Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Reporting and Analysis Plan for ViiV Healthcare-sponsored study 212482: A Phase 1, Two-part, Double-blind, Active-control, Randomized Study to Evaluate the Pharmacokinetics, Safety and Tolerability of Repeat-Dose Cabotegravir (CAB 400 mg/mL formulation) Long-Acting Injection Following Subcutaneous or Intramuscular Administration in Healthy Adult Participants
Compound Number	:	GSK1265744/CAB 400 mg/mL formulation
Clinical Study Identifier	:	212482
Effective Date	:	06-May-2022

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 212482 and preliminary analyses to support submission of key results to a scientific conference
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverables (Part 1, Part 2, and Final) and preliminary analyses (Cohort 1-4 and Cohort 1-5 interim analysis)

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CCI [redacted]

1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol 212482:

Revision Chronology:		
Original protocol	14-Feb-2020	Original
Amendment 1	22-Apr-2020	Reprioritising the cohorts: the order of Cohorts 2 and 3 has changed, i.e., the subcutaneous (SC) abdominal injection will now be evaluated in Cohort 2 and the intramuscular (IM) lateral thigh injection in Cohort 3; participants will be enrolled sequentially into Cohorts 1, 2, and 3. Adding permissible procedures during the COVID-19 Pandemic.
Amendment 2	26-Jun-2020	Revisions were made to the study eligibility criteria and safety assessments to further mitigate the potential risks for study conduct during the COVID-19 pandemic. Additional changes were made based on comments and recommendations for revisions of Protocol 212482 received from the FDA's Division of Antivirals as mentioned in the Division's 'Study May Proceed' letter dated 3 June 2020. Changes impacting data collection include: a) clarification that Randomization will occur on Day 1 of the Oral Lead-in (OLI) Phase prior to dosing of oral CAB, b) Participants will have pharmacokinetic (PK) monitoring up to and including Week 52 post their last CAB injection; Participants with undetectable CAB concentrations before Week 52 will be deemed to have completed follow up and return to the clinic for a last study visit at which activities specified for the Week 52/early withdrawal (EW) visit will be performed, c) Oral Lead-in Day 2 PK sample taken between 20 h and 28 h post first oral dose, d) Participants will be asked to collect their temperature daily for 14 days following each injection.
Amendment 3	29-OCT-2020	Revisions were made to study eligibility criteria, safety assessments and Appendix 8 for participant safety and to further mitigate the potential risks for study conduct during the COVID-19 pandemic and to rephrase sections that were ambiguous. Information on assessments required for sentinel participants in Cohorts 5 and 6 and the definition of what constitutes an overdose of oral cabotegravir have been updated. Revisions pertinent to analysis and reporting include: • Additional PK samples to be collected on Day 1 (at 8 h and 12 h post dose) during OLI phase for Cohorts 5 and 6 • Weight data to be collected during the follow-up phase

		• Part 2 Cohorts 5 and 6: Haematology, clinical chemistry, and urinalysis assessments added for Week 4 and 8 following each injection • Analysis populations redefined to align with GSK/IDSL standards
Amendment 4	28-FEB-2021	Revisions were made to provide further details on the conduct and future dosing regimens following the review of preliminary PK and safety data from Cohorts 1, 2, and 3: • Randomization in Part 2 will now occur on Day 1 of the injection phase • Objective and endpoints to describe the PK profiles of oral CAB added • Details on the conduct of Cohort 4, including doses agreed by the Study Team safety & PK Review (STR), added • Details on the conduct of Cohort 5 added, including a reduced maximum dose (up to 1200 mg rather than up to 1400 mg of CAB 400 mg/mL formulation), Inclusion of four sentinel participants (instead of two) and a 10-day safety review, an additional review of Cohort 4 safety data prior to starting the injection phase of Cohort 5, and staggered recruitment of non-sentinel participants • Dosing in Cohorts 2,3,4, and 5 has been updated • Participants will remain in the clinic for 7 days after each injection • Requirements for SARS-CoV-2 testing have been updated distinguishing between areas/countries where SARS-CoV-2 is circulating in the community and those where it is not • Further information on the assessment of injection site reactions, i.e. the measuring of injection site erythema and swelling, is provided • Further safety assessments during the first 7 days after each injection, i.e. electrocardiograms (ECGs) and clinical chemistry/hematology, are included • Risk mitigation strategies for Drug Induced Liver Injury and Injection Site reactions have been strengthened • A risk about the relationship between CAB plasma concentration and QTc was added and described where the median Cmax was 22.5 ug/mL and the maximum time-matched mean QTcF for CAB was 2.62 msec (1-sided 95% upper CI:5.26 msec). CAB did not prolong the QTc interval. PK and ECG mitigation strategies have been added • Section 4.2.3, Rationale Supporting Cmax criteria of 22.5 µg/mL in Part 2, is added • New sections regarding reporting for medical device deficiencies added

		• To provide details on who is unblinded at what stage of the study and what data will be reviewed by the study team and STR • To provide more details on the use of analgesics following injection site reactions and the use of COVID-19 vaccines • Further pausing criteria related to liver biochemistry are added • Section 10.4.5, Bayesian Predictive Probability for Cohort 5 and 6 Dose Selection, is added • Three further preliminary analyses included Introduce some flexibility in terms of timings of the preliminary analyses
Amendment 5	07-SEP-2021	The primary reason for this amendment is to include a further cohort in Part 1 (Cohort 4b) CCI [redacted] relevant sections throughout the protocol were updated accordingly. CCI [redacted] • Update to PK primary endpoints • New paragraph describing Cohort 4b added • A sentence describing timing of Injection 2 added • Overall participant numbers updated • Information on injections in Cohort 4b added and length of participants' stay in the clinic for different cohorts clarified • Schema for Cohort 4b added • '12-Lead ECG' replaced by 'triplicate12-Lead ECG' throughout • New sections regarding reporting for medical device deficiencies had been added in protocol amendment 4; these have been removed again • Cohort 4b schedule of activities added • Summary of CAB clinical studies updated based on information from most recent CAB IB • Mitigation strategies CCI [redacted] for Cohort 4b CCI [redacted] • Included another exploratory objectives and exploratory endpoints • New information on Cohort 4b added • CCI [redacted] in Cohort 4b included • CCI [redacted]

		• CCI [redacted] • CCI [redacted] Cohort 4b included • CCI [redacted] • Concomitant medications entered in diary cards to be recorded in the CRF • CCI [redacted] to be administered in Cohort 4b included • Overdose definition updated and requirement to record overdoses in the CRF removed • Section on Cohort 4b sample size added • Update to PK primary endpoints • An additional preliminary analysis has been added Formal Part 1 and Part 2 analyses following completion of the injection phases may be combined
Amendment 6	28-OCT-2021	Revisions were made to provide further details on the conduct and future dosing regimens following the review of preliminary PK and safety data from Cohorts 4h: • Overall design update for Cohort 4h. • Randomization of Cohort 4h participants will occur on Day 1 of the injection phase. • Overall participant numbers updated. 20 more participants are to be enrolled and randomized in the study (Cohort 4h). • Information on injection in Cohort 4h added. The doses and route of administration in Cohort 4h and to include information on length of clinic stay following injection in this cohort. • Participants in Cohort 4h will stay in the clinic for 4-7 days after the injection and may be discharged between Day 5 and Day 8; where SARS-CoV-2 is circulating in the community, a SARS-CoV-2 test is required upon discharge from the clinic between Day 5 and Day 8. • Schema for Cohort 4h added to describe the design of Cohort 4h. • Cohort 4h schedule of activities added and describe the type and timing of assessments in Cohort 4h. • Brief description of rHuPH20 and its use added. To provide information on rHuPH20. • Sentinel dosing strategy in Cohort 4h outlined and CAB has not been administered with rHuPH20 in humans before. • Potential risks and mitigation strategies for rHuPH20 included; the potential risks identified with rHuPH20 are well understood.

		• Data on the impact of rHuPH20 on the pharmacokinetics of CAB 200 mg/mL in rats added. • Section on what dose of rHuPH20 to use with CAB 200 mg/mL and CAB 400 mg/mL formulations included. • Exclusion criterion added: A known hypersensitivity to hyaluronidases. • Information on rHuPH20 added to table of study interventions. • New section on rHuPH20 included, to describe the use of rHuPH20 in Cohort 4h. • New section/information added. To reflect the use of rHuPH20 in Cohort 4h, i.e. collect plasma sample for storage of potential immunogenicity analyses if there are safety events suggestive of immune-mediated reactions to rHuPH20. • Information on Cohort 4h sample size added, To provide rationale for Cohort 4h sample size. • An additional preliminary analysis of data from Cohort 4h has been added Information on formal and interim analyses has been updated. • Minor editorial and document formatting revisions.

1.1. RAP Amendment

Revision chronology:

RAP Section	**Amendment Details**
Reporting and Analysis Plan_212482_Final	
Reporting and Analysis Plan_212482_Amendment	
The primary reason for this RAP amendment is to include reporting and analysis details for newly added cohorts 4b and 4h to align with the latest protocol amendment 6.	
RAP Section	**Amendment Details**
Section 2.2 Study Objectives and Estimands Section 3.3 Study Design Section 3 Planned Analyses	• Updated objectives, endpoints, study schematic, study design features and planned analyses, as described protocol amendment 6.
Section 3.2 Interim Analysis	• Updated description of interim analyses to align with protocol amendment 6 • Added decision to conduct an unblinded preliminary interim analysis for Cohort 1-5
Section 4 Analysis Populations	• Added analysis population details for the cohort 1-5 preliminary interim analysis: data displays will exclude cohort 4b data from participants who have received injection 1 but have not yet completed Injection 2 Day 1 or Follow-up Week 4; Cohort 4b will remain

	blinded to randomized CCI [redacted]. • Added Safety – LA Exposed population
Section 5.1 Study Treatment & Sub-group Displays Descriptors	• Added treatment groups for cohort 4b and cohort 4h and shorted treatment descriptors for all cohorts. • Update the list of PK pairwise between cohorts and cross study historical comparisons to be evaluated in statistical analyses.
Section 7.1 Adverse Events Analyses	• Added details for Cohort 4b: adverse event data will be summarized by injection CCI [redacted].
Section 7.4 Other Safety/Exploratory Analyses	• CCI [redacted]
Section 7.5 Exploratory Crossover Analysis for Cohort 4b	• CCI [redacted]
Section 8.1.1.2 Derived Pharmacokinetic Parameters	• Added dose normalized PK parameters for Cohort 3 injection 1 (footnoted) • Added PK parameters for Cohort 4b and 4h • Added C4 & AUC (0-4) PK parameters for Cohort 5
Section 8.1.5 Statistical Analyses/Methods	• Added additional Cohort 4b summary of PK concentrations and parameters by treatment sequence and period CCI [redacted]
Section 8.1.5.1 Statistical Methodology Specification	• Clarified plan to perform PK pairwise comparisons between cohorts receiving the same dose. • Updated dose proportionality assessment to be performed separately for each route rather than across routes.
Section 2.2 Study Objectives and Estimands	• Exploratory endpoint CCI [redacted]
Section 10.2 Appendix 2: Schedule of Activities	• Update protocol defined schedule of events per protocol amendment 6.
Section 10.3: Assessment Windows	• Clarified that all assessments/events, including PK, will be assigned to assessment windows/analysis visits. • Analysis windows were updated to incorporate cohort 4b and 4h assessments and other minor corrections.

Section 10.4: Appendix 4: Study Phases, Study Periods, and Treatment Emergent Adverse Events	• Added analysis period derivation details for CCI [redacted]
Section 10.6.3 Safety	• CCI [redacted] • CCI [redacted]
Section 10.10 Appendix 10: List of Data Displays	• CCI [redacted] • Added displays to summarize clinical chemistry, hematology, coagulation, ECG and vitals sign values (in addition to change from baseline) • Updated analysis population to Safety – LA Exposure for ISR displays • Updated delivery classifications (i.e., Cohort 1-5 IA, Cohort 1-5, EOS). • Combined separate Part 1 and Part 2 displays into a single display. • Additional programming notes added • Updated presentation of treatment groups in the table shells document.
General	• Minor editorial and document formatting revisions

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 through protocol amendment 6.

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

Objectives	Estimands / Endpoints
Primary	**Primary**
PK	**PK**
• To describe the pharmacokinetic (PK) profiles of CAB 400 mg/mL formulation following multiple injections administered intramuscularly (gluteus medius or vastus lateralis) or subcutaneously (abdominal) in healthy adult participants)	• Maximum observed plasma concentration (Cmax) [Injection 1 and 2] • Time of maximum observed plasma concentration (tmax) [Injection 1 and 2] • Area under the concentration – time curve (AUC) for each injected dose from time zero to last quantifiable time point or 4 weeks following injection whichever is earlier (AUC0-t) • Trough concentrations (Cτ) at 4 weeks following first injection (or earlier if the second injection occurs at <4-week interval) and 4 weeks following the second injection • Apparent terminal phase half-life (t½) and absorption rate constant (KALA) [Injection 2]

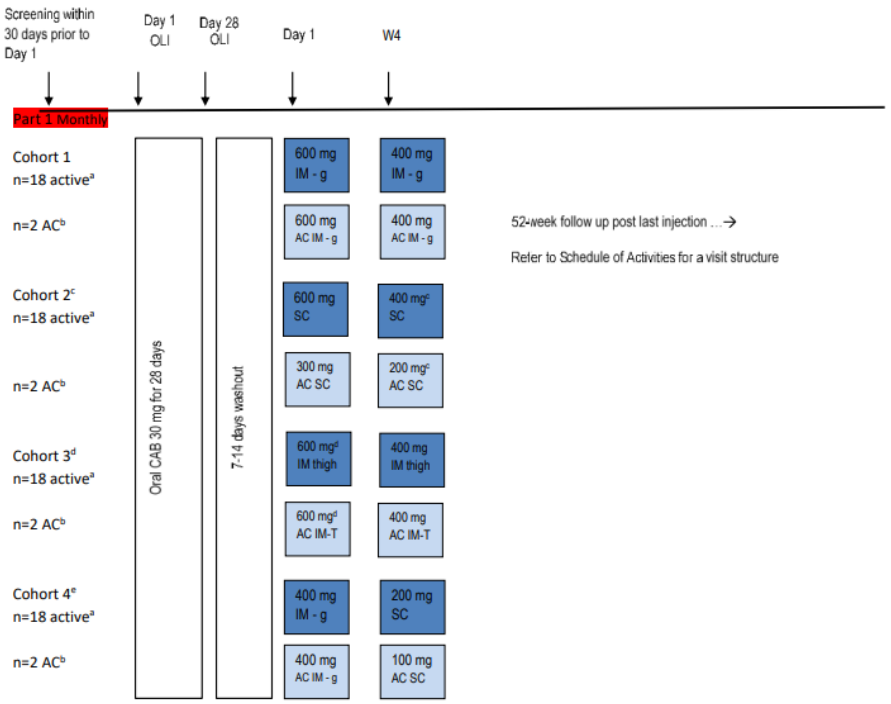
• To assess the relative bioavailability of a CAB 400 mg/mL formulation administered via different routes (i.e., IM (vastus lateralis), IM (gluteus medius) or SC routes) • To compare exposures after CAB 400 mg/mL formulation administered via different routes with historical data of CAB 200 mg/mL formulation administered IM (gluteus medius)	Pair-wise comparisons of geometric mean ratios of plasma trough concentrations (C_T), Cmax, and AUC0-t [injection phase] for Cohorts 1, 2, 3, 4, 4b, and 4h Geometric mean ratios of plasma trough concentrations (C_T) for Cohorts 1, 2, 3, 4, 4b, 4h, 5, and 6 (if conducted) compared to historical CAB 200 mg/mL data
Safety	**Safety**
• To assess safety and tolerability of CAB 400 mg/mL formulations following repeated intramuscular injections in the gluteus medius, vastus lateralis (lateral thigh) or subcutaneously (abdomen) of healthy adult participants. • To assess safety and tolerability of CAB 200 mg/mL with rHuPH20 following a subcutaneous (abdominal) injection in healthy adult participants. • To assess safety and tolerability of CAB 400 mg/mL with rHuPH20 following a subcutaneous (abdominal) injection in healthy adult participants.	• Safety and tolerability parameters including adverse events (AEs), clinical laboratory tests, and vital sign assessments.
Secondary	**Secondary**
Safety	**Safety**
• To assess the tolerability of CAB 400 mg/mL formulation following repeated IM injections in the gluteus medius, vastus lateralis (lateral thigh) or SC (abdomen) of healthy participants. • To assess safety and tolerability of CAB 200 mg/mL with rHuPH20 following a subcutaneous (abdominal) injection in healthy adult participants. • To assess safety and tolerability of CAB 400 mg/mL with rHuPH20 following a subcutaneous (abdominal) injection in healthy adult participants.	• Tolerability parameters (AEs) and liver biochemistry abnormalities.

Secondary	Secondary
PK	**PK**
• To describe the PK profiles of CAB 200 mg/mL and CAB 400 mg/mL formulations with rHuPH20 following a subcutaneous (abdominal) injection in healthy adult participants	• Maximum observed plasma concentration (Cmax) • Time of maximum observed plasma concentration (tmax) • Area under the concentration – time curve from time zero to last quantifiable time point or 4 weeks following the injection whichever is earlier (AUC0-t) • Trough concentrations (C_T) through the Follow-up Phase • Apparent terminal phase half-life ($t_{½}$) and absorption rate constant (KALA)
• To describe the pharmacokinetic (PK) profiles of oral CAB 30 mg following daily administration in healthy adult participants	• Cmax • tmax • AUC(0-t) • C24 • Day 29 C_T
Exploratory	**Exploratory**
CCI [redacted]	

2.3. Study Design

Overview of Study Design and Key Features

Figure 2-1 Study Design Schematic – Part 1 (Cohorts 1-4):

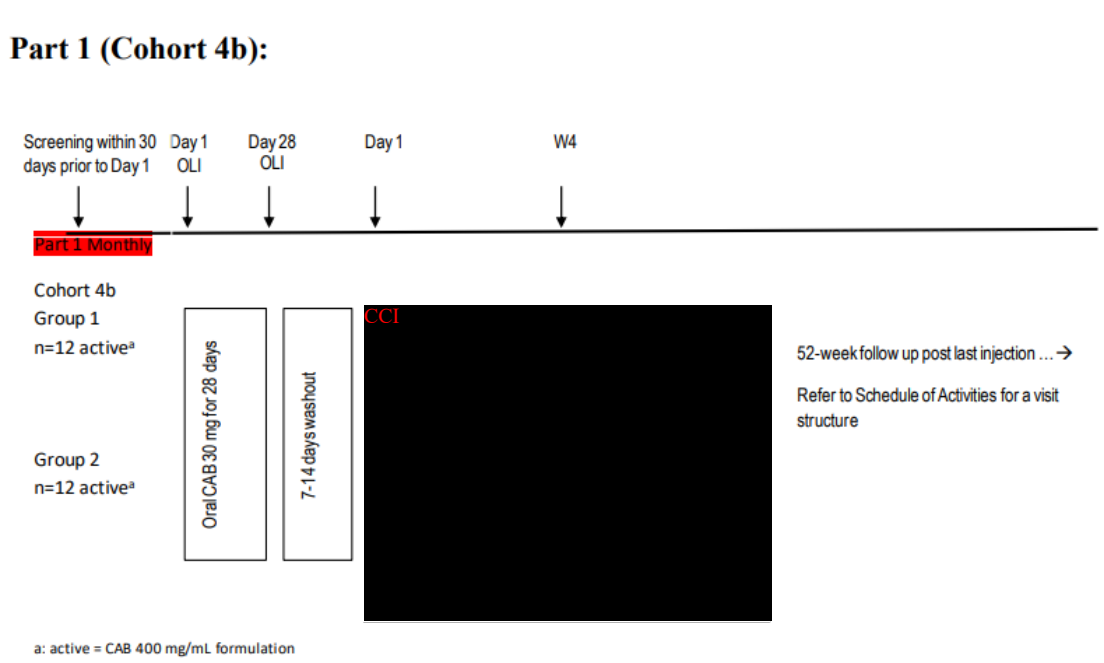


a: active = CAB 400 mg/mL formulation
b: AC = Active control CAB 200 mg/mL formulation
c: At the VSLC meeting on 13 November 2020, it was agreed to modify the conduct of Cohort 2 based upon interim data: participants will receive a second subcutaneous abdominal injection of CAB 200 mg given as 0.5 mL CAB 400 mg/mL formulation or 100 mg as 1 x 0.5 mL CAB 200 mg/mL.
d: At their meeting on 22 December 2020, the STR agreed to reduce the dose of the first IM lateral thigh injection for remaining Cohort 3 participants based on interim PK data from Cohorts 1 and 2, i.e. CAB 400 mg given as 1 x 1 mL of CAB 400 mg/mL formulation or 400 mg as 1 x 2 mL CAB 200 mg/mL.
e: At their meeting on 22 December 2020, the STR agreed to conduct optional Cohort 4.

At a 22 December 2020 STR meeting, it was agreed

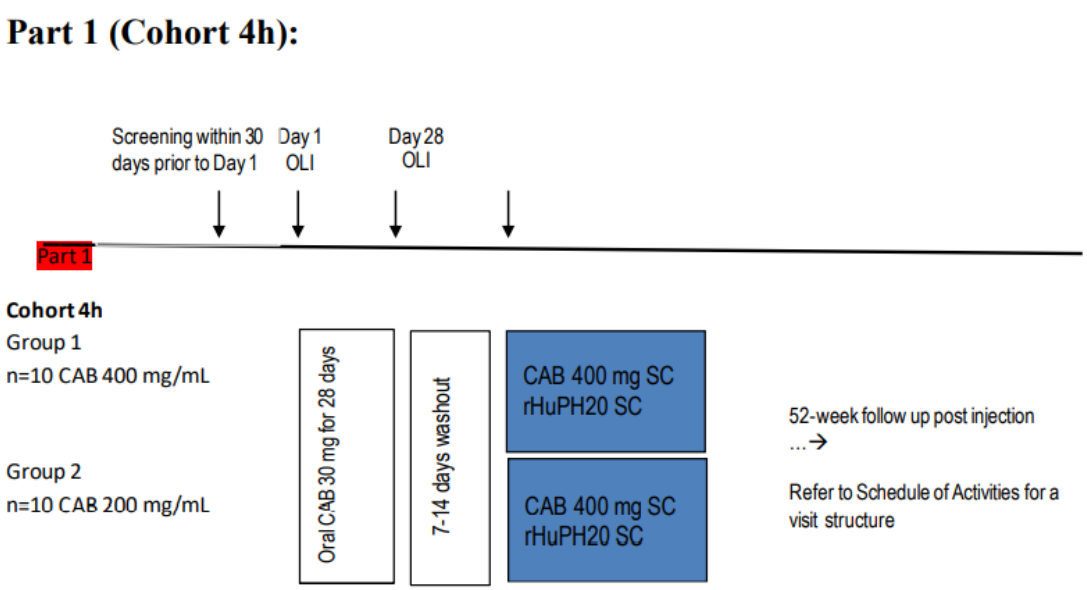
- to conduct Cohort 4 evaluating two 4-weeks apart (Q4W) injections of CAB 400 mg/mL 4 weeks apart (n=18, first injection 400 mg IM *gluteus medius* and second injection 200 mg SC) or two Q4W injections of CAB 200 mg/mL 4 weeks apart as active controls (n=2, first injection 400 mg IM *gluteus medius* and second injection 100 mg SC), and
- to reduce the dose of the first injection for the remaining Cohort 3 participants based on interim PK data from Cohorts 1 and 2. Participants yet to receive Injection 1# in Cohort 3 will receive CAB 400 mg given as 1 x 1 mL of CAB 400 mg/mL formulation or 400 mg as 1 x 2 mL CAB 200 mg/mL IM lateral thigh injection

Figure 2-2 Study Design Schematic – Part 1 (Cohort 4b):



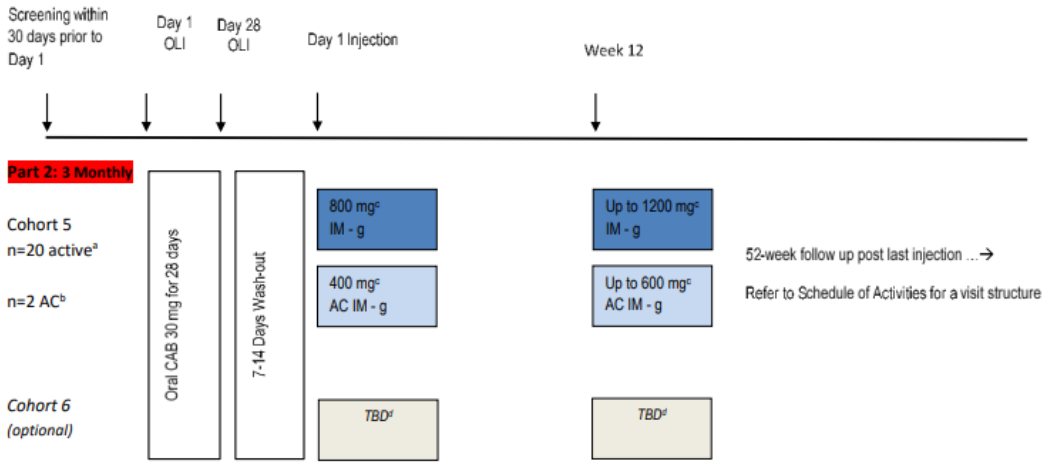
Cohort 4b will assess the PK, safety and CCI among 24 participants. All participants will receive two injections of 300 mg of CAB 400 mg/mL 4 weeks apart. CCI Participants (n=24) will be randomized according to a pre-generated randomization schedule to one of two sequences (i.e. 12 per sequence) of two treatments to be administered along with injection 1 and injection 2, respectively: CCI

Figure 2-3 Study Design Schematic – Part 1 (Cohort 4h):



Cohort 4h will assess the PK, safety and tolerability of long-acting CAB 400 mg/mL and CAB 200 mg/mL formulations administered subcutaneously (abdominal) following recombinant human hyaluronidase PH20 (rHuPH20) administration.

Figure 2-4 Study Design Schematic – Part 2



a: active = CAB 400 mg/mL formulation

b: AC = Active control CAB 200 mg/mL formulation

c: Cohort 5 will commence following preliminary analysis once data (Trough concentrations (Cτ) and Plasma AUC (0-τ) data up to and including week 8 data following injection one from all active subjects in Cohort 1, and safety and tolerability from each cohort 1-3) are reviewed and compared to historical data of the CAB 200 mg/mL formulation). The determination of the dose and dosing schedule will be governed by the STR. Further, the first injection in Cohort 5 will not be administered until data on ISRs observed within the first ten days after the first injection for at least 50% of Cohort 4 participants (n=10) have been reviewed by the STR. If pausing criteria due to ISRs are met in Cohort 4, Cohort 5 will be placed on hold until further discussion. The dose of the first injections has been agreed by the STR; the dose of the second injection will be guided by safety and PK data when ≥50% participants in Cohort 5 complete Injection 1 Week 4 assessments.

d: The requirement for an optional Cohort 6 will be based upon a review of the safety, tolerability and PK data from Cohorts 1-4 and safety, tolerability and PK data (12 weeks after injection 1 in cohort 5) from cohort 5 and comparison to historical data of the CAB 200 mg/mL formulation. This determination will be undertaken by the STR.

Part 2 will commence once data (trough concentrations [Cτ] and Plasma AUC0-t up to and including Week 8 following Injection 1 from all participants in Cohort 1, and any safety and tolerability data available at this time from Cohort 1-3) are reviewed and compared to historical PK data of the CAB 200 mg/mL formulation from the Phase 2/3 program. The determination of the dose and dosing schedule will be governed by the STR with the aim of selecting a safe dose predicted to achieve approximately 95% of dosed participants having trough concentrations higher than the Phase 3 benchmark. The dose of the second injection in Cohort 5 will be guided by safety and PK data when ≥50% participants in Cohort 5 complete Injection 1 Week 4 assessments.

The requirement for an optional further cohort (Cohort 6) will be based upon a review of the available safety, tolerability, and PK data from Cohorts 1-4 and safety, tolerability and PK data (12 weeks after injection 1) from Cohort 5 and comparison to historical PK data of the CAB 200 mg/mL formulation from the Phase 2/3 program. This determination will be undertaken by the STR. Cohort 6, if required, will assess the PK, safety and tolerability of alternative doses and/or dosing schedule among 22 participants (20 active and 2 active control). Sentinel dosing will also occur for this cohort.

At a 05 October 2021 STR meeting, it was agreed

- to stop the injection immediately in Cohort 5. As a consequent, all participants enrolled in Cohort 5 would not receive Injection 2
- that Cohort 6 was not needed

Analyses described in this RAP are adjusted accordingly

Dosing	• See Study Design Schematics above and Protocol Amendment 06 Section 6.1.2.

Design Features	• This is a phase 1, double-blind (sponsor-unblind), active control, and randomized study.
	• The study will consist of a screening period, an oral lead-in (OLI) phase, a wash-out phase, an injection phase, and a follow-up phase:
	  ○ A 30-day Screening Period
	  ○ A 28-day OLI phase, CAB 30 mg once daily (QD) with sparse PK sampling through Day 29
	  ○ A 7 to 14-day Washout Period (starting on Day 29)
	  ○ An Injection Phase
	  ○ up to Week 8 (Injection 2 Day 28) in Part 1 Cohorts 1, 2, 3, 4 and 4b
	  ○ up to Week 4 (Injection Day 28) in Part 1 Cohort 4h and
	  ○ up to Week 24 (Injection 2 Week 12) in Part 2 Cohorts 5 and 6 (if conducted)
	  ○ A 52-week Follow-up Phase post last injection or until CAB is no longer quantifiable (if this occurs prior to Week 52)
	• Part 1
	  ○ Twenty participants recruited to Cohort 1 first, then to Cohort 2 and followed by Cohort 3. Participants will be randomized (9:1 Active vs Active Control [AC]) according to a pre-generated randomization schedules in each cohort.
	  ○ Cohorts 1-3 are required and will be enrolled sequentially.
	  ○ Cohort 4 is optional and will be based on an interim review of the safety and tolerability data from Cohorts 1-3 and PK data through Week 4 from Cohorts 1-2.
	  ○ Cohort 4b: Two subcutaneous injections of CAB 400 mg/mL formulation 4-weeks apart (each 300 mg) CCI [redacted] Participants (n=24) will be randomized in equal numbers according to a pre-generated randomization schedule to one of two sequences (i.e. 12 per sequence) of two treatments to be administered along with Injection 1 and Injection 2, respectively
	  ○ Cohort 4h: One subcutaneous injection in the abdomen with rHuPH20 followed by CAB 400 mg/mL formulation (400 mg) or CAB 200 mg/mL (400 mg). Instructions regarding drug preparation and administration are provided in the pharmacy manual. Participants will be randomized to receive 5000 U of rHuPH20 followed by either CAB 200 mg/mL or CAB 400 mg/mL formulations at a dose of 400 mg (2 mL and 1 mL, respectively). Four sentinel participants (two each administered CAB 200 mg/mL and CAB400 mg/mL formulations) will be followed clinically for 10 days after dose administration and if there are no significant safety concerns upon a 10-day review of safety data, the remaining 16 participants will be dosed with rHuPH20 plus either CAB 200 mg/mL or CAB 400 mg/mL.
	• Part 2
	  ○ Cohort 5 in Part 2 will commence once $C\tau$ and plasma AUC0-t up to and including Week 8 following Injection 1 (i.e., Week 4 following Injection 2 [Injection 2 Day 28/Week 4 follow-up]) from all participants in Cohort 1, and available safety and tolerability collected from each Cohorts 1-3 are reviewed and compared to historical PK data of the CAB 200 mg/mL formulation from Phase 2/3 program.

	○ Cohort 6 is optional and will be based upon a review of the safety, tolerability, and PK data from Cohort 5 (12 weeks after Injection 1) and available safety, tolerability, and PK data from Cohorts 1-4, and comparison to historical PK data of the CAB 200 mg/mL formulation from the Phase 2/3 program. ○ Twenty-two participants will be enrolled (20:2 Active vs AC according to the randomization schedules) to ensure that at least 16 participants have evaluable data in each cohort. ○ The first 4 participants enrolled in each cohort will serve as sentinel participants (3:1 Active vs AC). ○ The remaining participants will be treated (17:1 Active vs AC) after 10-day safety review for the sentinel participants. ○ Dose administration for the remaining participants (n=18) will be staggered.
Dosing	• See Study Design Schematics above and Protocol Amendment 06 Section 6.1.2.
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	For each cohort, subjects will be assigned to study treatment (CAB 400 mg/ml or CAB200 mg/ml formulations) in accordance with the central randomization schedules generated by the Sponsor or their delegate using validated internal software.
Planned Analysis	At least two formal analyses will be conducted: 1. Injection Phase complete: when all participants in Part 1 Cohorts 1, 2, 3, 4 and 4b complete the 8-week Injection Phase, all Cohort 4h participants complete the 4-week Injection Phase and all participants in Part 2 complete the 24-week Injection Phase. 2. End of Study: when all subjects complete the 52-week Follow-up Phase in Part 1 and Part 2. If the recruitment time is prolonged, a formal unblinded interim analysis of data from Cohort 4b and/or Cohort 4h (i.e., prior to all participants in the cohort completing the injection phase) may be conducted to support timely dissemination of study results.
Preliminary Analyses	• Formal tables, listings, and figures as described in Appendix 10: List of Data Displays will only be provided for the Cohort 1-4 preliminary analysis, the preliminary Cohort 1-5 interim analysis, and formal analyses to be described in CSR(s). See Section 3.1 and Section 3.2 for additional details.

2.4. Statistical Hypotheses

This study is designed to describe the PK profiles of CAB 400 mg/mL injection administered in different routes. No formal hypothesis will be tested.

3. PLANNED ANALYSES

3.1. Part 1 and Part 2 Analyses

Formal analyses will be conducted and described in a CSR when all participants in Part 1 complete the 8-week injection phase and when all participants in Part 2 complete the 24-week injection phase. Depending on when participants complete the injection phases in Part 1 and Part 2, these two analyses for part 1 and Part 2 may be combined and described in a single CSR. A final CSR will be produced when all subjects complete the 52-week follow-up phase of Parts 1 and 2.

The following 13 preliminary analyses will be conducted for Study Team safety & PK Review (STR) review:

1. When all participants in Cohort 1 complete Week 8 (Injection 2 Day 28/Week 4 follow-up) assessments (*results of this analysis will determine Cohort 5 dose and dosing schedule*);

2. When all participants in Cohort 1 & Cohort 2 complete Week 4 (Injection 1 Day 28/Injection 2 Day 1) assessments (*results of this analysis will determine if optional Cohort 4 will proceed and the dose/dosing schedule*);

3. When all participants in Cohort 2 complete Week 8 (Injection 2 Day 28/Week 4 follow-up) assessments;

4. When ≥50% participants in Cohort 4 complete Injection 1 Day 10 assessments following Injection 1, data on injection site reactions will be reviewed prior to proceeding with Cohort 5 Injection 1;

5. When 50% participants in Cohort 4 complete Week 8 (Injection 2 Day 28) assessments PK and safety data will be reviewed;

6. When all participants in Cohort 3 & Cohort 4 complete Week 8 (Injection 2 Day 28/Week 4 follow-up) assessments;

7. When all participants in Cohort 4b complete Week 8 (Injection 2 Day 28) assessments, PK and safety data will be reviewed;

8. When ≥50% participants in Cohort 4h complete Week 4 (Injection Day 28) assessments, PK and safety data will be reviewed;

9. When all participants in Cohort 4h complete Week 4 (Injection Day 28) assessments, PK and safety data will be reviewed;

10. When ≥50% participants in Cohort 5 complete Injection 1 Week 4 assessments, the safety and PK data will be used to determine the dose for Injection 2;

11. When all participants in Cohort 5 complete Week 12 (Injection 1 Week 12 /Injection 2 Day 1) assessments (*results of this analysis will determine if optional Cohort 6 will proceed and the dose/dosing schedule*);

12. When all participants in Cohort 5 complete Week 24 (Injection 2 Week 12/Week 12 follow-up) assessments;

13. When all participants in Cohort 5 & Cohort 6 (if conducted) complete Week 24 (Injection 2 Week 12/Week 12 follow-up) assessments.

The timing or number of preliminary analyses above may be modified based upon emerging data for example if the planned dosing for a cohort is modified following an STR review due to safety pausing criteria described in Protocol Amendment 6 Section 7.1 being met the timing of the analysis may be modified accordingly.

A further unblinded preliminary analysis will be conducted when all participants in Part 1 Cohorts 1, 2, 3, 4 complete the 8-week Injection Phase to support an abstract submission of key results to a scientific conference (ViiV Healthcare group of companies Document Number TMF-13988926, 28-Oct-2021).

Formal tables, listings, and figures as described in Appendix 10: List of Data Displays will only be provided for the Cohort 1-4 preliminary analysis mentioned above (excluding PK), the preliminary Cohort 1-5 interim analysis (see Section 3.2) and formal analyses to be described in CSR(s).

The following steps will be followed sequentially for each formal analysis:

1. All required database cleaning activities have been completed and interim database release (DBR) up to the clinical cut-off have been declared by Data Management. Details of the cut-off and data cleanliness are specified in the Data Validation Manual (DVM).
2. All criteria for unblinding the randomization codes have been met.
3. Randomization codes have been distributed according to pre-generated central randomization procedures
4. Database freeze (DBF) has been declared by Data Management.

The planned tables, listings, and figures are described in Appendix 10: List of Data Displays.

3.2. Interim Analyses

If the recruitment time is prolonged, a formal unblinded interim analysis of data from Cohort 4b and/or Cohort 4h (i.e., prior to all participants in the cohort completing the injection phase) may be conducted to support timely dissemination of study results. The decision to conduct an interim analysis and planned analyses will be documented before unblinding treatment allocations. To minimise bias, the interim results will not be shared with any participants and investigators. However, when investigators are identified as authors of a potential conference presentation of interim results, those investigators and the other co-authors will have access to the interim results prior to its presentation. No other investigators will have knowledge of these data prior to the last participants completing their last visits for the injection phase. An interim analysis abstract may be submitted to a conference for consideration only if the conference convenes after all data collection for the injection phase has been completed. In order to avoid inflation of type I

error, no formal statistical analyses evaluating treatment comparisons will be performed for the interim analysis.

Once all participants in Cohort 1 complete 8 weeks post-injection 1, PK (trough concentrations [Cτ] and Plasma AUC0-t), safety and tolerability data will be reviewed along with any safety and tolerability data available at this time from Cohorts 2-3 to determine the dose and dosing schedule for cohort 5 in Part 2. This will be determined by the STR with the aim of selecting a safe dose predicted to achieve approximately 95% of dosed participants having trough concentrations higher than the Phase 3 benchmark for future efficacy studies.

An interim analysis will be performed once all participants in Cohort 1 and Cohort 2 complete their Week 4 assessments post-injection 1. This interim analysis will inform the need for optional Cohort 4 and its dose/dosing schedule and will be based upon review of PK data and all available safety and tolerability data. An interim analysis for Cohort 5 of PK and safety data up to 4 weeks after the first injection (≥50% participants) and 12 weeks after the first injection, including a review of available PK, safety and tolerability data from cohorts 1-5, will be undertaken to determine the dose for Injection 2 in Cohort 5 and to determine the need for and dose/dosing schedule for Cohort 6.

Due to slower than anticipated enrolment, the sponsor has decided to conduct an additional unblinded preliminary interim analysis of Cohort 1-5 data for the purpose of timely study results dissemination, which will take place before all participants in cohort 4b have completed injection phase assessments (i.e., injection 2 Week 4). Participants in all other cohorts will have completed the primary injection phase assessments, and all follow-up phase assessments for cohorts 1-3.

Data displays for the preliminary Cohort 1-5 interim analysis will exclude Cohort 4b data from participants who have received injection 1 but have not yet completed Injection 2 Day 1 or Follow-up Week 4 by the data analysis cut-off. Cohort 4b will remain blinded to the randomized mitigation treatments CCI [redacted] and results will not be presented by mitigation group for the interim analysis. All other cohorts will be unblinded.

3.3. Final Analyses

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

1. All participants have completed the study (52-week follow-up phase) as defined in the protocol.
2. All required database cleaning activities have been completed and final DBR, source database lock (SDL), and DBF have been declared by Data Management.

4. ANALYSIS POPULATIONS

For the Cohort 1-5 preliminary interim analysis, displays will exclude Cohort 4b data from participants who have received injection 1 but have not yet completed Injection 2 Day 1 or Follow-up Week 4 by the data analysis cut-off. Cohort 4b will remain blinded to the randomized mitigation treatments CCI [redacted] and results will not be presented by mitigation group for the interim analysis.

Population	Definition / Criteria	Analyses Evaluated
Screened	All participants who were screened for eligibility.	• Study Population
Enrolled	All participants who passed screening and entered the study. *Note: screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study are excluded from the Enrolled population as they did not enter the study.*	• Study Population
Randomized	All participants who were randomly assigned to treatment in the study.	• Study Population
Safety	All participants who received at least one dose of study treatment (oral or injection). This population will be based on the treatment the participant received.	• Safety, Baseline and Demographic Characteristics
Safety – LA Exposed	All participants who received at least one injection of long-acting study treatment. This population will be based on the treatment the participant received.	• Injection Site Reactions
Pharmacokinetic	All participants in the Safety population who received study treatment and had at least 1 non-missing PK assessment (non-quantifiable [NQ] values will be considered as non-missing values). *Note: 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.*	• PK Concentration and PK Parameter

Refer to Appendix 10: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management, or participant assessment) will be summarized and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study.

- Data will be reviewed prior to unblinding and DBF to ensure all significant deviations and deviations which may lead to exclusion from the analysis populations 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 listing of all inclusion/exclusion criteria deviations will also be provided. This listing will be based on data as recorded on the inclusion/exclusion page of the electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

In general, the following treatment group descriptors will be presented in data displays for reporting, with minor variations depending on whether a display is presenting treatment group information as a column or row.

For Cohort 4b, all data will be summarized by period (OLI, injection 1, injection 2, follow-up, overall) and selected safety and patient reported outcome endpoints will also be summarized by CCI [redacted] PK concentrations and parameters will also be summarized by treatment sequence and period, as appropriate.

Treatment Group Descriptions					
		Randomization		Data Displays for Reporting	
Part	Arm	Code	Description	Description	Order in TLF
Part 1	C1 CAB 400	A1	CAB 400 mg/mL IM injections 4-weeks apart in gluteus muscle (cohort 1)	Oral CAB 30 mg QD	1
				Inj.1 600 mg IM Gluteal	2
				Inj.2 400 mg IM Gluteal	3
				Follow-up	4
				Overall[1]	5
	C1 CAB 200	C1	CAB 200 mg/mL IM Injection 4-weeks apart in gluteus muscle (cohort 1)	Oral CAB 30 mg QD	6
				Inj.1 600 mg IM Gluteal	7
				Inj.2 400 mg IM Gluteal	8
				Follow-up	9
				Overall[1]	10
	C2 CAB 400	A2	CAB 400 mg/mL SC injections 4-weeks apart in abdomen (cohort 2)	Oral CAB 30 mg QD	11
				Inj.1 600 mg SC Abdomen	12
				Inj.2 200 mg SC Abdomen	13
				Follow-up	14
				Overall[1]	15
	C2 CAB 200	C2	CAB 200 mg/mL SC injections 4-weeks apart in abdomen (cohort 2)	Oral CAB 30 mg QD	16
				Inj.1 300 mg SC Abdomen	17
				Inj.2 100 mg SC Abdomen	18
				Follow-up	19
				Overall[1]	20
	C3 CAB 400	A3	CAB 400 mg/mL IM injections 4-weeks apart in	Oral CAB 30 mg QD	21
				Inj. 1 600 mg IM Lateral Thigh	22
				Inj. 1 400 mg IM Lateral Thigh	23

			lateral thigh (cohort 3)	Inj. 2 400 mg IM Lateral Thigh	24
				Follow-up	25
				Overall[1]	26
	C3 CAB 200	C3	CAB 200 mg/mL IM injections 4-weeks apart in lateral thigh (cohort 3)	Oral CAB 30 mg QD	27
				Inj.1 600 mg IM Lateral Thigh	28
				Inj.1 400 mg IM Lateral Thigh	29
				Inj.2 400 mg IM Lateral Thigh	30
				Follow-up	31
				Overall[1]	32
	C4 CAB 400	A4	CAB 400 mg/mL Injections 4-weeks apart (first IM injection in *gluteus medius* and second SC injection in abdomen; cohort 4)	Oral CAB 30 mg QD	33
				Inj.1 400 mg IM Gluteal	34
				Inj.2 200 mg SC Abdomen	35
				Follow-up	36
				Overall[1]	37
	C4 CAB 200	C4	CAB 200 mg/mL Injections 4-weeks apart (first IM injection in *gluteus medius* and second SC injection in abdomen; cohort 4)	Oral CAB 30 mg	38
				Inj.1 400 mg IM Gluteal	39
				Inj.2 100 mg SC Abdomen	40
				Follow-up	41
				Overall[1]	42
	C4b CAB 400 + Topical Steroid or NSAID 4	A4bG1	CAB 400 mg/mL Injections 4-weeks apart in [redacted]	Oral CAB 30 mg QD	43
				[redacted]	44
					45
				Follow-up	46
				Overall[1]	47
	C4b CAB 400 + Topical Steroid or NSAID 4	A4bG2	CAB 400 mg/mL Injections 4-weeks apart in [redacted]	Oral CAB 30 mg QD	4833
				[redacted]	49
					50
				Follow-up	51
				Overall[1]	52
		A4h		Oral CAB 30 mg QD	53

	C4h CAB 400 + rHUPH20		CAB 400 mg/mL Injection in the abdomen with rHuPH20	Inj. 1 CAB 400 mg + 5000 U rHUPH20 SC Abdomen	54
				Follow-up	55
				Overall[1]	56
	C4h CAB 200 + rHUPH20	A4h	CAB 200 mg/mL Injection in the abdomen with rHuPH20	Oral CAB 30 mg QD	57
				Inj. 1 CAB 400 mg + 5000 U rHUPH20 SC Abdomen	58
				Follow-up	59
				Overall[1]	60
	N/A	N/A	Pooled Group[2]	Pooled Oral CAB 30 mg QD OLI ONLY	61
				Pooled Oral CAB 30 mg QD	62
				Pooled CAB 400 mg/mL Q4W 400 mg IM Gluteal	63
				Pooled CAB 200 mg/mL Q4W 400 mg IM Gluteal	64
				Pooled CAB 400 mg/mL Q4W 200 mg SC	65
				Pooled CAB 200 mg/mL Q4W 100 mg SC	66
				Pooled CAB 400 mg/mL Q4W 400 mg Lateral Thigh	67
				Pooled CAB 200 mg/mL Q4W 400 mg Lateral Thigh	68
Part 2	C5 CAB 400 [3]	A5	CAB 400 mg/mL IM injections 12-weeks apart in gluteus muscle (cohort 5)	Oral CAB 30 mg QD	69
				Inj.1 800 mg IM Gluteal	70
				Follow-up	71
				Overall[1]	72
	C5 CAB 200	C5	CAB 200 mg/mL IM injections 12-weeks apart in gluteus muscle (cohort 5)	Oral CAB 30 mg QD	73
				Inj.1 400 mg IM Gluteal	74
				Follow-up	75
				Overall[1]	76
	N/A	N/A	Historical Data, CAB 200 mg/mL	(ATLAS/FLAIR) Inj. 1 CAB 600 mg IM Gluteal [3]	77
				(ATLAS/FLAIR) Inj. 2 CAB 400 mg IM Gluteal [3]	78
				(ÉCLAIR) Inj. 1 CAB 800 mg IM Gluteal [3]	79

Note: A1 = Active Drug in Cohort 1; A2 = Active Drug in Cohort 2; A3 = Active Drug in Cohort 3; A4 = Active Drug in Cohort 4; A4h = Active Drug in Cohort 4h; A5 = Active Drug in Cohort 5; A6 = Active Drug in Cohort 6; C1 = Cohort 1, C2 = Cohort 2, C3 = Cohort 3, C4 = Cohort 4, C4b = Cohort 4b, C4h = Cohort 4h, C5 = Cohort 5.

1. Overall group is not applicable for PK analyses.
2. Pooled active and AC groups are only applicable when there is more than one cohort at the stated dose (mg) to combine for the specific summary.
3. Historical data for formulation of 200 mg/mL from the Phase 3 program, only applicable for PK analyses.

Treatment comparisons for the PK pairwise and cross study historical comparison (See Section 8.1.5) will be displayed by injection using the following descriptors:

Pairwise Comparisons for AUC(0-τ), Cmax, and Cτ:

Injection 1 (CAB 400 mg/mL):

1. C2 CAB400 - Inj. 1 600 mg SC Abdomen vs C1 CAB400 - Inj. 1 600 mg IM Gluteal
2. C3 CAB400 - Inj. 1 600 mg IM Lateral Thigh vs C1 CAB400 - Inj. 1 600 mg IM Gluteal
3. C2 CAB400 - Inj. 1 600 mg SC Abdomen vs C3 CAB400 - Inj. 1 600 mg IM Lateral Thigh
4. C4h CAB400 + rHUPH20 - Inj. 1 CAB 400 mg + 5000 U rHUPH20 SC Abdomen vs C4 CAB400 - Inj. 1 400 mg IM Gluteal

Injection 2 (CAB 400 mg/mL):

1. C3 CAB400 - Inj. 2 400 mg IM Lateral Thigh [participants who received 600 mg for Injection 1] vs C1 CAB400 - Inj. 2 400 mg IM Gluteal

Historical Comparisons:

Injection 1 (CAB 400 mg/mL):

1. C1 CAB400 - Inj. 1 600 mg IM Gluteal vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W
2. C2 CAB400 - Inj. 1 600 mg SC Abdomen vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W
3. C3 CAB400 - Inj. 1 600 mg IM Lateral Thigh vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W
4. C4 CAB400 - Inj. 1 400 mg IM Gluteal vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W [dose normalize to 400 mg]
5. CCI [redacted]
6. C4h CAB400 + rHUPH20 - Inj. 1 CAB 400 mg + 5000 U rHUPH20 SC Abdomen vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W [dose normalize to 400 mg]
7. C4h CAB200 + rHUPH20 - Inj. 1 CAB 400 mg + 5000 U rHUPH20 SC Abdomen vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W [dose normalize to 400 mg]

8. C5 IM Gluteal CAB 800 mg (CAB 400 mg/mL) Q12W Week 12 post injection 1 vs Week 4 post injection 1 in ATLAS/FLAIR IM Gluteal CAB 600 mg (CAB 200 mg/mL) Q4W) [dose normalize to 800 mg]
9. C5 IM Gluteal CAB 800 mg (CAB 400 mg/mL) Q12W Week 12 post injection 1 vs Week 12 post injection 1 in ÉCLAIR IM Gluteal CAB 800 mg (CAB 200 mg/mL) Q12W
10. C5 IM Gluteal CAB 800 mg (CAB 400 mg/mL) Q12W Week 12 post injection 1 [Male participants only] vs Week 12 post injection 1 in ÉCLAIR IM Gluteal CAB 800 mg (CAB 200 mg/mL) Q12W

Injection 2 (CAB 400 mg/mL):

1. C1 CAB400 - Inj. 2 400 mg IM Gluteal vs Week 4 post injection 2 in ATLAS/FLAIR IM Gluteal CAB 400 mg (CAB 200 mg/mL) Q4W
2. C2 CAB400 - Inj. 2 200 mg SC Abdomen vs Week 4 post injection 2 in ATLAS/FLAIR IM Gluteal CAB 400 mg (CAB 200 mg/mL) Q4W [dose normalize to 200 mg]
3. C3 CAB400 - Inj. 2 400 mg IM Lateral Thigh vs Week 4 post injection 2 in ATLAS/FLAIR IM Gluteal CAB 400 mg (CAB 200 mg/mL) Q4W

5.2. Baseline Definitions

For all safety endpoints, the baseline value for the OLI phase, Injection Phase and Follow-up Phase, respectively, will be derived as follows:

Parameter	Phase	Study Assessments Considered as Baseline
Clinical Chemistry, Haematology, Coagulation, Vital Signs (pre-dose), ECG (pre-dose)[1]	OLI Phase	OLI Baseline = last non-missing pre-dose assessment collected <= Date of first OLI dose
	Injection Phase	Injection Phase Baseline = last non-missing assessment collected <= Date of first CAB injection, and > Date of last OLI dose
	Follow-up Phase	Follow-up Phase Baseline = last non-missing assessment collected <= Date of Nominal Follow-up Week 4 Visit [for Part 1 participants] / Date of Nominal Follow-up Week 12 Visit [for Part 2 participants]

- Average of the triplicate assessments for quantitative assessments and the worst-case of the triplicate assessments for qualitative assessments will be used as the baseline.

If time is not collected, Day 1 assessments are assumed to be taken prior to first dose of the respective phase.

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

5.3. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
10.1	Appendix 1: Exclusions from Per Protocol Population
10.2	Appendix 2: Schedule of Activities
10.3	Appendix 3: Assessment Windows
10.4	Appendix 4: Study Phases, Study Periods, and Treatment Emergent Adverse Events
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Reporting Standards for Missing Data
10.8	Appendix 8: Values of Potential Clinical Importance
10.9	Appendix 9: Abbreviations & Trademarks
10.10	Appendix 10: List of Data Displays
10.11	Appendix 11: AESI Identification

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

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

Study population analyses including analyses of participant's disposition, protocol deviations, inclusion/exclusion criteria deviations, study populations, demographic and baseline characteristics, prior and concomitant medications, medical history, and exposure will be based on GSK Core Data Standards.

The details of the planned displays are provided in Appendix 10: List of Data Displays.

7. SAFETY ANALYSES

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

7.1. Adverse Events Analyses

Adverse events analyses including the analysis of AEs, serious AEs (SAEs), injection site reaction related AEs, and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 10: List of Data Displays.

Injection site reactions will be summarized by preferred term and by the following grouped terms: 'Injection Site Induration/Swelling', 'Injection Site Pain/Tenderness', 'Injection Site Redness/Erythema', 'Injection Site Redness/Erythema/Pain/Tenderness/Induration/Swelling'.

For Cohort 4b, safety data will be summarized by period (OLI, injection 1, injection 2, follow-up, overall) where injection 1 and injection 2 data is aggregated across mitigation treatments CCI [redacted]

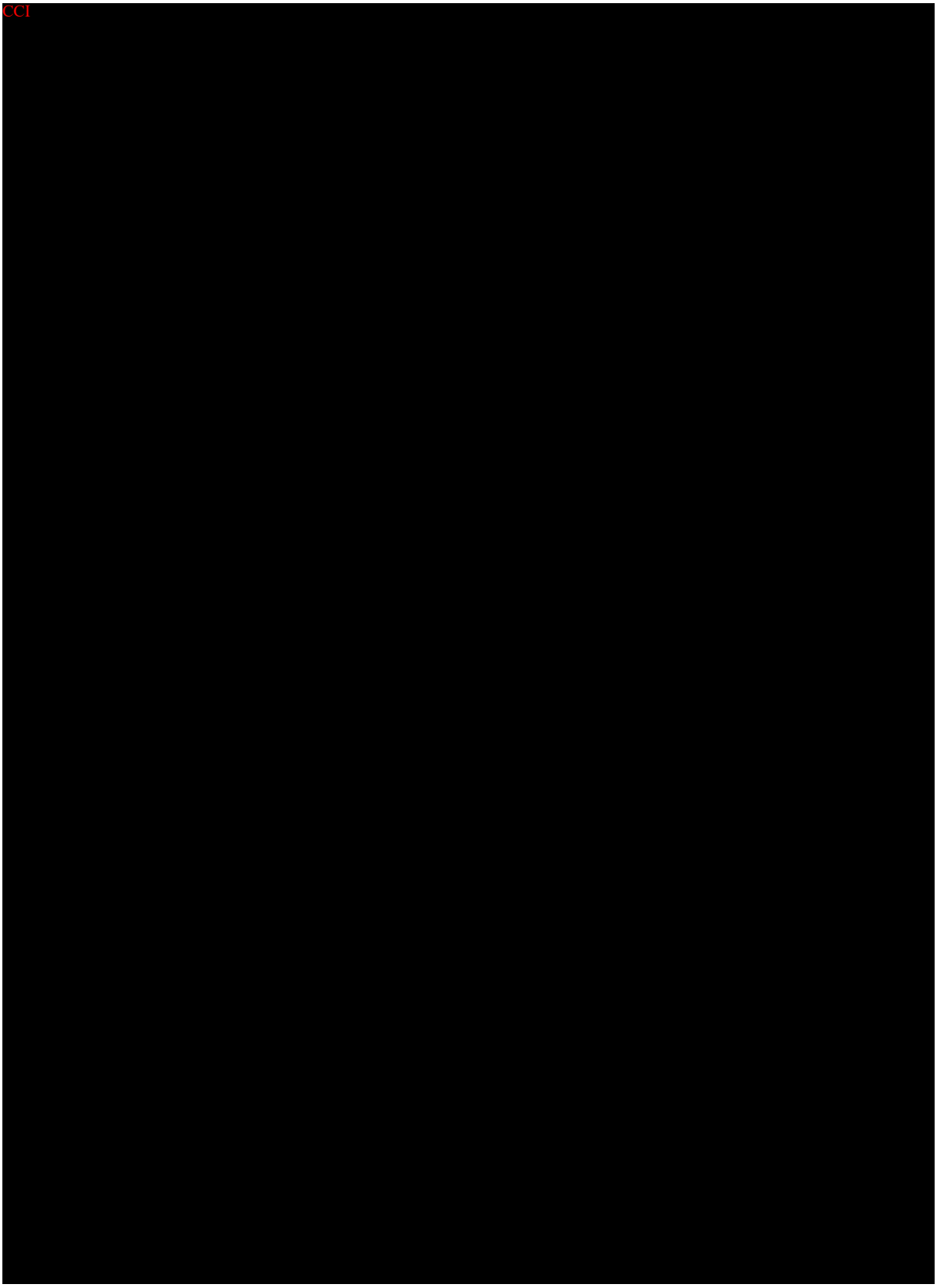
7.2. Adverse Events of Special Interest

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event for Adverse Events of Special Interest (AESI). [Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from ongoing studies may highlight additional AESIs, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting.] The details of the current planned grouping, including Standardized MedDRA Query (SMQ) values (as applicable), and planned displays are provided in Appendix 11: AESI Identification and Appendix 10: List of Data Displays.

7.3. Clinical Laboratory Analyses

Laboratory evaluations will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 10: List of Data Displays.

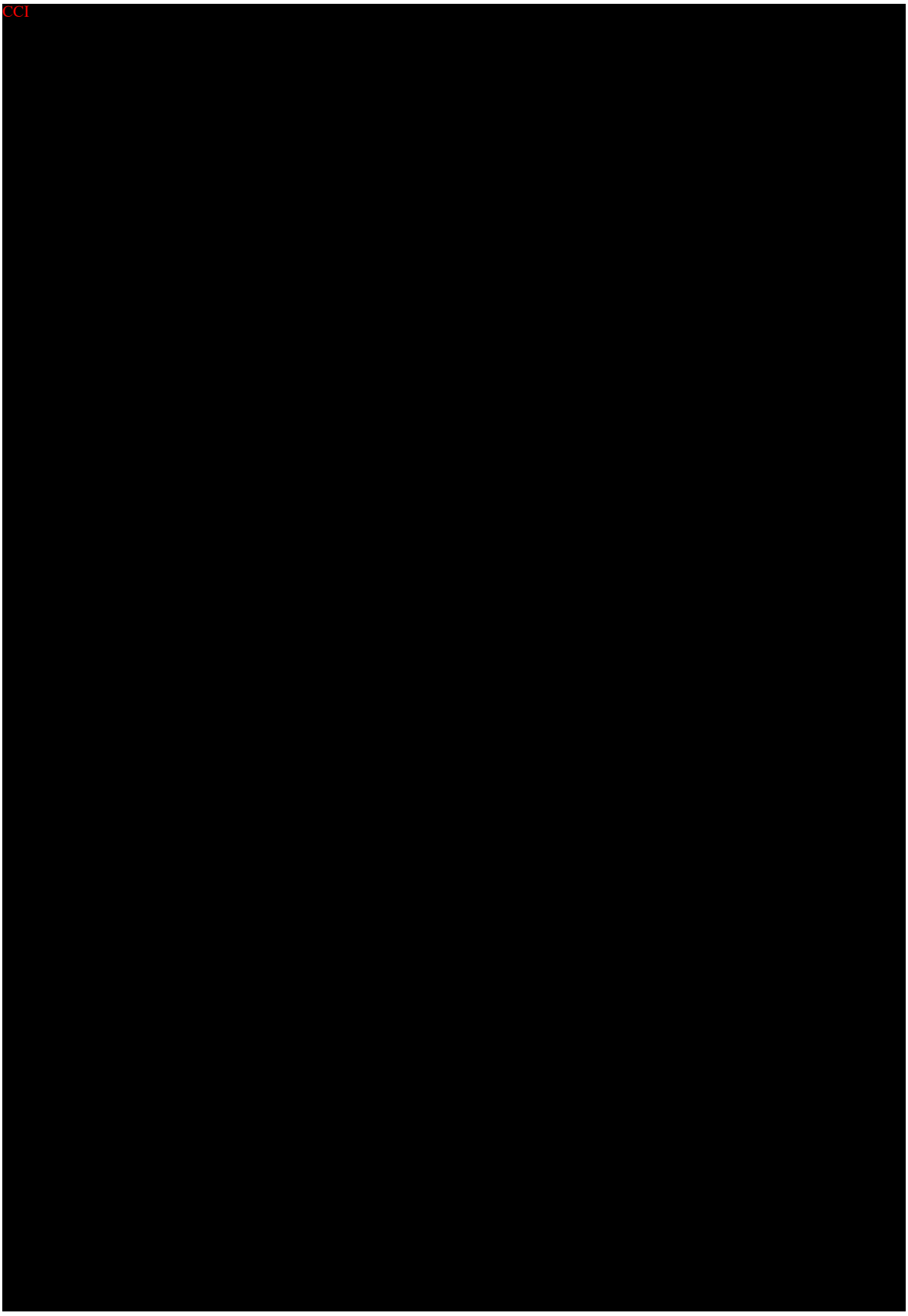
CCI



7.5. CCI [redacted]

CCI [redacted]

CCI



CCI

7.5.3. Ordinal Endpoint / Variables

The following ordinal endpoint/variable will be analysed in the crossover analysis comparing preference for topical steroids vs topical NSAIDs for Cohort 4b:

Ordinal Endpoint/Variable
• For the hypothesis test for evidence of a treatment difference (i.e., p-value), the 5-level ordinal endpoint for Injection Preference from the Preference Questionnaire will be coded as: • -2 (strongly prefer injection 2 compared to injection 1) • -1 (slightly prefer injection 2 compared to injection 1) • 0 (no preference between injection 1 and injection 2) • 1 (slightly prefer injection 1 compared to injection 2) • 2 (strongly prefer injection 1 compared to injection 2)

7.5.3.1. Summary Measure

The summary measure is the number and percentage of participants in each of the following derived response categories:

- Strongly prefer Injection with Topical NSAID
- Slightly prefer Injection with Topical NSAID
- No preference
- Slightly prefer Injection with Topical Steroid
- Strongly prefer Injection with Topical Steroid

7.5.3.2. Population of Interest

The Safety population will be used for Cohort 4b crossover analyses.

7.5.3.3. Strategy for Intercurrent (Post-Randomization) Events

A complete case analysis set will be used for the crossover analysis where participants with missing endpoint/variable are excluded. Missing data will not be imputed, regardless of the reason.

7.5.3.4. Statistical Analyses / Methods

The number and percentage of participants with preference corresponding to each of the 5 ordinal outcomes will be summarized. The number and percentage of participants reporting each statement supporting their preferences as collected in the eCRF will also be summarized.

Details for the planned display are provided in Appendix 10: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Statistical Methodology Specification
• Extended Mantel-Haenszel test using the SAS Proc Freq procedure. • Implementation notes/pseudo code: *proc freq;* *tables sequence*outcome/measures nocol norow nopct;* *exact mhchi;* *run;*
Results Presentation
• Exact two-sided p-value from extended Mantel-Haenszel test

8. PHARMACOKINETIC ANALYSES

8.1. Primary Pharmacokinetic Analyses

8.1.1. Endpoint / Variables

8.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Standards for Pharmacokinetic). Plasma concentrations of CAB will be measured and reported.

8.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher). All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data from OLI and Injection phases, as data permit.

Parameter	Parameter Description	OLI Phase	Injection Phase
Cmax	Maximum observed plasma concentration determined directly from the concentration-time data.	Day 1	For Injection 1 and 2 in Part 1 and Part 2
Cmax/D	Dose normalized Cmax, calculated as Cmax/Dose	Day 1	For Injection 1 and 2 in Part 1 and Part 2
tmax	Time of C_{max} determined directly from the concentration-time data.	Day 1	For Injection 1 and 2 in Part 1 and Part 2
AUC(0-t)	Area under the concentration time curve from time zero to last quantifiable time point calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.	Day 1	For Injection 1 & 2 in Part 1 and Part 2
AUC(0-t)/D	Dose normalized AUC(0-t), calculated as AUC(0-t)/Dose	Day 1	For Injection 1 & 2 in Part 1 and Part 2
AUC(0-τ)	Area under the concentration time curve from time zero to tau time point calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid. Tau=24 hours for OLI Day 1 Tau is 4 weeks for Cohort 1-4, 4b and 4h Tau is 12 weeks for cohort 5	Day 1	For Injection 1 & 2 in Part 1 and Part 2
AUC(0-τ)/D	Dose normalized AUC(0-τ) calculated as AUC(0-τ)/Dose	Day 1	For Injection 1 & 2 in Part 1 and Part 2

Parameter	Parameter Description	OLI Phase	Injection Phase
AUC(0-4) Cohort 5 only	Area under the concentration time curve from time zero to Week 4 calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.	NA	Injection 1 Part 2 (Cohort 5) (this parameter is used in the dose proportionality analysis).
AUC(0-∞)	Area under the concentration time curve from time zero to infinity	NA	For Injection 1 (Cohort 4h) & 2 in Part 1 and Part 2
AUC(0-∞)/D	Dose normalized AUC(0-∞), calculated as AUC(0-∞)/Dose	NA	For Injection 1 (Cohort 4h) & 2 in Part 1 and Part 2
Cτ	Trough concentrations (Cτ) Tau=24 hours for OLI Day 29 Tau is 4 weeks for Inj. Phase in Cohort 1-4, 4b, and 4h Tau is 12 weeks for Inj. Phase in cohort 5.	Day 29	For Injection 1 & 2 in Part 1 and Part 2
Cτ/D	Trough concentrations (Cτ)/Dose Tau=24 hours for OLI Day 29 Tau is 4 weeks for Inj. Phase in Cohort 1-4, 4b, and 4h Tau is 12 weeks for Inj. Phase in cohort 5.	Day 29	For Injection 1 & 2 in Part 1 and Part 2
C4 Cohort 5 only	Trough concentrations on Week 4	NA	For Injection 1 & 2 in Part 2
C24	Trough Concentrations on Day 2 (24 hour)	Day 1	
t½	Terminal absorption elimination half-life will be calculated as: t½ = ln2 / KALA	NA	For Injection 1 (Cohort 4h) & 2 in Part 1 and Part 2.
KALA	Terminal absorption elimination rate constant, Long-acting	NA	For Injection 1 (Cohort 4h) & 2 in Part 1 and Part 2

NOTES:

- Additional parameters may be included as required.
- In addition to the PK parameters calculated based on the observed concentrations for the 2 participants from Cohort 3 who received a CAB400 - Inj. 1 400 mg IM Lateral Thigh. PK parameters adjusted to a 600 mg dose will be calculated for these participants as well. The adjustment will be performed using a 50% increase of the plasma PK parameters.

8.1.2. Summary Measure

For PK concentrations and PK parameters: arithmetic mean, 95% confidence interval (CI) of arithmetic mean, geometric mean, 95% CI of geometric mean, SD, SD of log data, between-subject geometric coefficient of variation (CVb), median, minimum, maximum, and coefficient of variation (CV), as appropriate.

For pairwise comparisons of AUC(0-τ), Cmax, and Cτ (CAB 400 mg/mL) between cohorts: geometric mean ratio and corresponding 90% CI.

For cross study comparisons of Cτ to historical CAB 200 mg/mL data: geometric mean ratio and corresponding 90% CI.

For dose proportionality assessments of AUC(0-τ) [AUC(0-4) for Cohort 5], Cmax, and Cτ [C4 for Cohort 5] following injection 1 for CAB 400 mg/mL (across all cohorts in Part 1 and Part 2, excluding cohort 4h) for each route: mean slope estimated from the power model and the corresponding 90% CI.

8.1.3. Population of Interest

The primary PK analyses will be based on the PK population.

8.1.4. Strategy for Intercurrent (Post-Randomization) Events

No intercurrent events are expected, in addition to those defined as protocol deviations. Missing data will not be imputed, regardless of the reason.

8.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 10: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.1.1 will be summarized using descriptive statistics, graphically presented (where appropriate) and listed.

Summary statistics (N, n, arithmetic mean, 95% CI of arithmetic mean, geometric mean, 95% CI of geometric mean, SD, SD of log data, between-subject geometric CVb, median, minimum, maximum, and CV) for non-transformed and ln-transformed plasma CAB PK concentration and parameter values (Cmax, AUCs, Cτ, and C24) will be summarized by treatment and period, as appropriate.

Plasma CAB PK concentrations collected during the follow-up phase will only be summarized by visit for participants who received both injection 1 and injection 2 for cohorts 1-4 and 4b, and for participants who received injection 1 for cohort 4h and 5. All follow-up phase concentrations will be included in the individual CAB plasma concentration-time plots by injection and in data listings.

A population PK analysis using non-linear mixed effects modelling software NONMEM (ICON; Hanover, MD) maybe performed with the emergent data from this study to select optimal dosage regimens using simulations such that 5th percentile trough concentrations are maintained above Phase 3 trough concentrations benchmark. This analysis will be described and reported in a separate document(s) from the RAP.

8.1.5.1. Statistical Methodology Specification

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

Endpoint / Variables
• AUC(0-τ), Cmax, and Cτ for CAB 400 mg/mL following CAB IM (gluteus medius or vastus lateralis) or SC dosing
Model Specification for Pairwise and Historical Comparisons
• Pairwise comparisons between cohorts receiving the same dose of CAB400 but via different administration routes of CAB 400 mg/mL geometric mean plasma Cτ, Cmax, and plasma AUC(0-τ) for Cohorts 1, 2, 3, 4, 4b and 4h will be conducted, as specified in Section 5.1. • Cross study comparisons of geometric mean plasma Cτ for Cohorts 1, 2, 3, 4, 4b and 4h, and Cohort 5 compared to historical CAB 200 mg/mL data will be conducted, as specified in Section 5.1. • Following log transformation, PK parameters will be separately analyzed using a linear regression model with a fixed effect term for treatment, with allowance for unequal variances for each treatment group (using the repeated / group=treatment option in the MIXED procedure to model unequal variances and DDFM=KENWARDROGER option for adjusted degrees of freedom). Point estimates and corresponding 90% CIs will be constructed for the treatment differences. Point estimates and their 90% CIs will then be transformed back to provide point estimates and 90% CIs on the original scale.
Historical CAB 200 mg/mL Data
• Anonymized reference dataset(s) containing the historical PK data from the ATLAS [201585], FLAIR [201584], and ÉCLAIR [201120] studies will be used in the historical cross-study comparison analyses described above. • For ATLAS and FLAIR, concentrations meeting the definition of 'evaluable' as defined in the study-specific RAPs (e.g., excluding samples collected outside the ± 4 days evaluable sample window) will be used.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation
• Statistical analysis by analysis of variance (ANOVA) will be presented in tabular format with geometric mean ratios and corresponding 90% CI for the comparisons mentioned above.

Endpoint / Variables
• AUC(0-τ) [AUC(0-4) for Cohort 5], Cmax, and Cτ [C4 for Cohort 5] for CAB 400 mg/mL following Injection 1 of CAB IM (gluteus medius or vastus lateralis) or SC dosing, as data permit
Model Specification for Dose Proportionality Assessment
• AUC(0-τ) [AUC(0-4) for Cohort 5], Cmax, and Cτ [C4 for Cohort 5] following Injection 1 for CAB 400 mg/mL will be assessed separately for dose proportionality by route (IM gluteal, SC abdomen, IM lateral thigh) using pooled data across cohorts (Part 1 and Part 2, but excluding cohort 4h), where applicable, and the following power model: $y = \alpha * dose^{\beta}$

where y denotes the PK parameter and α is an intercept term. Dose proportionality in this model equates to $\beta=1$. A point estimate and 90% CI will be derived for β. β will be estimated by regressing the $\log_e$-transformed PK parameter on $\log_e$ dose (Log_e(PK parameter) = $\log_e(\alpha) + \beta * \log_e(\text{dose})$). • A fixed effects power model will be fitted by restricted maximum likelihood (REML) using SAS Proc Mixed.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation
• Statistical analysis by power model will be presented in tabular format with point estimates and corresponding 90% CI.

9. REFERENCES

Chevat C, Viala-Dante M, Dias-Barbosa C, Nguyen VH. Development and psychometric validation of a self-administered questionnaire assessing the acceptance of influenza vaccination: the Vaccinees' Perception of Injection (VAPI©) questionnaire. Health Qual Life Outcomes. 2009; 7: 21.

ViiV Healthcare group of companies Document Number TMF-11724805 (17-Feb-2021): A Phase 1, Two-part, Double-blind, Active-control, Randomized Study to Evaluate the Pharmacokinetics, Safety and Tolerability of Repeat-Dose Cabotegravir (CAB 400 mg/mL formulation) Long-Acting Injection Following Subcutaneous or Intramuscular Administration in Healthy Adult Participants.

10. APPENDICES

10.1. Appendix 1: Exclusions from Per Protocol Population

Instream and final analysis population reviews as per SOP 130050 are not planned for this study because it does not include a Per-Protocol population. Exclusions of subjects from any analysis populations will be determined and documented prior to the DBF.

PK samples collected outside the protocol defined time-windows and/or other protocol deviations will be reviewed by the study team to determine whether the sample will be excluded from PK analyses.

10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

Screening Period and Oral Lead-in Phase: All Cohorts

Study Period	Screening[1]		Oral Lead-in[8]			Day 29	Early withdrawal[10]	Washout Period
			Dosing Days 1-28					
Visit Window	**Within 30 days of oral lead-in**	**Within 5 days of admission to the clinic**	**Day 1**	**Day 2**	**Day 14**	**Within 24 hours of the Day 28 last dose**	**EW**	**7 – 14 days[11]**
Informed Consent	X							
Demographics	X							
Medical / Medication / Drug / Alcohol History	X							
Inclusion/Exclusion Criteria[2]	X		X					
Height, Weight, BMI	X						X	
Physical Exam	X						X	
Vital Signs[3]	X		X	X	X	X	X	
Triplicate 12-Lead ECG[3]	X		X			X	X	
Drug / Alcohol Screen[4]	X		X					
Pregnancy Test[3,4]	X		X		X	X	X	
Testing for SARS-CoV-2	X	X[5]						
Hepatitis B, Hepatitis C Screening	X							
HIV Test	X							
Haematology with differential; Clinical Chemistry Tests; Urinalysis[3,4]	X		X	X	X	X	X	
Coagulation Tests	X					X	X	
Admit to clinic			X[4,5]					
Dispense Oral lead-in IP[6]			X					
Administer oral CAB[6]			X	X	X			
Provide dosing diary card			X					
Discharge from clinic				X				
Drug accountability/ pill count/review drug diary				X	X	X	X	
Blood plasma PK sampling[7]			X	X	X	X	X	

Study Period	**Screening[1]**		**Oral Lead-in[8]**			**Day 29**	**Early withdrawal[10]**	**Washout Period**
			Dosing Days 1-28					
Visit Window	**Within 30 days of oral lead-in**	**Within 5 days of admission to the clinic**	**Day 1**	**Day 2**	**Day 14**	**Within 24 hours of the Day 28 last dose**	**EW**	**7 – 14 days[11]**
AE Assessment[8]			X	X	X	X	X	
Concomitant Medication Review	X		X	X	X	X	X	
Genetic sample[9]			X					

1. Screening may occur over more than one visit but within 30 days of the first dose in the oral lead in phase.
2. Eligibility criteria must be carefully assessed at the Screening visit and confirmed at the Day 1 Oral lead-in phase visit.
3. Prior to administering the first oral dose of CAB, study personnel must verify the following pre-dose assessments to be within normal limits prior to administration: vital signs, ECG, pregnancy test (negative; females of reproductive potential [FRP] only). The results of the Drug/Alcohol screen, haematology with differential, clinical chemistry tests and urinalysis on Day 1 are not required prior to administering the first oral dose of CAB but samples should be drawn/collected prior to CAB administration.
4. Participants may be admitted to the clinic before Day 1 of the Oral Lead-in Phase. They may have some assessments, such as drug/alcohol screen, pregnancy test and haematology/chemistry/urinalysis, done on the day before Day 1.
5. The second test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) should be performed within 5 days of admission (ideally within 24 hours), and negative results for both tests are required prior to dosing. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. **Where SARS-CoV-2 is circulating in the community**, participants are admitted for the second test for SARS-CoV-2; prior to the second test result being known, they should follow strict infection control procedures (personal protective equipment (PPE)/social distancing) and should be isolated within an area of the unit to avoid exposure to COVID-19 negative participants. Once the second test result is a confirmed negative, they can be released into the unit and follow infection control practices as per unit guidance. **Where SARS-CoV-2 is NOT circulating in the community**, the second test for SARS-CoV-2 may be performed within 5 days of admission to the clinic, and if participants are not admitted, they will be advised to avoid exposure to COVID-19 and self-quarantine until entrance to the unit while awaiting final testing clearance. Sponsor approval is required for site(s) to adopt SARS-CoV-2 testing within 5 days of admission to the clinic if study participants do not remain and isolate within the unit until test results are known.
6. Randomization in Part 1 to occur on Day 1 prior to oral dosing (randomization in Part 2 to occur on Day 1 of the injection phase prior to the first injection). Oral CAB dosing Days 1 to 28. Day 1, Day 2, and Day 14 doses should be administered in the clinic. The tablet should be taken at approximately the same time each day.
7. PK sampling – On Day 1 (1 h, 2 h, 3 h, 4 h, and 6 h, and in addition for Cohort 5 and Cohort 6 [if conducted] at 8 h, and 12 h) and Day 2 PK between 20 h and 28 h post first oral dose. Day 14 is a pre-dose PK sample. Day 29 assessments should occur between 20 h and 28 h of the last dose on Day 28. A total of 8 PK samples (10 PK samples for Cohorts 5 and 6) will be collected during oral lead-in phase. Please refer to Protocol Section 8.5 for permitted PK window for OLI phase.
8. AE assessment will include a brief, symptom-directed physical exam as needed.
9. Genetic sample Day 1 collect the sample at the earliest convenient time after the first dose in the oral lead in phase.
10. If a participant is withdrawn prior to receiving the CAB LA injection, a follow-up/withdrawal visit should be scheduled 10-14 days after the last oral dose of CAB.
11. The washout period may be extended if deemed necessary by the investigator and sponsor.

CAB 400 mg/mL or CAB 200 mg/mL LA Injection Phase and Follow- up: Part 1 Cohorts 1-4

		Injection Phase															Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 /EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	8 h	24 h																		
Permitted window for PK collection		Within 1 h prior to dosing	±15 min	±30 min	±1 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±1 day	±1 day	±1 day		±3 days	±3 days	±3 days	±3 days	±3 days	±3 days	±3 days	±3 days
Interim Medical /Medication/ Drug / Alcohol History		X																						
Pregnancy Test[3,8]		X											X				X	X	X			X	X	X
12-Lead ECG		X		X																				
Testing for SARS-CoV-2	X[3]										X[3]													

		Injection Phase															Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 /EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	8 h	24 h																		
HIV Test[3,9]		X															X							X
Haematology; Clinical Chemistry; Urinalysis[3]		X									X		X				X	X	X			X	X	X
Coagulation Tests[3]		X																						X
Brief Physical Exam		X				X					X						X	X	X			X	X	X
Weight																	X				X			X
Vital Signs		X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X			X	X	X
Admit to clinic		X[3]																						
Administer CAB 400 mg/mL or CAB 200 mg/mL LA[4]		X																						

		Injection Phase															Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 /EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	8 h	24 h																		
CCI																								
Provide diary card regarding injection site reactions		X																						
Discharge from the clinic											X													
Injection site reaction assessment[10]			X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
AE Assessment[6]			X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Device deficiencies		X	X																					
Concomitant Medication Review			X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X

		Injection Phase															Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 /EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	8 h	24 h																		
Blood plasma PK Sampling[7]		X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X

1. Participants will have PK monitoring up to and including Week 52 post last injection. Participants with undetectable CAB concentrations before this timepoint will be deemed to have completed follow up and return to the clinic for a last study visit at which activities specified for the Week 52/EW visit will be performed. Participants who withdraw from the study before week 52 post last injection will be asked to return to the site for a withdrawal visit.
2. On Day 1, study personnel must verify the following pre-dose assessments to be within normal limits prior to injection: ECG, brief physical exam, vital signs, pregnancy test (negative; FRP only), AE assessment, and concomitant medication assessment. If a clinical abnormality, clinically significant AE, or prohibited medication that precludes injection is observed/recorded, the medical monitor must be contacted for further instruction.
3. Participants may be admitted to the clinic before Injection 1 Day 1 and Injection 2 Day 1. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. **Where SARS-CoV-2 is circulating in the community**, participants should have one SARS-CoV-2 test approximately 1 week prior to admission to the clinic. A second test would be done upon admission; prior to the test result being known, participants should follow strict infection control procedures (PPE/social distancing) and should be isolated within an area of the unit to avoid exposure to COVID-19 negative participants until the test result is known. Once the test result is a confirmed negative, they can be released into the unit and follow infection control practices as per unit guidance. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. A further test will be done on Day 8 upon discharge from the clinic. **Where SARS-CoV-2 is NOT circulating in the community**, SARS-CoV-2 testing prior to dosing may be performed within 5 days of admission to the clinic, and if participants are not admitted, they will be advised to avoid exposure to COVID-19 and self-quarantine until entrance to the unit while awaiting final testing clearance. Sponsor approval is required for site(s) to adopt SARS-CoV-2 testing within 5 days of admission to the clinic if study participants do not remain and isolate within the unit until test results are known. A further test is NOT required on Day 8 upon discharge from the clinic. Participants may have some assessments, such as HIV test, drug/alcohol screen, pregnancy test, haematology/chemistry/urinalysis and coagulation tests, done on the day before Injection 1 Day 1 and Injection 2 Day 1.

4. CAB 400 mg/mL - injection 1 loading dose of 600 mg and injection 2 400 mg; Cohort 1 Q4WM IM- via gluteus medius, Cohort 2 Q4W SC and Cohort 3 Q4W IM – lateral thigh/vastus lateralis. Cohort 4 dose and dosing schedule determination by STR based upon data from cohorts 1-3 and historical CAB 200 mg/mL data. Active controls will be administered CAB 200 mg/mL formulation matched on dose or volume to the CAB 400 mg/mL participants in Cohorts 1 and 3 and Cohort 2, respectively.
5. CCI [redacted]
6. AE assessment will include a brief, symptom-directed physical exam as needed.
7. A total of 36 PK samples will be collected through the injection phase and Follow-up.
8. Urine or plasma pregnancy testing to be performed pre-injection where relevant
9. HIV antibody test (either a laboratory or point of care test).
10. See Protocol Section 8.2.6.

CAB 400 mg/mL LA Injection Phase and Follow- up: Part 1 Cohort 4b

			Injection Phase															Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day -1**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 4**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day -1**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 4**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures			Pre-dose[2]	1 h	2 h	8 h	24 h																		
Permitted window for PK collection			Within 1 h prior to dosing	±15 min	±30 min	±1 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±1 day	±1 day	±1 day		±3 days	±3 days	±3 days	±3 days	±3 days	±3 days	±3 days	±3 days
Interim Medical /Medication/ Drug / Alcohol History			X																						
Pregnancy Test[3,8]			X												X				X	X	X			X	X	X
Triplicate 12-Lead ECG			X		X																					
Testing for SARS-CoV-2	X[3]												X[3]													

			Injection Phase																Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day -1**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 4**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day -1**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 4**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures			Pre-dose[2]	1 h	2 h	8 h	24 h																			
HIV Test[3,9]			X																X							X
Haematology; Clinical Chemistry; Urinalysis[3]			X										X		X				X	X	X			X	X	X
Coagulation Tests[3]			X																							X
Brief Physical Exam			X				X						X						X	X	X			X	X	X
Weight																			X				X			X
Vital Signs			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X			X	X	X
Admit to clinic			X[3]																							
Administer CAB 400 mg/mL[4]			X																							
Administer topical NSAID or steroid[11]		X		X			X	X	X	X																

			Injection Phase																Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day -1**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 4**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day -1**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 4**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures			Pre-dose[2]	1 h	2 h	8 h	24 h																			
CCI																										
Provide diary card regarding injection site reactions			X																							
Discharge from the clinic													X													
Injection site reaction assessment[10]				X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
AE Assessment[6]				X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Concomitant Medication Review				X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X

			Injection Phase																Follow-up Phase							
Injection 1	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day -1**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 4**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	***Inj 1 Day 28 – proceed to Inj 2 Day 1***	**Follow-up post last injection**							
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day -1**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 4**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	***Inj 2 Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures			Pre-dose[2]	1 h	2 h	8 h	24 h																			
Blood plasma PK Sampling[7]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X

1. Participants will have PK monitoring up to and including Week 52 post last injection. Participants with undetectable CAB concentrations before this timepoint will be deemed to have completed follow up and return to the clinic for a last study visit at which activities specified for the Week 52/EW visit will be performed. Participants who withdraw from the study before week 52 post last injection will be asked to return to the site for a withdrawal visit.
2. On Day 1, study personnel must verify the following pre-dose assessments to be within normal limits prior to injection: triplicate 12-lead ECG, brief physical exam, vital signs, pregnancy test (negative; FRP only), AE assessment, and concomitant medication assessment. If a clinical abnormality, clinically significant AE, or prohibited medication that precludes injection is observed/recorded, the medical monitor must be contacted for further instruction.
3. Participants may be admitted to the clinic before Injection 1 Day 1 and Injection 2 Day 1. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. **Where SARS-CoV-2 is circulating in the community**, participants should have one SARS-CoV-2 test approximately 1 week prior to admission to the clinic. A second test would be done upon admission; prior to the test result being known, participants should follow strict infection control procedures (PPE/social distancing) and should be isolated within an area of the unit to avoid exposure to COVID-19 negative participants until the test result is known. Once the test result is a confirmed negative, they can be released into the unit and follow infection control practices as per unit guidance. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. A further test will be done on Day 8 upon discharge from the clinic. **Where SARS-CoV-2 is NOT circulating in the community**, SARS-CoV-2 testing prior to dosing may be performed within 5 days of admission to the clinic, and if participants are not admitted, they will be advised to avoid exposure to COVID-19 and self-quarantine until entrance to the unit while awaiting final testing clearance. Sponsor approval is required for site(s) to adopt SARS-CoV-2 testing within 5 days of admission to the clinic if study participants do not remain and isolate within the unit until test results are known. A further test is NOT required on Day 8 upon discharge from the clinic. Participants may have some assessments, such as HIV test, drug/alcohol screen, pregnancy test, haematology/chemistry/urinalysis and coagulation tests, done on the day before Injection 1 Day 1 and Injection 2 Day 1.
4. CAB 400 mg/mL - injection 1 loading dose of 300 mg and injection 2 300 mg Q4W SC.

5. CCI [redacted]
6. AE assessment will include a brief, symptom-directed physical exam as needed.
7. A total of 38 PK samples will be collected through the injection phase and Follow-up.
8. Urine or plasma pregnancy testing to be performed pre-injection where relevant
9. HIV antibody test (either a laboratory or point of care test).
10. See Protocol Section 8.2.6.
11. See Protocol Section 6.1.2. The topical steroid or placebo will be applied once daily (midday) and the topical NSAID or placebo twice daily (morning and evening) from Day -1 to Day 5 for Injections 1 and 2.
12. CCI [redacted]

CAB 400 mg/mL or CAB 200 mg/mL LA Injection Phase and Follow- up: Part 1 Cohort 4h (CAB 400 mg/mL or CAB 200 mg/mL with rHuPH20)

		Injection Phase																	Follow-up Phase							
Injection	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj Day 1**						**Inj Day 2**	**Inj Day 3**	**Inj Day 4**	**Inj Day 5**	**Inj Day 6**	**Inj Day 7**	**Inj Day 8**	**Inj Day 10**	**Inj Day 14**	**Inj Day 17**	**Inj Day 22**	***Inj Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	4 h	8 h	12 h	24 h																		
Permitted window for PK collection		Within 1 h prior to dosing	±15 min	±30 min	±1 h	±1 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±1 day	±1 day	±1 day		±3 days	±3 days	±3 days	±3 days	±3 days	±3 days	±3 days	±3 days
Interim Medical /Medication/ Drug / Alcohol History		X																								
Pregnancy Test[3,8]		X														X				X	X	X			X	X	X
12-Lead ECG		X		X				X	X	X	X	X	X	X	X												
Testing for SARS-CoV-2	X[3]													X[3]													
HIV Test[3,9]		X																		X							X
Haematology; Clinical Chemistry; Urinalysis[3]		X							X[13]		X[13]			X		X				X	X	X			X	X	X
Coagulation Tests[3]		X																									X

		Injection Phase																	Follow-up Phase							
Injection	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj Day 1**						**Inj Day 2**	**Inj Day 3**	**Inj Day 4**	**Inj Day 5**	**Inj Day 6**	**Inj Day 7**	**Inj Day 8**	**Inj Day 10**	**Inj Day 14**	**Inj Day 17**	**Inj Day 22**	***Inj Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	4 h	8 h	12 h	24 h																		
Brief Physical Exam		X						X						X						X	X	X			X	X	X
Weight																				X				X			X
Vital Signs		X	X	X		X		X	X		X	X	X	X	X	X	X	X		X	X	X			X	X	X
Admit to clinic		X[3]																									
Administer rHuPH20 followed by CAB 400 mg/mL or CAB 200 mg/mL[4]		X																									
CCI																											
Provide diary card regarding injection site reactions		X																									
Discharge from the clinic														X[12]													
Injection site reaction assessment[10]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE Assessment[6]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

		Injection Phase																	Follow-up Phase							
Injection	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj Day 1**						**Inj Day 2**	**Inj Day 3**	**Inj Day 4**	**Inj Day 5**	**Inj Day 6**	**Inj Day 7**	**Inj Day 8**	**Inj Day 10**	**Inj Day 14**	**Inj Day 17**	**Inj Day 22**	***Inj Day 28 – proceed to follow-up***	**Week 4/ Day 28**	**Week 8**	**Week 12**	**Week 20**	**Week 28**	**Week 36**	**Week 44**	**Week 52 / EW[1]**
Procedures		Pre-dose[2]	1 h	2 h	4 h	8 h	12 h	24 h																		
Concomitant Medication Review			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Blood plasma PK Sampling[7]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Blood plasma sampling (rHuPH20 immunogenicity)[11]		X														X				X							

1. Participants will have PK monitoring up to and including Week 52 post last injection. Participants with undetectable CAB concentrations before this timepoint will be deemed to have completed follow up and return to the clinic for a last study visit at which activities specified for the Week 52/EW visit will be performed. Participants who withdraw from the study before week 52 post last injection will be asked to return to the site for a withdrawal visit.
2. On Day 1, study personnel must verify the following pre-dose assessments to be within normal limits prior to injection: ECG, brief physical exam, vital signs, pregnancy test (negative; FRP only), AE assessment, and concomitant medication assessment. If a clinical abnormality, clinically significant AE, or prohibited medication that precludes injection is observed/recorded, the medical monitor must be contacted for further instruction.
3. Participants may be admitted to the clinic before Injection Day 1. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. **Where SARS-CoV-2 is circulating in the community**, participants should have one SARS-CoV-2 test approximately 1 week prior to admission to the clinic. A second test would be done upon admission; prior to the test result being known, participants should follow strict infection control procedures (PPE/social distancing) and should be isolated within an area of the unit to avoid exposure to COVID-19 negative participants until the test result is known. Once the test result is a confirmed negative, they can be released into the unit and follow infection control practices as per unit guidance. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. A further test will be done upon discharge from the clinic (between Day 5 and Day 8 – see footnote 12). **Where SARS-CoV-2 is NOT circulating in the community**, SARS-CoV-2 testing prior to dosing may be performed within 5 days of admission to the clinic, and if participants are not admitted, they will be advised to avoid exposure to COVID-19 and self-quarantine until entrance to the unit while awaiting final testing clearance. Sponsor approval is required for site(s) to adopt SARS-CoV-2 testing within 5 days of admission to the clinic if study participants do not remain and isolate within the unit until test results are known. A further test is NOT required upon discharge from the clinic. Participants may have some assessments, such as HIV test, drug/alcohol screen, pregnancy test, haematology/chemistry/urinalysis and coagulation tests, done on the day before Injection Day 1.

4. Randomization to occur on Day 1 prior to the injection. CAB 400 mg/mL and CAB 200 mg/mL - injection dose of 400 mg SC. Participants receive 5000 U of rHuPH20 followed by CAB 200 mg/mL or 400 mg/mL formulation via a subcutaneous injection via a single butterfly needle. Due to a dead volume of 0.331 mL in the butterfly tube, a larger volume of CAB 200 mg/mL or 400 mg/mL formulation will be required. Therefore, 1.4 mL of CAB 400 mg/mL and 2.4 mL of CAB 200 mg/mL for injection will be used, and the exact doses of CAB 400 mg/mL and CAB 200 mg/mL administered will be 427.6 mg (1.069 mL) and 413.8 mg (2.069 mL), respectively.
5. CCI [redacted]
6. AE assessment will include a brief, symptom-directed physical exam as needed.
7. A total of 25 PK samples will be collected through the injection phase and Follow-up.
8. Urine or plasma pregnancy testing to be performed pre-injection where relevant
9. HIV antibody test (either a laboratory or point of care test).
10. See Protocol Section 8.2.6.
11. Plasma samples (K3-EDTA) for optional rHuPH20 immunogenicity analysis at pre-dose, Day 14 and Day 28. Analysis will be event-driven, (e.g. only if there are safety observations suggestive of an immune-mediated event).
12. Participants may be discharged from the clinic between Injection Day 5 and Injection Day 8. If participants are discharged prior to Injection Day 8, they would return to the clinic for assessments on the days specified in the SoA. **Where SARS-CoV-2 is circulating in the community,** participants should have a SARS-CoV-2 test on the day they are being discharged from the clinic.
13. No urinalysis needs to be performed on Days 3 and 5.

CAB 400 mg/mL or CAB 200 mg/mL LA Injection Phase and Follow- up: Part 2 Cohorts 5 and 6

		Injection Phase																		Follow-up Phase			
Injection 1[10]	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	**Inj 1 Week 4**	**Inj 1 Week 6**	**Inj 1 Week 8**	**Inj 1 Week 10**	***Inj 1 Week 12 – proceed to Injection 2 Day 1***	**Follow-up post last injection**			
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	**Inj 2 Week 4**	**Inj 2 Week 6**	**Inj 2 Week 8**	**Inj 2 Week 10**	***Inj 2 Week 12 – proceed to follow-up***	**Week 12**	**Week 24**	**Week 40**	**Week 52/EW[1]**
		Pre-dose[2]	1 h	2 h	8 h	24 h																	
Permitted window for PK collection		Within 1 h prior to dosing	±15 min	±30 min	±1 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±2 h	±1 day	±1 day	±1 day	±1 day	±1 day	±1 day	±1 day		±3 days	±3 days	±3 days	±3 days
Interim Medical / Medication/ Drug / Alcohol History		X																					
Pregnancy Test[3,8]		X											X				X				X	X	X	X
Triplicate 12-Lead ECG		X		X		X	X	X	X	X	X	X												

		Injection Phase																		Follow-up Phase			
Injection 1[10]	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	**Inj 1 Week 4**	**Inj 1 Week 6**	**Inj 1 Week 8**	**Inj 1 Week 10**	***Inj 1 Week 12 – proceed to Injection 2 Day 1***	**Follow-up post last injection**			
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	**Inj 2 Week 4**	**Inj 2 Week 6**	**Inj 2 Week 8**	**Inj 2 Week 10**	***Inj 2 Week 12 – proceed to follow-up***	**Week 12**	**Week 24**	**Week 40**	**Week 52/EW[1]**
		Pre-dose[2]	1 h	2 h	8 h	24 h																	
Testing for SARS-CoV-2	X[3]										X[3]												
HIV Test[3,9]		X																			X			X
Haematology; Clinical Chemistry; Urinalysis[3]		X				X[11]	X[11]	X[11]		X		X	X		X	X		X			X	X	X	X
Coagulation Tests[3]		X													X									X
Brief Physical Exam		X				X			X			X			X		X				X		X	X
Weight		X																			X	X		X
Vital Signs		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Admit to clinic		X[3]																						

		Injection Phase																		Follow-up Phase			
Injection 1[10]	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	**Inj 1 Week 4**	**Inj 1 Week 6**	**Inj 1 Week 8**	**Inj 1 Week 10**	***Inj 1 Week 12 – proceed to Injection 2 Day 1***	**Follow-up post last injection**			
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	**Inj 2 Week 4**	**Inj 2 Week 6**	**Inj 2 Week 8**	**Inj 2 Week 10**	***Inj 2 Week 12 – proceed to follow-up***	**Week 12**	**Week 24**	**Week 40**	**Week 52/EW[1]**
		Pre-dose[2]	1 h	2 h	8 h	24 h																	
Administer CAB 400 mg/mL or CAB 200 mg/mL LA[4]		X																					
CCI																							
Provide diary card regarding injection site reactions		X																					
Discharge from the clinic											X[10]												
Injection site reaction assessment[12]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X

		Injection Phase																		Follow-up Phase			
Injection 1[10]	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 1 Day 1**				**Inj 1 Day 2**	**Inj 1 Day 3**	**Inj 1 Day 5**	**Inj 1 Day 6**	**Inj 1 Day 7**	**Inj 1 Day 8**	**Inj 1 Day 10**	**Inj 1 Day 14**	**Inj 1 Day 17**	**Inj 1 Day 22**	**Inj 1 Week 4**	**Inj 1 Week 6**	**Inj 1 Week 8**	**Inj 1 Week 10**	***Inj 1 Week 12 – proceed to Injection 2 Day 1***	**Follow-up post last injection**			
Injection 2	**Within 7 and/or 5 days of admission to the clinic[3]**	**Inj 2 Day 1**				**Inj 2 Day 2**	**Inj 2 Day 3**	**Inj 2 Day 5**	**Inj 2 Day 6**	**Inj 2 Day 7**	**Inj 2 Day 8**	**Inj 2 Day 10**	**Inj 2 Day 14**	**Inj 2 Day 17**	**Inj 2 Day 22**	**Inj 2 Week 4**	**Inj 2 Week 6**	**Inj 2 Week 8**	**Inj 2 Week 10**	***Inj 2 Week 12 – proceed to follow-up***	**Week 12**	**Week 24**	**Week 40**	**Week 52/EW[1]**
		Pre-dose[2]	1 h	2 h	8 h	24 h																	
AE Assessment[6]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Concomitant Medication Review		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Blood plasma PK Sampling[7]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X

1. Participants will have PK monitoring up to and including Week 52 post last injection. Participants with undetectable CAB concentrations before this timepoint will be deemed to have completed follow up and return to the clinic for a last study visit at which activities specified for the Week 52/EW visit will be performed. Participants who withdraw from the study before Week 52 post last injection will be asked to return to the site for a withdrawal visit.
2. On Day 1, study personnel must verify the following pre-dose assessments to be within normal limits prior to injection: ECG, brief physical exam, vital signs, pregnancy test (negative; FRP only), AE assessment, and concomitant medication assessment. If a clinical abnormality, clinically significant AE, or prohibited medication that precludes injection is observed/recorded, the medical monitor must be contacted for further instruction.
3. Participants may be admitted to the clinic before Injection 1 Day 1 and Injection 2 Day 1. Any new Phase I unit participating in this study will adhere to the following SARS-CoV-2 testing procedures. **Where SARS-CoV-2 is circulating in the community**, participants should have one SARS-CoV-2 test approximately 1 week prior to admission to the clinic. A second test would be done upon admission; prior to the test result being known, participants should follow strict infection control procedures (PPE/social distancing) and should be isolated within an area of the unit to avoid exposure to COVID-19 negative participants until the test result is known. Once the test result is a confirmed negative, they can be

released into the unit and follow infection control practices as per unit guidance. A further test will be done on Day 8 upon discharge from the clinic. **Where SARS-CoV-2 is NOT circulating in the community**, SARS-CoV-2 testing prior to dosing may be performed within 5 days of admission to the clinic, and if participants are not admitted, they will be advised to avoid exposure to COVID-19 and self-quarantine until entrance to the unit while awaiting final testing clearance. Sponsor approval is required for site(s) to adopt SARS-CoV-2 testing within 5 days of admission to the clinic if study participants do not remain and isolate within the unit until test results are known. A further test is NOT required on Day 8 upon discharge from the clinic. Participants may have some assessments, such as HIV test, drug/alcohol screen, pregnancy test, haematology/chemistry/urinalysis and coagulation tests, done on the day before Injection 1 Day 1 and Injection 2 Day 1.

4. Randomization in Part 2 to occur on Day 1 prior to the first injection. CAB 400 mg/mL – (dose determination by SRT following cohort 1) injection via *gluteus medius* on Day 1 and Week 12 (± 3 days for second injection). Active control participants will receive CAB 200 mg/mL matched on volume to CAB 400 mg/mL participants.
5. CCI [redacted]
6. AE assessment will include a brief, symptom-directed physical exam as needed.
7. A total of 40 PK samples will be collected through the injection phase and Follow-up.
8. Urine or plasma pregnancy testing to be performed pre-injection where relevant.
9. HIV antibody test (either a laboratory or point of care test).
10. The first four participants enrolled in Cohort 5 and Cohort 6 (if conducted) will serve as sentinel participants with three receiving CAB 400 mg/mL formulation and one receiving active control (based on 3:1 randomization). These sentinel participants will be followed clinically for 10 days after Injection 1 (including a stay in the clinic until Day 8) to monitor the emergence of adverse events and other assessments specified for Days 1 to 10. If there are no significant safety concerns upon 10-day review of safety data for the sentinel participants, the remaining participants will subsequently be treated with either CAB 400 mg/mL formulation (n=17) or AC (n=1). Dose administration for these remaining participants (n=18) will be staggered: a further 7 participants will have their first injection and following a review of safety data from the initial 7 participants 10 days post first injection, the remaining 11 participants will receive their first injection. All participants will remain in the clinic for 7 days following each injection.
11. No urinalysis needs to be performed on these Days 2, 3 and 5.
12. See Protocol Section 8.2.6.

10.3. Appendix 3: Assessment Windows

All assessments/events (including those from planned, unscheduled and withdrawal visits) will be assigned to assessment windows/analysis visits according to actual dates of collection rather than the nominal visit labels recorded on the eCRF or in the laboratory database.

For parameters which are not scheduled to be assessed at a particular visit, all-inclusive assessment windows will still be used; however, data displays summarizing measurements by visit will only report visits in which the parameter is a planned collection according to Appendix 2: Schedule of Activities.

Note: Prior to visit slotting, assessments are first assigned to a study period according to Table 5.

10.3.1. Definitions of Assessments Windows

Table 1 Assessment Windows for Screening and OLI Period Data

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
Assessments assigned to Period=Screening or OLI (per Table 5)			
Vital signs, Labs, ECG, Weight, Pregnancy Test, Drug/Alcohol Screen, Coagulation Tests	OLI Period Day <1	The day of earliest record	Screening
PK, Vital Signs, Labs, ECG, Pregnancy Test, Drug/Alcohol Screen	OLI Period Day = 1	1	Day 1
PK, Vital Signs, Labs	OLI Period Day = 2	2	Day 2
Vital Signs, Labs, Pregnancy Test	3 ≤ OLI Period Day ≤ 21	14	Day 14
PK	13 ≤ OLI Period Day ≤ 15	14	Day 14
ECG	2 ≤ OLI Period Day	29	Day 29
Vital Signs, Labs, Pregnancy Test	22 ≤ OLI Period Day	29	Day 29
PK	28 ≤ OLI Period Day ≤ 30	29	Day 29
Coagulation Tests	1 ≤ OLI Period Day	29	Day 29
Vital signs, Labs, ECG, Weight, PK, Coagulation Tests, Pregnancy Test	OLI Period Day > [(OLI Stop Date – OLI Start Date + 1) + 1]		Washout
Vital signs, Labs, ECG	Date of Assessment = Date of Injection 1		Injection 1 Day 1
If none of the above			Day X, where X=OLI period day

Note: if a record falls within more than one analysis window then the record will be assigned to the latest applicable analysis timepoint (e.g., if a record falls within the analysis window for Day 14 and Washout, then the record will be assigned to Washout; if a record falls within the analysis window for Washout and Injection 1 Day 1, then the record will be assigned to Injection 1 Day 1).

Table 2 Assessment Windows for Part 1 Injection and Follow Up Phase Data

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
Assessments assigned to Period=Injection 1 (per Table 5)			
PK, Vital Signs, Labs, ECG, NRS, Pregnancy Test, Brief Physical Exam, HIV Test	Injection 1 Period Day = 1	1	Day 1
PK, Vital Signs, NRS	Injection 1 Period Day = 2	2	Day 2
Brief Physical Exam	2 ≤ Injection 1 Period Day ≤ 5	2	Day 2
Cohort 4h: ECG	Injection 1 Period Day = 2	2	Day 2
Vital Signs	3 ≤ Injection 1 Period Day ≤ 4	3	Day 3
Cohort 4b: Vital Signs	Injection 1 Period Day = 3	3	Day 3
Cohort 4h: ECG	Injection 1 Period Day = 3	3	Day 3
PK	Injection 1 Period Day = 3	3	Day 3
Cohort 4b: PK, Vital Signs	Injection 1 Period Day = 4	4	Day 4
Cohort 4h: PK, ECG	Injection 1 Period Day = 4	4	Day 4
PK, Vital Signs, NRS	Injection 1 Period Day = 5	5	Day 5
Cohort 4h: ECG	Injection 1 Period Day = 5	5	Day 5
PK, Vital Signs	Injection 1 Period Day = 6	6	Day 6
Cohort 4h: ECG	Injection 1 Period Day = 6	6	Day 6
PK, Vital Signs	Injection 1 Period Day = 7	7	Day 7
Cohort 4h: ECG	Injection 1 Period Day = 7	7	Day 7
NRS, PIN, PK	Injection 1 Period Day = 8	8	Day 8
Cohort 4h: ECG	8 ≤ Injection 1 Period Day ≤ 9	8	Day 8
Vital Signs	8 ≤ Injection 1 Period Day ≤ 9	8	Day 8
Labs	2 ≤ Injection 1 Period Day ≤ 11	8	Day 8
Brief Physical Exam	6 ≤ Injection 1 Period Day ≤ 18	8	Day 8
PK	Injection 1 Period Day =10	10	Day 10
Vital Signs	10 ≤ Injection 1 Period Day ≤ 12	10	Day 10
Cohort 4h: ECG	10 ≤ Injection 1 Period Day	10	Day 10
PK, Vital Signs	13 ≤ Injection 1 Period Day <=15	14	Day 14
Labs	12 ≤ Injection 1 Period Day ≤ 21	14	Day 14
Pregnancy Test	2 ≤ Injection 1 Period Day ≤ 21	14	Day 14
Vital Signs	16 ≤ Injection 1 Period Day ≤ 19	17	Day 17
PK	16 ≤ Injection 1 Period Day ≤ 18	17	Day 17
Vital Signs	20 ≤ Injection 1 Period Day ≤ 25	22	Day 22
PK	21 ≤ Injection 1 Period Day ≤ 23	22	Day 22
Weight	15 ≤ Injection 1 Period Day	28	Week 4
Vital Signs	26 ≤ Injection 1 Period Day	28	Week 4
PK	25 ≤ Injection 1 Period Day ≤ 31	28	Week 4
Labs	22 ≤ Injection 1 Period Day	28	Week 4
Pregnancy Test	22 ≤ Injection 1 Period Day	28	Week 4
Brief Physical Exam	19 ≤ Injection 1 Period Day	28	Week 4
HIV Test	2 ≤ Injection 1 Period Day	28	Week 4

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
	If none of the above		Day X, where X=Injection 1 Period Day
Assessments assigned to Period=Injection 2 (per Table 5)			
PK, Vital Signs, Labs, ECG, NRS, Pregnancy Test, Brief Physical Exam, HIV Test,	Injection 2 Period Day = 1	1	Day 1
PK, Vital Signs, NRS	Injection 2 Period Day = 2	2	Day 2
Brief Physical Exam	2 ≤ Injection 2 Period Day ≤ 5	2	Day 2
Vital Signs	3 ≤ Injection 2 Period Day ≤ 4	3	Day 3
Cohort 4b: Vital Signs	Injection 2 Period Day = 3	3	Day 3
PK	Injection 2 Period Day = 3	3	Day 3
Cohort 4b: PK, Vital Signs	Injection 1 Period Day = 4	4	Day 4
PK, Vital Signs, NRS	Injection 2 Period Day = 5	5	Day 5
PK, Vital Signs	Injection 2 Period Day = 6	6	Day 6
PK, Vital Signs	Injection 2 Period Day = 7	7	Day 7
NRS, PIN, PK	Injection 2 Period Day = 8	8	Day 8
Vital Signs	8 ≤ Injection 2 Period Day ≤ 9	8	Day 8
Labs	2 ≤ Injection 2 Period Day ≤ 11	8	Day 8
Vital Signs	10 ≤ Injection 2 Period Day ≤ 12	10	Day 10
PK	Injection 2 Period Day =10	10	Day 10
PK, Vital Signs	13 ≤ Injection 2 Period Day ≤15	14	Day 14
Labs	12 ≤ Injection 2 Period Day ≤ 21	14	Day 14
Pregnancy Test	2 ≤ Injection 2 Period Day ≤ 21	14	Day 14
Vital Signs	16 ≤ Injection 2 Period Day ≤ 19	17	Day 17
PK	16 ≤ Injection 2 Period Day ≤ 18	17	Day 17
Vital Signs	20 ≤ Injection 2 Period Day ≤ 25	22	Day 22
PK	21 ≤ Injection 2 Period Day ≤ 23	22	Day 22
Weight	15 ≤ Injection 2 Period Day	28	Week 4
Vital Signs	26 ≤ Injection 2 Period Day	28	Week 4
PK	25 ≤ Injection 2 Period Day ≤ 31	28	Week 4
Labs	22 ≤ Injection 2 Period Day	28	Week 4
Pregnancy Test	22 ≤ Injection 2 Period Day	28	Week 4
Brief Physical Exam	19 ≤ Injection 2 Period Day	28	Week 4
HIV Test	2 ≤ Injection 2 Period Day	28	Week 4
	If none of the above		Day X, where X=Injection 2 Period Day
Assessments assigned to Period=Follow-up (per Table 5)			
Vital Signs, Labs, Pregnancy Test, Brief Physical Exam	(Date of Nominal Follow-up Week 4 Visit – Date of Final CAB Injection [a] + 1) < Follow-up Period Day ≤ 70	56	Week 8
PK	53 ≤ Follow-up Period Day ≤ 59	56	Week 8
Vital Signs, Labs, Pregnancy Test, Brief Physical Exam	71 ≤ Follow-up Period Day ≤ 168	84	Week 12
PK	81 ≤ Follow-up Period Day ≤ 87	84	Week 12

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
PK	137 ≤ Follow-up Period Day ≤ 143	140	Week 20
Weight	113 (week 16) ≤ Follow-up Period Day ≤ 280 (week 40)	196	Week 28
PK	193 ≤ Follow-up Period Day ≤ 199	196	Week 28
Vital Signs, Labs, Pregnancy Test, Brief Physical Exam	169 ≤ Follow-up Period Day ≤ 280 (week 40)	252	Week 36
PK	249 ≤ Follow-up Period Day ≤ 255	252	Week 36
Vital Signs, Labs, Pregnancy Test, Brief Physical Exam	281 ≤ Follow-up Period Day ≤ 336 (week 48)	308	Week 44
PK	305 ≤ Follow-up Period Day ≤ 311	308	Week 44
Weight	281 ≤ Follow-up Period Day	364	Week 52
Vital Signs, Labs, Pregnancy Test, Brief Physical Exam	337 ≤ Follow-up Period Day	364	Week 52
PK	361 ≤ Follow-up Period Day ≤ 367	364	Week 52
If none of the above			Day X, where X=Follow-up Period Day

NOTES:
- OLI Day, Injection 1 Day, Injection 2 Day and Follow-up Day are defined in Section 10.6.1.

Table 3 Assessment Windows for Part 2 Injection and Follow-up Phase Data

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
Assessments assigned to Period=Injection 1 (per Table 5)			
PK, Vital Signs, Labs, ECG, NRS, Weight, Pregnancy Test, Brief Physical Exam, HIV Test, Coagulation Tests	Injection 1 Period Day = 1	1	Day 1
PK, Vital Signs, Labs, ECG, NRS	Injection 1 Period Day = 2	2	Day 2
Brief Physical Exam	2 ≤ Injection 1 Period Day ≤ 4	2	Day 2
Vital Signs, Labs, ECG	3 ≤ Injection 1 Period Day ≤ 4	3	Day 3
PK	Injection 1 Period Day = 3	3	Day 3
PK, Vital Signs, ECG, NRS	Injection 1 Period Day = 5	5	Day 5
Labs	5 ≤ Injection 1 Period Day ≤ 6	5	Day 5
PK, Vital Signs, ECG	Injection 1 Period Day = 6	6	Day 6
Brief Physical Exam	5 ≤ Injection 1 Period Day ≤ 8	6	Day 6
PK, Vital Signs, ECG	Injection 1 Period Day = 7	7	Day 7
Labs	7 ≤ Injection 1 Period Day ≤ 8	7	Day 7
PK, NRS, PIN	Injection 1 Period Day = 8	8	Day 8
Vital Signs, ECG	8 ≤ Injection 1 Period Day ≤ 9	8	Day 8
Labs	9 ≤ Injection 1 Period Day ≤ 12	10	Day 10
Vital Signs, ECG	10 ≤ Injection 1 Period Day ≤ 12	10	Day 10

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
PK	Injection 1 Period Day = 10	10	Day 10
Brief Physical Exam	9 ≤ Injection 1 Period Day ≤ 16	10	Day 10
PK, Vital Signs	13 ≤ Injection 1 Period Day ≤ 15	14	Day 14
Labs	13 ≤ Injection 1 Period Day ≤ 18	14	Day 14
Pregnancy Test	2 ≤ Injection 1 Period Day ≤ 28	14	Day 14
Vital Signs	16 ≤ Injection 1 Period Day ≤ 19	17	Day 17
PK	16 ≤ Injection 1 Period Day ≤ 18	17	Day 17
Labs	19 ≤ Injection 1 Period Day ≤ 25	22	Day 22
Vital Signs	20 ≤ Injection 1 Period Day ≤ 25	22	Day 22
PK	21 ≤ Injection 1 Period Day ≤ 23	22	Day 22
Brief Physical Exam	17 ≤ Injection 1 Period Day ≤ 32	22	Day 22
Coagulation Tests	2 ≤ Injection 1 Period Day	22	Day 22
Labs	26 ≤ Injection 1 Period Day ≤ 42	28	Week 4
Vital Signs	26 ≤ Injection 1 Period Day ≤ 35	28	Week 4
PK	25 ≤ Injection 1 Period Day ≤ 31	28	Week 4
Vital Signs	36 ≤ Injection 1 Period Day ≤ 49	42	Week 6
PK	41 ≤ Injection 1 Period Day ≤ 43	42	Week 6
Pregnancy Test	29 ≤ Injection 1 Period Day ≤ 63	42	Week 6
Brief Physical Exam	33 ≤ Injection 1 Period Day ≤ 63	42	Week 6
Labs	43 ≤ Injection 1 Period Day ≤ 70	56	Week 8
Vital Signs	50 ≤ Injection 1 Period Day ≤ 63	56	Week 8
PK	55 ≤ Injection 1 Period Day ≤ 57	56	Week 8
Vital Signs	64 ≤ Injection 1 Period Day ≤ 77	70	Week 10
PK	69 ≤ Injection 1 Period Day ≤ 71	70	Week 10
Weight, HIV Test	2 ≤ Injection 1 Period Day	84	Week 12
Vital Signs	78 ≤ Injection 1 Period Day	84	Week 12
PK	81 ≤ Injection 1 Period Day ≤ 87	84	Week 12
Labs	71 ≤ Injection 1 Period Day	84	Week 12
Pregnancy Test, Brief Physical Exam	64 ≤ Injection 1 Period Day	84	Week 12
If none of the above			Day X, where X=Injection 1 Period Day
Assessments assigned to Period=Injection 2 (per Table 5)			
PK, Vital Signs, Labs, ECG, NRS, Weight, Pregnancy Test, Brief Physical Exam, HIV Test, Coagulation Tests	Injection 2 Period Day = 1	1	Day 1
PK, Vital Signs, Labs, ECG, NRS	Injection 2 Period Day = 2	2	Day 2
Brief Physical Exam	2 ≤ Injection 2 Period Day ≤ 4	2	Day 2
Vital Signs, Labs, ECG	3 ≤ Injection 2 Period Day ≤ 4	3	Day 3
PK	Injection 2 Period Day = 3	3	Day 3
PK, Vital Signs, ECG, NRS	Injection 2 Period Day = 5	5	Day 5
Labs	5 ≤ Injection 2 Period Day ≤ 6	5	Day 5
PK, Vital Signs, ECG	Injection 2 Period Day = 6	6	Day 6
Brief Physical Exam	5 ≤ Injection 2 Period Day ≤ 8	6	Day 6

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
PK, Vital Signs, ECG	Injection 2 Period Day = 7	7	Day 7
Labs	7 ≤ Injection 2 Period Day ≤ 8	7	Day 7
PK, NRS, PIN	Injection 2 Period Day = 8	8	Day 8
Vital Signs, ECG	8 ≤ Injection 2 Period Day ≤ 9	8	Day 8
Labs	9 ≤ Injection 2 Period Day ≤ 12	10	Day 10
Vital Signs, ECG	10 ≤ Injection 2 Period Day ≤ 12	10	Day 10
PK	Injection 2 Period Day = 10	10	Day 10
Brief Physical Exam	9 ≤ Injection 2 Period Day ≤ 16	10	Day 10
PK, Vital Signs	13 ≤ Injection 2 Period Day ≤ 15	14	Day 14
Labs	13 ≤ Injection 2 Period Day ≤ 18	14	Day 14
Pregnancy Test	2 ≤ Injection 2 Period Day ≤ 28	14	Day 14
Vital Signs	16 ≤ Injection 2 Period Day ≤ 19	17	Day 17
PK	16 ≤ Injection 2 Period Day ≤ 18	17	Day 17
Labs	19 ≤ Injection 2 Period Day ≤ 25	22	Day 22
Vital Signs	20 ≤ Injection 2 Period Day ≤ 25	22	Day 22
PK	21 ≤ Injection 2 Period Day ≤ 23	22	Day 22
Brief Physical Exam	17 ≤ Injection 2 Period Day ≤ 32	22	Day 22
Coagulation Tests	2 ≤ Injection 2 Period Day	22	Day 22
Labs	26 ≤ Injection 2 Period Day ≤ 42	28	Week 4
Vital Signs	26 ≤ Injection 2 Period Day ≤ 35	28	Week 4
PK	27 ≤ Injection 2 Period Day ≤ 29	28	Week 4
Vital Signs	36 ≤ Injection 2 Period Day ≤ 49	42	Week 6
PK	41 ≤ Injection 2 Period Day ≤ 43	42	Week 6
Pregnancy Test	29 ≤ Injection 2 Period Day ≤ 63	42	Week 6
Brief Physical Exam	33 ≤ Injection 2 Period Day ≤ 63	42	Week 6
Labs	43 ≤ Injection 2 Period Day ≤ 70	56	Week 8
Vital Signs	50 ≤ Injection 2 Period Day ≤ 63	56	Week 8
PK	55 ≤ Injection 2 Period Day ≤ 57	56	Week 8
Vital Signs	64 ≤ Injection 2 Period Day ≤ 77	70	Week 10
PK	69 ≤ Injection 2 Period Day ≤ 71	70	Week 10
Weight, HIV Test	2 ≤ Injection 2 Period Day	84	Week 12
Vital Signs	78 ≤ Injection 2 Period Day	84	Week 12
PK	81 ≤ Injection 2 Period Day ≤ 87	84	Week 12
Labs	71 ≤ Injection 2 Period Day	84	Week 12
Pregnancy Test, Brief Physical Exam	64 ≤ Injection 2 Period Day	84	Week 12
If none of the above			Day X, where X=Injection 2 Period Day
Assessments assigned to Period=Follow-up (per Table 5)			
Vital Signs, Labs, Pregnancy Test	(Date of Nominal Follow-up Week 12 Visit – Date of Final CAB Injection [a] + 1) < Follow-up Period Day ≤ 224 (week 32)	168	Week 24

Parameter	Analysis Window	Target Period Day	Analysis Timepoint
Weight	(Date of Nominal Follow-up Week 12 Visit – Date of Final CAB Injection [a] + 1) < Follow-up Period Day ≤ 266 (week 38)	168	Week 24
PK	165 ≤ Follow-up Period Day ≤ 171	168	Week 24
Vital Signs, Labs, Pregnancy Test	225 ≤ Follow-up Period Day ≤ 322 (week 46)	280	Week 40
PK	277 ≤ Follow-up Period Day ≤ 283	280	Week 40
Weight	267 ≤ Follow-up Period Day	364	Week 52
Vital Signs, Labs, Pregnancy Test	323 ≤ Follow-up Period Day	364	Week 52
PK	361 ≤ Follow-up Period Day ≤ 367	364	Week 52
If none of the above			Day X, where X=Follow-up Period Day

NOTES:

- OLI Period Day, Injection 1 Period Day, Injection 2 Period Day and Follow-up Period Day are defined in Section 10.6.1.

10.4. Appendix 4: Study Phases, Study Periods, and Treatment Emergent Adverse Events

10.4.1. Study Phases and Study Periods

All assessments and events (including those collected as planned, early withdrawal and unscheduled visits) will be classified in study phases and study periods according to Table 4 and Table 5, respectively.

Assessments/events are assigned to study phases, and study periods sequentially, starting from the top of each table.

Table 4 Assignment of Study Phases

Study Phase	Definition
Screen	Assessments/Events assigned to Period=Screen in Table 5
OLI	Assessments/Events assigned to Period=OLI in Table 5
Injection	Assessments/Events assigned to Period=Injection 1 or Period=Injection 2 in Table 5
Follow-up	Assessments/Events assigned to Period=Follow-up in Table 5

Table 5 Assignment of Study Periods

For Adverse Events	
Study Period	**Date range**
Screen	**If actual "Time of Day" for the assessment/event is collected:**
	AE Start Date and Time < OLI Treatment Start Date & Time
	If actual "Time of Day" for the assessment/event is not collected:
	AE Start Date < OLI Treatment Start Date
OLI	**If actual "Time of Day" for the assessment/event is collected:**
	For participants continuing into Injection Phase: OLI Treatment Start Date & Time ≤ **AE Start Date & Time** < Date & Time of First CAB Injection **For participants not continuing into Injection Phase:** **AE Start Date & Time** ≥OLI Treatment Start Date & Time
	If actual "Time of Day" for the assessment/event is not collected:
	For participants continuing into Injection Phase: OLI Treatment Start Date ≤ **AE Start Date** < Date of First CAB Injection **For participants not continuing into Injection Phase:** **AE Start Date** ≥OLI Treatment Start Date
Injection 1	**If actual "Time of Day" for the assessment/event is collected:**
	For participants receiving second CAB injection: Date & Time of First CAB Injection ≤ **AE Start Date & Time** < Date & Time of Second CAB Injection **For participants not receiving second CAB injection:** Date & Time of First CAB Injection ≤ **AE Start Date & Time** and **AE Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]

	If actual "Time of Day" for the assessment/event is not collected:
	For participants receiving second CAB injection: Date of First CAB Injection ≤ **AE Start Date** < Date of Second CAB Injection **For participants not receiving second CAB injection:** Date of First CAB Injection ≤ **AE Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
Injection 2	**If actual "Time of Day" for the assessment/event is collected:**
	Date & Time of Second CAB Injection ≤ **AE Start Date & Time and AE Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
	If actual "Time of Day" for the assessment/event is not collected:
	Date of Second CAB Injection ≤ **AE Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
Follow-up	**AE Start Date** > Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
For Injection Site Reaction Adverse Events (Where collected on the ISR form for study treatment associated reactions, including drug related and non-drug related)	
Injection 1	**If actual "Time of Day" for the assessment/event is collected:**
	For participants receiving second CAB injection: Date & Time of First CAB Injection ≤ **AE Start Date & Time** < Date & Time of Second CAB Injection **For participants not receiving second CAB injection:** Date & Time of First CAB Injection ≤ **AE Start Date & Time**
	If actual "Time of Day" for the assessment/event is not collected:
	For participants receiving second CAB injection: Date of First CAB Injection ≤ **AE Start Date** < Date of Second CAB Injection **For participants not receiving second CAB injection:** Date of First CAB Injection ≤ **AE Start Date**

Injection 2	**If actual "Time of Day" for the assessment/event is collected:**
	Date & Time of Second CAB Injection ≤ **AE Start Date & Time and AE Start Date**
	If actual "Time of Day" for the assessment/event is not collected:
	Date of Second CAB Injection ≤ **AE Start Date**
For PK Data	
Study Period	**Data Range**
OLI	**Excluding Injection 1 Day 1 Pre-dose Samples:** **Start Date & Time** < Date & Time of First CAB Injection
Injection 1	**a) Injection 1 Day 1 Pre-dose Samples:** **Start Date & Time** < Date & Time of First CAB Injection **b) All Other Samples:** **For participants receiving second CAB injection:** Date & Time of First CAB Injection ≤ **Start Date & Time** < Date & Time of Second CAB Injection **For participants not receiving second CAB injection:** Date & Time of First CAB Injection ≤ **Date & Time** and **Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants] / Nominal Follow-up Week 12 Visit [For Part 2 participants]
Injection 2	Date & Time of Second CAB Injection ≤ **Date & Time** and **Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants] / Nominal Follow-up Week 12 [for Part 2 Participants]
Follow-up	**Start Date** > Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants] / Nominal Follow-up Week 12 Visit [for Part 2 participants]
Injection 2 Day 1 Pre-dose Samples: The original record will be assigned to Period = Injection 1 (as defined above). A duplicate record will be created and assigned to Period = Injection 2.	

Follow-up Week 4 [for Part 1 Participants], Follow-up Week 12 [for Part 2 Participants] Samples: If participant is not receiving second injection, the original record will be assigned to Period = Injection 1 (as defined above). A duplicate record will be created and assigned to Period = Follow-up. If participant has received second injection, the original record will be assigned to Period = Injection 2 (as defined above). A duplicate record will be created and assigned to Period = Follow-up.	
For Other Assessments (Excluding AEs and PK)	
Study Period	**Date range**
Screen	**If actual "Time of Day" for the assessment/event is collected:**
	Date & Time < OLI Treatment Start Date & Time
	If actual "Time of Day" for the assessment/event is not collected:
	Date < OLI Treatment Start Date
OLI	**If actual "Time of Day" for the assessment/event is collected:**
	For participants continuing into Injection Phase: OLI Treatment Start Date & Time ≤ **Date & Time** < Date & Time of First CAB Injection **For participants not continuing into Injection Phase:** **Date & Time** ≥OLI Treatment Start Date & Time
	If actual "Time of Day" for the assessment/event is not collected:
	For participants continuing into Injection Phase: OLI Treatment Start Date ≤ **Date** < Date of First CAB Injection **For participants not continuing into Injection Phase:** **Date** ≥OLI Treatment Start Date
Injection 1	**If actual "Time of Day" for the assessment/event is collected:**
	For participants receiving second CAB injection: Date & Time of First CAB Injection ≤ **Date & Time** < Date & Time of Second CAB Injection **For participants not receiving second CAB injection:** Date & Time of First CAB Injection ≤ **Date & Time and Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
	If actual "Time of Day" for the assessment/event is not collected:

	For ECG (inj 2 Day 1 pre-dose), Vital Signs (inj 2 Day 1 pre-dose), PK (inj 2 Day 1 pre-dose), Labs (inj 2 Day 1) Assessments: [a] Date of First CAB Injection ≤ **Date** ≤ minimum of (Date of Second CAB Injection, Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]) ***For Other Assessments/Events:*** **For participants receiving second CAB injection:** Date of First CAB Injection ≤ **Date** < Date of Second CAB Injection **For participants not receiving second CAB injection:** Date of First CAB Injection ≤ **Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
Injection 2	Date of Second CAB Injection ≤ **Date** ≤ Date of Nominal Follow-up Week 4 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
Follow-up	**Date** > Date of Nominal Follow-up Week 4 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
For Preference Questionnaire (Cohort 4b)	
Study Period	**Date range**
Injection 2	**Date** ≥ Date of Nominal Follow-up Week 4 Visit

NOTES:

- Date = Date of assessment

a. Pre-dose based on nominal planned timepoint variable (PTM)

Table 6 Study Phases for Concomitant Medication

Concomitant during:	Date range
Prior	**Medication Taken** < OLI Treatment Start Date
OLI	**For participants continuing into Injection Phase:** OLI Treatment Start Date & Time ≤ **Medication Taken** < Injection Phase Treatment Start Date & Time **For participants not continuing into Injection Phase:** **Medication Taken** ≥ OLI Treatment Start Date & Time
Injection 1	**For participants receiving second CAB injection:** Date & Time of First CAB Injection ≤ **Medication Taken** < Date & Time of Second CAB Injection **For participants not receiving second CAB injection:** Date & Time of First CAB Injection ≤ **Medication Taken** and **Medication Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
Injection 2	Date & Time of Second CAB Injection ≤ **Medication Taken and Medication Start Date** ≤ Date of Nominal Follow-up Week 4/Day 28 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]
Follow-Up	**Medication Taken** ≥ Date of Nominal Follow-up Week 4 Visit [for Part 1 participants]/ Nominal Follow-up Week 12 Visit [for Part 2 participants]

NOTES:

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

10.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• AEs will be considered emergent in the OLI, Injection and Follow-up Phase according to the classification defined in Table 5

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software
• The currently supported versions of SAS software version 9.4 will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1.
Generation of RTF Files
• RTF files will be generated for all tables, listings, and figures in Appendix 10: List of Data Displays
Generation of xlm Files
• xlm files will not be generated.

10.5.2. Reporting Standards

General

• The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings

Formats
• GSK Statistical Display Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the GSK Standard Statistical Display Principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any important deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the participant's listings.

Unscheduled Visits
• Unscheduled visits will be assigned to a study visit using assessment windows defined in Section 10.3.

Descriptive Summary Statistics	
Continuous Data	Refer to GSK Standard Statistical Display Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Standard Statistical Display Principals 7.01 to 7.13.	

10.5.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	

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

Pharmacokinetic Parameter Data	
Descriptive Summary Statistics, Graphical Displays and Listings	N, n, arithmetic mean, 95% CI of arithmetic mean, geometric mean, 95% CI of geometric mean, SD, SD of logged data, CVb (%), minimum and maximum will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of Ln-Transformed data)
Untransformed PK parameter	tmax
PK parameter listed only	KALA, KALA lower, KALA upper, KALA no. of points, and Rsq_adjusted
Listings	Include the first point (KALA lower), last point (KALA upper) and number of points used in the determination of KALA (KALA no. of points), and Rsq_adjusted for listings.

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Analysis Time Point

• For non-ECG assessments:
  ○ If there are multiple measurements within a time window (per Section 10.3), 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 of the measurements (for quantitative parameters) or the worst-case of the measurements (for qualitative parameters) will be calculated and used in any derivation of summary statistics.
• For ECG assessments, the average value (for quantitative parameters) or the worst-case value (for interpretation) from the triplicate assessments will be calculated and used in all of the summary statistics.
• Only planned assessment timepoints (according to Appendix 2: Schedule of Activities) will be included in data displays summarizing measurements by visit.
• Measurements at timepoints not selected for summarization by visit will be included in worst-case post-baseline determinations and in data listings.
  ○ Worst-case post-baseline determination, details are outlined in the Programming Notes from Appendix 10: List of Data Displays.
• Participants having both High and Low values for Normal Ranges at any post-baseline visit for vital sign measurements in the relevant Potential Clinical Importance summary tables.

Study Day

• Calculated as the number of days from First Dose Date of CAB:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First Dose Date of CAB → Study Day = Ref Date – First Dose Date of CAB
  • Ref Data ≥ First Dose Date of CAB → Study Day = Ref Date – (First Dose Date of CAB) + 1

Period Day

• Calculated as the number of days from First Dose Date of CAB for the respective period (based on study period classifications in Table 5):
 	
Screening and OLI periods:
• If Assessment Date < First Dose Date of Oral CAB then
  • Period Day = Assessment Date – First Dose Date of Oral CAB
• If Assessment Date ≥ First Dose Date of Oral CAB then
  • Period Day = Assessment Date – First Dose Date of Oral CAB +1
 	
Injection 1 period:
• If Assessment Date < First Dose Date of Injection CAB then
  • Period Day = Assessment Date – First Dose Date of Injection CAB
• If Assessment Date ≥ First Dose Date of Injection CAB then
  • Period Day = Assessment Date – First Dose Date of Injection CAB +1
 	
Injection 2 period:
• If Assessment Date < Second Dose Date of Injection CAB then
  • Period Day = Assessment Date – Second Dose Date of Injection CAB
• If Assessment Date ≥ Second Dose Date of Injection CAB then
  • Period Day = Assessment Date – Second Dose Date of Injection CAB +1
 	
Follow-up period:
• If Assessment Date < Final Dose Date of Injection CAB then
  • Period Day = Assessment Date – Final Dose Date of Injection CAB
• If Assessment Date ≥ Final Dose Date of Injection CAB then
  • Period Day = Assessment Date – Final Dose Date of Injection CAB +1
 	
Where “Final Dose Date of Injection CAB” is the date of first CAB injection for participants who discontinue prior to receiving the second injection; otherwise this will be the date of the second CAB injection, if available.

10.6.2. Study Population

Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: o Age, in whole years, will be calculated with respect to: o The participant's first dose date, if at least 1 dose of CAB was taken. o The participant's first Screening visit, if the participant did not take any dose of CAB. o For the purpose of calculating age, the '30th June' is imputed as the date and month of birth for all participants. • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height $(m)^2$]
Oral CAB Exposure
• Time on Oral CAB Study Treatment = last dose date of oral CAB – first dose date of oral CAB + 1
CAB Injection 1 Group in Cohort 3
• If not collected on the eCRF, the dose for injection 1 of Cohort 3 will be derived as follows: If date of injection 1 is prior to 01JAN2021 then dose = 600 mg, otherwise it is 400 mg

10.6.3. Safety

12-Lead Electrocardiograms
General
• Only the average value (for quantitative parameter) or the worst-case value (for interpretation) from the triplicate ECG assessments will be included in the summary statistics, including the maximum QTc values and the maximum increase in QTc values post-baseline relative to baseline summaries.
QTc Interval
• When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements. If RR interval (in msec) is provided, then missing QTcB and/or QTcF will be derived as $$\mathrm{QTcB} = \frac{\mathrm{QT}}{\sqrt{\mathrm{RR}/1000}} \qquad \mathrm{QTcF} = \frac{\mathrm{QT}}{\sqrt[3]{\mathrm{RR}/1000}}$$ where uncorrected QT interval is also measured in msec. If RR interval is not provided directly and one of QTcB or QTcF has been entered, then RR interval can be obtained from the above formulas and used to calculate the other correction method value; i.e., $$\mathrm{QTcB} = \sqrt{\frac{\mathrm{QTcF}^3}{\mathrm{QT}}} \qquad \mathrm{QTcF} = \sqrt[3]{\mathrm{QT} \cdot \mathrm{QTcB}^2}$$ • Average value (for quantitative ECG parameters) and worst-case value (for ECG interpretation) of the triplicate ECG assessments will be used for summaries of ECG change from baseline and ECG interpretations.

- All post-dose assessments will be used to determine the maximum QTc values post-baseline or maximum QTc increase post-baseline.

CCI
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Adverse Events

Adverse Events of Special Interest (AESI)

- Please refer to Appendix 11: AESI Identification for AESI identification

CCI
CCI

CCI

CCI

CCI

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Withdrawn participants may be replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

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 by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays. • Where necessary, partial dates may be imputed for specific analysis purposes as outlined below. • Imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of AEs), or elapsed time variables (e.g., time since diagnosis), except for crossover analysis endpoints (see Section 7.5) in which date of last contact will be used to derive duration for ongoing events.
Adverse Events	• Imputations in the AEs dataset are used for slotting events to the appropriate study time periods and for sorting in data listings. • Partial dates for AE recorded in the eCRF will be imputed using the following conventions: Missing start day: • If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month. • Else if study treatment start date is not missing: ○ If month and year of start date = month and year of study treatment start date then ▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month. ▪ Else set start date = study treatment start date. ○ Else set start date = 1st of month.

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.
• Else if study treatment start date is not missing:
○ If year of start date = year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = January 1.
▪ Else set start date = study treatment start date.
○ Else set start date = January 1.</td></tr>
<tr><td>Missing stop day</td><td>Last day of the month will be used.</td></tr>
<tr><td>Missing stop day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• Completely missing start or end dates will remain missing, with no imputation applied.
</td></tr>
<tr><td>Concomitant Medications</td><td>
• Partial dates for any concomitant medications recorded in the eCRF will be imputed using the following convention:
<table>
<tr><td>Missing start day</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.
• Else if study treatment start date is not missing:
○ If month and year of start date = month and year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month.
▪ Else set start date = study treatment start date.
○ Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.
• Else if study treatment start date is not missing:
○ If year of start date = year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = January 1.
▪ Else set start date = study treatment start date.
• Else set start date = January 1.</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year)</td></tr>
<tr><td>Missing end day and month</td><td>A '31' will be used for the day and 'Dec' will be used for the month.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• The recorded partial date will be displayed in listings.
</td></tr>
</table>

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values and Site Reactions to Injections and Infusions

Laboratory values and site reactions to injections and infusions will be graded based on the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Version 2.1, July 2017, as specified in the protocol Appendix 11.7, and shown below. Only numeric portion will be used, and higher grade will be assigned if the same criteria is applied to multiple grades.

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

Coagulation				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
INR, High	1.1 to < 1.5 × ULN	1.5 to < 2.0 × ULN	2.0 to < 3.0 × ULN	≥ 3.0 × ULN
PTT, High	1.1 to < 1.66 × ULN	1.66 to < 2.33 × ULN	2.33 to < 3.00 × ULN	≥ 3.00 × ULN
PT, High	1.1 to < 1.25 × ULN	1.25 to < 1.50 × ULN	1.50 to < 3.00 × ULN	≥ 3.00 × ULN

Clinical Chemistry				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Alkaline Phosphatase, High	1.25 to < 2.5 × ULN	2.5 to < 5.0 × ULN	5.0 to < 10.0 × ULN	≥ 10.0 × ULN
Alanine Aminotransferase, High	1.25 to < 2.5 × ULN	2.5 to < 5.0 × ULN	5.0 to < 10.0 × ULN	≥ 10.0 ULN
Aspartate Aminotransferase, High	1.25 to < 2.5 × ULN	2.5 to < 5.0 × ULN	5.0 to < 10.0 × ULN	≥ 10.0 × ULN
Direct Bilirubin, High > 28 days of age	NA	NA	> ULN with other signs and symptoms of hepatotoxicity	> ULN with life-threatening consequences (e.g., signs and symptoms of liver failure)
Total Bilirubin, High > 28 days of age	1.1 to < 1.6 × ULN	1.6 to < 2.6 × ULN	2.6 to < 5.0 × ULN	≥ 5.0 × ULN
Calcium, High (mg/dL; mmol/L) ≥ 7 days of age	10.6 to < 11.5 2.65 to < 2.88	11.5 to < 12.5 2.88 to < 3.13	12.5 to < 13.5 3.13 to < 3.38	≥ 13.5 ≥ 3.38
Calcium, Low (mg/dL; mmol/L) ≥ 7 days of age	7.8 to < 8.4 1.95 to < 2.10	7.0 to < 7.8 1.75 to < 1.95	6.1 to < 7.0 1.53 to < 1.75	< 6.1 < 1.53
Creatine Kinase, High	3 to < 6 × ULN	6 to < 10 × ULN	10 to < 20 × ULN	≥ 20 × ULN
Creatinine, High *Choose the method that selects for the higher grade*	1.1 to 1.3 × ULN	> 1.3 to 1.8 × ULN OR Increase to 1.3 to < 1.5 × participant's baseline	> 1.8 to < 3.5 × ULN OR Increase to 1.5 to < 2.0 × participant's baseline	≥ 3.5 × ULN OR Increase of ≥ 2.0 × participant's baseline
Glucose Fasting, High (mg/dL; mmol/L)	110 to 125 6.11 to < 6.95	> 125 to 250 6.95 to < 13.89	> 250 to 500 13.89 to < 27.75	≥ 500 ≥ 27.75
Glucose, Low (mg/dL; mmol/L) ≥ 1 month of age	55 to 64 3.05 to < 3.55	40 to < 55 2.22 to < 3.05	30 to < 40 1.67 to < 2.22	< 30 < 1.67
Potassium, High (mEq/L; mmol/L)	5.6 to < 6.0 5.6 to < 6.0	6.0 to < 6.5 6.0 to < 6.5	6.5 to < 7.0 6.5 to < 7.0	≥ 7.0 ≥ 7.0
Potassium, Low (mEq/L; mmol/L)	3.0 to < 3.4 3.0 to < 3.4	2.5 to < 3.0 2.5 to < 3.0	2.0 to < 2.5 2.0 to < 2.5	< 2.0 < 2.0
Sodium, High (mEq/L; mmol/L)	146 to < 150 146 to < 150	150 to < 154 150 to < 154	154 to < 160 154 to < 160	≥ 160 ≥ 160
Sodium, Low (mEq/L; mmol/L)	130 to < 135 130 to < 135	125 to < 130 125 to < 130	121 to < 125 121 to < 125	≤ 120 ≤ 120

Site Reactions to Injections and Infusions				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Injection Site Erythema or Redness > 15 years of age	2.5 to < 5 cm in diameter OR 6.25 to < 25 cm^2 surface area	≥ 5 to < 10 cm in diameter OR ≥ 25 to < 100 cm^2 surface area	≥ 10 cm in diameter OR ≥ 100 cm^2 surface area	-
Injection Site Induration or Swelling > 15 years of age	2.5 to < 5 cm in diameter OR	≥ 5 to < 10 cm in diameter OR ≥ 25 to < 100	≥ 10 cm in diameter OR ≥	-

	6.25 to < 25 cm^2 surface area	cm^2 surface area	100 cm^2 surface area	

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

10.8.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		>450
Absolute PR interval	msec	<120	>220
Absolute QRS Interval	msec	<75	>120
Change from Baseline			
Increase from Baseline QTc	msec		>60

10.8.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	<85	>140
Diastolic Blood Pressure	mmHg	<45	>90
Heart Rate (Males)	bpm	<45	>100
Heart Rate (Females)	bpm	<50	>100

10.9. Appendix 9: Abbreviations & Trademarks

10.9.1. Abbreviations

Abbreviation	Description
AC	Active Control
ADaM	Analysis Data Model
AE	Adverse Event
ANOVA	Analysis of Variance
AUC	Area under Concentration-Time Curve
AUC0-t	AUC for each Injected Dose from Time Zero to Last Quantifiable Time Point or 4 Weeks Following the Injection, whichever is earlier
BMI	Body Mass Index
CAB	Cabotegravir
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
Cmax	Maximum Observed Plasma Concentration
CSR	Clinical Study Report
Cτ	Trough Concentrations at 4 Weeks Following First Injection (or Earlier If The Second Injection Occurs at <4-Week Interval) and 4 Weeks Following The Second Injection
DBF	Database Freeze
DBR	Database Release
DP	Decimal Place
DVM	Data Validation Manual
eCRF	Electronic Case Report Form
CV	Coefficient of Variation
CVb	Between-Subject Geometric CV
ECG	Electrocardiogram
GSK	GlaxoSmithKline
IA	Interim Analysis
ICF	Informed Consent Form
IDSL	Integrated Data Standards Library
IG	Implementation Guide
IM	Intramuscular
ISR	Injection Site Reaction
KALA	Terminal Absorption Elimination Rate Constant
LLN	Lower Limit of Normal
NQ	Not Quantifiable Value
CCI [redacted]	
OLI	Oral Lead-In
CCI [redacted]	
PK	Pharmacokinetic
Q4W	Four-Weekly

Q12W	Twelve-Weekly
QD	Once Daily
QTcB	QT Duration Corrected for Heart Rate by Bazett's Formula
QTcF	QT Duration Corrected for Heart Rate by Fridericia's Formula
RAP	Reporting and Analysis Plan
REML	Restricted Maximum Likelihood
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SAS	Statistical Analysis Software
SC	Subcutaneous
SD	Standard Deviation
SDL	Source Database Lock
SDTM	Study Data Tabulation Model
SMQ	Standardized MedDRA Query
SRT	Safety Review Team
STR	Study Team safety & PK Review
t½	Terminal Absorption Elimination Half-Life
tmax	Time of Cmax
ULN	Upper Limit of Normal

10.9.2. Trademarks

Trademarks of the ViiV Healthcare Group of Companies

Trademarks not owned by the ViiV Healthcare Group of Companies
WinNonlin
SAS
NONMEM

10.10. Appendix 10: List of Data Displays

All data displays will use the term "subject" rather than "participant" in accordance with CDSIC and GSK Statistical Display Standards.

10.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.19	
Safety	2.1 to 2.70	2.1 to 2.4
Pharmacokinetic	3.1 to 3.12	3.1 to 3.12
Section	**Listings**	
ICH Listings	1 to 82	
Other Listings	68 to 75	

10.10.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated and if required example mock-up displays provided in separate documents.

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 'GSK Statistical Display Standard / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

10.10.3. Deliverables

Delivery [Priority] [1]	Description
Cohort 1-5 IA	Preliminary Cohort 1-5 Interim Analysis: displays will exclude Cohort 4b data from participants who have received injection 1 but have not yet completed Injection 2 Day 1 or Follow-up Week 4 by the data analysis cut-off. Cohort 4b will remain blinded to the randomized mitigation treatments (topical steroids vs. NSAID) and results will not be presented by mitigation treatment.
Cohort 1-4	Cohort 1-4 Injection Phase Complete: when all participants in Part 1 Cohorts 1, 2, 3, 4 complete the 8-week Injection Phase.
Cohort 1-5	Injection Phase Complete: when all participants in Part 1 Cohorts 1, 2, 3, 4 and 4b complete the 8-week Injection Phase, all Cohort 4h participants complete the 4-week Injection Phase, and all participants in Part 2 complete the 24-week Injection Phase.

Delivery [Priority] [1]	Description
EOS	End of Study: when all participants complete the 52-week Follow-up Phase in Part 1 and Part 2.

NOTES:

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

10.10.4. Study Population Tables

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Enrolled	NS1	Summary of Number of Subjects Enrolled – Part 1 & Part 2		Cohort 1-5, EOS
1.2.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failures		Cohort 1-5, EOS
1.3.	Safety	ES1	Summary of Subject Disposition for the Subject Conclusion Record – Part 1 & Part 2		Cohort 1-5, EOS
1.4.	Safety	ES11	Summary of Outcome of Adverse Events which Led to Study Withdrawal at Each Study Period/Phase – Part 1 & Part 2		Cohort 1-5, EOS
1.5.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment – Part 1 & Part 2		Cohort 1-5, EOS
Protocol Deviations					
1.6.	Safety	DV1	Summary of Important Protocol Deviations – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
Population Analysed					
1.7.	Enrolled	SP1	Summary of Study Populations – Part 1 & Part 2		Cohort 1-5, EOS
Demographic and Baseline Characteristics					
1.8.	Safety	DM1	Summary of Demographic Characteristics – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
1.9.	Enrolled	DM11	Summary of Age Ranges – Part 1 & Part 2		Cohort 1-5, EOS
Exposure and Treatment Compliance					

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.10.	Safety	EX5	Summary of Exposure to CAB – Part 1 & Part 2		Cohort 1-5, EOS

10.10.5. Safety Tables

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE1	Summary of Adverse Events by System Organ Class and Preferred Term– Part 1 & Part 2	Include pooled treatment groups by dose & route	Cohort 1-5, EOS
2.2.	Safety – Injection Exposed	ISR1	Subject-Level Summary of Injection Site Reaction Adverse Events by Period and Preferred Term – Part 1 & Part 2	Injection 1 and Injection 2 periods only.	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.3.	Safety – Injection Exposed	ISR1a	Subject-Level Summary of Maximum Impact on Usual Social and Functional Activities across all Grade >=2 Injection Site Reaction Adverse Events of Erythema/Redness and/or Induration/Swelling by Period – Part 1 & Part 2 (Cohorts 2, 4, 4b and 5)	Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.4.	Safety – Injection Exposed	ISR2	Event-level Summary of Injection Site Reaction Adverse Events by Preferred Term – Part 1 & Part 2	Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.5.	Safety – LA Exposed	ISR2a	Summary of Injection Site Reaction Adverse Events by Preferred Term – Impact on Social & Function Activities, and Occurrence of Other Associated Grade 3 ISRs or Potentially Life-Threating Consequences – Part 1 Cohort 4h	Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route.	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.6.	Safety	AE1	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term – Part 1 & Part 2	Include pooled treatment groups by dose & route	Cohort 1-5, EOS
2.7.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term – Part 1 & Part 2 (Number of Subjects and Occurrences)	Include pooled treatment groups by dose & route	Cohort 1-5, EOS
2.8.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term – Part 1 & Part 2 (Number of Subjects and Occurrences)	Include pooled treatment groups by dose & route	Cohort 1-5, EOS
2.9.	Safety	AE5B	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Grade – Part 1 & Part 2	Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.10.	Safety	AE5B	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term and Maximum Grade – Part 1 & Part 2	Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.11.	Safety	ESI1	Summary of Characteristics of Seizures		Cohort 1-5, EOS
COVID-19 Assessment					
2.12.	Safety	PAN1	Summary of COVID-19 Assessments for Subjects with COVID-19 Adverse Events – Part 1 & Part 2		Cohort 1-5, EOS
2.13.	Safety	PAN2	Summary of COVID-19 Additional Assessments for Subjects with COVID-19 Adverse Events – Part 1 & Part 2		Cohort 1-5, EOS
2.14.	Safety	PAN3	Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events – Part 1 & Part 2		Cohort 1-5, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.15.	Safety	PAN4	Summary of COVID-19 Pandemic Visit Impacts – Part 1 & Part 2		Cohort 1-5, EOS
Laboratory: Chemistry					
2.16.	Safety	LB1	Summary of Clinical Chemistry Values – Part 1 & Part 2		Cohort 1-5, EOS
2.17.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline – Part 1 & Part 2		Cohort 1-5, EOS
2.18.	Safety	LB16A	Summary of Clinical Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1 & Part 2	Unscheduled visits are included for determining maximum grade	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
Laboratory: Hematology					
2.19.	Safety	LB1	Summary of Hematology Values – Part 1 & Part 2		Cohort 1-5, EOS
2.20.	Safety	LB1	Summary of Hematology Changes from Baseline – Part 1 & Part 2		Cohort 1-5, EOS
2.21.	Safety	LB16A	Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1 & Part 2	Unscheduled visits are included for determining maximum grade	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
Laboratory: Coagulation					
2.22.	Safety	LB1	Summary of Coagulation Values – Part 1 & Part 2		Cohort 1-5, EOS
2.23.	Safety	LB1	Summary of Coagulation Changes from Baseline – Part 1 & Part 2		Cohort 1-5, EOS
2.24.	Safety	LB16A	Summary of Coagulation Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1 & Part 2	Unscheduled visits are included for determining maximum grade	Cohort 1-5, EOS
ECG					

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.25.	Safety	SAFE_T1 (See EG1)	Summary of ECG Findings – Part 1 & Part 2–	Unscheduled visits are included for determining worst-case post-baseline	Cohort 1-5, EOS
2.26.	Safety	EG2	Summary of ECG Values – Part 1 & Part 2		Cohort 1-5, EOS
2.27.	Safety	EG2	Summary of ECG Changes from Baseline – Part 1 & Part 2		Cohort 1-5, EOS
2.28.	Safety	SAFE_T2 (See EG10A)	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part 1 & Part 2	Unscheduled visits are included for determining maximum QTc values	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.29.	Safety	SAFE_T3 (See EG11)	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category – Part 1 & Part 2	Unscheduled visits are included for determining maximum increase in QTc values	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
Vital Signs					
2.30.	Safety	VS1	Summary of Vital Sign Values - Part 1 & Part 2		
2.31.	Safety	VS1	Summary of Vital Sign Changes from Baseline – Part 1 & Part 2		Cohort 1-5, EOS
2.32.	Safety	SAFE_T4 (See VS3)	Summary of Vital Sign Results Relative to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline – Part 1 & Part 2	Unscheduled visits are included for determination of 'to Low' and 'to High'	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
Liver Events					
2.33.	Safety	LIVER1	Summary of Liver Stopping Event Reporting – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.34.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part 1 & Part 2	Unscheduled visits are included	Cohort 1-5, EOS
Questionnaires					
2.35.	Safety	SAFE_T5	Summary of Numeric Rating Scale – Part 1 & Part 2	For each period: by visit, maximum and AUC. AUC not needed for Cohort 1-5 IA	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.36.	Safety	SAFE_T6	Summary of Perception of Injection – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
Injection Site Area & Duration by Grade					
2.37.	Safety	SAFE_T7a	Event-Level Summary of Duration (Days) at Each Grade by Injection Site Reaction Preferred Term – Part 1 & Part 2	Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.38.	Safety	SAFE_T7b	Event-Level Summary of Duration (Days) at Each Grade – Grading determined according to DAIDS Impact on Social and Function Activities Categories and Occurrence of Other Associated Grade 3 ISRs or Potentially Life-Threating Consequences – Part 1 Cohort 4h	Repeat for each of the following grouped preferred terms: Erythema/Redness/Induration/Swelling, Erythema/Redness, and Induration/Swelling Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.39.	Safety	SAFE_T7c	Subject-Level Summary of Maximum Duration (Days) at Each Grade by Injection Site Reaction Preferred Term – Part 1 & Part 2	Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
2.40.	Safety	SAFE_T7d	Subject-Level Summary of Maximum Duration (Days) at Each Grade – Grading determined according to DAIDS Impact on Social and Function Activities Categories and Occurrence of Other Associated Grade 3 ISRs or Potentially Life-Threating Consequences – Part 1 Cohort 4h	Repeat for each of the following grouped preferred terms: Erythema/Redness/Induration/Swelling, Erythema/Redness, and Induration/Swelling Injection 1 and Injection 2 periods only. Include pooled treatment groups by dose & route	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.41.	Safety	SAFE_T8	Subject-CCI [redacted]	Injection 1 and Injection 2 periods only.	Cohort 1-4, Cohort 1-5, EOS
Crossover Statistical Analyses for Cohort 4b, including summaries of endpoints for other cohorts					
2.42.	Safety – LA Exposed (Complete Case)	SAFE_XO1	Statistical Analysis for Proportion of Participants with Injection Site Reactions –CCI [redacted]	CCI [redacted]	Cohort 1-5, EOS
2.43.	Safety – LA Exposed (Complete Case)	SAFE_XO2	CCI [redacted]		Cohort 1-5, EOS
2.44.	Safety – LA Exposed (Complete Case)	SAFE_XO3			Cohort 1-5, EOS
2.45.	Safety – LA Exposed (Complete Case)	PIN_XO1			Cohort 1-5, EOS
2.46.	Safety – LA Exposed (Complete Case)	PIN_XO2			Cohort 1-5, EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.47.	Safety – LA Exposed (Complete Case)	NRS_XO1	CCI [redacted]		Cohort 1-5, EOS
2.48.	Safety – LA Exposed (Complete Case)	PRF_XO1			Cohort 1-5, EOS

10.10.6. Safety Figures

Safety Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Injection Site Area					
2.1	Safety	SAFE_F1	Plot of Surface Area versus Day Since Injection by Injection Site Reaction Preferred Term – Part 1 & Part 2 (Cohorts 2, 4, 4b , 4h and 5)		Cohort 1-5, EOS

10.10.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.1.	Pharmacokinetic	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data (units) – Part 1 & Part 2, Oral Lead-in Phase		Cohort 1-5, EOS
3.2.	Pharmacokinetic	PKCT1	Summary of CAB Plasma Pharmacokinetic Concentration-Time Data (units) – Part 1 & Part 2, Injection and Follow-up Phase		Cohort 1-5 IA Cohort 1-5, EOS
PK Derived Parameters					
3.3.	Pharmacokinetic	PKPT4	Summary Statistics of Derived CAB Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Part 1 & Part 2	Parameters with units	Cohort 1-5 IA Cohort 1-5, EOS
3.4.	Pharmacokinetic	PKPT4	Summary Statistics of Derived CAB Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Part 1 & Part 2	Parameters with units	Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
PK Analysis Tables					
3.5.	Pharmacokinetic	PKPT3	Statistical Analysis of CAB Plasma Pharmacokinetic Parameters – Relative Bioavailability		Cohort 1-5 IA Cohort 1-5, EOS
3.6.	Pharmacokinetic	PKPT3	Statistical Analysis of CAB Plasma Trough Concentrations – CAB 400 mg/mL vs. Evaluable Historical CAB 200 mg/mL – Part 1 and Part 2	Historical data from ATLAS/FLAIR	Cohort 1-5, EOS
3.7.	Pharmacokinetic	PKPT3	Statistical Assessment of Dose Proportionality by Route for CAB 400 mg/mL – Injection 1 PK Parameters from Cohorts 1-5 (excluding Cohort 4h)		Cohort 1-5 IA Cohort 1-5, EOS

10.10.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Concentration Data					
3.1.	Pharmacokinetic	PKCF1P	Individual CAB Plasma Concentration-Time Plots by Cohort – Oral Lead-in Phase (Linear and Semi-Logarithmic)	Paginate by Cohort Dashed line represents the LLQ	Cohort 1-5, EOS
3.2.	Pharmacokinetic	PKCF1P	Individual CAB Plasma Concentration-Time Plots by Treatment – Injection and Follow-up Phase (Linear and Semi-Logarithmic)	Paginate by Treatment and Injection Dashed line represents the LLQ	Cohort 1-5, EOS
Mean / Median Concentration Plots					
3.3.	Pharmacokinetic	PKCF2	Mean (± Standard Deviation) CAB Plasma Concentration-Time Plots by Treatment – Oral Lead-in Phase (Linear and Semi-Logarithmic)	Treatments Overlaid	Cohort 1-5, EOS
3.4.	Pharmacokinetic	PKCF2	Mean (± Standard Deviation) CAB Plasma Concentration-Time Plots by Treatment – Injection and Follow-up Phase (Linear and Semi-Logarithmic)		Cohort 1-5, EOS
3.5.	Pharmacokinetic	PKCF3	Median (± Range) CAB Plasma Concentration-Time Plots by Treatment –Oral Lead-in Phase (Linear and Semi-Logarithmic)	Treatments Overlaid	Cohort 1-5, EOS
3.6.	Pharmacokinetic	PKCF3	Median (± Range) CAB Plasma Concentration-Time Plots by Treatment –Injection and Follow-up Phase (Linear and Semi-Logarithmic)	Treatments Overlaid	Cohort 1-5 IA Cohort 1-5, EOS

10.10.9. ICH Listings

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Randomized	TA1	Listing of Randomized and Actual Treatments – Part 1 & Part 2		Cohort 1-5, EOS
2.	Screened	ES7	Listing of Reasons for Screen Failure		Cohort 1-5, EOS
3.	Safety	ES2	Listing of Reasons for Study Withdrawal – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
4.	Safety	SD2xo	Listing of Reasons for Study Treatment Discontinuation – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
5.	Safety	BL1	Listing of Subjects for Whom the Treatment Blind was Broken During the Study – Part 1 & Part 2		Cohort 1-5, EOS
Protocol Deviations					
6.	Safety	DV2xo	Listing of Protocol Deviations (Important and/or COVID-19 Related) – Part 1 & Part 2		Cohort 1-5, EOS
7.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations – Part 1 & Part 2		Cohort 1-5, EOS
Populations Analysed					
8.	Safety	SP3xo	Listing of Subjects Excluded from Any Population – Part 1 & Part 2		Cohort 1-5, EOS
Demographic and Baseline Characteristics					
9.	Safety	DM2	Listing of Demographic Characteristics – Part 1 & Part 2		Cohort 1-5, EOS
10.	Safety	DM9	Listing of Race – Part 1 & Part 2		Cohort 1-5, EOS
Concomitant Medication and Medical History					

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
11.	Safety	CM3xo	Listing of Concomitant Medications – Part 1 & Part 2	Based on GSK Drug Dictionary	Cohort 1-5, EOS
12.	Safety	MH2	Listing of General Medical History – Part 1 & Part 2		Cohort 1-5, EOS
Exposure and Treatment Compliance					
13.	Safety	EX3	Listing of Exposure Data – Part 1	CCI [redacted]	Cohort 1-5, EOS
14.	Safety	POP_L1	Listing of Drug Accountability for Oral CAB – Part 1 & Part 2		Cohort 1-5, EOS
Adverse Events					
15.	Safety	AE2	Listing of Relationship Between System Organ Class and Verbatim Text		Cohort 1-5, EOS
16.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events – Part 1 & Part 2		Cohort 1-5, EOS
17.	Safety	AE8CPxo	Listing of All Adverse Events – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
18.	Safety	AE8CPxo	Listing of Injection Site Reaction Adverse Events – Part 1 & Part 2	Include variable from the AE ISR form: "Did the subject use or apply any treatment at home for the injection site related symptom?"	Cohort 1-5, EOS

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
19.	Safety	SAFE_L1	Listing of Details of Injection Site Reaction Adverse Events – Part 1 & Part2	Include additional variables collected on the impact on social & functional activities forms	Cohort 1-5, EOS
20.	Safety	AE8CPxo	Listing of Serious Adverse Events (Fatal & Non-Fatal) – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
21.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event – Part 1 & Part 2		Cohort 1-5, EOS
22.	Safety	AE8CPxo	Listing of Adverse Events Leading to Treatment Discontinuation and/or Withdrawal from Study – Part 1 & Part 2		Cohort 1-5 IA Cohort 1-4, Cohort 1-5, EOS
COVID-19 Assessment					
23.	Safety	AE8CPxo	Listing of COVID-19 Related Adverse Events – Part 1 & Part 2		Cohort 1-5, EOS
24.	Safety	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Subject with COVID-19 Adverse Events – Part 1 & Part 2		Cohort 1-5, EOS
25.	Safety	PAN7	Listing of All Subjects with Visits and Assessments Impacted by COVID-19 Pandemic – Part 1 & Part 2		Cohort 1-5, EOS
All Laboratory					
26.	Safety	LB5xo	Listing of All Clinical Chemistry Data for Subjects with any Toxicities – Part 1 & Part 2		Cohort 1-5, EOS
27.	Safety	LB5xo	Listing of All Hematology Data for Subjects with any Toxicities – Part 1 & Part 2		Cohort 1-5, EOS
28.	Safety	LB5xo	Listing of All Coagulation Data for Subjects with any Toxicities – Part 1 & Part 2		Cohort 1-5, EOS

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
29.	Safety	EG5xo	Listing of All ECG Findings for Subjects with an Abnormal Finding – Part 1 & Part 2		Cohort 1-5, EOS
30.	Safety	EG3xo	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance – Part 1 & Part 2		Cohort 1-5, EOS
Vital Sign					
31.	Safety	VS4xo	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance – Part 1 & Part 2		Cohort 1-5, EOS
Liver Event					
32.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting – Part 1 & Part 2		Cohort 1-5, EOS
33.	Enrolled	LIVER15	Liver Stopping Event Profile		Cohort 1-5, EOS
Questionnaire					
34.	Safety	SAFE_L3	Listing of Numeric Rating Scale – Part 1 & Part 2		Cohort 1-5, EOS
35.	Safety	SAFE_L4	Listing of Perception of Injection – Part 1 & Part 2		Cohort 1-5, EOS
Immunogenicity					
36.	Safety	LB5xo	Listing of All Immunogenicity Data – Part 1		Cohort 1-5, EOS

10.10.10. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**GSK Standard GSK Statistical Display Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
37.	Pharmacokinetic	PKCL1P	Listing of CAB Plasma Concentration-Time Data by Cohort – Oral Lead-in Phase		Cohort 1-5, EOS
38.	Pharmacokinetic	PKCL1P	Listing of CAB Plasma Concentration-Time Data by Cohort – Injection and Follow up Phase		Cohort 1-5, EOS
39.	Pharmacokinetic	PKPL1P	Listing of CAB Plasma Pharmacokinetic Parameters Based on Actual Time – Oral Lead-in Phase		Cohort 1-5, EOS
40.	Pharmacokinetic	PKPL1P	Listing of CAB Plasma Pharmacokinetic Parameters Based on Actual Time – Injection and Follow-up Phase		Cohort 1-5, EOS

10.11. Appendix 11: AESI Identification

SMQ and PT codes based on MedDRA dictionary version 24.0.

10.11.1. Seizures

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”.

SMQ: ‘Convulsions’ SMQ Code: 20000079 Category: A Scope: Narrow	
Preferred Term	PT Code
1p36 deletion syndrome	10082398
2-Hydroxyglutaric aciduria	10078971
Acquired epileptic aphasia	10052075
Acute encephalitis with refractory, repetitive partial seizures	10076948
Alcoholic seizure	10056347
Alpers disease	10083857
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
CDKL5 deficiency disorder	10083005
CEC syndrome	10083749
Change in seizure presentation	10075606
Clonic convulsion	10053398
Congenital bilateral perisylvian syndrome	10082716
Convulsion in childhood	10052391
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
Epilepsy with myoclonic-atonic seizures	10081179
Epileptic aura	10015049
Epileptic psychosis	10059232
Faciobrachial dystonic seizure	10084187
Febrile convulsion	10016284
Febrile infection-related epilepsy syndrome	10079438
Focal dyscognitive seizures	10079424
Frontal lobe epilepsy	10049424
Gelastic seizure	10082918
Generalised onset non-motor seizure	10083376
Generalised tonic-clonic seizure	10018100
Glucose transporter type 1 deficiency syndrome	10078727
GM2 gangliosidosis	10083933

Grey matter heterotopia	10082084
Hemiconvulsion-hemiplegia-epilepsy syndrome	10085010
Hemimegalencephaly	10078100
Hyperglycaemic seizure	10071394
Hypocalcaemic seizure	10072456
Hypoglycaemic seizure	10048803
Hyponatraemic seizure	10073183
Idiopathic generalised epilepsy	10071081
Infantile spasms	10021750
Jeavons syndrome	10084303
Juvenile absence epilepsy	10085031
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
Neonatal epileptic seizure	10082068
Neonatal seizure	10082067
Parietal lobe epilepsy	10085326
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
Transient epileptic amnesia	10081728
Tuberous sclerosis complex	10080584
Uncinate fits	10045476
Additional selected preferred terms from HLT “Disturbances in consciousness NEC” under SOC “Nervous systems disorders” and HLT “Confusion and disorientation” under SOC “Psychiatric disorders”.	
Preferred Term	PT Code
Confusional state	10010305

Loss of consciousness	10024855
Syncope	10042772
Sopor	10058709
Stupor	10042264
Altered state of consciousness	10001854
Depressed level of consciousness	10012373
Consciousness fluctuating	10050093