Statistical Analysis Plan

INCB 54707-203

A Phase 2, Dose-Escalation, Placebo-Controlled Study of the Safety of INCB054707 in Participants With Hidradenitis Suppurativa

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SAP Version:	**Original**
SAP Author:	[redacted]
Date of Plan:	**01 MAR 2019**

This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

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LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
AN	abscess and inflammatory nodule
BMI	body mass index
CRF	case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DLQI	Dermatology Quality of Life Index
eCRF	electronic case report form
ECG	electrocardiogram
EOS	end of study
FAS	full analysis set
HiSCR	Hidradenitis Suppurativa Clinical Response
[redacted]	[redacted]
HS	hidradenitis suppurativa
IBD	inflammatory bowel disease
[redacted]	[redacted]
MedDRA	Medical Dictionary for Regulatory Affairs
NCI	National Cancer Institute
NRS	numeric rating scale
PCOS	polycystic ovarian syndrome
[redacted]	[redacted]
PGIC	Patient Global Impression of Change
[redacted]	[redacted]
PT	preferred term
QD	once daily
QTcF	QT interval corrected for heart rate using Fridericia's formula
SAP	statistical analysis plan
SOC	system organ class
SRC	safety review committee
TB	tuberculosis
TEAE	treatment-emergent adverse event
WHO	World Health Organization

1. INTRODUCTION

This is a Phase 2, multicenter, randomized, placebo controlled, dose escalation study to evaluate the safety of INCB054707 [redacted] over an 8-week treatment period in men and women aged 18 to 75 years with moderate to severe HS.

The study includes 3 cohorts, and approximately 36 participants will be enrolled. In each cohort, approximately 12 participants will be randomized in a 3:1 ratio to receive either INCB054707 (n = 9) or placebo (n = 3). The total duration of therapy for all enrolled participants is 8 weeks followed by a 30-day safety follow-up period. After all participants in each cohort have completed the Week 4 study visit and assessments, a SRC will review safety data.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 54707-203 Protocol.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 54707-203 Protocol Amendment 1 dated 09 AUG 2018 and CRFs approved 28 AUG 2018. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the safety and tolerability of INCB054707.	• Frequency, duration, and severity of AEs, clinical laboratory test results, vital signs results, ECGs, and physical examination findings.
Secondary	
To determine the systemic exposure to INCB054707.	• Population PK parameters of INCB054707.
To determine the efficacy of INCB054707.	• Proportion of participants achieving a HiSCR at each visit. • Proportion of participants achieving an AN count of 0 to 2 at each visit. • Mean change from baseline in the HS Pain NRS scores, worst and average pain, at each visit. • Mean change from baseline to Week 8 in the modified Sartorius scale score. • Mean change from baseline in the number of draining fistulas count at each visit. • Proportion of participants at each category of Hurley Stage at baseline and Week 8. • Proportion of participants with change from baseline in Hurley Stage at Week 8. • Proportions of participants in each HS-PGIC category during the treatment period. • Actual measurements in HS-PGIC at each visit.
To assess the need for rescue lesional treatment.	• Proportion of participants requiring rescue lesional treatment. • Number of interventions with rescue lesional treatment.
To assess patient-reported quality-of-life burden.	• Proportion of participants at each scoring category of DLQI at each visit. • Mean change from baseline in DLQI total scores at each visit.
[redacted]	

3. STUDY DESIGN

This is a Phase 2, multicenter, randomized, placebo controlled, dose escalation study to evaluate the safety of INCB054707 [redacted] over an 8-week treatment period in men and women aged 18 to 75 years with moderate to severe HS with a targeted enrollment of approximately 36 participants.

The study includes 3 cohorts, and approximately 36 participants will be enrolled. In each cohort, approximately 12 participants will be randomized to receive either INCB054707 (n = 9) or placebo (n = 3; randomization 3:1). The total duration of therapy for all enrolled participants is 8 weeks followed by a 30-day safety follow-up period. After all participants in each cohort have completed the Week 4 study visit and assessments, a SRC will review safety data.

3.1. Randomization

The study includes 3 cohorts, and approximately 36 participants will be enrolled. In each cohort, approximately 12 participants will be randomized in a 3:1 ratio to receive either INCB054707 (n = 9) or placebo (n = 3).

3.2. Control of Type I Error

All statistical analyses are exploratory in nature. No alpha control will be implemented. Unless otherwise specified, all confidence intervals provided will be at the 95% confidence level.

3.3. Sample Size Considerations

The study is a standard dose-escalation design, and the sample size depends on the occurrence of safety findings. Approximately 9 participants will be randomized in each dose level, which will provide > 85% chance of detecting at least 1 AE of interest (eg, platelets, hemoglobin, absolute neutrophil count, liver functions, and infections) if the underlying rate is 20%.

3.4. Schedule of Assessments

See Protocol Amendment 1 dated 09 AUG 2018 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations

4.1.1. Day 1

Day 1 is the date that the first dose of study drug (INCB054707) or placebo is administered to the participants.

4.1.2. Study Day

If a visit/reporting date is on or after Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (Visit/Reporting Date – Day 1 date + 1).

If the visit/reporting date is before Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (Visit/Reporting Date – Day 1 date).

A study day of –1 indicates 1 day before Day 1.

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of INCB054707 or placebo.

When scheduled assessments and unscheduled assessments occur on the same day and time of the assessment or time of first dose is not available, use the following convention to determine baseline:

- If both a scheduled and an unscheduled visit are available on the day of the first dose and the time is missing, use the scheduled assessment as baseline.
- If all scheduled assessments are missing on the day of the first dose and an unscheduled assessment is available, use the unscheduled assessment as baseline.

4.1.4. Last Available Value

The last available value is the last nonmissing measurement obtained after starting INCB054707 or placebo and within 30 days after the last dose of INCB054707 or placebo.

4.1.5. Handling of Missing and Incomplete Data

In general, values for missing data will not be imputed unless methods for handling missing data are specified in relevant sections.

4.2. Variable Definitions

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

$$\text{BMI } (kg/m^2) = [\text{weight } (kg)] / [\text{height } (m)]^2$$

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB054707 or placebo.

Concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB054707 and is ongoing throughout the study or ends on/after the date of first study drug administration.
- On/after the date of first administration of INCB054707 and is ongoing or ends during the course of study drug administration.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first administration of INCB054707. In the listing, it will be indicated whether a medication is prior-only, concomitant-only, or both prior and concomitant.

The start/stop dates recorded in the eCRF by the investigator and his/her research staff will be used to identify when a concomitant medication was taken during the study. Any missing start date must be queried for resolution. Unresolved missing start dates will be handled as follows:

- If the date is completely missing, the medication will be considered both prior and concomitant.
- If only the day is missing, and the last day of the month is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as the last day of the month.
- If only the day is missing, and the first day of the month is after the first dose date on Day 1, then the concomitant medication will be considered as starting after Day 1, and the incomplete date will be imputed as the first day of the month.
- If only the day is missing, and the month is equal to the month of the first dose date on Day 1, then the incomplete date will be imputed as the first day of the month.
- If both the month and day are missing, and the last day of the year is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as if it is the last day of the year. Otherwise, the incomplete date will be imputed as if it is the first day of the year.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.1 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include, but not be limited to, the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is a randomized, dose-escalation, placebo-controlled study. Up to 90-mg doses will be tested. Data will be summarized overall and by treatment group based on the dose regimen initially assigned.

5.3. Analysis Populations

5.3.1. Full Analysis Set

The FAS includes all participants enrolled in the study who received at least 1 dose of study drug.

The FAS will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all efficacy and safety data.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

6.1. Baseline and Demographics, Physical Characteristics, and Disease History

6.1.1. Demographics

The following demographics will be summarized for the FAS: age, sex, race, ethnicity, weight, height, and BMI.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized for the FAS:

- Days since first onset of HS;
- Stable disease at least 90 days before screening (Yes/No);
- Other autoimmune disorders (Hyperlipidemia/Hypertension/Diabetes/Abdominal obesity/Arthritis/IBD: Crohn disease/IBD: Ulcerative colitis/Psoriasis/Spondylarthropathy/PCOS/Other/None).

6.1.3. Prior Therapy

Prior medication information for HS will be used to identify medication received by participants before enrollment into the study. Prior medications for HS will be summarized.

6.1.4. General Medical History

For participants in the FAS, general medical history will be summarized by assigned treatment group. This summation will include the number and percentage of participants with significant medical history for each body system/organ class as documented on the eCRF.

6.2. Disposition of Participants

The number and percentage of participants who were enrolled, randomized, treated, completed the study, discontinued study treatment with a primary reason for discontinuation, and discontinued from the study with a primary reason for withdrawal will be summarized for the FAS. The number of participants randomized/enrolled by site will also be provided by treatment group.

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be presented in the participant data listings and tables.

6.4. Exposure

For participants in the FAS, descriptive statistics will be provided by treatment group for duration of treatment, average daily dose, and total dose. Duration of treatment with INCB054707 is defined as the number of days from Day 1 to the date of last record of INCB054707 administration.

6.5. Study Drug Compliance

For participants in the FAS, overall compliance (%) for INCB054707 will be calculated for all participants as

Compliance (%) = 100 × [total number of tablets dispensed – total number of tablets returned] / [total intended number of tablets].

- The total intended number of tablets will be based on the earliest study day of permanent discontinuation of the study drug or last study drug record in the database.

6.6. Prior and Concomitant Medication

For participants in the FAS, prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized by WHO drug class and WHO drug term. Results will be summarized as number and percentage of participants with prior and concomitant medications by preferred term and WHO drug class.

7. EFFICACY

All efficacy analyses are exploratory. Hence, no p-values will be provided and multiple adjustment will not be made.

Appendix A provides a list of planned tables, figures, and listings.

7.1. Efficacy Parameters

An example of the lesion count worksheet is provided in the Study Manual and will be used for assessment of Hurley Stage, HiSCR, modified Sartorius scale, [redacted] It includes assessment of 12 anatomic regions:

- left/right axilla,
- left/right sub/inframammary area,
- intermammary area,
- left/right buttock,
- left/right inguino-crural fold,
- perianal area, perineal area,
- and other areas.

Additionally, the need for rescue lesional treatment, including number of interventions, will be documented in this worksheet.

7.1.1. Hurley Stages of Hidradenitis Suppurativa

Hurley Stages of HS are defined in Table 2. The investigator will determine the Hurley Stage in each affected anatomical region at the designated study visits. If more than 1 stage is present in a region, the worst stage in each region should be documented. The participant is assigned Hurley Stage corresponding to the Hurley Stage of his or her worst involved anatomic region.

Table 2: Hurley Stages of Hidradenitis Suppurativa

Stage	Description
I	Abscess formation (single or multiple) without sinus tracts and cicatrization
II	Recurrent abscesses with tract formation and cicatrization; single or multiple, widely separated lesions
III	Diffuse or near-diffuse involvement or multiple interconnected tracts and abscesses across the entire area

7.1.2. Hidradenitis Suppurativa Clinical Response (Abscess and Inflammatory Nodule Count)

A HiSCR definition is based on the following criteria relative to the baseline at each visit:

- at least 50% reduction in total of counts of the abscess and inflammatory nodule, and
- no increase in abscess count, and
- no increase in draining fistula count (refer to the Study Manual; Kimball et al 2016).

7.1.3. Modified Sartorius Scale

The modified Sartorius scale is a measure of the severity of HS (refer to the Study Manual; Sartorius et al 2003). A larger score denotes a more severe disease status. The total Sartorius score is the sum of 12 anatomic region Sartorius scores. The regional Sartorius score can be calculated as follows, using the parameters in Table 3:

Regional Sartorius Score = Region + (2 × Number of Inflammatory Nodules) + (2 × Number of Non-Inflammatory Nodules) + (4 × Number of Abscesses) + (4 × Number of Draining Fistulas) + (4 × Number of Non-Draining Fistulas) + (1 × Number of Hypertrophic Scars) + Distance + Separate.

Table 3: Sartorius Score

Region	0	Otherwise
	3	If any lesion count in this anatomic region > 0
Distance	0	If no active lesion
	2	If longest distance between two relevant lesions or size < 50 mm
	4	If longest distance between two relevant lesions or size ≥ 50 mm and < 100 mm
	6	If longest distance between two relevant lesions or size ≥ 100 mm
Separate	0	If all lesions clearly separated by normal appearing skin
	6	Otherwise

7.1.4. Need for Rescue Lesional Treatment

Study procedures must be performed before any interventions. Any lesion undergoing an intervention will be documented in the lesion count worksheet (refer to the Study Manual). The site will be required to count any lesion that undergoes an intervention as permanently present from the date of the intervention, and must account for it in the source and on the appropriate eCRF.

7.1.5. Hidradenitis Suppurativa Pain Numeric Rating Scale

The HS Pain NRS will be completed in a daily diary by participants from screening through the follow-up visit (EOS). An 11-point scale will be used to assess the worst skin pain and the average skin pain due to HS based on a recall period of the last 24 hours. Ratings for the 2 items range from 0 (no skin pain) to 10 (skin pain as bad as you can imagine).

7.1.6. Analgesic Use

From Day 1 through the follow-up visit (EOS), participants will complete a daily electronic diary of their analgesic use (yes/no; refer to the Study Manual). All analgesics and dose modifications will be captured in the source and on the appropriate eCRF.

7.1.7. Hidradenitis Suppurativa Patient Global Impression of Change

Participants will complete the HS-PGIC questionnaire at the designated study visits. The HS-PGIC consists of 1 self-administered item that assesses change in the severity of skin in the HS area. Participants are asked to indicate their impression of change compared with their last visit. The participant will answer the following: Since your last visit, your HS is: (1) very much improved, (2) much improved, (3) minimally improved, (4) no change, (5) minimally worse, (6) much worse, or (7) very much worse.

7.1.8. Dermatology Life Quality Index

Participants will complete a DLQI questionnaire from screening through the follow-up visit (EOS). The DLQI will be used to assess the symptoms and the impact of skin problems on quality of life (Hongbo et al 2005). The DLQI can be used to evaluate 6 areas: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Participants will be asked to respond to the 10 questions of the DLQI based on a recall period of "the last week." The scoring of each question is as follows:

Very much	Scored 3
A lot	Scored 2
A little	Scored 1
Not at all	Scored 0
Not relevant	Scored 0
Question 7, 'prevented work or studying'	Scored 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The meaning of DLQI scores can be categorized as:

Score	Interpretation
0-1	No effect at all on patient's life
2-5	Small effect on patient's life
6-10	Moderate effect on patient's life
11-20	Very large effect on patient's life
21-30	Extremely large effect on patient's life

[redacted]

[redacted]

7.2. Analysis of Efficacy Endpoints

The efficacy endpoints include:

- Proportion of participants with a HiSCR (at least 50% reduction in AN count with no increase in abscess count and no increase in draining fistula count relative to baseline) at each visit;
- Proportion of participants achieving an AN count of 0 to 2 at each visit;
- Mean change from baseline in the HS Pain NRS scores, worst and average pain, at each visit;
- Mean change from baseline to Week 8 in the modified Sartorius scale score;
- Mean change from baseline in the number of draining fistulas count at each visit;
- Proportion of participants at each category of Hurley Stage at baseline and Week 8;
- Proportion of participants with change from baseline in Hurley Stage at Week 8;
- Proportions of participants in each HS-PGIC category during the treatment period;
- Actual measurements in HS-PGIC at each visit;
- Proportion of participants requiring rescue lesional treatment;
- Number of interventions with rescue lesional treatment;
- Proportion of participants at each scoring category of DLQI at each visit;
- Mean change from baseline in DLQI total scores at each visit;
- [redacted]

Category variables will be summarized using descriptive statistics, including sample size, frequency, and percentages. Continuous variables will be summarized using descriptive statistics, including sample size, mean, median, standard deviation, standard error of the mean, minimum, and maximum.

[redacted]

8. SAFETY AND TOLERABILITY

Appendix A provides a list of planned tables, figures, and listings.

8.1. General Considerations

Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique preferred terms reported on relatively few participants.

Unless otherwise stated, table summaries will be limited to AEs occurring within 30 days of the last administration of study drug.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after first administration of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE. The CTCAE v4.03 is used for this study. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. The incidence of AEs and treatment-related AEs will be tabulated. Serious TEAEs will also be tabulated.

Any missing onset date, causality, or severity must be queried for resolution. Unresolved missing causality and severity will be handled according to the following rules:

- An unresolved missing causality will be considered treatment-related.
- An unresolved missing severity will be identified as an unknown severity.

For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

8.2.2. Adverse Event Summaries

An overall summary of AEs will include:

- Number (%) of participants reporting any TEAEs
- Number (%) of participants reporting any serious TEAEs
- Number (%) of participants reporting any Grade 3 or higher TEAEs
- Number (%) of participants reporting any treatment-related TEAEs
- Number (%) of participants who temporarily interrupted study treatment because of TEAEs

- Number (%) of participants who permanently discontinued study treatment because of TEAEs
- Number (%) of participants who had a TEAE leading to death

The following summaries will be produced by MedDRA term (if 2 or fewer participants appear in a table, a listing may be appropriate):

- Summary of TEAEs by SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of TEAEs by SOC, PT, and maximum severity
- Summary of treatment-related TEAEs by SOC and PT
- Summary of treatment-related TEAEs by PT in decreasing order of frequency
- Summary of treatment-related TEAEs by SOC, PT, and maximum severity
- Summary of Grade 3 or higher TEAEs by SOC and PT
- Summary of Grade 3 or higher treatment-related TEAEs by PT
- Summary of Grade 3 or higher TEAE by PT in decreasing order of frequency
- Summary of TEAEs leading to death by SOC and PT
- Summary of serious TEAEs by SOC and PT
- Summary of serious TEAEs by PT in descending order of frequency
- Summary of serious treatment-related TEAEs by SOC and PT
- Summary of TEAEs leading to dose interruption by SOC and PT
- Summary of TEAEs leading to discontinuation of treatment by SOC and PT
- Summary of nonserious TEAEs by SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

All laboratory assessments (refer to Protocol Table 11) will be performed using a central laboratory except for urine pregnancy tests (as applicable) or tests that are deemed necessary by the investigator for participant management (refer to Protocol Section 8.3.5). Laboratory values, change from baseline values, and percent change from baseline values will be summarized descriptively by visit. Baseline values will be determined using the nonmissing values collected before the first administration, prioritizing scheduled assessments over unscheduled visits. For baseline laboratory candidates with the same date and time in the same priority category, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline.

8.3.2. Laboratory Value Summaries

Clinical laboratory tests, including hematology, serum chemistry, urinalysis, lipid panel, serology, C-reactive protein, follicle-stimulating hormone, serum pregnancy test, urine pregnancy test, and QuantiFERON-TB Gold test (refer to Protocol Table 11), will be performed for each participant during the study in accordance with study schedule of assessments (refer to Protocol Table 3). If specific safety issues arise, additional unscheduled laboratory tests/analyses may be performed at the discretion of the investigator.

All test results and associated normal ranges from central laboratories will be reported in SI units. All tests with numeric values will have a unique unit per test. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units. For the limited number of cases where the associated normal ranges from a local laboratory cannot be obtained despite due diligence, associated central laboratory normal ranges will be applied. In the event that central laboratory normal ranges are not available, a set of standard normal ranges based upon documented reference ranges will be applied to facilitate reporting the test results.

When there are multiple laboratory nonmissing values for a participant's particular test within a visit window, the smallest laboratory sequence number will be used to identify the record for postbaseline visits.

Laboratory parameters identified in Protocol Table 11 will be summarized. Shift tables based on worst postbaseline value recorded will use all postbaseline values occurring within 30 days of stopping study treatment. Other laboratory parameters collected will only be listed in an appendix to the CSR in their original units without SI conversions.

Actual values and changes from baseline in clinical laboratory test results will be summarized using descriptive statistics. Laboratory test values outside the normal range will be assessed for severity based on the normal ranges for the clinical reference laboratory. The incidence of abnormal laboratory values will be tabulated.

Laboratory data will be classified into Grades 1 through 5 using CTCAE v4.03. The following summaries will be produced for the laboratory data:

- Number and percentage of participants with worst postbaseline CTCAE grade (regardless of baseline value). Each participant will be counted only for the worst grade observed postbaseline.
- Shift tables from baseline to the worst postbaseline value using CTCAE grade. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the treatment period.
- For laboratory parameters where CTCAE grades are not defined, shift tables to the worst postbaseline value using the low/normal/high classifications based on laboratory reference ranges.

8.4. Vital Signs

Values at each scheduled visit, change, and percentage change from baseline for vital signs, including systolic blood pressure, diastolic blood pressure, pulse, body temperature, and respiratory rate will be summarized descriptively.

Criteria for clinically notable vital sign abnormalities are defined in Table 4. The abnormal values for participants exhibiting clinically notable vital sign abnormalities will be listed. Alert vital signs are defined as an absolute value outside the defined range and percentage change greater than 25%. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 4: Criteria for Clinically Notable Vital Sign Abnormalities

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mmHg	< 85 mmHg
Diastolic blood pressure	> 100 mmHg	< 40 mmHg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38°C	< 35.5°C
Respiratory rate	> 24 breaths/min	< 8 breaths/min

8.5. Electrocardiograms

All 12-lead ECGs will be performed as indicated in Table 5 with the participant in a recumbent or semirecumbent position after at least 5 minutes of rest. Additional 12-lead ECGs may be performed at other visits as deemed clinically necessary. Electrocardiograms will be interpreted by the investigator at the site, and the results will be used for immediate management of the participant's care. The decision to include or exclude a participant or withdraw a participant from the study based on an ECG flagged as "Abnormal, Clinically Significant" is the responsibility of the investigator, in consultation with the sponsor's medical monitor, as appropriate. Any abnormalities that are considered clinically significant in the judgment of the investigator are to be reported as AEs.

Descriptive statistics and mean change from baseline will be determined for each ECG parameter at each assessment time. Change and percentage change from baseline will be calculated. Triple ECGs will be measured at baseline and postbaseline visits if necessary. Electrocardiogram abnormalities, both at baseline and postbaseline visits, will be tabulated. Incidences of abnormalities will be listed with study visit, and a description of the abnormality.

Table 5: Electrocardiogram Schedule

Study Visit	Timing of Electrocardiogram Relative to Administration of Study Drug		
	Not Applicable	Predose (Trough) ECG[a]	Postdose (Postdose 2) ECG[b]
Screening[c]	Single → Triple[d]		
Day 1		Triple[e]	Single → Triple[d]
Week 4		Single → Triple[d]	Single → Triple[d]
Week 8		Single → Triple[d]	

[a] Predose ECG should be performed 5 to 10 minutes before the predose [redacted].
[b] Postdose ECGs will be performed after participants complete all of the study assessments but before the collection of the second postdose (postdose 2) [redacted]. Postdose ECG will be measured 5 to 10 minutes before the postdose (postdose 2) [redacted] collection.
[c] Prolonged QTcF values of ≥ 450 ms at screening are to be confirmed by performing 2 additional ECGs and averaging the results to determine whether the averaged value meets the exclusion criterion.
[d] Single → Triple: Single ECG will be performed first. If prolonged QT interval (corrected for heart rate using Fridericia's formula [QTcF], defined as ≥ 450 ms) are observed, an additional 2 ECGs will be measured within the next 5 minutes.
[e] Day 1 predose ECG will be performed in triplicate, and values will be averaged to calculate the baseline values.

9. INTERIM ANALYSES

No formal interim analysis is planned in this study.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 6.

Table 6: Statistical Analysis Plan Versions

SAP Version	Date
Original	01 MAR 2019

10.1. Changes to Protocol-Defined Analyses

Not applicable.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

Kimball AB, Sobell JM, Zouboulis CC, et al. HiSCR (Hidradenitis Suppurativa Clinical Response): a novel clinical endpoint to evaluate therapeutic outcomes in patients with hidradenitis suppurativa from the placebo-controlled portion of a phase 2 adalimumab study. J Eur Acad Dermatol Venereol 2016;30:989-994.

Sartorius K, Lapins J, Emtestam L, Jemec GB. Suggestions for uniform outcome variables when reporting treatment effects in hidradenitis suppurativa. Br J Dermatol 2003;149:211-213.

Hongbo Y, Thomas CL, Harrison MA, Salek MS, Finlay AY. Translating the science of quality of life into practice: what do dermatology life quality index scores mean? J Invest Dermatol 2005;125:659-664.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the CSR. Shells are provided for nonstandard tables in a separate document. In-text tables are identical in structure and content as appendix tables, but follow a Rich Text Format.

The lists of tables, figures, and listings are to be used as guidelines. Modifications of the lists that do not otherwise affect the nature of the analysis will not warrant an amendment to the SAP.

Tables

Table No.	Title	Population
Baseline and Demographic Characteristics		
1.1 Disposition		
1.1.1	Analysis Populations	FAS
1.1.2	Summary of Participant Disposition	FAS
1.1.3	Summary of Number of Participants Enrolled By Site	FAS
1.2 Demography		
1.2.1	Summary of Demographics	FAS
1.3 Baseline Characteristics		
1.3.1	Summary of Baseline Disease Characteristics	FAS
1.4 Prior Medication and Concomitant Medication		
1.4.1	Summary of Prior Medications	FAS
1.4.2	Summary of Prior Medications for Hidradenitis Suppurativa	FAS
1.4.3	Summary of Concomitant Medications	FAS
1.5 Others		
1.5.1	Summary of General Medical History	FAS
1.5.2	Summary of Protocol Deviations	FAS
Efficacy		
2.1.1	Summary of Participants With a HiSCR by Visit	FAS
2.1.2	Summary of Participants Achieving an AN Count of 0 to 2 by Visit	FAS
2.1.3.1	Summary of HS Pain NRS Score From Baseline to End of Study (Worst Pain)	FAS
2.1.3.2	Summary of HS Pain NRS Score From Baseline to End of Study (Average Pain)	FAS
2.1.4	Summary of Modified Sartorius Scale Score From Baseline to Week 8	FAS
2.1.5	Summary of Draining Fistulas Count From Baseline to End of Study	FAS
2.1.6.1	Summary of Hurley Stage at Baseline and Week 8	FAS
2.1.6.2	Summary of Hurley Stage Change From Baseline to Week 8	FAS
2.1.7	Summary of HS-PGIC Category by Visit	FAS
2.1.7.1	Summary of HS-PGIC by Visit	FAS
2.1.8	Summary of Participants Requiring Rescue Lesional Treatment by Visit	FAS
2.1.9	Summary of Interventions With Rescue Lesional Treatment by Visit	FAS
2.1.10.1	Summary of DLQI Category by Visit	FAS
2.1.10.2	Summary of DLQI Score From Baseline to End of Study	FAS
[redacted]	[redacted]	[redacted]
2.1.13	Summary of Daily Analgesic Usage	FAS

Table No.	Title	Population
Safety		
3.1 Study Drug Exposure		
3.1.1	Summary of Drug Compliance	FAS
3.1.2	Summary of Study Drug Exposure	FAS
3.2 Adverse Events		
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	FAS
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	FAS
3.2.5	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS
3.2.6	Summary of Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	FAS
3.2.7	Summary of Treatment-Related Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS
3.2.8	Summary of Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	FAS
3.2.9	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term	FAS
3.2.9.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by Preferred Term in Decreasing Order of Frequency	FAS
3.2.10	Summary of Treatment-Emergent Adverse Events Leading to Death by MedDRA System Organ Class and Preferred Term	FAS
3.2.11	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS
3.2.12	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS
3.2.13	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS
3.2.14	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term	FAS
3.2.15	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Treatment by MedDRA System Organ Class and Preferred Term	FAS
3.2.16	Summary of Nonserious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term[a]	FAS
3.3 Laboratory		
3.3.1	Summary of Laboratory Values - Hematology	FAS
3.3.2	Shift Summary of Hematology Values - To the Worst Abnormal Value	FAS
3.3.3	Shift Summary of Hematology Laboratory Values in CTC Grade - To the Worst Abnormal Value	FAS
3.3.4	Summary of Laboratory Values - Chemistry	FAS
3.3.5	Shift Summary of Chemistry Values - To the Worst Abnormal Value	FAS
3.3.6	Shift Summary of Chemistry Laboratory Values in CTC Grade - To the Worst Abnormal Value	FAS

Table No.	Title	Population
3.4 Vital Signs		
3.4.1	Summary of Systolic Blood Pressure	FAS
3.4.2	Summary of Diastolic Blood Pressure	FAS
3.4.3	Summary of Pulse	FAS
3.4.4	Summary of Respiratory Rate	FAS
3.4.5	Summary of Body Temperature	FAS
3.5 ECG		
3.5.1	Summary of PR Interval (ms) From 12-Lead ECG	FAS
3.5.2	Summary of RR Interval (ms) From 12-Lead ECG	FAS
3.5.3	Summary of QT Interval (ms) From 12-Lead ECG	FAS
3.5.4	Summary of QRS Interval (ms) From 12-Lead ECG	FAS
3.5.5	Summary of QTcB Interval (ms) From 12-Lead ECG	FAS
3.5.6	Summary of QTcF Interval (ms) From 12-Lead ECG	FAS
3.5.7	Summary of Treatment Emergent, Clinically Significant ECG Abnormality From Baseline	FAS

[a] Nonserious adverse event table will be generated for the study for the express purpose of clinical trial results posting.

Listings

Listing No.	Title
Demographic and Baseline Characteristics	
1.1.1	Participant Enrollment and Disposition Status
1.1.2	Participant Inclusion and Exclusion Criteria Violations
1.1.3	Protocol Deviations
1.2.1	Demographic
1.2.2	Baseline Disease Characteristics
1.3	General Medical History
1.4.1	Prior and Concomitant Medications
1.4.2	Prior Medications for Hidradenitis Suppurativa
1.5	Study Drug Compliance
Efficacy	
2.1	HiSCR Response
2.2	AN Count
2.3	Draining Fistula Count
2.4	HS Pain NRS Score
2.5	Modified Sartorius Scale
2.6	Hurley Stage
2.7	HS-PGIC Category
2.8	Rescue Lesional Treatment
2.9	DLQI
[redacted]	[redacted]
Adverse Events and Exposure	
3.1	Study Drug Administration
3.2.1	Adverse Events
3.2.2	Serious Treatment-Emergent Adverse Events
3.2.3	Adverse Events Leading to Death
3.2.4	Treatment-Related Adverse Events
3.2.5	Adverse Events Leading to Dose Interruption
3.2.6	Adverse Events Leading to Discontinuation

Listing No.	Title
Laboratory Data	
3.3.1	Clinical Laboratory Values – Hematology
3.3.2	Clinical Laboratory Values – Serum Chemistry
3.3.3	Abnormal Clinical Laboratory Values – Hematology
3.3.4	Abnormal Clinical Laboratory Values – Serum Chemistry
[redacted]	[redacted]
3.3.6	Central Laboratory Collection Times
Vital Signs	
3.4.1	Vital Signs
3.4.2	Abnormal Vital Sign Values
3.4.3	Alert Vital Sign Values
ECG	
3.5.1	12-Lead ECG Values
3.5.2	Abnormal 12-Lead ECG Values
3.5.3	Alert 12-Lead ECG Values