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209713

Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Reporting and Analysis Plan for A Randomized, Open-Label, Single Dose, Four-Period Crossover Clinical Trial to Assess the Relative Bioavailability of a Tablet Compared to a Capsule of GSK3640254 and to Assess the Effect of Food on the GSK3640254 Tablet in Healthy Participants
Compound Number	:	GSK3640254
Effective Date	:	15-Jan-2020

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 209713.
- This RAP is intended to describe the full analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

TABLE OF CONTENTS

PAGE

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: 209713.

Due to a potential contamination issue in the study drug, the study was early terminated. Only an abbreviated set of outputs will be generated to support the clinical study report.

2. SUMMARY OF KEY PROTOCOL INFORMATION

This is a Phase 1, randomized, open-label, single-dose, 4-period crossover study to compare the relative bioavailability (BA) of a tablet formulation of GSK3640254 with the capsule formulation and to assess the effect of food on the pharmacokinetics (PK) of the tablet formulation in healthy participants.

2.1. Changes to the Protocol Defined Statistical Analysis Plan

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**
• None	• Randomized population is defined as all participants who were randomly assigned to a treatment sequence	• This is a randomized study and listing of randomization schedule will be produced based on randomized population.
• Pharmacokinetic concentration population will be used for the PK concentration listings, summary tables, and plotting of concentration-time data.	• Pharmacokinetic concentration population will be used for the PK concentration listings and summary tables.	• Study terminated earlier due to potential contamination issue. An abbreviated clinical study report will be reported, and PK figures are not needed.

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

Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To assess the relative BA of GSK3640254 mesylate tablets and GSK3640254 mesylate capsules (in the presence of a moderate fat meal) • To assess the effect of food (fasted, moderate fat meal, and high fat meal) on the PK of the GSK3640254 mesylate tablet formulation	• AUC(0-∞), AUC(0-t), Cmax, and Tmax for GSK3640254

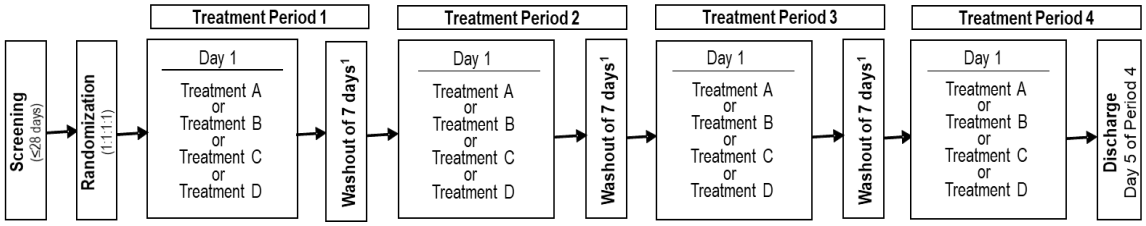
Objectives	Endpoints
Secondary Objectives	**Secondary Endpoints**
• To assess the safety and tolerability of GSK3640254 following single oral administration to healthy participants under fasted or fed (moderate fat or high fat) conditions	• Safety and tolerability parameters for AEs/SAEs, observed and change from baseline clinical laboratory assessments, ECGs, and vital sign measurements
• To characterize the PK of GSK3640254	• tlag, t1/2, CL/F, and Vz/F for GSK3640254 • GSK3640254 PK concentrations in plasma

AE = adverse event; AUC(0-∞) = area under the plasma concentration-time curve from time zero extrapolated to infinity; AUC(0-t) = area under the plasma concentration-time curve from time zero to time t; BA = bioavailability; CL/F = apparent oral clearance; Cmax = maximum observed concentration; ECG = electrocardiogram; PK = pharmacokinetics; SAE = serious adverse event; t1/2 = apparent terminal phase half-life; tlag = lag time for absorption; Tmax = time of maximum observed concentration; Vz/F = apparent volume of distribution.

2.3. Study Design

Overview of Study Design and Key Features

Figure 1 Study Design Schematic



Treatment A = GSK3640254 200 mg (capsules) administered under moderate fat conditions;
Treatment B = GSK3640254 200 mg (tablets) administered under moderate fat conditions;
Treatment C = GSK3640254 200 mg (tablets) administered under fasted conditions;
Treatment D = GSK3640254 200 mg (tablets) administered under high fat conditions.
[1] Washout will be at least 7 days minus 4 hours.

Design Features	• A phase 1, randomized, open-label, single-dose, 4-period crossover study. • The study will consist of a screening period and 4 sequential treatment periods. • There will be a single dose of study intervention per treatment period. • There will be at least 7 days (minus 4 hours) between each dose of study intervention. • Participants will be randomly assigned to 1 of 4 treatment sequences in 1:1:1:1 ratio. • Approximately 16 participants will be treated to ensure that 12 evaluable participants complete the study.
Dosing	• Treatment A: GSK3640254 200 mg (single dose given as 2 × 100-mg capsules) administered under moderate fat condition (reference) • Treatment B: GSK3640254 200 mg (single dose given as 2 × 100-mg tablets) administered under moderate fat conditions (test) • Treatment C: GSK3640254 200 mg (single dose given as 2 × 100-mg tablets) administered under fasted conditions (reference) • Treatment D: GSK3640254 200 mg (single dose given as 2 × 100-mg tablets) administered under high fat condition (test).
Time & Events	• Refer to Appendix 1: Schedule of Activities
Treatment Assignment	• This is an open-label study and randomized study. • Participants will be randomly assigned to 1 of 4 treatment sequences (ABCD, BADC, CDAB, or DCBA) in 1:1:1:1 ratio. • Site pharmacy group will use a computer-generated randomization schedule for treatment assignments. • The computer-generated randomization schedule will be produced by SAS software (9.4).
Interim Analysis	• No interim analysis is planned for this study

2.4. Statistical Hypotheses

There is no formal research hypothesis that will be statistically tested in this study.

3. PLANNED ANALYSES

3.1. Final Analyses

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

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) have been declared by Data Management.

The study early terminated due to potential contamination issue in study drug. All participants completed Treatment Period 2 before the study was terminated.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who signed the informed consent form • This population will be used for screen failure listing and summary.	• Study Population
Randomized	• All participants who were randomly assigned to a treatment sequence. • This population will be used for listing of randomization schedule.	• Study Population
Safety	• All participants who received at least 1 dose of study medication. • This population will be used for all demographic, disposition (exclude screen failure), and safety listings, summaries, and figures	• Study Population • Safety
Pharmacokinetic Concentration	• All participants who underwent plasma PK sampling and had evaluable PK assay results. • This population will be used for the PK concentration listings and summary tables.	• PK Concentration
Pharmacokinetic Parameter	• All participants who underwent plasma PK sampling and had evaluable PK parameters estimated. • This population will be used for PK parameter listings, summary tables, and statistical analysis tables.	• PK Parameter • PK statistical analysis

Refer to Appendix 9: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarized 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. The “significant” protocol deviation in the Protocol Deviation Management Plan is equivalent to “important” protocol deviations.

- Data will be reviewed prior to freezing the database to ensure all significant deviations and deviations which may lead to exclusion from the analysis are captured and categorized on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate listing of all inclusion/exclusion criteria deviations will also be provided. This listing will be based on data as recorded on the inclusion/exclusion page of the electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions		
Data Displays for Reporting		
Description	**Code**	**Order in TLF**
GSK3640254 200 mg (single dose given as 2 × 100-mg capsules) administered under moderate fat condition	Treatment A	1
GSK3640254 200 mg (single dose given as 2 × 100-mg tablets) administered under moderate fat conditions	Treatment B	2
GSK3640254 200 mg (single dose given as 2 × 100-mg tablets) administered under fasted conditions	Treatment C	3
GSK3640254 200 mg (single dose given as 2 × 100-mg tablets) administered under high fat condition	Treatment D	4

5.2. Baseline Definitions

For vital signs and 12-lead ECGs, the baseline value will be the average (for quantitative assessments) or the worst case (for interpretation) of the triplicate predose assessments within each period. For clinical laboratory parameters, the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits, before the first dose of study drug administration. If time is not collected, Day 1 assessments within each period are assumed to be taken prior to the dose and used as baseline.

Parameter	**Study Assessments Considered as Baseline**			**Baseline Used in Data Display**
	Screening	**Day -1**	**Day 1 (Pre-Dose)**	
Safety				
Vital Sign	X	X	X	Day 1 (Pre-Dose)[1] for each period
12-Lead ECG	X	X	X	Day 1 (Pre-Dose)[1] for each period
Hematology	X	X		Day -1
Clinical Chemistry	X	X		Day -1
Urinalysis	X	X		Day -1

ECG = Electrocardiogram.
[1] The average (for quantitative assessments) or the worst case (for interpretation) of the predose triplicate assessments will be used as the baseline.

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
10.1	Appendix 1: Schedule of Activities
10.2	Appendix 2: Study Phases and Treatment Emergent Adverse Events
10.3	Appendix 3: Data Display Standards & Handling Conventions
10.4	Appendix 4: Derived and Transformed Data
10.5	Appendix 5: Reporting Standards for Missing Data
10.6	Appendix 6: Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events
10.7	Appendix 7: 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 Safety or Screened or Randomized population, unless otherwise specified.

Study population analyses including analyses of randomization schedule, participant disposition, protocol deviations (including inclusion/exclusion criteria deviations), demographic and baseline characteristics, prior and concomitant medications, and exposure will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 9: List of Data Displays.

7. PHARMACOKINETIC ANALYSES

7.1. Primary Pharmacokinetic Analyses

7.1.1. Endpoint / Variables

7.1.1.1. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Standards for Pharmacokinetics). Plasma concentrations of GSK3640254 will be measured and presented in tabular form and will be summarized descriptively. Plasma GSK3640254 concentration-time data will be listed by participant, treatment group and sampling time and summarized by treatment group and sampling time for each period of the study.

7.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher). 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. Subjects who experience emesis at or before 2 times median T_{max} will be excluded from the calculation of summary statistics and statistical analysis for the respective treatment.

Parameter	Parameter Description
AUC(0-∞)	Area under the plasma concentration-time curve from time 0 extrapolated to infinity, to be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-t)	Area under the plasma concentration-time curve from time 0 to the last quantifiable concentration, to be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
Tmax	Time of maximum observed concentration

NOTES:

- Additional parameters may be included as required.

7.1.2. Summary Measure

Pharmacokinetic parameters AUC(0-∞), AUC(0-t), Cmax, and Tmax following single dose administration of GSK3640254 to healthy participants.

7.1.3. Population of Interest

The primary PK analyses will be based on the PK concentration population for plasma PK concentrations and the PK parameter population for plasma PK parameters and statistical analysis.

7.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.1.1 will be summarized using descriptive statistics and listed.

Primary plasma PK parameters (AUC[0-∞], AUC[0-t], Cmax, and Tmax) will be estimated for GSK3640254. Summary statistics (arithmetic mean, geometric mean, median, standard deviation (SD), coefficient of variation (CV), minimum, maximum, between-subject coefficient of variation (CVb), and 90% confidence interval (CI) for plasma GSK3640254 PK parameter values will be summarized by treatment.

7.1.4.1. Statistical Methodology Specification

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

Endpoint / Variables
• Plasma primary PK endpoints include AUC(0-∞), AUC(0-t), Cmax, and Tmax for GSK3640254 as data permit
Model Specification

• Analysis will be performed to compare the relative BA of a tablet formulation of GSK3640254 with the capsule formulation, as appropriate. Analyses will be performed on the natural logarithms of AUC(0-∞), AUC(0-t), and Cmax using linear mixed-effect models with treatment, period, and sequence as fixed effects and participant as a random effect. Effects will be estimated, and CIs will be constructed for the following treatment comparisons:
  ○ Treatment B (test) versus Treatment A (reference)
  ○ Point estimates and 90% CIs for treatment differences on the log scale derived from the model will be exponentiated to obtain estimates for geometric mean ratios and CIs on the original scale.
• The effect of food (moderate or high fat meal) on the PK of the tablet formulation of GSK3640254 will be similarly analyzed for the following treatment comparisons:
  ○ Treatment B (test) versus Treatment C (reference)
  ○ Treatment D (test) versus Treatment C (reference)
• Non-parametric analysis will be performed to compare the Tmax of a tablet formulation of GSK3640254 with the capsule formulation, as appropriate. The Hodges-Lehmann estimate will be used to produce the median, median difference, and 90% CIs for the following treatment comparison:
  ○ Treatment B (test) versus Treatment A (reference)
  ○ A p-value will be generated by the Wilcoxon signed-rank test
• The effect of food (moderate or high fat meal) on the Tmax of the tablet formulation of GSK3640254 will be similarly analyzed for the following treatment comparisons:
  ○ Treatment B (test) versus Treatment C (reference)

○ Treatment D (test) versus Treatment C (reference)
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation
• Statistical analysis for comparison of relative BA by analysis of variance (ANOVA) will be presented in tabular format with geometric mean ratios for the following treatment comparison: ○ Treatment B (test) versus Treatment A (reference) • Statistical analysis for the effect of food (moderate or high fat meal) by ANOVA will be presented in tabular format with geometric mean ratios for the following treatment comparisons: ○ Treatment B (test) versus Treatment C (reference) ○ Treatment D (test) versus Treatment C (reference) • Statistical analysis for comparison of Tmax of a tablet formulation with a capsule formulation by non-parametric analysis will be presented in tabular format with the median, median difference, and 90% CIs along with a p-value generated by the Wilcoxon signed-rank test for the following treatment comparison: ○ Treatment B (test) versus Treatment A (reference) • Statistical analysis for comparison of the effect of food (moderate or high fat meal) on the Tmax by non-parametric analysis will be presented in tabular format with the median, median difference, and 90% CIs along with a p-value generated by the Wilcoxon signed-rank test for the following treatment comparisons: ○ Treatment B (test) versus Treatment C (reference) ○ Treatment D (test) versus Treatment C (reference)

7.2. Secondary Pharmacokinetic Analyses

7.2.1. Endpoint / Variables

7.2.1.1. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Standards for Pharmacokinetic).

7.2.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher). All calculations of non-compartmental parameters will be based on actual sampling times.

Plasma pharmacokinetic parameters listed below will be determined from the plasma concentration-time data, as data permits:

Parameter	Parameter Description
tlag	Lag time for absorption
t1/2	Apparent terminal phase half-life
CL/F	Apparent oral clearance
Vz/F	Apparent volume of distribution

NOTES:

- Additional parameters may be included as required.

7.2.2. Summary Measure

Pharmacokinetic parameters tlag, t1/2, CL/F, and Vz/F following single dose administration of GSK3640254 to healthy participants.

7.2.3. Population of Interest

The secondary PK analyses will be based on the PK concentration population for plasma PK concentrations, and the PK parameter population for plasma PK parameters, unless otherwise specified.

7.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and statistical principles.

Unless otherwise specified, endpoints/variables defined in Section 7.2.1 will be summarized using descriptive statistics and listed.

Secondary plasma PK parameters (tlag, t1/2, CL/F, and Vz/F) will be estimated for GSK3640254. Summary statistics (arithmetic mean, geometric mean, median, CV, SD, minimum, maximum, CVb, and 90% CI) for secondary plasma PK parameters of GSK3640254 will be summarized by treatment.

Summary statistics (arithmetic mean, median, standard deviation, minimum, maximum, and coefficient of variation) for plasma GSK3640254 PK concentrations will be summarized by treatment using the PK Concentration Population.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

Adverse event analyses including the analysis of AEs, SAEs, and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 9: List of Data Displays.

8.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests, urinalysis, and liver function tests will be based on GSK Core Data Standards and will be graded using the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events (Version 2.1, July 2017). The details of the planned displays are in Appendix 9: List of Data Displays.

8.3. Adverse Events of Special Interest

At the end of the study, QT prolongation, gastrointestinal intolerability/toxicity, psychiatric events, and nervous system disorders will be summarized by treatment. A listing will also be provided accordingly.

QT prolongation AE of special interest will be defined as cardiac disorders system organ class (SOC) plus preferred terms (PTs) using the Medical Dictionary for Regulatory Activities (MedDRA) Standardized MedDRA Query (SMQ) “Torsade de pointes/QT Prolongation” (narrow and broad terms) plus seizure.

Gastrointestinal intolerability/toxicity AEs of special interest will be defined within three narrow sub-SMQs [Gastrointestinal nonspecific symptoms and therapeutic procedures SMQ; Gastrointestinal nonspecific dysfunction SMQ; Gastrointestinal nonspecific inflammation (SMQ)] plus a selection of relevant broad PTs from the Gastrointestinal non-specific symptoms and therapeutic procedures SMQ.

Psychiatric AEs of special interest will be defined within the following:

- Sub-SMQ “Suicide/self-injury” (SMQ) from parent SMQ of “Depression and Suicide/Self Injury”. Only narrow terms from the sub-SMQ selected.
- Sub-SMQ “Depression (excluding suicide and self-injury)” (SMQ) from parent SMQ of “Depression and Suicide/Self Injury”. Only narrow terms from the sub-SMQ selected.
- All preferred terms from high level group term (HLGT) “Manic and Bipolar mood disorders and disturbances” under SOC “Psychiatric disorders”.
- Narrow terms from SMQ “Psychosis and psychotic disorders” selected.
- All preferred terms from HLGT “Anxiety disorders and symptoms”, under SOC 'Psychiatric disorders'.

- All preferred terms from HLGT “Sleep Disorders and Disturbances” and HLGT “Sleep disturbances (incl subtypes)”.

Nervous system disorders AEs of special interest will be defined within the following:

- Four HLGTs under Nervous System Disorders SOC: “Headaches”; “Mental impairment disorders”; “Neurological disorders” and “Seizures”

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results including electrocardiograms (ECGs), and vital signs will be based on GSK Core Data Standards, unless otherwise specified. A figure of mean change from baseline in QTc using the Fridericia formula (QTcF) interval along with the 2-sided 95% CI using Student’s t distribution will be presented by treatment and visit. The details of the planned displays are presented in Appendix 9: List of Data Displays.

9. REFERENCES

ViiV Healthcare group of companies Document Number 2018N383392_00 (30-AUG-2019): A Randomized, Open-Label, Single Dose, Four-Period Crossover Clinical Trial to Assess the Relative Bioavailability of a Tablet Compared to a Capsule of GSK3640254 and to Assess the Effect of Food on the GSK3640254 Tablet in Healthy Participants.

10. APPENDICES

10.1. Appendix 1: Schedule of Activities

10.1.1. Protocol Defined Schedule of Events

Screening Visit

Procedure	Screening (up to 28 days before Day 1)
Outpatient visit	X
Informed consent	X
Inclusion and exclusion criteria	X
Demography	X
Full physical examination including height and weight [1]	X
Laboratory assessments (hematology, chemistry, urinalysis)	X
12-lead electrocardiogram	X
Vital sign measurements	X
Medication/drug/alcohol history	X
Past and current medical conditions	X
Columbia Suicide Severity Rating Scale	X
Serum pregnancy test	X
Follicle-stimulating hormone (as needed, to confirm postmenopausal status)	X
Drug, alcohol, and cotinine screen	X
Human immunodeficiency virus, hepatitis B and C Screening	X

1. A full physical examination will include at a minimum, assessments of the skin, cardiovascular, respiratory, gastrointestinal (GI), and neurological systems.

Time and Events Table

Procedure	Check-in	Periods 1, 2, and 3				Period 4 only				Notes
			Washout							
	Day –1	Day 1	Day 2	Days 3-5	Days 6-7	Day 1	Day 2	Days 3-4	Day 5[0]	
Admit to clinic	X									
Discharge from clinic									X	Discharge from clinic following completion of the last study procedure on Day 5 of Period 4.
Brief physical examination	X				D7 (Period 2 only)				X	Interim or symptom targeted physical examination will be performed at the discretion of the investigator. See Protocol Section 8.2.1 for description of brief physical examination.
Vital signs	X	X	X	D3-5		X	X	X	X	Blood pressure and pulse will be measured in triplicate predose on Day 1 in Periods 1-4. Single blood pressure and pulse will be measured predose on other study days.
12-lead ECG	X	X				X			X	All ECGs on Day 1 in Periods 1-4 will be predose, postdose at 2 hours, and postdose at 4 hours. The predose ECGs in Periods 1-4 will be taken in triplicate.
Drug, alcohol, and cotinine screen	X									See Protocol Appendix 2 for specific tests to be performed.
Laboratory assessments (hematology, chemistry, urinalysis)	X		X				X		X	See Protocol Appendix 2 for specific tests to be performed. Day 2 samples in each period to be collected 24 hours after dosing.
Pregnancy test	X								X	Serum testing at Day -1

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209713

Procedure	Check-in	Periods 1, 2, and 3				Period 4 only				Notes
			Washout							
	Day –1	Day 1	Day 2	Days 3-5	Days 6-7	Day 1	Day 2	Days 3-4	Day 5[0]	
Columbia-Suicide Severity Rating Scale	X				D7				X	
Genetic sample (optional)	X									
Study intervention: GSK3640254 200 mg (capsule or tablet)		X				X				Participants will fast overnight for at least 10 hours prior to dosing; be provided a moderate fat meal, a high fat meal, or no meal 30 minutes prior to dosing; and be provided standardized meals ≥4 hours postdose. See Protocol Section 4.1.
Serial PK sampling		X	X	X		X	X	X	X	Blood collection for PK analysis of GSK3640254 will be collected within 40 minutes prior to dosing and 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 12, 24, 48, 72, and 96 hours postdose in each period.
AE review		←==========X==========→								
SAE review	←==========X==========→									
Concomitant medications	←==========X==========→									

AE = adverse event; D = day; ECG = electrocardiogram; PK = pharmacokinetic; SAE = serious adverse event.
1 Evaluations scheduled for Day 5 in Period 4 will also be performed for participants who discontinue early.

10.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

10.2.1. Study States for Lab, Electrocardiograms, and Vital Signs

Assessments and events will be classified according to the time of occurrence relative to study treatment start date(/time) and stop date(/time).

Study Phase	Definition
Pre-Treatment	Date and Time ≤ Study Treatment Start Date and Time
On-Treatment	Study Treatment Start Date and Time < Date and Time ≤ Study Treatment Stop Date and Time + 5 days the Date and Time of Early Withdrawal Visit whichever is later.
Post-Treatment	Date and Time > Study Treatment Stop Date and Time + 5 days or the Date and Time of Early Withdrawal Visit whichever is later

10.2.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before Day -1
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 5: 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.

10.2.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date and time is on or after treatment start date and time & on or before treatment stop date and time + 5 days. • Study Treatment Start Date and Time ≤ AE Start Date and Time ≤ Study Treatment Stop Date and Time + 5 days. • If the AE onset date is completely missing, the AE is considered as treatment emergent.

NOTES:

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Please refer to Appendix 5: Reporting Standards for Missing Data for handling of missing and partial dates for adverse events. Use the rules in this table if the adverse event onset date is completely missing.

10.3. Appendix 3: Data Display Standards & Handling Conventions

10.3.1. Reporting Process

Software	
• The currently supported versions of SAS software (9.4) will be used.	
Reporting Area	
HARP Server	\\us1salx00259.corpnet2.com
HARP Compound	GSK3640254
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1). • For creation of ADaM datasets (ADC1/ADCM/ADAE), the same version of dictionary datasets will be implemented as those being used for conversion from SI to SDTM.	
Generation of RTF Files	
• RTF files will be generated for all reporting efforts described in the RAP.	

10.3.2. 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 participant level listings in the main body of the GSK CSR. All participant level listings should be located in the modular appendices as ICH or non-ICH listings.

Formats
• All data will be reported according to the actual treatment the participant received unless otherwise stated. • 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 participant's listings. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures (mean figures only for PK concentrations), summaries, and statistical analyses (excluding statistical analyses of PK parameters).
Unscheduled Visits
• Unscheduled visits will not be included in summary tables except for determining the worst-case values. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.
Descriptive Summary Statistics
Continuous Data: Refer to IDSL Statistical Principle 6.06.1
Categorical Data: N, n, frequency, %
Graphical Displays
• Refer to IDSL Statistical Principals 7.01 to 7.13.

10.3.3. Reporting Standards for Pharmacokinetics

Pharmacokinetic Concentration Data	

Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.
	Refer to IDSL Statistical Principle 6.06.1.
	For continuous data:
	• NQs at the beginning of a participant profile (i.e. before the first incidence of a measurable concentration) are deemed to be zero as it is assumed that in this circumstance no drug is yet measurable in the blood.
	• For NQs at the end of the participant profile (i.e. after the last incidence of a measurable concentration);
	  • for individual plots and pharmacokinetic analyses these are dropped (set to missing) as they do not provide any useful information (and can erroneously indicate that absolutely no drug is present)
	  • for summary statistics, these are set to 0 (to avoid skewing of the summary statistics)
	• Individual NQs which fall between two measurable concentrations are set to missing (individual values of this nature are assumed to be an anomaly)
	If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual participant plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing).
	Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.

Pharmacokinetic Parameter Data	
Descriptive Summary Statistics, Graphical Displays and Listings	N, n, arithmetic mean, 90% CI of arithmetic mean, geometric mean, 95% CI of geometric mean, SD, SD of logged data CV (%), and between-subject geometric coefficient of variation (CVb (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of Ln-Transformed data)

Parameters Not Being Ln-Transformed	Tmax, tlag, λz, λz lower, λz upper, and λz no. of points.
Parameters Not Being Summarized	λz, λz lower, λz upper, and λz no. of points.
Listings	Include the first point, last point and number of points used in the determination of λz and Rsq_adjusted for listings.

10.4. Appendix 4: Derived and Transformed Data

10.4.1. 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. • The worst finding/interpretation associated with multiple measurements as the finding/interpretation for that time point. • 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

• Calculated as the number of days from Dose Date on Period 1 Day 1:
  • Assessment Date = Missing
  → Study Day = Missing
  • Assessment Date < Dose Date on Period 1 Day 1
  → Study Day = Assessment Date –Dose Date on Period 1 Day 1
  • Assessment Date >= Dose Date on Period 1 Day 1
  → Study Day = Assessment Date – Dose Date on Period 1 Day 1 + 1

Period Day

• Calculated as the number of days from First Dose Date for the respective period:
  • Assessment Date = Missing
  → Period Day = Missing
  • Assessment Date < Dose Date on Period 1 Day 1
  → Period Day = Assessment Date – Dose Date on Period 1 Day 1
  • Dose Date on Period 1 Day 1 <= Assessment Date < Dose Date on Period 2 Day 1
  → Period Day = Assessment Date – Dose Date on Period 1 Day 1 + 1
  • Dose Date on Period 2 Day 1 <= Assessment Date < Dose Date on Period 3 Day 1
  → Period Day = Assessment Date – Dose Date on Period 2 Day 1 + 1
  • Dose Date on Period 3 Day 1 <= Assessment Date < Dose Date on Period 4 Day 1
  → Period Day = Assessment Date – Dose Date on Period 3 Day 1 + 1
  • Assessment Date >= Dose Date on Period 4 Day 1
  → Period Day = Assessment Date – Dose Date on Period 4 Day 1 + 1

10.4.2. Study Population

Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ Any participant with a missing day will have this imputed as day '15'.
  ○ Any participant with a missing day and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height $(m)^2$]

10.4.3. Safety

Adverse Events
AEs of Special Interest
• QT prolongation • Gastrointestinal intolerability/toxicity • Psychiatric events • Nervous system disorders

12-Lead Electrocardiograms
QTcB Interval
• QTc using the Bazett formula (QTcB) interval in msec will be calculated using QT interval (msec) and RR (msec) as $QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}}$ where RR interval in msec is calculated using QT interval (msec) and QTcF interval (msec) as $RR = (\frac{QT}{QTcF})^3 \times 1000$

10.5. Appendix 5: Reporting Standards for Missing Data

10.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as the participant had completed all phases of the study including the final date on which data were or are expected to be collected. • Withdrawn participants were not 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.

10.5.2. 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 participant 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 CSR.

10.5.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ 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 2: Study Phases and Treatment Emergent Adverse Events. ○ 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	• Partial dates for any concomitant medications recorded in the eCRF 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 (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.6. Appendix 6: Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events

10.6.1. Laboratory Values

Laboratory abnormalities will be graded according to the DAIDS grading table Version 2.1, July 2017. Laboratory results are converted to use SI units; only the numeric part of the criteria will be used. If for a laboratory parameter there are multiple grades sharing the same criteria, the maximum grade will be used.

HEMATOLOGY				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Absolute Lymphocyte Count, Low (cell/mm^3; cells/L) > 5 years of age (not HIV infected)	600 to < 650 0.600 × 10^9 to < 0.650 × 10^9	500 to < 600 0.500 × 10^9 to < 0.600 × 10^9	350 to < 500 0.350 × 10^9 to < 0.500 × 10^9	< 350 < 0.350 × 10^9
Absolute Neutrophil Count, Low (cells/mm^3; cells/L) > 7 days of age	800 to 1,000 0.800 × 10^9 to 1.000 × 10^9	600 to 799 0.600 × 10^9 to 0.799 × 10^9	400 to 599 0.400 × 10^9 to 0.599 × 10^9	< 400 < 0.400 × 10^9
Hemoglobin, Low (g/dL; mmol/L) ≥ 13 years of age (male only)	10.0 to 10.9 6.19 to 6.76	9.0 to < 10.0 5.57 to < 6.19	7.0 to < 9.0 4.34 to < 5.57	< 7.0 <4.34
Hemoglobin, Low (g/dL; mmol/L) ≥ 13 years of age (female only)	9.5 to 10.4 5.88 to 6.48	8.5 to < 9.5 5.25 to < 5.88	6.5 to < 8.5 4.03 to < 5.25	< 6.5 < 4.03
Platelets, Decreased (cells/mm^3; cells/L)	100,000 to < 125,000 100.000 × 10^9 to < 125.000 × 10^9	50,000 to < 100,000 50.000 × 10^9 to < 100.000 × 10^9	25,000 to < 50,000 25.000 × 10^9 to < 50.000 × 10^9	< 25,000 < 25.000 × 10^9
White Blood Cell, Decreased (cells/mm^3; cells/L) > 7 days of age	2,000 to 2,499 2.000 × 10^9 to 2.499 × 10^9	1,500 to 1,999 1.500 × 10^9 to 1.999 × 10^9	1,000 to 1,499 1.000 × 10^9 to 1.499 × 10^9	< 1,000 < 1.000 × 10^9

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Clinical Chemistry				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Albumin, Low (g/dL; g/L)	3.0 to < LLN 30 to < LLN	≥ 2.0 to < 3.0 ≥ 20 to < 30	< 2.0 < 20	NA
Alkaline Phosphatase, High	1.25 to < 2.5 × ULN	2.5 to < 5.0 × ULN	5.0 to < 10.0 × ULN	≥ 10.0 × ULN
Alanine Aminotransferase, High	1.25 to < 2.5 × ULN	2.5 to < 5.0 × ULN	5.0 to < 10.0 × ULN	≥ 10.0 ULN
Amylase (Total), High	1.1 to < 1.5 × ULN	1.5 to < 3.0 × ULN	3.0 to < 5.0 × ULN	≥ 5.0 × ULN
Aspartate Aminotransferase, High	1.25 to < 2.5 × ULN	2.5 to < 5.0 × ULN	5.0 to < 10.0 × ULN	≥ 10.0 × ULN
Bicarbonate, Low (mEq/L; mmol/L)	16.0 to < LLN 16.0 to < LLN	11.0 to < 16.0 11.0 to < 16.0	8.0 to < 11.0 8.0 to < 110.	< 8.0 < 8.0
Direct Bilirubin, High > 28 days of age	NA	NA	> ULN with other signs and symptoms of hepatotoxicity	> ULN with life-threatening consequences (e.g., signs and symptoms of liver failure)
Total Bilirubin, High > 28 days of age	1.1 to < 1.6 × ULN	1.6 to < 2.6 × ULN	2.6 to < 5.0 × ULN	≥ 5.0 × ULN
Calcium, High (mg/dL; mmol/L) ≥ 7 days of age	10.6 to < 11.5 2.65 to < 2.88	11.5 to < 12.5 2.88 to < 3.13	12.5 to < 13.5 3.13 to < 3.38	≥ 13.5 ≥ 3.38
Calcium, Low (mg/dL; mmol/L) ≥ 7 days of age	7.8 to < 8.4 1.95 to < 2.10	7.0 to < 7.8 1.75 to < 1.95	6.1 to < 7.0 1.53 to < 1.75	< 6.1 < 1.53
Creatine Kinase, High	3 to < 6 × ULN	6 to < 10 × ULN	10 to < 20 × ULN	≥ 20 × ULN
Creatinine, High *Choose the method that selects for the higher grade*	1.1 to 1.3 × ULN	> 1.3 to 1.8 × ULN OR Increase to 1.3 to < 1.5 × participant's baseline	> 1.8 to < 3.5 ULN OR Increase to 1.5 to < 2.0 × participant's baseline	≥ 3.5 × ULN OR Increase of ≥ 2.0 × participant's baseline
Glucose Fasting, High (mg/dL; mmol/L)	110 to 125 6.11 to < 6.95	> 125 to 250 6.95 to < 13.89	> 250 to 500 13.89 to < 27.75	≥ 500 ≥ 27.75
Glucose, Low (mg/dL; mmol/L) ≥ 1 month of age	55 to 64 3.05 to < 3.55	40 to < 55 2.22 to < 3.05	30 to < 40 1.67 to < 2.22	< 30 < 1.67
Lipase, High	1.1 to < 1.5 × ULN	1.5 to < 3.0 × ULN	3.0 to < 5.0 × ULN	≥ 5.0 × ULN
Cholesterol, Fasting, High (mg/dL; mmol/L) ≥ 18 years of age	200 to < 240 5.18 to < 6.19	240 to < 300 6.19 to < 7.77	≥ 300 ≥ 7.77	NA
Triglycerides, Fasting, High (mg/dL; mmol/L)	150 to 300 1.71 to 3.42	> 300 to 500 > 3.42 to 5.7	> 500 to < 1.000 > 5.7 to 11.4	> 1,000 > 11.4
Phosphate, Low (mg/dL; mmol/L) > 14 years of age	2.0 to < LLN 0.65 to < LLN	1.4 to < 2.0 0.45 to < 0.65	1.0 to < 1.4 0.32 to < 0.45	< 1.0 < 0.32

Clinical Chemistry				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Potassium, High (mEq/L; mmol/L)	5.6 to < 6.0 5.6 to < 6.0	6.0 to < 6.5 6.0 to < 6.5	6.5 to < 7.0 6.5 to < 7.0	≥ 7.0 ≥ 7.0
Potassium, Low (mEq/L; mmol/L)	3.0 to < 3.4 3.0 to < 3.4	2.5 to < 3.0 2.5 to < 3.0	2.0 to < 2.5 2.0 to < 2.5	< 2.0 < 2.0
Sodium, High (mEq/L; mmol/L)	146 to < 150 146 to < 150	150 to < 154 150 to < 154	154 to < 160 154 to < 160	≥ 160 ≥ 160
Sodium, Low (mEq/L; mmol/L)	130 to < 135 130 to < 135	125 to < 130 125 to < 130	121 to < 125 121 to < 125	≤ 120 ≤ 120
Uric Acid, High (mEq/L; mmol/L)	7.5 to < 10.0 0.45 to < 0.59	10.0 to < 12.0 0.59 to < 0.71	12.0 to < 15.0 0.71 to < 0.89	≥ 15.0 ≥ 0.89

NA=not applicable; LLN = lower limit of normal; ULN=upper limit of normal.

Urinalysis				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Glucose/Glycosuria (random collection tested by dipstick)	Trace to 1+ or ≤ 250 mg	2+ or > 250 to ≤ 500 mg	> 2+ or > 500 mg	NA
Protein/Proteinuria (random collection tested by dipstick)	1+	2+	3+ or higher	NA
Red Blood Cells (RBCs)/Hematuria (not to be reported based on dipstick findings or on blood believed to be of menstrual origin)	6 to < 10 RBCs per high power field	≥ 10 RBCs per high power field	Gross, with or without clots OR with RBC casts OR intervention indicated	Life-threatening consequences

NA=not applicable

10.7. Appendix 7: Values of Potential Clinical Importance

10.7.1. ECG

ECG Parameter	Units	Potential Clinically Important Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	<320	>450
Absolute PR Interval	msec	< 120	> 200
Absolute QRS Interval	msec	< 60	> 120
Change from Baseline			
Increase from Baseline QTc	msec		> 60

10.7.2. Vital Signs

Vital Sign Parameter (Absolute)	Units	Potential Clinically Important Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	< 85	> 140
Diastolic Blood Pressure	mmHg	< 45	> 90
Heart Rate	bpm	< 40	> 100

10.8. Appendix 8: Abbreviations & Trade Marks

10.8.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
ANOVA	Analysis of Variance
AUC	Area under the Plasma Concentration-Time Curve
AUC(0-∞)	AUC from Time 0 Extrapolated to Infinity
AUC(0-t)	AUC from Time 0 to Time t
BA	Bioavailability
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL/F	Apparent Oral Clearance
Cmax	Maximum Observed Concentration
C-SSRS	Columbia Suicide Severity Rating Scale
CV	Coefficient of Variation
CV_b	Coefficient of Variation (Between)
DAIDS	Division of AIDS
DBF	Database Freeze
DBR	Database Release
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
GSK	GlaxoSmithKline
HLGT	High Level Group Term
ICH	International Conference on Harmonization
IDSL	Integrated Data Standards Library
LLN	Lower Limit of Normal
MedDRA	Medical Dictionary for Regulatory Activities
PK	Pharmacokinetic
PT	Preferred Term
QTcB	QTc using the Bazett formula
QTcF	QTc using the Fridericia formula
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SMQ	Standardized MedDRA Query
SOC	System Organ Class
t1/2	Apparent Terminal Phase Half-life
tlag	Lag Time for Absorption
Tmax	Time of Maximum Observed Concentration
ULN	Upper Limit of Normal

Abbreviation	Description
Vz/F	Apparent Volume of Distribution

10.8.2. Trademarks

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10.9. Appendix 9: List of Data Displays

10.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.4	
Safety	2.1 to 2.15	2.1
Pharmacokinetic	3.1 to 3.7	
Section	**Listings**	
ICH Listings	1 to 32	
Other Listings	33 to 34	

10.9.2. Mock Example Shell Referencing

Non-IDSL specifications will be referenced as indicated and if required example mock-up displays provided in the Table/Listing/Figure Shells.

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

NOTES:

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

10.9.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

10.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition for the Subject Conclusion Record		SAC
1.2.	Screened	SD1	Summary of Screening Status and Reasons for Screen Failures		SAC
Demographic and Baseline Characteristics					
1.3.	Safety	DM1	Summary of Demographic Characteristics		SAC
1.4.	Safety	DM5	Summary of Race and Racial Combinations		SAC

10.9.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE1CP	Summary of Adverse Events by System Organ Class and Preferred Term		SAC
2.2.	Safety	AE1CP	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term		SAC
2.3.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
2.4.	Safety	AE1CP	Summary of Adverse Events of Special Interest by System Organ Class and Preferred Term		SAC
Laboratory: Chemistry					
2.5.	Safety	LB1	Summary of Clinical Chemistry Data		SAC
2.6.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline		SAC
Laboratory: Hematology					
2.7.	Safety	LB1	Summary of Hematology Data		SAC
2.8.	Safety	LB1	Summary of Hematology Changes from Baseline		SAC
Laboratory: Urinalysis					
2.9.	Safety	LB1	Summary of Urine Concentration		SAC
2.10.	Safety	LB1	Summary of Urine Concentration Changes from Baseline		SAC
ECG					
2.11.	Safety	EG2	Summary of ECG Values		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.12.	Safety	EG2	Summary of ECG Changes from Baseline		SAC
Vital Signs					
2.13.	Safety	VS1	Summary of Vital Signs		SAC
2.14.	Safety	VS1	Summary of Vital Sign Changes from Baseline		SAC
C-SSRS					
2.15.	Safety	CSSRS4	Listing of C-SSRS Suicidal Ideation and Behavior Data	Only include participants who have suicidal ideation or behavior	SAC

10.9.6. Safety Figures

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
2.1.	Safety	EG9	Mean (95% CI) Change from Baseline in QTcF Interval by Timepoint and Treatment		SAC

10.9.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.1.	PK Concentration	PKCT1	Summary of GSK3640254 Plasma Pharmacokinetic Concentration-Time Data (ng/mL) by Treatment		SAC
PK Derived Parameters					
3.2.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment	Parameters with units; present PK parameters in ug/mL or ug.h/mL	SAC
3.3.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment	Parameters with units; present PK parameters in ug/mL or ug.h/mL	SAC
PK Analysis Tables					
3.4.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA)- Relative Bioavailability	AUC(0-∞), AUC(0-t) and Cmax,	SAC
3.5.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA)- Food Effect	AUC(0-∞), AUC(0-t) and Cmax,	SAC
3.6.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Non-parametric analysis- Relative Bioavailability	Tmax	SAC
3.7.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Non-parametric analysis-Food Effect	Tmax	SAC

10.9.8. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Randomized	POP_L1	Listing of Randomization Schedule		SAC
2.	Safety	ES3	Listing of Reasons for Study Withdrawal		SAC
3.	Screened	ES7	Listing of Reasons for Screen Failure		SAC
Protocol Deviations					
4.	Safety	DV2	Listing of Important Protocol Deviations		SAC
5.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC
Populations Analyzed					
6.	Safety	SP3A	Listing of Subjects Excluded from Any Population		SAC
Demographic and Baseline Characteristics					
7.	Safety	DM2	Listing of Demographic Characteristics		SAC
8.	Safety	DM9	Listing of Race		SAC
Prior and Concomitant Medications					
9.	Safety	CM5	Listing of Concomitant Medications	Based on GSK Drug Dictionary	SAC
Exposure and Treatment Compliance					
10.	Safety	EX4	Listing of Exposure Data		SAC
11.	Safety	POP_L2	Listing of Meal Data		SAC
Adverse Events					
12.	Safety	AE2	Listing of Relationship Between System Organ Class and Verbatim Text		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
13.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC
14.	Safety	AE9CP	Listing of All Adverse Events		SAC
Serious and Other Significant Adverse Events					
15.	Safety	AE9CP	Listing of Study Drug Related Adverse Events		SAC
16.	Safety	AE9CP	Listing of Serious Adverse Events (Fatal & Non-Fatal)		SAC
17.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event		SAC
18.	Safety	AE9CP	Listing of Adverse Events Leading to Withdrawal from Study		SAC
19.	Safety	AE9CP	Listing of Adverse Events of Special Interest		SAC
Hepatobiliary (Liver)					
20.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events		SAC
21.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events		SAC
All Laboratory					
22.	Safety	LB5A	Listing of Clinical Chemistry with any Toxicities		SAC
23.	Safety	LB5A	Listing of All Clinical Chemistry Data for Subjects with any Toxicities		SAC
24.	Safety	LB5A	Listing of Hematology with any Toxicities		SAC
25.	Safety	LB5A	Listing of All Hematology Data for Subjects with any Toxicities		SAC
26.	Safety	LB5A	Listing of Urinalysis with any Toxicities		SAC
27.	Safety	LB5A	Listing of All Urinalysis Data for Subjects with any Toxicities		SAC
ECG					
28.	Safety	EG6	Listing of All ECG Findings		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29.	Safety	EG6	Listing of All Abnormal ECG Findings		SAC
30.	Safety	EG4	Listing of All ECG Values		SAC
Vital Signs					
31.	Safety	VS5	Listing of All Vital Signs of Potential Clinical Importance		SAC
32.	Safety	VS5	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance		SAC

10.9.9. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
33.	PK Concentration	PKCL1P	Listing of GSK3640254 Plasma Concentration-Time Data by Treatment		SAC
34.	PK Parameter	PKPL1P	Listing of GSK3640254 Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment		SAC