in conventional units.	SAC
3.23.	Safety	LB1	Summary of Chemistry Percent Changes from Baseline - Part A	By dose and 'All Treatment' for all parameters mentioned in the protocol Includes Baseline values. Baseline values are required Includes pre-specified parameters repeated in conventional units.	SAC
3.24.	Safety	LB1	Summary of Chemistry Percent Changes from Baseline - Part B	By dose for all parameters mentioned in the protocol Includes Baseline values. Baseline values are required Includes pre-specified parameters repeated in conventional units.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.25.	Safety	LB1	Summary of Chemistry Percent Changes from Baseline - Part C	By treatment group (fed/fasted) and 'Total' for all parameters mentioned in the protocol Includes Baseline values. Baseline values are required Includes pre-specified parameters repeated in conventional units.	SAC
Laboratory: Haematology					
3.26.	Safety	LB1	Summary of Haematology Values – Part A	By dose for all parameters mentioned in the protocol	SR, SAC
3.27.	Safety	LB1	Summary of Haematology Values – Part B	By dose for all parameters mentioned in the protocol	SR, SAC
3.28.	Safety	LB1	Summary of Haematology Values – Part C	By treatment group (fed/fasted) and 'Total' for all parameters mentioned in the protocol	SAC
3.29.	Safety	LB1	Summary of Haematology Changes from Baseline - Part A	By dose and 'All Treatment' (treatment vs placebo) for all parameters mentioned in the protocol	SR, SAC
3.30.	Safety	LB1	Summary of Haematology Changes from Baseline - Part B	By dose for all parameters mentioned in the protocol	SR, SAC
3.31.	Safety	LB1	Summary of Haematology Changes from Baseline - Part C	By treatment group (fed/fasted) and 'Total' for all parameters mentioned in the protocol	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.32.	Safety	LB1	Summary of Haematology Percent Changes from Baseline - Part A	By dose and 'All Treatment' (treatment vs placebo) for all parameters mentioned in the protocol Baseline values are required	SAC
3.33.	Safety	LB1	Summary of Haematology Percent Changes from Baseline - Part B	By dose for all parameters mentioned in the protocol Baseline values are required	SAC
3.34.	Safety	LB1	Summary of Haematology Percent Changes from Baseline - Part C	By treatment group (fed/fasted) and 'Total' for all parameters mentioned in the protocol Baseline values are required	SAC
Hormone Assessment					
3.35.	Safety	LB1	Summary of Hormone Assessment Values – Part B	By dose for all parameters mentioned in the protocol	SR, SAC
3.36.	Safety	LB1	Summary of Hormone Assessment Changes from Baseline - Part B	By dose for all parameters mentioned in the protocol	SR, SAC
3.37.	Safety	LB1	Summary of Hormone Assessment Percent Changes from Baseline - Part B	By dose for all parameters mentioned in the protocol Baseline values are required	SR, SAC
Laboratory: Urinalysis					
3.38.	Safety	UR3b	Summary of Urinalysis Dipstick Results – Part A	ICH E3 Page by test Includes Baseline values.	SAC
3.39.	Safety	UR3b	Summary of Urinalysis Dipstick Results – Part B	ICH E3 Page by test Includes Baseline values.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.40.	Safety	UR3b	Summary of Urinalysis Dipstick Results – Part C	ICH E3 Page by testIncludes Baseline values.	SAC
Laboratory: Liver Function					
3.41.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part A	IDSL	SAC
3.42.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part B	IDSL	SAC
3.43.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part C	IDSL	SAC
3.44.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part A	IDSL Listing may be sufficient if few events.	SAC
3.45.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part B	IDSL Listing may be sufficient if few events.	SAC
3.46.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part C	IDSL Listing may be sufficient if few events.	SAC
ECG					
3.47.	Safety	EG1	Summary of ECG Findings – Part A	IDSL As above for Chemistry, using ECG findings categories (and change from baseline categories, if applicable).	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.48.	Safety	EG1	Summary of ECG Findings – Part B	IDSL As above for Chemistry, using ECG findings categories (and change from baseline categories, if applicable).	SAC
3.49.	Safety	EG1	Summary of ECG Findings – Part C	IDSL As above for Chemistry, using ECG findings categories (and change from baseline categories, if applicable).	SAC
3.50.	Safety	EG2	Summary of Change from Baseline in ECG Values – Part A	IDSL Includes Baseline values.	SAC
3.51.	Safety	EG2	Summary of Change from Baseline in ECG Values – Part B	IDSL Includes Baseline values.	SAC
3.52.	Safety	EG2	Summary of Change from Baseline in ECG Values – Part C	IDSL Includes Baseline values.	SAC
3.53.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part A	IDSL Recommended for studies with sufficiently large sample size or frequency of values of interest.	SAC
3.54.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part B	IDSL Recommended for studies with sufficiently large sample size or frequency of values of interest.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.55.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part C	IDSL Recommended for studies with sufficiently large sample size or frequency of values of interest.	SAC
3.56.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part A	IDSL Recommended for studies with sufficiently large sample size or frequency of values of interest.	SAC
3.57.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part B	IDSL Recommended for studies with sufficiently large sample size or frequency of values of interest.	SAC
3.58.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part C	IDSL Recommended for studies with sufficiently large sample size or frequency of values of interest.	SAC
Vital Signs					
3.59.	Safety	VS1	Summary of Vital Signs – Part A	ICH E3 Includes Baseline values.	SAC
3.60.	Safety	VS1	Summary of Vital Signs – Part B	ICH E3 Includes Baseline values.	SAC
3.61.	Safety	VS1	Summary of Vital Signs – Part C	ICH E3 Includes Baseline values.	SAC
3.62.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part A	ICH E3 Includes Baseline values.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.63.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part B	ICH E3 Includes Baseline values.	SAC
3.64.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part C	ICH E3 Includes Baseline values.	SAC
3.65.	Safety	VS1	Summary of Percent Change from Baseline in Vital Signs – Part A	ICH E3 Includes Baseline values.	SAC
3.66.	Safety	VS1	Summary of Percent Change from Baseline in Vital Signs – Part B	ICH E3 Includes Baseline values.	SAC
3.67.	Safety	VS1	Summary of Percent Change from Baseline in Vital Signs – Part C	ICH E3 Includes Baseline values.	SAC

13.12.6. Safety Figures

- The requirements for each display (i.e. IDSL, ICH etc) specified in the programming notes may be retained, all other reference notes can be deleted.

- Select appropriate standard based on study design (i.e. parallel vs cross-over), when applicable.

- The ADaM datasets for the Core Study Population/Safety displays can be found in the IDSL Library under Reference →Statistical Displays →ADaM Datasets for Core RAP Displays.

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Chemistry					
3.1.	Safety	LB_PLOT1	Individual Plot of Clinical Chemistry Parameters Over Time by Dose – Part A	By dose	SAC
3.2.	Safety	LB_PLOT1	Individual Plot of Clinical Chemistry Parameters Over Time by Dose – Part B	By dose	SAC
3.3.	Safety	LB_PLOT1	Individual Plot of Clinical Chemistry Parameters Over Time by Dose – Part C	By dose	SAC
3.4.	Safety	LB_PLOT1	Individual Plot of Clinical Chemistry Parameters Over Time by Subject – Part A	By subject	SAC
3.5.	Safety	LB_PLOT1	Individual Plot of Clinical Chemistry Parameters Over Time by Subject – Part C	By subject	SAC
3.6.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Clinical Chemistry Parameters Over Time by Dose – Part A	By dose and treatment (treatment vs placebo) for all parameters mentioned in the protocol	SAC
3.7.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Clinical Chemistry Parameters Over Time by Dose – Part B	By dose for all parameters mentioned in the protocol	SAC
3.8.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Clinical Chemistry Parameters Over Time by Dose – Part C	By treatment group (fed/fasted) for all parameters mentioned in the protocol	SAC
3.9.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Clinical Chemistry Parameters Over Time by Dose – Part A	By dose and treatment (treatment vs placebo) for all parameters mentioned in the protocol	SAC
3.10.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Clinical Chemistry Parameters Over Time by Dose – Part B	By dose for all parameters mentioned in the protocol	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.11.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Clinical Chemistry Parameters Over Time by Dose – Part C	By treatment group (fed/fasted) for all parameters mentioned in the protocol	SAC
Laboratory: Haematology					
3.12.	Safety	LB_PLOT1	Individual Plot of Haematology Parameters Over Time by Dose – Part A	By dose	SAC
3.13.	Safety	LB_PLOT1	Individual Plot of Haematology Parameters Over Time by Dose – Part B	By dose	SAC
3.14.	Safety	LB_PLOT1	Individual Plot of Haematology Parameters Over Time by Dose – Part C		SAC
3.15.	Safety	LB_PLOT1	Individual Plot of Haematology Parameters Over Time by Subject – Part A	By Subject	SAC
3.16.	Safety	LB_PLOT1	Individual Plot of Haematology Parameters Over Time by Subject – Part C	By Subject	SAC
3.17.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Haematology Parameters Over Time by Dose – Part A	By dose and treatment (treatment vs placebo) for all parameters mentioned in the protocol	SAC
3.18.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Haematology Parameters Over Time by Dose – Part B	By dose for all parameters mentioned in the protocol	SAC
3.19.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Haematology Parameters Over Time by Dose – Part C	By treatment group (fed/fasted) for all parameters mentioned in the protocol	SAC
3.20.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Haematology Parameters Over Time by Dose – Part A	By dose and treatment (treatment vs placebo) for all parameters mentioned in the protocol	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.21.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Haematology Parameters Over Time by Dose – Part B	By dose for all parameters mentioned in the protocol	SAC
3.22.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Haematology Parameters Over Time by Dose – Part C	By treatment group (fed/fasted) for all parameters mentioned in the protocol	SAC
Hormone Assessment					
3.23.	Safety	LB_PLOT1	Individual Plot of Hormone Assessment Parameters Over Time by Dose – Part B	By dose	SAC
3.24.	Safety	LB_PLOT2	Mean ±SD Plot of Change from Baseline for Hormone Assessment Parameters Over Time by Dose – Part B	By dose for all parameters mentioned in the protocol	SAC
3.25.	Safety	LB_PLOT2	Mean ±SD Plot of Percent Change from Baseline for Hormone Assessment Parameters Over Time by Dose – Part B	By dose for all parameters mentioned in the protocol	SAC
Laboratory: Liver Function					
3.26.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT – Part A	Recommended for larger studies, but not required for smaller studies.	SAC
3.27.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT – Part B	Recommended for larger studies, but not required for smaller studies.	SAC

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.28.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT – Part C	Recommended for larger studies, but not required for smaller studies.	SAC

13.12.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK concentration					
4.1.	PK	PK01	Summary of Plasma GSK3439171 Pharmacokinetic Concentration-Time Data (ng/mL) – Part A		SAC
4.2.	PK	PK01	Summary of Plasma GSK3439171 Pharmacokinetic Concentration-Time Data (ng/mL) – Part B		SAC
4.3.	PK	PK01	Summary of Plasma GSK3439171 Pharmacokinetic Concentration-Time Data (ng/mL) – Part C		SAC
PK Urine					
4.4.	PK	PK02	Summary of Pharmacokinetic Urine Excretion Rate-Time Data – Part B		SAC
PK derived parameters					
4.5.	PK	PK03	Summary Statistics of Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part A		SAC
4.6.	PK	PK03	Summary Statistics of Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part B		SAC
4.7.	PK	PK03	Summary Statistics of Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part C		SAC
4.8.	PK	PK05	Summary Statistics of Log-Transformed Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part A		SAC
4.9.	PK	PK05	Summary Statistics of Log-Transformed Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part B		SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.10.	PK	PK05	Summary Statistics of Log-Transformed Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part C		SAC
4.11.	PK	PK_T1	Statistical Analysis of Plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part A	t1/2	SAC
4.12.	PK	PK_T1	Statistical Analysis of Plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part B	t1/2 Include 'Visit' as first column	SAC
4.13.	PK	PK_T1	Statistical Analysis of Plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part C	t1/2	SAC
4.14.	PK	PK_T2	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part A	AUC(0-t), AUC(0-24), AUC(0-∞), Cmax, Cτ, AUC(Rp)	SAC
4.15.	PK	PK_T2	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part B	AUC(0- τ), AUC(0-∞), Cmax, Cτ Include 'Visit' as first column	SAC
4.16.	PK	PK_T2	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part C	AUC(0-t), AUC(0-∞), Cmax	SAC
4.17.	PK	PK_T5	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Accumulation Ratio and Time Invariance – Part B		SAC
4.18.	PK	PK_T6	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Achievement of Steady State – Part B		SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.19.	PK	PK_T3	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Dose Proportionality (Power Model) – Part A	AUC(0-t), AUC(0-∞) and Cmax	SAC
4.20.	PK	PK_T4	Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Dose Proportionality (Power Model) – Part B	AUC(0-τ) and Cmax By timepoint	SAC
Pharmacogenetic					
4.21.	PK	GN1	Summary of Subject Accountability – Part A	By cohort	SAC
4.22.	PK	GN1	Summary of Subject Accountability – Part B		SAC
4.23.	PK	GN1	Summary of Subject Accountability – Part C		SAC
4.24.	PK	GN2	Summary of Genetic Consent Not Obtained/Withdrawn – Part A	By cohort	SAC
4.25.	PK	GN2	Summary of Genetic Consent Not Obtained/Withdrawn – Part B		SAC
4.26.	PK	GN2	Summary of Genetic Consent Not Obtained/Withdrawn – Part C		SAC

13.12.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Concentration Plots					
4.1.	PK	PK16b	Individual Plasma GSK3439171 Concentration-time Plot (Linear and Semi-log) by Subject – Part A		SAC
4.2.	PK	PK16a	Individual Plasma GSK3439171 Concentration-time Plot (Linear and Semi-log) by Subject – Part B		SAC
4.3.	PK	PK16b	Individual Plasma GSK3439171 Concentration-time Plot (Linear and Semi-log) by Subject – Part C		SAC
4.4.	PK	PK24	Individual Plasma GSK3439171 Concentration-time Plot (Linear and Semi-log) by Treatment – Part A		SAC
4.5.	PK	PK24	Individual Plasma GSK3439171 Concentration-time Plot (Linear and Semi-log) by Treatment – Part B		SAC
4.6.	PK	PK24	Individual Plasma GSK3439171 Concentration-time Plot (Linear and Semi-log) by Treatment – Part C		SAC
4.7.	PK	PK17	Mean Plasma GSK3439171 Concentration-Time Plots (Linear and Semi-log) – Part A		SAC
4.8.	PK	PK17	Mean Plasma GSK3439171 Concentration-Time Plots (Linear and Semi-log) – Part B		SAC
4.9.	PK	PK17	Mean Plasma GSK3439171 Concentration-Time Plots (Linear and Semi-log) – Part C		SAC
4.10.	PK	PK18	Median Plasma GSK3439171 Concentration-Time Plots (Linear and Semi-log) – Part A		SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.11.	PK	PK18	Median Plasma GSK3439171 Concentration-Time Plots (Linear and Semi-log) – Part B		SAC
4.12.	PK	PK18	Median Plasma GSK3439171 Concentration-Time Plots (Linear and Semi-log) – Part C		SAC
4.13.	PK	PK21	Individual GSK3439171 Urine Excretion Rate-Time Plots (Linear and Semi-log) – Part B		SAC
4.14.	PK	PK22	Mean GSK3439171 Urine Excretion Rate-Time Plots (Linear and Semi-log) – Part B		SAC
4.15.	PK	PK23	Median GSK3439171 Urine Excretion Rate-Time Plots (Linear and Semi-log) – Part B		SAC

13.12.9. Pharmacodynamic (and / or Biomarker) Tables

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Urinary Tetranor and Urinary Creatinine					
6.1.	PD	PK03	Summary Statistics of Urinary Tetranor and Urinary Creatinine Concentration Data– Part A		SAC

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.2.	PD	PK03	Summary Statistics of Urinary Tetranor and Urinary Creatinine Parameters – Part A	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Raw data (mass) 2)Creatinine corrected raw data, 3)Creatinine corrected aggregated data 0-12hrs, 4)Creatinine corrected aggregated data 12-24hrs 5)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value, Placebo corrected value and ratio of tPGDM/tPGEM for version 2,3 & 4 of the data mentioned above *PD parameters*: Creatinine *End points #*: • 1)Raw data (mass), 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4) Aggregated data 24-48hrs Baseline corrected value and Placebo corrected value for version 2,3 & 4 of the data mentioned above	SAC
6.3.	PD	PK03	Summary Statistics of Urinary Tetranor and Urinary Creatinine Concentration Data – Part B		SAC

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.4.	PD	PK03	Summary Statistics of Urinary Tetranor and Urinary Creatinine Parameters – Part B	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Raw data (mass) 2)Creatinine corrected raw data, 3)Creatinine corrected aggregated data 0-12hrs, 4)Creatinine corrected aggregated data 12-24hrs 5)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value and ratio of tPGDM/tPGEM for version 3,4 & 5 of the data mentioned above *PD parameters*: Creatinine *End points #*: • 1)Raw data (mass) 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs Baseline corrected value and Placebo corrected value for version 2,3 & 4 of the data mentioned above	SAC

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.5.	PD	PK05	Summary Statistics of Log-Transformed Urinary Tetranor and Urinary Creatinine Parameters – Part A	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Raw data (mass) Predose aggregated data – 24-12hr, 12-0hr 2) Raw data (mass) Post dose aggregated data 0-12hrs, 12-24 hr & 24-48 hr 3)Creatinine corrected data predose aggregated – 24-12hr, 12-0hr 4)Creatinine corrected data postdose aggregated 0-12hrs, 12-24 hr & 24-48 *PD parameters*: Creatinine *End points #*: 1)Raw data (mass) Predose aggregated data – 24-12hr, 12-0hr 2) Raw data (mass) Post dose aggregated data 0-12hrs, 12-24 hr & 24-48 hr	SAC

Pharmacodynamic (and or Biomarker): Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.6.	PD	PK05	Summary Statistics of Log-Transformed Urinary Tetranor and Urinary Creatinine Parameters – Part B	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Raw data (mass) Predose aggregated data – 24-12hr, 12-0hr 2) Raw data (mass) Post dose aggregated data 0-12hrs, 12-24 hr & 24-48 hr 3)Creatinine corrected data predose aggregated – 24-12hr, 12-0hr 4)Creatinine corrected data postdose aggregated 0-12hrs, 12-24 hr & 24-48 *PD parameters*: Creatinine *End points #*: • 1)Raw data (mass) Predose aggregated data – 24-12hr, 12-0hr 2) Raw data (mass) Post dose aggregated data 0-12hrs, 12-24 hr & 24-48 hr	SAC
6.7.	PD	PK05	Summary Statistics of Muscle Concentration Data – Part B		SAC
6.8.	PD	PD_T1	Statistical Analysis of Urinary Tetranor and Urinary Creatinine Parameters: Mixed Effect Model – Part A	tPGDM, tPGEM, Creatinine, Creatinine corrected tPGDM and Creatinine corrected tPGEM	SAC
6.9.	PD	PD_T1	Statistical Analysis of Urinary Tetranor and Urinary Creatinine Parameters: Mixed Effect Model – Part B	tPGDM, tPGEM, Creatinine, Creatinine corrected tPGDM and Creatinine corrected tPGEM	SAC

13.12.10. Pharmacodynamic (and / or Biomarker) Figures

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Urinary Tetranor					
6.1.	PD	LB_PLOT1	Plot of Urinary Tetranor and Urinary Creatinine vs Time by Dose– Part A	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value, Placebo corrected value and ratio of tPGDM/tPGEM for first 3 versions of the data mentioned above *PD parameters*: Creatinine *End points #*: • 1)Raw data, 2)Aggregated data 0-12hrs 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs • Baseline corrected value and Placebo corrected value for first 3 versions of the data mentioned above Note: X-axis values – actual midpoint of collection	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.2.	PD	LB_PLOT1	Plot of Urinary Tetranor and Urinary Creatinine vs Time by Dose– Part B	*PD parameters*: tPGDM, tPGEM for Day 1, 7, 9, 10 &17. *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value for first 3 versions of the data mentioned above *PD parameters*: Creatinine for Day 1, 7, 9, 10 &17 *End points #*: • 1)Raw data, 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs • Baseline corrected value for first 3 versions of the data mentioned above Note1: X-axis values – actual midpoint of collection Note2: Panel plot each day as panel. Data available on day 1 for all cohorts, day 7 & 10 for cohort 3 only, day 9 &17 for cohort 1&2.	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.3.	PD	LB_PLOT1	Plot of Urinary Tetranor and Urinary Creatinine vs Time by Subject– Part A	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value, Placebo corrected value and ratio of tPGDM/tPGEM for first 3 versions of the data mentioned above *PD parameters*: Creatinine *End points #*: • 1)Raw data, 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs • Baseline corrected value and Placebo corrected value for first 3 versions of the data mentioned above Note: X-axis values – actual midpoint of collection	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.4.	PD	LB_PLOT1	Plot of Urinary Tetranor and Urinary Creatinine vs Time by Subject– Part B	*PD parameters*: tPGDM, tPGEM for Day 1, 7, 9, 10 &17 *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value for first 3 versions of the data mentioned above *PD parameters*: Creatinine for Day 1, 7, 9, 10 &17 *End points #*: • 1)Raw data, 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs • Baseline corrected value for first 3 versions of the data mentioned above Note1: X-axis values – actual midpoint of collection Note2: Each line(profile) for each day. Data available on day 1 for all cohorts, 7 & 10 for cohort 3 only, day 9 &17 for cohort 1&2.	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.5.	PD	LB_PLOT2	Geometric mean and 95% CI Urinary Tetranor and Urinary Creatinine vs time – Part A	*PD parameters*: tPGDM, tPGEM *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value, Placebo corrected value and ratio of tPGDM/tPGEM for first 3 versions of the data mentioned above *PD parameters*: Creatinine *End points #*: • 1)Raw data, 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs • Baseline corrected value and Placebo corrected value for first 3 versions of the data mentioned above Note: X-axis values – planned midpoint of collection	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.6.	PD	LB_PLOT2	Geometric mean and 95% CI Urinary Tetranor and Urinary Creatinine vs time – Part B	*PD parameters*: tPGDM, tPGEM for Day 1, 7, 9, 10 &17 *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Baseline corrected value for first 3 versions of the data mentioned above *PD parameters*: Creatinine for Day 1, 7, 9, 10 &17 *End points #*: • 1)Raw data, 2)Aggregated data 0-12hrs & 3)Aggregated data 12-24hrs 4)Aggregated data 24-48hrs • Baseline corrected value for first 3 versions of the data mentioned above Note2: X-axis values – planned midpoint of collection Panel plot with each day as panel. Data available on day 1 for all cohorts, day 7 & 10 for cohort 3 only, day 9 &17 for cohort 1&2.	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.7.	PD	LIVER14	Plot of Urinary Tetranor and Urinary Creatinine vs PK Concentration by Dose– Part A	*PD parameters*: tPGDM and tPGEM *End points #*: • Creatinine corrected raw data • Baseline corrected value and Placebo corrected value for creatinine corrected raw data *PD parameters* Creatinine *End points #*: • Raw data • Baseline corrected value and Placebo corrected value for raw data Note: X-Axis- PD concentration &Y- Axis – PK concertation Different colour for each subject Note: For each PD marker interval, use the upper bound as target time; e.g. for 0-2hr interval, 2hr is the target time; Identify PK concentration with nominal time at the target time;If there is no PK sample taken at target time, use the PK concentration data with nominal time before but closest to target time; Use 0 PK concentration for placebo	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.8.	PD	LIVER14	Plot of Urinary Tetranor and Urinary Creatinine vs PK Concentration by Dose– Part B	*PD parameters*: tPGDM and Tpgem for Day 1, 10 &17 *End points #*: • Creatinine corrected raw data • Baseline corrected value for creatinine corrected raw data *PD parameter:* Creatinine for Day 1, 10 &17 *End points #*: • Raw data • Baseline corrected value for raw data Note: : X-Axis- PD concentration &Y- Axis – PK concertation . Panel plot with each day in separate panel and each subject different symbol. Data available on day 1 for all cohorts, day 10 for cohort 3 only, day 17 for cohort 1&2. Note: For each PD marker interval, use the upper bound as target time; e.g. for 0-2hr interval, 2hr is the target time; Identify PK concentration with nominal time at the target time;If there is no PK sample taken at target time, use the PK concentration data with nominal time before but closest to target time; Use 0 PK concentration for placebo	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.9.	PD	LIVER14	Plot of Urinary Tetranor and Urinary Creatinine vs PK Concentration by Subject – Part A	*PD parameters*: tPGDM and tPGEM *End points #*: • Creatinine corrected raw data • Baseline corrected value and Placebo corrected value for creatinine corrected raw data *PD parameters* Creatinine *End points #*: • Raw data • Baseline corrected value and Placebo corrected value for raw data Note: X-Axis- PD concentration &Y- Axis – PK concertation For each PD marker interval, use the upper bound as target time; e.g. for 0-2hr interval, 2hr is the target time; Identify PK concentration with nominal time at the target time;If there is no PK sample taken at target time, use the PK concentration data with nominal time before but closest to target time; Use 0 PK concentration for placebo	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.10.	PD	LIVER14	Plot of Urinary Tetranor and Urinary Creatinine vs PK Concentration by Subject – Part B	*PD parameters*: tPGDM and Tpgem for Day 1, 10 &17 *End points #*: • Creatinine corrected raw data • Baseline corrected value for creatinine corrected raw data *PD parameter:* Creatinine for Day 1, 10 &17 *End points #*: • Raw data • Baseline corrected value for raw data Note: X-Axis- PD concentration &Y- Axis – PK concertation. Different symbol for each day. (Data available on day 1 for all cohorts, day 10 for cohort 3 only, day 17 for cohort 1&2. Note: For each PD marker interval, use the upper bound as target time; e.g. for 0-2hr interval, 2hr is the target time; Identify PK concentration with nominal time at the target time;If there is no PK sample taken at target time, use the PK concentration data with nominal time before but closest to target time; Use 0 PK concentration for placebo	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.11.	PD	LB_PLOT1	Plot of Ratio of Urinary Tetranor Parameters vs Time by Dose – Part A	*Ratios of PD parameters to consider*: tPGDM/tPGEM *End points #*: • 1)Creatinine corrected data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Time matched ratio for above mentioned 4 versions of data Note: X-axis values – actual midpoint of collection	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.12.	PD	LB_PLOT1	Plot of Ratio of Urinary Tetranor Parameters vs Time by Dose– Part B	*Ratios of PD parameters to consider*: tPGDM/tPGEM for Day 1, 7, 9, 10 & 17 *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Time matched ratio for above mentioned 4 versions of data *Note:* Panel plot with each panel for each day. Data available on day 1 for all cohorts, 7 & 10 for cohort 3 only, 9 &17 for cohort 1&2.	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.13.	PD	LB_PLOT1	Plot of Ratio of Urinary Tetranor Parameters vs Time by Subject– Part A	*Ratios of PD parameters to consider:* tPGDM/tPGEM *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Time matched ratio for above mentioned 4 versions of data Note: X-axis values – actual midpoint of collection	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.14.	PD	LB_PLOT1	Plot of Ratio of Urinary Tetranor Parameters vs Time by Subject– Part B	*Ratios of PD parameters to consider*: tPGDM/tPGEM for Day 1, 7, 9, 10 & 17 *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Time matched ratio for above mentioned 4 versions of data *Note:* Each line(profile) for each day. Data available on day 1 for all cohorts, day 7 & 10 for cohort 3 only, day 9 &17 for cohort 1&2.	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.15.	PD	LB_PLOT2	Geometric mean and 95% CI Ratio of Urinary Tetranor Parameters vs time – Part A	*Ratios of PD parameters to consider:* tPGDM/tPGEM *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Time matched ratio for above mentioned 4 versions of data Note: X-axis values – actual midpoint of collection	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.16.	PD	LB_PLOT2	Geometric mean and 95% CI Ratio of Urinary Tetranor Parameters vs time – Part B	*Ratios of PD parameters to consider*: tPGDM/tPGEM for Day 1, 7, 9, 10 & 17 *End points #*: • 1)Creatinine corrected raw data, 2)Creatinine corrected aggregated data 0-12hrs, 3)Creatinine corrected aggregated data 12-24hrs 4)Creatinine corrected aggregated data 24-48hrs • Time matched ratio for above mentioned 4 versions of data *Note:* Panel plot with each panel for each day. Data available on day 1 for all cohorts, day 7 & 10 for cohort 3 only, day 9 &17 for cohort 1&2.	SAC

#Refer to Section 10.1.1 for derivation of PD endpoints

13.12.11. ICH Listings

- The requirements for each display (i.e. IDSL, ICH etc) specified in the programming notes may be retained, all other reference notes can be deleted.
- Select appropriate standard based on study design (i.e. parallel vs cross-over), when applicable.
- The ADaM datasets for the Core Study Population/Safety displays can be found in the IDSL Library under Reference →Statistical Displays →ADaM Datasets for Core RAP Displays.

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure – Part A	Journal Guidelines	SAC
2.	Screened	ES7	Listing of Reasons for Screen Failure – Part B	Journal Guidelines	SAC
3.	Screened	ES7	Listing of Reasons for Screen Failure – Part C	Journal Guidelines	SAC
4.	Safety	CP_ES10x	Listing of Reasons for Study Withdrawal – Part A	ICH E3	SAC
5.	Safety	ES2	Listing of Reasons for Study Withdrawal – Part B	ICH E3	SAC
6.	Safety	CP_ES10x	Listing of Reasons for Study Withdrawal – Part C	ICH E3	SAC
7.	Safety	SD2	Listing of Reasons for Study Treatment Discontinuation – Part B	ICH E3 Required for all studies except single dose studies.	SAC
8.	Safety	BL2	Listing of Participants for Whom the Treatment Blind was Broken – Part A	ICH E3 Blinded studies only.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
9.	Safety	BL1	Listing of Participants for Whom the Treatment Blind was Broken – Part B	ICH E3 Blinded studies only.	SAC
10.	Safety	BL2	Listing of Participants for Whom the Treatment Blind was Broken – Part C	ICH E3 Blinded studies only.	SAC
11.	Safety	TA2	Listing of Planned and Actual Treatments – Part A		SAC
12.	Safety	TA1	Listing of Planned and Actual Treatments – Part B		SAC
13.	Safety	TA2	Listing of Planned and Actual Treatments – Part C		SAC
Protocol Deviations					
14.	Safety	DV2A	Listing of Important Protocol Deviations – Part A	ICH E3 Listing also includes analysis population exclusions.	SAC
15.	Safety	DV2	Listing of Important Protocol Deviations – Part B	ICH E3 Listing also includes analysis population exclusions.	SAC
16.	Safety	DV2A	Listing of Important Protocol Deviations – Part C	ICH E3 Listing also includes analysis population exclusions.	SAC
17.	Safety	IE4	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part A	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
18.	Safety	IE3	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part B	ICH E3	SAC
19.	Safety	IE4	Listing of Participants with Inclusion/Exclusion Criteria Deviations – Part C	ICH E3	SAC
Populations Analysed					
20.	Randomized	SP3a	Listing of Participants Excluded from Any Population – Part A	ICH E3 e.g., participants screened but not randomized, participants randomized but not treated, participants with deviations leading to exclusion from per protocol population (can be separate listing per population).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
21.	Randomized	SP3	Listing of Participants Excluded from Any Population – Part B	ICH E3 e.g., participants screened but not randomized, participants randomized but not treated, participants with deviations leading to exclusion from per protocol population (can be separate listing per population).	SAC
22.	Randomized	SP3a	Listing of Participants Excluded from Any Population – Part C	ICH E3 e.g., participants screened but not randomized, participants randomized but not treated, participants with deviations leading to exclusion from per protocol population (can be separate listing per population).	SAC
Demographic and Baseline Characteristics					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
23.	Safety	DM4	Listing of Demographic Characteristics – Part A	ICH E3	SAC
24.	Safety	DM2	Listing of Demographic Characteristics – Part B	ICH E3	SAC
25.	Safety	DM4	Listing of Demographic Characteristics – Part C	ICH E3	SAC
26.	Safety	SU2	Listing of Substance Use – Part A		SAC
27.	Safety	SU2	Listing of Substance Use – Part B		SAC
28.	Safety	SU2	Listing of Substance Use – Part C		SAC
Prior and Concomitant Medications					
29.	Safety	CP_CM4	Listing of Concomitant Medications Using Generic Term – Part A		SAC
30.	Safety	CP_CM3	Listing of Concomitant Medications Using Generic Term – Part B		SAC
31.	Safety	CP_CM4	Listing of Concomitant Medications Using Generic Term – Part C		SAC
32.	Safety	MH3	Listing of Medical Conditions – Part A		SAC
33.	Safety	MH2	Listing of Medical Conditions – Part B		SAC
34.	Safety	MH3	Listing of Medical Conditions – Part C		SAC
35.	Safety	FH5	Listing of Family History Conditions – Part A		SAC
36.	Safety	FH5	Listing of Family History Conditions – Part B		SAC
37.	Safety	FH5	Listing of Family History Conditions – Part C		SAC
Exposure and Treatment Compliance					
38.	Safety	EX4	Listing of Exposure Data – Part A	ICH E3	SAC
39.	Safety	EX3	Listing of Exposure Data – Part B	ICH E3	SAC
40.	Safety	EX4	Listing of Exposure Data – Part C	ICH E3	SAC
Adverse Events					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
41.	Safety	CP_AE9	Listing of All Adverse Events – Part A	ICH E3	SAC
42.	Safety	CP_AE8	Listing of All Adverse Events – Part B	ICH E3	SAC
43.	Safety	CP_AE9	Listing of All Adverse Events – Part C	ICH E3	SAC
44.	Safety	CP_AE9	Listing of Drug Related Adverse Events – Part A	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., “Listing of Serious Adverse Events”).	SAC
45.	Safety	CP_AE8	Listing of Drug Related Adverse Events – Part B	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., “Listing of Serious Adverse Events”).	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
46.	Safety	CP_AE9	Listing of Drug Related Adverse Events – Part C	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., "Listing of Serious Adverse Events").	SAC
47.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events – Part A	ICH E3	SAC
48.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events – Part B	ICH E3	SAC
49.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events – Part C	ICH E3	SAC
50.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part A	IDSL	SAC
51.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part B	IDSL	SAC
52.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part C	IDSL	SAC
Serious and Other Significant Adverse Events					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
53.	Safety	CP_AE9a	Listing of Serious Adverse Events (Fatal & Non-Fatal) – Part A	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., "Listing of Serious Adverse Events").	SAC
54.	Safety	CP_AE8a	Listing of Serious Adverse Events (Fatal & Non-Fatal) – Part B	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., "Listing of Serious Adverse Events").	SAC
55.	Safety	CP_AE9a	Listing of Serious Adverse Events (Fatal & Non-Fatal) – Part C	ICH E3 Fatal and Non-Fatal SAEs are combined into a single listing for ClinPharm studies (i.e., "Listing of Serious Adverse Events").	SAC
56.	Safety	CP_AE9	Listing of Adverse Events Leading to Withdrawal from Study – Part A	ICH E3	SAC
57.	Safety	CP_AE8	Listing of Adverse Events Leading to Withdrawal from Study – Part B	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
58.	Safety	CP_AE9	Listing of Adverse Events Leading to Withdrawal from Study – Part C	ICH E3	SAC
Liver events					
59.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting – Part A	IDSL	SAC
60.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting – Part B	IDSL	SAC
61.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting – Part C	IDSL	SAC
62.	Safety	LIVER7	Listing of Liver Biopsy Details – Part A		SAC
63.	Safety	LIVER7	Listing of Liver Biopsy Details – Part B		SAC
64.	Safety	LIVER7	Listing of Liver Biopsy Details – Part C		SAC
65.	Safety	LIVER8	Listing of Liver Imaging Details – Part A		SAC
66.	Safety	LIVER8	Listing of Liver Imaging Details – Part B		SAC
67.	Safety	LIVER8	Listing of Liver Imaging Details – Part C		SAC
All Laboratory					
68.	Safety	LB14	Listing of Clinical Chemistry Laboratory Data with Character Results – Part A	ICH E3	SAC
69.	Safety	LB14	Listing of Clinical Chemistry Laboratory Data with Character Results – Part B	ICH E3	SAC
70.	Safety	LB14	Listing of Clinical Chemistry Laboratory Data with Character Results – Part C	ICH E3	SAC
71.	Safety	CP_LB6	Listing of All Clinical Chemistry Laboratory Data for Subjects with PCI Abnormalities – Part A	Add 'Lab test' column before 'Treatment/Period' column'	SAC
72.	Safety	CP_LB5	Listing of All Clinical Chemistry Laboratory Data for Subjects with PCI Abnormalities – Part B	Add 'Lab test' column before 'Treatment/Period' column'	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
73.	Safety	CP_LB6	Listing of All Clinical Chemistry Laboratory Data for Subjects with PCI Abnormalities – Part C	Add 'Lab test' column before 'Treatment/Period' column'	SAC
74.	Safety	CP_LB6	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance – Part A	Add 'Lab test' column before 'Treatment/Period' column'	SAC
75.	Safety	CP_LB5	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance – Part B	Add 'Lab test' column before 'Treatment/Period' column'	SAC
76.	Safety	CP_LB6	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance – Part C	Add 'Lab test' column before 'Treatment/Period' column'	SAC
77.	Safety	LB14	Listing of Haematology Laboratory Data with Character Results – Part A	ICH E3 'Treatment/Period' will be included as column and will be added after 'Lab Test'	SAC
78.	Safety	LB14	Listing of Haematology Laboratory Data with Character Results – Part B	ICH E3	SAC
79.	Safety	LB14	Listing of Haematology Laboratory Data with Character Results – Part C	ICH E3	SAC
80.	Safety	CP_LB6	Listing of All Haematology Laboratory Data for Subjects with PCI Abnormalities – Part A	Add 'Lab test' column before 'Treatment/Period' column'	SAC
81.	Safety	CP_LB5	Listing of All Haematology Laboratory Data for Subjects with PCI Abnormalities – Part B	Add 'Lab test' column before 'Treatment/Period' column'	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
82.	Safety	CP_LB6	Listing of All Haematology Laboratory Data for Subjects with PCI Abnormalities – Part C	Add 'Lab test' column before 'Treatment/Period' column'	SAC
83.	Safety	CP_LB6	Listing of Haematology Abnormalities of Potential Clinical Importance – Part A	Add 'Lab test' column before 'Treatment/Period' column'	SAC
84.	Safety	CP_LB5	Listing of Haematology Abnormalities of Potential Clinical Importance – Part B	Add 'Lab test' column before 'Treatment/Period' column'	SAC
85.	Safety	CP_LB6	Listing of Haematology Abnormalities of Potential Clinical Importance – Part C	Add 'Lab test' column before 'Treatment/Period' column'	SAC
86.	Safety	LB14	Listing of Hormone Assessment Data with Character Results – Part B	ICH E3	SAC
87.	Safety	LB14	Listing of Urinalysis Data with Character Results – Part A	ICH E3	SAC
88.	Safety	LB14	Listing of Urinalysis Laboratory Data with Character Results – Part B	ICH E3	SAC
89.	Safety	LB14	Listing of Urinalysis Laboratory Data with Character Results – Part C	ICH E3	SAC
90.	Safety	UR2B	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part A	ICH E3 Display ALL data for a subject who experienced a value of potential clinical importance.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
91.	Safety	UR2A	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part B	ICH E3 Display ALL data for a subject who experienced a value of potential clinical importance.	SAC
92.	Safety	UR2B	Listing of Urinalysis Data for Participants with Any Value of Potential Clinical Importance – Part C	ICH E3 Display ALL data for a subject who experienced a value of potential clinical importance.	SAC
ECG					
93.	Safety	CP_EG4	Listing of All ECG Values for Subjects with any Value of Potential Clinical Importance – Part A	IDSL Required for ClinPharm studies only. Display ALL ECGs for a subject who experienced a value of potential clinical importance.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
94.	Safety	CP_EG3	Listing of All ECG Values for Subjects with any Value of Potential Clinical Importance – Part B	IDSL Required for ClinPharm studies only. Display ALL ECGs for a subject who experienced a value of potential clinical importance.	SAC
95.	Safety	CP_EG4	Listing of All ECG Values for Subjects with any Value of Potential Clinical Importance – Part C	IDSL Required for ClinPharm studies only. Display ALL ECGs for a subject who experienced a value of potential clinical importance.	SAC
96.	Safety	CP_EG4	Listing of ECG Values of Potential Clinical Importance – Part A	IDSL Required for ClinPharm studies only.	SAC
97.	Safety	CP_EG3	Listing of ECG Values of Potential Clinical Importance – Part B	IDSL Required for ClinPharm studies only.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
98.	Safety	CP_EG4	Listing of ECG Values of Potential Clinical Importance – Part C	IDSL Required for ClinPharm studies only.	SAC
99.	Safety	CP_EG6	Listing of All ECG Findings for Subjects with an Abnormal Finding – Part A		SAC
100.	Safety	CP_EG5	Listing of All ECG Findings for Subjects with an Abnormal Finding – Part B		SAC
101.	Safety	CP_EG6	Listing of All ECG Findings for Subjects with an Abnormal Finding – Part C		SAC
102.	Safety	CP_EG6	Listing of Abnormal ECG Findings – Part A	IDSL Required for ClinPharm studies only.	SAC
103.	Safety	CP_EG5	Listing of Abnormal ECG Findings – Part B	IDSL Required for ClinPharm studies only.	SAC
104.	Safety	CP_EG6	Listing of Abnormal ECG Findings – Part C	IDSL Required for ClinPharm studies only.	SAC
Vital Signs					

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
105.	Safety	CP_VS5	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance – Part A	IDSL Required for ClinPharm studies only. Display ALL Vital Signs for a subject who experienced a value of potential clinical importance.	SAC
106.	Safety	CP_VS4	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance – Part B	IDSL Required for ClinPharm studies only. Display ALL Vital Signs for a subject who experienced a value of potential clinical importance.	SAC
107.	Safety	CP_VS5	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance – Part C	IDSL Required for ClinPharm studies only. Display ALL Vital Signs for a subject who experienced a value of potential clinical importance.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
108.	Safety	CP_VS5	Listing of Vital Signs of Potential Clinical Importance – Part A	IDSL Required for ClinPharm studies only.	SAC
109.	Safety	CP_VS4	Listing of Vital Signs of Potential Clinical Importance – Part B	IDSL Required for ClinPharm studies only.	SAC
110.	Safety	CP_VS5	Listing of Vital Signs of Potential Clinical Importance – Part C	IDSL Required for ClinPharm studies only.	SAC

13.12.12. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
111.	PK	PK08	Listing of Plasma GSK3439171 Pharmacokinetic Concentration (ng/mL) - Time Data – Part A		SAC
112.	PK	PK07	Listing of Plasma GSK3439171 Pharmacokinetic Concentration (ng/mL) - Time Data – Part B		SAC
113.	PK	PK08	Listing of Plasma GSK3439171 Pharmacokinetic Concentration (ng/mL) - Time Data – Part C		SAC
114.	PK	PK09	Listing of Urine Sample Collections – Part B		SAC
115.	PK	PK11	Listing of Urine Excretion Rate Data – Part B		SAC
116.	PK	PK14	Listing of Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part A		SAC
117.	PK	PK13	Listing of Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part B		SAC
118.	PK	PK14	Listing of Derived Plasma GSK3439171 Pharmacokinetic Parameters – Part C		SAC
119.	PK	NA	Raw SAS Output from Statistical Analysis plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part A		SAC
120.	PK	NA	Raw SAS Output from Statistical Analysis plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part B		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
121.	PK	NA	Raw SAS Output from Statistical Analysis plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part C		SAC
122.	PK	NA	Raw SAS Output from Statistical Analysis of Log Transformed plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part A		SAC
123.	PK	NA	Raw SAS Output from Statistical Analysis of Log Transformed plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part B		SAC
124.	PK	NA	Raw SAS Output from Statistical Analysis of Log Transformed plasma GSK3439171 Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Part C		SAC
125.	PK	NA	Raw SAS Output from Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Accumulation Ratio – Part B		SAC
	PK	NA	Raw SAS Output from Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Time Invariance – Part B		SAC
126.	PK	NA	Raw SAS Output from Statistical Analysis of Log-Transformed Plasma GSK3439171 Pharmacokinetic Parameters Assessing Achievement of Steady State – Part B		SAC
127.	PK	NA	Raw SAS Output from Statistical Analysis of log transformed plasma GSK3439171 Pharmacokinetic Parameters Assessing Dose Proportionality (Power Model) – Part A		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
128.	PK	NA	Raw SAS Output from Statistical Analysis of log transformed plasma GSK3439171 Pharmacokinetic Parameters Assessing Dose Proportionality (Power Model) – Part B		SAC
129.	PK		Listing of Entero-Test – Part B		SAC
Pharmacodynamics/Biomarkers					
130.	PD	PD_L1	Listing of All Pharmacodynamic Parameters – Part A		SAC
131.	PD	PD_L1	Listing of Urine Pharmacodynamic Parameters – Part B		SAC
132.	PD	PD_L1	Listing of Muscle Pharmacodynamic Parameters – Part B		SAC
133.	PD	NA	Raw SAS Output from Statistical Analysis of Log Transformed Pharmacodynamic Parameters: Analysis of Variance (ANOVA) – Part A		SAC
134.	PD	NA	Raw SAS Output from Statistical Analysis of Log Transformed Pharmacodynamic Parameters: Analysis of Variance (ANOVA) – Part B		SAC

13.12.13. Other Listings

Other Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population Tables					
135.	Screened	OT_L1	Listing of Rescreened Subjects		SAC

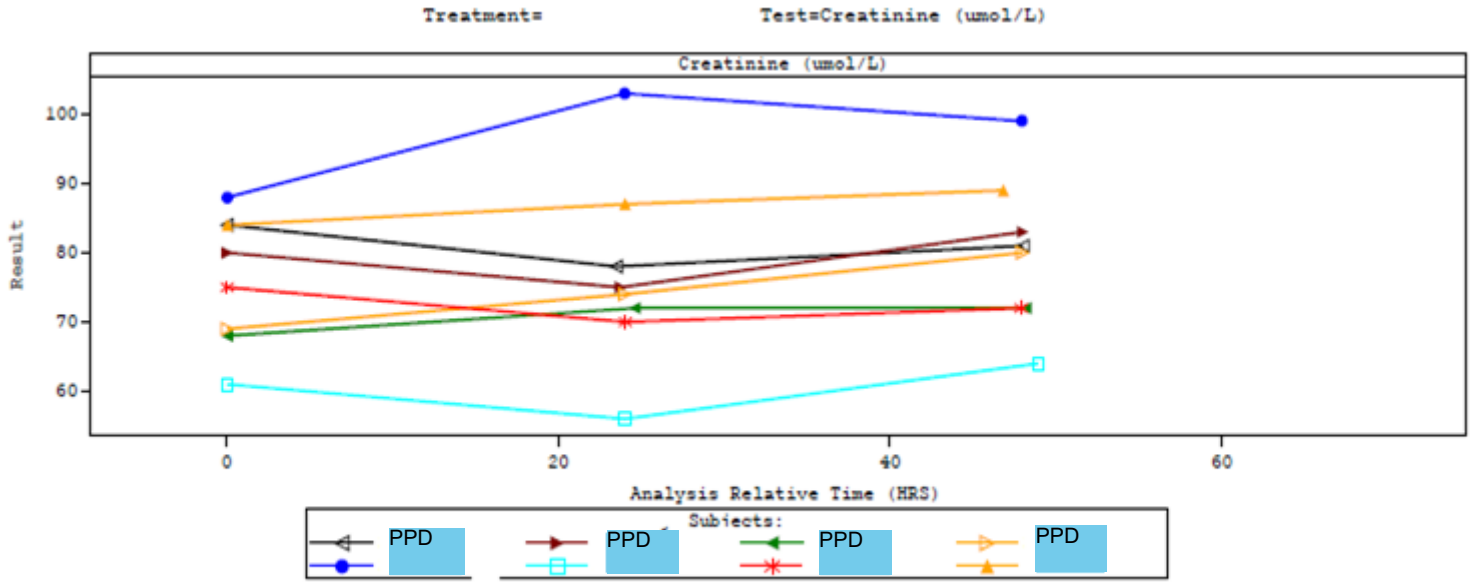
13.13. Example Mock Shells for Data Displays

Please note that the mock shells provided below are not study specific but example mock shells.

Example LB_PLOT1
Protocol: XYZ100001
Population: Safety/Other study specific

Figure 8.xx

Individual Plot of Clinical Chemistry Parameters Over Time by Dose – Part A

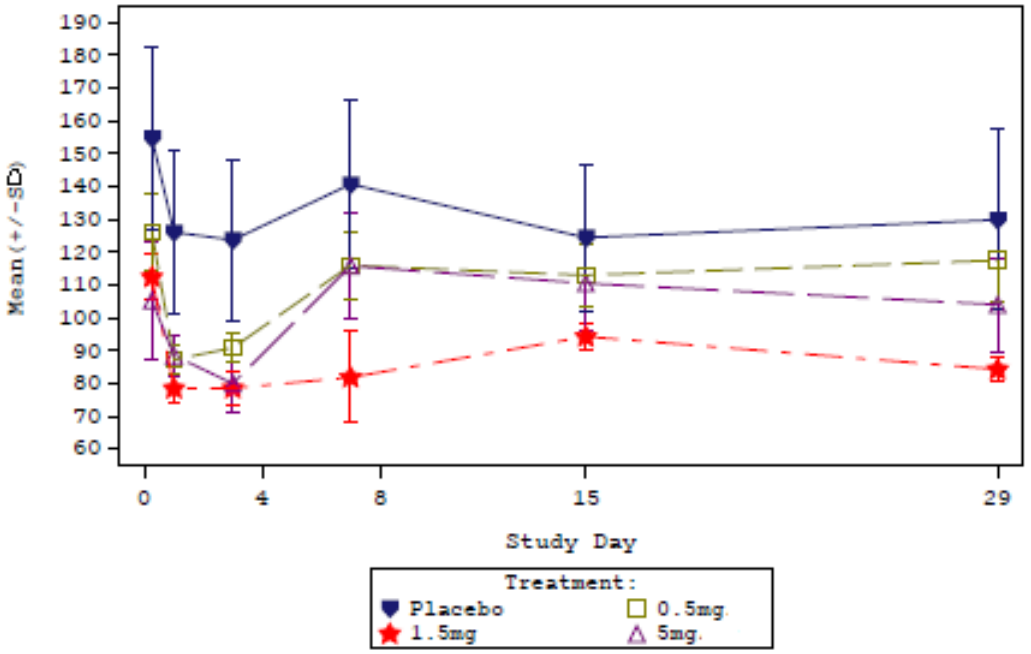


Please add lower and upper normal ranges in the plot.

Example LB_PLOT2
Protocol: XYZ100001
Population: Safety/Other study specific

Figure 8.xx

Mean ±SD Plot of Change from Baseline for Clinical Chemistry Parameters
Over time – Part A



Example : PK_T1
Protocol : GSKxxx
Population : Pharmacokinetic

Table PK_T1
Statistical Analysis of plasma GSKxxx Pharmacokinetic Parameters: ANOVA – Part A

Parameter	Treatment	N	n	LS Mean	95% CI (Lower,Upper)	{%CVw}
AUC(0-t) (units)	50mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	100mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	200mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
Cmax (units)	50mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	100mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	200mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx

Example : PK_T2
Protocol : GSKxxx
Population : Pharmacokinetic

Table PK_T2
Statistical Analysis of log transformed plasma GSKxxx Pharmacokinetic Parameters: ANOVA – Part A

Parameter	Treatment	N	n	LS Geom. Mean	95% CI (Lower,Upper)	{%CVw}
AUC(0-t) (units)	50mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	100mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	200mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
Cmax (units)	50mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	100mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx
	200mg	24	24	xxxx.xx	(xxxx.xx,xxxx.xx)	xx.xx

Example : PK_T3
Protocol : GSKxxx
Population : Pharmacokinetic

Table PK_T3
Statistical Analysis of log transformed plasma GSKxxx Pharmacokinetic Parameters Assessing Dose Proportionality (Power Model) - Part A

Parameter (units)	Slope	90% CI of the Slope
	Log Parameter vs Log Dose	
AUC(0-t) (µg.h/mL)	x.xx	(x.xxx, x.xxx)
AUC(0-∞) (µg.h/mL)	x.xx	(x.xxx, x.xxx)
AUC(0-τ) (µg.h/mL)	x.xx	(x.xxx, x.xxx)

Example : PK_T4
Protocol : GSKxxx
Population : Pharmacokinetic

Table PK_T4
Statistical Analysis of log transformed plasma GSKxxx Pharmacokinetic Parameters Assessing Dose Proportionality (Power Model) – Part B

Visit	Parameter (units)	Slope	90% CI of the Slope
		Log Parameter vs Log Dose	
Day 1	AUC(0-t) (μg.h/mL)	x.xx	(x.xxx, x.xxx)
	AUC(0-∞) (μg.h/mL)	x.xx	(x.xxx, x.xxx)
	AUC(0-τ) (μg.h/mL)	x.xx	(x.xxx, x.xxx)

Example : PK_T5
Protocol : GSKxxx
Population : Pharmacokinetic

Table PK_T5
Statistical Analysis of log transformed plasma GSKxxx Pharmacokinetic Parameters Assessing Accumulation Ratio and Time Invariance – Part B

Treatment	Parameter (units)	Comparison	Geom.LsMean				Ratio	90% Confidence Interval	
			n	Test	n	Ref			
XXmg	AUC(R0)(µg.h/mL)	Day 17 vs Day 1	XX	x.xxx	xx	x.xxx	x.xxx	(x.xxx,	x.xxx)
	Cmax(RCmax)(µg/mL)	Day 17 vs Day 1	XX	x.xxx	xx	x.xxx	x.xxx	(x.xxx,	x.xxx)
	AUC(R_{ss})(µg.h/mL)	Day 17 vs Day 1	XX	x.xxx	xx	x.xxx	x.xxx	(x.xxx,	x.xxx)

Example : PK_T6
Protocol : GSKxxx
Population : Pharmacokinetic

Table PK_T6
Statistical Analysis of log transformed plasma GSKxxx Pharmacokinetic Parameters Assessing Achievement of Steady State– Part B

Parameter	Treatment	Day	Back-Transformed Slope	90% Confidence Interval
Ctrough	xxmg	1-17	x.xxx	(x.xxx, x.xxx)
	xxmg	1-17	x.xxx	(x.xxx, x.xxx)

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Example : PD_T1
Protocol : GSKxxx
Population : Pharmacodynamic

Table
Statistical Analysis of Urinary Tetranor and Urinary Creatinine Parameters:
Mixed Effect Model – Part A

Parameter: tPGEM

Visit		Placebo (N=xxx)	Dose1 (N=xxx)	…….	Dose6 (N=xxx)
Day -1, 24-12hr	n	xxx	xxx		xxx
	Adjusted Geometric Mean	x.xxx	x.xxx		x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)		(x.xxx, x.xxx)
Day -1, 12-0hr	n	xxx	xxx		xxx
	Adjusted Geometric Mean	x.xxx	x.xxx		x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)		(x.xxx, x.xxx)
Day 1, 0-12hr	n	xxx	xxx		xxx
	Adjusted Geometric Mean	x.xxx	x.xxx		x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)		(x.xxx, x.xxx)
	Change from Baseline	x.xxx	x.xxx		x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)		(x.xxx, x.xxx)
Day 1, 12-24hr	n	xxx	xxx		xxx
	Adjusted Geometric Mean	x.xxx	x.xxx		x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)		(x.xxx, x.xxx)

	Change from Baseline	x.xxx	x.xxx	x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)	(x.xxx, x.xxx)
Day 1, 24-48hr	n	xxx	xxx	xxx
	Adjusted Geometric Mean	x.xxx	x.xxx	x.xxx
	90% C.I.	(x.xxx, x.xxx)	(x.xxx, x.xxx)	(x.xxx, x.xxx)

Example OT_L1

Protocol : GSKxxx
Population : Screened

Listing 11
Listing of Re-screened Subjects

Part	Unique Subject Id.	First Screening Number	Second Screening Number
Part A	XXXXXX.XXXXXX	XXXXXX	XXXXXX
	XXXXXX.XXXXXX	XXXXXX	XXXXXX
	XXXXXX.XXXXXX	XXXXXX	XXXXXX