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

Title	:	Reporting and Analysis Plan for 206898: An Open Label, Phase 1 Study to Evaluate the PK, Safety, Tolerability and Acceptability of Long Acting Injections of the HIV Integrase Inhibitor, Cabotegravir (CAB; GSK1265744) in HIV Uninfected Chinese Men
Compound Number	:	GSK1265744
Effective Date	:	22-APR-2019

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 206898.
- This RAP is intended to describe the safety, tolerability, and pharmacokinetic (PK) 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. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this reporting and analysis plan (RAP) is to describe any planned analyses and output to be included in the clinical study report for Protocol 206898.
Protocol	• This RAP is based on the Protocol Amendment 1 (Dated: 06JUN2018) of study Protocol 206898 (GSK Document No.: 2016N293702_01] and eCRF Version (2.00, Dated: 26SEP2018).
Primary Objective	• Evaluate the safety and tolerability of the injectable agent, cabotegravir (GSK1265744) long acting (CAB LA) injectable (600 mg dose administered every 4 weeks for 2 doses followed by every 8 weeks for 3 doses) through Week 5-41 in HIV-1 uninfected Chinese men. • Evaluate the plasma pharmacokinetics of CAB following repeat oral administration (Day 1 to Week 4) and CAB LA IM injections throughout the Injection Phase (Weeks 5-41).
Primary Endpoint	• Safety and tolerability parameters, including adverse events, clinical laboratory tests, study withdrawals due to AEs, vital signs assessments, and evaluation of injection site reactions (ISRs), for injection phase (Week 5-41). • Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F following daily oral administration of CAB through Day 1 to Week 4. • Plasma CAB AUC(0-τ), Cmax, Cτ, and tmax following IM injections of CAB LA once every 8 weeks through Weeks 5-41.
Secondary Objective	• Evaluate the plasma pharmacokinetics of CAB LA throughout the Injection and Long-term Follow-up Phases (Week 5 to Week 89). • Evaluate the safety and tolerability of oral CAB in HIV uninfected Chinese men during the oral lead-in Phase (Day 1 to Week 4) • Evaluate the acceptability of CAB LA injections through 41 weeks. • Explore concentration-effect relationships for various safety and tolerability parameters if relevant.
Secondary Endpoint	• Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F through Weeks 5-89. • Safety and tolerability parameters, including adverse events, study withdrawals due to AEs, vital signs assessments, and clinical laboratory assessments, for oral lead-in phase (Day 1 to Week 4). • Injection discontinuation rate, the number and severity of ISRs and additional acceptability measures. • Evaluation of relationships between significant safety and tolerability

Overview	Key Elements of the RAP
	parameters and CAB PK may be explored.
Study Design	• This will be an open label, non-randomized, single arm study. Participants will receive daily oral CAB (30mg tablets) for 4 weeks during the Oral Phase of the study and intramuscular (IM) injections of 600 mg of CAB LA at Week 5, Week 9, Week 17, Week 25 and Week 33. • Starting at 8 weeks post last injection, participants will be seen once every 12 weeks for 48 weeks during the follow-up phase. • Subjects who volunteer to participate in the intensive PK assessment will have serial blood sampling for measurement of plasma CAB concentrations following oral administration over a 24 h window starting on Day 27 and ending on Day 28 • PK samples at trough for Oral Phase will be collected for all subjects prior to dose within 20 to 28 hours following oral administration the day prior; Intensive oral PK samples will be collected from approximately 16 participants. • PK Samples for Injection Phase will be collected prior to CAB LA injections at Week 5, 9, 17, 25, and 33 with the exception of 1-week post injection samples at Weeks 6, 10, 18, 26, 34, 37 (4-week post injection sample) and Week 41 • Long-term follow up PK samples will be collected at Week 53, 65, 77, and 89.
Planned Analyses	• The primary safety analysis and PK analyses including both oral phase and injection phase through Weeks 5 to 41 will be performed after all ongoing participants complete the Week 41 visit or withdraw from the study treatment, whichever comes first. • The end of study analysis will be performed after all ongoing participants complete the Week 89 visit or withdraw from the study treatment, whichever comes first.
Analysis Populations	• The All Subjects Screened Population will include all subjects who consent to participate in the clinical study. Subjects in this population will be used for disposition summary • The Safety Population will include all subjects who receive at least one dose of the study treatment. Subjects in this population will be used for all demographic and safety summaries or listings, as well as for the analysis of acceptability of CAB LA. • Safety Injection Population will include all subjects received at least one CAB LA injection. Subjects in this population will be used to evaluate the safety and tolerability of CAB LA injection in primary analysis. • Oral PK Population: subjects in the 'Safety population' for whom an intensive oral pharmacokinetic sample was obtained and analysed. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of Oral PK data.

Overview	Key Elements of the RAP
	• Injection (Week 41) PK Population: subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 41. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of Injection PK data from Weeks 5 to 41. • Injection (Week 89) PK Population: subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 89. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of Injection PK data from Weeks 5 to 89.
Hypothesis	• No formal statistical hypotheses will be evaluated.
Primary Analyses	• To assess safety of CAB LA, the number and the percent of participants experiencing each safety endpoint will be tabulated including adverse events, clinical laboratory tests, study withdrawals due to AEs, and vital signs assessments. • To assess tolerability of CAB LA, the proportion of participants who terminate from receiving injections prior to the full course due to AE, intolerability of injection, frequency of injections, or burden of procedures related to injections out of those participants that received at least one injection. • To assess the plasma pharmacokinetics of CAB following repeat oral administration (Day 1 to Week 4) and CAB LA IM injections throughout the Injection Phase (Week 5 to Week 41).
Secondary Analyses	• To assess the plasma pharmacokinetics of CAB LA throughout the Injection and Long-term Follow-up Phases (Week 5 to Week 89). • To assess the safety and tolerability of oral CAB, each safety and tolerability endpoint will be tabulated including adverse events, study withdrawals due to AEs, vital signs assessments and clinical laboratory assessments. • To assess the acceptability of the CAB LA, injection discontinuation rate, the number and severity of ISRs, and the proportion (with 95% CI for the CAB LA arm) of participants who would consider using CAB LA for HIV prevention in the future will be tabulated among all enrolled participants (including those who terminated product use during the trial. • Overall treatment satisfaction score and answers to each individual question on HIV-PrevTSQc will be summarized to evaluate tolerability

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

The current adverse events of special interest (AESIs) included in the protocol are seizures and seizure like events, diarrhea, hypertriglyceridemia/hypercholesterolemia, decline in renal function, proximal renal tubule dysfunctions and proteinuria.

We are modifying the study AESIs to align them with the rest of the Cabotegravir programme, now that the AESIs related to CAB have now been fully developed.

The RAP AESIs will differ from the AESIs defined in the protocol. AESIs of hepatoxicity, hypersensitivity reactions, injection site reactions, impact on creatinine, and neuropsychiatric events have been added to the list of AESIs for the RAP.

The events of diarrhea, hypertriglyceridemia/hypercholesterolemia, have been removed for the list of AESIs in the RAP.

Seizures and seizure like events, Decline in renal function, proximal renal tubule dysfunctions, proteinuria, which were defined in the protocol, will be kept as the AESIs for the study.

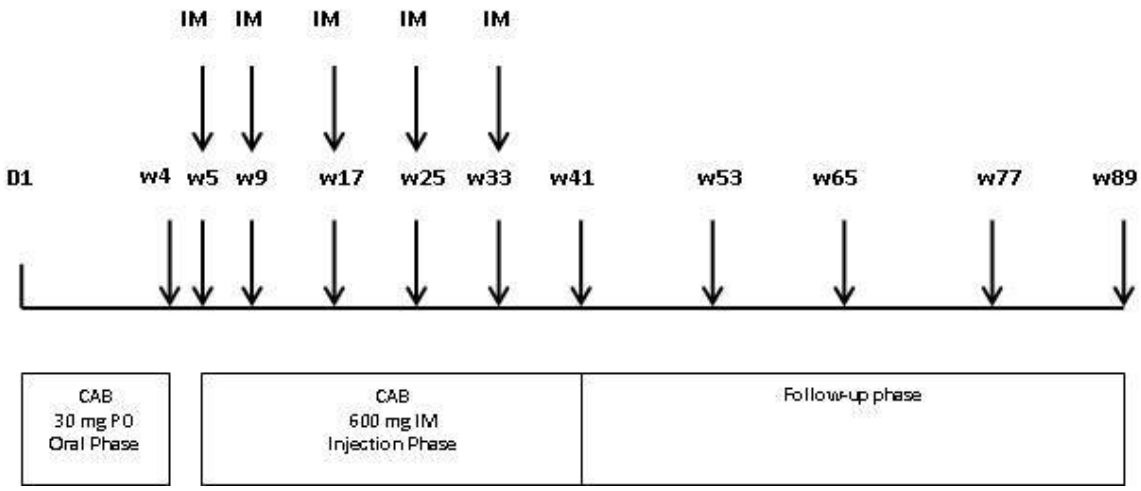
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
Evaluate the safety and tolerability of the injectable agent, cabotegravir (GSK1265744) long acting (CAB LA) injectable (600 mg dose administered every 4 weeks for 2 doses followed by every 8 weeks for 3 doses) through Week 5-41 in HIV-1 uninfected Chinese men.	Safety and tolerability parameters, including adverse events, clinical laboratory tests, study withdrawals due to AEs, vital signs assessments, and evaluation of injection site reactions (ISRs).
Evaluate the plasma pharmacokinetics of CAB following repeat oral administration (Day 1 to Week 4) and CAB LA IM injections throughout the Injection Phase (Week 5 to Week 41).	Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F at Week 4 following daily oral administration of CAB. Plasma CAB AUC(0-τ), Cmax, Cτ, and tmax at Week 41 following IM injections of CAB LA.
Secondary Objectives	**Secondary Endpoints**
Evaluate the plasma pharmacokinetics of CAB LA throughout the Injection and Long-term Follow-up Phases (Week 5 to Week 89)	Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F
Evaluate the safety and tolerability of oral CAB in HIV uninfected Chinese men during the oral lead-in Phase (Day 1 to Week 4)	Safety and tolerability parameters, including adverse events, study withdrawals due to AEs, vital signs assessments and clinical laboratory

Objectives	Endpoints
	assessments.
Evaluate the acceptability of CAB LA injections through 41 weeks.	Injection discontinuation rate, the number and severity of ISRs and additional acceptability measures.
Explore concentration-effect relationships for various safety and tolerability parameters if relevant.	Evaluation of relationships between significant safety and tolerability parameters and CAB PK may be explored.

2.3. Study Design

Overview of Study Design and Key Features



This study is an open label (OL) Phase 1, multi-site, study to evaluate the PK, safety, tolerability, and acceptability of CAB LA in adult male participants. Eligible participants will receive oral CAB tablets as well as open label CAB LA.

Design Features	Oral lead-in phase is from Day 1 to week 4; injection phase is from week 5 to week 41; and follow-up phase is from week 41 to week 89
Dosing	Oral CAB tablet is 30mg and dose level=1 tablet; CAB Sterile Suspension for Injection Vial is 200mg/mL and dose level = 600mg (3mL) Participants will receive daily oral CAB (30mg tablets) for 4 weeks during the Oral Phase of the study and IM injections of 600 mg of CAB LA at Week 5, Week 9, Week 17, Week 25 and Week 33.

Overview of Study Design and Key Features	
Treatment Assignment	Eligible participants will receive oral CAB tablets in the first four weeks, and will received CAB LA injections since Week 5 following planned schedules.
Interim Analysis	No interim analysis is planned in this study.

2.4. Statistical Hypotheses

No formal statistical hypotheses will be evaluated. The study is designed to evaluate the PK, safety, tolerability, and acceptability of the injectable agent, CAB LA (600 mg dose administered at 8-week intervals after 2 initial doses 4 weeks apart) in HIV-uninfected men in China where at least 60% of the men are of a population who have sex with men. Where appropriate, an estimation approach will be taken, and point estimates and confidence intervals will be constructed.

3. PLANNED ANALYSES

3.1. Interim Analyses

No formal interim analysis is planned in the study.

However, two preliminary PK analyses during the study will be performed in an informal manner. One will be after all planned participants complete the oral phase, and the other one will be after 50% of planned participants complete Week 17 visit. Safety data will be provided after all planned participants complete the oral phase as well. Study team will review preliminary safety and PK data.

3.2. Final Analyses

The primary safety analysis and PK analyses including both oral phase and injection phase through Weeks 5 to 41 will be performed after all ongoing participants complete the Week 41 visit and datasets have been authorized. Other secondary analyses as mentioned, where appropriate, will also be performed. The end of study analysis will be performed after all ongoing participants complete the Week 89 visit. All planned primary and secondary analyses will be included in the second formal analyses.

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

1. All subjects have completed the specific study visit (i.e. week 41 or week 89) as defined in the protocol.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects Screened	• Comprise of all subjects who consent to participate in the clinical study.	• Disposition summary
Safety	• Comprise of all subjects who receive at least one dose of the study treatment.	• All demographic • General safety analyses • Safety analysis for the oral phase • Analysis of acceptability of CAB LA
Safety Injection	• Comprise of all subjects received at least one CAB LA injection	• Safety and tolerability analyses of CAB LA in primary and extended analyses
Oral Pharmacokinetic (PK)	• Will consist of all subjects in the 'Safety population' for whom an intensive oral pharmacokinetic sample was obtained and analysed. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• Oral PK Concentration • Oral PK Parameters
Injection (Week 41) Pharmacokinetic (PK)	• Will consist of all subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 41. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• Injection PK Concentration • Injection PK Parameters
Injection (Week 89) Pharmacokinetic (PK)	• Will consist of all subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 89. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• Injection PK Concentration • Injection PK Parameters

NOTES:

Please refer to Appendix 14: List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.
    - Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 1 Overview of Appendices

Section	Component
10.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
10.2	Appendix 2: Time & Events
10.3	Appendix 3: Assessment Windows
10.4	Appendix 4: Treatment States and Phases
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
10.8	Appendix 8: Values of Potential Clinical Importance
10.9	Appendix 9: Multicenter Studies
10.10	Appendix 10: Examination of Covariates, Subgroups & Other Strata
10.11	Appendix 11: Multiple Comparisons & Multiplicity
10.12	Appendix 12: Model Checking and Diagnostics for Statistical Analyses.
10.13	Appendix 13: Abbreviations & Trade Marks
10.14	Appendix 14: List of Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The study population analyses will be based on the safety population, unless otherwise specified. All summary data and statistics are calculated from available data, unless otherwise specified.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Disposition			
Retention Rate and Reasons for Withdrawals	Y		Y
Demography and Baseline Characteristics			
General Demographics Characteristics	Y		Y
Medical History and Concomitant Medications			
Medical History	Y		Y
Prior Medications	Y		Y
Concomitant Medications	Y		Y
Protocol Deviations			
Deviation of Inclusion/Exclusion Criteria	Y		Y
Important Protocol Deviations	Y		Y

NOTES:
- Y = Yes display generated.

6.1.1. Disposition

The reasons of screening failure will be summarized based on the screened population. The number and percentage of each reason will be tabulated.

A summary of subject disposition by phase will be provided, including the number and percentage of subjects entering oral/injection phase, the number and percentage of subjects completing oral/injection phase and the number and percentage of subjects withdrawing from oral/injection phase.

Subject disposition data will be presented in a listing.

6.1.2. Demographics

General demographics including age, self-identified gender when entering the study, and ethnicity will be summarized.

A subject's age is calculated using the year part of informed consent form (ICF) – year of birth collected in CRF.

6.1.3. Medical History

Summaries of medical history will be presented by GSK pre-specified body system categories as collected in the eCRF. Number and percentage of subjects in each category will be tabulated.

6.1.4. Prior and Concomitant Medications

Medications will be coded to therapeutic drug classes and generic drug names using the GSKDRUG 1.4 or later. Medications initiated prior to the Day 1 of the study will be counted as prior medications. Concomitant medications are defined as medications that are taken on or after the Day 1. Medications initiated prior to the Day 1 and continued after the Day 1 will be counted as both prior and concomitant medications.

Summaries showing the number and percentage of subjects who take prior or concomitant medications will be presented by therapeutic drug class and generic drug name.

6.1.5. Protocol Deviation

Important protocol deviations (PD) will be summarized PD category and subcategory, and will also be presented in a listing. A separate summary table and a listing will be provided for subjects with deviation of the inclusion/exclusion criteria in the safety population

7. PRIMARY STATISTICAL ANALYSES

7.1. Safety Analyses of CAB LA

Four study phases are defined for this study: screening phase, oral phase, injection phase and follow-up phase (see Appendix 4 for the definition of each phase).

The primary safety analysis will be conducted after all ongoing participants complete the Week 41 visit and datasets have been authorized. All data from injected participants collected from Week 5 to Week 41 (i.e., in the injection phase) will be analysed. Analysis endpoints will include Grade 2 or higher clinical and laboratory events that occur from the initial injection to 8 weeks after the last injection among participants who receive at least one injection.

The extended safety analysis will be conducted after all ongoing participants complete the Week 89 visit and datasets have been authorized. All data from injected participants collected from Week 5 to Week 89 (i.e., in the injection phase and the follow-up phase) will be analysed. Analysis endpoints are the same as in the primary safety analysis.

To assess safety, the number and the percent of participants experiencing each safety endpoint will be tabulated. Each participant will contribute once in each category (i.e., only for the highest severity AE) for the evaluation of safety.

7.1.1. Injection Site Reaction

The number and percentage of participants experiencing each type of injection site reaction sign or symptom will be tabulated by severity from the safety injection population. For a given sign or symptom, each participant's ISR will be counted once under the maximum severity for all injection visits. Overall summary of ISR and summary of ISR by needle length will both be provided. ISR related details, such as cardiovascular activity, strength training exercise, will be listed only.

Table 3 provides an overview of the planned ISR analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 3 Overview of Planned ISR Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
ISR Analyses							
All ISR Symptoms				Y			Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.2. Adverse Events

Adverse events will be tabulated using MedDRA (v20.0 or above) system organ class (SOC) and preferred terms (PT), or preferred terms alone, by study phase. The number and percentage of participants experiencing each specific AEs (Grade 2 or higher, All AEs, SAEs, AEs leading to permanent treatment discontinuation or study withdrawal) will be tabulated. Number of subjects in the safety population who entered the study phase will be used as denominator in the calculation of percentages.

Drug-related AEs, SAEs, and Grade 2-4 AEs will also be tabulated. Any AE is assumed to be study treatment-related if relationship is marked 'YES' on CRF or value is missing. In addition, a summary table will be created for AEs by maximum severity by study phase. Common AEs are defined as AEs occurring in >=5% subjects during the study (based on preferred term). Common AEs, common non-serious AEs, common Grade 2-4 AEs, and common drug-related Grade 2-4 AEs will be tabulated.

All AE tables will be presented in a decreasing frequency order of SOC or PT unless otherwise specified.

Table 4 provides an overview of the planned AE analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 4 Overview of Planned AE Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
AE Analyses							
All AEs				Y			Y
Grade 2 or higher AEs				Y			Y
SAEs				Y			Y
AE leading to treatment discontinuation or study withdrawal				Y			Y
Drug-related AEs				Y			
Drug-related SAEs				Y			
Drug-related Grade 2 or higher AEs				Y			
Common AEs				Y			
Common non-serious AEs				Y			
Common Grade 2-4 AEs				Y			
Common drug-related Grade 2-4 AEs				Y			

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- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.3. Clinical Laboratory Tests

All clinical laboratory tests will be graded according to the Appendix 7 from the study protocol. Grade 2 or higher laboratory events will be tabulated by number and percentage of subjects with the event by study phase.

Change from baseline in hematology, fasting chemistry, fasting lipid profile, and coagulation profile will be summarized by visit. For the definition of baseline, refer to Section 10.5.2. Urinalysis and urine chemistry results will be summarized by visit as either categorical values or as continuous values, depending on the type of the parameter.

For each lab test, shift from baseline table will be provided based on toxicity grade, both by visit and for the shift to maximum toxicity grade in each study phase. Data collected at unscheduled visits will not be included in the by-visit summary, but will be used in the calculation of maximum grade in each study phase. Subjects having both high and low values will be counted in both High and Low categories for the summary by study phase.

All lab data, as well as lab data for subjects with Grade 2 or higher abnormalities, will be listed. Abnormal data will be listed with an indicator, which is low/high relative to normal range. All laboratory results from local labs, if any, will be listed only

Table 5 provides an overview of the planned lab test analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 5 Overview of Planned Lab Test Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Laboratory Test Analyses								
Grade 2 or high laboratory events	Y							
Clinical Chemistry				Y	Y			
Hematology				Y	Y			
Fasting Lipid Profile				Y	Y			
Coagulation Profile				Y	Y			
Urinalysis and Urine Chemistry	Y			Y	Y			
Other lab data including local lab				Y				

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- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.4. Vital Sign Assessments

Change from baseline in vital signs, including temperature, systolic and diastolic blood pressure, and pulse rate and respiratory rate will be summarized by study visit. For the

definition of baseline, refer to Section 10.5.2. Shift from baseline table (with respect to clinical concern range) will also be provided.

All vital signs, as well as vital signs for subjects with abnormalities of potential clinical importance, will be listed with an indicator, which is low/high relative to clinical concern range.

Table 6 provides an overview of the planned vital sign analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 6 Overview of Planned Vital Sign Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Vital Signs								
Vital signs				Y	Y			

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.5. Death

Both primary and secondary causes, if any, will be listed for each deceased participant.

Table 7 provides an overview of the planned death analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 7 Overview of Planned Death Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Death Analysis							
Death							Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.2. Tolerability Analyses of CAB LA

The tolerability analyses will be based on the safety injection population, unless otherwise specified. All summary data and statistics are calculated from available data, unless otherwise specified.

To assess tolerability of CAB LA, the proportion (with 95% confidence interval) of participants who terminate from receiving injections prior to the full course due to AE, intolerability of injection, frequency of injections, or burden of procedures related to injections will be calculated out of those participants that received at least one injection.

A questionnaire will also be used to assess participant tolerability and satisfaction to the treatment. For each question, the responses will be summarized by the proportion of participants reporting the response out of all those that answered the question. An overall treatment satisfaction score will be calculated for each participant.

Total score is defined as the sum of the scores for individual questions. If less than or equal to 50% of the questions for an individual participant are missing, the missing total scores will be estimated using the average of the existing questions multiplied by twelve; if more than 50% of the questions for an individual participant are missing, the total score will not be estimated and will be considered as missing. When calculating total scores, question CCI [redacted] will be used and question CCI [redacted] will be excluded.

Table 8 provides an overview of the planned tolerability analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 8 Overview of Planned Tolerability Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
CAB LA Discontinuation							
Injection Discontinuation Rate				Y			Y
Treatment Satisfaction Questionnaire							
Each question in the questionnaire				Y			Y
Treatment total satisfaction score				Y			Y

NOTES:
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- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data

7.3. Primary Pharmacokinetic Analyses

7.3.1. Overview of Planned Primary Pharmacokinetic Analyses

The primary pharmacokinetic (PK) analyses will be based on the Oral PK and Injection (Week 41) PK populations, unless otherwise specified.

Table 9 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 9 Overview of Planned Primary Pharmacokinetic Analyses

Display Type	Untransformed							Log-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Oral/Injection														
PK Concentrations				Y	Y [1]	Y [1]	Y							
Plasma PK Parameters	Y			Y			Y			Y	Y			

NOTES:
- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Linear and Semi-Logarithmic plots will be created on the same display.

7.3.2. Primary Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).

7.3.3. Primary Pharmacokinetic Parameters

7.3.3.1. Deriving Primary Pharmacokinetic Parameters

- Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin Version 6.4 or higher.
- All calculations of non-compartmental parameters will be based on actual sampling times, and all concentrations will be included in the estimation of PK parameters regardless of whether samples are collected within the specified time window or not.
- Pharmacokinetic parameters described in Table 10 will be determined from the plasma concentration-time data, as data permits.

Table 10 Derived Primary Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-τ)	Area under the concentration-time curve over the dosing interval 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.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
Cτ	Observed concentration at the end of the dosing interval, determined directly from the concentration-time data.
t½	Terminal absorption elimination half-life will be calculated as: $t_{½} = \ln 2 / \lambda z$
λz	Terminal absorption elimination rate constant
CL/F	Clearance (adjusted for bioavailability, F) will be calculated as: $CL/F = Dose / AUC(0-\tau)$
Vz/F	Volume of distribution (adjusted for bioavailability, F) will be calculated as: $Vz/F = CL / \lambda z$

NOTES:

- Additional parameters may be included as required.
- λz, CL/F, Vss and t½ will be determined for the Oral PK population only in the primary analysis; these parameters will be further explored for the Injection (Week 89) PK population (Section 8.1.3.1).

7.3.3.2. Statistical Analysis of Primary Pharmacokinetic Parameters

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

Pharmacokinetic Statistical Analyses
Endpoint(s)
• Plasma primary PK endpoints include Cτ, as data permit
Model Specification
Assessment of Accumulation (Injection Phase only): • To determine accumulation of plasma CAB following treatment with CAB LA, the log-transformed Cτ values for CAB will be analyzed using a mixed effects model (ANOVA) as appropriate to the study design, fitting fixed effect terms for visit and treating subject as a random effect. Point estimates and 90% confidence intervals (CIs) for the differences of interest (i.e. accumulation of CAB based on AUC(0-τ): Week 34 / Week 6) will be constructed using the residual variance. Attainment of Steady state (Injection Phase only): • If data permit, a statistical analysis of steady-state trough concentrations (Cτ) will be performed after log-transformation of Cτ on Weeks 17, 25, 33, and 41 to evaluate whether steady state was achieved using the Helmert transformation approach. A mixed effect model (ANOVA) will be fitted by visit (as a categorical covariate) as a fixed effect term and subject as a random effect term. The comparison will begin with Week 17 vs. the average of Weeks 25 through Week 41. If the p-value for Week 17 vs. the average of Week 25 through Week 41 comparison is ≤0.05 (i.e. steady state not achieved at Week 17), then the comparison will continue with Week 25 vs. Week 33 through Week 41.
Model Checking & Diagnostics
• Refer to Appendix 12: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Statistical analysis of accumulation of plasma CAB following treatment with CAB LA will be presented in tabular format with geometric mean ratios between Week 34 and Week 6, and 90% CIs for the ratios of Cτ for CAB. • In steady-state analysis, the ratio of Geometric LS means and its 95% CI will be presented for the comparison(s).

8. SECONDARY STATISTICAL ANALYSES

8.1. Secondary Pharmacokinetic Analyses

8.1.1. Overview of Planned Secondary Pharmacokinetic Analyses

The secondary pharmacokinetic (PK) analyses will be based on the Injection (Week 89) PK population, unless otherwise specified.

Table 11 provides an overview of the planned analyses, with full details being presented in Appendix 14: List of Data Displays.

Table 11 Overview of Planned Secondary Pharmacokinetic Analyses

Display Type	Untransformed							Log-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Oral/Injection														
PK Concentrations				Y	Y[1]	Y[1]	Y							
Plasma PK Parameters	Y			Y			Y			Y	Y			

NOTES:

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Linear and Semi-Logarithmic plots will be created on the same display.

8.1.2. Secondary Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).

8.1.3. Secondary Pharmacokinetic Parameters

8.1.3.1. Deriving Secondary Pharmacokinetic Parameters

- Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin Version 6.4 or higher.
- All calculations of non-compartmental parameters will be based on actual sampling times, and all concentrations will be included in the estimation of PK parameters regardless of whether samples are collected within the specified time window or not.
- Pharmacokinetic parameters described in Table 12 will be determined from the plasma concentration-time data, as data permits.

Table 12 Derived Secondary Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-τ)	Area under the concentration-time curve over the dosing interval 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.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
Cτ	Observed concentration at the end of the dosing interval, determined directly from the concentration-time data.
t½	Terminal absorption elimination half-life will be calculated as: $t_{½} = \ln 2 / \lambda z$
λz	Terminal absorption elimination rate constant
CL/F	Clearance (adjusted for bioavailability, F) will be calculated as: $CL/F = Dose / AUC(0-\tau)$
Vz/F	Volume of distribution (adjusted for bioavailability, F) will be calculated as: $Vz/F = CL / \lambda z$

NOTES:

- Additional parameters may be included as required.

8.2. Safety and Tolerability Analyses of Oral CAB

The safety and tolerability analyses of oral CAB will include Grade 2 or higher clinical and laboratory events occurred during the oral phase. Analysis time frame is from the first date of taking oral CAB tablet to the date right before the first CAB LA injection. For subjects who withdraw treatment from the oral phase, the analysis will include all safety and tolerability assessments from the first date of taking oral CAB tablet up to the date of last study visit.

Safety endpoints including adverse events, laboratory test, vital signs, and death will be analysed. The same analysis approaches will be conducted as in the primary analysis, but with different time frame.

Table 13 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 13 Overview of Planned AE, LB, VS, and Death Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
AE Analyses							
All AEs				Y			Y
Grade 2 or higher AEs				Y			Y
SAEs				Y			Y
AE leading to treatment discontinuation or study withdrawal				Y			Y
Drug-related AEs				Y			
Drug-related SAEs				Y			
Drug-related Grade 2 or higher AEs				Y			
Common AEs				Y			
Common non-serious AEs				Y			
Common Grade 2-4 AEs				Y			
Common drug-related Grade 2-4 AEs				Y			
Laboratory Tests							
Grade 2 or higher laboratory events				Y			
Clinical Chemistry				Y			Y
Hematology				Y			Y
Fasting Lipid Profile				Y			Y
Urinalysis				Y			Y
Coagulation Profile				Y			Y
Other lab data including local lab							Y
Vital Sign Analysis							
Vital Signs				Y			Y
Death Analysis							
Death							Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.3. Acceptability of CAB LA

The secondary acceptability analyses will be based on safety population, unless otherwise specified. All summary data and statistics are calculated from available data, unless otherwise specified.

To assess acceptability of the CAB LA, the proportion (with 95% confidence interval) of participants who would consider using CAB LA for HIV prevention in the future will be calculated among all subjects in the safety population (including those who terminated product use during the trial). Participants will be asked if they would consider using CAB LA for HIV prevention in the future at their Week 41 visit or at their withdrawal visit, whichever occurs first. Patients who are lost to follow up or with missing responses will be presented as such in a separate category.

Table 14 provides an overview of the planned acceptability analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 14 Overview of Planned Acceptability Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Acceptability of the CAB LA							
participants who would consider using CAB LA				Y			Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.4. Concentration-effect Relationships for Safety and Tolerability Parameters

Evaluation of relationships between significant safety and tolerability parameters and CAB PK may be explored.

8.5. General Safety Analyses

This section will describe safety analyses that are not mentioned in Section 7.1 or Section 8.2, but usually are performed as safety assessment.

8.5.1. Extent of Exposure to CAB

Duration of exposure to CAB and cumulative dose (see Section 10.6.2 for the definition) will be summarized for the oral phase and the injection phase separately. Overall exposure to the study drug and to the study (for safety evaluation) will also be calculated and summarized. Exposure data will also be listed.

Table 15 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 15 Overview of Planned Analyses for Extent of Exposure

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Extent of Exposure							
Extent of exposure				Y			Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.5.2. Possible suicidality-related Adverse Events

Possible suicidality-related will be listed.

Table 16 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 16 Overview of Analyses for possible suicidality-related AEs

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
AE Analyses							
Possible Suicidality-Related Adverse Event							Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.5.3. Social Harms

Details of social harms collected on the eCRF will be listed for each participant.

Table 17 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 17 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Social Harms			
All Social Harms			Y

NOTES:
- Y = Yes display generated.

8.5.4. ECG

ECG test will be performed at Screening only. Details collected on the eCRF will be listed for each subject. Baseline ECG findings (normal, abnormal – not clinically significant, or abnormal - clinically significant) will be summarized by number and percentage of subjects and presented as part of the 'Demographic Characteristics' table.

Table 18 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 18 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
ECG			
ECG Parameters and Results	Y		Y

NOTES:
- Y = Yes display generated.

8.5.5. Cardiovascular Events

Any cardiovascular events will be listed only.

Table 19 provides an overview of the planned cardiovascular event analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 19 Overview of Planned Cardiovascular Event Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
CV Event Analyses							
All CV events							Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.5.6. Liver Events

Number and percentage of subjects with liver events will be tabulated by study phase. Number and percentage of subjects with clinical significant hepatobiliary laboratory abnormalities during the study will also be tabulated. Full information of liver events will be listed.

Table 20 provides an overview of the planned liver event analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 20 Overview of Planned Liver Event Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Liver Event Analyses							
All liver events				Y			Y
Hepatobiliary laboratory abnormalities				Y			

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

9. REFERENCES

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10. APPENDICES

Section	Appendix
RAP Section 4 : Analysis Populations	
Section 10.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
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Section 10.12	Appendix 12: Model Checking and Diagnostics for Statistical Analyses
Other RAP Appendices	
Section 10.13	Appendix 13: Abbreviations & Trade Marks
Section 10.14	Appendix 14: List of Data Displays

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

Protocol waivers or exemptions are not allowed with the exception of immediate safety concerns that may arise after the oral administration of CAB.

Deviations from inclusion and exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or participant safety. Therefore, adherence to the criteria as specified in the protocol is essential

10.1.1. Exclusions from Per Protocol Population

Not applicable. Per protocol population is not defined in this study.

10.2. Appendix 2: Time & Events

10.2.1. Protocol Defined Time & Events

Table 21 Schedule of Activities[q]

Clinical Assessments	Screening[a]	Oral Phase[m]		Injection Phase												Follow-up Phase & Final Visit	
		Day 1	Day 28 (Week 4)	Day 35 (Week 5) Injection 1	Day 42 (Week 6)	Week 9 Injection 2	Week 10	Week 17 Injection 3	Week 18	Week 25 Injection 4	Week 26	Week 33 Injection 5	Week 34	Week 37	Week 41	Week 53, 65, 77	Week 89
Written informed consent	X																
Inclusion/Exclusion criteria[b]	X																
Demographic information	X																
Full physical exam/medical history[c]	X																X
Brief physical exam		X	X	X	X	X	X	X	X	X	X	X	X		X		
Height/weight/BMI[d]	X																X
Medication/drug/alcohol history	X																
HIV counseling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Offer condoms and lubricant	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dispense oral study medication (with counseling)[e]		X															
Drug accountability (pill counts)		X	X														

Clinical Assessments	Screening[a]	Oral Phase[m]		Injection Phase												Follow-up Phase & Final Visit	
		Day 1	Day 28 (Week 4)	Day 35 (Week 5) Injection 1	Day 42 (Week 6)	Week 9 Injection 2	Week 10	Week 17 Injection 3	Week 18	Week 25 Injection 4	Week 26	Week 33 Injection 5	Week 34	Week 37	Week 41	Week 53, 65, 77	Week 89
CAB LA Injection (with counseling)				X		X		X		X		X					
HIV-PrevTSQc[f]							X										
ISR AE Diary[g]				X		X		X		X		X					
AE		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SAE review (SAE will be collected from the signing of ICF)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication check		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs[h]	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Qualitative HIV RNA by NAAT[i]	X																
HIV PoC test[j]	X	X		X		X		X		X		X			X	X	X
ECG[k]	X																
HbsAg and HbsAb, HCV Antibody	X																
Hematology/Chemistry testing	X	X	X	X	X	X		X		X		X			X		X
Urinalysis	X														X		
Urine screen for Chlamydia and gonorrhea	X																
Liver Chemistry Tests[l]																X	

Clinical Assessments	Screening[a]	Oral Phase[m]		Injection Phase												Follow-up Phase & Final Visit	
		Day 1	Day 28 (Week 4)	Day 35 (Week 5) Injection 1	Day 42 (Week 6)	Week 9 Injection 2	Week 10	Week 17 Injection 3	Week 18	Week 25 Injection 4	Week 26	Week 33 Injection 5	Week 34	Week 37	Week 41	Week 53, 65, 77	Week 89
Fasting lipid profile		X													X		
Coagulation testing	X														X		
TRUST for Syphilis screen	X																
Plasma for CAB concentration[m,n,o]			X[m]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Plasma storage sample[p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

AE: Adverse events, BMI: Body mass index, CAB: Cabotegravir, CAB LA: Cabotegravir long-acting, ECG: Electrocardiogram, HbsAg: Hepatitis B surface antigen, HIV: Human Immunodeficiency Virus, HCV: Hepatitis C Virus, ISR: Injection site reactions, SAE: Serious adverse event, HIV-PrevTSQc: HIV-Prevention Treatment Satisfaction Questionnaire (change): TRUST: Toluidine Red Unheated Serum Test, RNA: Ribonucleic acid.

a. Screening (including drug screen) is to be performed within 30 days of the first dose in the Oral Phase of the study. See Appendix 2 from the study protocol
b. Inclusion/exclusion criteria will be fully assessed at the Screening visit. Changes between the screening visit and the Day 1 visit should be assessed to ensure eligibility, including additional assessments performed at Day 1.
c. A full physical exam will be performed at Week 89.
d. Weight will be collected at Screening and at Week 89. Height and BMI will be collected at Screening only.
e. Oral phase consists of 28 days with a 7 day washout period between Day 28 (last oral dose) and Day 35 (first injection visit).
f. HIV-PrevTSQc: HIV-Prevention Treatment Satisfaction Questionnaire (change) will be given at Week 10 only (after 2nd injection).
g. ISR AE 7 Day Post Injection Diary will be distributed at the injection visit at Week 5, 9, 17, 25 and 33 and returned to the clinic at weeks 6, 10, 18, 26, and 34. For participants having ISR on the last day of week 5, 9, 17, 25 and 33, additional ISR AE Weeks 2 – 12 Post Injection Diary will be distributed at weeks 6,10, 18, and 26,34. Participants will be asked to bring the diary to each clinic visit.
h. Vital sign measurements will be performed following 5 minutes of rest.
i. Qualitative HIV Nucleic Acid Amplification Testing (NAAT) will be performed at Screening. See Appendix 9 from the study protocol for the HIV testing algorithm at screening, Day 1 and during the course of the study.

j. HIV PoC (Point of care) test will be performed at each time point during the course of the study and must be reviewed prior to IM dosing. See Appendix 9 from the study protocol for the HIV testing algorithm at screening, Day 1 and during the course of the study.

k. ECGs will be performed following 5 minutes of rest in a semi-supine position.

l. Liver Chemistry Tests include Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Bilirubin total and direct.

m. Oral Pharmacokinetic (PK) sampling at trough will be collected for all subjects prior to dose within 20 to 28 hours following oral administration the day prior. Intensive oral PK sampling will be collected from approximately16 participants as shown in Table 20.

n. PK sampling for Injection phase: All PK samples will be collected prior to CAB LA injections at Week 5, 9, 17, 25, and 33 with the exception of 1-week post injection samples at Weeks 6, 10, 18, 26, 34, 37 (2-week post injection sample) and Week 41

o. Long-term follow up PK samples: PK sampling during follow up will occur at, Week 53, 65, 77, and 89.

p. Additional testing is required for participants who have a reactive or positive HIV test after enrolment. Stored plasma from the visit previous to the positive test should be tested for HIV using the 4th generation HIV test to best estimate time of infection. HIV acquisition must be confirmed by either western blot, HIV ½ Multispot or the Geenius HIV Confirmation ½ Assay, and HIV RNA.

q. Visit may occur in a window ±3 Day

Table 22 Schedule of Intensive Oral PK (Approximately 16 Participants) [a,b]

	Day 25	Day 26	Day 27							Day 28	
	Check- in	Oral dose administered (e.g. 8AM)	Prior to oral dose (e.g. 7:55AM)	Oral dose administered (e.g. 8AM)	1-hour post dose (e.g. 9AM)	2-hour post dose (e.g. 10AM)	3-hour post dose (e.g. 11AM)	4-hour post dose (e.g. 12AM)	8-hour post dose (e.g. 4PM)	24-hour post dose (e.g. 8AM)	Oral dose administered (e.g. after 8 AM)
Plasma for CAB concentration			X		X	X	X	X	X	X	

a. PK sampling may occur ± 15min

b. Central lab tests for the intensive oral PK subjects refer to Table 21.

10.3. Appendix 3: Assessment Windows

10.3.1. Assessment Windows

The nominal visit information collected on CRF will be used in the analysis. Analysis visit based on the time window will not be defined in this study.

10.4. Appendix 4: Study Phase and State

10.4.1. Treatment Phases

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

Treatment Phase	Definition
Screening Phase	Date < Date of first Oral CAB
Oral Phase	Date of First Oral CAB <= Date <= Date of First CAB LA Injection -1 day; for subjects who discontinued before receiving CAB LA Injection, the end date of the oral phase is the date of last study visit.
Injection Phase	Date of First CAB LA Injection <= Date <= 8 weeks after Last CAB LA Injection
Follow-up Phase	Date > 8 weeks after Last CAB LA Injection

10.4.2. Treatment States

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

10.4.2.1. Treatment States for AE Data

Treatment State	Definition
Screening Phase	AE Start Date < Date of First Oral CAB
On-Oral CAB-Treatment	Day 1 ≤ AE Start Date ≤ Date of First CAB LA Injection – 1; for subjects who withdraw from oral CAB treatment, Day 1 ≤ AE Start Date ≤ Withdrawal date + 7 days
On-CAB LA-treatment	Date of First CAB LA Injection ≤ AE Start Date ≤ Date of Week 41 Visit ; for subjects who withdraw from CAB LA injection, Date of First CAB LA Injection ≤ AE Start Date ≤ Date of Last CAB LA Injection + 8 Weeks
Post-Treatment	AE Start Date > Date of Last CAB LA Injection + 8 weeks
Onset Time Since 1st Dose (Days)	If Date of First Oral CAB (or CAB LA injection) >AE Onset Date, duration = AE Onset Date - Treatment Start Date If Date of First Oral CAB (or CAB LA injection) ≤ AE Onset Date, duration = AE Onset Date - Treatment Start Date +1 Missing otherwise.
AE Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on CRF OR value is missing

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
Study Group		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	CAB PO 30 mg QD	CAB 30 mg	1
B	CAB LA IM 600 mg Q8W	CAB LA 600 mg	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

10.5.2. Baseline Definition & Derivations

10.5.2.1. Baseline Definitions

The baseline or pre-dose assessment is the last available assessment prior to the time of the first dose unless it is specified otherwise.

10.5.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]
Maximum Change from Baseline	= Calculate the change from baseline at each given timepoint and determine the maximum change

NOTES:

- Unless otherwise specified, the baseline definitions specified in Section 10.5.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

10.5.3. Reporting Process & Standards

Reporting Process
Software
• The currently supported versions of SAS software 9.2 or higher and Phoenix WinNonlin will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards SDTMIG v3.2 & ADaMIG v1.0 • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.

Reporting Process
Generation of RTF Files
• RTF files will be generated for the TLFs. But only compiled PDF file will be used in the delivery.

Reporting Standards	
General	
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics	
Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • 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 : • Nominal visits collected on the eCRF will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate. • Reporting for Data Listings: • Planned and actual time relative to study drug dosing will be shown in Pharmacokinetic listings (Refer to IDSL Statistical Principle 5.05.1). • Unscheduled or unplanned readings will be presented within the subject's listings. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	
Unscheduled Visits	
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)

Reporting Standards	
Reporting of Pharmacokinetic Parameters	

• Reporting for PK tables, figures and listings:
  • Planned time relative to dosing will be used in mean concentration-time figures and summaries, and actual times will be used for individual concentration-time figures.
  • 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.
  • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in all PK figures, summaries and listings.	

Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and [between and or within] geometric coefficient of variation (CV_b (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)
Parameters Not Being Log Transformed	tmax, first point, last point, and number of points used in the determination of λz.
Summary Tables	The following PK parameters will not be summarised: first point, last point, and number of points used in the determination of λz
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Time Point
• If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target then the mean will be taken. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from Day 1 Visit:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Date of Day 1 Visit → Study Day = Ref Date –Date of Day 1 Visit
  • Ref Date ≥ Date of Day 1 Visit → Study Day = Ref Date –Date of Day 1 Visit + 1

10.6.2. Study Population

Demographics
Age
• As the month and date of birth will not be collected in the study, the age will be calculated as Year of ICF – Year of Birth; • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height $(m)^2$]

Extent of Exposure

• Duration of exposure to study drug will be calculated based on the formula:
  ○ The duration of exposure for oral phase is defined as the number of days starting from the first oral dose to the last oral dose.
  ○ Duration of exposure for injection phase is defined as the number of injections (1, 2, 3, 4 or 5)
  ○ Overall exposure to CAB is defined as number of days from the first oral dose to 8 weeks following the participant's last injection. If a participant does not enter the injection phase, the overall CAB exposure for the study will be defined as the number of days from the first oral dose to the last oral dose.
  ○ Overall exposure to the study (for safety evaluation) is defined as number of days from the first dose to last visit (including unscheduled visit) in days.
 	
• The cumulative dose will be based on the formula:
  ○ Cumulative dose in oral phase is defined as (number of tablets dispensed – number of tablets returned) * 30 mg

Extent of Exposure
○ Cumulative dose in injection phase is defined as number of injections * 600 mg

10.6.3. Safety

Adverse Events
Adverse Events of Special Interest
• Seizures and seizure like events • Decline in Renal Function • Proximal Renal Tubule Dysfunctions • Proteinuria • Hepatoxicity • Hypersensitivity Reactions • Injection Site Reactions • Impact on Creatinine • Neuropsychiatirc Events The adverse events of special interest that were used for data summaries are provided in Section 10.16

Laboratory Parameters
• HIV-1 RNA: For summaries and analyses which use HIV-1 RNA level as a continuous measure, the logarithm to base 10 of the value will be used. • 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

10.7. Appendix 7: Premature Withdrawals & Handling of Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completing all phases of the study including week 89. • If participants prematurely discontinue the oral phase of the study, additional replacement participants may be recruited at the discretion of the Sponsor. Participants who enter the injection phase of the study will not be replaced • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.7.2. 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 using a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.
	  ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.
	• Missing endpoints which are not covered in the following rule will not be imputed, unless otherwise specified.

Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Partial missing start or end dates will be imputed using the convention specified in Section 10.7.2.2 Handling of Partial Dates

10.7.2.2. Handling of Partial Dates

Element	Reporting Detail
Concomitant	• Partial dates for any concomitant medications recorded in the CRF will be

Element	Reporting Detail
Medications	imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.
Adverse Events	• Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. ○ However, if these results in a date prior to Week 1 Day 1 and the event could possibly have occurred during treatment from the partial information, then the Week 1 Day 1 date will be assumed to be the start date. The AE will then be considered to start on-treatment (worst case). ○ 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, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • The recorded partial date will be displayed in listings.

10.7.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
N/A	No statistical analysis is planned, unless otherwise specified.

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values

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

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

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

10.8.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	> 450 [1]	
		> 450 [1]	≤ 479 [1]
		≥ 480 [1]	≤ 499 [1]
		≥ 500 [1]	
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec	> 60 [1]	
	msec	> 30 [1]	≤ 59 [1]
	msec	≥ 60 [1]	

NOTES: [Remove footnotes for RAP development]
1. Represent standard ECG values of PCI for HV studies
2. Represent further subdivisions of ECG values for analysis whereby the RAP team needs to decide whether these need to be generated in addition to standard ECG values being flagged. IF not required, then delete.

10.8.3. Vital Signs

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

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper
Systolic Blood Pressure	mmHg	≥ 20	≥ 40	≥ 20	≥ 40
Diastolic Blood Pressure	mmHg	≥ 10	≥ 20	≥ 10	≥ 20
Heart Rate	bpm	≥ 15	≥ 30	≥ 15	≥ 30

NOTES: [Remove footnotes for RAP development]
Represent further subdivisions of BP & HR for analysis whereby the RAP team needs to decide whether these need to be generated in addition to standard absolute BP & HR values being flagged. IF not required, then delete.

10.9. Appendix 9: Multicenter Studies

10.9.1. Methods for Handling Centres

- In this multicentre study, enrolment will be presented by investigative site.

10.10. Appendix 10: Examination of Covariates, Subgroups & Other Strata

10.10.1. Handling of Covariates, Subgroups & Other Strata

- Demographic covariates that may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses.
- Additional covariates of clinical interest may also be considered.

10.11. Appendix 11: Multiple Comparisons & Multiplicity

10.11.1. Handling of Multiple Comparisons & Multiplicity

Not applicable.

10.12. Appendix 12: Model Checking and Diagnostics for Statistical Analyses

10.12.1. Statistical Analysis Assumptions

Endpoint(s)	• PK endpoint C_τ
Analysis	• ANOVA (primary)
• Model assumptions will be applied, but appropriate adjustments maybe 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.	

10.13. Appendix 13: Abbreviations & Trade Marks

10.13.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AUC(0-τ)	Area under the concentration-time curve (AUC) over the dosing interval
Cτ	The observed concentration at the end of the dosing interval
CAB	Cabotegravir
CAB LA	Cabotegravir Long Acting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL/F	The apparent clearance (adjusted for bioavailability, F)
Cmax	Maximum observed concentration
CSR	Clinical Study Report
CTMS	Clinical Trial Management System
CV_b	Coefficient of Variation (Between)
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
GSK	GlaxoSmithKline
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IM	Intramuscular
IP	Investigational Product
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligrams
PCI	Potential Clinical Importance
PK	Pharmacokinetic
PrEP	Pre-exposure prophylaxis
QC	Quality Control
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SAS	Statistical Analysis Software
SD	Standard deviation
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
t½	Terminal phase half-life
tmax	Time to first occurrence of Cmax
TFL	Tables, Figures & Listings
Vz/F	The volume of distribution associated with the terminal phase (adjusted for bioavailability, F)
λz	Terminal-phase rate constant

10.13.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

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

10.14. Appendix 14: List of Data Displays

10.14.1. Data Display Numbering

The following numbering will be applied for RAP generated display according to ICH standards:

Section	Tables	Figures
Study Population	1.1 to 1.10	NA
Safety	2.1 to 2.32	NA
Pharmacokinetic	3.1 to 3.11	3.1-3.8
Section	**Listings**	
ICH Listings	1-51	

10.14.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 15: 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

NOTES:

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

10.14.3. Deliverable [Priority]

Delivery [Priority] [1]	Description
W41 SAC [1]	Primary Statistical Analysis Complete at Week 41
SAC [1]	Final Statistical Analysis Complete at Week 89

NOTES:

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

10.14.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population, Disposition and Demographics					
1.1	Screened	SP1	Summary of Study Population		W41 SAC [1], SAC [1]
1.2	Screened	ES6	Summary of Screen Status and Reasons for Screen Failures		W41 SAC [1], SAC [1]
1.3	Screened	ES1	Summary of Subject Disposition for the Subject Conclusion Record		W41 SAC [1], SAC [1]
1.4	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment		W41 SAC [1], SAC [1]
1.5	Safety	DM1	Summary of Demographic Characteristics		W41 SAC [1], SAC [1]
Medical History and Concomitant Medications					
1.6	Safety	MH4	Summary of Medical Conditions	.	W41 SAC [1], SAC [1]
1.7	Safety	CM1	Summary of Prior Medications		W41 SAC [1], SAC [1]
1.8	Safety	CM1	Summary of Concomitant Medications		W41 SAC [1], SAC [1]
Protocol Deviations					
1.9	Safety	IE1	Summary of Inclusion/Exclusion Criteria Deviations		W41 SAC [1], SAC [1]
1.10	Safety	DV1A	Summary of Important Protocol Deviations		W41 SAC [1], SAC [1]

10.14.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
2.1	Safety	EX1	Summary of Extent of Exposure		W41 SAC [1], SAC [1]
Injection Site Reactions					
2.2	Safety Injection		Summary of Injection Site Reaction		W41 SAC [1], SAC [1]
Adverse Events					
2.3	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term		W41 SAC [1], SAC [1]
2.4	Safety	AE5B	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term		W41 SAC [1], SAC [1]
2.5	Safety	AE3	Summary of All Grade 2 or Higher Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.6	Safety	AE3	Summary of Serious Adverse Events		W41 SAC [1], SAC [1]
2.7	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		W41 SAC [1], SAC [1]
2.8	Safety	AE3	Summary of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study		W41 SAC [1], SAC [1]
2.9	Safety	AE1	Summary of Drug-Related Adverse Events		W41 SAC [1], SAC [1]
2.10	Safety	AE1	Summary of Drug-Related Serious Adverse Events		W41 SAC [1], SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.11	Safety	AE3	Summary of Drug-related Grade 2 or Higher Adverse Events		W41 SAC [1], SAC [1]
2.12	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.13	Safety	AE15	Summary of Common (>=5%) Non-Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		W41 SAC [1], SAC [1]
2.14	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.15	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
Laboratory Tests					
2.16	Safety		Summary of Grade 2 or Higher Laboratory Tests		W41 SAC [1], SAC [1]
2.17	Safety	ES11	Summary of Characteristics of Adverse Events of Special Interest		W41 SAC [1], SAC [1]
2.18	Safety	LB1	Summary of Change from Baseline in Hematology and Coagulation Data		W41 SAC [1], SAC [1]
2.19	Safety	LB1	Summary of Change from Baseline in Chemistry Data and Fasting Lipid Profile		W41 SAC [1], SAC [1]
2.20	Safety	UR3	Summary of Urinalysis and Urine Chemistry Results		W41 SAC [1], SAC [1]
2.21	Safety	LB18	Summary of Hematology and Coagulation Grade Shifts from Baseline Grade		W41 SAC [1], SAC [1]
2.22	Safety	LB18	Summary of Chemistry and Fasting Lipid Profile Grade Shifts from Baseline Grade		W41 SAC [1], SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.23	Safety	LB18	Summary of Urinalysis Grade Shifts from Baseline Grade		W41 SAC [1], SAC [1]
Vital Signs					
2.24	Safety	VS1	Summary of Change from Baseline in Vital Signs		W41 SAC [1], SAC [1]
2.25	Safety	VS8	Summary of Vital Sign Shifts from Baseline with Respect to Clinical Concern Range		W41 SAC [1], SAC [1]
Liver Events					
2.26	Safety	LIVER1	Summary of Liver Events Reporting		W41 SAC [1], SAC [1]
2.27	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities		W41 SAC [1], SAC [1]

10.14.6. Tolerability Tables

Tolerability: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Tolerability of CAB Injection					
2.28	Safety Injection		Summary of HIV-Prevention Treatment Satisfaction Scores		W41 SAC [1], SAC [1]

10.14.7. Acceptability Tables

Acceptability: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Acceptability of the CAB Injection					
2.29	Safety		Summary of Acceptability of the CAB LA		W41 SAC [1], SAC [1]

10.14.8. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Oral Phase					
3.1	Oral PK	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data – Oral Phase		SAC [1]
3.2	Oral PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) – Oral Phase	Parameters with units	SAC [1]
3.3	Oral PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Log-Transformed) – Oral Phase	Parameters with units	SAC [1]
Injection Phase (up to Week 41)					
3.4	Injection (Week 41) PK	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.5	Injection (Week 41) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) – Injection Phase (up to Week 41)	Parameters with units	W41 SAC [1], SAC [1]
3.6	Injection (Week 41) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Log-Transformed) – Injection Phase (up to Week 41)	Parameters with units	W41 SAC [1] SAC [1]
3.7	Injection (Week 41) PK	PKPT3	Statistical Analysis of CAB Plasma Accumulation – Injection Phase (up to Week 41)	$C\tau$ only for Injection Phase at Week 41.	W41 SAC [1], SAC [1]
3.8	Injection (Week 41) PK	PKPT3	Statistical Analysis of CAB Plasma Steady-state Pre-dose Concentrations – Injection Phase (up to Week 41)	$C\tau$ only for Injection Phase at Week 41.	W41 SAC [1], SAC [1]

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Injection Phase (up to Week 89)					
3.9	Injection (Week 89) PK	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 89)		SAC [1]
3.10	Injection (Week 89) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) – Injection Phase (up to Week 89)	Parameters with units	SAC [1]
3.11	Injection (Week 89) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Log-Transformed) – Injection Phase (up to Week 89)	Parameters with units	SAC [1]

10.14.9. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Oral Phase					
3.1	Oral PK	PKCF1P	Individual CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Oral Phase		SAC [1]
3.2	Oral PK	PKCF4	Mean (±SD) CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Oral Phase		SAC [1]
Injection Phase (up to Week 41)					
3.3	Injection (Week 41) PK	PKCF1P	Individual CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.4	Injection (Week 41) PK	PKCF4	Mean (±SD) CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.5	Injection (Week 41) PK	PK26	Individual CAB Plasma Pre-dose Concentration versus Week (Linear and Semi-Logarithmic) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.6	Injection (Week 41) PK	PK27	Median (range) CAB Plasma Pre-dose Concentration versus Week (Linear and Semi log) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
Injection Phase (up to Week 89)					
3.7	Injection (Week 89) PK	PKCF1P	Individual CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 89)		SAC [1]
3.8	Injection (Week 89) PK	PKCF4	Mean (±SD) CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 89)		SAC [1]

10.14.10. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population, Disposition and Demographics					
1	Screened	SP3	Listing of Subjects Excluded from Any Population		W41 SAC [1], SAC [1]
2	Screened	ES7	Listing of Reasons for Screen Failure		W41 SAC [1], SAC [1]
3	Safety	ES2	Listing of Reasons for Withdrawal		W41 SAC [1], SAC [1]
4	Safety	SD2	Listing of Study Drug Discontinuation Record		W41 SAC [1], SAC [1]
5	Safety	DM2	Listing of Demographic Characteristics		W41 SAC [1], SAC [1]
6	Safety	EX3	Listing of Exposure Data – Oral Dose		W41 SAC [1], SAC [1]
7	Safety		Listing of Exposure Data – Injection		W41 SAC [1], SAC [1]
Medical History and Concomitant Medication					
8	Safety	MH2	Listing of Medical Conditions		W41 SAC [1], SAC [1]
9	Safety	CM5	Listing of Prior Medications		W41 SAC [1], SAC [1]
10	Safety	CM5	Listing of Concomitant Medications		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Protocol Deviations					
11	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		W41 SAC [1], SAC [1]
12	Safety	DV2	Listing of Important Protocol Deviations		W41 SAC [1], SAC [1]
Injection Site Reaction					
13	Safety Injection		Listing of Injection Site Reaction – Daily Diary Card 1		W41 SAC [1], SAC [1]
14	Safety Injection		Listing of Injection Site Reaction – Daily Diary Card 2		W41 SAC [1], SAC [1]
Adverse Events					
15	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		W41 SAC [1], SAC [1]
16	Safety	AE8	Listing of All Adverse Events		W41 SAC [1], SAC [1]
17	Safety	AE8CPA	Listing of Serious Adverse Events (Fatal and Non-Fatal)		W41 SAC [1], SAC [1]
18	Safety	AE8	Listing of Grader 2 or Higher Adverse Events		W41 SAC [1], SAC [1]
19	Safety	AE8	Listing of All Adverse Events Leading to Premature Discontinuation of Study Drug or Withdrawal from Study		W41 SAC [1], SAC [1]
20	Safety	AE8	Listing of Adverse Events of Special Interest		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
21	Safety		Listing of Possible Suicidality-Rated Adverse Events		W41 SAC [1], SAC [1]
22	Safety	AE2	Listing of Relationship Between System Organ Classes and Verbatim Text		W41 SAC [1], SAC [1]
23	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event		W41 SAC [1], SAC [1]
Deaths					
24	Safety		Listing of Death		W41 SAC [1], SAC [1]
Laboratory Tests					
25	Safety	LB5	Listing of Chemistry Data and Fasting Lipid Profile		W41 SAC [1], SAC [1]
26	Safety	LB5	Listing of Hematology and Coagulation Data		W41 SAC [1], SAC [1]
27	Safety	UR2a	Listing of Urinalysis and Urine Chemistry Data		W41 SAC [1], SAC [1]
28	Safety	LB5	Listing of Laboratory Data for Subjects with Grade 2 or Higher Abnormalities		W41 SAC [1], SAC [1]
29	Safety	LB14	Listing of HIV Tests		W41 SAC [1], SAC [1]
30	Safety	LB5	Listing of Local Lab Data		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Sign					
31	Safety	VS4	Listing of Vital Signs		W41 SAC [1], SAC [1]
32	Safety	VS4	Listing of Vital Signs for Subjects with Any Value of Potential Clinical Importance		W41 SAC [1], SAC [1]
ECG's					
33	Safety		Listing of ECG Results		W41 SAC [1], SAC [1]
Social Harm					
34	Safety		Listing of Social Harm		W41 SAC [1], SAC [1]
Cardiovascular Event					
35	Safety		Listing of Cardiovascular Event		W41 SAC [1], SAC [1]
Liver Event					
36	Safety		Listing of Liver Event		W41 SAC [1], SAC [1]
Tolerability of CAB Injection					
37	Safety Injection		Listing of HIV-Prevention Treatment Satisfaction Questionnaire		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Acceptability of the CAB Injection					
38	Safety		Listing of Acceptability of the CAB LA		W41 SAC [1], SAC [1]
Pharmacokinetic					
39	Oral PK	PKCL1P	Listing of CAB Plasma Pharmacokinetic Concentration-Time Data – Oral Phase	Please list all the concentration data including unscheduled.	SAC [1]
40	Oral PK	PKPL1P	Listing of Derived CAB Plasma Pharmacokinetic Parameters – Oral Phase		SAC [1]
41	Injection (Week 41) PK	PKCL1P	Listing of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 41)	Please list all the concentration data including unscheduled.	W41 SAC [1], SAC [1]
42	Injection (Week 41) PK	PKPL1P	Listing of Derived CAB Plasma Pharmacokinetic Parameters – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
43	Injection (Week 89) PK	PKCL1P	Listing of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 89)	Please list all the concentration data including unscheduled.	SAC [1]
44	Injection (Week 89) PK	PKPL1P	Listing of Derived CAB Plasma Pharmacokinetic Parameters – Injection Phase (up to Week 89)		SAC [1]

10.14.11. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**

10.15. Appendix 15: Example Mock Shells for Data Displays

Data Display Specification will be made available on Request

10.16. Appendix 16: Adverse Events of Special Interest Used for Data Summaries

AESI Item	Product of Interest	PT Selection*
Hepatic Safety Profile: Assessment of risk of hepatoxicity	CAB +RPV	Sub- SMQ** x2
Hypersensitivity reactions (HSR)	CAB	SMQ (modified) plus selected PTs from HLGT
Severe cutaneous adverse reactions (SCAR)	RPV	SMQ plus selected PTs from HLTs
Prolongation of the corrected QT interval of the ECG in supratherapeutic doses	RPV	SMQ plus selected PT from HLT
Neuropsychiatric Events •Suicidal ideation/behaviour •Depression •Bipolar disorder •Psychosis •Mood disorders •Anxiety •Sleep disorders	CAB +RPV	SMQ , Sub- SMQ or HLGT
Injection Site Reactions (ISR)	CAB +RPV	Use CRF terms for ISRs
Seizures and seizure-like events	CAB	SMQ plus selected PTs from HLTs
Impact on Creatinine/Decline in Renal function	CAB+RPV	SMQ plus selected PTs from HLT
Safety in Pregnancy	CAB	Use AE terms co-reported in pregnancy exposures to CAB
Protenuria	CAB+RPV	SMQ
Proximal Renal Tubule Dysfunctions	CAB+RPV	SMQ

* All PTs, SMQs, HLT, HLGTs from MedDRA V21
** All SMQs use narrow terms unless otherwise specified

Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions (SMQ)	20000013

*Notes: Medical concept of hepatic failure and hepatitis. Sub- SMQs (1) 'Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions' **and** (2) 'Hepatitis, non-infectious', both of parent SMQ 'Hepatic Disorders'; only narrow terms selected from sub-SMQs. Some preferred terms e.g PT 'hepatitis fulminant' are duplicated.*

PT	PT Code
Acquired hepatocerebral degeneration	10080860
Acute hepatic failure	10000804
Acute on chronic liver failure	10077305
Acute yellow liver atrophy	10070815
Ascites	10003445
Asterixis	10003547
Bacterascites	10068547
Biliary cirrhosis	10004659
Biliary fibrosis	10004664
Cholestatic liver injury	10067969
Chronic hepatic failure	10057573
Coma hepatic	10010075
Cryptogenic cirrhosis	10063075
Diabetic hepatopathy	10071265
Drug-induced liver injury	10072268
Duodenal varices	10051010
Gallbladder varices	10072319
Gastric variceal injection	10076237
Gastric variceal ligation	10076238
Gastric varices	10051012
Gastric varices haemorrhage	10057572
Hepatectomy	10061997
Hepatic atrophy	10019637
Hepatic calcification	10065274
Hepatic cirrhosis	10019641
Hepatic encephalopathy	10019660
Hepatic encephalopathy prophylaxis	10066599
Hepatic failure	10019663
Hepatic fibrosis	10019668
Hepatic hydrothorax	10067365
Hepatic infiltration eosinophilic	10064668
Hepatic lesion	10061998
Hepatic necrosis	10019692
Hepatic steato-fibrosis	10077215
Hepatic steatosis	10019708
Hepatitis fulminant	10019772
Hepatobiliary disease	10062000
Hepatocellular foamy cell syndrome	10053244
Hepatocellular injury	10019837

PT	PT Code
Hepatopulmonary syndrome	10052274
Hepatorenal failure	10019845
Hepatorenal syndrome	10019846
Hepatotoxicity	10019851
Intestinal varices	10071502
Intestinal varices haemorrhage	10078058
Liver and small intestine transplant	10052280
Liver dialysis	10076640
Liver disorder	10024670
Liver injury	10067125
Liver operation	10062040
Liver transplant	10024714
Lupoid hepatic cirrhosis	10025129
Minimal hepatic encephalopathy	10076204
Mixed liver injury	10066758
Nodular regenerative hyperplasia	10051081
Non-alcoholic fatty liver	10029530
Non-alcoholic steatohepatitis	10053219
Non-cirrhotic portal hypertension	10077259
Oedema due to hepatic disease	10049631
Oesophageal varices haemorrhage	10030210
Peripancreatic varices	10073215
Portal fibrosis	10074726
Portal hypertension	10036200
Portal hypertensive colopathy	10079446
Portal hypertensive enteropathy	10068923
Portal hypertensive gastropathy	10050897
Portal vein cavernous transformation	10073979
Portal vein dilatation	10073209
Portopulmonary hypertension	10067281
Primary biliary cholangitis	10080429
Regenerative siderotic hepatic nodule	10080679
Renal and liver transplant	10052279
Retrograde portal vein flow	10067338
Reye's syndrome	10039012
Reynold's syndrome	10070953
Splenic varices	10067823
Splenic varices haemorrhage	10068662
Steatohepatitis	10076331
Subacute hepatic failure	10056956
Varices oesophageal	10056091
Varicose veins of abdominal wall	10072284
White nipple sign	10078438

Hepatitis, non-infectious (SMQ)		20000010
PT	**PT Code**	
Acute graft versus host disease in liver	10066263	
Allergic hepatitis	10071198	
Alloimmune hepatitis	10080576	
Autoimmune hepatitis	10003827	
Chronic graft versus host disease in liver	10072160	
Chronic hepatitis	10008909	
Graft versus host disease in liver	10064676	
Hepatitis	10019717	
Hepatitis acute	10019727	
Hepatitis cholestatic	10019754	
Hepatitis chronic active	10019755	
Hepatitis chronic persistent	10019759	
Hepatitis fulminant	10019772	
Hepatitis toxic	10019795	
Immune-mediated hepatitis	10078962	
Ischaemic hepatitis	10023025	
Lupus hepatitis	10067737	
Non-alcoholic steatohepatitis	10053219	
Radiation hepatitis	10051015	
Steatohepatitis	10076331	

Drug reaction with eosinophilia and systemic symptoms syndrome (SMQ) -	20000225
PT	**PT Code**
Drug reaction with eosinophilia and systemic symptoms	10073508
Pseudolymphoma	10037127

Notes: Medical concept of hypersensitivity reactions/DRESS. Only narrow terms selected from Category A of SMQ 'Drug reaction with eosinophilia and systemic symptoms syndrome'. Algorithmic approach for this SMQ not used due to complexity in applying and poor specificity of remaining categories. Category A selected as PTs because more specific for concept (only narrow terms) and a pre-requisite for any combination in algorithmic search. Overlap of some preferred terms with SMQ 'Severe Cutaneous Adverse Reactions' . ***Plus*** *additional preferred terms selected from HGLT 'Allergic conditions' under SOC 'Immune system disorders'*

PTs (Selective)	
Drug hypersensitivity	10013700
Hypersensitivity	10020751
Type IV Hypersensitivity reaction	10053613
Eosinophillia	10014950
Eye swelling	10015967
Eyelid oedema	10015993
Lip swelling	10024570
Angioedema	10002424
Circumoral oedema	10052250
Face oedema	10016029
Idiopathic angioedema	10073257
Lip oedema	10024558
Mouth swelling	10075203
Oedema mouth	10030110
Periorbital oedema	10034545
Swelling face	10042682

Severe cutaneous adverse reactions (SMQ)		20000020
PT	**PT Code**	
Acute generalised exanthematous pustulosis	10048799	
Cutaneous vasculitis	10011686	
Dermatitis bullous	10012441	
Dermatitis exfoliative	10012455	
Dermatitis exfoliative generalised	10012456	
Drug reaction with eosinophilia and systemic symptoms	10073508	
Epidermal necrosis	10059284	
Erythema multiforme	10015218	
Exfoliative rash	10064579	
Oculomucocutaneous syndrome	10030081	
Skin necrosis	10040893	
Stevens-Johnson syndrome	10042033	
Toxic epidermal necrolysis	10044223	
Toxic skin eruption	10057970	

*Notes: Medical concept of severe cutaneous adverse reactions. Only narrow terms from SMQ 'Severe cutaneous adverse reactions' selected. **Plus** several additional preferred terms [only G3 and higher] selected from HLTs 'Rashes, eruptions and exanthems NEC', 'Pruritus NEC', 'Pustular conditions', 'Dermatitis ascribed to specific agent' all under SOC 'Skin and subcutaneous tissue disorders'*

PTs (Selective)G3 and higher		
Eyelid rash	10074620	
Genital rash	10018175	
Mucocutaneous rash	10056671	
Nodular rash	10075807	
Perineal rash	10075364	
Rash	10037844	
Rash erythematous	10037855	
Rash generalised	10037858	
Rash macular	10037867	
Rash maculo-papular	10037868	
Rash maculovesicular	10050004	
Rash morbilliform	10037870	
Rash papular	10037876	
Rash rubelliform	10057984	
Rash scarlatiniform	10037890	
Rash vesicular	10037898	
Rash pruritic	10037884	
Rash follicular	10037857	
Rash pustular	10037888	
Drug eruption	10013687	

Torsade de pointes/QT prolongation (SMQ)	20000001
PT	**PT Code**
Electrocardiogram QT interval abnormal	10063748
Electrocardiogram QT prolonged	10014387
Long QT syndrome	10024803
Long QT syndrome congenital	10057926
Torsade de pointes	10044066
Ventricular tachycardia	10047302

*Notes: Medical concept of QT prolongation and complications. Only narrow terms from SMQ 'Torsade de pointes/QT prolongation' selected **plus** one additional PT under HLT 'ECG investigations'.*

PTs (Selective)	
Electrocardiogram repolarisation abnormality	10052464

Suicide/self-injury (SMQ)	20000037	*Notes: Medical concept of suicidal ideation and behaviour. Sub-SMQ 'Suicide/self-injury' (SMQ) from parent SMQ of 'Depression and Suicide/Self Injury'. Only narrow terms from the sub-SMQ selected.*
PT	**PT Code**	
Assisted suicide	10079105	
Columbia suicide severity rating scale abnormal	10075616	
Completed suicide	10010144	
Depression suicidal	10012397	
Intentional overdose	10022523	
Intentional self-injury	10022524	
Poisoning deliberate	10036000	
Self-injurious ideation	10051154	
Suicidal behaviour	10065604	
Suicidal ideation	10042458	
Suicide attempt	10042464	
Suicide threat	10077417	

Depression (excl suicide and self injury) (SMQ) -	20000167	*Notes: Medical concept of Depression. Sub-SMQ 'Depression (excl suicide and self injury)' (SMQ) from parent SMQ of 'Depression and Suicide/Self Injury'.Only narrow terms from the sub-SMQ selected.*
PT	**PT Code**	
Activation syndrome	10066817	
Adjustment disorder with depressed mood	10001297	
Adjustment disorder with mixed anxiety and depressed mood	10001299	
Agitated depression	10001496	
Anhedonia	10002511	
Antidepressant therapy	10054976	
Childhood depression	10068631	
Decreased interest	10011971	
Depressed mood	10012374	
Depression	10012378	
Depression postoperative	10012390	
Depressive symptom	10054089	
Dysphoria	10013954	
Electroconvulsive therapy	10014404	
Feeling guilty	10049708	
Feeling of despair	10016344	
Feelings of worthlessness	10016374	
Helplessness	10077169	
Major depression	10057840	
Menopausal depression	10067371	
Mixed anxiety and depressive disorder	10080836	
Perinatal depression	10078366	
Persistent depressive disorder	10077804	
Post stroke depression	10070606	
Postictal depression	10071324	

HLGT Manic and Bipolar mood disorders and disturbances	
PT	**PT Code**
Bipolar I disorder	10004939
Bipolar II disorder	10004940
Bipolar disorder	10057667
Cyclothymic disorder	10011724
Hypomania	10021030
Mania	10026749

Notes: Medical concept of bipolar disorder. All preferred terms from HLGT 'Manic and Bipolar mood disorders and disturbances' under SOC 'Psychiatric disorders'.

Psychosis and psychotic disorders (SMQ) 20000117	20000117
PT	PT Code
Acute psychosis	10001022
Alcoholic psychosis	10001632
Alice in wonderland syndrome	10001666
Brief psychotic disorder with marked stressors	10048549
Brief psychotic disorder without marked stressors	10056395
Brief psychotic disorder, with postpartum onset	10006362
Charles Bonnet syndrome	10063354
Childhood psychosis	10061040
Clang associations	10009232
Cotard's syndrome	10059591
Delusion	10012239
Delusion of grandeur	10012241
Delusion of reference	10012244
Delusion of replacement	10012245
Delusional disorder, erotomanic type	10012249
Delusional disorder, grandiose type	10012250
Delusional disorder, jealous type	10012251
Delusional disorder, mixed type	10012252
Delusional disorder, persecutory type	10053195
Delusional disorder, somatic type	10012254
Delusional disorder, unspecified type	10012255
Delusional perception	10012258
Dementia of the Alzheimer's type, with delusions	10012295
Depressive delusion	10063033
Derailment	10012411
Epileptic psychosis	10059232
Erotomanic delusion	10015134
Flight of ideas	10016777
Hallucination	10019063
Hallucination, auditory	10019070
Hallucination, gustatory	10019071
Hallucination, olfactory	10019072
Hallucination, synaesthetic	10062824
Hallucination, tactile	10019074
Hallucination, visual	10019075
Hallucinations, mixed	10019079
Hypnagogic hallucination	10020927
Hypnopompic hallucination	10020928
Hysterical psychosis	10062645

Notes: Medical concept of psychosis. Only narrow terms from SMQ 'Psychosis and psychotic disorders' selected.

PT	PT Code
Ideas of reference	10021212
Illusion	10021403
Jealous delusion	10023164
Loose associations	10024825
Mixed delusion	10076429
Neologism	10028916
Neuroleptic-induced deficit syndrome	10075295
Paranoia	10033864
Paranoid personality disorder	10033869
Parkinson's disease psychosis	10074835
Paroxysmal perceptual alteration	10063117
Persecutory delusion	10034702
Postictal psychosis	10070669
Post-injection delirium sedation syndrome	10072851
Posturing	10036437
Psychosis postoperative	10065617
Psychotic behaviour	10037249
Psychotic disorder	10061920
Psychotic disorder due to a general medical condition	10061921
Reactive psychosis	10053632
Rebound psychosis	10074833
Schizoaffective disorder	10039621
Schizoaffective disorder bipolar type	10068889
Schizoaffective disorder depressive type	10068890
Schizophrenia	10039626
Schizophreniform disorder	10039647
Schizotypal personality disorder	10039651
Senile psychosis	10039987
Shared psychotic disorder	10040535
Somatic delusion	10041317
Somatic hallucination	10062684
Substance-induced psychotic disorder	10072388
Tangentiality	10043114
Thought blocking	10043495
Thought broadcasting	10052214
Thought insertion	10043496
Thought withdrawal	10043497
Transient psychosis	10056326
Waxy flexibility	10047853

HLGT Mood disorders and disturbances NEC, Psychiatric disorders SOC	
PT	**PT Code**
Crying	10011469
Mood swings	10027951
Boredom	10048909
Mood altered	10027940
Apathy	10002942
Affective ambivalence	10077173
Emotional poverty	10014557
Euphoric mood	10015535
Premenstrual dysphoric disorder	10051537
Alexithymia	10077719
Laziness	10051602
Blunted affect	10005885
Constricted affect	10010778
Affect lability	10054196
Anger	10002368
Affective disorder	10001443
Lethargy	10024264
Listless	10024642
Inappropriate affect	10021588
Dysphoria	10013954
Mood disorder due to a general medical con	10027944
Morose	10027977
Screaming	10039740
Steroid withdrawal syndrome	10042028
Emotional disorder	10014551
Irritability	10022998
Moaning	10027783
Premenstrual syndrome	10036618
Neuroleptic-induced deficit syndrome	10075295
Substance-induced mood disorder	10072387
Flat affect	10016759
Diencephalic syndrome of infancy	10012774
Emotional distress	10049119
Frustration tolerance decreased	10077753
Seasonal affective disorder	10039775

Notes: Medical concept of mood disorders. All preferred terms from HLGT 'Mood disorders and disturbances NEC', under SOC 'Psychiatric disorders'.

HLGT Anxiety disorders and symptoms	
PT	**PT Code**
Acrophobia	10000605
Activation syndrome	10066817
Acute stress disorder	10001084
Aerophobia	10080300
Agitation	10001497
Agitation neonatal	10001500
Agitation postoperative	10049989
Agoraphobia	10001502
Akathisia	10001540
Algophobia	10078056
Animal phobia	10002518
Anniversary reaction	10074066
Anticipatory anxiety	10002758
Anxiety	10002855
Anxiety disorder	10057666
Anxiety disorder due to a general medical condition	10002859
Arachnophobia	10051408
Astraphobia	10078372
Autophobia	10071070
Body dysmorphic disorder	10052793
Burnout syndrome	10065369
Claustrophobia	10009244
Compulsions	10010219
Compulsive cheek biting	10076510
Compulsive handwashing	10071263
Compulsive hoarding	10068007
Compulsive lip biting	10066241
Compulsive shopping	10067948
Dermatillomania	10065701
Dysmorphophobia	10049096
Emetophobia	10070637
Fear	10016275
Fear of animals	10016276
Fear of closed spaces	10016277
Fear of crowded places	10050365
Fear of death	10066392
Fear of disease	10016278
Fear of eating	10050366

Notes: Medical concept of anxiety disorders. All preferred terms from HLGT 'Anxiety disorders and symptoms', under SOC 'Psychiatric disorders'.

PT	PT Code
Fear of falling	10048744
Fear of injection	10073753
Fear of open spaces	10016279
Fear of pregnancy	10067035
Fear of weight gain	10016280
Fear-related avoidance of activities	10080136
Generalised anxiety disorder	10018075
Glossophobia	10080077
Haemophobia	10073458
Haphephobia	10067580
Hydrophobia	10053317
Hyperarousal	10080831
Immunisation anxiety related reaction	10075205
Kinesiophobia	10078430
Limited symptom panic attack	10024511
Mysophobia	10078769
Nail picking	10066779
Nervousness	10029216
Neurosis	10029333
Noctiphobia	10057946
Nocturnal fear	10057948
Nosophobia	10063546
Obsessive need for symmetry	10077179
Obsessive rumination	10056264
Obsessive thoughts	10029897
Obsessive-compulsive disorder	10029898
Obsessive-compulsive symptom	10077894
Ochlophobia	10050095
Osmophobia	10060765
Paediatric autoimmune neuropsychiatric disorders assoc	10072147
Panic attack	10033664
Panic disorder	10033666
Panic reaction	10033670
Paruresis	10069024
Performance fear	10034432
Phagophobia	10050096
Pharmacophobia	10069423
Phobia	10034912
Phobia of driving	10056676
Phobia of exams	10034913
Phobic avoidance	10034918

PT	PT Code
Phonophobia	10054956
Photaugiaphobia	10064420
Post-traumatic stress disorder	10036316
Postpartum neurosis	10036419
Postpartum stress disorder	10056394
Procedural anxiety	10075204
Pseudoangina	10056610
Selective mutism	10039917
Separation anxiety disorder	10040045
Sitophobia	10080170
Social anxiety disorder	10041242
Social fear	10041247
Stress	10042209
Tension	10043268
Terminal agitation	10077416
Thanatophobia	10064723
Thermophobia	10075147
Trichotemnomania	10072752
Trichotillomania	10044629

HLGT Sleep Disorders and Disturbances	Notes: Medical concept of sleep disorders. All preferred terms from (1) HLGT 'Sleep Disorders and Disturbances', 'Psychiatric disorders' SOC ***plus*** (2)HLGT 'Sleep disturbances (incl subtypes)', 'Nervous system' SOC. Numerous duplicated preferred terms e.g. middle insomnia

PT	PT Code
Behavioural insomnia of childhood	10072072
Hyposomnia	10067530
Initial insomnia	10022035
Insomnia	10022437
Middle insomnia	10027590
Terminal insomnia	10068932
Breathing-related sleep disorder	10006344
Dyssomnia	10061827
Hypersomnia	10020765
Periodic limb movement disorder	10064600
Pickwickian syndrome	10035004
Poor quality sleep	10062519
Sleep apnoea syndrome	10040979
Somnolence	10041349
Somnolence neonatal	10041350
Stupor	10042264
Upper airway resistance syndrome	10063968
Cataplexy	10007737
Hypnagogic hallucination	10020927
Hypnopompic hallucination	10020928
Narcolepsy	10028713
Sleep attacks	10040981
Sleep paralysis	10041002
Abnormal dreams	10000125
Abnormal sleep-related event	10061613
Confusional arousal	10067494
Exploding head syndrome	10080684
Loss of dreaming	10065085
Nightmare	10029412
Parasomnia	10061910
Rapid eye movement sleep behaviour disorder	10077299
Rapid eye movements sleep abnormal	10037841
Sleep inertia	10067493
Sleep sex	10067492
Sleep talking	10041009
Sleep terror	10041010
Sleep-related eating disorder	10067315
Somnambulism	10041347
Hypersomnia related to another mental condition	10020767
Hypersomnia-bulimia syndrome	10053712
Insomnia related to another mental condition	10022443
Sleep disorder	10040984
Sleep disorder due to a general medical condition	10063910
Sleep disorder due to general medical condition, hypersomnia type	10040985
Sleep disorder due to general medical condition, insomnia type	10040986
Sleep disorder due to general medical condition, mixed type	10040987
Sleep disorder due to general medical condition, parasomnia type	10040988

PT	PT Code
Sopor	10058709
Advanced sleep phase	10001423
Circadian rhythm sleep disorder	10009191
Delayed sleep phase	10012209
Irregular sleep phase	10022995
Irregular sleep wake rhythm disorder	10080301
Non-24-hour sleep-wake disorder	10078086
Shift work disorder	10078088

HLGT Sleep disturbances (incl subtypes)	
PT	**PT Code**
Abnormal dreams	10000125
Abnormal sleep-related event	10061613
Confusional arousal	10067494
Loss of dreaming	10065085
Sleep inertia	10067493
Sleep paralysis	10041002
Sleep sex	10067492
Sleep talking	10041009
Sleep terror	10041010
Sleep-related eating disorder	10067315
Somnambulism	10041347
Behavioural insomnia of childhood	10072072
Hyposomnia	10067530
Initial insomnia	10022035
Insomnia	10022437
Middle insomnia	10027590
Terminal insomnia	10068932
Advanced sleep phase	10001423
Circadian rhythm sleep disorder	10009191
Delayed sleep phase	10012209
Irregular sleep phase	10022995
Irregular sleep wake rhythm disorder	10080301
Non-24-hour sleep-wake disorder	10078086
Shift work disorder	10078088
Cataplexy	10007737
Hypersomnia	10020765
Narcolepsy	10028713
Central-alveolar hypoventilation	10007982
Sleep apnoea syndrome	10040979
Breathing-related sleep disorder	10006344
Dyssomnia	10061827
Fatal familial insomnia	10072077
Microsleep	10076954
Periodic limb movement disorder	10064600
Pickwickian syndrome	10035004
Poor quality sleep	10062519
Rapid eye movement sleep behaviour disorder	10077299
Rapid eye movements sleep abnormal	10037841
Sleep deficit	10080881
Sudden onset of sleep	10050014

PT	PT Code
Upper airway resistance syndrome	10063968

Convulsions (SMQ)	20000079
PT	PT Code
2-Hydroxyglutaric aciduria	10078971
Acquired epileptic aphasia	10052075
Acute encephalitis with refractory, repetitive partial seizures	10076948
Alcoholic seizure	10056347
Aspartate-glutamate-transporter deficiency	10079140
Atonic seizures	10003628
Atypical benign partial epilepsy	10056699
Automatism epileptic	10003831
Autonomic seizure	10049612
Baltic myoclonic epilepsy	10054895
Benign familial neonatal convulsions	10067866
Benign rolandic epilepsy	10070530
Biotinidase deficiency	10071434
Change in seizure presentation	10075606
Clonic convulsion	10053398
Convulsion in childhood	10052391
Convulsion neonatal	10010911
Convulsions local	10010920
Convulsive threshold lowered	10010927
CSWS syndrome	10078827
Deja vu	10012177
Double cortex syndrome	10073490
Dreamy state	10013634
Drug withdrawal convulsions	10013752
Early infantile epileptic encephalopathy with burst-suppression	10071545
Eclampsia	10014129
Epilepsy	10015037
Epilepsy surgery	10079824
Epileptic aura	10015049
Epileptic psychosis	10059232
Febrile convulsion	10016284
Febrile infection-related epilepsy syndrome	10079438
Focal dyscognitive seizures	10079424
Frontal lobe epilepsy	10049424
Generalised non-convulsive epilepsy	10018090
Generalised tonic-clonic seizure	10018100
Glucose transporter type 1 deficiency syndrome	10078727
Gray matter heterotopia	10080533
Hemimegalencephaly	10078100
Hyperglycaemic seizure	10071394

*Notes: Medical concept of seizures. Only narrow terms from SMQ 'Convulsions' selected **plus** selected PTs of possible seizure events from HLT 'Disturbances in consciousness NEC' under SOC 'Nervous systems disorders' and HLT 'Confusion and disorientation' under SOC 'Psychiatric disorders' .*

PT	PT Code
Hypocalcaemic seizure	10072456
Hypoglycaemic seizure	10048803
Hyponatraemic seizure	10073183
Idiopathic generalised epilepsy	10071081
Infantile spasms	10021750
Juvenile myoclonic epilepsy	10071082
Lafora's myoclonic epilepsy	10054030
Lennox-Gastaut syndrome	10048816
Migraine-triggered seizure	10076676
Molybdenum cofactor deficiency	10069687
Multiple subpial transection	10079825
Myoclonic epilepsy	10054859
Myoclonic epilepsy and ragged-red fibres	10069825
Partial seizures	10061334
Partial seizures with secondary generalisation	10056209
Petit mal epilepsy	10034759
Polymicrogyria	10073489
Post stroke epilepsy	10076982
Post stroke seizure	10076981
Postictal headache	10052470
Postictal paralysis	10052469
Postictal psychosis	10070669
Postictal state	10048727
Post-traumatic epilepsy	10036312
Schizencephaly	10073487
Seizure	10039906
Seizure anoxic	10039907
Seizure cluster	10071350
Seizure like phenomena	10071048
Severe myoclonic epilepsy of infancy	10073677
Simple partial seizures	10040703
Status epilepticus	10041962
Sudden unexplained death in epilepsy	10063894
Temporal lobe epilepsy	10043209
Tonic clonic movements	10051171
Tonic convulsion	10043994
Tonic posturing	10075125
Topectomy	10073488
Tuberous sclerosis complex	10080584
Uncinate fits	10045476

PTs (Selective)	
Confusional state	10010305

PT	PT Code
Loss of consciousness	10024855
Syncope	10042772
Sopor	10058709
Stupor	10042264
Altered state of consciousness	10050093
Depressed level of consciousness	10012373
Consciousness fluctuating	10050093

Acute renal failure (SMQ)	20000003
PT	**PT Code**
Acute kidney injury	10069339
Acute phosphate nephropathy	10069688
Anuria	10002847
Azotaemia	10003885
Continuous haemodiafiltration	10066338
Dialysis	10061105
Foetal renal impairment	10078987
Haemodialysis	10018875
Haemofiltration	10053090
Hyponatriuria	10077515
Neonatal anuria	10049778
Nephropathy toxic	10029155
Oliguria	10030302
Peritoneal dialysis	10034660
Prerenal failure	10072370
Renal failure	10038435
Renal failure neonatal	10038447
Renal impairment	10062237
Renal impairment neonatal	10049776

*Notes: Medical concept of worsening renal function/renal failure in the context of impact on creatinine. Only narrow terms from SMQ 'Acute renal failure' **plus** all PTs from HLT 'Renal failure and impairment', under SOC 'Renal and urinary disorders'. Numerous duplicated preferred terms e.g. renal failure*

Renal Failure and Impairment HLT	
PT	**PT Code**
Acute Kidney injury	10069339
Anuria	10002847
Atypical haemolytic uraemic syndrome	10079840
Cardiorenal syndrome	10068230
Chronic kidney disease	10064848
Crush syndrome	10050702
Diabetic end stage renal disease	10012660
End stage renal disease	10077512
Foetal renal impairment	10078987
Haemolytic uraemic syndrome	10018932
Hepatorenal failure	10019845
Hepatorenal syndrome	10019846

PT	PT Code
Nail-patella syndrome	10063431
Neonatal anuria	10049778
Oliguria	10030302
Pancreatorenal syndrome	10056277
Postoperative renal failure	10056675
Postrenal failure	10059345
Prerenal failure	10072370
Propofol infusion syndrome	10063181
Renal failure	10038435
Renal failure neonatal	10038447
Renal impairment	10062237
Renal impairment neonatal	10049776
Renal injury	10061481
Scleroderma renal crisis	10062553
Traumatic anuria	10044501

Tubulointerstitial diseases (SMQ)	20000221	*Notes: Medical concept of Proximal Renal Tubule Dysfunction. Only narrow terms from SMQ 'Tubulointerstitial diseases'.*
PT	**PT Code**	
Acidosis hyperchloraemic	10000489	
Acquired aminoaciduria	10073515	
Acute phosphate nephropathy	10069688	
Aminoaciduria	10001939	
Beta-N-acetyl-D-glucosaminidase increased	10004511	
Crystal nephropathy	10071503	
Eosinophils urine present	10058363	
Fanconi syndrome acquired	10052607	
Hyperphosphaturia	10051232	
Isosthenuria	10023077	
Nephritis allergic	10029120	
Nephrogenic diabetes insipidus	10029147	
Nephropathy toxic	10029155	
Renal glycosuria	10038457	
Renal papillary necrosis	10038491	
Renal tubular acidosis	10038535	
Renal tubular atrophy	10038536	
Renal tubular disorder	10038537	
Renal tubular dysfunction	10050335	
Tubulointerstitial nephritis	10048302	
Tubulointerstitial nephritis and uveitis syndrc	10069034	
Urine phosphorus increased	10055030	
Urine retinol binding protein increased	10061432	

Proteinuria (SMQ)	20000220	Notes: Medical concept of Proteinuria. Only narrow terms from narrow SMQ 'Proteinuria' included.
PT	PT Code	
Albumin globulin ratio increased	10001567	
Albumin urine present	10001582	
Albuminuria	10001580	
Bence Jones protein urine present	10053112	
Bence Jones proteinuria	10004231	
Beta 2 microglobulin urine increased	10004501	
Globulinuria	10018352	
Microalbuminuria	10027525	
Myoglobinuria	10028629	
Orthostatic proteinuria	10031129	
Protein urine	10037018	
Protein urine present	10053123	
Proteinuria	10037032	
Urine albumin/creatinine ratio increased	10053541	
Urine protein/creatinine ratio abnormal	10053539	
Urine protein/creatinine ratio increased	10053538	

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

Title	:	Reporting and Analysis Plan for 206898: An Open Label, Phase 1 Study to Evaluate the PK, Safety, Tolerability and Acceptability of Long Acting Injections of the HIV Integrase Inhibitor, Cabotegravir (CAB; GSK1265744) in HIV Uninfected Chinese Men
Compound Number	:	GSK1265744
Effective Date	:	28-SEP-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 206898.
- This RAP is intended to describe the safety, tolerability, and pharmacokinetic (PK) 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.

Author's Name and Functional Area:

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this reporting and analysis plan (RAP) is to describe any planned analyses and output to be included in the clinical study report for Protocol 206898.
Protocol	• This RAP is based on the Protocol Amendment 1 (Dated: 06JUN2018) of study Protocol 206898 (GSK Document No.: 2016N293702_00] and eCRF Version (1.00, Dated: 09MAR2018).
Primary Objective	• Evaluate the safety and tolerability of the injectable agent, cabotegravir (GSK1265744) long acting (CAB LA) injectable (600 mg dose administered every 4 weeks for 2 doses followed by every 8 weeks for 3 doses) through Week 5-41 in HIV-1 uninfected Chinese men. • Evaluate the plasma pharmacokinetics of CAB following repeat oral administration (Day 1 to Week 4) and CAB LA IM injections throughout the Injection Phase (Weeks 5-41).
Primary Endpoint	• Safety and tolerability parameters, including adverse events, clinical laboratory tests, study withdrawals due to AEs, vital signs assessments, and evaluation of injection site reactions (ISRs), for injection phase (Week 5-41). • Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F following daily oral administration of CAB through Day 1 to Week 4. • Plasma CAB AUC(0-τ), Cmax, Cτ, and tmax following IM injections of CAB LA once every 8 weeks through Weeks 5-41.
Secondary Objective	• Evaluate the plasma pharmacokinetics of CAB LA throughout the Injection and Long-term Follow-up Phases (Week 5 to Week 89). • Evaluate the safety and tolerability of oral CAB in HIV uninfected Chinese men during the oral lead-in Phase (Day 1 to Week 4) • Evaluate the acceptability of CAB LA injections through 41 weeks. • Explore concentration-effect relationships for various safety and tolerability parameters if relevant.
Secondary Endpoint	• Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F through Weeks 5-89. • Safety and tolerability parameters, including adverse events, study withdrawals due to AEs, vital signs assessments, and clinical laboratory assessments, for oral lead-in phase (Day 1 to Week 4). • Injection discontinuation rate, the number and severity of ISRs and additional acceptability measures.

Overview	Key Elements of the RAP
	• Evaluation of relationships between significant safety and tolerability parameters and CAB PK may be explored.
Study Design	• This will be an open label, non-randomized, single arm study. Participants will receive daily oral CAB (30mg tablets) for 4 weeks during the Oral Phase of the study and intramuscular (IM) injections of 600 mg of CAB LA at Week 5, Week 9, Week 17, Week 25 and Week 33. • Starting at 8 weeks post last injection, participants will be seen once every 12 weeks for 48 weeks during the follow-up phase. • Subjects who volunteer to participate in the intensive PK assessment will have serial blood sampling for measurement of plasma CAB concentrations following oral administration over a 24 h window starting on Day 27 and ending on Day 28 • PK samples at trough for Oral Phase will be collected for all subjects prior to dose within 20 to 28 hours following oral administration the day prior; Intensive oral PK samples will be collected from approximately 16 participants. • PK Samples for Injection Phase will be collected prior to CAB LA injections at Week 5, 9, 17, 25, and 33 with the exception of 1-week post injection samples at Weeks 6, 10, 18, 26, 34, 37 (4-week post injection sample) and Week 41 • Long-term follow up PK samples will be collected at Week 53, 65, 77, and 89.
Planned Analyses	• The primary safety analysis and PK analyses including both oral phase and injection phase through Weeks 5 to 41 will be performed after all ongoing participants complete the Week 41 visit or withdraw from the study treatment, whichever comes first. • The end of study analysis will be performed after all ongoing participants complete the Week 89 visit or withdraw from the study treatment, whichever comes first.
Analysis Populations	• The All Subjects Screened Population will include all subjects who consent to participate in the clinical study. Subjects in this population will be used for disposition summary • The Safety Population will include all subjects who receive at least one dose of the study treatment. Subjects in this population will be used for all demographic and safety summaries or listings, as well as for the analysis of acceptability of CAB LA. • Safety Injection Population will include all subjects received at least one CAB LA injection. Subjects in this population will be used to evaluate the safety and tolerability of CAB LA injection in primary analysis. • Oral PK Population: subjects in the 'Safety population' for whom an intensive oral pharmacokinetic sample was obtained and analysed. PK samples that may

Overview	Key Elements of the RAP
	be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of Oral PK data. • Injection (Week 41) PK Population: subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 41. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of Injection PK data from Weeks 5 to 41. • Injection (Week 89) PK Population: subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 89. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of Injection PK data from Weeks 5 to 89.
Hypothesis	• No formal statistical hypotheses will be evaluated.
Primary Analyses	• To assess safety of CAB LA, the number and the percent of participants experiencing each safety endpoint will be tabulated including adverse events, clinical laboratory tests, study withdrawals due to AEs, and vital signs assessments. • To assess tolerability of CAB LA, the proportion of participants who terminate from receiving injections prior to the full course due to AE, intolerability of injection, frequency of injections, or burden of procedures related to injections out of those participants that received at least one injection. • To assess the plasma pharmacokinetics of CAB following repeat oral administration (Day 1 to Week 4) and CAB LA IM injections throughout the Injection Phase (Week 5 to Week 41).
Secondary Analyses	• To assess the plasma pharmacokinetics of CAB LA throughout the Injection and Long-term Follow-up Phases (Week 5 to Week 89). • To assess the safety and tolerability of oral CAB, each safety and tolerability endpoint will be tabulated including adverse events, study withdrawals due to AEs, vital signs assessments and clinical laboratory assessments. • To assess the acceptability of the CAB LA, injection discontinuation rate, the number and severity of ISRs, and the proportion (with 95% CI for the CAB LA arm) of participants who would consider using CAB LA for HIV prevention in the future will be tabulated among all enrolled participants (including those who terminated product use during the trial. • Overall treatment satisfaction score and answers to each individual question on

Overview	Key Elements of the RAP
	HIV-PrevTSQc will be summarized to evaluate tolerability

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

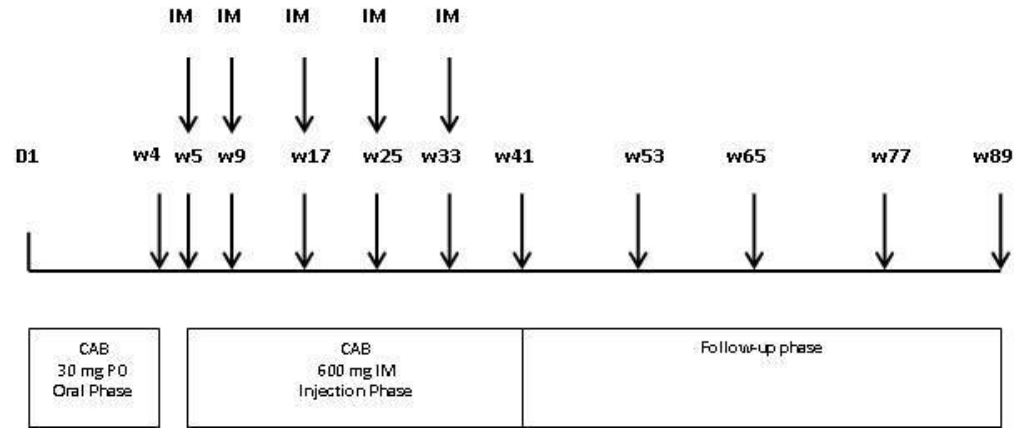
There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 06/JUN/2018).

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
Evaluate the safety and tolerability of the injectable agent, cabotegravir (GSK1265744) long acting (CAB LA) injectable (600 mg dose administered every 4 weeks for 2 doses followed by every 8 weeks for 3 doses) through Week 5-41 in HIV-1 uninfected Chinese men.	Safety and tolerability parameters, including adverse events, clinical laboratory tests, study withdrawals due to AEs, vital signs assessments, and evaluation of injection site reactions (ISRs).
Evaluate the plasma pharmacokinetics of CAB following repeat oral administration (Day 1 to Week 4) and CAB LA IM injections throughout the Injection Phase (Week 5 to Week 41).	Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F at Week 4 following daily oral administration of CAB. Plasma CAB AUC(0-τ), Cmax, Cτ, and tmax at Week 41 following IM injections of CAB LA.
Secondary Objectives	**Secondary Endpoints**
Evaluate the plasma pharmacokinetics of CAB LA throughout the Injection and Long-term Follow-up Phases (Week 5 to Week 89)	Plasma CAB AUC(0-τ), Cmax, Cτ, tmax, λz, t½, CL/F, and Vz/F
Evaluate the safety and tolerability of oral CAB in HIV uninfected Chinese men during the oral lead-in Phase (Day 1 to Week 4)	Safety and tolerability parameters, including adverse events, study withdrawals due to AEs, vital signs assessments and clinical laboratory assessments.
Evaluate the acceptability of CAB LA injections through 41 weeks.	Injection discontinuation rate, the number and severity of ISRs and additional acceptability measures.
Explore concentration-effect relationships for various safety and tolerability parameters if relevant.	Evaluation of relationships between significant safety and tolerability parameters and CAB PK may be explored.

2.3. Study Design

Overview of Study Design and Key Features



This study is an open label (OL) Phase 1, multi-site, study to evaluate the PK, safety, tolerability, and acceptability of CAB LA in adult male participants. Eligible participants will receive oral CAB tablets as well as open label CAB LA.

Design Features	Oral lead-in phase is from Day 1 to week 4; injection phase is from week 5 to week 41; and follow-up phase is from week 41 to week 89
Dosing	Oral CAB tablet is 30mg and dose level=1 tablet; CAB Sterile Suspension for Injection Vial is 200mg/mL and dose level = 600mg (3mL) Participants will receive daily oral CAB (30mg tablets) for 4 weeks during the Oral Phase of the study and IM injections of 600 mg of CAB LA at Week 5, Week 9, Week 17, Week 25 and Week 33.
Treatment Assignment	Eligible participants will receive oral CAB tablets in the first four weeks, and will received CAB LA injections since Week 5 following planned schedules.
Interim Analysis	No interim analysis is planned in this study.

2.4. Statistical Hypotheses

No formal statistical hypotheses will be evaluated. The study is designed to evaluate the PK, safety, tolerability, and acceptability of the injectable agent, CAB LA (600 mg dose administered at 8-week intervals after 2 initial doses 4 weeks apart) in HIV-uninfected men in China where at least 60% of the men are of a population who have sex with men.

Where appropriate, an estimation approach will be taken, and point estimates and confidence intervals will be constructed.

3. PLANNED ANALYSES

3.1. Interim Analyses

No formal interim analysis is planned in the study.

However, two preliminary PK analyses during the study will be performed in an informal manner. One will be after all planned participants complete the oral phase, and the other one will be after 50% of planned participants complete Week 17 visit. Study team will review preliminary safety and PK data.

3.2. Final Analyses

The primary safety analysis and PK analyses including both oral phase and injection phase through Weeks 5 to 41 will be performed after all ongoing participants complete the Week 41 visit and datasets have been authorized. Other secondary analyses as mentioned, where appropriate, will also be performed. The end of study analysis will be performed after all ongoing participants complete the Week 89 visit. All planned primary and secondary analyses will be included in the second formal analyses.

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

a. All subjects have completed the specific study visit (i.e. week 41 or week 89) as defined in the protocol.

b. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects Screened	• Comprise of all subjects who consent to participate in the clinical study.	• Disposition summary
Safety	• Comprise of all subjects who receive at least one dose of the study treatment.	• All demographic • General safety analyses • Safety analysis for the oral phase • Analysis of acceptability of CAB LA
Safety Injection	• Comprise of all subjects received at least one CAB LA injection	• Safety and tolerability analyses of CAB LA in primary and extended analyses
Oral Pharmacokinetic (PK)	• Will consist of all subjects in the 'Safety population' for whom an intensive oral pharmacokinetic sample was obtained and analysed. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• Oral PK Concentration • Oral PK Parameters
Injection (Week 41) Pharmacokinetic (PK)	• Will consist of all subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 41. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• Injection PK Concentration • Injection PK Parameters
Injection (Week 89) Pharmacokinetic (PK)	• Will consist of all subjects in the 'Safety population' for whom an injection pharmacokinetic sample was obtained and analysed during Weeks 5 to 89. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• Injection PK Concentration • Injection PK Parameters

NOTES:
Please refer to Appendix 14: List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.
    - Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 1 Overview of Appendices

Section	Component
10.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
10.2	Appendix 2: Time & Events
10.3	Appendix 3: Assessment Windows
10.4	Appendix 4: Treatment States and Phases
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
10.8	Appendix 8: Values of Potential Clinical Importance
10.9	Appendix 9: Multicenter Studies
10.10	Appendix 10: Examination of Covariates, Subgroups & Other Strata
10.11	Appendix 11: Multiple Comparisons & Multiplicity
10.12	Appendix 12: Model Checking and Diagnostics for Statistical Analyses.
10.13	Appendix 13: Abbreviations & Trade Marks
10.14	Appendix 14: List of Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The study population analyses will be based on the safety population, unless otherwise specified. All summary data and statistics are calculated from available data, unless otherwise specified.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Disposition			
Retention Rate and Reasons for Withdrawals	Y		Y
Demography and Baseline Characteristics			
General Demographics Characteristics	Y		Y
Medical History and Concomitant Medications			
Medical History	Y		Y
Prior Medications	Y		Y
Concomitant Medications	Y		Y
Protocol Deviations			
Deviation of Inclusion/Exclusion Criteria	Y		Y
Important Protocol Deviations	Y		Y

NOTES:

- Y = Yes display generated.

6.1.1. Disposition

The reasons of screening failure will be summarized based on the screened population. The number and percentage of each reason will be tabulated.

A summary of subject disposition by phase will be provided, including the number and percentage of subjects entering oral/injection phase, the number and percentage of subjects completing oral/injection phase and the number and percentage of subjects withdrawing from oral/injection phase.

Subject disposition data will be presented in a listing.

6.1.2. Demographics

General demographics including age, self-identified gender when entering the study, and ethnicity will be summarized.

A subject's age is calculated using the year part of informed consent form (ICF) – year of birth collected in CRF.

6.1.3. Medical History

Summaries of medical history will be presented by GSK pre-specified body system categories as collected in the eCRF. Number and percentage of subjects in each category will be tabulated.

6.1.4. Prior and Concomitant Medications

Medications will be coded to therapeutic drug classes and generic drug names using the GSKDRUG 1.4 or later. Medications initiated prior to the Day 1 of the study will be counted as prior medications. Concomitant medications are defined as medications that are taken on or after the Day 1. Medications initiated prior to the Day 1 and continued after the Day 1 will be counted as both prior and concomitant medications.

Summaries showing the number and percentage of subjects who take prior or concomitant medications will be presented by therapeutic drug class and generic drug name.

6.1.5. Protocol Deviation

Important protocol deviations (PD) will be summarized PD category and subcategory, and will also be presented in a listing. A separate summary table and a listing will be provided for subjects with deviation of the inclusion/exclusion criteria in the safety population

7. PRIMARY STATISTICAL ANALYSES

7.1. Safety Analyses of CAB LA

Four study phases are defined for this study: screening phase, oral phase, injection phase and follow-up phase (see Appendix 4 for the definition of each phase).

The primary safety analysis will be conducted after all ongoing participants complete the Week 41 visit and datasets have been authorized. All data from injected participants collected from Week 5 to Week 41 (i.e., in the injection phase) will be analysed. Analysis endpoints will include Grade 2 or higher clinical and laboratory events that occur from the initial injection to 8 weeks after the last injection among participants who receive at least one injection.

The extended safety analysis will be conducted after all ongoing participants complete the Week 89 visit and datasets have been authorized. All data from injected participants collected from Week 5 to Week 89 (i.e., in the injection phase and the follow-up phase) will be analysed. Analysis endpoints are the same as in the primary safety analysis.

To assess safety, the number and the percent of participants experiencing each safety endpoint will be tabulated. Each participant will contribute once in each category (i.e., only for the highest severity AE) for the evaluation of safety.

7.1.1. Injection Site Reaction

The number and percentage of participants experiencing each type of injection site reaction sign or symptom will be tabulated by severity from the safety injection population. For a given sign or symptom, each participant's ISR will be counted once under the maximum severity for all injection visits. Overall summary of ISR and summary of ISR by needle length will both be provided. ISR related details, such as cardiovascular activity, strength training exercise, will be listed only.

Table 3 provides an overview of the planned ISR analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 3 Overview of Planned ISR Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
ISR Analyses							
All ISR Symptoms				Y			Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.2. Adverse Events

Adverse events will be tabulated using MedDRA (v20.0 or above) system organ class (SOC) and preferred terms (PT), or preferred terms alone, by study phase. The number and percentage of participants experiencing each specific AEs (Grade 2 or higher, All AEs, SAEs, AEs leading to permanent treatment discontinuation or study withdrawal) will be tabulated. Number of subjects in the safety population who entered the study phase will be used as denominator in the calculation of percentages.

Drug-related AEs, SAEs, and Grade 2-4 AEs will also be tabulated. Any AE is assumed to be study treatment-related if relationship is marked 'YES' on CRF or value is missing. In addition, a summary table will be created for AEs by maximum severity by study phase. Common AEs are defined as AEs occurring in >=5% subjects during the study (based on preferred term). Common AEs, common non-serious AEs, common Grade 2-4 AEs, and common drug-related Grade 2-4 AEs will be tabulated.

All AE tables will be presented in a decreasing frequency order of SOC or PT unless otherwise specified.

Table 4 provides an overview of the planned AE analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 4 Overview of Planned AE Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
AE Analyses							
All AEs				Y			Y
Grade 2 or higher AEs				Y			Y
SAEs				Y			Y
AE leading to treatment				Y			Y

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
discontinuation or study withdrawal							
Drug-related AEs				Y			
Drug-related SAEs				Y			
Drug-related Grade 2 or higher AEs				Y			
Common AEs				Y			
Common non-serious AEs				Y			
Common Grade 2-4 AEs				Y			
Common drug-related Grade 2-4 AEs				Y			

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.3. Clinical Laboratory Tests

All clinical laboratory tests will be graded according to the Appendix 7 from the study protocol. Grade 2 or higher laboratory events will be tabulated by number and percentage of subjects with the event by study phase.

Change from baseline in hematology, fasting chemistry, fasting lipid profile, and coagulation profile will be summarized by visit. For the definition of baseline, refer to Section 10.5.2. Urinalysis and urine chemistry results will be summarized by visit as either categorical values or as continuous values, depending on the type of the parameter.

For each lab test, shift from baseline table will be provided based on toxicity grade, both by visit and for the shift to maximum toxicity grade in each study phase. Data collected at unscheduled visits will not be included in the by-visit summary, but will be used in the calculation of maximum grade in each study phase. Subjects having both high and low values will be counted in both High and Low categories for the summary by study phase.

All lab data, as well as lab data for subjects with Grade 2 or higher abnormalities, will be listed. Abnormal data will be listed with an indicator, which is low/high relative to normal range. All laboratory results from local labs, if any, will be listed only

Table 4 provides an overview of the planned lab test analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 5 Overview of Planned Lab Test Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Laboratory Test Analyses								
Grade 2 or high laboratory events	Y							
Clinical Chemistry				Y	Y			
Hematology				Y	Y			
Fasting Lipid Profile				Y	Y			
Coagulation Profile				Y	Y			
Urinalysis and Urine Chemistry	Y			Y	Y			
Other lab data including local lab				Y				

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.4. Vital Sign Assessments

Change from baseline in vital signs, including temperature, systolic and diastolic blood pressure, and pulse rate and respiratory rate will be summarized by study visit. For the definition of baseline, refer to Section 10.5.2. Shift from baseline table (with respect to clinical concern range) will also be provided.

All vital signs, as well as vital signs for subjects with abnormalities of potential clinical importance, will be listed with an indicator, which is low/high relative to clinical concern range.

Table 6 provides an overview of the planned vital sign analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 6 Overview of Planned Vital Sign Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Vital Signs								
Vital signs				Y	Y			

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.1.5. Death

Both primary and secondary causes, if any, will be listed for each deceased participant.

Table 7 provides an overview of the planned death analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 7 Overview of Planned Death Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Death Analysis							
Death							Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.2. Tolerability Analyses of CAB LA

The tolerability analyses will be based on the safety injection population, unless otherwise specified. All summary data and statistics are calculated from available data, unless otherwise specified.

To assess tolerability of CAB LA, the proportion (with 95% confidence interval) of participants who terminate from receiving injections prior to the full course due to AE, intolerability of injection, frequency of injections, or burden of procedures related to injections will be calculated out of those participants that received at least one injection.

A questionnaire will also be used to assess participant tolerability and satisfaction to the treatment. For each question, the responses will be summarized by the proportion of participants reporting the response out of all those that answered the question. An overall treatment satisfaction score will be calculated for each participant.

Total score is defined as the sum of the scores for individual questions. If less than or equal to 50% of the questions for an individual participant are missing, the missing total scores will be estimated using the average of the existing questions multiplied by twelve; if more than 50% of the questions for an individual participant are missing, the total score will not be estimated and will be considered as missing. When calculating total scores, question CCI [redacted] will be used and question CCI [redacted] will be excluded.

Table 8 provides an overview of the planned tolerability analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 8 Overview of Planned Tolerability Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
CAB LA Discontinuation							
Injection Discontinuation Rate				Y			Y
Treatment Satisfaction Questionnaire							
Each question in the questionnaire				Y			Y
Treatment total satisfaction score				Y			Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data

7.3. Primary Pharmacokinetic Analyses

7.3.1. Overview of Planned Primary Pharmacokinetic Analyses

The primary pharmacokinetic (PK) analyses will be based on the Oral PK and Injection (Week 41) PK populations, unless otherwise specified.

Table 9 provides an overview of the planned efficacy analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 9 Overview of Planned Primary Pharmacokinetic Analyses

Display Type	Untransformed							Log-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Oral/Injection														
PK Concentrations				Y	Y[1]	Y[1]	Y							
Plasma PK Parameters	Y			Y			Y			Y	Y			

NOTES:

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Linear and Semi-Logarithmic plots will be created on the same display.

7.3.2. Primary Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).

7.3.3. Primary Pharmacokinetic Parameters

7.3.3.1. Deriving Primary Pharmacokinetic Parameters

- Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin Version 6.4 or higher.
- All calculations of non-compartmental parameters will be based on actual sampling times, and all concentrations will be included in the estimation of PK parameters regardless of whether samples are collected within the specified time window or not.
- Pharmacokinetic parameters described in Table 10 will be determined from the plasma concentration-time data, as data permits.

Table 10 Derived Primary Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-τ)	Area under the concentration-time curve over the dosing interval 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.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
Cτ	Observed concentration at the end of the dosing interval, determined directly from the concentration-time data.
t½	Terminal absorption elimination half-life will be calculated as: $t½ = ln2 / λz$
λz	Terminal absorption elimination rate constant
CL/F	Clearance (adjusted for bioavailability, F) will be calculated as: $CL/F = Dose / AUC(0-τ)$
Vz/F	Volume of distribution (adjusted for bioavailability, F) will be calculated as: $Vz/F = CL / λz$

NOTES:

- Additional parameters may be included as required.
- λz, CL/F, Vss and t½ will be determined for the Oral PK population only in the primary analysis; these parameters will be further explored for the Injection (Week 89) PK population (Section 8.1.3.1).

7.3.3.2. Statistical Analysis of Primary Pharmacokinetic Parameters

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

Pharmacokinetic Statistical Analyses
Endpoint(s)
• Plasma primary PK endpoints include Cτ, as data permit
Model Specification
Assessment of Accumulation (Injection Phase only): • To determine accumulation of plasma CAB following treatment with CAB LA, the log-transformed Cτ values for CAB will be analyzed using a mixed effects model (ANOVA) as appropriate to the study design, fitting fixed effect terms for visit and treating subject as a random effect. Point estimates and 90% confidence intervals (CIs) for the differences of interest (i.e. accumulation of CAB based on AUC(0-τ): Week 34 / Week 6) will be constructed using the residual variance. Attainment of Steady state (Injection Phase only): • If data permit, a statistical analysis of steady-state trough concentrations (Cτ) will be performed

Pharmacokinetic Statistical Analyses
after log-transformation of Cτ on Weeks 17, 25, 33, and 41 to evaluate whether steady state was achieved using the Helmert transformation approach. A mixed effect model (ANOVA) will be fitted by visit (as a categorical covariate) as a fixed effect term and subject as a random effect term. The comparison will begin with Week 17 vs. the average of Weeks 25 through Week 41. If the p-value for Week 17 vs. the average of Week 25 through Week 41 comparison is ≤0.05 (i.e. steady state not achieved at Week 17), then the comparison will continue with Week 25 vs. Week 33 through Week 41.
Model Checking & Diagnostics
• Refer to Appendix 12: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Statistical analysis of accumulation of plasma CAB following treatment with CAB LA will be presented in tabular format with geometric mean ratios between Week 34 and Week 6, and 90% CIs for the ratios of Cτ for CAB. • In steady-state analysis, the ratio of Geometric LS means and its 95% CI will be presented for the comparison(s).

8. SECONDARY STATISTICAL ANALYSES

8.1. Secondary Pharmacokinetic Analyses

8.1.1. Overview of Planned Secondary Pharmacokinetic Analyses

The secondary pharmacokinetic (PK) analyses will be based on the Injection (Week 89) PK population, unless otherwise specified.

Table 11 provides an overview of the planned analyses, with full details being presented in Appendix 14: List of Data Displays.

Table 11 Overview of Planned Secondary Pharmacokinetic Analyses

Display Type	Untransformed							Log-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Oral/Injection														
PK Concentrations				Y	Y[1]	Y[1]	Y							
Plasma PK Parameters	Y			Y			Y			Y	Y			

NOTES:

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

[1] Linear and Semi-Logarithmic plots will be created on the same display.

8.1.2. Secondary Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).

8.1.3. Secondary Pharmacokinetic Parameters

8.1.3.1. Deriving Secondary Pharmacokinetic Parameters

- Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin Version 6.4 or higher.
- All calculations of non-compartmental parameters will be based on actual sampling times, and all concentrations will be included in the estimation of PK parameters regardless of whether samples are collected within the specified time window or not.

- Pharmacokinetic parameters described in Table 12 will be determined from the plasma concentration-time data, as data permits.

Table 12 Derived Secondary Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-τ)	Area under the concentration-time curve over the dosing interval 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.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
Cτ	Observed concentration at the end of the dosing interval, determined directly from the concentration-time data.
t½	Terminal absorption elimination half-life will be calculated as: $t_{½} = \ln 2 / \lambda z$
λz	Terminal absorption elimination rate constant
CL/F	Clearance (adjusted for bioavailability, F) will be calculated as: $CL/F = Dose / AUC(0-\tau)$
Vz/F	Volume of distribution (adjusted for bioavailability, F) will be calculated as: $Vz/F = CL / \lambda z$

NOTES:

- Additional parameters may be included as required.

8.2. Safety and Tolerability Analyses of Oral CAB

The safety and tolerability analyses of oral CAB will include Grade 2 or higher clinical and laboratory events occurred during the oral phase. Analysis time frame is from the first date of taking oral CAB tablet to the date right before the first CAB LA injection. For subjects who withdraw treatment from the oral phase, the analysis will include all safety and tolerability assessments from the first date of taking oral CAB tablet up to the date of last study visit.

Safety endpoints including adverse events, laboratory test, vital signs, and death will be analysed. The same analysis approaches will be conducted as in the primary analysis, but with different time frame.

Table 13 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 13 Overview of Planned AE, LB, VS, and Death Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
AE Analyses							
All AEs				Y			Y
Grade 2 or higher AEs				Y			Y
SAEs				Y			Y
AE leading to treatment discontinuation or study withdrawal				Y			Y
Drug-related AEs				Y			
Drug-related SAEs				Y			
Drug-related Grade 2 or higher AEs				Y			
Common AEs				Y			
Common non-serious AEs				Y			
Common Grade 2-4 AEs				Y			
Common drug-related Grade 2-4 AEs				Y			
Laboratory Tests							
Grade 2 or higher laboratory events				Y			
Clinical Chemistry				Y			Y
Hematology				Y			Y
Fasting Lipid Profile				Y			Y
Urinalysis				Y			Y
Coagulation Profile				Y			Y
Other lab data including local lab							Y
Vital Sign Analysis							
Vital Signs				Y			Y
Death Analysis							
Death							Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.3. Acceptability of CAB LA

The secondary acceptability analyses will be based on safety population, unless otherwise specified. All summary data and statistics are calculated from available data, unless otherwise specified.

To assess acceptability of the CAB LA, the proportion (with 95% confidence interval) of participants who would consider using CAB LA for HIV prevention in the future will be calculated among all subjects in the safety population (including those who terminated product use during the trial). Participants will be asked if they would consider using CAB LA for HIV prevention in the future at their Week 41 visit or at their withdrawal visit, whichever occurs first. Patients who are lost to follow up or with missing responses will be presented as such in a separate category.

Table 14 provides an overview of the planned acceptability analyses, with further details of data displays being presented in Appendix 14: List of Data Displays.

Table 14 Overview of Planned Acceptability Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Acceptability of the CAB LA							
participants who would consider using CAB LA				Y			Y

NOTES:

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.4. Concentration-effect Relationships for Safety and Tolerability Parameters

Evaluation of relationships between significant safety and tolerability parameters and CAB PK may be explored.

8.5. General Safety Analyses

This section will describe safety analyses that are not mentioned in Section 7.1 or Section 8.2, but usually are performed as safety assessment.

8.5.1. Extent of Exposure to CAB

Duration of exposure to CAB and cumulative dose (see Section 10.6.2 for the definition) will be summarized for the oral phase and the injection phase separately. Overall exposure to the study drug and to the study (for safety evaluation) will also be calculated and summarized. Exposure data will also be listed.

Table 15 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 15 Overview of Planned Analyses for Extent of Exposure

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Extent of Exposure							
Extent of exposure				Y			Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.5.2. Possible suicidality-related Adverse Events

Possible suicidality-related will be listed.

Table 16 provides an overview of the planned analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 16 Overview of Analyses for possible suicidality-related AEs

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
AE Analyses							
Possible Suicidality-Related Adverse Event							Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.5.3. Social Harms

Details of social harms collected on the eCRF will be listed for each participant.

Table 17 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 17 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Social Harms			
All Social Harms			Y

NOTES:
- Y = Yes display generated.

8.5.4. ECG

ECG test will be performed at Screening only. Details collected on the eCRF will be listed for each subject. Baseline ECG findings (normal, abnormal – not clinically significant, or abnormal - clinically significant) will be summarized by number and percentage of subjects and presented as part of the 'Demographic Characteristics' table.

Table 18 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 18 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
ECG			
ECG Parameters and Results	Y		Y

NOTES:
- Y = Yes display generated.

8.5.5. Cardiovascular Events

Any cardiovascular events will be listed only.

Table 19 provides an overview of the planned cardiovascular event analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 19 Overview of Planned Cardiovascular Event Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
CV Event Analyses							
All CV events							Y

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L

- Individual = Represents FL related to any displays of individual subject observed raw data.

8.5.6. Liver Events

Number and percentage of subjects with liver events will be tabulated by study phase. Number and percentage of subjects with clinical significant hepatobiliary laboratory abnormalities during the study will also be tabulated. Full information of liver events will be listed.

Table 20 provides an overview of the planned liver event analyses, with full details of data displays being presented in Appendix 14: List of Data Displays.

Table 20 Overview of Planned Liver Event Analyses

Display Type	Data Displays Generated						
	Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L
Liver Event Analyses							
All liver events				Y			Y
Hepatobiliary laboratory abnormalities				Y			

NOTES:
- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

9. REFERENCES

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10. APPENDICES

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RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
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10.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

Protocol waivers or exemptions are not allowed with the exception of immediate safety concerns that may arise after the oral administration of CAB.

Deviations from inclusion and exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or participant safety. Therefore, adherence to the criteria as specified in the protocol is essential

10.1.1. Exclusions from Per Protocol Population

Not applicable. Per protocol population is not defined in this study.

10.2. Appendix 2: Time & Events

10.2.1. Protocol Defined Time & Events

Table 21 Schedule of Activities[q]

Clinical Assessments	Screening[a]	Oral Phase[m]		Injection Phase												Follow- up Phase & Final Visit	
		Day 1	Day 28 (Week 4)	Day 35 (Week 5) Injection 1	Day 42 (Week 6)	Week 9 Injection 2	Week 10	Week 17 Injection 3	Week 18	Week 25 Injection 4	Week 26	Week 33 Injection 5	Week 34	Week 37	Week 41	Week 53, 65, 77	Week 89
Written informed consent	X																
Inclusion/Exclusion criteria[b]	X																
Demographic information	X																
Full physical exam/medical history[c]	X																X
Brief physical exam		X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Height/weight/BMI[d]	X																X
Medication/drug/alcohol history	X																
HIV counseling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Offer condoms and lubricant	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dispense oral study medication (with counseling)[e]		X															
Drug accountability (pill counts)		X	X														

Clinical Assessments	Screening[a]	Oral Phase[m]		Injection Phase												Follow- up Phase & Final Visit	
		Day 1	Day 28 (Week 4)	Day 35 (Week 5) Injection 1	Day 42 (Week 6)	Week 9 Injection 2	Week 10	Week 17 Injection 3	Week 18	Week 25 Injection 4	Week 26	Week 33 Injection 5	Week 34	Week 37	Week 41	Week 53, 65, 77	Week 89
CAB LA Injection (with counseling)				X		X		X		X		X					
HIV-PrevTSQc[f]							X										
ISR AE Diary[g]				X		X		X		X		X					
AE		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SAE review (SAE will be collected from the signing of ICF)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication check		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs[h]	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Qualitative HIV RNA by NAAT[i]	X																
HIV PoC test[j]	X	X		X		X		X		X		X			X	X	X
ECG[k]	X																
HbsAg and HbsAb, HCV Antibody	X																
Hematology/Chemistry testing	X	X	X	X	X	X		X		X		X			X		X
Urinalysis	X														X		
Urine screen for Chlamydia and gonorrhea	X																
Liver Chemistry Tests[l]																X	

Clinical Assessments	Screening[a]	Oral Phase[m]		Injection Phase												Follow- up Phase & Final Visit	
		Day 1	Day 28 (Week 4)	Day 35 (Week 5) Injection 1	Day 42 (Week 6)	Week 9 Injection 2	Week 10	Week 17 Injection 3	Week 18	Week 25 Injection 4	Week 26	Week 33 Injection 5	Week 34	Week 37	Week 41	Week 53, 65, 77	Week 89
Fasting lipid profile		X													X		
Coagulation testing	X														X		
TRUST for Syphilis screen	X																
Plasma for CAB concentration[m,n,o]			X[m]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Plasma storage sample[p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

AE: Adverse events, BMI: Body mass index, CAB: Cabotegravir, CAB LA: Cabotegravir long-acting, ECG: Electrocardiogram, HbsAg: Hepatitis B surface antigen, HIV: Human Immunodeficiency Virus, HCV: Hepatitis C Virus, ISR: Injection site reactions, SAE: Serious adverse event, HIV-PrevTSQc: HIV-Prevention Treatment Satisfaction Questionnaire (change): TRUST: Toluidine Red Unheated Serum Test, RNA: Ribonucleic acid.

a. Screening (including drug screen) is to be performed within 30 days of the first dose in the Oral Phase of the study. See Appendix 2 from the study protocol
b. Inclusion/exclusion criteria will be fully assessed at the Screening visit. Changes between the screening visit and the Day 1 visit should be assessed to ensure eligibility, including additional assessments performed at Day 1.
c. A full physical exam will be performed at Week 89.
d. Weight will be collected at Screening and at Week 89. Height and BMI will be collected at Screening only.
e. Oral phase consists of 28 days with a 7 day washout period between Day 28 (last oral dose) and Day 35 (first injection visit).
f. HIV-PrevTSQc: HIV-Prevention Treatment Satisfaction Questionnaire (change) will be given at Week 10 only (after 2nd injection).
g. ISR AE 7 Day Post Injection Diary will be distributed at the injection visit at Week 5, 9, 17, 25 and 33 and returned to the clinic at weeks 6, 10, 18, 26, and 34. For participants having ISR on the last day of week 5, 9, 17, 25 and 33, additional ISR AE Weeks 2 – 12 Post Injection Diary will be distributed at weeks 6,10, 18, and 26,34. Participants will be asked to bring the diary to each clinic visit.
h. Vital sign measurements will be performed following 5 minutes of rest.
i. Qualitative HIV Nucleic Acid Amplification Testing (NAAT) will be performed at Screening. See Appendix 9 from the study protocol for the HIV testing algorithm at screening, Day 1 and during the course of the study.

j. HIV PoC (Point of care) test will be performed at each time point during the course of the study and must be reviewed prior to IM dosing. See Appendix 9 from the study protocol for the HIV testing algorithm at screening, Day 1 and during the course of the study.

k. ECGs will be performed following 5 minutes of rest in a semi-supine position.

l. Liver Chemistry Tests include Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Bilirubin total and direct.

m. Oral Pharmacokinetic (PK) sampling at trough will be collected for all subjects prior to dose within 20 to 28 hours following oral administration the day prior. Intensive oral PK sampling will be collected from approximately16 participants as shown in Table 20.

n. PK sampling for Injection phase: All PK samples will be collected prior to CAB LA injections at Week 5, 9, 17, 25, and 33 with the exception of 1-week post injection samples at Weeks 6, 10, 18, 26, 34, 37 (2-week post injection sample) and Week 41

o. Long-term follow up PK samples: PK sampling during follow up will occur at, Week 53, 65, 77, and 89.

p. Additional testing is required for participants who have a reactive or positive HIV test after enrolment. Stored plasma from the visit previous to the positive test should be tested for HIV using the 4th generation HIV test to best estimate time of infection. HIV acquisition must be confirmed by either western blot, HIV ½ Multispot or the Geenius HIV Confirmation ½ Assay, and HIV RNA.

q. Visit may occur in a window ±3 Day

Table 22 Schedule of Intensive Oral PK (Approximately 16 Participants) [a,b]

	Day 25	**Day 26**	**Day 27**							**Day 28**	
	Check-in	Oral dose administered (e.g. 8AM)	Prior to oral dose (e.g. 7:55AM)	Oral dose administered (e.g. 8AM)	1-hour post dose (e.g. 9AM)	2-hour post dose (e.g. 10AM)	3-hour post dose (e.g. 11AM)	4-hour post dose (e.g. 12AM)	8-hour post dose (e.g. 4PM)	24-hour post dose (e.g. 8AM)	Oral dose administered (e.g. after 8 AM)
Plasma for CAB concentration			X		X	X	X	X	X	X	

a. PK sampling may occur ±15min

b. Central lab tests for the intensive oral PK subjects refer to Table 21.

10.3. Appendix 3: Assessment Windows

10.3.1. Assessment Windows

The nominal visit information collected on CRF will be used in the analysis. Analysis visit based on the time window will not be defined in this study.

10.4. Appendix 4: Study Phase and State

10.4.1. Treatment Phases

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

Treatment Phase	Definition
Screening Phase	Date < Date of first Oral CAB
Oral Phase	Date of First Oral CAB <= Date <= Date of First CAB LA Injection -1 day; for subjects who discontinued before receiving CAB LA Injection, the end date of the oral phase is the date of last study visit.
Injection Phase	Date of First CAB LA Injection <= Date <= 8 weeks after Last CAB LA Injection
Follow-up Phase	Date > 8 weeks after Last CAB LA Injection

10.4.2. Treatment States

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

10.4.2.1. Treatment States for AE Data

Treatment State	Definition
Screening Phase	AE Start Date < Date of First Oral CAB
On-Oral CAB-Treatment	Day 1 ≤ AE Start Date ≤ Date of First CAB LA Injection – 1; for subjects who withdraw from oral CAB treatment, Day 1 ≤ AE Start Date ≤ Withdrawal date + 7 days
On-CAB LA-treatment	Date of First CAB LA Injection ≤ AE Start Date ≤ Date of Week 41 Visit ; for subjects who withdraw from CAB LA injection, Date of First CAB LA Injection ≤ AE Start Date ≤ Date of Last CAB LA Injection + 8 Weeks
Post-Treatment	AE Start Date > Date of Last CAB LA Injection + 8 weeks
Onset Time Since 1st Dose (Days)	If Date of First Oral CAB (or CAB LA injection) >AE Onset Date, duration = AE Onset Date - Treatment Start Date If Date of First Oral CAB (or CAB LA injection) ≤ AE Onset Date, duration = AE Onset Date - Treatment Start Date +1 Missing otherwise.
AE Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on CRF OR value is missing

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
Study Group		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	CAB PO 30 mg QD	CAB 30 mg	1
B	CAB LA IM 600 mg Q8W	CAB LA 600 mg	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

10.5.2. Baseline Definition & Derivations

10.5.2.1. Baseline Definitions

The baseline or pre-dose assessment is the last available assessment prior to the time of the first dose unless it is specified otherwise.

10.5.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]
Maximum Change from Baseline	= Calculate the change from baseline at each given timepoint and determine the maximum change

NOTES:

- Unless otherwise specified, the baseline definitions specified in Section 10.5.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

10.5.3. Reporting Process & Standards

Reporting Process
Software
• The currently supported versions of SAS software 9.2 or higher and Phoenix WinNonlin will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards SDTMIG v3.2 & ADaMIG v1.0 • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.

Reporting Process
Generation of RTF Files
• RTF files will be generated for the TLFs. But only compiled PDF file will be used in the delivery.

Reporting Standards	
General	
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics	
Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • 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 : • Nominal visits collected on the eCRF will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate. • Reporting for Data Listings: • Planned and actual time relative to study drug dosing will be shown in Pharmacokinetic listings (Refer to IDSL Statistical Principle 5.05.1). • Unscheduled or unplanned readings will be presented within the subject's listings. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	
Unscheduled Visits	
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)

Reporting Standards	
Reporting of Pharmacokinetic Parameters	

• Reporting for PK tables, figures and listings:
  • Planned time relative to dosing will be used in mean concentration-time figures and summaries, and actual times will be used for individual concentration-time figures.
  • 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.
  • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in all PK figures, summaries and listings.	

Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and [between and or within] geometric coefficient of variation (CV_b (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)
Parameters Not Being Log Transformed	tmax, first point, last point, and number of points used in the determination of λz.
Summary Tables	The following PK parameters will not be summarised: first point, last point, and number of points used in the determination of λz
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Time Point
• If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target then the mean will be taken. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from Day 1 Visit:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Date of Day 1 Visit → Study Day = Ref Date –Date of Day 1 Visit
  • Ref Date ≥ Date of Day 1 Visit → Study Day = Ref Date –Date of Day 1 Visit + 1

10.6.2. Study Population

Demographics
Age
• As the month and date of birth will not be collected in the study, the age will be calculated as Year of ICF – Year of Birth; • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height $(m)^2$]

Extent of Exposure

• Duration of exposure to study drug will be calculated based on the formula:
  ○ The duration of exposure for oral phase is defined as the number of days starting from the first oral dose to the last oral dose.
  ○ Duration of exposure for injection phase is defined as the number of injections (1, 2, 3, 4 or 5)
  ○ Overall exposure to CAB is defined as number of days from the first oral dose to 8 weeks following the participant's last injection. If a participant does not enter the injection phase, the overall CAB exposure for the study will be defined as the number of days from the first oral dose to the last oral dose.
  ○ Overall exposure to the study (for safety evaluation) is defined as number of days from the first dose to last visit (including unscheduled visit) in days.
• The cumulative dose will be based on the formula:
  ○ Cumulative dose in oral phase is defined as (number of tablets dispensed – number of tablets returned) * 30 mg
  ○ Cumulative dose in injection phase is defined as number of injections * 600 mg

10.6.3. Safety

Adverse Events
Adverse Events of Special Interest
• Diarrhea • Hypertriglyceridemia/ Hypercholesterolemia • Decline in Renal Function • Proximal Renal Tubule Dysfunctions • Proteinuria

Laboratory Parameters
• HIV-1 RNA: For summaries and analyses which use HIV-1 RNA level as a continuous measure, the logarithm to base 10 of the value will be used. • If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value. o Example 1: 2 Significant Digits = '< x' becomes x – 0.01 o Example 2: 1 Significant Digit = '> x' becomes x + 0.1 o Example 3: 0 Significant Digits = '< x' becomes x – 1

10.7. Appendix 7: Premature Withdrawals & Handling of Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completing all phases of the study including week 89. • If participants prematurely discontinue the oral phase of the study, additional replacement participants may be recruited at the discretion of the Sponsor. Participants who enter the injection phase of the study will not be replaced • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.7.2. 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 using a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such. • Missing endpoints which are not covered in the following rule will not be imputed, unless otherwise specified.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Partial missing start or end dates will be imputed using the convention specified in Section 10.7.2.2 Handling of Partial Dates

10.7.2.2. Handling of Partial Dates

Element	Reporting Detail
Concomitant Medications	• 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.
Adverse Events	• Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made: 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 However, if these results in a date prior to Week 1 Day 1 and the event could possibly have occurred during treatment from the partial information, then the Week 1 Day 1 date will be assumed to be the start date. The AE will then be considered to start on-treatment (worst case). 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, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • The recorded partial date will be displayed in listings.

10.7.2.3. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
N/A	No statistical analysis is planned, unless otherwise specified.

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values

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

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

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

10.8.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	> 450 [1]	
		> 450 [1]	≤ 479 [1]
		≥ 480 [1]	≤ 499 [1]
		≥ 500 [1]	
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec	> 60 [1]	
	msec	> 30 [1]	≤ 59 [1]
	msec	≥ 60 [1]	

NOTES: [Remove footnotes for RAP development]

1. Represent standard ECG values of PCI for HV studies
2. Represent further subdivisions of ECG values for analysis whereby the RAP team needs to decide whether these need to be generated in addition to standard ECG values being flagged. IF not required, then delete.

10.8.3. Vital Signs

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

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper
Systolic Blood Pressure	mmHg	≥ 20	≥ 40	≥ 20	≥ 40
Diastolic Blood Pressure	mmHg	≥ 10	≥ 20	≥ 10	≥ 20
Heart Rate	bpm	≥ 15	≥ 30	≥ 15	≥ 30

NOTES: [Remove footnotes for RAP development]

Represent further subdivisions of BP & HR for analysis whereby the RAP team needs to decide whether these need to be generated in addition to standard absolute BP & HR values being flagged. IF not required, then delete.

10.9. Appendix 9: Multicenter Studies

10.9.1. Methods for Handling Centres

- In this multicentre study, enrolment will be presented by investigative site.

10.10. Appendix 10: Examination of Covariates, Subgroups & Other Strata

10.10.1. Handling of Covariates, Subgroups & Other Strata

- Demographic covariates that may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses.
- Additional covariates of clinical interest may also be considered.

10.11. Appendix 11: Multiple Comparisons & Multiplicity

10.11.1. Handling of Multiple Comparisons & Multiplicity

Not applicable.

10.12. Appendix 12: Model Checking and Diagnostics for Statistical Analyses

10.12.1. Statistical Analysis Assumptions

Endpoint(s)	• PK endpoint $C\tau$
Analysis	• ANOVA (primary)
• Model assumptions will be applied, but appropriate adjustments maybe 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.	

10.13. Appendix 13 – Abbreviations & Trade Marks

10.13.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AUC(0-τ)	Area under the concentration-time curve (AUC) over the dosing interval
Cτ	The observed concentration at the end of the dosing interval
CAB	Cabotegravir
CAB LA	Cabotegravir Long Acting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL/F	The apparent clearance (adjusted for bioavailability, F)
Cmax	Maximum observed concentration
CSR	Clinical Study Report
CTMS	Clinical Trial Management System
CV_b	Coefficient of Variation (Between)
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
GSK	GlaxoSmithKline
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IM	Intramuscular
IP	Investigational Product
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligrams
PCI	Potential Clinical Importance
PK	Pharmacokinetic
PrEP	Pre-exposure prophylaxis
QC	Quality Control
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SAS	Statistical Analysis Software
SD	Standard deviation
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
t½	Terminal phase half-life
tmax	Time to first occurrence of Cmax
TFL	Tables, Figures & Listings
Vz/F	The volume of distribution associated with the terminal phase (adjusted for bioavailability, F)
λz	Terminal-phase rate constant

10.13.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

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

10.14. Appendix 14: List of Data Displays

10.14.1. Data Display Numbering

The following numbering will be applied for RAP generated display according to ICH standards:

Section	Tables	Figures
Study Population	1.1 to 1.10	NA
Safety	2.1 to 2.32	NA
Pharmacokinetic	3.1 to 3.11	3.1-3.8
Section	**Listings**	
ICH Listings	1-51	

10.14.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 15: 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

NOTES:

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

10.14.3. Deliverable [Priority]

Delivery [Priority] [1]	Description
W41 SAC [1]	Primary Statistical Analysis Complete at Week 41
SAC [1]	Final Statistical Analysis Complete at Week 89

NOTES:

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

10.14.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population, Disposition and Demographics					
1.1	Screened	SP1	Summary of Study Population		W41 SAC [1], SAC [1]
1.2	Screened	ES6	Summary of Screen Status and Reasons for Screen Failures		W41 SAC [1], SAC [1]
1.3	Screened	ES1	Summary of Subject Disposition for the Subject Conclusion Record		W41 SAC [1], SAC [1]
1.4	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment		W41 SAC [1], SAC [1]
1.5	Safety	DM1	Summary of Demographic Characteristics		W41 SAC [1], SAC [1]
Medical History and Concomitant Medications					
1.6	Safety	MH4	Summary of Medical Conditions	.	W41 SAC [1], SAC [1]
1.7	Safety	CM1	Summary of Prior Medications		W41 SAC [1], SAC [1]
1.8	Safety	CM1	Summary of Concomitant Medications		W41 SAC [1], SAC [1]
Protocol Deviations					
1.9	Safety	IE1	Summary of Inclusion/Exclusion Criteria Deviations		W41 SAC [1], SAC [1]
1.10	Safety	DV1A	Summary of Important Protocol Deviations		W41 SAC [1], SAC [1]

10.14.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
2.1	Safety	EX1	Summary of Extent of Exposure		W41 SAC [1], SAC [1]
Injection Site Reactions					
2.2	Safety Injection		Summary of Injection Site Reaction		W41 SAC [1], SAC [1]
Adverse Events					
2.3	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term		W41 SAC [1], SAC [1]
2.4	Safety	AE5B	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term		W41 SAC [1], SAC [1]
2.5	Safety	AE3	Summary of All Grade 2 or Higher Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.6	Safety	AE3	Summary of Serious Adverse Events		W41 SAC [1], SAC [1]
2.7	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		W41 SAC [1], SAC [1]
2.8	Safety	AE3	Summary of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study		W41 SAC [1], SAC [1]
2.9	Safety	AE1	Summary of Drug-Related Adverse Events		W41 SAC [1], SAC [1]
2.10	Safety	AE1	Summary of Drug-Related Serious Adverse Events		W41 SAC [1], SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.11	Safety	AE3	Summary of Drug-related Grade 2 or Higher Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.12	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.13	Safety	AE15	Summary of Common (>=5%) Non-Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		W41 SAC [1], SAC [1]
2.14	Safety	AE3	Summary of Common (>=5%) Grade 2-4 Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
2.15	Safety	AE3	Summary of Common (>=5%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency		W41 SAC [1], SAC [1]
Laboratory Tests					
2.16	Safety		Summary of Grade 2 or Higher Laboratory Tests		W41 SAC [1], SAC [1]
2.17	Safety	ES11	Summary of Characteristics of Adverse Events of Special Interest		W41 SAC [1], SAC [1]
2.18	Safety	LB1	Summary of Change from Baseline in Hematology and Coagulation Data		W41 SAC [1], SAC [1]
2.19	Safety	LB1	Summary of Change from Baseline in Fasting Chemistry Data and Lipid Profile		W41 SAC [1], SAC [1]
2.20	Safety	UR3	Summary of Urinalysis and Urine Chemistry Results		W41 SAC [1], SAC [1]
2.21	Safety	LB18	Summary of Hematology and Coagulation Grade Shifts from Baseline Grade		W41 SAC [1], SAC [1]
2.22	Safety	LB18	Summary of Fasting Chemistry and Lipid Profile Grade Shifts from Baseline Grade		W41 SAC [1], SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.23	Safety	LB18	Summary of Urinalysis Grade Shifts from Baseline Grade		W41 SAC [1], SAC [1]
Vital Signs					
2.24	Safety	VS1	Summary of Change from Baseline in Vital Signs		W41 SAC [1], SAC [1]
2.25	Safety	VS8	Summary of Vital Sign Shifts from Baseline with Respect to Clinical Concern Range		W41 SAC [1], SAC [1]
Liver Events					
2.26	Safety	LIVER1	Summary of Liver Events Reporting		W41 SAC [1], SAC [1]
2.27	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities		W41 SAC [1], SAC [1]

10.14.6. Tolerability Tables

Tolerability: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Tolerability of CAB Injection					
2.28	Safety Injection		Summary of HIV-Prevention Treatment Satisfaction Scores		W41 SAC [1], SAC [1]

10.14.7. Acceptability Tables

Acceptability: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Acceptability of the CAB Injection					
2.29	Safety		Summary of Acceptability of the CAB LA		W41 SAC [1], SAC [1]

10.14.8. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Oral Phase					
3.1	Oral PK	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data – Oral Phase		SAC [1]
3.2	Oral PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) – Oral Phase	Parameters with units	SAC [1]
3.3	Oral PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Log-Transformed) – Oral Phase	Parameters with units	SAC [1]
Injection Phase (up to Week 41)					
3.4	Injection (Week 41) PK	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.5	Injection (Week 41) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) – Injection Phase (up to Week 41)	Parameters with units	W41 SAC [1], SAC [1]
3.6	Injection (Week 41) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Log-Transformed) – Injection Phase (up to Week 41)	Parameters with units	W41 SAC [1] SAC [1]
3.7	Injection (Week 41) PK	PKPT3	Statistical Analysis of CAB Plasma Accumulation – Injection Phase (up to Week 41)	$C\tau$ only for Injection Phase at Week 41.	W41 SAC [1], SAC [1]
3.8	Injection (Week 41) PK	PKPT3	Statistical Analysis of CAB Plasma Steady-state Pre-dose Concentrations – Injection Phase (up to Week 41)	$C\tau$ only for Injection Phase at Week 41.	W41 SAC [1], SAC [1]

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Injection Phase (up to Week 89)					
3.9	Injection (Week 89) PK	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 89)		SAC [1]
3.10	Injection (Week 89) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) – Injection Phase (up to Week 89)	Parameters with units	SAC [1]
3.11	Injection (Week 89) PK	PKPT4	Summary of Derived CAB Plasma Pharmacokinetic Parameters (Log-Transformed) – Injection Phase (up to Week 89)	Parameters with units	SAC [1]

10.14.9. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Oral Phase					
3.1	Oral PK	PKCF1P	Individual CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Oral Phase		SAC [1]
3.2	Oral PK	PKCF4	Mean (±SD) CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Oral Phase		SAC [1]
Injection Phase (up to Week 41)					
3.3	Injection (Week 41) PK	PKCF1P	Individual CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.4	Injection (Week 41) PK	PKCF4	Mean (±SD) CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.5	Injection (Week 41) PK	PK26	Individual CAB Plasma Pre-dose Concentration versus Week (Linear and Semi-Logarithmic) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
3.6	Injection (Week 41) PK	PK27	Median (range) CAB Plasma Pre-dose Concentration versus Week (Linear and Semi log) – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
Injection Phase (up to Week 89)					
3.7	Injection (Week 89) PK	PKCF1P	Individual CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 89)		SAC [1]
3.8	Injection (Week 89) PK	PKCF4	Mean (±SD) CAB Plasma Concentration-Time Plots (Linear and Semi-Logarithmic) – Injection Phase (up to Week 89)		SAC [1]

10.14.10. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population, Disposition and Demographics					
1	Screened	SP3	Listing of Subjects Excluded from Any Population		W41 SAC [1], SAC [1]
2	Screened	ES7	Listing of Reasons for Screen Failure		W41 SAC [1], SAC [1]
3	Safety	ES2	Listing of Reasons for Withdrawal		W41 SAC [1], SAC [1]
4	Safety	SD2	Listing of Study Drug Discontinuation Record		W41 SAC [1], SAC [1]
5	Safety	DM2	Listing of Demographic Characteristics		W41 SAC [1], SAC [1]
6	Safety	EX3	Listing of Exposure Data – Oral Dose		W41 SAC [1], SAC [1]
7	Safety		Listing of Exposure Data – Injection		W41 SAC [1], SAC [1]
Medical History and Concomitant Medication					
8	Safety	MH2	Listing of Medical Conditions		W41 SAC [1], SAC [1]
9	Safety	CM5	Listing of Prior Medications		W41 SAC [1], SAC [1]
10	Safety	CM5	Listing of Concomitant Medications		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Protocol Deviations					
11	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		W41 SAC [1], SAC [1]
12	Safety	DV2	Listing of Important Protocol Deviations		W41 SAC [1], SAC [1]
Injection Site Reaction					
13	Safety Injection		Listing of Injection Site Reaction – Daily Diary Card 1		W41 SAC [1], SAC [1]
14	Safety Injection		Listing of Injection Site Reaction – Daily Diary Card 2		W41 SAC [1], SAC [1]
Adverse Events					
15	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		W41 SAC [1], SAC [1]
16	Safety	AE8	Listing of All Adverse Events		W41 SAC [1], SAC [1]
17	Safety	AE8CPA	Listing of Serious Adverse Events (Fatal and Non-Fatal)		W41 SAC [1], SAC [1]
18	Safety	AE8	Listing of Grader 2 or Higher Adverse Events		W41 SAC [1], SAC [1]
19	Safety	AE8	Listing of All Adverse Events Leading to Premature Discontinuation of Study Drug or Withdrawal from Study		W41 SAC [1], SAC [1]
20	Safety	AE8	Listing of Adverse Events of Special Interest		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
21	Safety		Listing of Possible Suicidality-Rated Adverse Events		W41 SAC [1], SAC [1]
22	Safety	AE2	Listing of Relationship Between System Organ Classes and Verbatim Text		W41 SAC [1], SAC [1]
23	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event		W41 SAC [1], SAC [1]
Deaths					
24	Safety		Listing of Death		W41 SAC [1], SAC [1]
Laboratory Tests					
25	Safety	LB5	Listing of Chemistry Data and Fasting Lipid Profile		W41 SAC [1], SAC [1]
26	Safety	LB5	Listing of Hematology and Coagulation Data		W41 SAC [1], SAC [1]
27	Safety	UR2a	Listing of Urinalysis and Urine Chemistry Data		W41 SAC [1], SAC [1]
28	Safety	LB5	Listing of Laboratory Data for Subjects with Grade 2 or Higher Abnormalities		W41 SAC [1], SAC [1]
29	Safety	LB14	Listing of HIV Tests		W41 SAC [1], SAC [1]
30	Safety	LB5	Listing of Local Lab Data		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Sign					
31	Safety	VS4	Listing of Vital Signs		W41 SAC [1], SAC [1]
32	Safety	VS4	Listing of Vital Signs for Subjects with Any Value of Potential Clinical Importance		W41 SAC [1], SAC [1]
ECG's					
33	Safety		Listing of ECG Results		W41 SAC [1], SAC [1]
Social Harm					
34	Safety		Listing of Social Harm		W41 SAC [1], SAC [1]
Cardiovascular Event					
35	Safety		Listing of Cardiovascular Event		W41 SAC [1], SAC [1]
Liver Event					
36	Safety		Listing of Liver Event		W41 SAC [1], SAC [1]
Tolerability of CAB Injection					
37	Safety Injection		Listing of HIV-Prevention Treatment Satisfaction Questionnaire		W41 SAC [1], SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Acceptability of the CAB Injection					
38	Safety		Listing of Acceptability of the CAB LA		W41 SAC [1], SAC [1]
Pharmacokinetic					
39	Oral PK	PKCL1P	Listing of CAB Plasma Pharmacokinetic Concentration-Time Data – Oral Phase	Please list all the concentration data including unscheduled.	SAC [1]
40	Oral PK	PKPL1P	Listing of Derived CAB Plasma Pharmacokinetic Parameters – Oral Phase		SAC [1]
41	Injection (Week 41) PK	PKCL1P	Listing of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 41)	Please list all the concentration data including unscheduled.	W41 SAC [1], SAC [1]
42	Injection (Week 41) PK	PKPL1P	Listing of Derived CAB Plasma Pharmacokinetic Parameters – Injection Phase (up to Week 41)		W41 SAC [1], SAC [1]
43	Injection (Week 89) PK	PKCL1P	Listing of CAB Plasma Pharmacokinetic Concentration-Time Data – Injection Phase (up to Week 89)	Please list all the concentration data including unscheduled.	SAC [1]
44	Injection (Week 89) PK	PKPL1P	Listing of Derived CAB Plasma Pharmacokinetic Parameters – Injection Phase (up to Week 89)		SAC [1]

10.14.11. Non-ICH Listings

Non-ICH: Listings					
No.	Population	IDSL / TST ID / Example Shell	Title	Programming Notes	Deliverable [Priority]

10.15. Appendix 15: Example Mock Shells for Data Displays

Data Display Specification will be made available on Request