Statistical Analysis Plan

Official Title of Study: Reporting and Analysis Plan for A Randomized, Double-Blind (Sponsor-unblinded), Placebo-Controlled, Adaptive Trial to Investigate the Antiviral Effect, Safety, Tolerability and Pharmacokinetics of GSK3640254 in HIV-1 Infected Treatment-Naïve Adults

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The GlaxoSmithKline group of companies 208132

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

Title	:	Reporting and Analysis Plan for A Randomized, Double-Blind (Sponsor-unblinded), Placebo-Controlled, Adaptive Trial to Investigate the Antiviral Effect, Safety, Tolerability and Pharmacokinetics of GSK3640254 in HIV-1 Infected Treatment-Naïve Adults
Compound Number	:	GSK3640254
Effective Date	:	06-FEB-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 208132.
- This RAP is intended to describe the safety, tolerability, pharmacokinetic, and antiviral 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 end of analyses to be included in the Clinical Study Report for Protocol.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 26/AUG/2019 Version: 208132/03).

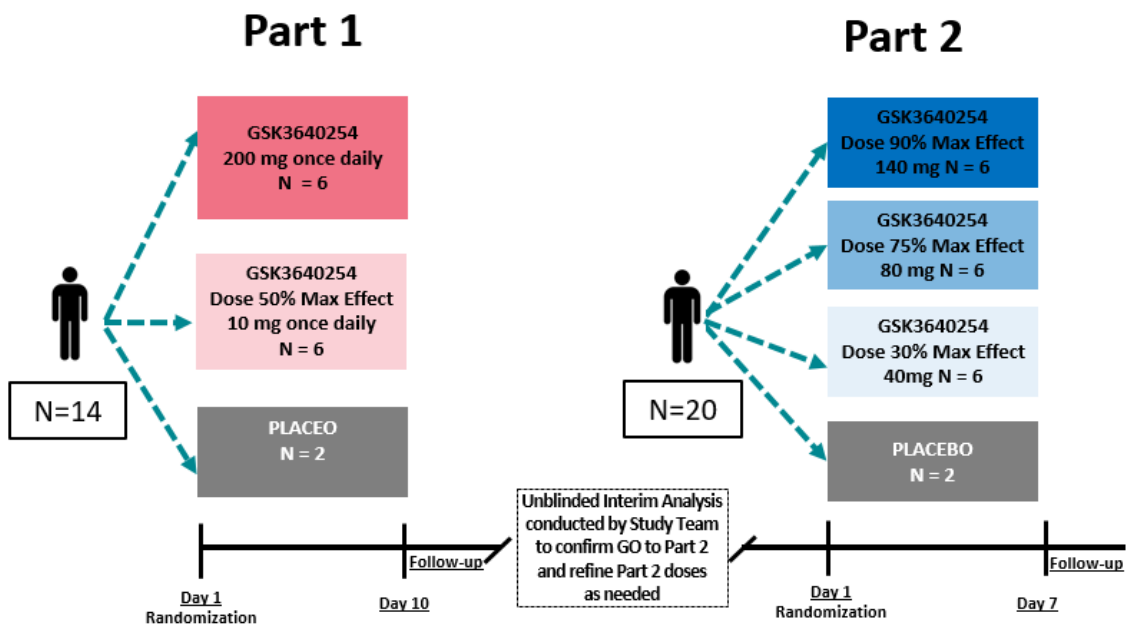
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To evaluate the antiviral activity of GSK3640254 in HIV-1 infected Treatment-Naïve(TN) participants during 10 days of monotherapy in Part 1 and during 7 days of monotherapy in Part 2	• Maximum change from baseline (Day 1) in plasma HIV-1 ribonucleic acid (RNA)
Secondary Objectives	**Secondary Endpoints**
• To assess the safety and tolerability of GSK3640254 when administered as monotherapy over 10 days in Part 1 and over 7 days in Part 2 in HIV-1 infected TN participants	• GSK3640254 safety and tolerability parameters: adverse events (AE) ; post-baseline values and changes over time of clinical laboratory evaluations, vital signs, and electrocardiogram (ECG) parameters
• To characterize the pharmacokinetics of GSK3640254 dosing for 10 days in Part 1 and for 7 days in Part 2 in HIV-1 infected patients	• GSK3640254 PK parameters at the following dose administration: Day 1: area under the plasma concentration time curve from zero to 24 (AUC[0-24]), maximum observed concentration (Cmax), time to maximum observed concentration (tmax), concentration at 24 hours post dose (C24), absorption lag time (tlag). Following repeat administration: Area under the curve (Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval at steady state (AUC[0-τ]), Cmax, tmax, pre-dose concentration (C0), concentration at end of dosing interval (Cτ), apparent terminal phase half-life (t1/2), and apparent oral clearance (CL/F), if data permit.
• To explore the relationship between GSK3640254 exposure and change in plasma HIV-1 RNA	• GSK3640254 repeat-dose PK parameters AUC(0-τ), Cmax, Cτ with maximum HIV-1 RNA change from baseline
• To estimate GSK3640254 accumulation following administration of GSK3640254 for 10 days in Part 1 and for 7 days in Part 2 in HIV-1 infected patients	• Accumulation: GSK3640254 PK accumulation ratios (R): repeat -dose AUC (0-τ), Cmax, and Cτ compared to Day 1 AUC (0-24), Cmax, C24, respectively

Objectives	Endpoints
• To examine dose proportionality of GSK3640254 PK parameters following dosing for 10 days in Part 1 and for 7 days in Part 2	• Relationship between Day 1 AUC (0-24), Cmax, C24, and repeat-dose AUC (0-τ), Cmax and Cτ and GSK3640254 dose levels
Exploratory Objectives	**Exploratory Endpoints**
• To assess the development of viral resistance (genotypic and phenotypic) over 10 days in Part 1 and over 7 days in Part 2 and correlate with viral response, if appropriate.	• Emergence of drug resistance mutations, if appropriate
• To assess attainment of steady state following administration of GSK3640254 for 10 days in Part 1 and for 7 days in Part 2 in HIV-1 infected patients.	• Steady State: pre-morning dose concentrations (C0) on Day 2 through Day 10 Cτ (Day 11) in Part 1 and on Day 2 through Day 7 Cτ (Day 8)
• To assess the immunologic effects of GSK3640254 when administered over 10 days in Part 1 and 7 days in Part 2 in HIV-1 infected adults	• Change from baseline in CD4+ T-cell count to Day 11 in Part 1 and to Day 8 in Part 2
• To explore the relationship between GSK3640254 exposure and safety or immunologic parameters, if appropriate	• GSK3640254 repeat-dose PK parameters: AUC (0-τ), Cmax, Cτ with Day 11 change from baseline in CD4+ cell count in Part 1 and with Day 8 change from baseline in CD4+ cell count in Part 2

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• This is a Phase 2a, global, multicentre, randomized, double-blind (Sponsor-unblinded), placebo-controlled, adaptive clinical trial to evaluate the antiviral effect, safety, tolerability and PK/ pharmacodynamics (PD) of GSK3640254 over 10 days in study Part 1 and over 7 days in study Part 2 in ART naïve HIV-1 infected adults, who are termed "participants" in the study. • All participants will be screened for eligibility before being randomized, preferably within 14 days, into a 10-day treatment period in Part 1 and into a 7-day treatment in Part 2. The 14-day screening period may be extended to 28 days in some cases to allow receipt of all screening results and/or to accommodate scheduling.
Dosing	• Part 1 will include approximately 14 randomized participants and will evaluate two active doses of GSK3640254, 200 mg once daily or 10 mg once daily, in cohorts of 6 participants each for 10 days. A cohort of 2 participants will be randomized to receive placebo for 10 days. • Part 2 will include approximately 20 randomized participants and will evaluate three active doses of GSK3640254, 140/80/40 mg once daily, in cohorts of 6 participants each for 7 days. A cohort of 2 participants will be randomized to receive placebo for 7 days.
Time & Events	• See Appendix 2: Schedule of Activities for additional details of activities
Treatment Assignment	• All participants will be centrally randomized using an Interactive Voice/Web Response System (IVRS/IWRS).
Interim Analysis	• An informal unblinded interim analysis of preliminary safety, tolerability, PK and antiviral activity occurred after participants of Part 1 completed their Day 12 visit.

2.4. Statistical Hypotheses / Statistical Analyses

Study 208132 is a proof of concept (POC), randomized double blind (Sponsor-unblinded) study to characterize antiviral activity, safety/tolerability, PK, and the relationship between PK and antiviral activity of GSK3640254 given once daily (QD), administered across a range of doses over 10 days in Part 1 and over 7 days in Part 2 in HIV-1 infected treatment naïve adults. No formal hypotheses will be tested.

3. PLANNED ANALYSES

3.1. Interim Analyses

An informal unblinded interim analysis of preliminary safety, tolerability, PK and antiviral activity occurred after participants of Part 1 complete their Day 12 visit. The analysis was accomplished following criterion defined in protocol Section 10.3.1.

Based on the results of the interim analysis, the dose levels for Part B were determined to be 140 mg, 80 mg, and 40 mg GSK3640254. Details of the Interim analysis displays are presented in Appendix 11: List of Data Displays. The main statistical results are included in the ICPSR [GlaxoSmithKline Document Number 2019N405148_01. Study 208132].

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) and database freeze (DBF) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Study Population
Enrolled	• All participants who passed screening and entered the study. • Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (Reserve, Not Used) are excluded from the Enrolled population as they did not enter the study.	• Study Population
Randomized	• All participants who were randomly assigned to treatment in the study. • This population will be based on the treatment the participant was randomized to.	• Study Population
Safety	• All randomized participants who received at least one dose of study treatment. • This population will be analysed based on the treatment the participant actually received.	• Study Population • Safety
Intent-To-Treat Exposed (ITT)	• All randomized participants who meet the study criteria and are enrolled into the study with documented evidence of having received at least one dose of treatment and at least one post-baseline HIV-1 RNA measurement. • This will be the primary population for the final efficacy analysis for all active treatment groups. • This population will be based on the treatment the participant was randomized to.	• Efficacy
Per-Protocol (PP)	• all participants who meet study criteria and are enrolled into the study with documented evidence of having received all doses and all post-baseline HIV-1 RNA measurement. • Protocol deviations that would exclude participants from the PP population are defined in Section 4.1 (Protocol Deviations) and Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population). • The PP set will not be analysed if no participants drop out of ITT population.	• Efficacy
Pharmacokinetic (PK)	• The PK Population will include all participants who receive GSK3640254 and undergo plasma PK sampling during the study. Participants for whom a plasma PK sample is obtained and assayed will be included in the listing of plasma GSK3640254 concentration-time data. Results from samples collected from a participant with emesis occurring within 2 hours of the dose will not be considered as evaluable.	• PK
Pharmacokinetic/ Pharmacodynamic (PK/PD)	• Participants who meet criteria for Per-Protocol and Pharmacokinetic Population analysis sets and who undergo PD sampling during the study.	• Pharmacokinetic/ Pharmacodynamic

Refer to Appendix 11: 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, patient management or patient assessment) will be summarised and listed.

Important deviations which result in exclusion from the analysis population will also be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population).

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP) [04 Nov 2019 Version 2].

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

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Part 1 Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TLF
D1	GSK3640254 10 mg	GSK 10 mg	1
D2	GSK3640254 200 mg	GSK 200 mg	2
P	Placebo	Part 1 Placebo	3

Part 2 Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TLF
D3	GSK3640254 Dose 3	GSK 40 mg	4
D4	GSK3640254 Dose 4	GSK 80 mg	5
D5	GSK3640254 Dose 5	GSK 140 mg	6
P	Placebo	Part 2 Placebo	7

Data collected from protocol planned visits (ex. Lab, ECG, vital signs and PK etc.) will be analysed and reported separately for each part of the study, unless otherwise specified. Data collected from unplanned visits (ex. Adverse events, concomitant medications etc) or collected only once in study i.e. study population(ex. Demography , medical history etc.) will be reported two parts in single output. Unless otherwise indicated (in statistical models), randomized placebo participants from Parts 1 and 2 will always be treated as two groups for summaries tables. Besides, overall column will be added in all summary output.

5.2. Baseline Definitions

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

Parameter	Study Assessments Considered as Baseline		Baseline Used in Data Display
	Screening	Day 1 (Pre-Dose)	
Efficacy			
All efficacy endpoints	X	X	Day 1
Safety			
All laboratory, vital signs and ECG measurement endpoints	X	X	Day 1

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

5.3. Multicentre Studies

Data will be summarised for all centres combined.

5.4. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
13.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
13.2	Appendix 2: Schedule of Activities
13.3	Appendix 3: Assessment Windows
13.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
13.4.1	Appendix 5: Data Display Standards & Handling Conventions
13.5.1	Appendix 6: Derived and Transformed Data
13.7	Appendix 7: Reporting Standards for Missing Data
13.8	Appendix 8: Values of Potential Clinical Importance
13.9	Appendix 9: Biomarker Analyses
13.10	Appendix 10: Abbreviations & Trade Marks
13.11	Appendix 11: List of Data Displays
13.12	Appendix 12: Example Mock Shells for Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the ITT population, unless otherwise specified. The study population analysis will include part 1 and part 2 together in one display (Part 1 placebo and Part 2 placebo displayed separately).

Study population analyses including analyses of participant's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, medical history and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 11: List of Data Displays.

6.2. Display Details

6.2.1. Subject Disposition

The disposition table will consist of all intent-to-treat participants

The number and percentage of participants who failed screening and were, therefore, not enrolled into the study, overall and by reason, will be summarized. A listing of the screen failure record for all participants who failed screening, including the reasons for screen failure will be presented.

Reasons for study treatment discontinuation will be summarized by treatment group and overall. A by-subject listing of reasons for study withdrawal, a by-subject listing of reasons for study treatment discontinuation, and a by-subject listing of planned and actual treatment received will be produced.

The number and percentage of participants at each visit will be summarized for each treatment group and overall.

6.2.2. Protocol Deviations

Please refer to Section 4.1 for details.

Inclusion and exclusion criteria deviations will be listed.

6.2.3. Populations analysed

The number of participants who were enrolled into the study, and the number of participants within each analysis population (screened, enrolled, randomized, ITT, Per Protocol, Safety, PK and PK/PD) will be summarized for each treatment group and overall.

The number and percentage of participants will be summarized by centre for each treatment group and overall.

Participants excluded from any population, including participants excluded from the Per Protocol population, will be listed.

6.2.4. Demography

The demographic and baseline characteristics age, sex, race, ethnicity, height, weight, BMI, and baseline CDC HIV-1 classification will be summarized by treatment group and overall for the safety population. The count, mean, standard deviation, median, minimum, and maximum value will be computed for age, BMI, height, and weight. A separate summary will be provided for age ranges.

A by-subject listing of demographic and baseline characteristics will also be produced.

Summaries of race and racial combinations will be produced for each treatment group and overall. A listing of race by subject will also be produced.

6.2.5. Medical Conditions and Medications

6.2.5.1. Medical Conditions

The number and percentage of participants with each past and current medical condition will be summarized for each treatment group and overall. Past conditions are those reported as ‘past’ and current conditions are those reported as ‘current’ at screening. Past and current conditions will be reported separately. Medical conditions will be summarised by category according to eCRF. By-subject listings of past and current medical conditions will also be produced.

A by-subject listing for HIV associated conditions will be produced.

6.2.5.2. Medications

For reporting purposes, medications will be classified as prior, concomitant using the associated start and stop dates recorded in the eCRF and relative to the first and last dose dates of investigational product (IP) (see Appendix 4). Medications will be coded using the GSK Drug coding dictionary (current version at the time of DBF).

Concomitant and prior medications will be summarised by GSK-Drug Anatomical Therapeutic Chemical (ATC) classification level 1 (body system) and ingredient. Drugs that are composed of a combination of ingredients will be displayed according to the ATC classifications of the ingredients, not of the combination.

The relationship between ATC level 1, ingredients and verbatim text for all medications in the study will be listed.

6.2.6. Exposure and Treatment Compliance

The complete dosing experience will be listed for all participants. The total duration of exposure (number of days on study drug), average daily dose, and cumulative dose will be summarized by treatment group.

For participants who completed the 10-day treatment period in Part 1 and 7-day treatment period in Part 2 of the study, the expected number of doses is 10 for Part 1 and 7 for Part 2. For participants who permanently discontinued the study treatment and/or withdrew from the study, the expected number of doses during the treatment period will be calculated using "Days on study drug" where "Days on study drug" is Last Dose Date – First Dose Date +1.

A summary of study medication compliance will be produced by treatment group: >0-<100%, 100%, >100%. The compliance will be calculated for the whole study treatment period as the percentage of cumulative dose [100*(actual cumulative dose) / (expected cumulative dose for the participant's treatment duration)].

For participants who completed the 10-day treatment period in Part 1 or 7-day treatment period in Part 2, the expected cumulative dose of GSK3640254 taken during the treatment period would be planned dose*10 days or planned dose*7 days. E.g. For participants who received 200 mg GSK3640254 in Part 1, the expected cumulative dose is 2,000 mg GSK3640254 (the 200 mg of IP is comprised of two 100 mg capsules of GSK3640254 administered daily over the 10-day treatment period).

For participants who permanently discontinued study treatment or withdrew early from the study, the expected cumulative dose of GSK3640254 taken during the treatment period would be the planned dose*(Last Dose Date – First Dose Date + 1).

The actual cumulative dose of GSK3640254 for all participants is the sum of all doses, in mg, of study drug consumed for the duration of the study. (Approach for handling missing treatment stopping dates is discussed in Section 13.7.2)

7. EFFICACY ANALYSES

Efficacy data will be listed and summarized according to GSK reporting standards, where applicable. Unless specified, efficacy tables will be reported separately for Part 1 and Part 2. Listings will be paginated by part, sorted by participant, day, and time, noting treatment; Descriptive statistics (n, mean, median, SD, min and max) will be calculated for continuous data and n and percentages will be calculated for categorical data.

Both the ITT and PP populations will be used for all efficacy analyses when there are participants excluded from the PP population. If there are no exclusions (i.e., if the PP and ITT population do not differ), then only the ITT population will be used for all efficacy analyses.

For summary tables, Plasma HIV-1 RNA values below lower limit of detection (LLOD = 50 copies/mL), will be imputed to 49 copies/mL. Otherwise, for listings, it will be listed as collected.

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

- Change from baseline to the nadir (maximum change from baseline) in Plasma HIV-1 RNA
- Change from baseline to Visit 6 (Day 11 in Part 1 and Day 8 in Part 2) in Plasma HIV-1 RNA

7.1.2. Summary Measure

- Mean rate of maximum change from baseline to the nadir
- Mean rate of change from baseline to Visit 6 (Day 11 in Part 1 and Day 8 in Part 2)

7.1.3. Statistical Analyses / Methods

Statistical models will be fitted separately for Part 1 and Part 2.

Plasma HIV-1 RNA maximum change from baseline (on original scale and log10 scale) and time to nadir will be calculated for each subject and summarized by treatment for each part.

Details of the planned displays are provided in Appendix 11: 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 summarised using descriptive statistics, graphically presented (where appropriate) and listed.

7.1.3.1. Statistical Methodology Specification

Endpoint / Variables
• Change from baseline to the nadir in Plasma HIV-1 RNA (on log10 scale) • Change from baseline to Visit 6 (Day 11 in Part 1 and Day 8 in Part 2) in Plasma HIV-1 RNA (on log10 scale)
Model Specification
• Plasma HIV-1 RNA change from baseline (on log10 scale) to nadir and change from baseline to Visit 6 (Day 11 in Part 1 or Day 8 in Part 2) (on log10 scale) will be fitted in a mixed-effects linear model by treatment, with baseline plasma HIV-1 RNA (on log10 scale) and visit fitted as fixed effects and subject fitted as a random effect.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation

• Statistical analysis for maximum change from baseline to the nadir and change from baseline will be presented in tabular format. The linear model will be used to estimate slope, intercept and a 90% CI of the slope. The model will be fitted for Part 1 and Part 2 data respectively.
Example SAS Code:
proc mixed data=dataset;
class dose visit subjid;
model chgRNA = baseRNA visit dose;
random subjid / type=un solution;
run;

Sensitivity and Supportive Analyses
Both ITT and PP population will be used for the above analyses if PP population is differed from ITT population.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

- Plasma HIV-1 RNA and log10 Plasma HIV-1 RNA on each assessment visit
- Change from baseline of plasma HIV-1 RNA and log10 plasma HIV-1 RNA on each assessment visit
- Proportion of participants with plasma HIV-1 RNA <400 copies/mL and < 50 copies/mL
- Proportion of participants with plasma HIV-1 RNA change from baseline > 1.5 log10 copies/mL decrease

7.2.2. Summary Measure

Descriptive summaries will include n, mean, standard deviation (SD), median, minimum, and maximum for continuous variables, whereas n and percent will be used as summary statistics for categorical variables.

7.2.3. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

Plasma HIV-1 RNA will be listed by treatment, subject, and assessment visit and summarized by treatment and assessment visit along with change from baseline.

A plot of mean and median log10 plasma HIV-1 RNA and change from baseline data will be generated by treatment and assessment visit.

7.3. Exploratory Efficacy Analyses

7.3.1. Immunology

7.3.1.1. Endpoint / Variables

- CD4+ and CD8+ T-cell count at each assessment visit along with change from baseline

7.3.1.2. Summary Measure

Descriptive summaries will include n, mean, standard deviation (SD), median, minimum, and maximum for continuous variables, whereas n and percent will be used as summary statistics for categorical variables.

In addition, mean rate of change for CD4+ T-cell count change from baseline to Visit 6 (Day 11 in Part 1 and Day 8 in Part 2) will be calculated based on the following linear mixed model.

7.3.1.3. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.3.1will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

7.3.1.4. Statistical Methodology Specification

Endpoint / Variables
• Change from baseline in CD4+ T-cell count to Visit 6 (Day 11 in Part 1 and Day 8 in Part 2) (on log10 scale)
Model Specification
• Change from baseline to Visit 6 (Day 11 in Part or Day 8 in Part 2) in CD4+ T-cell count (on log10 scale) will be fitted in a mixed-effects linear model by treatment, with baseline CD4+ (on log10 scale) and VISIT fitted as fixed effects and subject fitted as a random effect.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation

• Statistical analysis for change from baseline will be presented in tabular format. The linear model will be used to estimate slope, intercept and a 90% CI of the slope. The model will be fitted for Part 1 and Part 2 data respectively.
Example SAS Code:
proc mixed data=dataset
class dose visit subjid;
model chgCD4 = baseCD4 visit dose;
random subjid / type=un solution;
run;

Sensitivity and Supportive Analyses
Both ITT and PP population will be used for the above analyses if PP population is differed from ITT population.

7.3.2. Clinical Virology

If virology data is available and up to analysis standards by DBF, viral genotypic and phenotypic data will be listed by treatment group, subject, and assessment day as in Appendix 11: List of Data Displays and will be based on GSK data standards and statistical principles. If virology data is not available by DBF, a separate virology analysis report will be generated.

8. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified. Safety data will be presented in tabular format and summarized descriptively according to GSK's Integrated Data Standards Library standards and data will be in Clinical Data Interchange Standards Consortium (CDISC) format. No formal statistical analysis of the safety data will be conducted.

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 11: List of Data Displays. The AE analysis will include part 1 and part 2 in one display (Part 1 placebo and Part 2 placebo displayed separately) for summary tables and listings.

The following summaries will be provided:

- Adverse events overview
- All adverse events by SOC and PT and all adverse events by maximum grade and SOC and PT
- Drug related adverse events by SOC and PT and drug related adverse events by maximum grade and SOC and PT
- Serious Adverse Events by SOC and PT (Number of Participants and Occurrences)
- Adverse events leading to withdrawal from study/permanent discontinuation of study treatment
- Common (>= 5%) adverse events by overall frequency
- Common (>= 5%) non-serious adverse events (Number of Subjects and Occurrences)

The following listings will be provided:

- All adverse events
- Subject numbers for individual AEs
- Serious adverse events
- Drug related adverse events
- Adverse events leading to withdrawal from study/permanent discontinuation of study treatment
- Fatal serious adverse events
- Non-fatal serious adverse events

8.2. Adverse Events of Special Interest Analyses

At the end of the study, all Cardiac System Organ Class / Preferred Terms, seizure, and syncope (regardless of Grade/Relationship), will be summarized by treatment. A listing will also be provided accordingly.

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 preferred terms 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 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 (include 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"

8.3. Clinical Laboratory Analyses

Unless specified, clinical laboratory tables will be reported separately for Part 1 and Part 2. Corresponding listings will be paginated by part, sorted by participant, day, and time, noting treatment.

Haematology and clinical chemistry parameters collected are listed below.

Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters			
Haematology	Platelet Count Red blood cells (RBC) Count Haemoglobin Haematocrit	RBC Indices: Mean corpuscular volume (MCV) Mean corpuscular haemoglobin (MCH) %Reticulocytes	White blood cells (WBC) count with Differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils	
Clinical Chemistry[1]	BUN	Potassium	Aspartate Aminotransferase (AST)/ Serum Glutamic-Oxaloacetic Transaminase (SGOT)	Total and direct bilirubin
	Amylase and Lipase	Sodium, Bicarbonate, and Chloride	Alanine Aminotransferase (ALT)/ Serum Glutamic-Pyruvic Transaminase (SGPT)	Total Protein
	Glucose (nonfasting)	Calcium, Magnesium, and Phosphate	Alkaline phosphatase	Fasting Lipid Panel (Cholesterol, Triglycerides, High density lipoprotein [HDL], low density lipoprotein [LDL])
Routine Urinalysis	• Specific gravity • pH, glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase by dipstick • Microscopic examination (if blood or protein is abnormal)			
Other Screening Tests	• Follicle-stimulating hormone and estradiol (if needed to determine women of non-childbearing potential) • Urine human chorionic gonadotropin (hCG) pregnancy test (as needed)[2] • Serology (HIV antibody, hepatitis B surface antigen [HBsAg], and hepatitis C virus antibody [HCVAb], with reflex to HCV RNA if positive). • PCR (HIV-1 diagnostic PCR)			

Laboratory Assessments	Parameters
	• Alcohol and drug screen (to include at minimum: amphetamines, barbiturates, cocaine, opiates, cannabinoids and benzodiazepines) • All study-required laboratory assessments will be performed by a central laboratory The results of each test may be entered into the CRF.

NOTES :
1. Details of liver chemistry stopping criteria and required actions and follow-up assessments after liver stopping or monitoring event are given in Section 8.1 and Appendix 7 All events of ALT ≥3 × upper limit of normal (ULN) and bilirubin ≥2 × ULN (>35% direct bilirubin) or ALT ≥3 × ULN and international normalized ratio (INR) >1.5, if INR measured, which may indicate severe liver injury (possible Hy's Law), must be reported as an SAE (excluding studies of hepatic impairment or cirrhosis).
2. Local urine testing will be standard for the protocol unless serum testing is required by local regulation or IRB/IEC.

Laboratory values, treatment emergent toxicities, and change from baseline for haematology, clinical chemistry, and liver function parameters will be summarized by visit and by treatment group. Laboratory values for haematology, clinical chemistry, liver function, and urinalysis will also be listed by subject. In addition, the number and percentage of participants with on-treatment laboratory abnormalities worsened from baseline by maximum grade will be reported for haematology, clinical chemistry. The participants with laboratory values of potential clinical importance will be summarised and listed (potential clinical importance criteria are specified in Section 13.8). The details of the planned displays are in Appendix 11: List of Data Displays.

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs, vital signs and Hepatobiliary will be based on GSK Core Data Standards, unless otherwise specified. Similar as clinical laboratory analysis, tables for other safety analyses will be reported separately for Part 1 and Part 2. Corresponding listings will be paginated by part, sorted by participant, day, and time, noting treatment. The details of the planned displays are presented in Appendix 11: List of Data Displays.

8.4.1. Electrocardiograms

ECG is collected triplicates at certain visits and for those visits average values will be reported in summary tables and triplicate readings will be listed in listings. A summary of the number and percentage of participants with ECG findings will be displayed by treatment. For abnormal ECG findings, the most recent one will be used if there's multiple records in the same visit. Additionally, summary statistics of change from baseline in ECG values will be presented. Maximum QTc values and maximum increase in QTc values post-baseline relate to baseline will be summarized by category. Mean (95% CI) change from baseline in QTcB-interval and QTcF interval will be plotted by time and treatment. All ECG Values for Participants with a Value of Potential Clinical Importance will be listed (potential clinical importance criteria are specified in Appendix

8: Values of Potential Clinical Importance). QTc interval data for subjects with QTc measurement > 500msec or increase from baseline > 60msec will also be listed.

8.4.2. Vital Signs

Vital sign parameter (systolic blood pressure, diastolic blood pressure, pulse rate and heart rate) change from baseline at every assessed time point will be summarized (n, mean, standard deviation, median, minimum, and maximum). The number of subjects with worst case vital sign results relative to normal range criteria which are post-baseline relative to baseline will be summarized by test and category. A by-subject listing of vital signs for all participants with potential clinical importance will be produced. Potential clinical importance criteria are specified in Appendix 8: Values of Potential Clinical Importance.

8.4.3. Columbia Suicide Severity Rating Scale (C-SSRS)

Summaries of Columbia Suicide Severity Rating Scale (CSSRS) will be produce for each treatment group in Part 1 and Part 2.

8.4.4. Combination anti-retroviral therapy (cART)

In Part 2 of the study, participant must be willing and able to start cART on Study Day 8. Summary and listing of cART medication will be produced accordingly.

9. PHARMACOKINETIC ANALYSES

Unless specified, pharmacokinetic analyses tables will be reported separately for Part 1 and Part 2. Listings will be paginated by part, sorted by participant, day, time, and noting treatment.

9.1. Primary Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

9.1.1.1. Drug Concentration Measures

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

9.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin Version 6.1 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.

Parameter	Parameter Description
Visit 1 (Day 1)	
AUC(0-24)	Area under the concentration-time curve from time zero to the concentration at 24-hour post dose. AUC will 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.
C24	Concentration at 24 hours post dose
tmax	Time to reach Cmax, determined directly from the concentration-time data.
tlag	absorption lag time
Visit 5 (Day 8, 9 or 10 for Part 1 and Day 7 for Part 2)	
AUC(0-τ)	Area under the concentration-time curve over the dosing interval. AUC will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
C0	Concentration at pre-dose
Cτ	Concentration at the end of the dosing interval
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
λz	The slope of the apparent terminal phase
t½	Apparent terminal half-life will be calculated as: t½ = ln2 / λz
CL/F	Apparent oral clearance will be calculated as: CL/F = Dose / AUC(0-τ)

Parameter	Parameter Description
R_AUC	The accumulation ratio of AUC will be calculated as: will be calculated as: R_AUC = AUC(0-τ) Visit 5 / AUC(0-24) Visit 1
R_Cmax	The accumulation ratio of Cmax will be calculated as: will be calculated as: R_Cmax = Cmax Visit 5 / Cmax Visit 1
R_Cτ	The accumulation ratio of Cτ will be calculated as: will be calculated as: R_Cτ = Cτ Visit 5 / C24 Visit 1

NOTES:

- Additional parameters may be included as required.

9.1.2. Summary Measure

For each of these parameters, except tmax, tmin, and tlag, the following summary statistics will be calculated for each active treatment group: median, maximum, minimum, arithmetic mean, standard deviation, coefficient of variation on arithmetic mean, geometric mean, coefficient of variation on geometric mean, 95% confidence interval for the geometric mean and standard deviation of logarithmically transformed data. For tmax, tmin, and tlag, median, maximum, minimum, arithmetic mean and standard deviation will be calculated.

9.1.3. Population of Interest

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

9.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK Data Standards and statistical principles.

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

9.1.4.1. Dose proportionality

9.1.4.1.1. Statistical Methodology Specification

The following pharmacokinetic statistical analyses will only be performed if sufficient data is available (i.e. if participants have well defined plasma profiles). The statistical model will be fitted for Part 1 and Part 2 combined data.

Endpoint / Variables
• Plasma primary PK endpoints on log10 scale include **Day 1**: AUC(0-24), Cmax and C24; **Day 8/9/10 in Part 1 and Day 7 in Part 2**: AUC(0-τ) and Cmax and Cτ.
Model Specification
• To assess the dose proportionality of plasma GSK3640254, PK parameters on log10 scale from Day1 [AUC(0-24) , Cmax and C24] and Day 8/9/10 for Part 1 or Day 7 for Part 2 [AUC(0-τ), Cmax and Cτ] will be assessed using a power model if multiple dose levels are assessed. The power model will be fitted by restricted maximum likelihood (REML) using SAS Proc Mixed. A fixed effects power model will be used. The mean slope will be estimated from the power model with the corresponding 90% CI, separately for Day 1 and Day 8/9/10 for Part 1 or Day 7 for Part 2. • Additionally, if power model does not show dose proportionality, dose proportionality may be assessed by pair-wise analysis of variance(ANOVA) using the SAS Mixed model procedure. A reference dose of 10 mg will be used and the other doses would be treated as test dose. PK parameters will be normalized to the reference dose and then log-transformed prior to the analysis. Point estimates and 90% confidence intervals for AUC and Cmax will be reported to 4 decimal places with no rounding. An example of SAS code is also included here for the ANOVA approach.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data. • The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used. • Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure.
Model Results Presentation

Statistical analysis for dose proportionality from Day 1 [AUC(0-24) , Cmax and C24] and Day 8/9/10 in Part 1 and Day 7 in Part 2 [AUC(0-τ), Cmax and Cτ] will be presented in tabular format, respectively. The linear model will be used to provide a slope, intercept and a 90% CI of the slope.
Example SAS Code for power model:
PROC MIXED;
MODEL LNPKPARM=LNDOSE /SOLUTION CL ALPHA=0.1;
ODS OUTPUT SOLUTIONF=SOLUTION1(RENAME=(ESTIMATE=EST STDERR=SE));
RUN;
 	
Example SAS Code for ANOVA model:
ODS output solutionf=stat;
Proc Mixed;
class treatment; /* treatments are different dose groups */
model logdnPKvar = treatment/ddfm=kr;
lsmeans treatment; /* assuming one ref and four test treatments */
estimate 'test1 vs ref' treatment -1 1 0 0 0 /cl alpha=0.1;
estimate 'test2 vs ref' treatment -1 0 1 0 0/cl alpha=0.1;
run;

9.1.4.2. Steady State

9.1.4.2.1. Statistical Methodology Specification

The following pharmacokinetic statistical analyses will only be performed if sufficient data is available (i.e. if participants have well defined plasma profiles). Statistical model will be fitted for Part 1 and Part 2 respectively.

Endpoint / Variables
• Plasma primary PK endpoints include Visit 2 to visit 6 Pre-dose concentrations C0 and visit 5 $C\tau$
Model Specification
• To assess the achievement of steady state with the pre-dose concentrations between Visit 2~6 for each treatment. A linear mixed model using Day as fixed effects and subject as a random effect on the ln-transformed pre-dose values will be performed evaluating whether steady state was achieved using Helmert transformation approach. The comparison will begin with Visit 2~6 then Visit 3~6, etc. The estimate and 90% CI of the slope for the day will be presented for the comparison(s).
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data. • Statistical analysis of steady state will be analyze using Helmert transformation approach.
Model Results Presentation
Code will be separated for Part 1 and Part 2 due to the different study design of the two parts. Example SAS Code for Part 1: PROC MIXED; BY TREATMENT; WHERE (DAY IN (2,3,4,5,6,7,8,9,10,11)); CLASS SUBJECT; MODEL LOGCTAU = DAY/CL ALPHA=0.1 SOLUTION; RANDOM INTERCEPT/SUBJECT=SUBJECT TYPE=UN; RUN;

10. PHARMACODYNAMIC ANALYSES

10.1. Primary Pharmacodynamic Analyses

Relationships between dose and PD measures (maximum change (in Day 1 to Day 8) in log10 plasma HIV-1 RNA from baseline) will be explored with an Emax and linear models. Part 1 and Part 2 doses combined in the model fitting. Model selection will be based on Akaike Information Criteria (AIC) value, where model with the lowest AIC value will be considered the best model.

10.1.1. Endpoint / Variables

- Log10 Maximum change from baseline to Day 8 and change from baseline to Day 8 in plasma HIV-1 RNA

10.1.2. Summary Measure

- Parameter estimates for Emax, ED50 and variance along with their standard error, and 95% CI

10.1.3. Population of Interest

The primary pharmacodynamics analyses will be based on the PP population, unless otherwise specified.

10.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 10.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

Descriptive Summary tables are separated for Part 1 and Part 2 while the summary table for statistical modelling results are combined for two Parts.

In endpoint descriptive summary tables, the maximum change from baseline includes all visits while in model fitting it only includes visits from baseline to Day 8 in HIV-1 RNA for both parts.

10.1.4.1. Statistical Methodology Specification

Model Specification

- To model the dose-response relationship, a frequentist simplified Emax model is planned. This model assumes the following form:

$$\Delta VL = \frac{(Emax)}{1 + (\frac{ED50}{Dose})} + \epsilon$$

Where:

- ΔVL is the change from baseline, defined as Log10 Maximum change from baseline to Day 8 and change from baseline to Day 8 (both parts) in plasma HIV-1 RNA on log10 scale.
- Emax is the maximum response
- ED50 is the dose that attains the 50% of the maximal effect ε is a random error assumed to be normally distributed with mean zero and constant variance (σ^2)

The observed maximum change from baseline in Plasma HIV-1 RNA will be used as the response variable in the Emax model.

- The derived data from this Emax model (estimates Emax, ED50 and Variance along with their standard error, and 95% CI) will be tabulated and a dose-response curve will also be produced.
- If problems are encountered Emax model or if the Emax shape is a poor fit for the data and a linear relationship looks plausible across the dose range, then a linear model will be considered of the form:

$$\Delta VL = \alpha * Dose + \epsilon$$

Model Checking & Diagnostics

- Model assumptions will be applied, but appropriate adjustments may be made based on the data.

Model Results Presentation

- The statistical model will use doses from both parts for model fitting.
- The derived data from this Emax model (estimates Emax, ED50 and Variance along with their standard error, and 95% CI) will be tabulated and an exposure-response curve will also be produced.

Example SAS Code:

```
PROC NLMIXED;
PARMS E0 = EST EMAX = EST ED50 = EST S2E = SE;
BOUNDS E0>0 EMAX>0 ED50>0 S2E>0;
PRED = E0 +(EMAX-E0)/(1+(ED50/DOSE));
MODEL RESPONSE ~ NORMAL (PRED, S2E);
PREDICT PRED OUT=DOSE;
RUN;
```

11. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

11.1. PK/PD Analyses of HIV-1 RNA

11.1.1. Statistical Analyses / Methods

Scatter plots of plasma HIV-1 RNA change from baseline to Day 8 vs. plasma GSK3640254 PK parameters (AUC(0-τ), Cmax and Cτ) will be generated separately for each active treatment. The Pearson's correlations between plasma HIV-1 RNA change from baseline to Day 8 and plasma GSK3640254 PK parameters will be summarized by treatment and overall.

Relationships between various PK parameters (AUC(0-τ), Cmax and Cτ) and PD measures (Log10 maximum change from baseline to Day 8 in plasma RNA and Log10 change from baseline to Day 8 in plasma HIV-1 RNA) will be explored with various Emax models. Model selection will be based on Akaike Information Criteria (AIC) value, where model with the lowest AIC value will be considered the best model.

11.1.2. Population of Interest

The primary pharmacodynamics analyses will be based on the PK/PD population, unless otherwise specified. Part 1 Day 9~11 HIV RNA are excluded to fulfil the same dosing days and be used in one statistical model.

11.1.3. Statistical Methodology Specification

Endpoint / Variables
• Log10 maximum change from baseline to day 8 in plasma RNA, Log10 change from baseline to Day 8 in plasma HIV-1 RNA relative to the PK parameters (AUC(0-τ), Cmax and Cτ) Day 8/9/10 from Part 1 and Day 7 from Part 2
Model Specification
• To model the exposure-response relationship, a frequentist three-parameter Emax model is planned. This model assumes the following form $$\Delta VL = E0 + \frac{Emax}{1 + (\frac{EC50}{PK})} + \epsilon$$ Where: • ΔVL is the log10 maximum viral load change from baseline to day 8 or change to Day 8 in plasma HIV-1 RNA • E0 is the baseline response • Emax is the maximum response

- EC50 is the corresponding exposure/PK parameter value that attains the 50% of the maximal effect
- PK is the PK parameter
- ε is a random error assumed to be normally distributed with mean zero and constant variance (σ^2)
- If problems are encountered Emax model or if the Emax shape is a poor fit for the data and a linear relationship looks plausible across the dose range, then a linear model will be considered of the form:

$$\Delta VL = \alpha * PK + \epsilon$$

Model Checking & Diagnostics

- Model assumptions will be applied, but appropriate adjustments may be made based on the data.

Model Results Presentation

- The derived data from this Emax model (estimates E0, Emax, EC50 and Variance along with their standard error, and 95% CI) will be tabulated and an exposure-response curve will also be produced. If E0 turns out as not significant, the reduced Emax model without baseline E0 will be selected as the final model.

Example SAS Code:

```
PROC NLMIXED;
PARMS E0 = EST EMAX = EST EC50 = EST S2E = SE;
BOUNDS E0>0 EMAX>0 EC50>0 S2E>0;
PRED = E0 +(EMAX-E0)/(1+(EC50/PARAM));
MODEL RESPONSE ~ NORMAL (PRED, S2E);
PREDICT PRED OUT=DOSE;
RUN;
```

11.2. Concentration-QTcF Analyses

For each ECG assessment, the individual subject's QTcF change from baseline will be calculated and will be merged with time-matched PK concentration values, when available. QTcF change from baseline (y-axis) to Day 8 for all doses in Part 1 and Part 2 will be plotted against the PK concentration data (x-axis) with a linear regression overlay. The placebo arms from Part 1 and Part 2 would be combined as one group (with PK concentration value as 0) and included in the figure.

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13. APPENDICES

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

13.1.1. Exclusions from Per Protocol Population

A participant meeting any of the following criteria will be excluded from the Per Protocol population:

Number	Exclusion Description
1	Participant who deviated from any inclusion/exclusion criteria
2	Participant who did not receive correct treatment which the participant was randomized to
3	Participant who have missed at least one dose of GSK3640254
4	Participant who did not have Visit 6 HIV-RNA measurement
5	Not withdrawn after meeting the following stopping criteria • Liver chemistry stopping criteria • QTc stopping criteria • Stopping criteria based on Laboratory Abnormality and Adverse Event
6	Informed Consent • Study-specific assessments conducted prior to obtaining proper consent.
7	Study visits performed out of window • Consecutive participant study visits performed out of window • Multiple study visits performed out of window by various Participants (Trending)
8	Incorrect study treatment • Unresolved IP accountability discrepancy • IP storage guidelines not followed • IP incorrectly administered • IP accountability not done
9	Lack of PI oversight
10	Participant Used prohibited medication
11	Participant became pregnant while on study
12	Safety assessments not performed when clinically relevant • Central safety lab samples not collected and/or not properly sent to Q2 when clinically relevant

13.2. Appendix 2: Schedule of Activities

Study Part 1:

Procedure[1]	Treatment Period Day 1 – Day 10										Post-Dosing Follow Up Period Day 11 – 17			Final Follow-up Day 18-24
	Day 1	Day 2	Day 3, 4 Choose one day for the Clinic Visit 3. The other day will be a virtual event.		Day 5, 6, 7 Choose one day for the Clinic Visit 4. The other days will be virtual events.			Day 8, 9, 10 Choose one day for the Clinic Visit 5. The other days will be virtual events.			Day 11	Day 12	Day 13, 14, 15, 16 or 17	Day 18, 19, 20, 21, 22, 23 or 24
	Clinic Visit 1	Clinic Visit 2	Clinic Visit 3	Virtual	Clinic Visit 4	Virtual	Virtual	Clinic Visit 5	Virtual	Virtual	Clinic Visit 6	Clinic Visit 7	Clinic Visit 8	Clinic Visit 9
Clinical Assessments														
Outpatient Visit[2]	X	X	X		X			X			X	X	X	X
Video/Phone Call				X		X	X		X	X				
Verify Inclusion/ Exclusion Criteria	X													
Medical/medication/drug/alcohol history	X													
Prior Anti-retroviral (ARV) Check	X													
CDC Classification	X													X

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Procedure[1]	Treatment Period Day 1 – Day 10										Post-Dosing Follow Up Period Day 11 – 17			Final Follow-up Day 18-24
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6, 7** Choose one day for the Clinic Visit 4. The other days will be virtual events.			**Day 8, 9, 10** Choose one day for the Clinic Visit 5. The other days will be virtual events.			**Day 11**	**Day 12**	**Day 13, 14, 15, 16 or 17**	**Day 18, 19, 20, 21, 22, 23 or 24**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Virtual**	**Clinic Visit 5**	**Virtual**	**Virtual**	**Clinic Visit 6**	**Clinic Visit 7**	**Clinic Visit 8**	**Clinic Visit 9**
HIV-associated conditions assessments[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse event (AE)/SAE assessment[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication review[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight, BMI and Physical exam[4]	X													
Vital Signs	X	X	X					X						X
C-SSRS Administration (*Since Last Visit* form)											X			

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Procedure[1]	Treatment Period Day 1 – Day 10										Post-Dosing Follow Up Period Day 11 – 17			Final Follow-up Day 18-24
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6, 7** Choose one day for the Clinic Visit 4. The other days will be virtual events.			**Day 8, 9, 10** Choose one day for the Clinic Visit 5. The other days will be virtual events.			**Day 11**	**Day 12**	**Day 13, 14, 15, 16 or 17**	**Day 18, 19, 20, 21, 22, 23 or 24**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Virtual**	**Clinic Visit 5**	**Virtual**	**Virtual**	**Clinic Visit 6**	**Clinic Visit 7**	**Clinic Visit 8**	**Clinic Visit 9**
Clinical Procedures														
12-lead ECG (triplicate reading, pre-dose; single readings at PK draws 2hr, 4hr, and 6hr)	X													
12-lead ECG (single reading, pre-dose at Visits 2 and 3)		X	X											X
12-lead ECG (single reading pre-dose and at PK draws 2hr, 4hr, and 6hr)								X						
Pharmacogenetics (PGX) Collection (if consented)	X													

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Procedure[1]	Treatment Period Day 1 – Day 10										Post-Dosing Follow Up Period Day 11 – 17			Final Follow-up Day 18-24
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6, 7** Choose one day for the Clinic Visit 4. The other days will be virtual events.			**Day 8, 9, 10** Choose one day for the Clinic Visit 5. The other days will be virtual events.			**Day 11**	**Day 12**	**Day 13, 14, 15, 16 or 17**	**Day 18, 19, 20, 21, 22, 23 or 24**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Virtual**	**Clinic Visit 5**	**Virtual**	**Virtual**	**Clinic Visit 6**	**Clinic Visit 7**	**Clinic Visit 8**	**Clinic Visit 9**
Hematology/Chemistry/Urine	X	X	X		X			X			X			X
Fasting Lipid Panel (approximately 8 hrs)	X										X			X
Lymphocyte T-cell subsets (CD4, CD8)	X										X			
Plasma for HIV-1 genotype/phenotype[5]	X	X	X		X			X			X	X	X	X
Plasma for storage[6]	X	X	X		X			X			X	X	X	X
HIV-1 RNA	X	X	X		X			X			X	X	X	X

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Procedure[1]	Treatment Period Day 1 – Day 10										Post-Dosing Follow Up Period Day 11 – 17			Final Follow-up Day 18-24
	Day 1	Day 2	Day 3, 4 Choose one day for the Clinic Visit 3. The other day will be a virtual event.		Day 5, 6, 7 Choose one day for the Clinic Visit 4. The other days will be virtual events.			Day 8, 9, 10 Choose one day for the Clinic Visit 5. The other days will be virtual events.			Day 11	Day 12	Day 13, 14, 15, 16 or 17	Day 18, 19, 20, 21, 22, 23 or 24
	Clinic Visit 1	Clinic Visit 2	Clinic Visit 3	Virtual	Clinic Visit 4	Virtual	Virtual	Clinic Visit 5	Virtual	Virtual	Clinic Visit 6	Clinic Visit 7	Clinic Visit 8	Clinic Visit 9
Single, Pharmacokinetic (PK) sample (pre-dose at Visits 3 and 4)			X		X						X[7]	X	X	
Intensive PK sampling[8] (with sample at 24hr time point the next morning)	X							X[9]						
Observed dosing with GSK3640254/placebo[3]	X	X	X	X	X	X	X	X	X	X				
IWRS (RAMOS) activity[10]	X													

1. Procedures should be performed in the following order: ECG, Vitals, Blood Draws, followed by dose administration.
2. The study requires 9 in-clinic visits. Flexibility is offered for Visits 3, 4, 5, 8 and 9. The visit schedule for each participant should be pre-planned to be sure weekend, work schedules and clinic hours are appropriately considered. No visit interval during the treatment period can be greater than 3 days.
3. These assessments must be conducted with a participant during each day indicated, to include the days when the participant is not in the clinic. This can be done in via phone, preferably via a visual method (as locally permitted) of Skype, Facetime, WhatsApp, et. al.
4. Physical Exam will include, at a minimum, assessments of the Skin, Heart, Lungs, and Abdomen (liver and spleen).
5. Genotypic/Phenotypic testing will be conducted on Day 1 and Day 11 samples, with other visits tested as appropriate.
6. Plasma samples for storage will be collected at each visit starting at Day 1, including unscheduled visits. These samples will be used when needed, such as when samples are lost or where quantity is insufficient for testing. In the event samples are not used by study completion, they will be utilized for additional research on ARV resistance and/or HIV-1 disease biology/host immune response (excluding any human genetic testing)
7. If the Intensive PK day occurs on Day 10, do not collect the Day 11 pre-dose PK sample (as it is redundant with the 24-hr PK collection (completing the sample set started on Day 10).
8. Intensive Plasma PK samples will be collected as outlined in Protocol Table 4 in Section 9.5
9. If Day 8 or 9 is the Clinic Visit 5 to include the Intensive PK collection, the participant must return the following day for the 24-hr PK collection, meal and dosing. The assessments to be done as indicated on what is a “virtual visit day” should be captured as a virtual visit, even if the questions are asked in the clinic.
10. Log in to RAMOS on Day 1 to randomize the participant and to receive blinded study treatment. Subsequently log-in to RAMOS for study treatment supply as needed. If a participant is discontinued from the study early, log in to RAMOS to record the discontinuation.

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

- Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol amendment. The IRB/IEC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICF.

Study Part 2:

Procedure[1]	Treatment Period Day 1 – Day 7							Post-Dosing Follow Up Period	Final Follow-up
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6** Choose one day for the Clinic Visit 4. The other day will be a virtual event.		**Day 7**	**Day 8**	**Day 10, 11 or 12**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Clinic Visit 5**	**Clinic Visit 6**	**Clinic Visit 7**
Clinical Assessments									
Outpatient Visit[2]	X	X	X		X		X	X	X
Video/Phone Call				X		X			
Verify Inclusion/ Exclusion Criteria	X								
Medical/medication/drug/alcohol history	X								
Prior Anti-retroviral (ARV) Check	X								
CDC Classification	X								X

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Procedure[1]	Treatment Period Day 1 – Day 7							Post-Dosing Follow Up Period	Final Follow-up
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6** Choose one day for the Clinic Visit 4. The other day will be a virtual event.		**Day 7**	**Day 8**	**Day 10, 11 or 12**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Clinic Visit 5**	**Clinic Visit 6**	**Clinic Visit 7**
HIV-associated conditions assessments[3]	X	X	X	X	X	X	X	X	X
Adverse event (AE)/SAE assessment[3]	X	X	X	X	X	X	X	X	X
Concomitant medication review[3]	X	X	X	X	X	X	X	X	X
Weight, BMI and Physical exam[4]	X								
Vital Signs	X	X	X				X		X
C-SSRS Administration (*Since Last Visit* form)								X	

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Procedure[1]	Treatment Period Day 1 – Day 7							Post-Dosing Follow Up Period	Final Follow-up
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6** Choose one day for the Clinic Visit 4. The other day will be a virtual event.		**Day 7**	**Day 8**	**Day 10, 11 or 12**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Clinic Visit 5**	**Clinic Visit 6**	**Clinic Visit 7**
Clinical Procedures									
12-lead ECG (triplicate reading, done pre-dose; single readings at PK draws 2hr, 4hr, and 6hr)	X								
12-lead ECG (single reading, done pre-dose at Visits 2 and 3)		X	X						X
12-lead ECG (single reading done pre-dose and at PK draws 2hr, 4hr, and 6hr)							X		

Procedure[1]	Treatment Period Day 1 – Day 7							Post-Dosing Follow Up Period	Final Follow-up
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6** Choose one day for the Clinic Visit 4. The other day will be a virtual event.		**Day 7**	**Day 8**	**Day 10, 11 or 12**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Clinic Visit 5**	**Clinic Visit 6**	**Clinic Visit 7**
Pharmacogenetics (PGX) Collection (if consented)	X								
Hematology/Chemistry/Urine	X	X	X		X		X	X	X
Fasting Lipid Panel (approximately 8 hrs)	X							X	X
Lymphocyte T-cell subsets (CD4, CD8)	X							X	
Plasma for HIV-1 genotype/phenotype[5]	X	X	X		X		X	X	
Plasma for storage[6]	X	X	X		X		X	X	X

Procedure[1]	Treatment Period Day 1 – Day 7							Post-Dosing Follow Up Period	Final Follow-up
	Day 1	Day 2	Day 3, 4 Choose one day for the Clinic Visit 3. The other day will be a virtual event.		Day 5, 6 Choose one day for the Clinic Visit 4. The other day will be a virtual event.		Day 7	Day 8	Day 10, 11 or 12
	Clinic Visit 1	Clinic Visit 2	Clinic Visit 3	Virtual	Clinic Visit 4	Virtual	Clinic Visit 5	Clinic Visit 6	Clinic Visit 7
HIV-1 RNA	X	X	X		X		X	X	X
Single, Pharmacokinetic (PK) sample done pre-dose			X		X				
Intensive PK sampling (to include the 24hr samples drawn the next day)	X						X		
Observed dosing with GSK3640254 /placebo[3]	X	X	X	X	X	X	X		

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Procedure[1]	Treatment Period Day 1 – Day 7							Post-Dosing Follow Up Period	Final Follow-up
	Day 1	**Day 2**	**Day 3, 4** Choose one day for the Clinic Visit 3. The other day will be a virtual event.		**Day 5, 6** Choose one day for the Clinic Visit 4. The other day will be a virtual event.		**Day 7**	**Day 8**	**Day 10, 11 or 12**
	Clinic Visit 1	**Clinic Visit 2**	**Clinic Visit 3**	**Virtual**	**Clinic Visit 4**	**Virtual**	**Clinic Visit 5**	**Clinic Visit 6**	**Clinic Visit 7**
Observed dosing with Investigator-selected, prescribed and provided CART, and eCRF completion								X	
IWRS (RAMOS) activity[8]	X								

1. Procedures should be performed in the following order: ECG, Vitals, Blood Draws, followed by dose administration.
2. The study requires 7 in-clinic visits. Flexibility is offered for Visits 3, 4 and 7. The visit schedule for each participant should be pre-planned to be sure weekend, work schedules and clinic hours are appropriately considered. No visit interval during the treatment period can be greater than 3 days.
3. These assessments must be conducted with a participant during each day indicated, to include the days when the participant is not in the clinic. This can be done in via phone, preferably via a visual method (as locally permitted) of Skype, Facetime, WhatsApp, et. al.
4. Physical Exam will include, at a minimum, assessments of the Skin, Heart, Lungs, and Abdomen (liver and spleen).
5. Genotypic/Phenotypic testing will be conducted on Day 1 and Day 8 samples, with other visits tested as appropriate.
6. Plasma samples for storage will be collected at each visit starting at Day 1, including unscheduled visits. These samples will be used when needed, such as when samples are lost or where quantity is insufficient for testing. In the event samples are not used by study completion, they will be utilized for additional research on ARV resistance and/or HIV-1 disease biology/host immune response (excluding any human genetic testing)
7. Intensive Plasma PK samples will be collected as outlined in Protocol Table 4 in Section 9.5
8. Log in to RAMOS on Day 1 to dispense blinded study treatment. Subsequently log-in to RAMOS for study treatment supply as needed. If a participant is discontinued from the study early, log in to RAMOS to record the discontinuation.

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

- Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The IRB/IEC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICF

13.3. Appendix 3: Assessment Windows

13.3.1. Definitions of Assessment Windows for Analyses

Analyses will be presented by scheduled visits as collected in the CRF. The following table presents protocol defined assessment windows.

Part 1

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
Safety and Efficacy	All	14 - 28 days prior to first dose	28 days prior to first dose	Day -1	Screen
Efficacy	HIV-1 RNA, HIV-1 genotype / phenotype	Day 1	Day 1	Day 1	Visit 1
		Day 2	Day 2	Day 2	Visit 2
		Day 3 or 4	Day 3	Day 4	Visit 3
		Day 5, 6, or 7	Day 5	Day 7	Visit 4
		Day 8, 9, or 10	Day 8	Day 10	Visit 5
		Day 11	Day 11	Day 11	Visit 6
		Day 12	Day 12	Day 12	Visit 7
		Day 13, 14, 15, 16, or 17	Day 13	Day 17	Visit 8
		Days 18 to final follow up visit day	Day 18	final follow up visit day	Follow-up
	CD4 and CD8	Day 1	Day 1	Day 1	Visit 1
		Day 11	Day 11	Day 11	Visit 6
Safety	Laboratory: Chemistry/ Haematology/ Urinalysis	Day 1	Day 1	Day 1	Visit 1
		Day 2	Day 2	Day 2	Visit 2
		Day 3 or 4	Day 3	Day 4	Visit 3
		Day 5, 6, or 7	Day 5	Day 7	Visit 4
		Day 8, 9, or 10	Day 8	Day 10	Visit 5
		Day 11	Day 11	Day 11	Visit 6
		Days 18 to final follow up visit day	Day 18	final follow up visit day	Follow-up
	Fasting Lipid Panel	Day 1	Day 1	Day 1	Visit 1
		Day 11	Day 11	Day 11	Visit 6
		Days 18 to final follow up visit day	Day 18	final follow up visit day	Follow-up
	ECG	Day 1[1]	Day 1	Day 1	Visit 1
		Day 2[2]	Day 2	Day 2	Visit 2
		Day 3 or 4[2]	Day 3	Day 4	Visit 3
		Day 8, 9, or 10[3]	Day 8	Day 10	Visit 5
		Days 18 to final follow up visit day[2]	Day 18	final follow up visit day	Follow-up

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
	Vital Signs	Day 1	Day 1	Day 1	Visit 1
		Day 2	Day 2	Day 2	Visit 2
		Day 3 or 4	Day 3	Day 4	Visit 3
		Day 8, 9, or 10	Day 8	Day 10	Visit 5
		Days 18 to final follow up visit day	Day 18	final follow up visit day	Follow-up

NOTES:

[1] 12-lead ECG (triplicate reading, pre-dose; single readings at PK draws 2hr, 4hr, and 6hr)

[2] 12-lead ECG (single reading, pre-dose)

[3] 12-lead ECG (single reading pre-dose and at PK draws 2hr, 4hr, and 6hr)

Part 2

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
Safety and Efficacy	All	14 - 28 days prior to first dose	28 days prior to first dose	Day -1	Screen
Efficacy	HIV-1 RNA, HIV-1 genotype / phenotype	Day 1	Day 1	Day 1	Visit 1
		Day 2	Day 2	Day 2	Visit 2
		Day 3 or 4	Day 3	Day 4	Visit 3
		Day 5 or 6	Day 5	Day 6	Visit 4
		Day 7	Day 7	Day 7	Visit 5
		Day 8	Day 8	Day 8	Visit 6
		Days 10 to final follow up visit day	Day 10	final follow up visit day	Visit 7
	CD4 and CD8	Day 1	Day 1	Day 1	Visit 1
		Day 8	Day 8	Day 8	Visit 6
Safety	Laboratory: Chemistry/ Haematology/ Urinalysis	Day 1	Day 1	Day 1	Visit 1
		Day 2	Day 2	Day 2	Visit 2
		Day 3 or 4	Day 3	Day 4	Visit 3
		Day 5 or 6	Day 5	Day 6	Visit 4
		Day 7	Day 7	Day 7	Visit 5
		Day 8	Day 8	Day 8	Visit 6
		Days 10 to final follow up visit day	Day 10	final follow up visit day	Visit 7
	Fasting Lipid Panel	Day 1	Day 1	Day 1	Visit 1
		Day 8	Day 8	Day 8	Visit 6
		Days 10 to final follow up visit day	Day 10	final follow up visit day	Visit 7
	ECG	Day 1[1]	Day 1	Day 1	Visit 1

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
		Day 2[2]	Day 2	Day 2	Visit 2
		Day 3 or 4[2]	Day 3	Day 4	Visit 3
		Day 7[3]	Day 7	Day 7	Visit 5
		Days 10 to final follow up visit day	Day 10	final follow up visit day	Visit 7
	Vital Signs	Day 1	Day 1	Day 1	Visit 1
		Day 2	Day 2	Day 2	Visit 2
		Day 3 or 4	Day 3	Day 4	Visit 3
		Day 7	Day 7	Day 7	Visit 5
		Days 10 to final follow up visit day	Day 10	final follow up visit day	Visit 7

NOTES:

[1] 12-lead ECG (triplicate reading, pre-dose; single readings at PK draws 2hr, 4hr, and 6hr)

[2] 12-lead ECG (single reading, pre-dose)

[3] 12-lead ECG (single reading pre-dose and at PK draws 2hr, 4hr, and 6hr)

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

13.4.1. Study Phases

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

Study Phase	Definition
Screening Period	Day -28 to Day -1
Treatment Period	Day 1 to Day 10 / study treatment stop date in Part 1 and Day 1 to Day 7 / study treatment stop date in Part 2
Follow-up Period	Study treatment stop date + 1 to Day 24 in Part 1 and study treatment stop date + 1 to Day 12 in Part 2

13.4.1.1. Study Phases for Concomitant Medication

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

NOTES:

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

13.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	Study Treatment Start Date ≤ AE Start Date ≤ Final Follow-up Visit.

NOTES:

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

13.5. Appendix 5: Data Display Standards & Handling Conventions

13.5.1. Reporting Process

Software	
• The currently supported versions of SAS software 9.4 or higher will be used.	
Reporting Area	
HARP Server	:\\us1salx00259.corpnet2.com
HARP Compound	:\arwork\gsk3640254\mid208132\final_01
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1.	
Generation of RTF Files	
RTF files will be generated for Tables, one RTF file per item. Listings will be generated in L10 format, and Figures will be generated in PDF format. •	

13.5.2. Reporting Standards

General
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx): o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics
Formats
• GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time
• Reporting for tables, figures and formal statistical analyses: o Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. o 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: o Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). o Unscheduled or unplanned readings will be presented within the participant's listings.
Unscheduled Visits
• Unscheduled visits will not be included in summary tables and/or figures. • All unscheduled visits will be included in listings.
Descriptive Summary Statistics

Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

13.5.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non-compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to PK One document (Standards for the Transfer and Reporting of PK Data using HARP). Note: Concentration values will be imputed as per GUI_51487
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
NONMEM/Pop PK File	Not applicable.
NONMEM/PK/PD File	PK/PD file (CSV format) for the PK/PD analysis will be created according to the data specification detailed in Section 13.9 Pharmacokinetic/Pharmacodynamic Dataset Specification.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	The following PK parameters will be derived by the Programmer: R_AUC, R_Cmax, R_Cτ
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	Yes, refer to Standards for Handling NQ Impacted PK Parameters.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.
Units for PK Parameters	ug/mL for PK parameters; Original units (ng/mL) for listings, summary tables and figures of concentration-time data

13.6. Appendix 6: Derived and Transformed Data

13.6.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • Triplicate 12-lead ECGs will be recorded at each study-specified visit. Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • 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 First Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date
  • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

13.6.2. Study Population

Demographics
Age
Due to local privacy regulations, only the year of birth is recorded in the eCRF. The following algorithm will be used for imputation: • All dates of birth will be imputed using the 30th day of June. Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the participant will not be calculated and will remain missing. In listings of demographic data, the year of birth as entered will be displayed.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**

13.6.3. Efficacy

Efficacy Parameters
Plasma HIV-1 RNA
• If there are two values within a time window, the latest value will be used for summaries and analyses
CD4+ T-cell
• If there are two values within a time window, the average value will be used for summaries and analyses

13.6.4. Safety

ECG Parameters

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as:
  [1] If QTcB is machine read & QTcF is not provided, then:

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

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

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

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

Corrected QT Intervals

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

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

Laboratory Parameters

- If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value.
  - Example 1: 2 Significant Digits = '< x ' becomes x – 0.01
  - Example 2: 1 Significant Digit = '> x' becomes x + 0.1
  - Example 3: 0 Significant Digits = '< x' becomes x – 1

13.7. Appendix 7: Reporting Standards for Missing Data

13.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as a participant who has completed all phases of the study including the follow-up visit. • Withdrawn participants may be replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

13.7.2. 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.
Exposure	• If study treatment stop date is missing, then for the purposes of calculating exposure, it will be imputed using the date of last visit or the recorded date of withdrawal/completion whichever is earlier. • Partially Missing Stop Day: Last day of the month or last month of the year will be used, unless this is after the date of last visit or the recorded date of withdrawal/completion; in this case the earliest of the two dates will be used.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

13.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in 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 4: 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.

Element	Reporting Detail
	Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: 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.

13.8. Appendix 8: Values of Potential Clinical Importance

Haematology					
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**		
			Low Flag (< x)	**High Flag (>x)**	
Hematocrit	Ratio of 1	Male		0.54	
		Female		0.54	
		Δ from BL	↓0.075		
Hemoglobin	g/L	Male		180	
		Female		180	
		Δ from BL	↓25		
Lymphocytes	$x10^9$/ L		0.8		
Neutrophil Count	$x10^9$/ L		1.5		
Platelet Count	$x10^9$/ L		100	550	
White Blood Cell Count (WBC)	$x10^9$/ L		3	12	
Clinical Chemistry					
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**		**Comments**
			Low Flag (< x)	**High Flag (>x)**	
Bicarbonates	mmol/L		18	32	
BUN	mmol/L			9	
Calcium	mmol/L		2	2.75	
Chloride	mmol/L		98	107	
Creatinine	µmol/L	Δ from BL		44.2	
Glucose	mmol/L		3	11	
Potassium	mmol/L		3	5.5	
Sodium	mmol/L		130	150	
Total Protein	g/L	Δ from BL	-15	15	
Liver Function					
Test Analyte	**Units**	**Category**	**Clinical Concern Range**		
ALT/SGPT	U/L	High	≥ 2x ULN		
AST/SGOT	U/L	High	≥ 2x ULN		
AlkPhos	U/L	High	≥ 2x ULN		
Total Bilirubin	µmol/L	High	≥ 1.5xULN		

ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
PR Interval	msec	< 120	> 200
QRS Duration	msec	< 60	> 120
QT Interval	msec	< 320	> 450
QTc Interval (Bazett)	msec	< 320	> 450
QTc Interval (Fridericia)	msec	< 320	> 450
RR Interval	msec	< 600	> 1200
Change from Baseline			
Increase from Baseline QTc	msec		>60

Vital Signs

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

13.9. Appendix 9: Biomarker Analyses

13.9.1. Viral Genotyping and Phenotyping

Whole venous blood samples will be obtained from each participant to provide plasma for viral genotype and phenotype analysis, at the times listed in the Time and Events Table in Appendix 2. Details concerning the handling, labelling and shipping of these samples will be supplied separately.

Genotypic and phenotypic analyses will be carried out by Monogram Biosciences using their GAG/PR, PR/RT, and IN formats, in which PCR amplification is used to generate HIV cDNA products including the Gag, the PR and RT, and IN coding regions, respectively. Phenotypic analyses of the GAG/PR region will include susceptibility to GSK3640254. Analysis will be done on Day 1 and Day 11 samples in Part 1 and Day 1 and Day 8 samples in Part 2. In the case of rebound HIV-1 viral load, analysis will be completed on samples corresponding to time point of rebound occurrence.

13.9.2. Genetics

Information regarding genetic research is included in Appendix 6, Section 12.6 of protocol Amendment 2 (Dated: 10/JAN/2019).

13.10. Appendix 10: Abbreviations & Trade Marks

13.10.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
AIDS	Auto immunodeficiency syndrome
A&R	Analysis and Reporting
ALT	Alanine aminotransferase
ART	Antiretroviral therapy
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration time curve
AUC(0-τ)	Area under the plasma concentration time curve over the dosing interval
AUC(0-24)	Area under the plasma concentration time curve from time zero to the concentration at 24 hours post dose
A&R	Analysis and Reporting
Bpm	beats per minute
BIL	Bilirubin
C0	Concentration at pre-dose
Cτ	Concentration at the end of the dosing interval
C24	Concentration at 24 hours post dose
cART	Combination anti-retroviral therapy
CDISC	Clinical Data Interchange Standards Consortium
CL/F	Apparent oral clearance
CI	Confidence Interval
Cmax	Maximum observed concentration
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DOB	Date of Birth
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IP	Investigational Product
ITT	Intent-To-Treat
g	gram
GSK	GlaxoSmithKline
GUI	Graphical User Interface
H	Hour(s)
HIV	Human Immunodeficiency Virus
Kg	Kilogram

Abbreviation	Description
λz	The slope of the apparent terminal phase
L	Litre
LOC	Last Observation Carries Forward
MedDRA	Medical Dictionary for Regulatory Activities
mL	Milliliter
mg	milligrams
MMRM	Mixed Model Repeated Measures
ng/mL	Nanogram per millilitre
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PT	Preferred Term
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
R_AUC	The accumulation ratio of AUC from Day 10 to Day 1 in Part 1 or Day 7 to Day 1 in Part 2
R_Cmax	The accumulation ratio of Cmax from Day 10 to Day 1 in Part 1 or Day 7 to Day 1 in Part 2
R_Cτ	The accumulation ratio of Cτ from Day 10 to Day 1 in Part 1 or Day 7 to Day 1 in Part 2
RAP	Reporting & Analysis Plan
Rsq	The correlation coefficient of the slope of the terminal phase
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SOP	Standard Operation Procedure
t½	Apparent terminal half-life
tlag	Absorption lag time
tmax	Time to reach Cmax
TFL	Tables, Figures & Listings
U	Units
LLOD	Lower limit of detection

13.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
NONMEM
SAS
WinNonlin

13.11. Appendix 11: List of Data Displays

13.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.19	Not applicable
Efficacy	2.1 to 2.32	2.1 to 2.6
Safety	3.1 to 3.57	3.1 to 3.2
Pharmacokinetic	4.1 to 4.13	4.1 to 4.12
Population Pharmacokinetic (PopPK)	Not applicable	Not applicable
Pharmacodynamic	5.1	5.1
Pharmacokinetic / Pharmacodynamic	6.1	6.1 to 6.3
Section	**Listings**	
ICH Listings	1 to 31	
Other Listings	32~56	

13.11.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 12: Example Mock Shells for Data Displays.

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

NOTES:

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

13.11.3. Deliverables

Delivery [Priority] [1]	Description
HL	Headline report
SAC [1]	Final Statistical Analysis Complete

NOTES:

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

13.11.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Participant Disposition					
1.1.	Safety	ES1	Summary of Subject Status and Reason for Study Withdrawal	ICH E3, FDAAA, EudraCT	HL, SAC
1.2.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment	ICH E3	SAC
1.3.	Safety	ES4	Summary of Subject Disposition	ICH E3	SAC
1.4.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations	ICH E3	SAC
1.6.	Safety	DV1A	Summary of Deviations Leading to Exclusions from Per Protocol Population		SAC
1.7.	Safety	IE1	Summary of Inclusion/Exclusion Criteria Deviations		SAC
Population Analysed					
1.8.	All Screened	SP1	Summary of Study Populations	IDSL	SAC
1.9.	Safety	SP2	Summary of Exclusions from the Per Protocol Population	IDSL	SAC
1.10.	Safety	NS1	Summary of Number of Subjects by Centre	IDSL/EudraCT/Clinical Operations	SAC
Demographic and Baseline Characteristics					
1.11.	Safety	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	HL, SAC
1.12.	Safety	DM11	Summary of Age Ranges	EudraCT	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.13.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT For details on Race categories shown in this table, please see GSK IDSL Demography Statistical Display Standards, Section 1.1.2 Summary of Race and Racial Combinations	SAC
Prior and Concomitant Medications					
1.14.	Safety	MH1	Summary of Past Medical Conditions	ICH E3 Categories of medical conditions will be sorted in descending order of "Total" incidence, and medical conditions within each category will be sorted in descending order of "Total" incidence. If the "Total" incidence for any two or more medical conditions is equal, then they will be presented in alphabetical order.	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.15.	Safety	MH1	Summary of Current Medical Conditions	ICH E3 Categories of medical conditions will be sorted in descending order of "Total" incidence, and medical conditions within each category will be sorted in descending order of "Total" incidence. If the "Total" incidence for any two or more medical conditions is equal, then they will be presented in alphabetical order.	SAC
1.16.	Safety	CM1	Summary of Prior Concomitant Medications ATC Level 1 by Ingredient	ICH E3 Medications will be sorted in descending order of "Total" incidence for the ATC level 1 and in descending order of total incidence for the ingredient within each ATC level. If the total incidence of for any two or more ingredients is equal, the events will be presented in alphabetical order. See GSK IDSL "CONCOMITANT MEDICATIONS STATISTICAL DISPLAY STANDARDS" (Version 12), Section 1.1.1	SAC
1.17.	Safety	CM1	Summary of Current Concomitant Medications ATC Level 1 by Ingredient	ICH E3 Same as Table 1.16 notes	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure and Treatment Compliance					
1.18.	Safety	COMP1	Summary of Study Treatment Overall Compliance		SAC
1.19.	Safety	EX1	Summary of Exposure to Study Treatment	ICH E3	HL, SAC

13.11.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Plasma HIV-1 RNA (ITT)					
2.1.	ITT	EFF_T1	Summary of Plasma HIV-1 RNA – Part 1	On original and log10 scale	SAC
2.2.	ITT	EFF_T1	Summary of Plasma HIV-1 RNA – Part 2	On original and log10 scale	SAC
2.3.	ITT	EFF_T2	Summary of Change from Baseline to Nadir and Change from Baseline to Visit 6 (Day 11) in Plasma HIV-1 RNA – Part 1	On original and log10 scale	SAC
2.4.	ITT	EFF_T2	Summary of Change from Baseline to Nadir and Change from Baseline to Visit 6 (Day 8) in Plasma HIV-1 RNA – Part 2	On original and log10 scale	SAC
2.5.	ITT	EFF_T2	Summary of Time to Nadir in Plasma HIV-1 RNA – Part 1		SAC
2.6.	ITT	EFF_T2	Summary of Time to Nadir in Plasma HIV-1 RNA – Part 2		SAC
2.7.	ITT	EFF_T3	Summary of Modelled Plasma HIV-1 RNA Mean Rate of Change from baseline to Visit 6 (Day 11) and Maximum Change by Treatment – Part 1	On log10 scale	SAC
2.8.	ITT	EFF_T3	Summary of Modelled Plasma HIV-1 RNA Mean Rate of Change from baseline to Visit 6 (Day 8) and Maximum Change by Treatment – Part 2	On log10 scale	SAC
2.9.	ITT	EFF_T4	Summary of Proportion of Participants with Plasma HIV-1 RNA <400 and < 50 copies/mL – Part 1	By visit and by treatment	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.10.	ITT	EFF_T4	Summary of Proportion of Participants with Plasma HIV-1 RNA <400 and < 50 copies/mL – Part 2	By visit and by treatment	SAC
2.11.	ITT	EFF_T5	Summary of Proportion of Participants with Plasma HIV-1 RNA Change from Baseline >1.5 log10 copies/mL Decrease -Part 1	By visit and by treatment	SAC
2.12.	ITT	EFF_T5	Summary of Proportion of Participants with Plasma HIV-1 RNA Change from Baseline >1.5 log10 copies/mL Decrease -Part 2	By visit and by treatment	SAC
Immunology (ITT)					
2.13.	ITT	EFF_T6	Summary of CD4+ and CD8+ and Change from Baseline by Visit – Part 1	Please include both absolute CD4 count and CD4 percentage, Same to CD8	SAC
2.14.	ITT	EFF_T6	Summary of CD4+ and CD8+ and Change from Baseline by Visit – Part 2	Please include both absolute CD4 count and CD4 percentage, same to CD8	SAC
2.15.	ITT	EFF_T3	Summary of Modelled CD4+ Cell Count Mean Rate of Change from baseline to Visit 6 (Day 11) by Treatment – Part 1	On log10 scale	SAC
2.16.	ITT	EFF_T3	Summary of Modelled CD4+ Cell Count Mean Rate of Change from baseline to Visit 6 (Day 8) by Treatment – Part 2	On log10 scale	SAC
Plasma HIV-1 RNA (PP)					
2.17.	PP	EFF_T1	Summary of Plasma HIV-1 RNA – Pat 1	To be generated if there are participants excluded from the Per Protocol population	SAC
2.18.	PP	EFF_T1	Summary of Plasma HIV-1 RNA – Pat 2	To be generated if there are participants excluded from the Per Protocol population	SAC
2.19.	PP	EFF_T2	Summary of Change from Baseline to Visit 6 (Day 11) and Maximum Decline from Baseline in plasma HIV-1 RNA – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.20.	PP	EFF_T2	Summary of Change from Baseline to Visit 6 (Day 8) and Maximum Decline from Baseline in plasma HIV-1 RNA – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC
2.21.	PP	EFF_T2	Summary of Time to Nadir in Plasma HIV-1 RNA – Part 1		SAC
2.22.	PP	EFF_T2	Summary of Time to Nadir in Plasma HIV-1 RNA – Part 2		SAC
2.23.	PP	EFF_T2	Summary of Modelled Plasma HIV-1 RNA Mean Rate of Change from baseline to Visit 6 (Day 11) and Maximum Change by Treatment – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC
2.24.	PP	EFF_T3	Summary of Modelled Plasma HIV-1 RNA Mean Rate of Change from baseline to Visit 6 (Day 8) and Maximum Change by Treatment – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC
2.25.	PP	EFF_T4	Summary of Proportion of Participants with Plasma HIV-1 RNA <400 and < 50 copies/mL – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC
2.26.	PP	EFF_T4	Summary of Proportion of Participants with Plasma HIV-1 RNA <400 and < 50 copies/mL – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC
2.27.	PP	EFF_T5	Summary of Proportion of Participants with Plasma HIV-1 RNA Change from Baseline >1.5 log10 copies/mL Decrease – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC
2.28.	PP	EFF_T5	Summary of Proportion of Participants with Plasma HIV-1 RNA Change from Baseline >1.5 log10 copies/mL Decrease – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC
Immunology (PP)					
2.29.	PP	EFF_T6	Summary of CD4+ Cell Count and Change from Baseline by Visit – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.30.	PP	EFF_T6	Summary of CD4+ Cell Count and Change from Baseline by Visit – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC
2.31.	PP	EFF_T3	Summary of Modelled CD4+ Cell Count Mean Rate of Change from baseline to Visit 6 (Day 11) by Treatment – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC
2.32.	PP	EFF_T3	Summary of Modelled CD4+ Cell Count Mean Rate of Change from baseline to Visit 6 (Day 8) by Treatment – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC

13.11.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Plasma HIV-1 RNA					
2.1.	ITT	EFF_F1	Plot of Mean and Median Change from Baseline (Day 1) in Plasma HIV-1 RNA by Treatment – Part 1	Overlay all treatment groups together. 95% CI will also be provided based on T-distribution.	HL, SAC
2.2.	ITT	EFF_F1	Plot of Mean and Median Change from Baseline (Day 1) in Plasma HIV-1 RNA by Treatment – Part 2	Overlay all treatment groups together. 95% CI will also be provided based on T-distribution.	HL, SAC
2.3.	ITT	PK24	Plot of Individual Change from Baseline (Day 1) in Plasma HIV-1 RNA by Treatment and Day – Part 1	Present individual change from baseline profile on same plot. Use different legend to denote the treatment arms. Day used for x axis.	SAC
2.4.	PP	EFF_F1	Plot of Mean and Median Change from Baseline (Day 1) in Plasma HIV-1 RNA by Treatment – Part 1	To be generated if there are participants excluded from the Per Protocol population	SAC
2.5.	PP	EFF_F1	Plot of Mean and Median Change from Baseline (Day 1) in Plasma HIV-1 RNA by Treatment – Part 2	To be generated if there are participants excluded from the Per Protocol population	SAC
2.6.	PP	PK24	Plot of Individual Change from Baseline (Day 1) in Plasma HIV-1 RNA by Treatment and Day – Part 2	Present individual change from baseline profile on same plot. Use different legend to denote the treatment arms. Day used for x axis.	SAC

13.11.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE13	Adverse Events Overview		SAC
3.2.	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	HL, SAC
3.3.	Safety	AE5B	Summary of All Adverse Events by System Organ Class and Preferred Term and Maximum Grade	ICH E3	SAC
3.4.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Preferred Term	ICH E3	SAC
3.5.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	SAC
3.6.	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3	HL, SAC
3.7.	Safety	AE5B	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Grade	ICH E3	SAC
3.8.	Safety	AE1	Summary of Adverse Events of Special Interest		SAC
Serious and Other Significant Adverse Events					
3.9.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAAA, EudraCT	SAC
3.10.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term	IDSL	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Chemistry					
3.11.	Safety	LB1	Summary of Clinical Chemistry Data by Visit – Part 1	ICH E3	SAC
3.12.	Safety	LB1	Summary of Clinical Chemistry Data by Visit – Part 2	ICH E3	SAC
3.13.	Safety	LB1	Summary of Changes from Baseline in Clinical Chemistry Data by Visit – Part 1	ICH E3 .	SAC
3.14.	Safety	LB1	Summary of Changes from Baseline in Clinical Chemistry Data by Visit – Part 2	ICH E3 .	SAC
3.15.	Safety	LB18	Summary of Worst-Case Chemistry Grade Shifts from Baseline Grade – Part 1	ICH E3 Display only worst case post baseline visits.	HL, SAC
3.16.	Safety	LB18	Summary of Worst-Case Chemistry Grade Shifts from Baseline Grade – Part 2	ICH E3 Display only worst case post baseline visits.	HL, SAC
3.17.	Safety	LB17	Summary of Chemistry Laboratory Abnormalities of Potential Clinical Importance – Part 1		SAC
3.18.	Safety	LB17	Summary of Chemistry Laboratory Abnormalities of Potential Clinical Importance – Part 2		SAC
3.19.	Safety	SAFE_T1	Summary of Treatment Emergent Clinical Chemistry Toxicities – Part 1	Exclude Liver tests(AST, ALT , ALP, TBIL)	SAC
3.20.	Safety	SAFE_T1	Summary of Treatment Emergent Clinical Chemistry Toxicities – Part 2	Exclude Liver tests(AST, ALT , ALP, TBIL)	SAC
Laboratory: Haematology					
3.21.	Safety	LB1	Summary of Haematology Data by Visit – Part 1	ICH E3	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.22.	Safety	LB1	Summary of Haematology Data by Visit – Part 2	ICH E3	SAC
3.23.	Safety	LB1	Summary of Changes from Baseline in Haematology by Visit – Part 1	ICH E3	SAC
3.24.	Safety	LB1	Summary of Changes from Baseline in Haematology by Visit – Part 2	ICH E3	SAC
3.25.	Safety	LB18	Summary of Worst-Case Haematology Grade Shifts from Baseline Grade – Part 1	ICH E3	HL, SAC
3.26.	Safety	LB18	Summary of Worst-Case Haematology Grade Shifts from Baseline Grade – Part 2	ICH E3	HL, SAC
3.27.	Safety	LB17	Summary of Haematology Laboratory Abnormalities of Potential Clinical Importance – Part 1		
3.28.	Safety	LB17	Summary of Haematology Laboratory Abnormalities of Potential Clinical Importance – Part 2		
3.29.	Safety	SAFE_T1	Summary of Treatment Emergent Haematology Toxicities – Part 1		SAC
3.30.	Safety	SAFE_T1	Summary of Treatment Emergent Haematology Toxicities – Part 2		SAC
Laboratory: Urinalysis					
3.31.	Safety	LB1	Summary of Urine Concentration Data by Visit – Part 1	ICH E3	SAC
3.32.	Safety	LB1	Summary of Urine Concentration Data by Visit – Part 2	ICH E3	SAC
3.33.	Safety	LB1	Summary of Changes from Baseline in Urine Concentration by Visit – Part 1	ICH E3	SAC
3.34.	Safety	LB1	Summary of Changes from Baseline in Urine Concentration by Visit – Part 2	ICH E3	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.35.	Safety	UR1	Summary of Worst-Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline – Part 1	ICH E3	SAC
3.36.	Safety	UR1	Summary of Worst-Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline – Part 2	ICH E3	SAC
Laboratory: Hepatobiliary (Liver)					
3.37.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 1	IDSL	SAC
3.38.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 2	IDSL	SAC
3.39.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part 1	IDSL	SAC
3.40.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part 2	IDSL	SAC
3.41.	Safety	SAFE_T2	Summary of Treatment Emergent Liver Toxicities – Part 1		SAC
3.42.	Safety	SAFE_T2	Summary of Treatment Emergent Liver Toxicities – Part 2		SAC
ECG					
3.43.	Safety	EG1	Summary of ECG Findings – Part 1	IDSL	HL. SAC
3.44.	Safety	EG1	Summary of ECG Findings – Part 2	IDSL	HL. SAC
3.45.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit – Part 1	IDSL	SAC
3.46.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit – Part 2	IDSL	SAC
3.47.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part 1	IDSL	SAC
3.48.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part 2	IDSL	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.49.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part 1	IDSL	SAC
3.50.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part 2	IDSL	SAC
3.51.	Safety	ING111207, Table 10.30	Listing of QTc Interval Data for Subjects with QTc Measurement > 500msec or Increase from Baseline > 60msec- Part 1 and 2	For subjects with QTcB or QTcF measurement > 500msec or increase from baseline > 60msec, list QTcB and QTcF data (both value and change from baseline) at all time points, and flag the values > 500msec and increases > 60msec	SAC
Vital Signs					
3.52.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 1	ICH E3	SAC
3.53.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 2	ICH E3	SAC
3.54.	Safety	VS3	Summary of Worst-Case Vital Signs Relative to Normal Range Post-Baseline Relative to Baseline – Part 1	IDSL	SAC
3.55.	Safety	VS3	Summary of Worst-Case Vital Signs Relative to Normal Range Post-Baseline Relative to Baseline – Part 2	IDSL	SAC
C-SSRS					
3.56.	Safety	CSSRS4	Listing of C-SSRS Suicidal Ideation or Behaviour Data	IDSL. Part 1 and Part 2 in one table.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
cART					
3.57.	Safety	CM1	Summary of cART Medications ATC Categories by Ingredient – Part 2	IDSL. Part 2 only.	SAC

13.11.8. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
3.1.	Safety	SAFE_F1	Plot of Mean (95% CI) Change from Baseline in QTc Interval by Treatment and Time – Part 1	For both QTcB-interval and QTcF interval	SAC
3.2.	Safety	SAFE_F1	Plot of Mean (95% CI) Change from Baseline in QTc Interval by Treatment and Time – Part 2	For both QTcB-interval and QTcF interval	SAC

13.11.9. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
4.1.	PK	PK01	Summary of Plasma GSK3640254 Pharmacokinetic Concentration-Time Data – Part 1		SAC
4.2.	PK	PK01	Summary of Plasma GSK3640254 Pharmacokinetic Concentration-Time Data – Part 2		SAC
PK Derived Parameters					
4.3.	PK	PKPL1P	Listing of Derived Plasma GSK3640254 Pharmacokinetic Parameters by Treatment - Visit 1 – Part 1	Parameters with units	SAC
4.4.	PK	PKPL1P	Listing of Derived Plasma GSK3640254 Pharmacokinetic Parameters by Treatment - Visit 1 – Part 2	Parameters with units	SAC
4.5.	PK	PKPL1P	Listing of Derived Plasma GSK3640254 Pharmacokinetic Parameters by Treatment – Visit 5 – Part 1	Parameters with units	SAC
4.6.	PK	PKPL1P	Listing of Derived Plasma GSK3640254 Pharmacokinetic Parameters by Treatment – Visit 5 – Part 2	Parameters with units	SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.7.	PK	PKPT2	Summary Statistics of Derived Plasma GSK3640254 Pharmacokinetic Parameters by Treatment and Visit – Part 1	Parameters with units	SAC
4.8.	PK	PKPT2	Summary Statistics of Derived Plasma GSK3640254 Pharmacokinetic Parameters by Treatment and Visit – Part 2	Parameters with units	SAC
4.9.	PK	PKPT4	Summary Statistics of Log-Transformed Derived Plasma GSK3640254 Pharmacokinetic Parameters and Visit -Part 1	Parameters with units	SAC
4.10.	PK	PKPT4	Summary Statistics of Log-Transformed Derived Plasma GSK3640254 Pharmacokinetic Parameters and Visit -Part 2	Parameters with units	SAC
4.11.	PK	PK_T1	Assessment of Dose Proportionality of GSK3640254 by Days	Part 1 and Part 2 doses all included in the statistical mode. Day 1: AUC(0-24), Cmax and C24; Day 8: AUC(0-tau) and Cmax and C-tau.	SAC
4.12.	PK	PK_T2	Assessment of Plasma GSK3640254 Steady State Concentrations – Part 1	Pre-dose concentration values for Visit 2~6	SAC
4.13.	PK	PK_T2	Assessment of Plasma GSK3640254 Steady State Concentrations – Part 2	Pre-dose concentration values for Visit 2~6	SAC

13.11.10. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Concentration Plots					
4.1.	PK	PKCF1P	Individual Plasma GSK3640254 Concentration-Time Plot by Visit (Linear and Semi-Log)	Present individual Visit 1 and Visit 5 profile on same plot. Paginate by Subject and Part	SAC
4.2.	PK	PK26	Individual Plasma GSK3640254 Trough Concentration-Time Plot (Linear and Semi-Log)	Present Pre-dose and 24 hr time points only. Paginate by Subject and Part	SAC
Mean/Median Concentration Plots					
4.3.	PK	PKCF2	Mean Plasma GSK3640254 Concentration-Time Plots by Treatment and Visit (Linear and Semi-Log) – Part 1	Paginate by Visit	SAC
4.4.	PK	PKCF2	Mean Plasma GSK3640254 Concentration-Time Plots by Treatment and Visit (Linear and Semi-Log) – Part 2	Paginate by Visit	SAC
4.5.	PK	PK27	Mean Plasma GSK3640254 Trough Concentration-Time Plots by Treatment (Linear and Semi-Log) – Part 1	Pre-dose and 24 hr time points only. Time scale by Visit	SAC
4.6.	PK	PK27	Mean Plasma GSK3640254 Trough Concentration-Time Plots by Treatment (Linear and Semi-Log) – Part 2	Pre-dose and 24 hr time points only. Time scale by Visit	SAC
4.7.	PK	PKCF3	Median Plasma GSK3640254 Concentration-Time Plots by Treatment and Visit (Linear and Semi-Log) – Part 1	Paginate by Visit	SAC
4.8.	PK	PKCF3	Median Plasma GSK3640254 Concentration-Time Plots by Treatment and Visit (Linear and Semi-Log) – Part 2	Paginate by Visit	SAC
4.9.	PK	PK27	Median Plasma GSK3640254 Trough Concentration-Time Plots by Treatment (Linear and Semi-Log) – Part 1	Pre-dose and 24 hr time points only. Time scale by Visit	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.10.	PK	PK27	Median Plasma GSK3640254 Trough Concentration-Time Plots by Treatment (Linear and Semi-Log) – Part 2	Pre-dose and 24 hr time points only. Time scale by Visit	SAC
PK Parameter Plots					
4.11.	PK	PK28	Individual and Geometric Mean (95% CI) of Plasma PK Parameters versus Dose by Visit – Part 1	Paginate by Parameter and Visit. Present overlay of individual parameters with Geometric mean and 95%CI for parameters and results for Table 4.4 for regression line	SAC
4.12.	PK	PK28	Individual and Geometric Mean (95% CI) of Plasma PK Parameters versus Dose by Visit – Part 2	Paginate by Parameter and Visit. Present overlay of individual parameters with Geometric mean and 95%CI for parameters and results for Table 4.4 for regression line	SAC

13.11.11. Pharmacodynamic Tables

Pharmacodynamic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PD Linear and Emax Models					
5.1.	PP	PD_T1	Summary of Estimates from Dose-Response Model	Only include visits from Day 1 to Day 8 for the HIV-RNA change. Part 1 and Part 2 doses all included in the statistical mode.	SAC

13.11.12. Pharmacodynamic Figures

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK/PD – RNA Change from Baseline					
5.1	PP	PK28	Scatter Plot of HIV RNA Maximum Decline from Baseline versus Dose	Only include visits from Day 1 to Day 8 for the HIV-RNA change. Part 1 and Part 2 doses in one plot.	SAC

13.11.13. Pharmacokinetic / Pharmacodynamic Tables

Pharmacokinetic / Pharmacodynamic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
6.1.	PK/PD	PK28	Summary of Estimates from Exposure Response Model	Part 1 and Part 2 doses all included in the statistical mode.	SAC

13.11.14. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK/PD – RNA Change from Baseline					
6.1.	PK/PD	PK28	Scatter Plot of Day 8 HIV RNA Change from Baseline versus Plasma PK Parameters	Present Day 8 HIV RNA Change from Baseline vs AUC(0-τ), Cmax and Cτ, for all doses in Part 1 and Part 2	SAC
6.2.	PK/PD	PK28	Scatter Plot of HIV RNA Maximum Change from Baseline to day 8 versus Plasma PK Parameters	Maximum change from baseline to day 8 HIV RNA vs AUC(0-τ), Cmax and Cτ, for all doses in Part 1 and Part 2	SAC
PK/PD – QTcF Change from Baseline					
6.3.	PK/PD	PK28	Scatter Plot of QTcF Change from Baseline versus Time-matched PK Concentration	Placebo group included with PK concentration value as 0. Day 1 to Day 8 in Part 1 and Part 2.	SAC

13.11.15. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Participant Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	ITT	ES2	Listing of Reasons for Study Withdrawal	ICH E3	HL, SAC
3.	Safety	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC
4.	ITT	BL1	Listing of Participants for Whom the Treatment Blind was Broken	ICH E3	SAC
5.	ITT	TA1	Listing of Planned and Actual Treatments	IDSL.	SAC
Protocol Deviations					
6.	ITT	DV2	Listing of Important Protocol Deviations	ICH E3, add one flag for denoting the protocol deviation leading to exclusion from PP population.	SAC
7.	ITT	IE3	Listing of Inclusion/Exclusion Criteria Deviations	ICH E3	SAC
Populations Analysed					
8.	ITT	SP3	Listing of Participants Excluded from Any Population	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
9.	ITT	DM2	Listing of Demographic Characteristics	ICH E3 Age, sex, race, ethnicity, height, weight, and BMI. For details on Race categories shown in this table, please see GSK IDSL Demography Statistical Display Standards, Section 1.1.1 Summary of Demographic Characteristics	SAC
10.	ITT	DM9	Listing of Race and Racial Combinations	ICH E3 For details on Race categories shown in this table, please see GSK IDSL Demography Statistical Display Standards, Section 1.1.2 Summary of Race and Racial Combinations	SAC
Prior and Concomitant Medications					
11.	Safety	CP_CM3	Listing of Prior Concomitant Medications	IDSL	SAC
12.	Safety	CP_CM3	Listing of Current Concomitant Medications	IDSL	SAC
Exposure and Treatment Compliance					
13.	Safety	EX3	Listing of Exposure Data	ICH E3	SAC
Adverse Events					
14.	Safety	AE8	Listing of All Adverse Events	ICH E3	HL, SAC
15.	Safety	AE7	Listing of Participant Numbers for Individual Adverse Events	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
16.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
17.	Safety	AE8	Listing of Serious Adverse Events		HL, SAC
18.	Safety	AE8	Listing of Fatal Serious Adverse Events	ICH E3	SAC
19.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3	SAC
20.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC
21.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	HL, SAC
22.	Safety	AE8	Listing of Cardiovascular Adverse Events of Special Interest		SAC
Hepatobiliary (Liver)					
23.	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	SAC
24.	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events	IDSL	SAC
All Laboratory					
25.	Safety	LB5	Listing of Clinical Chemistry Laboratory Data for Participants with Any Value of Potential Clinical Importance	ICH E3	SAC
26.	Safety	LB5	Listing of Haematology Laboratory Data for Participants with Any Value of Potential Clinical Importance	ICH E3	SAC
27.	Safety	LB5	Listing of Liver Function Laboratory Data for Participants with Any Value of Potential Clinical Importance	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
28.	Safety	EG3	Listing of All ECG Values for Participants with Any Value of Potential Clinical Importance	IDSL	HL, SAC
29.	Safety	EG5	Listing of All ECG Findings for Participants with an Abnormal ECG Finding	IDSL	HL, SAC
Vital Signs					
30.	Safety	VS5	Listing of All Vital Signs Data for Participants with Any Value of Potential Clinical Importance	IDSL	HL, SAC
cART					
31.	Safety	CM2	Listing of cART Medications – Part 2	IDSL, for Part 2 only	SAC

13.11.16. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Populations Analysed					
32.	All Screened	POP_L1	Listing of Study Populations		SAC
Demography & Disease Characteristics at Screening					
33.	ITT	POP_L2	Listing of Cardiovascular Risk Assessment		SAC
34.	ITT	POP_L3	Listing of HIV Risk Factors		SAC
Medical Condition & Concomitant Medications					
35.	ITT	MH2	Listing of Current and Past Medical Conditions		SAC
36.	ITT	POP_L4	Listing of HIV Associated Conditions		SAC
37.	ITT	CM6	Listing Relationship Between ATC Level 1, Ingredients and Verbatim Text		SAC
Adverse Event					
38.	Safety	AE8	Listing of Drug Related Adverse Events		SAC
Laboratory Values					
39.	Safety	LB5	Listing of Clinical Chemistry Data	Exclude Liver tests(AST, ALT , ALP, TBIL)	SAC
40.	Safety	LB5	Listing of Haematology Data		SAC
41.	Safety	LB5	Listing of Liver Function Data		SAC
42.	Safety	UR2A	Listing of Urinalysis Data		SAC
Efficacy					
43.	ITT	EFF_L1	Listing of Plasma HIV-1 RNA		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
44.	ITT	EFF_L2	Listing of CD4+ T-cell counts	Please include both absolute CD4 count and CD4 percentage.	SAC
45.	ITT	EFF_L2	Listing of CD8+ T-cell counts	Please include both absolute CD8 count and CD8 percentage.	SAC
Virology					
46.	ITT	VR_L1	Listing of Viral Genotypic Data		SAC
47.	ITT	VR_L2	Listing of Viral Phenotypic Data		SAC
Pharmacokinetic					
48.	PK	PKCL1P	Listing of Plasma GSK3640254 Concentrations (ng/mL) by Treatment	List all the concentration data including unscheduled. Repeat for all treatments.	SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Statistical Output					
49.	ITT		Statistical Output Listing of Modelled Plasma HIV-1 RNA Maximum Change by Treatment		SAC
50.	ITT		Statistical Output Listing of Modelled Plasma HIV-1 RNA Mean Rate of Change by Treatment		SAC
51.	PP		Statistical Output Listing of Modelled Plasma HIV-1 RNA Maximum Change by Treatment		SAC
52.	PP		Statistical Output Listing of Modelled Plasma HIV-1 RNA Mean Rate of Change by Treatment		SAC
53.	PK		Statistical Output Listing of Assessment of Dose Proportionality of GSK3640254 by Day		SAC
54.	PK		Statistical Output Listing of Assessment of Plasma GSK3640254 Steady State Concentrations		SAC
55.	PP		Statistical Output Listing of Summary of Estimates from Dose-Response Model		SAC
56.	PK/PD		Statistical Output Listing of Summary of Estimates from Exposure Response Model		SAC

13.12. Appendix 12: Example Mock Shells for Data Displays

Data Display Specification will be made available on request

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