STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2/3 Study to Evaluate the Safety and Efficacy of Long Acting Capsid Inhibitor GS-6207 in Combination with an Optimized Background Regimen in Heavily Treatment Experienced People Living with HIV-1 Infection with Multidrug Resistance
Name of Test Drug:	Lenacapavir (LEN; previously referred to as GS-6207)
Study Number:	GS-US-200-4625
Protocol Version (Date):	Amendment 2 (01 September 2020)
Analysis Type:	DMC/Primary Efficacy Endpoint Analysis
Analysis Plan Version:	Version 1.0
Analysis Plan Date:	30 September 2020
Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ARV	antiretroviral
BMI	body mass index
CAI	capsid inhibitor
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
COBI	cobicistat
CSR	clinical study report
DAIDS	Division of AIDS
DMC	data monitoring committee
ECG	Electrocardiogram
eCRF	electronic case report form
FAS	Full Analysis Set
FDA	Food and Drug Administration
GLPS	Global Patient Safety (formerly known as Pharmacovigilance and Epidemiology [PVE])
HLGT	high-level group term
HLT	high-level term
ID	Identification
INSTI	integrase inhibitor
ISR	injection site reaction
LEN	Lenacapavir; GS-6207
LTT	lower-level term
LOQ	limit of quantitation
M = E	missing = excluded
M = F	missing = failure
MDR	multidrug resistance
MedDRA	Medical Dictionary for Regulatory Activities
NNRTI	non-nucleoside reverse transcriptase inhibitors
NRTI	nucleoside reverse transcriptase inhibitors
OBR	optimized background regimen
PI	protease inhibitor
PK	pharmacokinetics
PLWH	people living with HIV
PP	per protocol
PT	preferred term
RTV	Ritonavir
Q1, Q3	first quartile, third quartile
SAE	serious adverse event

SAP	statistical analysis plan
SC	Subcutaneous
SD	standard deviation
SE	standard error
SOC	system organ class
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
US	United States
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) of the Data Monitoring Committee (DMC) analysis for Study GS-US-200-4625. The DMC analysis will be a formal interim analysis for the primary efficacy endpoint and will be performed when all participants in Cohort 1 have completed assessments or discontinued the study drug in the Functional Monotherapy Period. The purpose of this DMC analysis is to assess the primary efficacy endpoint, to evaluate safety, and to determine whether to continue with the study. The stopping criteria is described in Section 2.1.1 of the SAP.

This SAP is based on the study protocol amendment 2 dated 01 September 2020 and the electronic case report form (eCRF). The SAP will be finalized prior to data snapshot for the DMC analysis. Any critical changes (eg, changes related to the primary efficacy endpoint) after the finalization of the DMC SAP will be documented in the Week 26 SAP and the corresponding clinical study report (CSR).

1.1. Study Objectives

The primary objective of this study is as follows:

- To evaluate the antiviral activity of LEN administered as an add-on to a failing regimen (functional monotherapy) for people living with HIV (PLWH) with multidrug resistance (MDR) as determined by the proportion of participants achieving at least 0.5 $\log_{10}$ reduction from baseline in HIV-1 RNA at the end of the Functional Monotherapy Period

The secondary objective of this study is as follows:

- To evaluate the safety and efficacy of LEN in combination with an optimized background regimen (OBR) at Weeks 26 and 52

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Only the primary objective of this study will be evaluated in the DMC analysis.

1.2. Study Design

This is a Phase 2/3 global multicenter study of LEN together with an OBR in PLWH with MDR infection. Participants who complete a Screening visit will return to the clinic between 14 and 30 days after the Screening visit, for a Cohort Selection visit. HIV-1 RNA results from the Cohort Selection visit will be used to determine whether eligible participants will participate in Cohort 1 or Cohort 2.

Cohort 1 (n 36)

Functional Monotherapy Period

Eligible participants with a < 0.5 $\log_{10}$ HIV-1 RNA decline compared to the Screening visit and HIV-1 RNA ≥ 400 copies/mL at the Cohort Selection visit will be randomized in a 2:1 ratio to receive either oral LEN or placebo to match LEN for 14 days. Treatment assignment will be blinded to the sponsor, participants, investigators and study staff at the site. Functional Monotherapy will be assessed while participants continue their failing regimen. After each participant completes the Functional Monotherapy Period, their treatment assignment will be unblinded.

Maintenance Period

Participants who were randomized to receive oral LEN will receive subcutaneous (SC) LEN and initiate their OBR on Day 1 SC (14 days after the first dose of oral LEN) **(Cohort 1A)**.

Participants who were randomized to receive placebo will receive oral LEN and initiate their OBR on Day 15 **(Cohort 1B)**. They will receive SC LEN at Day 1 SC (14 days after the first dose of oral LEN) while continuing their OBR.

After the Day 1 SC visit, all Cohort 1 participants will continue with study visits and receive their subsequent SC LEN injection at the Week 26 visit. At the Week 52 visit, participants will be given an option to receive SC LEN injection and continue on the study to receive SC LEN injections every 6 months (26 weeks).

Cohort 2 (n 64)

Oral Lead-in Period

Participants will be enrolled into Cohort 2 if Cohort 1 is fully enrolled or if they do not meet the criteria for randomization in Cohort 1 (ie, they had ≥ 0.5 $\log_{10}$ HIV-1 RNA decline compared to the Screening visit and/or HIV-1 RNA < 400 copies/mL at the Cohort Selection visit). All Cohort 2 participants will receive oral LEN for 14 days starting at Day 1. Participants will initiate an OBR on Day 1.

Maintenance Period

At Day 1 SC (14 days after the first dose of oral LEN), participants will receive SC LEN and will continue their OBR. After the Day 1 SC visit, participants will continue with study visits and receive their subsequent SC LEN injection at the Week 26 visit. At the Week 52 visit, participants will be given an option to receive SC LEN injection and continue the study to receive SC LEN injections every 6 months (26 weeks).

For both Cohorts 1 and 2, data collected through Week 52 (52 weeks from the first dose of SC LEN) refer to as the "Main Phase" of the study. Data collected post Week 52 refer to as the "Extension Phase" of the study.

Schedule of Assessments is provided in Section 11.

1.3. Sample Size and Power

A total of 36 participants in Cohort 1 will provide at least 90% power to detect a 60% difference in the proportion of participants achieving a ≥ 0.5 $\log_{10}$ reduction from baseline at Day 15 of the Functional Monotherapy Period between the treatment groups (LEN in Cohort 1A and placebo in Cohort 1B).

In this sample size and power computation, it is assumed that 70% and 10% of participants achieve a ≥ 0.5 $\log_{10}$ reduction from baseline in HIV-1 RNA in the LEN group (Cohort 1A) and the placebo group (Cohort 1B), respectively (based on data from Trogarzo Phase 3 TMB-301 study {Emu 2018}), and the Fisher exact test is conducted at 2-sided significant level of 0.05.

A total sample size of 36 participants from Cohorts 1A and 1B will provide reasonable assessment of safety through at least 24 weeks of LEN treatment in heavily treatment experienced participants.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

2.1.1. DMC Interim Analysis

One external multidisciplinary DMC analysis is planned to review the progress of the study and to perform interim reviews of the efficacy and safety data. The DMC will convene after all participants in Cohort 1 have completed or discontinued the study drug in the Functional Monotherapy Period. Treatment assignment will be unblinded for the DMC analysis.

No formal stopping rules will be used by the DMC for safety outcomes. Rather, a clinical assessment will be made to determine if the nature, frequency, and severity of adverse events (AEs) associated with a study regimen warrant the early termination of the study in the best interest of the participants.

Gilead does not have a prior intent to ask the DMC to consider early termination of the study even if there is an early evidence of favorable efficacy. However, Gilead will stop further enrollment if 50% or more of the participants in the LEN group fail in Cohort 1 to achieve at least 0.5 $\log_{10}$ reduction from baseline in HIV-1 RNA at the end of the Functional Monotherapy Period. The decision whether to continue with the study and the development of LEN will be based on the magnitude of the HIV-1 RNA decline at the end of the Functional Monotherapy Period.

The DMC's role and responsibilities and the scope of analysis to be provided to the DMC are defined in a mutually agreed upon charter, which defines the DMC membership, meeting logistics, and meeting frequency, and in this SAP.

2.1.2. Interim Analysis at Week 26 (Primary Analysis)

Interim analysis at Week 26 is the primary analysis and will be conducted after all participants in Cohort 1 have completed the Week 26 visit (ie, 26 weeks after the first dose of SC LEN) or have prematurely discontinued the study drug, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized for the analysis. The data from this analysis will be used to support the LEN regulatory filing for the indication in the heavily treatment experienced PLWH.

2.1.3. Interim Analysis at Week 52 (Secondary Analysis)

Interim analysis at Week 52 is the secondary analysis and will be conducted after all participants in Cohort 1 have completed the Week 52 visit (ie, 52 weeks after the first dose of SC LEN) and/or after all participants in Cohort 2 have completed the Week 26 visit (ie, 26 weeks after the first dose of SC LEN) or have prematurely discontinued the study drug, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized for the analysis.

2.2. Final Analysis

After all participants have completed the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized, final analysis of the data will be performed.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

The following 2 sets of analyses are defined for this study. Data included in each analysis are defined as follows:

Functional Monotherapy Period Analysis

Functional Monotherapy Period analysis includes data collected from participants randomized in the Functional Monotherapy Period. All data collected up to the first dose date of the open-label study drug, defined as the earliest date from SC LEN or open-label oral LEN, will be included in this analysis except for data on AEs and death. For AEs and death, only data collected **prior to** the first dose date of the open-label study drug will be included.

Data included in this analysis will be used to assess the primary efficacy endpoint and safety data collected during the blinded phase of the study. Results will be summarized by treatment group (LEN vs. Placebo).

All LEN Analysis

All LEN analysis include data collected from participants who receive at least one dose of LEN (ie, blinded or open-label LEN). Data collected **on and after** the first dose of LEN are included in this analysis. Data included in this analysis will be used to assess efficacy and safety of LEN. Results will be summarized by cohort and total, unless specified otherwise.

General Analysis Approaches

Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of participants in each category will be presented; for continuous variables, the number of participants (n), mean, standard deviation (SD) or standard error (SE), median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

By-participant listings will be presented for all participants in the All Enrolled Analysis Set and sorted by participant identification (ID) number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within the participant. The treatment group to which participants were enrolled will be used in the listings. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the participants to be included in an analysis. Analysis sets and their definitions are provided in this section. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

For each analysis set, the number and percentage of participants will be summarized by cohort based on the All Enrolled Analysis Set.

3.1.1. All Enrolled Analysis Set

All Enrolled Analysis Set includes all participants who were randomized into Cohort 1 or enrolled into Cohort 2. This is the primary analysis set for by-participant listings.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) is the primary analysis set for efficacy analyses. Two FASs are defined for this study:

- FAS for the Functional Monotherapy Period analysis: this analysis set includes all participants who are randomized in the Functional Monotherapy Period and receive at least one dose of blinded study drug. This is the primary analysis set for the primary efficacy endpoint.

- FAS for the All LEN analysis: this analysis set includes all participants who are enrolled into the study and receive at least one dose of SC LEN. This is the primary analysis set for the secondary efficacy endpoints and other efficacy endpoints.

3.1.3. Per-Protocol Analysis Set

A Per-Protocol (PP) Analysis Set is defined for the primary efficacy analysis. This analysis set includes all participants in the FAS for the Functional Monotherapy Period analysis excluding participants meeting any of the following criteria:

- Received partial or missed doses on Day 1, Day 2, or Day 8

- Did not have any postbaseline HIV-1 RNA collected during the Functional Monotherapy Period

- Added a new antiretroviral (ARV) during the Functional Monotherapy Period

- Did not meet the criteria for randomization in Cohort 1, that is, participants had ≥ 0.5 $\log_{10}$ HIV-1 RNA decline compared to the Screening visit and/or HIV-1 RNA < 400 copies/mL at the Cohort Selection visit

3.1.4. Safety Analysis Set

The Safety Analysis Set includes all participants who are enrolled and receive at least one dose of study drug. This is the primary analysis set for safety analyses. This analysis set will be used to describe baseline information as well as safety summary for the Functional Monotherapy Period analysis and All LEN analysis.

3.2. Participant Grouping

For analyses based on the FAS, participants will be grouped according to the treatment to which they were enrolled. For analyses based on the PP and Safety Analysis Sets, participants will be grouped according to the actual treatment received.

3.3. Strata and Covariates

This study does not use a stratified randomization schedule when enrolling participants. No covariates will be included in efficacy analyses.

3.4. Examination of Participant Subgroups

Examination of participant subgroups will not be performed in the DMC analysis.

3.5. Multiple Comparisons

The primary efficacy endpoint will be evaluated at the time when all participates in Cohort 1 have completed the Functional Monotherapy Period or discontinued from the study drug. There will be no interim analyses before the analysis of the primary efficacy endpoint; therefore, no alpha level adjustment will be applied to the primary efficacy endpoint.

3.6. Missing Data and Outliers

3.6.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified. Exceptions are presented in this document.

For missing last study date, imputation rules are described in Section 4.3. The handling of missing or incomplete dates for AE onset is described in Section 7.1.5.2, and for ARV medications and concomitant medications in Section 7.3.

3.6.2. Outliers

Outliers will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. All data will be included in the data analysis.

3.7. Data Handling Conventions and Transformations

Only year of birth is collected in this study. The following conventions will be used for the imputation of full date of birth:

- If year of birth is collected, “01 July” will be imputed as the day and month of birth
- If year of birth is missing, date of birth will not be imputed

In general, age collected at baseline (in years) will be used for analyses and presented in listings. If age at baseline is not available for a participant, age derived based on date of birth and the baseline visit date will be used instead. If an enrolled participant was not dosed with any study drug, the randomization/enrollment date will be used instead of the baseline visit date. For screen failures, the date the first informed consent was signed will be used for the age derivation. Age required for longitudinal and temporal calculations and analyses (eg, estimates of creatinine clearance) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

Non-PK data that are continuous in nature but are less than the lower limit of quantitation (LOQ) or above the upper LOQ will be imputed as follows:

- A value that is 1 unit less than the LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the LOQ). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used to calculate summary statistics. An exception to this rule is any value reported as < 1 or < 0.1, etc. For values reported as < 1 or < 0.1, a value of 0.9 or 0.09, respectively, will be used to calculate summary statistics.

- A value that is 1 unit above the LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the LOQ). Values with decimal points will follow the same logic as above.

- The LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the LOQ).

Logarithmic (base 10) transformations will be applied to HIV-1 RNA data for efficacy analysis. HIV-1 RNA results of 'No HIV-1 RNA detected' and "<20 cp/mL HIV-1 RNA Detected" will be imputed as 19 copies/mL for analysis purposes.

3.8. Analysis Visit Windows

3.8.1. Definition of Key Dates and Study Day

Definitions of the first dose date and the last dose date for each analysis are provided in Table 3-1.

Table 3-1. Definitions of First Dose Date and Last Dose Date for Each Analysis

Analysis	First Dose Date	Last Dose Date
Functional Monotherapy Period Analysis	First dose date of blinded study drug (LEN or Placebo)	Last dose date of blinded study drug (LEN or Placebo)[a]
All LEN Analysis	The earliest dose date from blinded or open-label oral LEN	The latest dose date from blinded or open-label oral LEN or SC LEN[b]

a. This date is defined for participants who receive the open label LEN (ie, completion the Functional Monotherapy Period) or who do not receive the open label LEN with study drug completion eCRF for the main phase marked as early termination (ie, discontinuation during the Functional Monotherapy Period).
b. This date is defined for participants who prematurely discontinue study drug in any phase (ie, main phase or extension phase) of the study or who complete study drug in the main phase and do not continue into the extension phase of the study

Last Dose Date for the study is defined for participants who prematurely discontinue study drug in any phase of the study or who complete study drug in the main phase and do not continue into the extension phase of the study as the latest dose date of any study drug including blinded study drug, open-label oral LEN, and SC LEN.

Last Study Date is defined as the latest clinic visit dates and the laboratory visit dates, including the 30, 60, 90 and 180-day follow-up visit dates for participants who prematurely discontinue study or for participants who complete the main phase of the study and decide not to continue into the extension phase of the study.

Study Day will be calculated from the first dose date of study drug and derived as follows:

- For postdose study days: Assessment Date First Dose Date + 1
- For study days prior to the first dose: Assessment Date First Dose Date

3.8.2. Analysis Visit Windows

Analysis visit windows are not defined for the Functional Monotherapy Period analysis due to short duration of follow-up and close monitor of the visit dates. The nominal visit as recorded on the eCRF will be used when data are summarized by visit.

For the All LEN analysis, participants visits might not occur on protocol-specified visits. Therefore, for the purpose of analysis, observations will be assigned to analysis windows (see Table 3-2).

Table 3-2. Analysis Windows for All LEN Analysis

Analysis Visit	Nominal Study Day	Analysis Window Study Day Range	
		HIV-1 RNA	Hematology, (Urine) Chemistry, Urinalysis, CD4 Cell Count, and CD4%
Baseline		≤ First Dose Date, if time not available ≤ First Dose Date/Time, if time available	≤ First Dose Date, if time not available ≤ First Dose Date/Time, if time available
Day 1 (Postdose)[a]	1	> First Dose Date/Time, 1	> First Dose Date/Time, 1
Day 2	2	2, 5	NP
Day 8	8	6, 11	2, 11
Day 1 SC	15	12, 29	12, 29
Week 4	43	30, 64	30, 64
Week 10	85	65, 106	65, 106
Week 16	127	107, 148	107, 148
Week 22	169	149, 183	149, 183
Week 26	197	184, 232	184, 232
Week 36	267	233, 323	233, 323
Week 52	379	324, 414	324, 414
CCI			

NP Not planned by the protocol
a. Day 1 postdose will be used to label the records collected on Day 1 with collection time after the Day 1 dosing time. The Day 1 postdose will be used in listings to identify such records. Day 1 postdose visit will not be included in by visit table summary.

3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Visit Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value, whereas a time-to-event analysis would not require 1 value per analysis window.

If multiple valid, nonmissing measurements exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- For baseline, the last nonmissing value with collection date (and time, if available) on or prior to the first dose date (and time) of study drug will be selected, unless specified differently. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the average of the measurements for continuous data (except

for HIV-1 RNA, see below), or the measurement with the lowest severity (eg, normal will be selected over abnormal for safety electrocardiogram [ECG] findings) for categorical data.

- For postbaseline values (ie, data with collection date [and time, if available] after the first dose date [and time] of study drug):

  The record closest to the nominal day for that visit will be selected with the exception of CD4 cell counts and CD4% in which the latest record will be selected and HIV-1 RNA level (see below).

  If there are 2 records that are equidistant from the nominal day, the later record will be selected.

  If there is more than 1 record on the selected day, the average will be taken for continuous data (except for HIV-1 RNA, see below) and the worse severity will be taken for categorical data, unless otherwise specified.

- For baseline HIV-1 RNA, the latest (considering both date and time) record(s) on or prior to the first dose date and time of study drug will be selected. For postbaseline HIV-1 RNA, the latest record(s) on the window will be selected. For both baseline and postbaseline HIV-1 RNA, if both "HIV RNA Taqman 2.0" and "HIV RNA Repeat" (ie, the HIV-1 RNA result obtained from an additional aliquot of the original sample) are available with the same collection time, the results from the "HIV RNA Repeat" will be selected for analysis purposes; otherwise, if there are multiple "HIV RNA Taqman 2.0" records with the same collection time, the geometric mean will be taken for analysis purposes.

4. PARTICIPANT DISPOSITION

4.1. Participant Enrollment and Disposition

A summary of participant enrollment will be provided by cohort, treatment group, and total. The number and percentage of participants enrolled in each country, investigator within a country, and overall will be summarized. For each column, the denominator for the percentage calculation will be the total number of participants analyzed for that column.

A summary of participant disposition will be provided by cohort, treatment group, and total based on all enrolled participants. This summary will present the number of participants enrolled, the number of participants enrolled but never treated (if applicable), number of participants in the Safety Analysis Set, and the number of participants in each of the categories listed below:

Participant Disposition on Study Drug by Phase

- Main Phase (Up to Week 52)

  Before SC dosing

  - Continuing study drug (if applicable)
  - Completed study drug
  - Did not complete study drug with reasons for premature discontinuation of study drug (if applicable)

  After SC dosing

  - Received Day 1 SC injection
  - Continuing study drug
  - Completed study drug
  - Did not complete study drug with reasons for premature discontinuation of study drug (if applicable)

- Extension Phase (Post Week 52) (if applicable)

  Treated in the extension phase

  Continuing study drug

  Completed study drug

  Did not complete study drug with reasons for premature discontinuation of study drug

Participant Disposition throughout the Study

- Continuing study
- Completed study
- Did not complete study with reasons for premature discontinuation of study drug

The denominator for the percentage calculation for the main phase categories and for study disposition categories will be the total number of participants in the Safety Analysis Set corresponding to that column. The denominator for the percentage calculation for the extension phase categories will be the total number of participants treated in the extension phase corresponding to that column.

4.2. Study Drug Administration

Study drug administration and study drug dispensing information will be collected in the Study Drug Administration and Study Drug Accountability eCRFs. Number of participants receiving oral LEN and SC LEN at each protocol specified visit (Day 1, Day 2, Day 8, Day 15, Day 16, and Day 22 for oral LEN and Day 1 SC, Week 26, Week 52, etc for SC LEN) will be summarized. Number of participants receiving oral reload before the first SC injection due to missing scheduled oral dosing or due to missing scheduled SC dosing will also be provided.

Study drug administration will be listed.

4.3. Study Duration

Due to long-acting feature of the study drug, study duration will be calculated for the Functional Monotherapy Period analysis and All LEN analysis, respectively, using the Safety Analysis set.

For the Functional Monotherapy Period analysis, study duration is calculated as the open-label first dose date (defined as the earliest date from SC LEN or open-label oral LEN) minus first dose date of the blinded study drug plus 1. For participants who discontinued study drug prior to receive open-label study drug, last study date will be used to calculate study duration.

For the All LEN analysis, study duration is calculated as the last study date minus the first dose date of LEN plus 1. For participants who are still on study at the time of the DMC analysis, the data snapshot date will be used to impute the last study day.

Study duration will be expressed in weeks using up to 1 decimal place (eg, 4.5 weeks) and will be summarized using descriptive statistics and using the number and percentage of participants stayed through the following applicable time periods: 1 day, 2 days, 8 days, 15 days, 43 days, 85 days, 127 days, 169 days, 197 days, etc.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Participant demographic variables (ie, age, sex at birth, gender identify, sexual orientation, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2]) will be summarized by cohort, treatment group, and total using descriptive statistics for continuous variables and using number and percentage of participants for categorical variables. The summary of demographic data will be provided for the Safety Analysis Set.

For Cohort 1, the Cochran-Mantel-Haenszel (CMH) test will be used to compare the 2 treatment groups (LEN vs. Placebo) for categorical data. The 2-sided Wilcoxon rank sum test will be used to compare the treatment groups (LEN vs. Placebo) for continuous data.

A by-participant demographic and baseline characteristics listing, including the informed consent date, will be provided by participant ID number in ascending order.

5.2. Other Baseline Characteristics

Other baseline characteristics include disease characteristics, HIV and ARV medication history (prior ARV drugs), and ARV drugs at baseline:

Disease characteristics will include the following:

- HIV-1 RNA (log_{10} copies/mL)
- HIV-1 RNA categories (copies/mL): (a) ≤ 100,000, (b) > 100,000
- CD4 cell counts (/uL)
- CD4 cell counts categories (/uL): (a) ≤ 200, (b) > 200
- CD4 percentage (%)

HIV and ARV medication history will include the following:

- Number of years since HIV diagnosis
- Number of years since first started HIV treatment
- Number of prior ARV drugs (see definition in Section 7.3.1.1 excluding cobicistat [COBI] and ritonavir [RTV] used as a boosting agent)

- Prior ARV drug class exposure: (a) nucleoside reverse transcriptase inhibitors (NRTI), (b) non-nucleoside reverse transcriptase inhibitors (NNRTI), (c) protease inhibitor (PI), (d) integrase inhibitor (INSTI), (e) fusion inhibitor (eg, enfuvirtide), (f) CCR5 entry inhibitor (eg, maraviroc), (g) CD4-directed post-attachment inhibitor (eg, ibalizumab), (h) attachment inhibitor (eg, fostemsavir), (i) Other, if applicable

- Number of ARV drugs at baseline (see definition in Section 7.3.1.2 excluding COBI and RTV used as a boosting agent)

- ARV drugs at baseline drug class exposure (a) NRTI, (b) NNRTI, (c) PI, (d) INSTI, (e) fusion inhibitor, (f) CCR5 entry inhibitor, (g) CD4-directed post-attachment inhibitor (eg, ibalizumab), (h) attachment inhibitor (eg, fostemsavir), (i) Other, if applicable

Other baseline characteristics will be summarized by cohort and treatment group and overall using descriptive statistics for continuous variables and using number and percentage of participants for categorical variables. The summary of other baseline characteristics will be provided for the Safety Analysis Set.

For Cohort 1, the CMH test will be used to compare the 2 treatment groups for categorical data and the 2-sided Wilcoxon rank sum test will be used to compare the treatment groups for continuous data.

A by-participant listing of other baseline characteristics will be provided by participant ID number in ascending order.

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the proportion of participants in Cohort 1 achieving ≥ 0.5 $\log_{10}$ reduction from baseline in HIV-1 RNA at the end of the Functional Monotherapy Period. Only data collected up to Day 1 SC or Day 15 visit will be included in the primary efficacy analysis. If Day 1 SC or Day 15 visit is missing, only data collected within 15 days from the first dose date of the blinded study drug or up to the first dose date of open-label study drug, whichever is the earliest, will be included. The primary analysis of the efficacy endpoint will be based on the FAS for the Functional Monotherapy Period analysis.

The null hypothesis is that there is no difference in the proportion of participants achieving ≥ 0.5 $\log_{10}$ reduction from baseline at the end of the Functional Monotherapy Period (between the LEN group and the Placebo group in Cohort 1); the alternative hypothesis is that there is a difference (LEN Placebo) in the proportion of participants achieving ≥ 0.5 $\log_{10}$ reduction from baseline at the end of the Functional Monotherapy Period between the 2 treatment groups in Cohort 1. For participants with missing HIV-1 RNA values at the end of the Functional Monotherapy Period, the value will be imputed using the last observation carried forward method. The difference in proportions between 2 treatment groups will be compared using an unconditional exact method using 2 invert 1-sided tests {Chan and Zhang 1999} with an alpha level at 0.05 to evaluate superiority. The p-value and 95% confidence interval (CI) for the point estimate of treatment difference in proportions will be estimated and constructed using the Chan and Zhang method carried out by the following SAS codes:

```
proc freq data    example;
table trt*outcome /riskdiff(CL  (exact)) alpha  0.05;
exact barnard RISKDIFF(METHOD  SCORE);
output out  ciexact (keep  _RDIF1_ XL_RDIF1 XU_RDIF1) riskdiff;
run;
```

A secondary analysis of the primary efficacy endpoint based on the PP analysis set for the Functional Monotherapy Period analysis will also be performed to evaluate the robustness of the primary endpoint based on the FAS.

6.2. Secondary Efficacy Endpoints

The secondary efficacy endpoints are the proportion of participants in Cohort 1 with HIV-1 RNA < 50 and < 200 copies/mL at Weeks 26 and 52 using the United States (US) Food and Drug Administration (FDA)-defined snapshot algorithm. Secondary efficacy endpoints will not be performed in the DMC analysis given the majority of participants will not have reached the timepoints of interest.

6.3. Other Efficacy Endpoints

6.3.1. Definition of Other Efficacy Endpoints

Other efficacy endpoints that will be performed for the specified analysis are provided below.

Other Efficacy Endpoints	Functional Monotherapy Period Analysis	ALL LEN Analysis
Change from baseline in HIV-1 RNA (copies/mL) by visit	X	X
Change from baseline in CD4 cell count (/uL) by visit		X
Proportion of participants with HIV-1 RNA < 50 copies/mL by visit based on Missing = Failure and Missing = Excluded analyses		X

6.3.2. Analysis of Other Efficacy Endpoints

Baseline and the change from baseline in HIV-1 RNA (log_{10} copies/mL) and CD4 cell count (/uL) by visit will be summarized using descriptive statistics.

Number and percentage of participants with HIV-1 RNA < 50 copies/mL by visit will be analyzed using the following analyses:

- Missing Failure (M F):

  In this approach, missing data will be treated as virologic failure and summarized into the "missing" category (see list of HIV-RNA categories below). The denominator for percentages at a visit is the number of participants in the FAS, excluding ongoing participants who have missing HIV-1 RNA at a visit and have not reached the upper limit of the analysis window for the corresponding visit.

- Missing Excluded (M E):

  In this approach, missing data will be excluded in the computation of the percentages (ie, missing data points will be excluded from both the numerator and denominator in the computation). The denominator for percentages at a visit is the number of participants in the FAS with nonmissing HIV-1 RNA value at that visit.

No statistical testing is planned. The number and percentage of participants with HIV-1 RNA in the following categories will be summarized:

- < 50 copies/mL

  < 20 copies/mL

  - < 20 copies/mL Not Detectable

- < 20 copies/mL Detectable

  20 to < 50 copies/mL

- 50 to < 200 copies/mL
- 200 to < 400 copies/mL
- 400 to < 1000 copies/mL
- ≥ 1000 copies/mL
- Missing (only applicable to M F analysis)

Analysis of the other efficacy endpoints will be based on the FAS.

6.4. Changes from Protocol-Specified Efficacy Analyses

No change from protocol-specified efficacy analysis is planned.

7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory AEs will be coded using the current version of MedDRA. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lower-level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to toxicity criteria specified in the protocol. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE eCRF to the question of "Related to Study Treatment." Relatedness will always represent the investigator's choice, not that of the medical monitor. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-participant data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if the AEs met the definitions of SAEs that were specified in the study protocol. SAEs captured and stored in the clinical database will be reconciled with the SAE database from the Global Patient Safety (formerly known as Pharmacovigilance and Epidemiology [PVE]) before data finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

The TEAEs are defined as any AEs that begins on or after the date of first dose of study drug or any AEs leading to premature discontinuation of study drug.

7.1.5.2. Incomplete Dates

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dose date of study drug, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if the AE onset is the same as or after the month and year (or year) of the first dose date of study drug.

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dose date of study drug, will be considered to be treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dose date of study drug will be considered treatment emergent.

7.1.6. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be summarized based on the Safety Analysis Set.

7.1.6.1. Summaries of AE Incidence in Combined Severity Grade Subsets

A brief, high-level summary of the number and percentage of participants who experienced at least 1 TEAE in the categories described below will be provided for the Functional Monotherapy Period analysis and the All LEN analysis. All deaths observed in the study will also be included in this summary.

- TEAEs
- TEAEs with Grade 3 or higher
- TEAEs with Grade 2 or higher
- TE treatment-related AEs
- TE treatment-related AEs with Grade 3 or higher
- TE treatment-related AEs with Grade 2 or higher
- TE SAEs
- TE treatment-related SAEs
- TEAEs leading to premature discontinuation of study drug

The number and percentage of participants who experienced at least 1 TEAE will be provided and summarized by PT only for the following AE categories:

- TEAEs
- TEAEs with Grade 3 or higher
- TE treatment-related AEs
- TE SAEs
- TEAEs leading to premature discontinuation of study drug

Multiple events will be counted only once per participant in each summary. Adverse events will be summarized and listed by PT in descending order of total frequency. For summaries by severity grade, the most severe grade will be used for those AEs that occurred more than once in an individual participant during the study.

In addition, data listings will be provided for the following:

- All AEs
- All SAEs
- All Deaths
- All AEs with severity of Grade 3 or higher
- All AEs leading to discontinuation of study drug

For each listing, whether the event is treatment emergent will be indicated.

7.1.7. Additional Analysis of Adverse Events

Additional analysis of AEs will be performed for injection site reaction (ISR) events. An ISR event is defined as an AE related to study drug with HLT of "Injection Site Reactions". The following summaries will be provided for each SC injection visit (eg, Day 1 SC, Week 26) and the overall using the All LEN analysis.

- Number of participants received SC injection
- Number and percentage of participants with any ISRs by the highest toxicity grade
- Number and percentage of participants with any ISRs by PT term
- Duration of ISR events in days

The denominator for the percentage calculation for the by visit summary and the overall summary will be based on the total number of participants who receive at least 1 SC injection at the visit of interest and the total number of participants who receive at leave 1 SC injection at any injection visit, respectively.

Duration of a given ISR event is defined as the ISR stop date minus the ISR onset date plus 1 day. Duration of ISR events in days will be summarized using descriptive statistics.

A by-participant listing for ISR events and the corresponding duration will be provided.

7.2. Laboratory Evaluations

7.2.1. Graded Laboratory Values

The Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1 dated July 2017, will be used to assign toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (ie, increased, decreased) will be presented separately.

7.2.1.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline visit. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed at any postbaseline visit will be considered treatment emergent.

7.2.1.2. Summaries of Laboratory Abnormalities

The summaries (number and percentage of participants) for treatment-emergent laboratory abnormalities will be provided by lab test; participants will be categorized according to the most severe postbaseline abnormality grade for a given lab test.

Graded laboratory abnormalities will be summarized for the Functional Monotherapy and All LEN analyses, separately. For all summaries of laboratory abnormalities, the denominator is the number of participants with nonmissing postbaseline values.

A by-participant listing of treatment-emergent laboratory abnormalities will be provided by participant ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the lab test of interest, with all applicable severity grades displayed.

7.3. Antiretroviral Medications and Concomitant Medications

7.3.1. Antiretroviral Medications

The ARV medications are defined as nonstudy drug ARV medications used prior to, during, or after the study (if collected). The ARV medications are recorded on the ARV eCRF and will be coded using the Gilead-modified World Health Organization (WHO) Drug Dictionary for ARV medications. The WHO preferred name and drug code will be attached to the clinical database. All ARV medications recorded on the ARV eCRF will be listed.

7.3.1.1. Prior Antiretroviral Medications

Prior ARV medications are defined as any nonstudy drug ARV medications with a start date prior to the first dose date of study drug regardless of when the stop date is. If a partial start date is entered, the medication will be considered prior unless the month and year (if day is missing)

or year (if day and month are missing) of the start date are after the first dose date. Medications with a completely missing start date will be included in the prior medication summary, unless otherwise specified.

Prior ARV medications will be summarized by drug class and preferred name (based on the Gilead-modified WHO coding terms) using the number and percentage of participants for each cohort and treatment group. A participant reporting the same medication more than once will be counted only once within each drug class when calculating the number and percentage of participants who received that medication. The summary will be ordered alphabetically by drug class and then by preferred term in descending order of the total frequency. For drugs with the same frequency, sorting will be done alphabetically.

In addition, number of prior ARVs (excluding COBI and RTV used as a boosting agents) each participant has been taken and prior ARV drug class exposure will be summarized in the baseline characteristics table mentioned in Section 5.2.

7.3.1.2. Antiretroviral Medications at Baseline

The ARV medications at baseline is defined as any nonstudy drug ARV medications that are used on the first dose date of study drug. The ARV at baseline will be summarized in the same manner as the prior ARV medications by drug class and preferred term. In addition, the number of ARVs and ARVs by drug class will be included in the baseline characteristics table mentioned in Section 5.2.

7.3.1.3. Optimized Background Regimen at Baseline

The OBR at baseline is defined as any nonstudy drug ARV medications that were started on or prior to Study Day 28 from the first dose date of open-label LEN and were used for a minimum duration of 28 days on or after the first dose of open-label LEN. The ARV medications with temporary interruption will be considered as the same ARV. The earliest start date and the latest end date of the same ARV will be used in the calculation to define baseline OBR. The OBR will be flagged in the ARV listing.

7.4. Changes from Protocol-Specified Safety Analyses

No change from protocol-specified safety analyses is planned.

8. REFERENCES

Chan IS, Zhang Z. Test-based exact confidence intervals for the difference of two binomial proportions. Biometrics 1999;55 (4):1202-9.

Emu B, Fessel J, Schrader S, Kumar P, Richmond G, Win S, et al. Phase 3 Study of Ibalizumab for Multidrug-Resistant HIV-1. N Engl J Med 2018;379 (7):645-54.

9. SOFTWARE

SAS® Version 9.4 (SAS Institute Inc., Cary, NC.) is to be used for all programming of tables, listings, and figures.

nQuery Advisor® Version 7.0 (Statistical Solutions, Cork, Ireland.) is to be used for sample size and power calculation.

10. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision

11. APPENDICES

Appendix 1. Schedule of Assessments

	Screening[a]	Cohort Selection[b]	Day 1[c]	Day 2	Day 5	Day 8	Day 15[d]	Day 16[d]	Day 19[d]	Day 22[d]	Day 1 SC	Weeks 4, 10, 16, 22, 26, 36	Week 52 and visits thereafter[e]	30, 90 and 180 Day Follow-Up[f]	Early Termination[g]
Written Informed Consent/Assent/Parental Consent	X														
Medical History	X														
Demographic Information	X														
Complete Physical Examination	X		X				X				X	X[h]	X[h]		X
Symptom Directed Physical Examination				X		X		X		X		X[h]	X[h]	X	
Vital Signs[i] (include weight)	X		X	X		X	X	X		X	X	X	X	X	X
12 lead ECG (supine)	X														
Height	X														
Hematology[j], Chemistry[k], Estimated GFR, Urinalysis[l], Urine Chemistry[l], CD4+ Cell Count	X		X			X	X			X	X	X	X	X	X
Urine Storage Sample			X	X		X	X	X		X	X	X	X		X
Serum Pregnancy Test[m]	X														
Serum FSH[n]	X														
Urine Pregnancy Test[m]			X			X	X			X	X	X	X	X	X
HBV, HCV Testing	X														

	Screening[a]	Cohort Selection[b]	Day 1[c]	Day 2	Day 5	Day 8	Day 15[d]	Day 16[d]	Day 19[d]	Day 22[d]	Day 1 SC	Weeks 4, 10, 16, 22, 26, 36	Week 52 and visits thereafter[e]	30, 90 and 180 Day Follow-Up[f]	Early Termination[g]
HIV 1 Genotyping/Phenotyping	X														
Plasma HIV 1 RNA	X	X	X	X		X	X	X		X	X	X	X	X	X
Plasma Storage Sample	X	X	X	X		X	X	X		X	X	X	X	X	X
CCI															
CCI															
CCI															
Oral GS 6207 Administration[t]			X	X		X	X	X		X					
Begin Optimized Background Regimen[u]			X				X				X				
SC GS 6207 Administration[v]											X	X	X		
Symptoms Distress Module, SF 36, EQ 5D 5L[w]			X									X	X		
Numeric Pain Scale[x]											X	X	X		
Injection Site Reaction Worksheet[x]											X	X	X		
Adverse Events/ Concomitant Meds	X	X	X	X	X	X	X	X	**X**	X	X	X	X	X	X

a. Screening evaluations must be completed within 42 days prior to Day 1.
b. Cohort Selection visit to be completed 14 to 30 days after the Screening visit until Cohort 1 is fully enrolled
c. Day 1 tests and procedures must be completed prior to study drug administration
d. Day 15, 16, 19 and 22 visits will be completed by Cohort 1B participants only

e. At the Week 52 visit, CCI [redacted] Participants will receive SC GS 6207 every 6 months (26 weeks) starting at Week 52 visit, while continuing their OBR, until the product becomes accessible to participants through an access program or until Gilead Sciences elects to discontinue the study in the country.
f. Participants may be required to return to the clinic for a 30, 90 and 180 Day Follow Up Visit after Early Termination visit as noted in section 6.4.1.
g. Early Termination visit to be completed, if participant decides to discontinue study drug prior to completing Week 52 visit or prior to study completion. Investigators should counsel participant regarding the importance of continuing a complete ARV therapy in accordance to standard of care, and refer participant to an appropriate HIV treatment facility
h. Complete physical examination to be completed at Weeks 26 and 52, symptom directed physical examination to be completed at all other visits
i. Vital signs blood pressure, pulse, respiration rate, and temperature, weight
j. Hematology: CBC with differential and platelet count
k. Chemistries: alkaline phosphatase, AST, ALT, GGT, total bilirubin, direct and indirect bilirubin, total protein, albumin, LDH, CPK, bicarbonate, BUN, calcium, chloride, creatinine, glucose, lipase, magnesium, phosphorus, potassium, sodium, uric acid (except at Cohort Selection, Days 2, 5, 16 and 19 visits)
l. Urinalysis and Urine Chemistry: including color & clarity, specific gravity, pH, glucose, ketones, bilirubin, urobilinogen, blood, nitrite, leukocyte esterase and microscopic (if microscopic elements are seen), urine protein, albumin, creatinine, phosphate, calcium, magnesium and uric acid (except at Cohort Selection, Days 2, 5, 16 and 19 visits)
m. All women will have a serum test performed at Screening. Urine pregnancy test will be performed at all subsequent visits for women of child bearing potential (except at Days 2, 5, 16 and 19). Positive urine pregnancy tests will be confirmed with a serum test
n. FSH test is required for women who are < 54 years old and have stopped menstruating for ≥ 12 months but do not have documentation of ovarian hormonal failure
[redacted]
q. During the Maintenance Period, at all visits without SC GS 6207 injections: CCI [redacted]
r. During the Maintenance Period, at all visits with SC GS 6207 injections: CCI [redacted]
t. Cohort 1 participants will be administered oral GS 6207 or placebo to match GS 6207 at Days, 1, 2 and 8. Participants who receive placebo to match GS 6207 at Days 1, 2 and 8 will receive oral GS 6207 at Days 15, 16 and 22. Cohort 2 participants will be administered oral GS 6207 at Days 1, 2 and 8
u. Cohort 1 participants will begin an OBR on Day 15 (Cohort 1B) or Day 1 SC (Cohort 1A). Cohort 2 participants will begin an OBR on Day 1. An OBR should be selected based on the screening and/or available historical HIV resistance reports.
v. All participants will be administered SC GS 6207 at Day 1 SC (14 days after the first dose of oral GS 6207) and will continue to receive SC GS 6207 every 6 months (26 weeks). Each SC GS 6207 dosing should occur within 26 and 28 weeks of the previous SC GS 6207 dosing.
w. Participants ≥ 18 years of age at Day 1 visit will complete Symptoms Distress Module, SF 36, EQ 5D 5L at Day 1, Weeks 4, 16, 26 and 52, if available (before completing other study procedures).
x. Participants ≥ 18 years of age at Day 1 visit will complete the Numeric Pain Rating Scale at Day 1 SC, Weeks 26 and 52 (after they receive SC GS 6207 injections)
y. Provide injection site reaction assessment worksheet and instruct the participants to measure and report injection site reactions following the administration of the SC injections

Appendix 2. Programming Specifications

1) Study drug disposition in Main Phase

- Before SC dosing

  Completed study drug: participants who received SC LEN injection on Day 1 SC.

  Did not complete study drug with reasons for premature discontinuation of study drug: participants who did not receive SC LEN injection on Day 1 SC and whose Study Drug Completion eCRF for the Study Phase "Treatment" was marked as "No".

  Continuing study drug: participants who did not receive SC LEN on Day 1 SC and Study Drug Completion eCRF for the Study Phase "Treatment" has not been filled out.

- After SC dosing

  Received Day 1 SC injection

  Completed study drug: participants who received Day 1 SC injection and whose Study Drug Completion eCRF for the Study Phase "Treatment" was marked as "Yes".

  Did not complete study drug with reasons for premature discontinuation of study drug: participants who received Day 1 SC injection and whose Study Drug Completion eCRF for the Study Phase "Treatment" was marked as "No"

  Continuing study drug: participants who received Day 1 SC injection and Study Drug Completion eCRF for the Study Phase "Treatment" has not been filled out.

2) Additional specifications for Functional Monotherapy Period Analysis:

- Efficacy data included for the Functional Monotherapy Period analysis: The "Day 1 SC or Day 15 visit" specified in Section 6.1 of the SAP refers to the visit associated with the first oral lead-in dosing. The Day 1 SC or Day 15 visit associated with oral redosing after participants have been unblinded will not be included in the Functional Monotherapy Period analysis.

- PP Analysis Set:

  a) The 3rd PP exclusion criteria, "Added a new ARV during the Functional Monotherapy Period", mentioned in Section 3.1.3 of the SAP is for ARVs added on or after the first dose date of blinded study drug and prior to the Day 1 SC or Day 15 visit date. If Day 1 SC or Day 15 visit date is missing, the date that is 15 days from the date of the first dose of blinded study drug or the date of the first dose of open-label LEN, whichever is earlier, will be used to replace the Day 1 SC and Day 15 visit date in above algorithm.

  b) "Partial dose" is defined for participants who receive 1 dose of 300 mg LEN tablet on Day 1 and/or Day 2.

3) Drug class and abbreviation of the generic name is tabulated below:

Drug Class	Generic Name	Generic Name Abbreviation
NRTI	Abacavir	ABC
	Zidovudine	AZT or ZDV
	Didanosine	ddI
	Stavudine	d4T
	Emtricitabine	FTC
	Tenofovir alafenamide	TAF
	Tenofovir Disoproxil Fumarate	TDF
	Lamivudine	3TC
	Zalcitabine	DDC
NNRTI	Delavirdine	DLV
	Doravirine	DOR
	Efavirenz	EFV
	Etravirine	ETR
	Nevirapine	NVP
	Rilpivirine	RPV
PI	Amprenavir	APV
	Atazanavir	ATV
	Darunavir	DRV
	Indinavir	IDV
	Fosamprenavir	FPV
	Lopinavir	LPV
	Nelfinavir	NFV
	Ritonavir	RTV or /r when used with other PI[1]
	Saquinavir	SQV
	Tipranavir	TPV
INSTI	Bictegravir	BIC
	Dolutegravir	DTG
	Elvitegravir	EVG
	Raltegravir	RAL
Fusion Inhibitor	Enfuvirtide	T20
CCR5 co-receptor Antagonist	Maraviroc	MVC
CD4-Directed Post Attachment	Ibalizumab	IMAB
Attachment Inhibitor (AI)	Fostemsavir	FTR
Pharmacokinetic Enhancers	Cobicistat	COBI or /c when used with PI[2]

1. RTV is not considered as an ARV when used as a boosting agent, defined as RTV used as 100 mg QD or BID or as 200 mg QD or BID.
2. COBI is not considered as an ARV.

4) Study drug administration: Oral reload will be recorded as an "Unscheduled" visit in the Study Drug Administration eCRF. Participants with oral reload prior to the 1st dose of SC have "Unscheduled" dosing visits occurred prior to Day 1 SC visit. Participants who received a total of 5 tablets of LEN (300 mg) (ie, 2 x 300 mg LEN tablets each for the first 2 days and 1 x 300 mg LEN tablet on the 8th day) prior to "Unscheduled" dosing visits followed by Day 1 SC visit will be classified as oral reload due to missing scheduled SC dosing. Otherwise, participants will be classified as oral reload due to missing scheduled oral dosing visit.

GS-US-200-4625-DMC-Primary Efficacy Endpoint-SAP-v1.0

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Biostatistics eSigned	01-Oct-2020 19:50:58
PPD	Clinical Research eSigned	02-Oct-2020 03:57:16