## Reporting and Analysis Plan for a Two-Part, Randomized, Open-Label, Single Dose, 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

<table>
<thead>
<tr>
<th>Division</th>
<th>Worldwide Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information Type</td>
<td>Reporting and Analysis Plan (RAP)</td>
</tr>
<tr>
<td>Title</td>
<td>Reporting and Analysis Plan for A Two-Part, Randomized, Open-Label, Single Dose, 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</td>
</tr>
<tr>
<td>Compound Number</td>
<td>GSK3640254</td>
</tr>
<tr>
<td>Effective Date</td>
<td>16-APR-2020</td>
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**Description:**
- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 213567.
- 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.

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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 (CSR) for Protocol: 213567.

### Revision Chronology:

<table>
<thead>
<tr>
<th>Original Protocol</th>
<th>27-DEC-2019</th>
<th>Original</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019N425126_00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Amendment 01</th>
<th>20-FEB-2020</th>
<th>Removed eligibility of participants who enter Part 1 from entering into Part 2.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019N425126_01</td>
<td></td>
<td>Added details of a planned preliminary pharmacokinetic (PK) interim analyses following completion of Part 1</td>
</tr>
</tbody>
</table>

2. **SUMMARY OF KEY PROTOCOL INFORMATION**

This is a Phase 1, 2-part, randomized, open-label, single-dose, crossover study to compare the relative bioavailability (BA) of a tablet formulation of GSK3640254 with capsule formulation (Part 1) and to assess the effect of food on the PK of the tablet formulation in healthy participants (Part 2).

2.1. **Changes to the Protocol Defined Statistical Analysis Plan**

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Statistical Analysis Plan</th>
<th>Rationale for Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pharmacokinetic concentration population will be used for concentration listing.</td>
<td>• Pharmacokinetic concentration population will be used for the PK concentration listings, summary tables, and plotting of concentration-time data.</td>
<td>• Align with reporting and analysis plan (RAP) for previous GSK3640254 studies.</td>
</tr>
<tr>
<td>• Pharmacokinetic parameter population will be used for PK parameter listing, PK concentration and parameter summary tables, statistical analysis tables, and plotting of the PK concentration-time data.</td>
<td>• Pharmacokinetic parameter population will be used for PK parameter listings, summary tables, and statistical analysis tables.</td>
<td>• Align with reporting and analysis plan (RAP) for previous GSK3640254 studies.</td>
</tr>
<tr>
<td>• This is an open-label study</td>
<td>• Biostatistics and Programming teams from both GSK and PPD will remain blinded to the actual randomization schedule. Other teams including PPD Pharmacology team will remain open-label</td>
<td>• Biostatistics and Programming teams remain blinded following GSK’s requirement</td>
</tr>
</tbody>
</table>
## 2.2. Study Objective(s) and Endpoint(s)

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Objectives</strong></td>
<td><strong>Primary Endpoints</strong></td>
</tr>
<tr>
<td>• To assess the relative BA of GSK3640254 mesylate tablets and GSK3640254 mesylate capsules (in the presence of a moderate fat meal)</td>
<td>• AUC(0–∞), AUC(0–t), Cmax, and Tmax for GSK3640254</td>
</tr>
<tr>
<td>• To assess the effect of food (fasted moderate fat meal, and high fat meal) on the PK of the GSK3640254 mesylate tablet formulation</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary Objectives</strong></td>
<td><strong>Secondary Endpoints</strong></td>
</tr>
<tr>
<td>• 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</td>
<td>• Safety and tolerability parameters for AEs/SAEs, observed and change from baseline clinical laboratory assessments, ECGs, and vital sign measurements</td>
</tr>
<tr>
<td>• To characterize the PK of GSK3640254</td>
<td>• tlag, t1/2, CL/F, and Vz/F for GSK3640254</td>
</tr>
<tr>
<td>• GSK3640254 PK concentrations in plasma</td>
<td></td>
</tr>
</tbody>
</table>

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.
## Study Design

### Overview of Study Design and Key Features

#### Figure 1  Study Design Schematic – Part 1

<table>
<thead>
<tr>
<th>Screening (≤28 days)</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Discharge (Day 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 Treatment A or Treatment B</td>
<td>Washout 7 Days</td>
<td>Day 1 Treatment A or Treatment B</td>
<td></td>
</tr>
</tbody>
</table>

Treatment A = GSK3640254 200 mg (as 2x 100mg capsules) administered under moderate fat conditions (reference); Treatment B = GSK3640254 200 mg (as 2x 100mg tablets) administered under moderate fat conditions (test).

#### Figure 2  Study Design Schematic – Part 2

<table>
<thead>
<tr>
<th>Screening (≤28 days)</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Period 3</th>
<th>Discharge (Day 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 Treatment C or Treatment D or Treatment E</td>
<td>Washout 7 Days</td>
<td>Day 1 Treatment C or Treatment D or Treatment E</td>
<td>Washout 7 Days</td>
<td>Day 1 Treatment C or Treatment D or Treatment E</td>
</tr>
</tbody>
</table>

Treatment C = GSK3640254 200 mg (as 2x 100mg tablets) administered under moderate fat conditions (test); Treatment D = GSK3640254 200 mg (as 2x 100mg tablets) administered under fasted conditions (reference); Treatment E = GSK3640254 200 mg (as 2x 100mg tablets) administered under high fat conditions (test).

### Design Features

- A phase 1, 2-part, randomized, open-label, single-dose, and crossover study.
- Participants in Part 1 will be randomly assigned to 1 of 2 treatment sequences in a 1:1 ratio; participants in Part 2 will be randomly assigned to 1 of 3 treatment sequences in 1:1:1 ratio.
- Part 1 will consist of a Screening period and 2 sequential treatment periods; Part 2 will consist of a Screening period and 3 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.
- Approximately 18 participants will be enrolled to ensure that 14 evaluable participants complete Part 1; approximately 21 participants will be enrolled to ensure that 16 evaluable participants complete Part 2.

### Dosing

- Part 1
  - Treatment A: GSK3640254 200 mg (as 2x 100mg capsules) administered under moderate fat condition (reference)
  - Treatment B: GSK3640254 200 mg (as 2x 100mg tablets) administered under moderate fat conditions (test)

- Part 2
  - Treatment C: GSK3640254 200 mg (as 2x 100mg tablets) administered under moderate fat conditions (test)
  - Treatment D: GSK3640254 200 mg (as 2x 100mg tablets) administered under fasted conditions (reference)
- Treatment E: GSK3640254 200 mg (as 2x 100mg tablets) administered under high fat conditions (test_)

| Time & Events | • Refer to Appendix 1: Schedule of Activities |
| Treatment Assignment | • This is a randomized study. Biostatistics and Programming teams from both GSK and PPD will remain blinded to the actual randomization schedule. Other teams including PPD PK team will remain open-label.  
• In Part 1, participants will be randomly assigned to 1 of 2 treatment sequences (AB or BA) in 1:1 ratio; in Part 2, participants will be randomly assigned to 1 of 3 treatment sequences (CDE, DEC, or ECD) in 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 (version 9.4). |
| Interim Analysis | • After completion of the study Part 1, preliminary PK data based on nominal time will be analyzed by PPD Pharmacology as soon as PK data are available, the decision will be used for the selection of formulations to proceed with in future Phase II clinical trials.  
• The interim outputs will be produced by WinNonlin (8.0 or higher). |

2.4. **Statistical Hypotheses**

There is no formal research hypothesis that will be statistically tested in this study.
3. **PLANNED ANALYSES**

3.1. **Interim Analyses**

There is no formal interim analysis planned for this study. After completion of the study Part 1, preliminary PK data based on nominal time will be analyzed by PPD Pharmacology as soon as PK data are available, the decision will be used for the selection of formulations to proceed with in future Phase II clinical trials.

The interim outputs will be produced by WinNonlin (8.0 or higher).

3.2. **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).
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed by PPD Randomization Team to PPD Biostatistics and Programming team.
5. Database freeze (DBF) has been declared by GSK Data Management after reviewing the unblinded SDTM datasets.
6. Only after DBF has been declared by GSK Data Management can GSK Biostatistics and Programming be unblinded.

4. **ANALYSIS POPULATIONS**

<table>
<thead>
<tr>
<th>Population</th>
<th>Definition / Criteria</th>
<th>Analyses Evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened</td>
<td>• All participants who signed the informed consent form</td>
<td>• Study Population</td>
</tr>
<tr>
<td></td>
<td>• This population will be used for screen failure listing and summary.</td>
<td></td>
</tr>
<tr>
<td>Randomized</td>
<td>• All participants who were randomly assigned to a treatment sequence.</td>
<td>• Study Population</td>
</tr>
<tr>
<td></td>
<td>• This population will be used for listing of randomization schedule.</td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>• All participants who received at least 1 dose of study medication.</td>
<td>• Study Population</td>
</tr>
<tr>
<td></td>
<td>• This population will be used for all demographic, disposition (exclude screen failure), and safety listings, summaries, and figures</td>
<td>• Safety</td>
</tr>
<tr>
<td>Pharmacokinetic Concentration</td>
<td>• All participants who underwent plasma PK sampling and had evaluable PK assay results.</td>
<td>• PK Concentration</td>
</tr>
<tr>
<td></td>
<td>• This population will be used for the PK concentration listings, summary tables, and plotting of concentration-time data.</td>
<td></td>
</tr>
</tbody>
</table>
### 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 unblinding and 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).

---

**Population** | **Definition / Criteria** | **Analyses Evaluated**
--- | --- | ---
Pharmacokinetic Parameter | • All participants who underwent plasma PK sampling and had evaluable PK parameters estimated. • This population will be used for PK parameter listings, PK parameter 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.
5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

<table>
<thead>
<tr>
<th>Treatment Group Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data Displays for Reporting – Part 1</strong></td>
</tr>
<tr>
<td><strong>Description</strong></td>
</tr>
<tr>
<td>GSK3640254 200 mg (as 2 × 100mg capsules) administered under moderate fat conditions (reference)</td>
</tr>
<tr>
<td>GSK3640254 200 mg (as 2 × 100mg tablets) administered under moderate fat conditions (test)</td>
</tr>
<tr>
<td><strong>Data Displays for Reporting – Part 2</strong></td>
</tr>
<tr>
<td><strong>Description</strong></td>
</tr>
<tr>
<td>GSK3640254 200 mg (as 2 × 100mg tablets) administered under moderate fat conditions (test)</td>
</tr>
<tr>
<td>GSK3640254 200 mg (as 2 × 100mg tablets) administered under fasted conditions (reference)</td>
</tr>
<tr>
<td>GSK3640254 200 mg (as 2 × 100mg tablets) administered under high fat conditions (test)</td>
</tr>
</tbody>
</table>

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 pre-dose 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.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study Assessments Considered as Baseline</th>
<th>Baseline Used in Data Display</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Screening</td>
<td>Day -1</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital Sign</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>12-Lead ECG</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hematology</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Clinical Chemistry</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Section</th>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1</td>
<td>Appendix 1: Schedule of Activities</td>
</tr>
<tr>
<td>10.2</td>
<td>Appendix 2: Study Phases and Treatment Emergent Adverse Events</td>
</tr>
<tr>
<td>10.3</td>
<td>Appendix 3: Data Display Standards &amp; Handling Conventions</td>
</tr>
<tr>
<td>10.4</td>
<td>Appendix 4: Derived and Transformed Data</td>
</tr>
<tr>
<td>10.5</td>
<td>Appendix 5: Reporting Standards for Missing Data</td>
</tr>
<tr>
<td>10.6</td>
<td>Appendix 6: Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events</td>
</tr>
<tr>
<td>10.7</td>
<td>Appendix 7: Values of Potential Clinical Importance</td>
</tr>
</tbody>
</table>
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, study populations, 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 for each study part and summarized by treatment group and sampling time for each study part.

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 permit. Participants who experience emesis at or before 2 times median $T_{max}$ or participants whose predose concentrations are $>5\%$ their $C_{max}$ value for the given treatment will be excluded from the calculation of summary statistics and statistical analysis for the respective treatment.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC(0-∞)</td>
<td>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.</td>
</tr>
<tr>
<td>AUC(0-t)</td>
<td>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.</td>
</tr>
<tr>
<td>Cmax</td>
<td>Maximum observed concentration, determined directly from the concentration-time data.</td>
</tr>
<tr>
<td>Tmax</td>
<td>Time of maximum observed concentration</td>
</tr>
</tbody>
</table>

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 95% confidence interval (CI) for plasma GSK3640254 PK parameter values will be summarized by treatment for each study part.

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).

<table>
<thead>
<tr>
<th>Endpoint / Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Plasma primary PK endpoints include AUC(0-∞), AUC(0-t), Cmax, and Tmax for GSK3640254 as data permit</td>
</tr>
</tbody>
</table>

**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 C (test) versus Treatment D (reference)
  - Treatment E (test) versus Treatment D (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:
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 C (test) versus Treatment D (reference)
  - Treatment E (test) versus Treatment D (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 C (test) versus Treatment D (reference)
  - Treatment E (test) versus Treatment D (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. Participants who experience emesis at or before 2 times median T_{max} or participants whose predose concentrations are >5% their C_{max} value for the given treatment will be excluded from the calculation of summary statistics for the respective treatment.
Plasma pharmacokinetic parameters listed below will be determined from the plasma concentration-time data, as data permits:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>tlag</td>
<td>Lag time for absorption</td>
</tr>
<tr>
<td>t1/2</td>
<td>Apparent terminal phase half-life</td>
</tr>
<tr>
<td>CL/F</td>
<td>Apparent oral clearance</td>
</tr>
<tr>
<td>Vz/F</td>
<td>Apparent volume of distribution</td>
</tr>
</tbody>
</table>

**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 2019N425126_01 (20-FEB-2020): A Two-Part, Randomized, Open-Label, Single Dose, 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**

**Table 1**  
**Screening Visit (Part 1 and Part 2)**

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

\(^1\) A full physical examination will include at a minimum, assessments of the skin, cardiovascular, respiratory, gastrointestinal, and neurological systems.
## Table 2  
**Time and Events Table – Part 1**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Check-in</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day -1</td>
<td>Day 1</td>
<td>Washout</td>
<td>Period 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Day 2</td>
<td>Days 3-5</td>
</tr>
<tr>
<td>Admit to clinic</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge from clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brief physical examination</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital signs</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>D3-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-lead ECG</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug, alcohol, and cotinine screen</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory assessments (hematology, chemistry, urinalysis)</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy test</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discharge from clinic following completion of the last study procedure on Day 5 of Period 2.

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.

Blood pressure and pulse will be measured in triplicate pre-dose on Day 1 in both periods. Single blood pressure and pulse will be measured on other study days.

The ECGs on Day 1 in both periods will be taken at pre-dose, and post-dose at 2 and 4 hours. The pre-dose ECGs in both periods will be taken in triplicate. The post-dose ECGs are single ECGs.

See Protocol Appendix 2 for specific tests to be performed.

See Protocol Appendix 2 for specific tests to be performed. Day 2 samples in each period to be collected 24 hours after dosing.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Check-in</th>
<th>Period 1</th>
<th>Period 2</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Washout</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day -1</td>
<td>Day 1</td>
<td>Day 2</td>
<td>Days 3-5</td>
</tr>
<tr>
<td>Columbia-Suicide Severity Rating Scale</td>
<td>X</td>
<td></td>
<td></td>
<td>D7</td>
</tr>
<tr>
<td>Genetic sample (optional)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study intervention: GSK3640254 200 mg</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>(as 2x 100mg capsule or tablet)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants will fast overnight for at least 10 hours prior to dosing; will be provided a moderate fat meal 30 minutes prior to dosing; and will be provided standardized meals ≥24 hours post-dose. See Protocol Section 4.1.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serial PK sampling</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Blood 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 post-dose in both periods.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AE = adverse event; D = day; ECG = electrocardiogram; PK = pharmacokinetic; SAE = serious adverse event.

¹ Evaluations scheduled for Day 5 in Period 2 will also be performed for participants who discontinue early.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Check-in</th>
<th>Periods 1 and 2</th>
<th>Period 3 only</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Washout</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day -1</td>
<td>Day 1</td>
<td>Day 2</td>
<td>Days 3-5</td>
</tr>
<tr>
<td>Admit to clinic</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge from clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brief physical examination</td>
<td>X</td>
<td></td>
<td>D7 (Period 1 and 2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital signs</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>D3-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-lead ECG</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug, alcohol, and cotinine screen</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory assessments</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(hematology, chemistry, urinalysis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure</td>
<td>Check-in</td>
<td>Periods 1 and 2</td>
<td>Period 3 only</td>
<td>Notes</td>
</tr>
<tr>
<td>----------------------------------------------------------------</td>
<td>----------</td>
<td>----------------</td>
<td>---------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Day -1</td>
<td>Day 1</td>
<td>Day 2</td>
<td>Days 3-5</td>
</tr>
<tr>
<td>Pregnancy test</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Columbia-Suicide Severity Rating Scale</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic sample (optional)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study intervention: GSK3640254 200 mg tablet</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study intervention:</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serial PK sampling</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>AE review</td>
<td>≫</td>
<td>≫</td>
<td>≫</td>
<td>≫</td>
</tr>
<tr>
<td>SAE review</td>
<td>≫</td>
<td>≫</td>
<td>≫</td>
<td>≫</td>
</tr>
<tr>
<td>Concomitant medications</td>
<td>≫</td>
<td>≫</td>
<td>≫</td>
<td>≫</td>
</tr>
</tbody>
</table>

AE = adverse event; D = day; ECG = electrocardiogram; PK = pharmacokinetic; SAE = serious adverse event.
1 Evaluations scheduled for Day 5 in Period 3 will also be performed for participants who discontinue early.

Participants will fast overnight for at least 10 hours prior to dosing; will be provided no meal, a moderate fat meal, or a high fat meal 30 minutes prior to dosing; and will be provided standardized meals ≥4 hours post-dose. See Protocol Section 4.1.

Blood 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 post-dose in each period.
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).

<table>
<thead>
<tr>
<th>Study Phase</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Treatment</td>
<td>Date and Time ≤ Study Treatment Start Date and Time</td>
</tr>
<tr>
<td>On-Treatment</td>
<td>Study Treatment Start Date and Time &lt; Date and Time ≤ Study Treatment Stop Date and Time + 5 days the Date and Time of Early Withdrawal Visit whichever is later.</td>
</tr>
<tr>
<td>Post-Treatment</td>
<td>Date and Time &gt; Study Treatment Stop Date and Time + 5 days or the Date and Time of Early Withdrawal Visit whichever is later</td>
</tr>
</tbody>
</table>

10.2.1.1. Study Phases for Concomitant Medication

<table>
<thead>
<tr>
<th>Study Phase</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior</td>
<td>If medication end date is not missing and is before Day -1</td>
</tr>
<tr>
<td>Concomitant</td>
<td>Any medication that is not a prior</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Flag</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Emergent</td>
<td>• If AE onset date and time is on or after treatment start date and time &amp; on or before treatment stop date and time + 5 days.</td>
</tr>
<tr>
<td></td>
<td>• Study Treatment Start Date and Time ≤ AE Start Date and Time ≤ Study Treatment Stop Date and Time + 5 days.</td>
</tr>
<tr>
<td></td>
<td>• If the AE onset date is completely missing, the AE is considered as treatment emergent.</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>HARP Server</th>
<th>``gsk3640254`mid213567`final_01</th>
</tr>
</thead>
<tbody>
<tr>
<td>HARP Compound</td>
<td>GSK3640254</td>
</tr>
</tbody>
</table>

**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 presented by study part separately.
- 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**

<table>
<thead>
<tr>
<th>Continuous Data</th>
<th>Refer to IDSL Statistical Principle 6.06.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Categorical Data</td>
<td>N, n, frequency, %</td>
</tr>
</tbody>
</table>

**Graphical Displays**
- Refer to IDSL Statistical Principals 7.01 to 7.13.

### 10.3.3. Reporting Standards for Pharmacokinetics

**Pharmacokinetic Concentration Data**

<table>
<thead>
<tr>
<th>Descriptive Summary Statistics, Graphical Displays and Listings</th>
<th>Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. For continuous data:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 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.</td>
<td></td>
</tr>
<tr>
<td>- For NQs at the end of the participant profile (i.e. after the last incidence of a measurable concentration);</td>
<td></td>
</tr>
<tr>
<td>- 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)</td>
<td></td>
</tr>
<tr>
<td>- for summary statistics, these are set to 0 (to avoid skewing of the summary statistics)</td>
<td></td>
</tr>
<tr>
<td>- Individual NQs which fall between two measurable concentrations are set to missing (individual values of this nature are assumed to be an anomaly)</td>
<td></td>
</tr>
<tr>
<td>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).</td>
<td></td>
</tr>
<tr>
<td>Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.</td>
<td></td>
</tr>
</tbody>
</table>
### Pharmacokinetic Parameter Data

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
</table>
| **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.  
  \( CV_b(\%) = \sqrt{\exp(\text{SD}^2) - 1} \times 100 \)  
  (SD = SD of Ln-Transformed data)                                      |
| **Parameters Not Being Ln-Transformed**                                    | Tmax, tlag, \( \lambda_z \), \( \lambda_z \) lower, \( \lambda_z \) upper, and \( \lambda_z \) no. of points.                                |
| **Parameters Not Being Summarized**                                        | \( \lambda_z \), \( \lambda_z \) lower, \( \lambda_z \) upper, and \( \lambda_z \) no. of points.                                     |
| **Listings**                                                                | Include the first point, last point and number of points used in the determination of \( \lambda_z \) 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
  - Assessment Date >= Dose Date on Period 3 Day 1
    → Period Day = Assessment Date – Dose Date on Period 3 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

\[
QTcB = \frac{QT}{\sqrt{RR/1000}}
\]

where RR interval in msec is calculated using QT interval (msec) and QTcF interval (msec) as

\[
RR = \left(\frac{QT}{QTcF}\right)^3 \times 1000
\]
10.5. **Appendix 5: Reporting Standards for Missing Data**

10.5.1. **Premature Withdrawals**

<table>
<thead>
<tr>
<th>Element</th>
<th>Reporting Detail</th>
</tr>
</thead>
</table>
| 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**

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

10.5.2.1. **Handling of Missing and Partial Dates**

<table>
<thead>
<tr>
<th>Element</th>
<th>Reporting Detail</th>
</tr>
</thead>
</table>
| General    | • Partial dates will be displayed as captured in participant listing displays.  
  • The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:  
  o **Missing Start Day**: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 2: Study Phases and Treatment Emergent Adverse Events.  
  o **Missing Stop Day**: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used.  
  • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. |
| Adverse Events | • Partial dates for any concomitant medications recorded in the eCRF will be imputed using the following convention:  
  o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month  
  o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month.  
  • The recorded partial date will be displayed in listings. |
## 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.

<table>
<thead>
<tr>
<th><strong>HEMATOLOGY</strong></th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absolute Lymphocyte Count, Low (cell/mm(^3); cells/L)</strong></td>
<td>600 to &lt; 650 0.600 × 10(^9) to &lt; 0.650 × 10(^9)</td>
<td>500 to &lt; 600 0.500 × 10(^9) to &lt; 0.600 × 10(^9)</td>
<td>350 to &lt; 500 0.350 × 10(^9) to &lt; 0.500 × 10(^9)</td>
<td>&lt; 350 0.350 × 10(^9)</td>
</tr>
<tr>
<td><strong>Absolute Neutrophil Count, Low (cells/mm(^3); cells/L)</strong></td>
<td>800 to 1,000 0.800 × 10(^9) to 1.000 × 10(^9)</td>
<td>600 to 799 0.600 × 10(^9) to 0.799 × 10(^9)</td>
<td>400 to 599 0.400 × 10(^9) to 0.599 × 10(^9)</td>
<td>&lt; 400 0.400 × 10(^9)</td>
</tr>
<tr>
<td><strong>Hemoglobin, Low (g/dL; mmol/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 13 years of age (male only)</td>
<td>10.0 to 10.9 6.19 to 6.76</td>
<td>9.0 to ≤ 10.0 5.57 to ≤ 6.19</td>
<td>7.0 to &lt; 9.0 4.34 to &lt; 5.57</td>
<td>&lt; 7.0 &lt;=4.34</td>
</tr>
<tr>
<td>≥ 13 years of age (female only)</td>
<td>9.5 to 10.4 5.88 to 6.48</td>
<td>8.5 to &lt; 9.5 5.25 to &lt; 5.57</td>
<td>6.5 to &lt; 8.5 4.03 to &lt; 5.25</td>
<td>&lt; 6.5 &lt;=4.03</td>
</tr>
<tr>
<td><strong>Platelets, Decreased (cells/mm(^3); cells/L)</strong></td>
<td>100,000 to &lt; 125,000 100,000 × 10(^9) to &lt; 125,000 × 10(^9)</td>
<td>50,000 to &lt; 100,000 50,000 × 10(^9) to &lt; 100,000 × 10(^9)</td>
<td>25,000 to &lt; 50,000 25,000 × 10(^9) to &lt; 50,000 × 10(^9)</td>
<td>&lt; 25,000 25,000 × 10(^9)</td>
</tr>
<tr>
<td><strong>White Blood Cell, Decreased (cells/mm(^3); cells/L)</strong></td>
<td>2,000 to 2,499 2.000 × 10(^9) to 2.499 × 10(^9)</td>
<td>1,500 to 1,999 1.500 × 10(^9) to 1.999 × 10(^9)</td>
<td>1,000 to 1,499 1.000 × 10(^9) to 1.499 × 10(^9)</td>
<td>&lt; 1,000 1.000 × 10(^9)</td>
</tr>
<tr>
<td>Clinical Chemistry</td>
<td>Grade 1</td>
<td>Grade 2</td>
<td>Grade 3</td>
<td>Grade 4</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------------------------</td>
<td>--------------------------</td>
<td>--------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td><strong>Albumin, Low (g/dL; g/L)</strong></td>
<td>3.0 to &lt; LLN</td>
<td>≥ 2.0 to &lt; 3.0</td>
<td>&lt; 2.0</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>30 to &lt; LLN</td>
<td>≥ 20 to &lt; 30</td>
<td>&lt; 20</td>
<td></td>
</tr>
<tr>
<td><strong>Alkaline Phosphatase, High</strong></td>
<td>1.25 to &lt; 2.5 × ULN</td>
<td>2.5 to &lt; 5.0 × ULN</td>
<td>5.0 to &lt; 10.0 × ULN</td>
<td>≥ 10.0 × ULN</td>
</tr>
<tr>
<td><strong>Alanine Aminotransferase, High</strong></td>
<td>1.25 to &lt; 2.5 × ULN</td>
<td>2.5 to &lt; 5.0 × ULN</td>
<td>5.0 to &lt; 10.0 × ULN</td>
<td>≥ 10.0 ULN</td>
</tr>
<tr>
<td><strong>Amylase (Total), High</strong></td>
<td>1.1 to &lt; 1.5 × ULN</td>
<td>1.5 to &lt; 3.0 × ULN</td>
<td>3.0 to &lt; 5.0 × ULN</td>
<td>≥ 5.0 × ULN</td>
</tr>
<tr>
<td><strong>Aspartate Aminotransferase, High</strong></td>
<td>1.25 to &lt; 2.5 × ULN</td>
<td>2.5 to &lt; 5.0 × ULN</td>
<td>5.0 to &lt; 10.0 × ULN</td>
<td>≥ 10.0 × ULN</td>
</tr>
<tr>
<td><strong>Bicarbonate, Low (mEq/L; mmol/L)</strong></td>
<td>16.0 to &lt; LLN</td>
<td>11.0 to &lt; 16.0</td>
<td>8.0 to &lt; 11.0</td>
<td>&lt; 8.0</td>
</tr>
<tr>
<td></td>
<td>16.0 to &lt; LLN</td>
<td>11.0 to &lt; 16.0</td>
<td>8.0 to &lt; 110.</td>
<td></td>
</tr>
<tr>
<td><strong>Direct Bilirubin, High &gt; 28 days of age</strong></td>
<td>NA</td>
<td>NA</td>
<td>&gt; ULN with other signs and symptoms of hepatotoxicity</td>
<td>&gt; ULN with life-threatening consequences (e.g., signs and symptoms of liver failure)</td>
</tr>
<tr>
<td><strong>Total Bilirubin, High &gt; 28 days of age</strong></td>
<td>1.1 to &lt; 1.6 × ULN</td>
<td>1.6 to &lt; 2.6 × ULN</td>
<td>2.6 to &lt; 5.0 × ULN</td>
<td>≥ 5.0 × ULN</td>
</tr>
<tr>
<td><strong>Calcium, High (mg/dL; mmol/L) ≥ 7 days of age</strong></td>
<td>10.6 to &lt; 11.5</td>
<td>11.5 to &lt; 12.5</td>
<td>12.5 to &lt; 13.5</td>
<td>≥ 13.5</td>
</tr>
<tr>
<td></td>
<td>2.65 to &lt; 2.88</td>
<td>2.88 to &lt; 3.13</td>
<td>3.13 to &lt; 3.38</td>
<td>≥ 3.38</td>
</tr>
<tr>
<td><strong>Calcium, Low (mg/dL; mmol/L) ≥ 7 days of age</strong></td>
<td>7.8 to &lt; 8.4</td>
<td>7.0 to &lt; 7.8</td>
<td>6.1 to &lt; 7.0</td>
<td>&lt; 6.1</td>
</tr>
<tr>
<td></td>
<td>1.95 to &lt; 2.10</td>
<td>1.75 to &lt; 1.95</td>
<td>1.53 to &lt; 1.75</td>
<td>&lt; 1.53</td>
</tr>
<tr>
<td><strong>Creatine Kinase, High</strong></td>
<td>3 to &lt; 6 × ULN</td>
<td>6 to &lt; 10 × ULN</td>
<td>10 to &lt; 20 × ULN</td>
<td>≥ 20 × ULN</td>
</tr>
<tr>
<td><strong>Creatinine, High Choose the method that selects for the higher grade</strong></td>
<td>1.1 to 1.3 × ULN</td>
<td>&gt; 1.3 to 1.8 × ULN OR Increase to 1.3 to &lt; 1.5 × participant’s baseline</td>
<td>&gt; 1.8 to &lt; 3.5 ULN OR Increase to 1.5 to &lt; 2.0 × participant’s baseline</td>
<td>≥ 3.5 × ULN OR Increase of ≥ 2.0 × participant’s baseline</td>
</tr>
<tr>
<td><strong>Glucose Fasting, High (mg/dL; mmol/L) ≥ 18 years of age</strong></td>
<td>110 to 125</td>
<td>125 to 250</td>
<td>250 to 500</td>
<td>≥ 500</td>
</tr>
<tr>
<td></td>
<td>6.11 to 6.95</td>
<td>6.95 to &lt; 13.89</td>
<td>13.89 to &lt; 27.75</td>
<td>≥ 500</td>
</tr>
<tr>
<td><strong>Glucose, Low (mg/dL; mmol/L) ≥ 1 month of age</strong></td>
<td>55 to 64</td>
<td>40 to &lt; 55</td>
<td>30 to &lt; 40</td>
<td>&lt; 30</td>
</tr>
<tr>
<td></td>
<td>3.05 to 3.55</td>
<td>2.22 to &lt; 3.05</td>
<td>1.67 to &lt; 2.22</td>
<td>&lt; 1.67</td>
</tr>
<tr>
<td><strong>Lipase, High</strong></td>
<td>1.1 to &lt; 1.5 × ULN</td>
<td>1.5 to &lt; 3.0 × ULN</td>
<td>3.0 to &lt; 5.0 × ULN</td>
<td>≥ 5.0 × ULN</td>
</tr>
<tr>
<td><strong>Cholesterol, Fasting, High (mg/dL; mmol/L) ≥ 18 years of age</strong></td>
<td>200 to &lt; 240</td>
<td>240 to &lt; 300</td>
<td>≥ 300</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>5.18 to 6.19</td>
<td>6.19 to &lt; 7.77</td>
<td>≥ 7.77</td>
<td></td>
</tr>
<tr>
<td><strong>Triglycerides, Fasting, High (mg/dL; mmol/L)</strong></td>
<td>150 to 300</td>
<td>300 to 500</td>
<td>500 to &lt; 1.000</td>
<td>&gt; 1,000</td>
</tr>
<tr>
<td></td>
<td>1.71 to 3.42</td>
<td>3.42 to 5.7</td>
<td>5.7 to 11.4</td>
<td></td>
</tr>
<tr>
<td><strong>Phosphate, Low (mg/dL; mmol/L) &gt; 14 years of age</strong></td>
<td>2.0 to &lt; LLN</td>
<td>1.4 to &lt; 2.0</td>
<td>1.0 to &lt; 1.4</td>
<td>&lt; 1.0</td>
</tr>
<tr>
<td></td>
<td>0.65 to &lt; LLN</td>
<td>0.45 to &lt; 0.65</td>
<td>0.32 to &lt; 0.45</td>
<td></td>
</tr>
</tbody>
</table>
### Clinical Chemistry

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

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

### Urinalysis

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

NA=not applicable
10.7. Appendix 7: Values of Potential Clinical Importance

10.7.1. ECG

<table>
<thead>
<tr>
<th>ECG Parameter</th>
<th>Units</th>
<th>Potential Clinically Important Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td><strong>Absolute</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute QTc Interval</td>
<td>msec</td>
<td>&lt;320</td>
</tr>
<tr>
<td>Absolute PR Interval</td>
<td>msec</td>
<td>&lt; 120</td>
</tr>
<tr>
<td>Absolute QRS Interval</td>
<td>msec</td>
<td>&lt; 60</td>
</tr>
<tr>
<td><strong>Change from Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase from Baseline QTc</td>
<td>msec</td>
<td></td>
</tr>
</tbody>
</table>

10.7.2. Vital Signs

<table>
<thead>
<tr>
<th>Vital Sign Parameter (Absolute)</th>
<th>Units</th>
<th>Potential Clinically Important Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>mmHg</td>
<td>&lt; 85</td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>mmHg</td>
<td>&lt; 45</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>bpm</td>
<td>&lt; 40</td>
</tr>
</tbody>
</table>
10.8. Appendix 8: Abbreviations & Trade Marks

10.8.1. Abbreviations

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

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ULN</td>
<td>Upper Limit of Normal</td>
</tr>
<tr>
<td>Vz/F</td>
<td>Apparent Volume of Distribution</td>
</tr>
</tbody>
</table>

#### 10.8.2. Trademarks

<table>
<thead>
<tr>
<th>Trademarks of the GlaxoSmithKline Group of Companies</th>
<th>Trademarks not owned by the GlaxoSmithKline Group of Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>NONE</td>
<td>SAS, WinNonlin</td>
</tr>
</tbody>
</table>
10.9. Appendix 9: List of Data Displays

10.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

<table>
<thead>
<tr>
<th>Section</th>
<th>Tables</th>
<th>Figures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Population</td>
<td>1.1 to 1.14</td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>2.1 to 2.50</td>
<td>2.1 to 2.2</td>
</tr>
<tr>
<td>Pharmacokinetic</td>
<td>3.1 to 3.10</td>
<td>3.1 to 3.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Section</th>
<th>Listings</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH Listings</td>
<td>1 to 63</td>
</tr>
<tr>
<td>Other Listings</td>
<td>64 to 67</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Section</th>
<th>Figure</th>
<th>Table</th>
<th>Listing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Population</td>
<td>POP_Fn</td>
<td>POP_Tn</td>
<td>POP_Ln</td>
</tr>
<tr>
<td>Safety</td>
<td>SAFE_Fn</td>
<td>SAFE_Tn</td>
<td>SAFE_Ln</td>
</tr>
<tr>
<td>Pharmacokinetic</td>
<td>PK_Fn</td>
<td>PK_Tn</td>
<td>PK_Ln</td>
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</tbody>
</table>

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

10.9.3. Deliverables

<table>
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<tr>
<td>SAC</td>
<td>Final Statistical Analysis Complete</td>
</tr>
</tbody>
</table>
## 10.9.4. Study Population Tables

<table>
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<tr>
<th>Study Population Tables</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No.</strong></td>
</tr>
<tr>
<td><strong>Subject Disposition</strong></td>
</tr>
<tr>
<td>1.1.</td>
</tr>
<tr>
<td>1.2.</td>
</tr>
<tr>
<td>1.3.</td>
</tr>
<tr>
<td>1.4.</td>
</tr>
<tr>
<td>1.5.</td>
</tr>
<tr>
<td>1.6.</td>
</tr>
<tr>
<td><strong>Protocol Deviations</strong></td>
</tr>
<tr>
<td>1.7.</td>
</tr>
<tr>
<td>1.8.</td>
</tr>
<tr>
<td><strong>Demographic and Baseline Characteristics</strong></td>
</tr>
<tr>
<td>1.9.</td>
</tr>
<tr>
<td>1.10.</td>
</tr>
<tr>
<td>1.11.</td>
</tr>
<tr>
<td>1.13.</td>
</tr>
</tbody>
</table>
### Study Population Tables

<table>
<thead>
<tr>
<th>No.</th>
<th>Population</th>
<th>IDSL / Example Shell</th>
<th>Title</th>
<th>Programming Notes</th>
<th>Deliverable [Priority]</th>
</tr>
</thead>
</table>
## 10.9.5. Safety Tables

<table>
<thead>
<tr>
<th>No.</th>
<th>Population</th>
<th>IDSL / Example Shell</th>
<th>Title</th>
<th>Programming Notes</th>
<th>Deliverable [Priority]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse Events (AEs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1</td>
<td>Safety</td>
<td>AE1CP</td>
<td>Summary of Adverse Events by System Organ Class and Preferred Term – Part 1</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.2</td>
<td>Safety</td>
<td>AE1CP</td>
<td>Summary of Adverse Events by System Organ Class and Preferred Term – Part 2</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.3</td>
<td>Safety</td>
<td>AE1CP</td>
<td>Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term – Part 1</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.4</td>
<td>Safety</td>
<td>AE1CP</td>
<td>Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term – Part 2</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.5</td>
<td>Safety</td>
<td>AE3</td>
<td>Summary of Common (&gt;=5%) Adverse Events by Overall Frequency – Part 1</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.6</td>
<td>Safety</td>
<td>AE3</td>
<td>Summary of Common (&gt;=5%) Adverse Events by Overall Frequency – Part 2</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.7</td>
<td>Safety</td>
<td>AE15</td>
<td>Summary of Common (&gt;=5%) Non-serious Adverse Events by System Organ Class and Preferred Term – Part 1 (Number of Subjects and Occurrences)</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.8</td>
<td>Safety</td>
<td>AE15</td>
<td>Summary of Common (&gt;=5%) Non-serious Adverse Events by System Organ Class and Preferred Term – Part 2 (Number of Subjects and Occurrences)</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.9</td>
<td>Safety</td>
<td>AE16</td>
<td>Summary of Serious Adverse Events by System Organ Class and Preferred Term – Part 1 (Number of Subjects and Occurrences)</td>
<td></td>
<td>SAC</td>
</tr>
</tbody>
</table>
## Safety: Tables

<table>
<thead>
<tr>
<th>No.</th>
<th>Population</th>
<th>IDSL / Example Shell</th>
<th>Title</th>
<th>Programming Notes</th>
<th>Deliverable</th>
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<tbody>
<tr>
<td>2.10</td>
<td>Safety</td>
<td>AE16</td>
<td>Summary of Serious Adverse Events by System Organ Class and Preferred Term – Part 2 (Number of Subjects and Occurrences)</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.11</td>
<td>Safety</td>
<td>AE5A</td>
<td>Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Intensity – Part 1</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.12</td>
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<td>AE5A</td>
<td>Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Intensity – Part 2</td>
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<td>SAC</td>
</tr>
<tr>
<td>2.13</td>
<td>Safety</td>
<td>AE1CP</td>
<td>Summary of Adverse Events of Special Interest by System Organ Class and Preferred Term – Part 1</td>
<td></td>
<td>SAC</td>
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<td>2.14</td>
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<td>Summary of Adverse Events of Special Interest by System Organ Class and Preferred Term – Part 2</td>
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### Laboratory: Chemistry

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<td>LB1</td>
<td>Summary of Clinical Chemistry Data – Part 1</td>
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<tr>
<td>2.16</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Clinical Chemistry Data – Part 2</td>
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<td>SAC</td>
</tr>
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<td>Safety</td>
<td>LB1</td>
<td>Summary of Clinical Chemistry Changes from Baseline – Part 1</td>
<td></td>
<td>SAC</td>
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<tr>
<td>2.18</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Clinical Chemistry Changes from Baseline – Part 2</td>
<td></td>
<td>SAC</td>
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<tr>
<td>2.19</td>
<td>Safety</td>
<td>LB16</td>
<td>Summary of Clinical Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1</td>
<td></td>
<td>SAC</td>
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<tr>
<td>2.20</td>
<td>Safety</td>
<td>LB16</td>
<td>Summary of Clinical Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 2</td>
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<td>SAC</td>
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### Laboratory: Hematology

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<th>No.</th>
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<th>Programming Notes</th>
<th>Deliverable</th>
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<tbody>
<tr>
<td>2.21</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Hematology Data – Part 1</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.22</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Hematology Data – Part 2</td>
<td></td>
<td>SAC</td>
</tr>
<tr>
<td>2.23</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Hematology Changes from Baseline – Part 1</td>
<td></td>
<td>SAC</td>
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</tbody>
</table>
## Safety: Tables

<table>
<thead>
<tr>
<th>No.</th>
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</tr>
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<td>2.25</td>
<td>Safety</td>
<td>LB16</td>
<td>Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1</td>
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<td>2.26</td>
<td>Safety</td>
<td>LB16</td>
<td>Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 2</td>
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### Laboratory: Urinalysis

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<tbody>
<tr>
<td>2.27</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Urine Concentration – Part 1</td>
</tr>
<tr>
<td>2.28</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Urine Concentration – Part 2</td>
</tr>
<tr>
<td>2.29</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Urine Concentration Changes from Baseline – Part 1</td>
</tr>
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<td>2.30</td>
<td>Safety</td>
<td>LB1</td>
<td>Summary of Urine Concentration Changes from Baseline – Part 2</td>
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<td>2.31</td>
<td>Safety</td>
<td>UR3</td>
<td>Summary of Urinalysis Dipstick Results – Part 1</td>
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<td>2.32</td>
<td>Safety</td>
<td>UR3</td>
<td>Summary of Urinalysis Dipstick Results – Part 2</td>
</tr>
<tr>
<td>2.33</td>
<td>Safety</td>
<td>LB16</td>
<td>Summary of Urinalysis by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1</td>
</tr>
<tr>
<td>2.34</td>
<td>Safety</td>
<td>LB16</td>
<td>Summary of Urinalysis by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 2</td>
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### ECG

<table>
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<th>Title</th>
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<td>Safety</td>
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<td>Summary of ECG Findings – Part 1</td>
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<tr>
<td>2.36</td>
<td>Safety</td>
<td>SAFE_T1</td>
<td>Summary of ECG Findings – Part 1</td>
</tr>
<tr>
<td>2.37</td>
<td>Safety</td>
<td>EG2</td>
<td>Summary of ECG Values – Part 1</td>
</tr>
<tr>
<td>2.38</td>
<td>Safety</td>
<td>EG2</td>
<td>Summary of ECG Values – Part 2</td>
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</tbody>
</table>
### Safety: Tables

<table>
<thead>
<tr>
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<th>Title</th>
<th>Programming Notes</th>
<th>Deliverable [Priority]</th>
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<td>Summary of ECG Changes from Baseline – Part 1</td>
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<td>SAC</td>
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<td>Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part 2</td>
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### Vital Signs

<table>
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<tr>
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<th>Population</th>
<th>IDSL / Example Shell</th>
<th>Title</th>
<th>Programming Notes</th>
<th>Deliverable [Priority]</th>
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<td>SAC</td>
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<td>2.46</td>
<td>Safety</td>
<td>VS1</td>
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### C-SSRS

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# Pharmacokinetic Figures

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| 16. | Safety | CM5 | Listing of Concomitant Medications – Part 1 | Based on GSK Drug Dictionary | SAC
| 17. | Safety | CM5 | Listing of Concomitant Medications – Part 2 | Based on GSK Drug Dictionary | SAC

| Exposure and Treatment Compliance |
| 18. | Safety | EX4 | Listing of Exposure Data – Part 1 | | SAC
| 19. | Safety | EX4 | Listing of Exposure Data – Part 2 | | SAC
| 20. | Safety | POP_L2 | Listing of Meal Data – Part 1 | | SAC
| 21. | Safety | POP_L2 | Listing of Meal Data – Part 2 | | SAC

| Adverse Events |
| 22. | Safety | AE2 | Listing of Relationship Between System Organ Class and Verbatim Text – Part 1 | | SAC
| 23. | Safety | AE2 | Listing of Relationship Between System Organ Class and Verbatim Text – Part 2 | | SAC
| 24. | Safety | AE7 | Listing of Subject Numbers for Individual Adverse Events – Part 1 | | SAC
| 25. | Safety | AE7 | Listing of Subject Numbers for Individual Adverse Events – Part 2 | | SAC
| 26. | Safety | AE9CP | Listing of All Adverse Events – Part 1 | | SAC
| 27. | Safety | AE9CP | Listing of All Adverse Events – Part 2 | | SAC

| Serious and Other Significant Adverse Events |
| 28. | Safety | AE9CP | Listing of Study Drug Related Adverse Events – Part 1 | | SAC
| 29. | Safety | AE9CP | Listing of Study Drug Related Adverse Events – Part 2 | | SAC
| 30. | Safety | AE9CP | Listing of Serious Adverse Events (Fatal & Non-Fatal) – Part 1 | | SAC

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## ICH: Listings

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### Hepatobiliary (Liver)

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