STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 1a/1b Study to Evaluate the Safety and Tolerability of Repeated Doses of Nonreplicating Arenavirus Vector Therapeutic Vaccines GS-2829 and GS-6779 in Healthy Participants and Participants with Chronic Hepatitis B (CHB)
Name of Test Drug:	GS-2829 and GS-6779
Study Number:	GS-US-642-5670
Protocol Version (Date):	Original (01 September 2022) Amendment 1 (22 November 2022) Amendment 2 (20 July 2023)
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Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

LIST OF IN-TEXT FIGURES

LIST OF ABBREVIATIONS

AASLD	American Association for the Study of Liver Diseases
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BAP	Biomarker Analysis Plan
BMI	body mass index
CHB	Chronic Hepatitis B
CI	confidence interval
CK	creatine kinase
COVID-19	Coronavirus Disease 2019
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
ECG	electrocardiogram
eCRF	electronic Case Report Form
$eGFR_{CG}$	estimated Glomerular Filtration Rate (Cockcroft-Gault formula)
EliSpot	Enzyme-linked ImmunoSpot
ET	early termination
FAS	Full Analysis Set
FFU	focus forming units
FIH	first-in-human
FSH	follicle stimulating hormone
FU-WK xx	Follow-Up Week xx
HBV	Hepatitis B virus
HIV-1	Human Immunodeficiency Virus Type 1
HLT	high-level term
HP	Healthy Participant
ICH	International Conference on Harmonization (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
ID	Identification
IFNɣ	interferon gamma
INR	International Normalized Ratio
IPD	Important Protocol Deviation
IRT	Interactive Response Technology
LDH	lactic dehydrogenase
LLT	lower-level term
LOQ	limit of quantitation
LPLV	last patient last visit
MedDRA	Medical Dictionary for Regulatory Activities

MST	MedDRA Search Term
PBO	Placebo
PT	preferred term
Q1, Q3	first quartile, third quartile
RNA	ribonucleic acid
SAP	statistical analysis plan
SD	standard deviation
SMQ	Stardardized MedDRA Query
SOC	system organ class
SRT	Safety Review Team
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
ULN	upper limit of normal
WBC	white blood cell
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) for the final clinical study report (CSR) for Study GS-US-642-5670. This SAP is based on the Amendment 2 study protocol dated 20 July 2023 and the electronic case report form (eCRF). The SAP will be finalized before database finalization. Any changes made after SAP finalization will be documented in the CSR.

1.1. Study Objectives and Endpoints

Primary Objective	**Primary Endpoint**
• To evaluate the safety and tolerability of repeated dosing of GS-2829 and GS-6779 in healthy participants and in virally suppressed participants with CHB	• Proportion of participants with treatment-emergent AEs, SAEs, and laboratory abnormalities
Secondary Objective	**Secondary Endpoints**
• To evaluate the immunogenicity of repeated dosing of GS-2829 and GS-6779 in healthy participants and in virally suppressed participants with CHB	• Incidence and magnitude of vaccine-induced T-cell responses
Exploratory Objectives	**Exploratory Endpoints**
• To evaluate the impact of GS-2829 and GS-6779 on HBV-specific viral biomarkers in participants with CHB	• Change in HBsAg from baseline • Proportion of participants with HBsAg loss with or without HBsAg seroconversion • Changes in quantitative hepatitis B e antigen (HBeAg) from baseline

Note: Only exploratory objectives to be analyzed under this SAP are included. Exploratory objectives may be analyzed outside of this SAP will not be described here.

1.2. Study Design

This is a randomized, blinded, placebo-controlled, Phase 1a and Phase 1b study to evaluate the safety, tolerability, and immunogenicity of repeated doses of GS-2829 and GS-6779 in healthy participants (Phase 1a) and participants with virally suppressed CHB (Phase 1b). The study will comprise 8 cohorts, which will enroll approximately 10 participants each, with a 4:1 randomization to either active viral vectors (GS-2829 and/or GS-6779) or Placebo (PBO).

The investigational products GS-2829 and GS-6779 are available as $\geq 1.0 \times 10^7$ FFU/mL. There are 2 doses in this study: high dose (0.5 mL of the undiluted solution) and low dose (0.5 mL of the 10-fold dilution of the high dose).

Phase 1a activities will be performed in healthy participants who are 18 to 60 years of age at a single study site in New Zealand (refer to protocol for complete inclusion and exclusion criteria).

Healthy participants will be enrolled into 1 of 5 cohorts to receive the investigational product as follows:

Cohort 1* – Single low dose of GS-2829 or PBO on Day 1 and Day 57.

Cohort 2* – Single low dose of GS-6779 or PBO on Day 1 and Day 57.

Cohort 3 – Single low dose of GS-2829 on Day 1 and Day 57; and single low dose of GS-6779 on Day 29 and Day 85 or PBO on Days 1, 29, 57, and 85.

Cohort 4 – Single high dose of GS-2829 on Day 1 and Day 57; single high dose of GS-6779 on Day 29 and Day 85 or PBO on Days 1, 29, 57, and 85.

Cohort 8 – Single high dose of GS-2829 on Day 1, Day 57, and Day 113; and single high dose of GS-6779 on Day 29, Day 85, and Day 141 or PBO on Days 1, 29, 57, 85, 113, and 141.

*Cohorts 1 and 2 will enroll concurrently and will receive investigational product in 2 groups, a sentinel group (2 active and 1 PBO, randomly assigned) and the remainder (6 active and 1 PBO), for a total of approximately 10 healthy participants per cohort. Dosing the remainder of Cohorts 1 and 2 and initiation of Cohort 3 will commence at the discretion of the investigator in consultation with the sponsor's medical monitor upon evaluation of available safety data through at least 14 days after the first dose of investigational product in Cohort 1 and 2 sentinel group participants.

Phase 1b activities will be performed at multiple study sites (approximately 15) in participants who are 18 to 65 years of age, diagnosed with CHB, and are HBV virally suppressed (Cohort 5, 6, and 7)--refer to protocol for complete inclusion and exclusion criteria. These participants will be enrolled into 1 of 3 cohorts to receive the investigational product as follows:

Cohort 5 – Single low dose of GS-2829 on Day 1 and Day 57; and single low dose of GS-6779 on Day 29 and Day 85 or PBO on Days 1, 29, 57, and 85.

Cohort 6 – Single high dose of GS-2829 on Day 1 and Day 57; and single high dose of GS-6779 on Day 29 and Day 85 or PBO on Days 1, 29, 57, and 85.

Cohort 7 - Single high dose of GS-2829 on Day 1, Day 57 and Day 113; and single high dose of GS-6779 on Day 29, Day 85, and Day 141 or PBO on Days 1, 29, 57, 85, 113, and 141.

All participants will be followed for safety for 6 months after their last dose of investigational product. The dosing schedules by cohort are provided in Table 1-1.

Table 1-1. Investigational Product Dose Timing

Cohort	1	2	3	4	8	5	6	7
Population	**HP**	**HP**	**HP**	**HP**	**HP**	**CHB**	**CHB**	**CHB**
Dose Level	**Low[a]**	**Low[a]**	**Low[a]**	**High[b]**	**High[b]**	**Low[a]**	**High[b]**	**High[b]**
Study Day 1	GS-2829 or PBO IM	GS-6779 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM
Study Day 29			GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM
Study Day 57	GS-2829 or PBO IM	GS-6779 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM	GS-2829 or PBO IM
Study Day 85			GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM	GS-6779 or PBO IM
Study Day 113					GS-2829 or PBO IM			GS-2829 or PBO IM
Study Day 141					GS-6779 or PBO IM			GS-6779 or PBO IM

CHB = chronic hepatitis B [participants were required to be HBV virally suppressed per protocol]; FFU = focus-forming unit; HP = healthy participant; IM = intramuscular; PBO = placebo

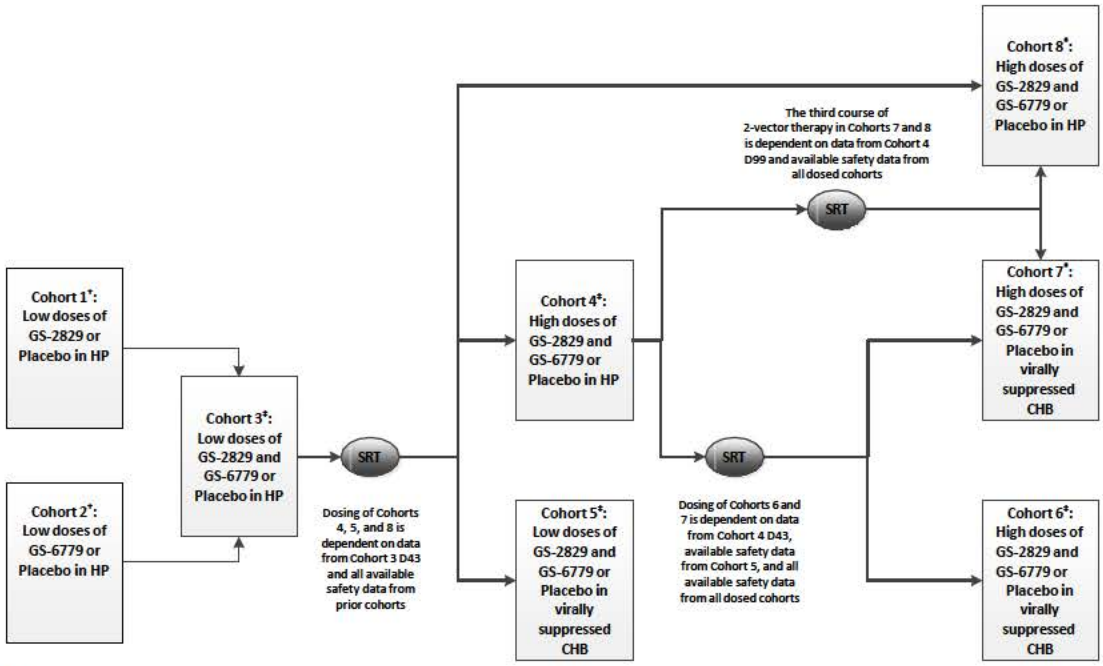
a Low dose = 0.5 mL of a 10-fold dilution of high-dose investigational product.

b High dose = 0.5 mL of high-dose investigational product ($\geq 1.0 \times 10^7$ FFU/mL).

A Safety Review Team (SRT) will make decisions on initiating enrollment of higher dose cohorts and initiating the third dose of alternating viral vector investigational product based on available safety data at the time of a snapshot. There are 3 planned SRT reviews specified in the protocol (see Section 2.2 of this SAP for the timing of these reviews). Ad hoc reviews can be convened at the discretion of the SRT during the study based on new safety concerns; and dosing of an individual cohort may be suspended if cohort stopping rules are met (see Section 3.3.3 of the study protocol).

An SRT charter defining team membership, meeting conduct, and the decision-making process will be agreed upon by all SRT members before the first meeting. The data reviewed at the SRT meetings to make cohort transition decisions will be defined in the SRT charter. Source data verification may not be performed before SRT meetings. The quality control checks performed on the data reviewed and used for making these decisions will also be described in the charter. The overall study schema is shown below in Figure 1.

Figure 1. Overall Study Schema, Phase 1a and Phase 1b



† Total 2 doses
‡ Total 4 doses
* Total of 6 doses
CHB = chronic hepatitis B; D = Day; HBV = hepatitis B virus; HP = healthy participants; SRT = Safety Review Team.

Cohorts 1, 2, and 3: Cohorts 1 and 2 will enroll concurrently and will receive investigational product in 2 groups, a sentinel group (2 active and 1 PBO, randomly assigned) and the remainder (6 active and 1 PBO), for a total of approximately 10 healthy participants per cohort. Dosing the remainder of Cohorts 1 and 2, and initiation of Cohort 3 will commence at the discretion of the investigator in consultation with the sponsor's medical monitor upon evaluation of available safety data through at least 14 days after the first dose of investigational product in Cohort 1 and 2 sentinel group participants. The duration of this review period may be increased based on emerging preliminary safety data. Decisions to initiate a higher dose level cohort and any required revisions to postdose monitoring will be made upon the review of all available safety data by the SRT.

Cohorts 4 and 5: Initiation of Cohorts 4 and 5, which will run concurrently, will be determined at the discretion of the SRT based on the evaluation of available safety data through Day 43 (14 Days after the initial dose of both investigational products for all participants enrolled in Cohort 3), in addition to all available safety data from Cohorts 1 and 2. The decision on cohort initiation will be based on prespecified criteria agreed upon by the SRT and documented in the SRT charter. The duration of this review period may be increased based on the emerging and cumulative safety data.

Cohort 8: Initiation of Cohort 8 will be determined at the discretion of the SRT based on the evaluation of available safety data through Day 43 (14 days after all participants in Cohort 3 have completed the initial dose of both investigational products), in addition to all available safety data from prior cohorts. Initiation of a third dose of 2-vector combination, therapy will be determined at the discretion of the SRT based on the evaluation of the available safety data through Day 99 (14 days after all participants in Cohort 4 have completed the second dose of both investigational products), in addition to all available safety data. The decision on cohort initiation will be based on prespecified criteria agreed upon by the SRT and documented in the SRT charter. The duration of this review period may be increased based on the emerging and cumulative safety data.

Cohort 6: Initiation of Cohort 6 will be determined at the discretion of the SRT based on the evaluation of available safety data through Day 43 (14 days after initial dose of both the investigational products for all participants enrolled in Cohort 4), available safety data from participants enrolled in Cohort 5, and all available safety data from all dosed cohorts, and dosing will be initiated only in the absence of dose-limiting toxicity and/or meeting any prespecified stopping criteria. The duration of this review period may be increased based on the emerging and cumulative safety data.

Cohort 7: Initiation of Cohort 7 will be determined at the discretion of the SRT based on the evaluation of available safety data through 14 days (Day 43) after initial dose of both the investigational products for all participants enrolled in Cohort 4, available safety data from participants enrolled in Cohort 5, and all available safety data from all dosed cohorts. Initiation of the third dose of 2 vector combination therapy will be determined at the discretion of the SRT based on the evaluation of the available safety data through Day 99 **(**14 days after all participants in Cohort 4 have completed the second dose of both investigational products), in addition to all available safety data. The decision on cohort initiation will be based on prespecified criteria agreed upon by the SRT and documented in the SRT charter. The duration of this review period may be increased based on the emerging and cumulative safety data.

All participants will provide informed consent, complete all screening procedures and assessments, and must meet all eligibility criteria prior to administration of investigational product on Day 1.

Study procedures including investigational product administration, safety follow-up via collection of AEs, laboratory assessments, participant diary review, immunogenicity, and biomarker assessments, HBV genomic sequencing and phenotyping, and other procedures are described in study protocol sections 5 and 6. Assessments will be conducted per the schedule of assessment table (see Schedule of Assessments, Appendix 1).

1.3. Sample Size and Power

The sample size for this study was determined based on practical considerations and empirical experience with similar types of studies. No formal power and sample size calculations were performed. Overall, a total sample size of approximately 80 participants (10 participants per cohort, including 8 active and 2 PBO) is expected to provide a suitable assessment of the safety, tolerability, and immunogenicity for treatment with the investigational products.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analysis

Prior to the final analysis, interim analyses may be conducted at the discretion of the sponsor and the results from these analyses may be submitted to regulatory agencies to facilitate the overall clinical program development or to scientic meetings or journals to disseminate the findings.

2.1.1. Dose Escalation Analysis

For the purposes of making the decision to escalate from the low dose to the high dose or to increase the number of (high-dose) alternating viral vector courses of treatment from 2 to 3 courses, interim analyses of relevant safety data will be conducted by Gilead. These dosing decisions will be determined at the discretion of the SRT based on stopping rules and the criteria outlined in the protocol and SRT Charter. Safety assessments (eg, AEs, ECGs, laboratory test results) will be displayed by population and cohort to facilitate the decision to dose escalate while preserving the blind at the participant level. Three planned SRT meetings will occur when a minimum of the following data is available:

Safety data through 14 days (Day 43) after the initial dose of both investigational products for all participants enrolled in Cohort 3 in addition to all available safety data from Cohorts 1 and 2. Purpose: Initiation of Cohorts 4, 5 (to be run concurrently) and Cohort 8.

Available safety data through 14 days (Day 43) after initial dose of both investigational products for all participants enrolled in Cohort 4 in addition to all available safety data at the time of the snapshot. Purpose: Initiation of Cohort 6 and Cohort 7 (see paragraph below for additional criteria required for Cohorts 7 and 8 and dosing of 3rd course of alternating viral vector therapy).

Safety data through 14 days (Day 99) after all participants in Cohort 4 have completed the second dose of both investigational products (total 4 doses) in addition to all available safety data. Purpose: Initiation of a third dose of 2-vector alternating combination therapy in Cohorts 7 and 8.

The SRT may lengthen the duration of follow-up required for planned SRT meetings and/or hold additional ad-hoc SRT meetings at their discretion.

2.2. Final Analysis

The unblinded final analysis will be performed 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. The analysis of the primary endpoint will be conducted at the time of the final analysis.

2.3. Changes from Protocol-Specified Analysis

No changes from protocol-specified analyses are planned.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented separately for the 2 participant populations (healthy participants [phase 1a] and virally suppressed CHB participants [phase 1b]) using descriptive statistics. Summaries will be presented by treatment group (active participants within each cohort followed by all participants [within population] assigned to placebo). 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 separately for the 2 populations (healthy participants [phase 1a] and virally suppressed CHB participants [phase 1b]) for the All Randomized Analysis Set. Listings will be sorted by cohort and 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 cohort and treatment group to which participants were initially assigned 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 (and are determined prior to unblinding). The analysis set will be identified and included as a subtitle for each table, figure, and listing.

For each analysis set, the number and percentage of participants eligible for inclusion, will be summarized separately for each population by treatment group (active participants within each cohort followed by all participants [within population] assigned to placebo) and overall for all participants in the population.

A listing of reasons for exclusion from analysis sets will be provided by participant.

3.1.1. All Randomized Analysis Set

All Randomized Analysis Set includes all participants who were randomized into the study (ie, received a study participant ID number in the interactive response technology [IRT]).

All Randomized Analysis Set is the primary analysis set for by-participant listings.

3.1.2. Safety Analysis Set

The Safety Analysis Set includes all participants who received at least 1 dose of study drug.

The Safety Analysis Set is the primary analysis set for safety analyses.

3.1.3. Immunogenicity Analysis Set

The Immunogenicity Analysis Set includes all randomized participants who received at least 1 dose of study drug and have at least 1 value for HBV-specific T-cell total response using the interferon gamma (IFN-ɣ) enzyme-linked immunospot (EliSpot) assay after administration of the investigational product.

The Immunogenicity Analysis Set will be the primary analysis set for immunogenicity analysis utilizing the IFN-ɣ EliSpot assay.

3.1.4. Full Analysis Set (Virally Suppressed CHB Participants only)

The Full Analysis Set (FAS) will include all virally suppressed CHB participants who were randomized, and received at least 1 dose of investigational product.

The FAS will be the primary analysis set for efficacy analysis for phase 1b participants.

3.2. Participant Grouping

For analyses using the Immunogenicity Analysis Set (both populations) and analyses in virally suppressed CHB participants only using the FAS, participants will be grouped according to population, treatment group (active group within each cohort followed by all participants [within population] assigned to placebo) to which they were randomized. For all other analyses, participants will be grouped according to population, treatment group (active group within each cohort followed by all participants [within population] assigned to placebo) based on actual treatment received. The actual treatment received will differ from the randomized treatment only when the participant's actual treatment differs from their randomized treatment for the entire treatment duration.

For enrollment, disposition, analysis sets, demographics and baseline characteristics, and baseline disease characteristics [virally suppressed CHB participants only], an additional total column for population (healthy participants or virally suppressed CHB participants) will be included. For all other tables, a population total column will not be presented.

Data will be summarized separately for healthy participants (Phase 1a) and virally suppressed CHB participants (Phase 1b). Within each population, displays will be by "cohort" for participants randomized to/taking active study drug within each cohort plus a pooled "placebo" group for the relevant population. Participants randomized to/taking placebo will be pooled across all cohorts within the population to form a single "placebo" group for summaries.

3.3. Strata and Covariates

No covariates will be included in efficacy analyses.

3.4. Examination of Participant Subgroups

There are no prespecified participant subgroups for efficacy or safety analyses.

3.5. Multiple Comparisons

Adjustments for multiplicity will not be made, because no formal statistical testing will be performed in this study.

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.

The handling of missing or incomplete dates for AE start is described in Section 7.1.6.2, and for prior and concomitant medications in Section 7.4.

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

The following conventions will be used for the imputation of date of birth when it is partially missing or not collected:

- If only month and year of birth is collected, then "15" will be imputed as the day of birth
- If only year of birth is collected, then "01 July" will be imputed as the day and month of birth
- If year of birth is missing, then date of birth will not be imputed.

In general, age collected at Day 1 (in years) from the demographics eCRF will be used for analyses and presented in listings. If age at Day 1 is not available for a participant, then age derived based on date of birth and the Day 1 visit date will be used instead. If a randomized participant was not dosed with any study drug, the randomization date will be used instead of the Day 1 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 (e.g., age on date of laboratory assessment) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

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 lower LOQ at the same precision level of the originally reported value will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the lower 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 upper LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the upper LOQ). Values with decimal points will follow the same logic as above.

- The lower or upper 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 lower or upper LOQ, respectively).

If methods based on the assumption that the data are normally distributed are not adequate, analyses may be performed on transformed data or nonparametric analysis methods may be used.

3.8. Visit Definitions

3.8.1. Definition of Baseline, Postbaseline, Study Day, and Follow-Up Day

Baseline is defined as the last available value collected on or prior to the first dose date (and time, where applicable) of investigational product (i.e., prior to taking first dose of investigational product).

Postbaseline is defined as any value collected after the first dose of investigational product.

Study day will be calculated from the first dosing date of investigational product and derived as follows:

- For postdose study days: Assessment Date – First Dosing Date + 1

- For days prior to the first dose: Assessment Date – First Dosing Date

Therefore, study day 1 is the day of first dose of investigational product.

Last Dose Date is defined as the date of the last injection of GS-2829 or GS-6779 [or PBO].

Follow-Up (FU) Day will be calculated from the last dosing date of investigational product and will be derived as follows:

- Assessment date – Last Dose Date

Both Study Day and FU Day will be displayed in listings of data for endpoints remapped to FU visits in Table 3-1 to Table 3-4 in Section 3.8.2 (when possible).

Last Study Date is the latest of clinic visit dates and laboratory visit dates, including all follow-up visits for participants who prematurely discontinued study or who completed study according to the Study Completion eCRF.

3.8.2. Analysis Visits

The nominal visit as recorded on the eCRF will be used for all "on treatment" visits and for "post-treatment" visits for parameters not described below. For the parameters specified below, nominal visits will be remapped to FU-WKxx for post-treatment visits. Both "Study Day" and "FU Day" of the assessment will be displayed in listings (when possible) for these parameters. The remapping of nominal visits in the post-treatment period is to align FU visits for post-dose weeks due to differences in duration of dosing. Specifically, the study day of last dose received is as follows: Cohorts 1 and 2 (Day 57); Cohorts 3, 4, 5, and 6 (Day 85); and Cohorts 7 and 8 (Day 141).

Any data relating to unscheduled visits will not be assigned to a particular visit or time point and in general will not be included in summaries. However, the following exceptions will be made:

- An unscheduled visit prior to the first dose of study drug may be included in the calculation of baseline value, if applicable. However, if 2 laboratory records for the same laboratory test have the same date and time and one is marked as an unscheduled test (VISITTYP='U'), the result marked as scheduled visit (VISITTYPE='S') will be used for analysis (ie, Participant ID 08465-10107 for lab test "HBsAg antibody quantitative" on Study Day 1).

- Unscheduled visits after the first dose date of study drug will be included in determining the maximum postbaseline toxicity grade.

- For participants who prematurely discontinue from the study, early termination (ET) data will be assigned to what would have been the next scheduled visit where the respective data were scheduled to be collected.

Note: For LabCorp laboratory dataset, unscheduled visits have VISITTYP='U' and are assigned to the previous nominal visit (these records will not be included in analysis if there is a measurement for the nominal visit that is a "scheduled" visit).

The remapped post last dose visits for laboratory values (including both safety and viral biomarkers), vital signs, ELISpot, and ECGs are displayed in Table 3-1, Table 3-2, Table 3-3, and Table 3-4 respectively.

Table 3-1. Remapped Follow-Up Visits for Hematology, Chemistry, Liver Function, Coagulation, Viral Biomarker [Phase 1b] and Antibody to HBsAg [Phase 1a] tests

Nominal Visit	Cohorts 1, 2	Cohorts 3, 4, 5, 6	Cohorts 7, 8
Last Value prior to first dose date=Baseline	Baseline*$	Baseline*#$	Baseline*#$
Day 15	Day 15	Day 15#	Day 15#
Day 29	Day 29*$	Day 29*#$	Day 29*#$
Day 43	–	Day 43	Day 43
Day 57	Day 57*$	Day 57*#$	Day 57*#$
Day 71	***FU-WK2***	Day 71	Day 71
Day 85	***FU-WK4$***	Day 85*#$	Day 85*#$
Day 99	–	***FU-WK2***	Day 99
Day 113	–	***FU-WK4#$***	Day 113*#$
Day 127	–	–	Day 127
Day 141	***FU-WK12$***	–	Day 141*#$
Day 155	–	–	***FU-WK2***
Day 169	–	***FU-WK12#$***	***FU-WK4#$***
Day 225	***FU-WK24*$***	–	***FU-WK12*#$***
Day 253	–	***FU-WK24*#***	–
Day 309	–	–	***FU-WK24*#***

*Creatinine Clearance (estimated using Cockcroft-Gault method) collected at this subset of visits.
#Viral biomarkers (HBV DNA, quantitative HBsAg, anti-HBsAg antibody, HBcrAg, HBeAg and anti-HBeAg antibody) collected at this subset of visits for participants in Cohorts 5, 6, and 7 (only).
$ Antibody to HBsAg [Phase 1a participants only]..

Table 3-2. Remapped Follow-Up Visits for Vital Signs, Weight, and BMI

Nominal Visit	Cohorts 1, 2	Cohorts 3, 4, 5, 6	Cohorts 7, 8
Last Value prior to first dose date=Baseline	Baseline*#	Baseline*#	Baseline*#
Day 8	Day 8	–	–
Day 15	Day 15	Day 15	Day 15
Day 29	Day 29	Day 29*#	Day 29*#
Day 43	–	Day 43	Day 43
Day 57	Day 57*#	Day 57*#	Day 57*#
Day 64	***FU-WK1***	–	–
Day 71	***FU-WK2***	Day 71	Day 71
Day 85	***FU-WK4***	Day 85*#	Day 85*#
Day 92	–	***FU-WK1***	–
Day 99	–	***FU-WK2***	Day 99
Day 113	–	***FU-WK4***	Day 113*#
Day 127	–	–	Day 127
Day 141	***FU-WK12***	–	Day 141*#
Day 148	–	–	***FU-WK1***
Day 155	–	–	***FU-WK2***
Day 169	–	***FU-WK12***	***FU-WK4***
Day 225	***FU-WK24****	–	***FU-WK12***
Day 253	–	***FU-WK24****	–
Day 309	–	–	***FU-WK24****

*Weight (and the calculation of BMI) performed at this subset of the visits.
"Pre-dose" and "Post-dose" timepoints will be displayed for vitals signs that were collected on injection days.

Table 3-3. Remapped Follow-Up Visits for IFNγ ELISpot Assay

Nominal Visit	Cohorts 1, 2	Cohorts 3, 4, 5, 6	Cohorts 7, 8
Last Value prior to first dose date=Baseline	Baseline	Baseline	Baseline
Day 15	Day 15	Day 15	–
Day 29	Day 29	Day 29	–
Day 43	–	Day 43	–
Day 57	Day 57	Day 57	Day 57
Day 71	***FU-WK2***	Day 71	Day 71
Day 85	***FU-WK4***	Day 85	Day 85
Day 99	–	***FU-WK2***	Day 99
Day 113	–	***FU-WK4***	Day 113
Day 127	–	–	Day 127
Day 141	***FU-WK12***	–	Day 141
Day 155	–	–	***FU-WK2***
Day 169	–	***FU-WK12***	***FU-WK4***
Day 225	***FU-WK24***	–	***FU-WK12***

Table 3-4. Remapped Follow-Up Visits for ECGs

Nominal Visit	Cohorts 1, 2	Cohorts 3, 4, 5, 6	Cohorts 7, 8
Last Value prior to first dose date=Baseline	Baseline	Baseline	Baseline
Day 85	–	Day 85	Day 85
Day 141	–	–	Day 141
Day 225	***FU-WK24***	–	–
Day 253	–	***FU-WK24***	–
Day 309	–	–	***FU-WK24***

Note: Day 85 is after 2 cycles of injections; Day 141 is after 3 cycles of injections.

4. PARTICIPANT DISPOSITION

4.1. Participant Randomization and Disposition

Key study dates (ie, first participant screened, first participant randomized, last participant randomized, last participant last visit for the primary endpoint, and last participant last visit for the clinical study report) will be provided separately for each population (healthy participants [phase 1a] and virally suppressed CHB participants [phase 1b]).

A summary of participant randomization into this study will be provided separately for each population (healthy participants [phase 1a] and virally suppressed CHB participants [phase 1b]). Displays will be presented by treatment group (active participants within each cohort followed by all participants assigned to placebo [within population]) and overall for all participants in the population for each country, and investigator within country. The denominator for the percentage calculation will be the total number of participants randomized for that column.

The randomization schedule used for the study will be provided.

A summary of participant disposition will be provided separately for each population (healthy participants [phase 1a] and virally suppressed CHB participants [phase 1b]) for the All Randomized Analysis Set. Displays will be by treatment group (active participants within each cohort followed by all participants [within population] assigned to placebo) and overall for all participants in the population. The denominator for the percentage calculation for completion status and reasons for premature discontinuation will be the total number of participants in the Safety Analysis Set for each column. The number and percentage of participants in each of the categories listed below will be summarized:

- All Randomized Analysis Set
- All Randomized but Never Dosed
- Safety Analysis Set
- Completed study drug
- Did not complete study drug with reasons for premature discontinuation of study drug
- Completed study
- Did not complete the study with reasons for premature discontinuation of study

For the status of study drug and study completion and reasons for premature discontinuation, the number and percentage of participants in each category will be provided. In addition, a flowchart for each of the participant populations will be provided to depict the disposition.

The following by-participant listings will be provided separately for each participant population to support the above summary tables:

- Reasons for screen failure (will be provided by screening ID number in ascending order)
- Analysis set status (participants excluded from any of the analysis sets)
- Participants who prematurely discontinued any of the study drugs

By-participant listings of disposition including cohort, treatment group, date of the last dose of study drug (study days), study drug completion status, reason for study drug discontinuation, study completion status, and reason for study discontinuation will be produced for each of the 2 participant populations.

4.2. Extent of Study Drug Exposure

For each participant, the number of injections received for each type of vector (GS-2829 and/or GS-6779) and dose level (high dose or low dose for participants receiving active treatment) or placebo for each vector will be calculated. For each population and treatment group (active participants within each cohort followed by all participants [within population] assigned to placebo), the number of participants taking 0, 1, 2, or 3 doses of the vector and dose level combination or placebo for the vector will be provided. Dosing information will be summarized based on data collected on the Study Drug Administration eCRF. Subjects who took only one of the vectors (eg, GS-2829 in Cohort 1 and GS-6779 in Cohort 2) will have 0, 1, or 2 injections for the vector administered/Low Dose or placebo for the vector. Cohorts 3 to 8 will have the number of injections received (0, 1, 2, or 3) for each of the following categories:

- GS-2829 Low Dose
- GS-2829 High Dose
- GS-2829 Placebo
- GS-6779 Low Dose
- GS-6779 High Dose
- GS-6779 Placebo

A by-participant listing of study drug administration will be provided separately for each participant population. Sort order will be as described in Section 3 of this SAP.

4.3. Protocol Deviations

Protocol deviations occurring after participants entered the study are documented during routine monitoring. The number and percentage of participants with at least 1 important protocol deviation (IPD) will be summarized by treatment group for the All Randomized Analysis Set. The following subcategories will also be displayed by treatment group:

- Number of IPDs for each participant (1, 2, or 3 or more IPDs)

- Total Number of Important Protocol Deviations
  Note: A participant may be counted across multiple important protocol deviation categories.

A by-participant listing will be provided for those participants with protocol deviations. The listing of protocol deviations (IPDs and non-IPDs) will include a column to specify whether the protocol deviation is an IPD.

Participants who did not meet eligibility criteria for study entry but were enrolled will be listed separately for each population.

4.4. Assessment of Disaster or Public Health Emergency Impact

This study was ongoing during the novel coronavirus (COVID-19) pandemic which had an impact on the study conduct. Some participants were unable to attend onsite visits due to shelter in place guidelines, site closures, or other reasons. This section describes how special situations due to COVID-19 will be handled in the analysis.

4.4.1. Study Drug or Study Discontinuation Due to Disaster or Public Health Emergency

A by-participant listing of reasons for premature study drug or study discontinuation due to COVID-19 will be provided, if applicable.

4.4.2. Protocol Deviations Due to Disaster or Public Health Emergency

A by-participant listing will be provided for participants with protocol deviations related to COVID-19 (if applicable). The listing of protocol deviations due to COVID-19 (IPDs and non-IPDs) will include a column to specify whether the protocol deviation is an IPD.

4.4.3. Missed and Virtual Visits Due to Disaster or Public Health Emergency

A by-participant listing of participants with missed or virtual visits due to COVID-19 will be provided.

Missed or virtual visits due to COVID-19 are collected on the Visit Date eCRF.

4.4.4. Adverse Events Due to Disaster or Public Health Emergency

AEs of COVID-19 will be included in analyses of AEs if applicable, and will be determined through a COVID-19 Standardized MedDRA Query (SMQ) narrow search.

A by-participant listing of AEs of COVID-19 will be provided.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Participant demographic variables (i.e., age on Day 1, sex at birth, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2]) will be summarized separately for each participant population and be displayed by treatment group (active participants within each cohort followed by all participants [within population] assigned to placebo) and overall for the population, 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.

A by-participant demographic listing, including the informed consent date, will be provided separately for each participant population.

5.2. Baseline Disease Characteristics (Virally Suppressed CHB Participants)

Baseline disease characteristics for virally suppressed CHB paticipants (Cohorts 5 to 7) include:

- years since HBV diagnosis
- HBsAg (IU/mL)
- HBsAg (log_{10} IU/mL)
- HBsAg Category (≤ 2, > 2 to < 3, ≥ 3 to < 4, or ≥ 4 log_{10} IU/mL)
- HBsAb Category (< 5 or ≥ 5 mIU/mL)
- Hepatits B Core Total (Positive, Negative)
- HBV DNA Category (< LLOQ [with subcategories for "< LLOQ target not detected" and "< LLOQ target detected") or ≥ LLOQ [with subcategories for "10 to < 69 IU/mL" and "≥ 69 IU/mL])
- HBV genotype (provided by the Gilead Clinical Virology Group)
- HBeAg Qualitative (Positive or Negative)
- HBeAb Qualitative (Positive, Negative, or Equivocal)
- ALT (U/L)
- ALT Category (≤ ULN or > ULN) using Central Laboratory criteria

- ALT Category (≤ ULN or > ULN) using AASLD criteria (ie, ULN of 35 U/L for males; 25 U/L for females)

- eGFR (mL/min) estimated by Cockcroft-Gault formula

- Prior Interferon

Note: If only the month and year are collected for "date of HBV diagnosis" the day will be set to '01' when imputing the full date. If both the day and month are missing, then '01 July' will be used for the day and month unless the full imputed date is after the first dose date of study drug. If HBV diagnosis date is imputed to be after the first dose date of study drug, set the imputed HBV diagnosis date to the date of first dose of study drug to avoid having a negative duration. The formula to calculate years with HBV disease is as follows:

Duration of HBV Disease (years) =

(First Dose Date of study drug – Date of HBV Diagnosis + 1) / 365.25

A by-participant listing of baseline disease characteristics will be provided for virally suppressed CHB participants (phase 1b).

5.3. Medical History

General medical history will be coded. A by-participant listing of medical history data will be provided.

6. IMMUNOLOGIC (BOTH POPULATIONS) AND OTHER ANALYSES IN VIRALLY SUPPRESSED CHB PARTICIPANTS

6.1. Secondary Immunologic Endpoint (Phase 1a and Phase 1b)

The incidence and magnitude of vaccine-induced T-cell response will be evaluated for the Immunogenicity Analysis Set and will be based on results from the IFN-ɣ ELISpot assay.

Immunogenicity will be evaluated using the IFN-ɣ ELISpot assay with a readout of spot forming cells (SFCs) per 10^6 PBMCs. This assay will be performed using stimulation with 4 overlapping HBV peptide pools (HBV core, HBV Pol A, HBV Pol B, and HBV sAg) that span the bivalent immunogen sequence. All 4 HBV peptide responses will have their value at a visit (mean of 3 replicates) background subtracted using the average unstimulated response (DMSO in triplicate) at the visit. Total vaccine-induced HBV-specific T-cell response will be calculated by adding the response to the 4 peptide pools. An individual participant will be classified as having a T-cell response on IFN-ɣ EliSpot assay if they exhibit a ≥ 3x increase in total vaccine-induced HBV-specific T-cell response over their baseline value at peak (maximum postbaseline value). Participants who have missing values for fold change from baseline will be counted as failures.

The number and percentage of participants with a postbaseline HBV-specific vaccine-induced T-cell response on IFN-ɣ EliSpot assay will be presented separately for each population (healthy participants and virally suppressed CHB participants) by treatment group (active participants within each cohort followed by all participants [within population] assigned to placebo).

Separate 8-number summaries for the absolute total T-cell response (SFC/10^6 PBMCs), change from baseline in total T-cell response (SFC/10^6 PBMCs), and X-fold increase over the result at baseline for the peak (highest value postbaseline) HBV-specific vaccine-induced total T-cell response (for each participant) measured using the IFN-ɣ ELISpot assay will be presented separately for each population (healthy participants and virally suppressed CHB participants) by treatment group.

A stacked bar plot using a different color (or shade of gray [when photocopied] ranging from white to black) to represent the contribution of each of the 4 HBV peptide pools to the total vaccine-induced HBV-specific T-cell response (SFC/10^6 PBMCs) will be produced for each of the 2 populations by treatment group. A spaghetti plot of the fold change from baseline by visit in total vaccine response will be created for each population by treatment group.

A listing of the average DMSO-adjusted IFN-ɣ ELISpot data for each of the 4 HBV peptides and the total for each participant at each visit will be provided. Separate listings will be produced for the 2 participant populations.

The analyses for other exploratory biomarker endpoints listed in the protocol will be described in a separate biomarker analysis plan (BAP).

6.2. Exploratory Analysis of Immune Response to Hepatitis B in Healthy Participants (Phase 1a)

A summary of antibody to HBsAg (mIU/mL) and change from baseline by visit will be summarized for healthy participants assigned to active treatment within each cohort (1, 2, 3, 4, and 8) and for healthy participants assigned to placebo for the Safety Analysis Set.

A listing of HBsAg (qualitative), antibody to HBsAg (mIU/mL), and Hepatitis B core antibody (qualitative) will be provided for healthy participants.

6.3. Exploratory Analysis of HBV Endpoints in Virally Suppressed CHB Participants (Phase 1b)

An 8-number summary of quantitative HBeAg (IU/mL) and change from baseline by visit will be summarized by treatment group for virally suppressed CHB participants in the FAS who were HBeAg positive at baseline (and had HBeAg quantitative data collected) by treatment group for participants in cohorts 5, 6, and 7. Listings will include all data collected for quantitative HBeAg regardless of the participant's HBeAg status at baseline.

Listings of HBV serology results and HBV DNA will be provided for virally suppressed CHB participants.

6.3.1. Maximum Postbaseline Decrease from Baseline in HBsAg (log_{10} IU/mL)

The baseline value and lowest change from baseline value after study Day 1 for each participant will be summarized for virally suppressed CHB participants assigned to active treatment within each cohort (5, 6, and 7), and all CHB participants assigned to placebo using an 8-number summary.

Maximum Postbaseline Decrease from Baseline in HBsAg (log_{10} IU/mL) is calculated as:

(Lowest change from baseline value after Day 1 for HBsAg [log_{10} IU/mL]) × −1

The maximum postbaseline decrease from baseline in HBsAg (log_{10}) for each participant will be used to classify the participant's best HBsAg (log_{10} IU/mL) response: ≥ 1 log_{10} decrease from baseline; 0.5 to < 1.0 log_{10} decrease from baseline, < 0.5 log_{10} IU/mL decrease from baseline.

6.3.2. HBsAg Serology Results

A summary table will be provided for HBsAg-related serology results for participants on active treatment within each cohort (5, 6, and 7), and for all CHB participants assigned to placebo for the FAS (participants with HBsAg positive at baseline). The proportion of participants who have ever had HBsAg loss, confirmed HBsAg loss, HBsAg loss with HBsAb seroconversion, HBsAg loss with HBsAb seroreversion, and HBsAg loss reversion with or without HBsAb seroconversion will be summarized.

HBV serology definitions:

- **HBsAg loss**: HBsAg changing from positive at baseline to negative at any postbaseline visit.
- **Confirmed HBsAg loss**: HBsAg loss confirmed by any 2 consecutive results.
- **HBsAg loss reversion**: Any postbaseline HBsAg positive result following HBsAg loss.
- **HBsAb seroconversion**: HBsAb changing from negative or missing at baseline to positive at any postbaseline visit.
- **Confirmed HBsAb seroconversion**: HBsAb changing from negative or missing at baseline to positive at any postbaseline visit confirmed by any 2 consecutive results.
- **HBsAb seroreversion**: Any postbaseline HBsAb negative result following HBsAb seroconversion.

Both baseline and postbaseline borderline results for HBeAg, HBeAb, HBsAg, and HBsAb will be imputed as follows:

- HBsAg and HBeAg results reported as "Equivocal" will be considered HBsAg positive and HBeAg positive, respectively. HBsAb and HBeAb reported as "Equivocal" will be considered HBsAb negative and HBeAb negative, respectively for purposes of analysis
- HBsAg result reported as "Positive Confirmed" will be considered HBsAg "Positive"

Missing data will be treated as a nonevent unless otherwise specified (eg, no HBsAg loss, no seroconversion, etc.)

6.3.3. HBeAg Serology Results

A summary table will be provided for HBeAg-related serology results for participants on active treatment within each cohort (5, 6, and 7), and for all CHB participants assigned to placebo for the FAS (participants with HBeAg positive at baseline). The proportion of participants who have ever had HBeAg loss, confirmed HBeAg loss, HBeAg loss with HBeAb seroconversion, HBeAg loss with HBeAb seroreversion, and HBeAg loss reversion with or without HBeAb seroconversion will be summarized.

HBeAg-related terminology is defined similarly to the HBsAg-related terminology.

No statistical testing is planned.

7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

Displays for AEs and deaths will be presented separately for each population by treatment group (active group within each cohort and all participants [within population] who received placebo) for the Safety Analysis Set.

7.1.1. Adverse Event Dictionary

Clinical and laboratory adverse events (AEs) will be coded using the current version of Medical Dictionary for Regulatory Activities (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 Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0 (November 2017). 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 the 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 default to the investigator's choice, not that of the medical monitor. For this study, relationship is recorded separately for GS-2829/PBO and GS-6779/PBO and for related to any study drug (eg, related to either [or both] of the 2 study drugs). Events for which the investigator did not record relationship to study drug will show the relationship as missing.

7.1.4. Relationship of Adverse Events to Study Procedure

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

7.1.5. 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 Gilead Patient Safety Department before database finalization.

7.1.6. Treatment-Emergent Adverse Events

7.1.6.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as any AE with a start date on or after the study drug start date; or any AE that led to premature disocontinuation of study drug.

7.1.6.2. Incomplete Dates

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

An AE with completely missing start and stop dates, or with the start date missing and a stop date later than the first dosing date of study drug, will be considered to be treatment emergent. In addition, an AE with the start 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 dosing date of study drug will be considered treatment emergent.

7.1.7. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be presented separately for each population and summarized by treatment group (active group within each cohort and all participants [within population] assigned to placebo) for the Safety Analysis Set. For displays of AEs "related to study drug", events marked as related to either GS-2829/PBO or to GS-6779/PBO in the database will be included. For displays of AEs related to each of the individual study drugs (eg, related to GS-2829 and related to GS-6779), the relatedness for the study drug of interest recorded in the database will be used. For the placebo group, events related to "GS-2829 PBO" or "GS-6779 PBO" will be counted as related to placebo for the viral vector of interest; and only participants taking at least 1 dose of active drug (or placebo for placebo group) for the viral vector of interest will be included in the denominator for the percentage calculations.

7.1.7.1. 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 separately for each population by treatment group (active group within each cohort and all participants [within population] assigned to placebo). 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
- TEAEs Related to Study Drug
- TEAEs Related to Study Drug with Grade 3 or Higher
- TEAEs Related to Study Drug with Grade 2 or Higher
- TEAEs Related to GS-2829/PBO
- TEAEs Related to GS-2829/PBO with Grade 3 or Higher
- TEAEs Related to GS-2829/PBO with Grade 2 or Higher
- TEAEs Related to GS-6779/PBO
- TEAEs Related to GS-6779/PBO with Grade 3 or Higher
- TEAEs Related to GS-6779/PBO with Grade 2 or Higher
- TE Serious AEs
- TE Serious AEs Related to Study Drug
- TE Serious AEs Related to GS-2829/PBO
- TE Serious AEs Related to GS-6779/PBO
- TEAEs Leading to Premature Discontinuation of Study Drug
- TEAEs Leading to Premature Discontinuation of Study
- Death During the Study

Multiple events will be counted only once per participant in each category.

For the AE categories described below, summaries will be provided separately for each population and will be summarized by treatment group (active group within each cohort and all participants [within population] assigned to placebo), SOC and PT:

- TEAEs by severity
- TEAEs with Grade 3 or Higher, by severity
- TEAEs with Grade 2 or Higher
- TE Treatment-Related AEs, by severity
- TEAEs Related to Each of the Individual Study Drugs
- TE Treatment-Related AEs with Grade 3 or Higher, by severity
- TE Treatment-Related AEs with Grade 2 or Higher
- TE Serious AEs
- TE Treatment-Related Serious AEs
- TEAEs Leading to Interruption of Any Study Drug
- TEAEs Leading to Premature Discontinuation of Any Study Drug

Multiple events will be counted only once per participant in each summary. Adverse events will be summarized first in alphabetic order of SOC, and then by PT in descending order of total frequency for the population within SOC. 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 to the above summary tables, all TEAEs, TE SAEs, and TE treatment-related AEs, will be summarized separately for each population by treatment group (active group within each cohort and all participants [within population] assigned to placebo), and PT only, in descending order of total frequency of PT within population. Preferred terms with the same total population frequency will additionally be sorted in alphabetic order.

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

- All AEs, indicating whether the event is treatment emergent
- All SAEs
- All Deaths

- All AEs with severity of Grade 3 or higher
- All AEs leading to premature discontinuation of any study drug
- All AEs for COVID-19 and Suspected COVID-19 infection (eg, identified by COVID-19 Standardized MedDRA Query (SMQ) [narrow scope]).

7.1.8. Additional Analysis of Adverse Events

The incidences of drug hypersensitivity, injection site reactions, immune-mediated autoimmune disorders, and flu-like symptoms will be examined. The AE preferred terms or higher level terms (HLTs) corresponding to these events will be determined through the following MedDRA search terms (MST):

A) Hypersensitivity (MedDRA preferred terms that match any of those in MST list "KUR_Hypersensitivity")

B) Injection site reactions (TEAEs with HLT='Injection site reactions' or 'Administration site reactions NEC' [as defined by MST list "KUR_Injection site reactions"])

C) Immune-mediated/Autoimmune Disorders (MedDRA preferred terms that match any of those in MST list "KUR_Immune-mediated disorders")

D) Flu-like Symptoms as defined in MST list for "Flu-Like Symptoms". A separate table will be created for flu-like symptoms related to any of the study drugs.

The number and percentage of participants who experienced the above events (1 table for each AE of interest) will be summarized separately for each population by treatment group and PT.

A corresponding listing for each participant population will be provided for each of the 4 types of AEs.

7.2. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. Summaries of laboratory data will be provided separately for each population by treatment group (active group within each cohort and all participants [within population] assigned to placebo) for the Safety Analysis Set. All data collected after the first dose date of study drug will be included. The analysis will be based on values reported in conventional units. When values are below the limit of quantitation (BLQ), they will be listed as such, and the imputed value will be used for the purpose of calculating summary statistics. Hemolyzed test results will not be included in the analysis, but they will be listed in by-participant laboratory listings.

A by-participant listing for laboratory test results will be provided for each participant population by cohort, participant ID, and visit in chronological order for hematology, coagulation, serum chemistry, urinalysis, screening serology tests (HBV tests [for healthy participants], HIV-1 and HCV), and FSH and pregnancy testing (for females only). Values falling outside of the relevant reference range and/or having a severity Grade of 1 or higher according to CTCAE Version 5.0 will be flagged in the data listings, as appropriate.

No formal statistical testing is planned.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics will be provided separately for each participant population by treatment group (active group within each cohort and all participants [within population] assigned to placebo) and visit for selected laboratory tests (hematocrit, hemoglobin, lymphocytes, neutrophils, white blood cells [WBC], platelets, alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP], total bilirubin, creatine kinase [CK], serum glucose, total cholesterol, lactate dehydrogenase [LDH], creatinine, $eGFR_{CG,}$ and international normalized ratio [INR]) as follows:

- Baseline values
- Values at each postbaseline visit
- Change from baseline at each postbaseline visit

A baseline laboratory value will be defined as the last measurement obtained on or prior to the first dose of study drug. Change from baseline to a postbaseline visit will be defined as the visit value minus the baseline value. The mean, SD, median, Q1, Q3, minimum, and maximum values will be displayed to the reported number of digits; SD values will be displayed to the reported number of digits plus 1.

Median (Q1, Q3*)* change from baseline by visit will be plotted using a line plot for: lymphocytes, neutrophils, WBC, platelets, ALT, AST, and CK. Plots will be produced separately for each population with a line displayed for each treatment group (active group within each cohort and all participants [within population] assigned to placebo).

7.2.2. Graded Laboratory Values

The CTCAE, Version 5.0, 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 (i.e., increased, decreased) will be presented separately.

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

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

7.2.2.2. Summaries of Laboratory Abnormalities

The following summaries (number and percentage of participants) for treatment-emergent laboratory abnormalities will be provided separately for each participant population by treatment group (active group within each cohort and all participants [within population] assigned to placebo) for each lab test. Participants will be categorized according to the most severe postbaseline abnormality grade for a given lab test:

- Graded laboratory abnormalities
- Grade 3 or 4 laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of participants with ≥ 1 nonmissing postbaseline value for the lab test of interest.

A by-participant listing of treatment-emergent laboratory abnormalities, and Grade 3 or 4 laboratory abnormalities will be provided by participant population, cohort, participant ID, 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 and abnormal flags displayed.

7.2.3. Liver-related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing will be examined and summarized separately for each participant population by treatment group (active group within each cohort and all participants [within population] assigned to placebo) using the number and percentage of participants who were reported to have the following laboratory test values for postbaseline measurements:

- ALT and/or AST > 5 × ULN
- ALT > 3 × ULN and Total Bilirubin > 2 × ULN
- AST > 3 × ULN and Total Bilirubin > 2 × ULN

The summary will include data from all postbaseline visits. For individual laboratory tests, subjects will be counted once based on the most severe postbaseline value. For composite endpoints, participants will be counted once when the criteria are met at the same postbaseline visit date. The denominator is the number of participants in the Safety Analysis Set who have at least 1 nonmissing postbaseline value for all relevant tests at the same postbaseline visit date.

A listing of participants who met at least 1 of the criteria above will be provided with ALT, AST, total bilirubin and alkaline phosphatase displayed in the listing for the participant's entire laboratory profile during study. Values that met criteria will be flagged in the listing.

7.3. Body Weight, Height, and Vital Signs

For vital signs data (systolic and diastolic blood pressure, pulse, and temperature) collected on the same date as an injection (eg, Days 1 and 57 for Cohorts 1 and 2; Days 1, 29, 57 and 85 for Cohorts 3, 4, 5, and 6; and Days 1, 29, 57, 85, 113 and 141 for Cohorts 7 and 8) both "Pre-Dose" and "Post-Dose" measurements were to be collected per protocol and will be displayed in summary tables. For displays of BMI and weight and visits where injections were <u>not</u> administered, only the pre-dose measurement [VSTPT_STD='VSPD' in VSPERF eCRF] will be presented in by visit displays (ie, no splitting for "pre-dose" and "post-dose" is required at any of the visits for weight or BMI or for non-injection days where vital signs were collected).

Descriptive statistics will be provided separately for each participant population and will be presented by treatment group (active group within each cohort and all participants [within population] assigned to placebo) for body weight, BMI, and vital signs (both pre-dose and post-dose measurements will be displayed for vital signs collected on dosing dates) as follows:

- Baseline value
- Values at each postbaseline time point [visit or visit/timepoint on injection days for vital signs data]
- Change from baseline at each postbaseline time point [visit or visit/timepoint on injection days for vital signs data]

A baseline value will be defined as the last available value collected on or prior to the first dose of study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value. For vital signs collections on the same date as a study drug injection, separate summary statistics will be displayed for "Day X Pre-dose" and "Day X Post-Dose" for by visit displays. Vital signs visits with no injections administered will be displayed under "Day X Pre-dose"; and for all weight and BMI data.

A by-participant listing of vital signs will be provided separately for each participant population and be sorted by cohort, participant ID number, visit, date and time in chronological order (and the timepoint [pre-dose or post-dose] will be displayed in tbe listing). Body weight, height, and BMI will be provided in a separate listing.

7.4. Prior and Concomitant Medications and Disease-Specific Medications

Prior and concomitant medications collected at screening and during the study will be coded using the current version of the World Health Organization (WHO) Drug Dictionary.

7.4.1. Prior Disease-Specific Medications

Prior disease-specific medications are defined as medications taken before a participant took their first dose of study drug that were recorded on the HBV Treatment eCRF (applicable only for virally suppressed CHB participants in Cohorts 5 to 7). A summary of Hepatitis B Prior Medications will be summarized by treatment group (active group within each cohort and all participants [within population] assigned to placebo) for virally suppressed CHB population.

Disease-specific prior (e.g., anti-HBV)] medications will be listed on the Prior and Concomitant HBV medications listing.

For the purposes of analysis, any medication with a start date prior to the first dosing date of study drug will be included as a prior medication regardless of the stop date. 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 dosing date for study drug. Medications with a completely missing start date will be included as prior medications, unless otherwise specified.

7.4.2. Disease-Specific Concomitant Medications and Concomitant Medications

Concomitant medications are defined as medications taken on or after the first dose of study drug. Healthy Participants (Cohorts 1 to 4; and Cohort 8) will have a single summary of concomitant medications produced.

For the virally suppressed CHB population [participants in cohorts 5 to 7], separate displays will be provided for “disease-specific medications” (eg, medications recorded on the HBV Treatment eCRF) and for “other concomitant medications” (eg, medications recorded on the CM eCRF). Use of concomitant medications will be summarized by preferred name using the number and percentage of participants for each treatment group (active group within each cohort and all participants [within population] assigned to placebo). A participant reporting the same medication more than once will be counted only once when calculating the number and percentage of participants who received that medication. The summary will be ordered by descending overall frequency for preferred term. For preferred terms with the same frequency, sorting will be done alphabetically by preferred term.

For the purposes of analysis, any medications with a start date prior to or on the first dosing date of study drug that continued to be taken after the first dosing date, or medications started after the first dosing date of study drug will be considered to be concomitant medications. Medications started and stopped on the same day as the first dosing date of study drug will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study drug will be excluded from the concomitant medication summary. If a partial stop date is

entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will be excluded from the concomitant medication summary. Medications with completely missing start and stop dates will be included in the concomitant medication summary, unless otherwise specified. Summaries will be based on the Safety Analysis Set.

No formal statistical testing is planned.

All prior and concomitant medications (other than per-protocol study drugs [and HBV medications for virally suppressed CHB participants]) will be provided in by-participant listings for each participant population and be sorted by cohort, participant ID number, and administration date in chronological order.

7.5. Investigator Assessment of Electrocardiogram Results

A shift table of the investigators' assessment of ECG results at each postbaseline visit (Day 85, Day 141, and FU-WK24) compared with the baseline values will be presented separately by participant population. Displays will be by treatment group (active group within each cohort and all participants [within population] assigned to placebo) using the following categories: normal; abnormal, not clinically significant; abnormal, clinically significant; or missing. The number and percentage of participants in each cross-classification group of the shift table will be presented. Participants with a missing value at predose or postdose will not be included in the denominator for percentage calculation. No formal statistical testing is planned.

A by-participant listing for investigator ECG assessment results will be provided separately for each participant population. The listing will be sorted by cohort, participant ID, and date in chronological order.

7.6. Other Safety Measures

A by-participant listing of subject pregnancies during the study will be provided.

No additional safety measures are specified in the protocol.

Although not necessarily related to safety, a by-participant listing of all comments received during the study on the comments eCRF will be provided.

8. PHARMACOKINETIC EVALUATION/ANALYSIS

No pharmacokinetic data was collected for this study.

9. REFERENCES

None.

10. SOFTWARE

SAS® Software Version 9.X. SAS Institute Inc., Cary, NC, USA.

11. SAP REVISION

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

12. APPENDICES

Appendix 1. STUDY PROCEDURES TABLES

Table 12-1. Schedule of Assessments, Phase 1a – Cohorts 1 and 2 (Two Total Doses)

Study Period	**Screen**	**Active Dosing Safety Follow-up**													
Study Day		**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 57**	**Day 64**	**Day 71**	**Day 85**	**Day 113[a]**	**Day 141**	**Day 169[a]**	**Day 197[a]**	**Day 225**	**ET**
Visit Window (Days)	**45 Days**	**N/A**	**± 1**	**± 1**	**± 3**	**± 3**	**± 1**	**± 1**	**± 3**	**± 7**	**± 7**	**± 7**	**± 7**	**± 7**	**N/A**
Study Weeks		**1**	**1**	**2**	**4**	**8**	**9**	**10**	**12**	**16**	**20**	**24**	**28**	**32**	
Dosing (PBO or IP)[b]		X				X									
Written informed consent; I/E criteria; medical history	X														
Adverse events and concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
General Assessments and Laboratory Assessments															
Complete physical examination[c]	X	X				X								X	X
Symptom-directed physical examination[d]			X	X	X		X	X	X		X				
HIV-1, HBV, and HCV testing	X	X[c]				X[c,e]								X[e]	X
Height	X														
Weight	X	X				X								X	X
12-lead ECG	X													X	X
Vital signs	X	X[f]	X	X	X	X[f]	X	X	X		X			X	X

Study Period	**Screen**	**Active Dosing Safety Follow-up**													
Study Day		**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 57**	**Day 64**	**Day 71**	**Day 85**	**Day 113[a]**	**Day 141**	**Day 169[a]**	**Day 197[a]**	**Day 225**	**ET**
Visit Window (Days)	**45 Days**	**N/A**	**± 1**	**± 1**	**± 3**	**± 3**	**± 1**	**± 1**	**± 3**	**± 7**	**± 7**	**± 7**	**± 7**	**± 7**	**N/A**
Study Weeks		**1**	**1**	**2**	**4**	**8**	**9**	**10**	**12**	**16**	**20**	**24**	**28**	**32**	
Urinalysis	X	X[c]		X	X	X[c]		X	X		X			X	X
Hematology[g]	X	X[c]		X	X	X[c]		X	X		X			X	X
FSH[h]	X														
Serum pregnancy test[i]	X	X[c]			X	X[c]			X	X	X	X	X	X	X
Urine pregnancy test[i]		X				X									
Urine drug and alcohol screen	X	X[c]													
Chemistry and liver function tests[j]	X	X[c]		X	X	X[c]		X	X		X			X	X
Creatinine clearance[k]	X	X			X	X								X	X
Coagulation[l]	X	X[c]		X	X	X[c]		X	X		X			X	X
Local and Systemic Reactogenicity															
Dispense participant diary[m]		X				X									
Review Participant diary[m]			X	X			X	X							
Immunology and Biomarkers															
PBMC collection for biomarker cellular assays		X[c]	X	X	X	X[c]	X	X	X		X			X	X

Study Period	**Screen**	**Active Dosing Safety Follow-up**													
Study Day		**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 57**	**Day 64**	**Day 71**	**Day 85**	**Day 113[a]**	**Day 141**	**Day 169[a]**	**Day 197[a]**	**Day 225**	**ET**
Visit Window (Days)	**45 Days**	**N/A**	**± 1**	**± 1**	**± 3**	**± 3**	**± 1**	**± 1**	**± 3**	**± 7**	**± 7**	**± 7**	**± 7**	**± 7**	**N/A**
Study Weeks		**1**	**1**	**2**	**4**	**8**	**9**	**10**	**12**	**16**	**20**	**24**	**28**	**32**	
Serum collection for HBV-targeting antibody measurements		X[c]			X	X[c]			X		X			X	X
Whole blood collection for biomarker analysis		X[c]		X		X[c]		X							X
Clinical Virology															
Serum collection for HBV neutralizing antibody and antivector antibody assessment		X[c]		X	X	X[c]			X		X			X	X

ECG = electrocardiogram; ET = early termination; FSH = follicle-stimulating hormone; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV-1 = human immunodeficiency virus type 1; I/E = inclusion/exclusion; IP = investigational product; N/A = not applicable; PBMC = peripheral blood mononuclear cell; PBO = placebo; Screen = screening

a These visits are only required for pregnancy testing for women of childbearing potential. Participants who are able to access an at-home urine pregnancy test from the clinical site may conduct their pregnancy test at home and will be contacted by site staff to confirm the result. If urine pregnancy results are equivocal or positive, a serum pregnancy test will be required.

b Participant shall receive the appropriate investigational product or PBO, as detailed in Section 5.3 and Table 8 of the study protocol. Sentinel participants will be observed at the study site for at least 8 hours after investigational product administration on Day 1, and for at least 4 hours following each administration of investigational product for all subsequent doses. All other Phase 1a participants will be monitored in the clinic for at least 4 hours following each dose of investigational product. Participants will receive a follow-up phone call for 2 consecutive days following each dose to review protocol restrictions, adverse events, any concomitant medication usage, and completion of participant diaries.

c Collection of vital signs, physical examination, and blood/urine samples should be completed prior to investigational product administration.

d Symptom-driven physical examinations shall be performed as deemed necessary.

e At the discretion of the investigator.

f Indicated assessment shall be performed prior to dosing and within 15 to 30 minutes following investigational product administration.

g Hematology assessments are listed in Section 6.4.5 of the study protocol.

h An FSH test is required for participants assigned female at birth who are younger than 54 years, not on hormonal contraception, and who have stopped menstruating for at least 12 months but do not have documentation of ovarian hormonal failure.

i For participants assigned female at birth and of childbearing potential. On days of investigational product administration, urine pregnancy testing is also required to determine pregnancy status prior to dosing.

j Chemistry and liver function assessments are listed in Section 6.4.5 of the study protocol.
k Central laboratory will calculate creatinine clearance.
l Coagulation assessments are listed in Section 6.4.5 of the study protocol.
m Participants will be asked to record potential vaccine reactions based on solicited events via diary for 7 days following each administration of investigational product. Review of participant reactogenicity data will occur at each visit after vaccination up to 7 days postdose or beyond for cases with ongoing events after 7 days postdose.

Table 12-2. Schedule of Assessments, Phase 1a – Cohorts 3, 4 and Phase 1b - Cohorts 5 and 6 (Four Total Doses)

Study Period	**Screen**	**Active Dosing**								**Safety Follow-up**								
Study Day		**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 43**	**Day 57**	**Day 71**	**Day 85**	**Day 92**	**Day 99**	**Day 113**	**Day 141[a]**	**Day 169**	**Day 197[a]**	**Day 225[a]**	**Day 253**	**ET**
Visit Window (Days)	**45 Days**	**N/A**	**± 1**	**± 1**	**± 3**	**± 1**	**± 3**	**± 1**	**± 3**	**± 1**	**± 1**	**± 3**	**± 7**	**± 7**	**± 7**	**± 7**	**± 7**	**N/A**
Study Weeks		**1**	**1**	**2**	**4**	**6**	**8**	**10**	**12**	**13**	**14**	**16**	**20**	**24**	**28**	**32**	**36**	
Dosing (PBO or IP)[b]		X			X		X		X									
Written informed consent; I/E criteria; medical history	X																	
Adverse events and concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
General Assessments and Laboratory Assessments																		
Complete physical examination[c]	X	X			X		X		X								X	X
Symptom-directed physical examination[d]			X	X		X		X		X	X	X		X				
HIV-1 testing	X																X[e]	X
HBV testing[p]	X	X[c]							X[c,e]								X[e]	X
HCV testing	X																X[e]	X
HDV testing[l]	X																	
Height	X																	
Weight	X	X			X		X		X								X	X
12-lead ECG	X								X								X	X
Vital signs	X	X[f]		X	X[f]	X	X[f]	X	X[f]	X	X	X		X			X	X
Urinalysis	X	X[c]			X[c]		X[c]	X	X[c]		X	X		X			X	X
Hematology[g]	X	X[c]		X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
FSH[h]	X																	
Serum pregnancy test[i]	X	X[c]			X[c]		X[c]		X[c]			X	X	X	X	X	X	X

Study Period	**Screen**	**Active Dosing**								**Safety Follow-up**								
Study Day		**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 43**	**Day 57**	**Day 71**	**Day 85**	**Day 92**	**Day 99**	**Day 113**	**Day 141[a]**	**Day 169**	**Day 197[a]**	**Day 225[a]**	**Day 253**	**ET**
Visit Window (Days)	**45 Days**	**N/A**	**± 1**	**± 1**	**± 3**	**± 1**	**± 3**	**± 1**	**± 3**	**± 1**	**± 1**	**± 3**	**± 7**	**± 7**	**± 7**	**± 7**	**± 7**	**N/A**
Study Weeks		**1**	**1**	**2**	**4**	**6**	**8**	**10**	**12**	**13**	**14**	**16**	**20**	**24**	**28**	**32**	**36**	
Urine pregnancy test[i]		X[c]			X[c]		X[c]		X[c]									
Urine drug and alcohol screen	X	X																
Chemistry and liver function tests[j]	X	X[c]		X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
Creatinine clearance[k]	X	X			X		X		X								X	X
Autoantibody test[l]		X																
FibroScan for participants with none in past 6 months[l]	X																	
Coagulation[m]	X	X[c]		X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
Local and Systemic Reactogenicity																		
Dispense participant diary[n]		X			X		X		X									
Review participant diary[n]			X	X		X		X		X	X							
Immunology and Biomarkers																		
PBMC collection for biomarker cellular assays		X[c]	X	X	X[c]	X	X[c]	X	X[c]	X	X	X		X				X
Serum collection for HBV-targeting antibody measurements		X[c]			X[c]		X[c]		X[c]			X		X				X
Whole blood collection for biomarker analysis		X[c]		X	X[c]	X	X[c]	X	X[c]		X							X

Study Period	Screen	Active Dosing								Safety Follow-up								
Study Day		**Baseline Day 1**	**Day 8**	**Day 15**	**Day 29**	**Day 43**	**Day 57**	**Day 71**	**Day 85**	**Day 92**	**Day 99**	**Day 113**	**Day 141[a]**	**Day 169**	**Day 197[a]**	**Day 225[a]**	**Day 253**	**ET**
Visit Window (Days)	**45 Days**	**N/A**	**± 1**	**± 1**	**± 3**	**± 1**	**± 3**	**± 1**	**± 3**	**± 1**	**± 1**	**± 3**	**± 7**	**± 7**	**± 7**	**± 7**	**± 7**	**N/A**
Study Weeks		**1**	**1**	**2**	**4**	**6**	**8**	**10**	**12**	**13**	**14**	**16**	**20**	**24**	**28**	**32**	**36**	
Clinical Virology																		
HBV neutralizing antibody and antivector antibody assessment		X[c]		X	X[c]		X[c]		X[c]			X		X			X	X
HBV viral biomarkers[o,l]		X[c]		X	X[c]		X[c]		X[c]			X		X			X	X
HBV genomic sequencing[l]		X[c]			X[c]		X[c]		X[c]			X		X			X	X
HBV genotyping[l]	X	X[c]																

DNA = deoxyribonucleic acid; ECG = electrocardiogram; ET = early termination; FSH = follicle-stimulating hormone; HBcrAg = hepatitis B core-related antigen; HBeAg = hepatitis B e antigen; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HDV = hepatitis D virus; HIV-1 = human immunodeficiency virus type 1; I/E = inclusion/exclusion; IP = investigational product; N/A = not applicable; PBMC = peripheral blood mononuclear cell; PBO = placebo; RNA = ribonucleic acid; Screen = screening

a These visits are only required for pregnancy testing for women of childbearing potential. Participants who are able to access an at-home urine pregnancy test from the clinical site may conduct their pregnancy test at home and will be contacted by site staff to confirm the result. If urine pregnancy results are equivocal or positive, a serum pregnancy test will be required.

b Participant shall receive the appropriate investigational product or PBO, as detailed in Section 5.3 and Table 8 of the study protocol. Participants in Cohorts 3 and 4 will be monitored in the clinic for at least 4 hours following each dose of investigational product. Participants in Cohorts 5 and 6 will be monitored in the clinic for at least 2 hours following each dose of investigational product. Participants may be required to remain in the clinic for additional observation at the discretion of the investigator. Participants will receive a follow-up phone call for 2 consecutive days following each dose to review protocol restrictions, adverse events, any concomitant medication usage, and completion of participant diaries.

c Collection of vital signs, physical examinations, and blood/urine samples should be completed prior to investigational product administration.

d Symptom-driven physical examinations shall be performed as deemed necessary.

e At the discretion of the investigator.

f Indicated assessment shall be taken prior to dosing and within 15 to 30 minutes following investigational product administration.

g Hematology assessments are listed in Section 6.4.5 of the study protocol.

h An FSH test is required for participants assigned female at birth who are younger than 54 years, not on hormonal contraception, and who have stopped menstruating for at least 12 months but do not have documentation of ovarian hormonal failure.

i For participants assigned female at birth and of childbearing potential. On days of investigational product administration, urine pregnancy testing is also required to determine pregnancy status prior to dosing.

j Chemistry and liver function assessments are listed in Section 6.4.5 of the study protocol.

k Central laboratory will calculate creatinine clearance.

l Required for Phase 1b only.

m Coagulation assessments are listed in Section 6.4.5 of the study protocol.
n Participants will be asked to record potential vaccine reactions based on solicited events via diary for 7 days following each administration of investigational product. Review of participant reactogenicity data will occur at each visit after vaccination up to 7 days postdose or beyond for cases with ongoing events after 7 days postdose.
o To include the assessments of: HBV DNA, quantitative HBsAg, anti-HBsAg antibody, HBcrAg, HBeAg, HBV RNA.
p Phase 1a: HBV testing is for HBsAg with reflex to HBV DNA, and hepatitis B core antibody. Phase 1b: HBV testing is for HBsAg, hepatitis B core antibody, HBV DNA, and quantitative HBsAg.

Table 12-3. Schedule of Assessments, Phase 1a – Cohort 8 and Phase 1b - Cohort 7 (Six Total Doses)

Study Period	Screen	Active Dosing												Safety Follow-up								
Study Day		Base-line Day 1	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85	Day 99	Day 113	Day 127	Day 141	Day 148	Day 155	Day 169	Day 197[a]	Day 225	Day 253[a]	Day 281[a]	Day 309	ET
Visit Window (Days)	45 Days	N/A	±1	±1	±3	±1	±3	±1	±3	±1	±3	±3	±3	±3	±7	±7	±7	±7	±7	±7	±7	N/A
Study Weeks		1	1	2	4	6	8	10	12	14	16	18	20	21	22	24	28	32	36	40	44	
Dosing (PBO or IP)[b]		X			X		X		X		X		X									
Written informed consent; I/E criteria; medical history	X																					
Adverse events and concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
General Assessments and Laboratory Assessments																						
Complete physical examination[c]	X	X			X		X		X		X		X								X	X
Symptom-directed physical examination[d]			X	X		X		X		X		X		X	X	X		X				
HIV-1 testing	X																				X[e]	X
HBV testing[p]	X	X[c]							X[c,e]												X[e]	X
HCV testing	X																				X[e]	X
HDV testing[l]	X																					
Height	X																					
Weight	X	X			X		X		X		X		X								X	X
12-lead ECG	X								X				X								X	X
Vital signs	X	X[f]		X	X[f]	X	X[f]	X	X[f]	X	X[f]	X	X[f]	X	X	X		X			X	X
Urinalysis	X	X[c]			X[c]		X[c]	X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
Hematology[g]	X	X[c]		X	X[c]	X	X[c]	X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
FSH[h]	X																					
Serum pregnancy test[i]	X	X[c]			X[c]		X[c]		X[c]		X[c]		X[c]			X	X	X	X	X	X	X

Study Period	Screen	Active Dosing												Safety Follow-up								
Study Day		Base-line Day 1	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85	Day 99	Day 113	Day 127	Day 141	Day 148	Day 155	Day 169	Day 197[a]	Day 225	Day 253[a]	Day 281[a]	Day 309	ET
Visit Window (Days)	45 Days	N/A	± 1	± 1	± 3	± 1	± 3	± 1	± 3	± 1	± 3	± 3	± 3	± 3	± 7	± 7	± 7	± 7	± 7	± 7	± 7	N/A
Study Weeks		1	1	2	4	6	8	10	12	14	16	18	20	21	22	24	28	32	36	40	44	
Urine pregnancy test[i]		X[c]			X[c]		X[c]		X[c]		X[c]		X[c]									
Urine drug and alcohol screen	X	X																				
Chemistry and liver function tests[j]	X	X[c]		X	X[c]	X	X[c]	X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
Creatinine clearance[k]	X	X			X		X		X		X		X					X			X	X
Autoantibody test[l]		X																				
FibroScan for participants with none in past 6 months[l]	X																					
Coagulation[m]	X	X[c]		X	X[c]	X	X[c]	X	X[c]	X	X[c]	X	X[c]		X	X		X			X	X
Local and Systemic Reactogenicity																						
Dispense participant diary[n]		X			X		X		X		X		X									
Review participant diary[n]			X	X		X		X		X		X			X							
Immunology and Biomarkers																						
PBMC collection for biomarker cellular assays		X[c]	X				X[c]	X	X[c]	X	X[c]	X	X[c]	X	X	X		X				X
Serum collection for HBV-targeting antibody measurements		X[c]			X[c]		X[c]		X[c]		X[c]		X[c]			X		X				X

Study Period	Screen	Active Dosing												Safety Follow-up								
Study Day		Base-line Day 1	Day 8	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85	Day 99	Day 113	Day 127	Day 141	Day 148	Day 155	Day 169	Day 197[a]	Day 225	Day 253[a]	Day 281[a]	Day 309	ET
Visit Window (Days)	45 Days	N/A	± 1	± 1	± 3	± 1	± 3	± 1	± 3	± 1	± 3	± 3	± 3	± 3	± 7	± 7	± 7	± 7	± 7	± 7	± 7	N/A
Study Weeks		1	1	2	4	6	8	10	12	14	16	18	20	21	22	24	28	32	36	40	44	
Whole blood collection for biomarker analysis		X[c]					X[c]	X	X[c]	X	X[c]	X	X[c]		X							X
Clinical Virology																						
HBV neutralizing antibody and antivector antibody assessment		X[c]		X	X[c]		X[c]		X[c]		X[c]		X[c]			X		X			X	X
HBV viral biomarkers[o,l]		X[c]		X	X[c]		X[c]		X[c]		X[c]		X[c]			X		X			X	X
HBV genomic sequencing[l]		X[c]			X[c]		X[c]		X[c]		X[c]		X[c]			X		X			X	X
HBV genotyping[l]	X	X[c]																				

DNA = deoxyribonucleic acid; ECG = electrocardiogram; ET = early termination; FSH = follicle-stimulating hormone; HBcrAg = hepatitis B core-related antigen; HBeAg = hepatitis B e antigen; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; HDV = hepatitis D virus; HIV-1 = human immunodeficiency virus type 1; I/E = inclusion/exclusion; IP = investigational product; N/A = not applicable; PBMC = peripheral blood mononuclear cell; PBO = placebo; RNA = ribonucleic acid; Screen = screening

a These visits are only required for pregnancy testing for women of childbearing potential. Participants who are able to access an at-home urine pregnancy test from the clinical site may conduct their pregnancy test at home and will be contacted by site staff to confirm the result. If urine pregnancy results are equivocal or positive, a serum pregnancy test will be required.

b Participant shall receive the appropriate investigational product or PBO, as detailed in Section 5.3 and Table 8 of the study protocol. Participants in Cohort 7 will be monitored in the clinic for at least 2 hours following each dose of investigational product. Participants may be required to remain in the clinic for additional observation at the discretion of the investigator. Participants will receive a follow-up phone call for 2 consecutive days following each dose to review protocol restrictions, adverse events, any concomitant medication usage, and completion of participant diaries.

c Collection of vital signs, physical examinations, and blood/urine samples should be completed prior to investigational product administration.

d Symptom-driven physical examinations shall be performed as deemed necessary.

e At the discretion of the investigator.

f Indicated assessment shall be taken prior to dosing and within 15 to 30 minutes following investigational product administration.

g Hematology assessments are listed in Section 6.4.5 of the study protocol.

h An FSH test is required for participants assigned female at birth who are younger than 54 years, not on hormonal contraception, and who have stopped menstruating for at least 12 months but do not have documentation of ovarian hormonal failure.

i For participants assigned female at birth and of childbearing potential. On days of investigational product administration, urine pregnancy testing is also required to determine pregnancy status prior to dosing.
j Chemistry and liver function assessments are listed in Section 6.4.5 of the study protocol.
k Central laboratory will calculate creatinine clearance.
l Required for Phase 1b only.
m Coagulation assessments are listed in Section 6.4.5 of the study protocol.
n Participants will be asked to record potential vaccine reactions based on solicited events via diary for 7 days following each administration of investigational product. Review of participant reactogenicity data will occur at each visit after vaccination up to 7 days postdose or beyond for cases with ongoing events after 7 days postdose.
o To include the assessments of: HBV DNA, quantitative HBsAg, anti-HBsAg antibody, HBcrAg, HBeAg, HBV RNA.
p HBV testing is for HBV surface antigen and antibody