STATISTICAL ANALYSIS PLAN

Study Title:	A Randomized, Blinded, Placebo-Controlled, Phase 1b Study of GS-5718 in Subjects with Cutaneous Lupus Erythematosus (CLE)
Name of Test Drug:	GS-5718
Study Number:	GS-US-497-5888
Protocol Version (Date):	Amendment 1 (01 July 2021)
Analysis Type:	Final Analysis
Analysis Plan Version:	Final 1.0
Analysis Plan Date:	13 February 2023
Analysis Plan Author(s):	PPI PPI

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

ACLE	acute cutaneous lupus erythematosus
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BLQ	below the limit of quantitation
BMI	body mass index
CI	confidence interval
CLASI	cutaneous lupus erythematosus disease area and severity index
CLASI-A	CLASI-Activity
CLASI-D	CLASI-Damage
CLE	cutaneous lupus erythematosus
CRF	case report form
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
ECG	electrocardiogram
eCRF	electronic case report form
ET	early termination
FAS	Full Analysis Set
HLGT	high-level group term
HLT	high-level term
HLT	high-level term
LOQ	limit of quantitation
LTT	lower-level term
MedDRA	Medical Dictionary for Regulatory Activities
PK	pharmacokinetics
PT	preferred term
PTM	Placebo-to-match
Q1, Q3	first quartile, third quartile
QD	Once a day
SAE	Serious adverse events
SAP	statistical analysis plan
SCLE	subacute cutaneous lupus erythematosus
SD	standard deviation
SE	standard error
SGA	subject’s global assessment
SLE	systemic lupus erythematosus
SLEDAI-2K	systemic lupus erythematosus disease activity index - 2000
SOC	system organ class

TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
ULN	upper limit of normal
VAS	Visual Analog Scale
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) in the clinical study report (CSR) for Study GS-US-497-5888. This SAP is based on the study protocol amendment 1 dated 01 July 2021 and the electronic case report forms (eCRF). The SAP will be finalized before database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

The decision to discontinue the study has been made on 18 October 2022. The screening has been stopped on 20 December 2021, with total 3 participants enrolled in the study. Of the 3 enrolled participants, 2 participants completed the study and 1 participant was prematurely terminated by sponsor.

This SAP describes the analyses to support the abbreviated CSR.

1.1. Study Objectives

The primary objective of this study is as follows:

- To evaluate the safety and tolerability of GS-5718 in participants with CLE with or without systemic lupus erythematosus (SLE)

The secondary objectives of this study are as follows:

- To characterize the PK of GS-5718 in participants with CLE with or without SLE

The exploratory objectives of this study are as follows:

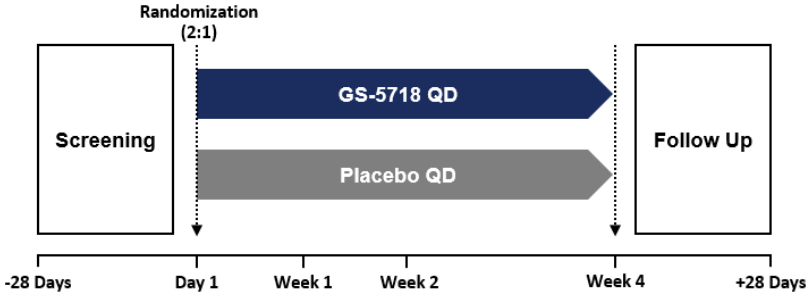
1.2. Study Design

This is a Phase 1b, multicenter, randomized, sponsor-unblinded, placebo-controlled, 4-week study evaluating the safety and tolerability of GS-5718 in participants with CLE. Adult male or female participants at ≥ 18 and ≤ 75 years of age who either fulfill EULAR/ACR 2019 classification criteria for SLE or have biopsy-proven CLE and have acute CLE (ACLE)/subacute CLE (SCLE) with cutaneous lupus erythematosus disease area and severity index {Klein 2010} (CLASI) activity score of ≥ 6 during screening and Day 1 may be eligible for entry (refer to the protocol for complete inclusion and exclusion criteria). Eligible participants are randomly assigned to 1 of the following 2 treatment groups in a 2:1 ratio:

- GS-5718 115 mg once a day in addition to standard of care for 4 weeks (n = 8)
- Placebo-to-match (PTM) once a day in addition to standard of care for 4 weeks (n = 4)

A schematic of this study is provided in Figure 1-1.

Figure 1-1. Study Design Schema



1.3. Sample Size and Power

Sample size was determined based on practical considerations and no sample size calculation was performed. A sample size of 12 participants (8 participants randomized to GS-5718 and 4 participants randomized to placebo) would provide a suitable assessment of the descriptive safety and pharmacokinetics (PK) profile.

The enrollment was stopped after 3 participants were randomized.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

No interim analysis is planned.

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.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

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

By-participant listings will be presented for all participants in the All Randomized Analysis Set and sorted by participant ID number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within the participant. The treatment group to which participants were randomized 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. Participants included in each analysis set will be determined before the study blind is broken for analysis. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

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 in the study.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes all randomized participants who took at least 1 dose of study drug. This is the primary analysis set for efficacy analyses.

3.1.3. Safety Analysis Set

The Safety Analysis Set includes all participants who took at least 1 dose of study drug. This is the primary analysis set for safety analyses.

3.2. Participant Grouping

For analyses based on the FAS, participants will be grouped according to the treatment to which they were randomized. For analyses based on the Safety Analysis Set, participants will be grouped according to the actual treatment received. The actual treatment received will differ from the randomized treatment only when their actual treatment differs from randomized treatment for the entire treatment duration.

3.3. Strata and Covariates

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

3.4. Examination of Participant Subgroups

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

3.5. Multiple Comparisons

Adjustments for multiplicity will not be made.

3.6. Missing Data and Outliers

3.6.1. Missing Data

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

For missing last dosing date of study drug, imputation rules are described in Section 4.2. The handling of missing or incomplete dates for AE onset is described in Section 7.1.5.2, 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.

Partial CLE/SLE diagnosis dates will be imputed using same rules as for the partial dates of birth.

In general, age collected at Day 1 (in years) 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 an enrolled 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., estimates of creatinine clearance, age at date of AE) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

The 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).

3.8. Analysis Visit Windows

3.8.1. Definition of Study Day

Study day will be calculated from the first dosing date of study drug 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 study drug administration.

3.8.2. Definition of Baseline

Baseline will be defined as the last nonmissing value on or prior to the first dosing date of study drug. All visits, including unscheduled visits, prior to the first dosing date of study drug, will be used for baseline derivation. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the average of the measurements for continuous data, or the measurement with the lowest severity (e.g., normal will be selected over abnormal for safety electrocardiogram [ECG] findings) for categorical data.

3.8.3. Analysis Visit Windows

No analysis visit windows will be derived for this study. The baseline and relevant nominal visits as recorded on the CRF will be used when data are summarized by visit. Any data relating to unscheduled visits will not be assigned to a particular visit or time point. However, the following exceptions will be made:

- An unscheduled visit prior to the first dosing of study drug may be included in the calculation of the baseline value, if applicable.
- Unscheduled visits after the first dose 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 summarized as a separate visit, labeled as “Early Termination Visit”.
- Data collected on a follow-up visit will be summarized as a separate visit and labeled “Follow-up Visit”.
- Data obtained after the follow-up visit or last dose date plus 28 days (whichever is later) will be excluded from the summaries but will be included in the listings.

All records will be listed by collection date.

4. PARTICIPANT DISPOSITION

4.1. Participant Enrollment and Disposition

Key study dates (i.e., 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.

No summary of participant enrollment will be provided. Relevant patient enrollment information will be presented in a by-participant listing.

The randomization schedule used for the study will be provided as an appendix to the CSR. Randomization scheme will be presented in a by-participant listing.

A summary of participant disposition will be provided by treatment group. This summary will present the number of participants in each of the categories listed below:

- Screened
- All Randomized Analysis Set
- Safety Analysis Set
- Full 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. The denominator for the percentage calculation will be the total number of participants in the Safety Analysis Set corresponding to that column. In addition, a flowchart will be provided to depict the disposition.

The following by-participant listings will be provided by participant identification (ID) number in ascending order to support the above summary tables:

- Reasons for premature study drug or study discontinuation
- Reasons for exclusion from analysis sets
- Lot number and bottle ID of assigned study drugs

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and the level of adherence relative to the study drug regimen specified in the protocol.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (e.g., 4.5 weeks). If the last study drug dosing date is missing, the latest date among the study drug end date, clinical visit date, laboratory sample collection date, and vital signs assessment date that occurred during the on-treatment period will be used for participants included in the final analyses. If month and year of the last dose are known, and the last study drug dosing date imputed above is different from the month collected, the last date of that month will be used. If only year of the last dose is known, and the last study drug dosing date imputed above is after the year collected, the last date of that year will be used; if the last study drug dosing date imputed above is before the year collected, the first date of that year will be used.

The total duration of exposure to study drug will be summarized using descriptive statistics and using the number (i.e., cumulative counts) and percentage of participants exposed through the following time periods: Baseline (Day 1), Week 1 (Day 8), Week 2 (Day 15) and Week 4 (Day 29). Summaries will be provided by treatment group for the Safety Analysis Set.

No formal statistical testing is planned.

4.2.2. Prescribed Adherence to Study Drug

The presumed total number of doses administered to a participant will be determined by the data collected on the drug accountability CRF using the following formula:

$$\text{Total Number of Doses Administered} = \left(\sum \text{No. of Doses Dispensed}\right) - \left(\sum \text{No. of Doses Returned}\right)$$

The level of prescribed adherence to the study drug regimen will be determined by the total amount of study drug administered relative to the total amount of study drug specified by the protocol for a participant who completes treatment in the study.

The level of prescribed adherence will be expressed as a percentage using the following formula:

$$\text{Prescribed Adherence (\%)} = \left(\frac{\text{Total Amount of Study Drug Administered}}{\text{Total Amount of Study Drug Specified by Protocol}} \right) \text{x } 100$$

If a bottle was dispensed and returned empty, then the number of tablets returned will be entered as zero. If a bottle is dispensed but not returned (missing) then the number of tablets from that bottle will be counted as zero.

If calculated adherence is greater than 100%, the result will be set to 100%.

The prescribed adherence to study drug will not be summarized but listed.

A by-participant listing of study drug administration and drug accountability will be provided separately by participant ID number (in ascending order) and visit (in chronological order).

4.3. Protocol Deviations

A by-participant listing will be provided for those participants who did not meet at least 1 eligibility (inclusion or exclusion) criterion, but enrolled in the study. The listing will present the eligibility criterion (or criteria if more than 1 deviation) that participants did not meet and related comments, if collected.

Important protocol deviations occurring after participants entered the study are documented during routine monitoring. A by-participant listing will be provided for those participants with important protocol deviation.

4.4. Assessment of COVID-19 Impact

Study conduct was not impacted by the novel coronavirus (COVID-19) pandemic. No analyses will be provided for the assessment of COVID-19 impact.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Participant demographic variables (i.e., age, sex, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2]) will be summarized by treatment group and overall 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 by participant ID number in ascending order.

5.2. Other Baseline Characteristics

Other baseline characteristics include:

- Time from CLE diagnosis to enrollment (years)
- CLE disease subtype
- SLE diagnosis (yes/ no)
- Time from SLE diagnosis to enrollment (years)
- CLASI-Activity (CLASI-A) score at baseline
- CLASI-Damage (CLASI-D) score at baseline
- Subject's global assessment (SGA) of CLE activity (mm) at baseline
- Physician's global assessment (PGA) of CLE activity (mm) at baseline

These baseline characteristics will be summarized by treatment group and overall using descriptive statistics for continuous variables and using number and percentage of participants for categorical variables. The summary of these baseline characteristics will be provided for the Safety Analysis Set. No formal statistical testing is planned.

The time from CLE/SLE diagnosis to enrollment will be calculated in years between the date of enrollment and the date of diagnosis, as (the date of enrollment – the date of diagnosis +1)/365.25.

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

5.3. Medical History

Medical history will be collected at screening for disease-specific and general conditions (i.e., conditions not specific to the disease being studied). Both medical history data will not be coded and will be listed only.

6. EFFICACY ANALYSES

6.1. Exploratory Efficacy Endpoint

6.1.1. Definition of Exploratory Efficacy Endpoints

The exploratory efficacy endpoints include:

6.1.2. Analysis Methods for Exploratory Efficacy Endpoints

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7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

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

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to toxicity criteria using CTCAE v5.0. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

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

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if the AEs met the definitions of SAEs that were specified in the study protocol. SAEs captured and stored in the clinical database will be reconciled with the SAEs in the Patient Safety database before data finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as 1 or both of the following:

- Any AEs with an onset date on or after the study drug start date and no later than 28 days after permanent discontinuation of study drug
- Any AEs leading to premature discontinuation of study drug.

7.1.5.2. Incomplete Dates

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dosing date of study drug, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset is the same as or after the month and year (or year) of the first dosing date of study drug, and
- The AE onset date is the same as or before the month and year (or year) of the date corresponding to 28 days after the date of the last dose of study drug

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

7.1.6. Summaries of Adverse Events and Deaths

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

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 by treatment group. All deaths observed in the study will also be included in this summary.

The number and percentage of participants who experienced at least 1 TEAE will be provided and summarized by treatment group for the following:

- TEAEs
- TEAEs with Grade 3 or higher
- TEAEs with Grade 2 or higher
- TEAE Related to Study Drug
- TEAE Related to Study Drug with Grade 3 or Higher
- TEAE Related to Study Drug with Grade 2 or Higher
- TE Serious AE
- TE Serious AE Related to Study Drug
- TEAE leading to discontinuation of study drug
- TEAE leading to discontinuation of study
- TE AE leading to death (i.e., outcome of death)

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

In addition, data listings will be provided for all AEs and all SAEs indicating whether the event is treatment emergent, and all deaths.

7.2. Laboratory Evaluations

A by-participant listings for laboratory test results will be provided by participant ID number and visit in chronological order for hematology, serum chemistry, and urinalysis separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on the Common Terminology Criteria for Adverse Events (CTCAE severity grade) 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 for laboratory tests will not be provided. Hematology, chemistry and urinalysis results will be listed.

7.2.2. Graded Laboratory Values

The CTCAE v5.0 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 postbaseline time point, up to and including the date of last dose of study drug plus 28 days for participants who permanently discontinued study drug. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent.

7.2.2.2. Summaries of Laboratory Abnormalities

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

For all summaries of laboratory abnormalities, the denominator is the number of participants with nonmissing postbaseline values up to 28 days after last dosing date.

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

7.2.3. Liver-related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing will be examined using following criteria based on the laboratory test values for postbaseline measurements:

- Aspartate aminotransferase (AST): (a) > 3 times of the upper limit of reference range (ULN); (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Alanine aminotransferase (ALT): (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- AST or ALT: (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Total bilirubin: > 2 x ULN
- Alkaline phosphatase (ALP) > 1.5 x ULN
- AST or ALT > 3 x ULN and total bilirubin: (a) > 1.5 x ULN; (b) > 2 x ULN

A listing of liver test results by visit for participants who met at least 1 of the above criteria will be provided.

7.3. Body Weight , Height, and Vital Signs

A by-participant listing of vital signs will be provided by participant ID number and visit in chronological order. In the same manner, a by-participant listing of body weight, height, and BMI will be provided separately.

7.4. Prior and Concomitant Medications

Medications collected at screening and during the study will be coded using the March 2022 version of the World Health Organization (WHO) Drug dictionary version.

7.4.1. Prior Medications

Prior medications are defined as any medications taken before a participant took the first study drug.

Any medication with a start date prior to the first dosing date of study drug will be considered prior regardless of when the stop date is. If a partial start date is entered the medication will be considered prior unless the month and year (if day is missing) or year (if day and month are missing) of the start date are after the first dosing date. Medications with a completely missing start date will be considered prior, unless otherwise specified.

7.4.2. Concomitant Medications

Concomitant medications are defined as medications taken while a participant took study drug.

Any medications with a start date prior to or on the first dosing date of study drug and continued to be taken after the first dosing date, or started after the first dosing date but prior to or on the last dosing date of study drug will be considered concomitant medications. Medications started and stopped on the same day as the first dosing date or the last 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 or a start date after the last dosing date of study drug will not be considered concomitant. 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 not be considered concomitant. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date not be considered concomitant. Medications with completely missing start and stop dates will be cosidered concomitant, unless otherwise specified.

Prior and concomitant medications will not be summarized in the study.

All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-participant listing sorted by participant ID number and administration date in chronological order. The general prior and concomitant medication and CLE/SLE-specific prior and concomitant medications will be presented separately.

7.5. Electrocardiogram Results

By-participant listings for overall assessment of electrocardiogram (ECG) and 12-lead ECG results will be provided by participant ID number and visit in chronological order.

7.5.1. Corrected QT Intervals

The QT interval (measured in millisecond [msec]) is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. The QT interval represents electrical depolarization and repolarization of the ventricles. The QT interval is affected by heart rate, and a number of methods have been proposed to correct QT for heart rate.

Corrected QT (QTc) intervals will be derived using Fridericia's correction (QTcF) as follows:

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

where QT is measured in msec; RR = 60/Heart Rate (beats per min [bpm]) and RR is measured in seconds.

7.6. Other Safety Measures

No additional safety measures are specified in the protocol.

7.7. Changes From Protocol-Specified Safety Analyses

Only limited safety summaries are provided due to small number of participants enrolled in the study prior to study termination.

8. PHARMACOKINETIC (PK) ANALYSES

Pharmacokinetic analyses will not be performed.

9. REFERENCES

Klein RS, Morganroth PA, Werth VP. Cutaneous Lupus and the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) Instrument. Rheumatic diseases clinics of North America 2010;36 (1):33-51, vii.

10. SOFTWARE

SAS® Software Version 9.4. 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. Schedule of Assessments

Procedure	Screening V0	Study Treatment Period				Early Termination[b]	Follow Up	Instructions
		Day 1	Week 1	Week 2	Week 4			
	−28[a]	0[a]	+7 Days[a] (±2 Days)	+14 Days[a] (±2 Days)	+28 Days[a] (±2 Days)	Any	+28 Days[a] (±5 Days)	
Informed Consent	X							Written, signed, and dated informed consent **must** be obtained prior to screening
Inclusion/Exclusion Criteria	X	X						Documentation of select criteria **must** be submitted to the study sponsor for review and confirmation of participant eligibility
Medical History, Demographics, Substance Use	X							Medical history will include demographics, a review of surgical history, and CLE/SLE history
Prior and Concomitant Medications	X	X	X	X	X	X	X	
Height	X							Participants should be instructed to remove shoes prior to baseline height measurement
Weight	X	X	X	X	X	X	X	
Vital Signs	X	X	X	X	X	X	X	Blood pressure, Pulse, Respiratory Rate, Temperature
12-Lead ECG	X			X	X	X	X	Resting ECG, performed and assessed locally; for participants with chest lesions, study assessments should precede ECG, as applicable
Complete Physical Examination	X							
Symptom-Driven Physical Examination		X	X	X	X	X	X	Performed, as needed, based on signs and symptoms
CLASI Assessment	X	X	X	X	X	X	X	Participants **must** have a CLASI activity (CLASI-A) score of ≥ 6 (excluding the alopecia component) during screening and Day 1

Procedure	Screening V0 −28[a]	Study Treatment Period: Day 1 0[a]	Week 1 +7 Days[a] (±2 Days)	Week 2 +14 Days[a] (±2 Days)	Week 4 +28 Days[a] (±2 Days)	Early Termination[b] Any	Follow Up +28 Days[a] (±5 Days)	Instructions
Photography of Skin Lesion(s)	X	X	X	X	X	X	X	Participant identifying features should be obscured, as much as possible. Follow-up photographs **must** target the same area of clinically active disease evaluated and photographed at baseline.
SLEDAI-2K Assessment		X		X	X	X	X	To be completed for participants with concurrent SLE
Subject's Global Assessment	X	X	X	X	X	X	X	Subject's global assessment of CLE disease activity (visual analogue scale)
Physician's Global Assessment	X	X	X	X	X	X	X	Physician's global assessment of CLE disease activity (visual analogue scale)
Chemistry	X	X	X	X	X	X	X	See protocol
Hematology	X	X	X	X	X	X	X	See protocol
Fasting Lipids		X			X			No food or drinks, except water for at least 8 hours prior to blood sample collection
Serum Pregnancy Test	X							Females of childbearing potential only (see protocol)
Urine Pregnancy Test		X	X	X	X	X	X	Females of childbearing potential only (see protocol)
FSH Test	X							Females of nonchildbearing potential only (see protocol)
Urine drug and Alcohol screen	X							
Urinalysis	X	X	X	X	X	X	X	
Urine Biomarkers		X		X	X	X	X	Day 1 sample to be taken predose
Urine Spot Protein/Creatinine Ratio		X		X	X	X	X	
QuantiFERON®-TB Gold In-Tube test	X							Not required for participants with prior latent TB who have been treated with a full course of prophylaxis
HIV, HBV, and HCV Serology	X							

Procedure	Screening V0	Study Treatment Period				Early Termination[b]	Follow Up	Instructions
		Day 1	Week 1	Week 2	Week 4			
	−28[a]	0[a]	+7 Days[a] (±2 Days)	+14 Days[a] (±2 Days)	+28 Days[a] (±2 Days)	Any	+28 Days[a] (±5 Days)	
HCV Serology					X			Only applicable for participants with baseline positive HCV antibody and negative HCV RNA VL
Skin Biopsy FFPE (4 mm)		X			X			A separate manual will be provided for skin biopsy instructions. Skin biopsies should be performed at the end of the respective visit after all other study procedures have been completed, as much as possible. Day 1 biopsies are to be taken predose.
Skin Biopsy RNA later (2-4 mm)		X			X			
PaxGene RNA Sample		X	X	X	X	X	X	Day 1 sample to be taken predose
Immunophenotyping Whole Blood		X		X	X	X	X	
TBNK Whole Blood		X		X	X	X	X	
Antinuclear Antibody by IFA	X							
ENA panel (anti-Sm, -RNP, -Ro, -La) and antiphospholipid antibodies		X						
Anti-dsDNA antibody		X		X	X	X	X	Day 1 sample to be taken for all participants. Samples thereafter only applicable for participants with concurrent SLE.
Complement Panel (C3, C4, CH50)		X		X	X	X	X	Day 1 sample to be taken predose
Quantitative Serum Immunoglobulin Test		X			X	X	X	
Serum Biomarker		X	X	X	X	X	X	Day 1 sample to be taken predose
Plasma Biomarker		X	X	X	X	X	X	Day 1 sample to be taken predose
Viably Frozen PBMC		X		X	X	X	X	Day 1 sample to be taken predose
CCI								

Procedure	Screening V0 −28[a]	Study Treatment Period: Day 1 0[a]	Week 1 +7 Days[a] (±2 Days)	Week 2 +14 Days[a] (±2 Days)	Week 4 +28 Days[a] (±2 Days)	Early Termination[b] Any	Follow Up +28 Days[a] (±5 Days)	Instructions
Intensive Plasma PK					X[d]			Participants will be instructed to fast prior to this clinic visit and take the dose at the clinic on the intensive PK sampling day
Randomization (IRT)		X						
Study Drug Dispensed		X						Final Day 1 procedure
Study Drug Accountability		X			X	X		
Adverse Event(s)	X	X	X	X	X	X	X	AE reporting begins after the participant signs the ICF until 28 days after the last dose of study drug, regardless of causality

CLE = cutaneous lupus erythematosus; dsDNA = double-stranded deoxyribonucleic acid; ECG = electrocardiogram; ENA = extractable nuclear antigen; FFPE = formalin-fixed paraffin-embedded; FSH = follicle-stimulating hormone; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; ICF = informed consent form; IFA = indirect fluorescent antibody; IRT = interactive response technology; PBMC = peripheral blood mononuclear cell; PK = pharmacokinetic; RNA = ribonucleic acid; SLE = systemic lupus erythematosus; TB = tuberculosis; TBNK = T cell/B cell/Natural Killer cell; VL = viral load

a All visits are anchored to Day 1 (eg, screening is up to 28 days prior to Day 1, the Week 1 visit is 7 days after Day 1, with a window of plus or minus 2 days)

b The early termination (ET) visit can satisfy the follow up (FU) visit if it takes place ≥ 28 days following the last dose of study drug

c CCI [redacted]

d Intensive plasma PK sampling will occur prior to the dose (≤ 5 min before dose) (at the Week 4 visit) and at 0.5, 1, 2, 3, 4, and 6 hours postdose (collection window: ± 5 minutes for the 0.5 and 1 hour PK sample; ± 15 minutes for the other time points)