Janssen Research & Development *

Clinical Protocol

Protocol Title
A Phase 2, Multicenter, Randomized, Placebo-Controlled, Double-Blind, Proof-of-Concept Study to Evaluate Guselkumab for the Treatment of Subjects with Moderate to Severe Hidradenitis Suppurativa

NOVA

Short Title
A Proof-of-Concept Study of Guselkumab in the Treatment of Subjects with Moderate to Severe Hidradenitis Suppurativa

Protocol CNTO1959HDS2001; Phase 2
AMENDMENT 1

CNTO 1959 (guselkumab)

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US sites of this study will be conducted under US Food & Drug Administration IND regulations (21 CFR Part 312).

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GCP Compliance: This study will be conducted in compliance with Good Clinical Practice, and applicable regulatory requirements.

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PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

DOCUMENT HISTORY	
Document	**Date**
Amendment 1	2 May 2019
Original Protocol	14 May 2018

Amendment 1 [02 May 2019]

Overall Rationale for the Amendment: The overall rationale for the changes implemented in the protocol amendment was to include an additional urine pregnancy test at Week 48 of the study, increase the percentage of total participants who are in Hurley Stage III, make necessary corrections to the total blood volume to be collected from each participant during the study, eliminate certain laboratory tests identified as not needed, resolve inconsistencies identified in the duration of continued contraception after the subject receives their last dose, and other minor typographical issues.

Section number and Name	Description of Change	Brief Rationale
1.1 Synopsis Objectives and Endpoints Other Secondary Endpoints	Added the following word where indicated: • The proportion of participants with HS-IGA (investigator's global assessment) score of inactive (0), almost inactive (1), or mild **activity** (2) and with at least 2-grade improvement relative to baseline at Week 16. • The proportion of participants with HS-IGA score of inactive (0) or almost inactive (1) at Week 16 among participants with HS-IGA score of moderate **activity** (3) or severe **activity** (4) at baseline.	Included the word "activity" to be consistent with terminology used in the HS-IGA assessment tool.
1.1 Synopsis Efficacy Analyses	Added the following text: "If a given comparison is not significant at the 2-sided α level of 0.05, **nominal p values will be provided for the subsequent treatment group comparisons and** the subsequent treatment group comparisons will be considered as supportive."	Provide clarification of multiple testing procedure.
1.3 Schedule of Activities Study Procedures Urine pregnancy test	Included an **additional urine pregnancy test to be performed at Week 48 or at early termination visit.**	Added based on health authority feedback.
3. Objectives and Endpoints Other Secondary Endpoints	Added the following word where indicated: • The proportion of participants with HS-Investigator's Global Assessment (HS-IGA) score of inactive (0), almost inactive (1), or mild **activity** (2) and with at least 2-grade improvement relative to baseline at Week 16. • The proportion of participants with HS-IGA score of inactive (0) or almost inactive (1) at Week 16 among participants with HS-IGA score of moderate **activity** (3) or severe **activity** (4) at baseline.	Included the word "activity" to be consistent with terminology used in the HS-IGA assessment tool.
4.2.1. Study-Specific Ethical Design Considerations	Revised the amount for the total blood volume in the following sentence: "The total blood volume to be collected from each participant in each group	The total blood volume to be collected from each participant in each group over the course of the

Section number and Name	Description of Change	Brief Rationale
	(~~approximately 150~~ approximately **181.5** mL over approximately 48 weeks) is far less than the American Red Cross standard limit for whole blood donation (approximately 475 mL q8w) and is therefore considered an acceptable amount of blood to be collected over this time period."	study was updated.
5.1 Inclusion Criteria Criterion #16a	Corrected to the appropriate units: a. Hemoglobin 10 g/dL (SI: 100 ~~g/L~~**mmol/L**)	Editorial correction: SI units corrected to mmol/L.
6.3 Measures to Minimize Bias: Randomization and Blinding Intervention Allocation *Procedures for Randomization and Stratification*	Revised the percentage provided in the following sentence: "Additionally, the number of participants in Hurley stage III should be limited to approximately ~~30%~~ **50%** of the total planned number of participants."	The percentage of participants in Hurley stage III out of the total number of study participants was increased due to fewer than expected subjects with Hurley stage I status screened or randomized at the time of this protocol amendment.
6.5.5. Prohibited Therapy	Added some clarification text to the following bullets: • Concomitant use of oral antibiotic therapy for HS or inflammatory disorders. Systemic antibiotic use (including oral) is allowed for the treatment of acute infections such as bacterial, viral, or **fungal**. • Oral or injectable corticosteroids for the **treatment of HS, except for protocol allowed intralesional rescue therapy as outlined in Section 6.5.1.**	Clarification related to the prohibited therapy.
6.5.6 Concomitant Corticosteroid use for Conditions Other than HS	Added a new section regarding Concomitant Corticosteroid use for Conditions Other than HS. **The use of systemic corticosteroids for indications other than HS should be limited to situations for which, in the opinion of the treating physician, there are no adequate alternatives. They should be used on a short-term basis, preferably for ≤2 weeks. Longer-term use of corticosteroids should be discussed with the medical monitor or designee and may require discontinuation of study drug. Inhaled, otic, ocular, nasal or other routes of mucosal delivery of corticosteroids are allowed throughout the study.**	Clarification related to the Concomitant Corticosteroid use for Conditions Other than HS
8. Study Assessments and Procedures Blood Sample Collection	Revised the amount for the total blood volume in the following sentence: "The total blood volume to be collected from each participant through Week 48 of the study will be ~~approximately 150~~ approximately **181.5** mL."	The total blood volume to be collected from each participant over the course of the study was updated.
8.2.4 Clinical Safety Laboratory Assessments	Added the following information to the end of the sentence: "Female participants of childbearing potential will undergo a urine pregnancy test at screening, before each study intervention administration, **and at the Week 48 or early termination visit."**	Added based on health authority feedback.

Section number and Name	Description of Change	Brief Rationale
9.4.1 Statistical Method	Added the following sentence: "**In case the number of subjects that are Hurley Stage I at baseline is much less than was expected, subjects that were Hurley Stage I will be pooled with subjects that were Hurley Stage II at baseline when baseline Hurley Stage is adjusted for in analyses."**	New text added due to few Hurley I subjects screened or randomized at the time of this protocol amendment.
9.4.2.1 Primary Analysis	Deleted text where indicated: "To address the primary objective, a CMH chi-squared statistic stratified by baseline weight (≤95 kg, >95 kg) and baseline Hurley stage ~~(I, II, and III)~~ at an alpha level of 0.05 will be used for each of the following hypotheses:"	Text deleted since Hurley Stage I and II could be pooled in the analyses. This was already clarified in Section 9.4.1.
9.4.2.2 Major Secondary Analyses	Added the following text: "With the sequential analyses specified above within each dose group vs placebo, each of the hypotheses will be tested at a 2-sided α level of 0.05 provided that the significance is achieved for the preceding hypothesis **test** in the specified order shown in Figure 2. If a given comparison is not significant at the 2-sided α level of 0.05, **nominal p values will be provided for the subsequent treatment group comparisons** and the subsequent treatment group comparisons will be considered as supportive."	Provided clarification of multiple testing procedure.
9.4.2.3 Other Efficacy Analyses	Added the following word where indicated: • The proportion of participants with HS-IGA score of inactive (0), almost inactive (1), or mild **activity** (2) and with at least 2-grade improvement relative to baseline at Week 16 will be compared between each of the guselkumab groups and the placebo group. • The proportion of participants with HS-IGA score of inactive (0), almost inactive (1) at Week 16 among participants with HS-IGA score of moderate **activity** (3) or severe **activity** (4) at baseline will be compared between each of the guselkumab groups and the placebo group.	Included the word "activity" to be consistent with terminology used in the HS-IGA assessment tool.
9.4.3 Safety Analyses Adverse Events	Modified the following text: • The incidence and type of **AEs temporally associated with infusion (defined as an AE that occurred on the same day of infusion, with a start time during infusion or ≤ 60 minutes after the end of infusion).** ~~infusion reactions.~~	Clarified the definition of AEs temporally associated with infusion of study intervention.
10.3 Appendix 3: Clinical Laboratory Tests Protocol-Required Safety Laboratory Assessments Other Laboratory Tests	The following tests were deleted: • ~~serum antibody titers to varicella, measles, mumps, and rubella~~) • ~~Serum IgG, IgM, IgA levels~~	Laboratory tests identified as not performed were deleted.
10.7 Appendix 7: Contraceptive and Barrier Guidance and Collection of	Changed the text as follows: "As noted in Inclusion Criterion 8, study participants who are women of childbearing potential must be practicing a highly effective method of contraception and remain on a	The duration of continuing to practice contraception after receiving the last dose of study intervention was changed to

Section number and Name	Description of Change	Brief Rationale
Pregnancy Information	highly effective method while receiving study intervention and until ~~16 weeks~~**12 weeks** after last dose."	12 weeks to align with Inclusion Criterion 8.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted and corrected.

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES AND FIGURES

TABLES

FIGURES

1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 2, Multicenter, Randomized, Placebo-Controlled, Double-Blind, Proof-of-Concept Study to Evaluate Guselkumab for the Treatment of Subjects with Moderate to Severe Hidradenitis Suppurativa

Protocol number: CNTO1959HDS2001

Guselkumab (CNTO 1959) is a fully human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody that binds to the p19 protein subunit of human interleukin (IL)-23 with high specificity and affinity. The binding of guselkumab to the IL-23p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23-specific intracellular signaling and subsequent activation and cytokine production. Guselkumab has been studied in Phase 1, Phase 2, and ongoing Phase 3 studies for the treatment of moderate to severe plaque psoriasis in adults. Guselkumab has been approved for the treatment of adults with moderate to severe plaque psoriasis in the United States, Europe, Canada, and several other countries. Guselkumab is also being studied globally for the treatment of psoriatic arthritis (PsA), Crohn's disease, and pediatric psoriasis.

OBJECTIVES AND ENDPOINTS

Objectives

Primary Objective

The primary objective of this study is to evaluate the initial efficacy, safety, and tolerability of guselkumab in adult participants with moderate to severe hidradenitis suppurativa (HS).

Secondary Objectives

The secondary objectives of this study are:

- To evaluate the efficacy of guselkumab in adult participants with moderate to severe HS during the maintenance phase.
- To evaluate the effect of guselkumab on the dermatologic health-related quality of life in adult participants with moderate to severe HS.
- To evaluate the pharmacokinetics (PK), immunogenicity, and pharmacodynamics (PD) of guselkumab therapy in adult participants with moderate to severe HS.

Endpoints

Primary Endpoint

The proportion of participants achieving Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 16

Major Secondary Endpoints

- The change from baseline in total abscess and inflammatory nodule (AN) count at Week 16.
- The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16.
- The change from baseline in HS-related pain in the past 24 hours based on Hidradenitis Suppurativa Symptom Diary (HSSD) at Week 16.

Other Secondary Endpoints

- The proportion of participants achieving at least 50%, 75%, 90%, and 100% reduction in total AN count at Week 16.
- The proportion of participants achieving an AN count of 1 and 2, respectively, at Week 16.
- The proportion of participants achieving complete elimination of abscesses at Week 16 among those participants with abscesses at baseline.
- The change from baseline in the number of abscesses at Week 16.
- The change from baseline in HSSD symptom scale score (other than pain the past 24 hours) at Week 16.
- The change from baseline in HSSD total symptom score at Week 16.
- The proportion of participants achieving complete elimination of draining fistulas at Week 16 among those participants with draining fistulas at baseline.
- The change from baseline in number of draining fistulas at Week 16.
- The proportion of participants achieving complete elimination of inflammatory nodules at Week 16 among those participants with inflammatory nodules at baseline.
- The change from baseline in number of inflammatory nodules at Week 16.
- The proportion of participants with HS-IGA (investigator's global assessment) score of inactive (0), almost inactive (1), or mild activity (2) and with at least 2-grade improvement relative to baseline at Week 16.
- The proportion of participants with HS-IGA score of inactive (0) or almost inactive (1) at Week 16 among participants with HS-IGA score of moderate activity (3) or severe activity (4) at baseline.
- The change from baseline in Hospital Anxiety and Depression Scale (HADS) scores at Week 16.
- The change from baseline in high-sensitivity C-reactive protein (hs-CRP) at Week 16.
- The distribution of the Patient Global Impression of Change (PGIC) of HS severity at Week 16.

Hypotheses

The primary hypothesis is that guselkumab treatment is superior to placebo as assessed by the proportion of participants achieving HiSCR at Week 16.

The major secondary hypotheses are that guselkumab treatment is:

- Superior to placebo as assessed by the change from baseline in AN count at Week 16.
- Superior to placebo as assessed by the improvement in patient-reported outcomes (PRO) as measured by:
  - The change from baseline in DLQI score at Week 16.
  - The change from baseline in HS-related pain in the past 24 hours based on HSSD at Week 16.

OVERALL DESIGN

This is a Phase 2, multicenter, randomized, placebo-controlled, double-blind study evaluating the efficacy, safety, PK, and immunogenicity of subcutaneous (SC) and intravenous (IV) administered guselkumab for the treatment of moderate to severe HS in adult participants. The participant population will comprise men and women who have had moderate to severe HS for at least 1 year.

Two database locks (DBLs) are planned for this study at Week 16 and Week 48, respectively. An interim analysis will be conducted when a subset of participants have completed the Week 16 visit.

An independent Data Monitoring Committee (DMC) will be commissioned for this study for safety evaluation.

NUMBER OF PARTICIPANTS

180 participants, ≥18 years of age, with HS, that is moderate to severe, and has been present for at least 1 year before the first administration of study intervention, and stable for at least 1 month (28 days) prior to screening as determined by the investigator through patient interview and/or review of the medical history. Participants must also have HS lesions in at least 2 distinct anatomic areas, had an inadequate response to an adequate course of oral antibiotics for treatment of HS in the investigator's opinion, and have a total AN count of ≥3 at the screening and baseline visits. Participants must agree to daily use of soap and water, or a topical antiseptic wash containing chlorhexidine gluconate, triclosan, or benzoyl peroxide, or a dilute bleach bath to all areas affected by HS throughout the study.

INTERVENTION GROUPS AND DURATION

All participants will be randomized in a 1:1:1 ratio to 1 of 3 treatment groups as described below:

Group 1: Guselkumab Regimen 1 (1200 mg IV q4w x 3 → 200 mg SC q4w)

Participants will receive guselkumab 1200 mg IV at Week 0, Week 4, and Week 8 (ie, a total of 3 IV guselkumab doses and 3 SC placebo doses). At Week 12, participants will continue treatment with guselkumab 200 mg SC q4w through Week 36.

Group 2: Guselkumab Regimen 2 (200 mg SC q4w x 3 → 200 mg SC q4w)

Participants will receive guselkumab 200 mg SC at Week 0, Week 4, and Week 8 (ie, a total of 3 SC guselkumab doses and 3 IV placebo doses). At Week 12, participants will switch treatment to guselkumab 200 mg SC q4w through Week 36.

Group 3: Placebo

Participants will receive placebo IV and SC at Week 0, Week 4, and Week 8 (ie, a total of 3 IV and 3 SC placebo doses) and an additional SC placebo dose at Week 12. At Week 16, participants will be rerandomized at a 1:1 ratio to either guselkumab 200 mg SC q4w through Week 36 or guselkumab 100 mg SC at Weeks 16, 20, 28, 36 and placebo at Weeks 24 and 32.

A screening period will take approximately 4 weeks. All participants will enter safety follow-up after Week 36 through Week 48.

EFFICACY EVALUATIONS

Efficacy evaluations include:

- HS-Investigator's Global Assessment
- Lesion Counts
- Hurley Staging
- HSSD
- DLQI

- HADS
- PGIC of HS Severity
- Photographs of HS lesions

PHARMACOKINETIC AND IMMUNOGENICITY EVALUATIONS

Venous blood samples will be collected for the measurement of serum guselkumab concentrations and detection of antibodies to guselkumab at the time points presented in the Schedule of Activities. Serum samples will also be collected at the final visit from participants who terminate study participation early.

BIOMARKER EVALUATIONS

Biomarker assessments will include the evaluation of relevant markers in serum for all participants and will be collected at the time points presented in the Schedule of Activities.

Serum samples will be analyzed for circulating factors such as cytokines and other inflammatory markers (eg, IL-17A, IL-17F, IL-23, TNFα, IL-6, IL-22), and other categories of biomarkers potentially associated with the development and progression of HS or related to the guselkumab mechanism of action.

SAFETY EVALUATIONS

Safety evaluations conducted at each study visit will include the assessment of adverse events (AEs, at the visit and those occurring between evaluation visits), a tuberculosis evaluation and other infection assessment, clinical laboratory blood tests (complete blood count and serum chemistries), physical examinations, vital sign measurements, echocardiogram, suicidality assessment measured using C-SSRS, concomitant medication review, and observations for injection-site reactions, reactions temporally associated with an infusion, and/or allergic reactions.

STATISTICAL METHODS

Sample Size Determination

This study is designed to enroll approximately 180 participants, in order to have sufficient power achieving the primary efficacy endpoint. The assumptions for the sample size and power calculations were based on the clinical data from the 2 adalimumab (Humira®) Phase 3 clinical studies M11-313 (PIONEER I) and M11-810 (PIONEER II) that evaluated the safety and efficacy of adalimumab in the treatment of adult participants with moderate to severe HS. With 60 participants in each of the guselkumab treatment group and 60 participants in the placebo group, there will be more than 90% power to detect a treatment difference of 30% between each guselkumab group and the placebo group for the primary efficacy endpoint with a significance level of 0.05.

Efficacy Analyses

All randomized participants who received at least 1 dose of study intervention will be included in the efficacy analyses. Participants will be analyzed according to the treatment group to which they were randomized, regardless of the treatment they actually received.

For response efficacy endpoints, treatment comparisons will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by the baseline weight (≤95 kg, >95 kg) and baseline Hurley stage (I, II, and III). For continuous efficacy endpoints, treatment comparisons will be performed using either a Mixed-Effect Model Repeated Measure (MMRM) model or an analysis of covariance (ANCOVA) model. All of the models will have treatment group, baseline weight (≤95 kg, >95 kg), baseline Hurley stage (I, II, and III), and baseline value as explanatory factors. MMRM models will additionally include visit, treatment by visit, and baseline value by visit interaction terms. All statistical tests will be performed at a

2-sided significance level of α=0.05. In addition, graphical data displays (eg, line plots) and participant listings may also be used to summarize/present the data.

In order to control the overall Type 1 error rate for comparisons between each guselkumab group and the placebo group, the primary analysis and major secondary analyses will be tested in a fixed sequence for the comparisons at an alpha level of 0.05. If a given comparison is not significant at the 2-sided α-level of 0.05, nominal p values will be provided for the subsequent treatment group comparisons and the subsequent treatment group comparisons will be considered as supportive.

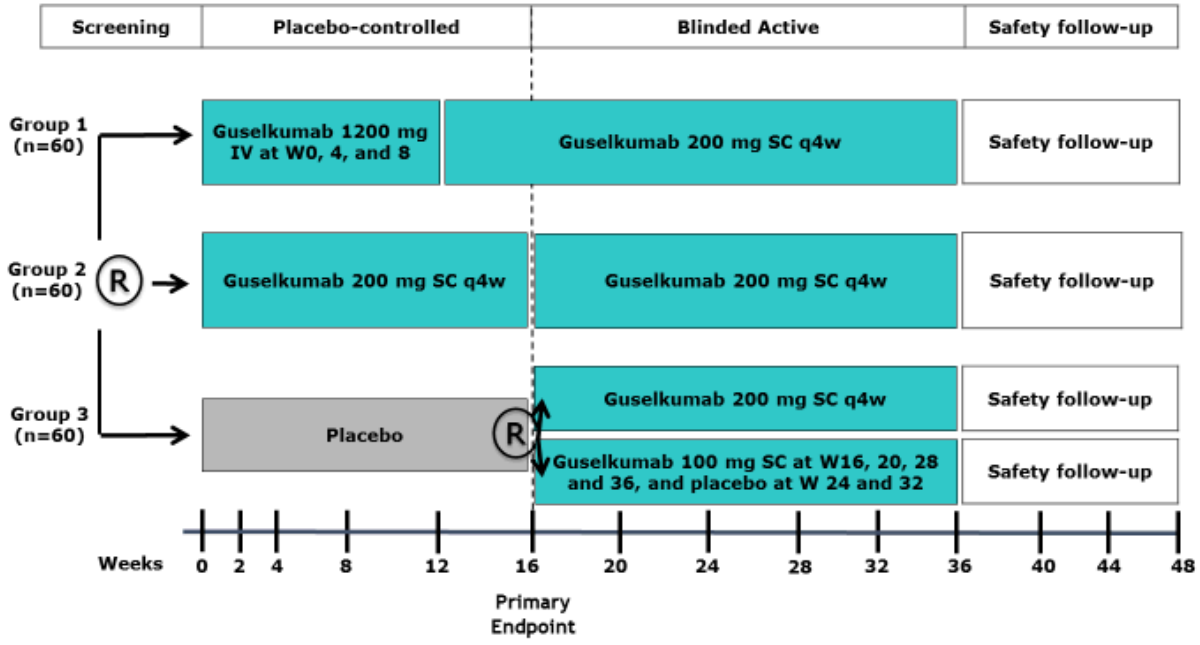
Analyses for other efficacy endpoints will be performed and nominal p-values will be provided.

Safety Analyses

Safety data, including but not limited to, AE, serious adverse events (SAE), infections, serious infections, mortality, suicidality assessment, changes in laboratory assessments, and changes in vital signs will be summarized. Intervention-emergent AEs will be summarized by treatment group and Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred terms.

1.2. Schema

Figure 1: Schematic Overview of CNTO1959HDS2001



1.3. Schedule of Activities (SoA)

From Screening through Week 48															
Period	Screening[a]	Placebo-Controlled Period						Blinded Active Treatment Period					Safety Follow-up		
Week		0	2	4	8	12	16	20	24	28	32	36	40	44	48 or Early Termination Visit[b]
Study Procedures[c]															
Screening/Administrative															
Informed consent	X														
Medical history and demographics	X														
Inclusion/ exclusion criteria	X	X													
Nicotine Use		X					X						X		
Alcohol Use		X					X						X		
Study Intervention Administration															
Randomization		X					X[d]								
Study intervention IV administration[e]		X		X	X										
Study intervention SC administration[e]		X		X	X	X	X	X	X	X	X	X			
Safety Assessments															
Physical examination (including skin)	X														X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Waist Circumference		X													X
Tuberculosis evaluation	X	X----------													----------X
Columbia-Suicide Severity Rating Scale (C-SSRS)[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chest radiograph	X														
12-lead ECG	X														

From Screening through Week 48															
Period	Screening[a]	Placebo-Controlled Period						Blinded Active Treatment Period					Safety Follow-up		
Week		0	2	4	8	12	16	20	24	28	32	36	40	44	48 or Early Termination Visit[b]
Study Procedures[c]															
Urine pregnancy test[g]	X	X		X	X	X	X	X	X	X	X	X			X
Height		X													
Weight		X					X								X
Concomitant therapy		X----------													----------X
Adverse events		X----------													----------X
Efficacy Assessments															
Hurley stage	X	X					X						X		
Lesion Counts	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HS-IGA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DLQI[f]		X					X						X		
HADS[f]		X					X						X		
Hidradenitis Suppurativa Symptom Diary (HSSD)[f]		X	X	X	X	X	X						X		
Patient global impression of change (PGIC) of HS severity[f]			X	X			X						X		
Photographs of skin lesions[h]		X					X						X		
Clinical Laboratory Assessment															
QuantiFERON®-TB test[i]	X														
Hepatitis B and C serology	X														
HIV antibody test	X														
Hematology	X	X					X						X		X

From Screening through Week 48															
Period	Screening[a]	Placebo-Controlled Period						Blinded Active Treatment Period					Safety Follow-up		
Week		0	2	4	8	12	16	20	24	28	32	36	40	44	48 or Early Termination Visit[b]
Study Procedures[c]															
Chemistry	X	X					X						X		X
Lipid panel[j]		X													
High sensitivity C-reactive protein (hs-CRP)		X		X			X						X		
Pharmacokinetics and Immunogenicity[k,l]															
Serum guselkumab concentration		X	X	X	X	X	X	X		X			X		X
Antibodies to guselkumab		X	X	X	X		X			X			X		X
Biomarkers															
Serum biomarkers[c]		X		X			X						X		X

Footnotes:

a. The screening visit should occur no more than 4 weeks before the Week 0 visit.
b. The Early Termination Visit should occur approximately 12 weeks after the last administration of study intervention (unless consent is withdrawn).
c. All study procedures and evaluations are to be completed before study intervention is administered except where otherwise indicated.
d. Randomization at Week 16 is for placebo group only and will not affect blinding.
e. IV infusions and SC injections for Weeks 0, 4, 8 and SC injections for Weeks 12 through 36.
f. The C-SSRS should be completed as the first assessment at screening after signing informed consent and before any tests, procedures, or other consultations, with the exception of the urine pregnancy test, and as the first assessment for baseline and all post-baseline visits, before any tests, procedures, or other consultations, with the exception of the urine pregnancy test, to prevent influencing participant perceptions. DLQI, HADS, HSSD, and PGIC should be performed before any tests, procedures, or other evaluations (Hurley stage, HS-IGA, Lesion counts), with the exception of the urine pregnancy test, for that visit.
g. Women of childbearing potential must have a negative urine pregnancy test result before randomization and before receiving study intervention at all study intervention administration visits, and at Week 48 or early termination visit.
h. Photographs to be taken at selected sites for participants who provide an additional consent; if such participants discontinue administration of study intervention early, however, photographs are not required at the final study visit.
i. A tuberculin skin test is additionally required if the QuantiFERON®-TB test is not approved/registered in the country in which this study is being conducted.
j. Participants must fast (ie, no food or beverages [except water]) for at least 8 hours before blood is drawn for lipid panel.
k. For all visits where study intervention will be administrated, one blood sample should be collected prior to study intervention administration for evaluation of serum concentration of guselkumab and/or antibodies to guselkumab. In addition, for IV infusion-related visits (ie, Weeks 0, 4, and 8), another blood draw should be taken approximately 60 minutes after completion of the infusion for serum concentration of guselkumab.
l. Participants who terminated study participation early should have a safety follow-up visit approximately 12 weeks after their last administration of study intervention. Serum samples should be collected at this visit for serum drug concentration measurement and antibody to drug assessment.

2. INTRODUCTION

Guselkumab (CNTO 1959) is a fully human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody (mAb) that binds to human interleukin (IL)-23 with high specificity and affinity. The binding of guselkumab to the IL-23p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23-specific intracellular signaling and subsequent activation and cytokine production. In this manner, guselkumab inhibits the biological activity of IL-23 in all in vitro assays examined.

Guselkumab has been approved in the United States, the European Union, Canada, and several other countries for the treatment of adult patients with moderate to severe plaque psoriasis. Data supporting the approval of the plaque psoriasis indication in adults included safety and efficacy data from 2,700 participants from 3 global Phase 3 studies (CNTO1959PSO3001 [VOYAGE 1], CNTO1959PSO3002 [VOYAGE 2], and CNTO1959PSO3003 [NAVIGATE]). Studies CNTO1959PSO3001 and CNTO1959PSO3002 have ongoing long-term extensions (LTE). In addition, guselkumab is being studied globally for the treatment of psoriatic arthritis (PsA), Crohn's disease, and pediatric psoriasis.

The approved dosage in the moderate to severe adult plaque psoriasis indication is 100 mg administered by subcutaneous (SC) injection at Week 0, Week 4, and every 8 weeks (q8w) thereafter. Guselkumab is not currently approved for use for the treatment of adult patients with moderate to severe hidradenitis suppurativa (HS).

For the most comprehensive nonclinical and clinical information regarding guselkumab, refer to the latest version of the Investigator's Brochure (IB) for guselkumab.

The term "sponsor" used throughout this document refers to the entities listed in the Contact Information page(s), which will be provided as a separate document.

2.1. Study Rationale

This is a proof-of-concept (POC) study to evaluate the efficacy, safety, and tolerability of guselkumab for the treatment of moderate to severe HS in adult participants by means of:

- Comparing the initial efficacy of 2 dose regimens (intravenous [IV] and SC) of guselkumab to placebo
- Evaluating the longer-term efficacy resulting from the initial IV vs. SC dose regimens of guselkumab
- Collecting safety and tolerability data for guselkumab in these HS participants

In addition, this study will evaluate the pharmacokinetics (PK), immunogenicity, and pharmacodynamics (PD) of guselkumab therapy in patients with HS.

2.2. Background

Hidradenitis suppurativa is a chronic skin disease of unclear etiology that affects 1% to 4% of the general population.[5,10,21,23] HS typically manifests as recurrent, inflamed, tender, subcutaneous nodules that are generally restricted to the axillary, inguinal, and anogenital regions.[5,10,21] While some nodules resolve spontaneously, others progress to form sterile abscesses, which then rupture into the skin, leading to the formation of fistulas and sinus tracts that can spontaneously release purulent drainage.[5,10,21] Over time, chronic inflammation can lead to irreversible scarring and fibrosis, which in severe cases can result in contractures and limitations in limb mobility, especially in the axilla.[5,10,21] Disease onset is typically after puberty and women are affected 2 to 5 times more commonly than men.[5,10] Multiple factors including genetics, cigarette smoking, and obesity are believed to predispose a person to HS.[5,23]

The chronic pain, drainage, and progressive, irreversible scarring associated with HS has been shown to have a particularly profound effect on patients' health-related quality of life relative to other common skin disorders.[23] Patients with HS experience considerable impact on activities of daily living, work/school attendance and productivity, physical activities, and emotional state.[20]

Although a variety of treatments are utilized to manage HS, including medical treatments (eg, systemic combination therapy with clindamycin and rifampicin, tetracyclines, intralesional steroids, systemic cyclosporine, anti-androgen treatment in women, systemic dapsone, systemic retinoids and metformin)[20] and surgical treatments (eg, incision and drainage of active lesions, local marsupialization and deroofing procedures, and radical excision), most have not been well studied and none appear particularly effective. The biologic anti-TNF inhibitor adalimumab (Humira®) has recently been approved to treat moderate to severe HS, but even this agent has not shown satisfactory treatment effects in many patients. Across two Phase 3 studies, the primary endpoint of Hidradenitis Suppurativa Clinical Response (HiSCR), defined as at least 50% reduction in total abscess and inflammatory nodule (AN) count with no increase in abscess count and no increase in draining fistula count relative to baseline,[4,9] was achieved in 42% and 59%, respectively, of adalimumab-treated patients compared with 26% and 28%, respectively, of placebo-treated patients.[8] Therefore, a substantial, unmet medical need exists for safe and more effective HS management options with alternative mechanisms of action.

Although the pathogenesis of HS remains somewhat unclear, there is evidence that inflammation associated with increased IL-17 pathway activity mediated by IL-23 may be involved. Genetic variations within the gene encoding the common IL-12βR1 subunit of the IL-12/IL-23 receptor have been shown to be associated with a more severe course of HS, and tissue obtained from HS lesions showed increased IL-23/Th17 pathway gene expression and distinct infiltration of IL-17-producing T helper cells compared with healthy skin.[3,22] Moreover, an uncontrolled, open-label, investigator-initiated clinical study of ustekinumab (STELARA®), a monoclonal antibody that inhibits both IL-12 and IL-23, using the standard weight-based psoriasis dosage, demonstrated that the primary outcome (a moderate to marked improvement based on the modified Sartorius Score) was achieved in 82% of participants at Week 40.[1] Furthermore, in a post-hoc analysis, 47% of participants achieved a HiSCR.[1] These results suggest that reducing IL-23-mediated

inflammation with guselkumab may improve the signs and symptoms of active HS and potentially allow for better treatment of this distressing disease.

Nonclinical Studies

A comprehensive overview of the nonclinical development program for guselkumab is available in Section 3 of the latest version of the guselkumab IB.

This section provides a summary of the sponsor's assessment of how the overall nonclinical data support the safety of the proposed dosing for guselkumab in this Phase 2 program in HS. Details regarding the proposed dose regimen and dose rationale are described in Section 4.3 of this protocol.

To place the proposed clinical dosing for guselkumab in HS participants into perspective relative to the existing preclinical data, the predicted cumulative human exposures during the placebo-controlled phase (1200 mg IV given at Weeks 0, 4, 8) were compared to the exposure at the no-observed-adverse-effect level (NOAEL) in cynomolgus monkeys following weekly IV administration in the 5-week arm of the subchronic toxicology study. In addition, predicted cumulative 12-week human exposures during the induction phase were compared to the exposure at the NOAEL in cynomolgus monkeys following weekly SC administration in the 24-week arm of the subchronic toxicology study. Thereafter, the predicted human exposure at steady-state (based on the highest SC dose being tested in this protocol, ie, 200 mg SC q4w) was compared with the exposure at the NOAEL in cynomolgus monkeys following weekly SC administration in the 24-week arm of the subchronic toxicology study. These data are presented in Appendix 8 (Section 10.8).

From a nonclinical perspective, the risk to HS patients is considered low when guselkumab is administered IV once every 4 weeks at doses up to 1200 mg (approximately 16 mg/kg in humans) followed by the proposed maintenance doses of up to 200 mg SC q4w, based on no adverse findings observed in cynomolgus monkeys following 5 weeks of once-weekly subchronic IV dosing at 50 mg/kg and 24 weeks of chronic once-weekly SC dosing. As summarized above, the actual exposure data (area under the serum concentration versus time curve [AUC]) achieved in monkeys relative to the predicted Week 8 to Week 12 IV clinical induction dosing interval AUC, or steady-state SC maintenance interval AUC (both normalized to weekly dosing to compare with the monkey dosing interval) provide ample exposure margins for the proposed clinical doses. This is further supported by the fact that guselkumab is an approved biotherapeutic with a good clinical safety profile in patients with plaque or other types of psoriasis, administered guselkumab at a dose of 100 mg SC, but also at doses up to 300 mg SC and 10 mg/kg IV in a limited number of patients with plaque psoriasis and in healthy normal volunteers, respectively, during Phase 1 of clinical development.

Clinical Studies

This protocol represents the first study of guselkumab in participants with HS.

This section provides a summary of the sponsor's assessment of how the overall clinical experience with guselkumab across various indications supports the investigation of guselkumab in HS. Details about the guselkumab clinical development programs across various indications are provided in Section 4 of the latest version of the guselkumab IB.

Guselkumab is currently approved in the United States, European Union, Canada, and several other countries for the treatment of moderate to severe plaque psoriasis. Also, Japan recently approved guselkumab for the treatment of patients with psoriasis, generalized pustular psoriasis (GPP), erythrodermic psoriasis (EP), and PsA.

In addition, guselkumab is being evaluated in adult PsA, Crohn's disease, and pediatric psoriasis globally, and in palmoplantar pustular psoriasis (PPP) in Japan.

Through the current IB cutoff date of 30 June 2017, 2,805 participants have been exposed to guselkumab across all indications in completed and ongoing clinical studies, including 185 healthy participants, 2,336 participants with psoriasis, 129 participants with PsA, and 155 participants in other indications.

The largest clinical experience to date with guselkumab has been in plaque psoriasis, primarily based on dosing at 100 mg SC q8w in the global Phase 2 and Phase 3 clinical development program (n=1,748), but also at doses up to 300 mg SC in a small number of participants (n=10) during Phase 1 clinical development. The safety profile of guselkumab in participants with moderate to severe plaque psoriasis based on data from the Phase 2 study (CNTO1959PSO2001) and three Phase 3 studies (CNTO1959PSO3001, CNTO1959PSO3002, and CNTO1959PSO3003) is described in Section 4.4 of the latest version of the guselkumab IB. Briefly, of the 1,748 guselkumab-treated participants in the Phase 2 and Phase 3 studies, 1,393 participants were exposed for at least 6 months and 728 participants were exposed for at least 1 year. The LTEs of two of the Phase 3 studies (CNTO1959PSO3001 and CNTO1959PSO3002) are ongoing and will evaluate the safety and efficacy of guselkumab through up to 5 years of follow-up.

The totality of the safety data available to date show that guselkumab, administered SC at doses of 100 mg q8w in participants with plaque psoriasis, is well tolerated, has a safety profile comparable to placebo over 16 weeks, and safety remained favorable when referenced versus an active comparator (adalimumab) over 1 year. Additional safety data in other indications (in participants who also receive concomitant immunomodulators as background therapy) with guselkumab doses as high as 200 mg SC q8w (in a Phase 2 rheumatoid arthritis study; n=54) did not identify any clinically significant safety signals through 1 year. Finally, a limited number of healthy participants (n=30) received single doses of IV guselkumab between 0.03 mg/kg and up to 10 mg/kg. Of the 6 participants in the 10 mg/kg dose group, the highest dose received was 987 mg in 1 participant. No clinically significant safety signals were identified.

2.3. Benefit/Risk Assessment

Based on the available data and the proposed safety measures discussed below, the risks of the dose regimens of guselkumab to be investigated in this protocol appear to be acceptable relative to the potential benefit.

Guselkumab has undergone extensive nonclinical and clinical development in inflammatory diseases such as PsA, Crohn's disease, GPP, EP, PPP, and pediatric psoriasis, as summarized in the latest version of the IB and described briefly in Section 2.2. The collective efficacy and safety results of the Phase 1, Phase 2, and Phase 3 clinical studies in healthy volunteers and patients with plaque psoriasis, and the recent regulatory approval for the adult plaque psoriasis indication, established a favorable benefit-risk profile for guselkumab in the treatment of plaque psoriasis.

There is evidence that inflammation associated with increased IL-17 pathway activity mediated by IL-23 may be involved in the pathogenesis of HS. Efficacy from an open-label ustekinumab study further suggested that reducing IL-23-mediated inflammation may improve the signs and symptoms of active HS (Section 2.2).

The approved dose regimen for guselkumab in psoriasis (100 mg SC at Week 0 and Week 4, and then q8w) has a favorable benefit/risk profile, and dose regimens as high as 200 mg SC q8w have been shown to be safe in a Phase 2 trial in rheumatoid arthritis. Clinical evidence suggests that meaningful efficacy in HS may require higher drug doses and exposures than psoriasis (Section 4.3). To determine the efficacy of guselkumab that results from the maximum exposure feasible, while maintaining an adequate safety margin to the available guselkumab nonclinical toxicology data (Section 2.2), a dose of 1200 mg IV given q4w for 3 doses will be utilized for this POC study in HS. Of note, this 1200 mg IV dose regimen is also being utilized and evaluated in a large ongoing Crohn's disease Phase 2b/3 clinical program. Unblinded safety will be evaluated on an ongoing basis throughout this trial by an independent Data Monitoring Committee (DMC), in addition to the standard safety oversight performed by the sponsor.

Details about the safety evaluations that will be utilized to continue or modify the protocol as the trial progresses are outlined in Section 9.6 and in the DMC charter.

More detailed information about the known and expected benefits and risks of guselkumab may be found in the IB.

3. OBJECTIVES AND ENDPOINTS

OBJECTIVES

Primary Objective

The primary objective of this study is to evaluate the initial efficacy, safety, and tolerability of guselkumab in adult participants with moderate to severe HS.

Secondary Objectives

The secondary objectives of this study are:

- To evaluate the efficacy of guselkumab in adult participants with moderate to severe HS during the maintenance phase.
- To evaluate the effect of guselkumab on the dermatologic health-related quality of life in adult participants with moderate to severe HS.
- To evaluate the PK, immunogenicity, and PD of guselkumab therapy in adult participants with moderate to severe HS.

ENDPOINTS

Primary Endpoint

- The proportion of participants achieving HiSCR at Week 16

Major Secondary Endpoints

- The change from baseline in total abscess and inflammatory nodule (AN) count at Week 16.
- The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16.
- The change from baseline in HS-related pain in the past 24 hours based on Hidradenitis Suppurativa Symptom Diary (HSSD) at Week 16.

Other Secondary Endpoints

- The proportion of participants achieving at least 50%, 75%, 90%, and 100% reduction in total AN count at Week 16.
- The proportion of participants achieving an AN count of 1 and 2, respectively, at Week 16.
- The proportion of participants achieving complete elimination of abscesses at Week 16 among those participants with abscesses at baseline.
- The change from baseline in the number of abscesses at Week 16.
- The change from baseline in HSSD symptom scale score (other than pain in the past 24 hours) at Week 16.
- The change from baseline in HSSD total symptom score at Week 16.
- The proportion of participants achieving complete elimination of draining fistulas at Week 16 among those participants with draining fistulas at baseline.
- The change from baseline in number of draining fistulas at Week 16.
- The proportion of participants achieving complete elimination of inflammatory nodules at Week 16 among those participants with inflammatory nodules at baseline.
- The change from baseline in number of inflammatory nodules at Week 16.

- The proportion of participants with HS-Investigator's Global Assessment (HS-IGA) score of inactive (0), almost inactive (1), or mild activity (2) and with at least 2-grade improvement relative to baseline at Week 16.
- The proportion of participants with HS-IGA score of inactive (0) or almost inactive (1) at Week 16 among participants with HS-IGA score of moderate activity (3) or severe activity (4) at baseline.
- The change from baseline in Hospital Anxiety and Depression Scale (HADS) scores at Week 16.
- The change from baseline in high-sensitivity C-reactive protein (hs-CRP) at Week 16.
- The distribution of the Patient Global Impression of Change (PGIC) of HS severity at Week 16.

Refer to Section 8, Study Assessments and Procedures, for evaluations related to endpoints.

HYPOTHESES

The primary hypothesis is that guselkumab treatment is superior to placebo as assessed by the proportion of participants achieving HiSCR at Week 16.

The major secondary hypotheses are that guselkumab treatment is:

- Superior to placebo as assessed by the change from baseline in AN count at Week 16.
- Superior to placebo as assessed by the improvement in patient-reported outcomes (PRO) as measured by:
  - The change from baseline in DLQI score at Week 16.
  - The change from baseline in HS-related pain in the past 24 hours based on HSSD at Week 16.

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 2, multicenter, randomized, placebo-controlled, double-blind, POC study evaluating the efficacy, safety, PK, and immunogenicity of SC and IV administered guselkumab for the treatment of moderate to severe HS in adult participants. The participant population will comprise men and women who have had moderate to severe HS for at least 1 year.

A diagram of the study design (Figure 1) is provided in Section 1.2, Schema.

As depicted in Figure 1, approximately 180 participants who satisfy all inclusion and exclusion criteria will be randomized in a 1:1:1 ratio to 1 of 3 groups:

Group 1: Guselkumab Regimen 1 (1200 mg IV q4w x 3 → 200 mg SC q4w)

Participants will receive guselkumab 1200 mg IV at Week 0, Week 4, and Week 8 (ie, a total of 3 IV guselkumab doses and 3 SC placebo doses). At Week 12, participants will continue treatment with guselkumab 200 mg SC q4w through Week 36.

Group 2: Guselkumab Regimen 2 (200 mg SC q4w x 3 → 200 mg SC q4w)

Participants will receive guselkumab 200 mg SC at Week 0, Week 4, and Week 8 (ie, a total of 3 SC guselkumab doses and 3 IV placebo doses). At Week 12, participants will switch treatment to guselkumab 200 mg SC q4w through Week 36.

Group 3: Placebo

Participants will receive placebo IV and SC at Week 0, Week 4, and Week 8 (ie, a total of 3 IV and 3 SC placebo doses) and an additional SC placebo dose at Week 12. At Week 16, participants will be rerandomized in a 1:1 ratio to either guselkumab 200 mg SC q4w through Week 36 or guselkumab 100 mg SC at Weeks 16, 20, 28, and 36, and placebo at Weeks 24 and 32.

A screening period will take approximately 4 weeks. All participants will enter safety follow-up after Week 36 through Week 48. Two planned database locks (DBLs) will occur, at Week 16 and at Week 48.

Efficacy assessments (HS-IGA, lesion counts, Hurley staging, HSSD, DLQI, HADS, and PGIC) will be performed according to the Schedules of Activities. Serum samples for PK, immunogenicity, and biomarker analyses will be collected at the timepoints shown in the Schedules of Activities (Section 1.3).

An interim analysis is planned and an independent DMC will be commissioned for this study for safety evaluation. Refer to Section 9.5 (Interim Analysis) and Section 9.6 (Data Monitoring Committee) for details.

4.2. Scientific Rationale for Study Design

Blinding, Control, Study Phase/Periods, Intervention Groups

Blinded treatment for guselkumab and placebo will be used to reduce potential bias during data collection and evaluation of endpoints. A placebo control will be used to establish the frequency and magnitude of changes in clinical endpoints that may occur in the absence of active treatment. Randomization will be used to minimize bias in the assignment of participants to treatment groups, to increase the likelihood that known and unknown participant attributes (eg, demographic and baseline characteristics) are evenly balanced across treatment groups, and to enhance the validity of statistical comparisons across treatment groups.

4.2.1. Study-Specific Ethical Design Considerations

Potential participants will be fully informed of the risks and requirements of the study and, during the study, participants will be given any new information that may affect their decision to continue participation. They will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only participants who are fully able to understand the risks, benefits, and potential adverse events (AEs) of the study and provide their consent voluntarily will be enrolled.

The total blood volume to be collected from each participant in each group (181.5 mL over approximately 48 weeks) is far less than the American Red Cross standard limit for whole blood donation (approximately 475 mL q8w) and is therefore considered an acceptable amount of blood to be collected over this time period. For more details regarding blood collection, see Blood Sample Collection in Section 8.

4.3. Justification for Dose

The following guselkumab dose regimens are selected for this Phase 2 POC study in participants with moderate to severe HS:

- Guselkumab 1200 mg IV at Weeks 0, 4, and 8, followed by 200 mg SC q4w through Week 36
- Guselkumab 200 mg SC q4w from Week 0 through Week 36
- Placebo IV and SC administration through Week 16. At Week 16, participants in the placebo group will cross over to:
  - Guselkumab 200 mg SC (q4w from Week 16 to Week 36), or
  - Guselkumab 100 mg SC (Weeks 16, 20, 28 and 36; placebo SC at Weeks 24 and 32).

These guselkumab dose regimens were selected based on existing safety information from relevant preclinical and clinical studies, the approved dose regimen for psoriasis, and the objective of determining the maximum efficacy of guselkumab possible for treatment of HS. Published information about adalimumab (an anti-TNFα monoclonal antibody) on relative dosing requirements among Crohn's disease, psoriasis, and HS patients also contributed to the choice of these dose regimens, along with data from an open-label HS clinical trial using ustekinumab (an anti-IL-12/IL-23 monoclonal antibody).[1,2,17,18,19]

This is a POC study, therefore, the maximum feasible dose (1200 mg IV), based on safety margins from preclinical and clinical studies, is being evaluated to define the maximum efficacy of guselkumab possible in HS. Single IV doses of guselkumab as high as 10 mg/kg, with the highest IV single dose tested being 987 mg, have been previously studied in a Phase 1 plaque psoriasis study. Additionally, guselkumab IV doses of up to 50 mg/kg weekly for 5 weeks, and guselkumab SC doses of up to 50 mg/kg weekly for 24 weeks, were well tolerated in cynomolgus monkeys (Section 2.2). These data support an acceptable exposure margin between

the predicted guselkumab exposures at the proposed dose regimens compared to those observed in toxicology studies; the estimated safety margins are approximately 4-to-6-fold for the 1200 mg IV dosing (See Appendix 8 [Section 10.8]). Of note, the 1200 mg IV dose is the same as the high guselkumab dose to be studied in Crohn's disease (NCT01369355, ClinicalTrials.gov). The 1200 mg IV dose regimen will help assess if incremental HS efficacy is possible with guselkumab exposure exceeding what can be practicably achieved with SC dosing.

A guselkumab 200 mg SC q4w dose, approximately 4-fold of the approved psoriasis dose (ie, 100 mg SC at Weeks 0 and 4, then 100 mg SC q8w thereafter), is also included in this POC study to determine the HS efficacy resulting from the maximally practicable SC dose of guselkumab.

Participants randomized to placebo will cross over to blinded guselkumab treatment at Week 16, including the 200 mg SC q4w dose and a lower 100 mg SC dose at Weeks 16 and 20, followed by q8w through Week 36, which is the approved psoriasis dose. Based on the results from an open-label ustekinumab HS study, it is likely that the psoriasis dose regimen could provide some clinical benefits.[1] Comparison of the relative efficacy of these two dose groups will provide useful data for determining if a dose higher than the optimal psoriasis dose provides incremental efficacy in HS.

Available preclinical observations and clinical data from other therapies suggest that a dose higher than the psoriasis dose may be needed in HS to achieve optimal efficacy. For example, IL-17+ CD4 T cells were shown to be enriched more than 40-fold in HS-involved skin compared with normal skin,[11] while the ratio was only approximately 2-fold for psoriasis.[6] IL-17A gene expression and protein levels have been reported to be highly up-regulated in HS affected skin compared to unaffected skin.[7] Additionally, studies have shown similar IL-23/Th17 pathway gene expression in HS- and Crohn's disease-affected tissues, indicating potential commonality in the pathophysiology of these autoinflammatory conditions.[16,22] Moreover, an adalimumab Phase 2 dose-ranging HS study found that an adalimumab dosage comparable with that used for Crohn's disease and ulcerative colitis, and essentially twice the psoriasis dose, provided better efficacy compared with the approved psoriasis dose,[8] and ultimately became the adalimumab dose approved for HS treatment. Finally, HS patients are generally heavier than patients with psoriasis (median body weight of approximately 94 kg and 89 kg, respectively)[12,14] and guselkumab exposure has been shown to be lower in heavier participants.

4.4. End of Study Definition

A participant will be considered to have completed the study if he or she has completed all scheduled study interventions through Week 36 and has completed all assessments at Week 48 of the safety follow-up period.

The end of study is considered as the last visit for the last participant in the study. The final data from the study-site will be sent to the sponsor (or designee) after completion of the final participant assessment at that study-site, in the time frame specified in the clinical trial agreement.

5. STUDY POPULATION

A target of 180 participants will be enrolled under the CNTO1959HDS2001 protocol.

Screening for eligible participants will be performed within 4 weeks before administration of the study intervention. Refer to Section 5.4, Screen Failures for conditions under which the repeat of any screening procedures is allowed.

The inclusion and exclusion criteria for enrolling participants in this study are described below. If there is a question about these criteria, the investigator must consult with the appropriate sponsor representative and resolve any issues before enrolling a participant in the study. Waivers are not allowed.

For a discussion of the statistical considerations of participant selection, refer to Section 9.2, Sample Size Determination.

5.1. Inclusion Criteria

Each potential participant must satisfy all of the following criteria to be enrolled in the study:

1. Be a man or a woman at least 18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place).

2. Have moderate to severe HS for at least 1 year (365 days) prior to the baseline visit as determined by the investigator through patient interview and/or review of the medical history.

3. Have HS lesions present in at least 2 distinct anatomic areas (examples include but are not limited to left and right axilla; or left axilla and left inguinocrural fold).

4. Had an inadequate response to an adequate course of appropriate oral antibiotics for treatment of HS (or demonstrated intolerance to, or had a contraindication to, oral antibiotics for treatment of their HS) in the investigator's opinion.

5. Have stable HS for at least 1 month (28 days) prior to the screening visit as determined by the investigator through patient interview and/or review of the medical history.

6. Have a total abscess and inflammatory nodule (AN) count of ≥3 at the screening and baseline visit.

7. Must agree to daily use (throughout the entirety of the study) of one of the following over-the-counter treatments to the body areas affected with HS lesions: either soap and water, or a topical antiseptic wash containing chlorhexidine gluconate, triclosan, or benzoyl peroxide, or a dilute bleach bath.

8. Before randomization, a woman must be either:

   - Not of childbearing potential: premenarchal; postmenopausal (>45 years of age with amenorrhea for at least 12 months or any age with amenorrhea for at least 6 months and a serum follicle-stimulating hormone (FSH) level >40 IU/L); permanently sterilized (eg, tubal occlusion, hysterectomy, bilateral salpingectomy); or otherwise be incapable of pregnancy.
   - Of childbearing potential and practicing a highly effective (failure rate of <1% per year when used consistently and correctly) method of birth control, prior to receiving study intervention, during the study and for at least 12 weeks after receiving the last administration of study intervention, consistent with local regulations regarding the use of birth control methods for participants participating in clinical studies: eg, established use of oral, injected or implanted hormonal methods of contraception; placement of an intrauterine device or intrauterine system; barrier methods: condom or occlusive cap (diaphragm or cervical/vault caps) plus spermicidal foam/gel/film/cream/suppository (if available in their locale); male partner sterilization (the vasectomized partner should be the sole partner for that participant); true abstinence (when this is in line with the preferred and usual lifestyle of the participant).

   Note: If a female participant's childbearing potential changes after start of the study (eg, a woman who is not heterosexually active becomes active, a premenarchal woman experiences menarche), she must begin practicing a highly effective method of birth control, as described above.

9. A woman of childbearing potential must have a negative urine pregnancy test (β-human chorionic gonadotropin [β-hCG]) at screening and at Week 0 prior to administration of study intervention.

10. A woman must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the study and for at least 12 weeks after receiving the last administration of study intervention.

11. A man who is sexually active with a woman of childbearing potential and who has not had a vasectomy must agree to use a barrier method of birth control (eg, either a condom [with spermicidal foam/gel/film/cream/suppository if available in their locale] or a partner with an occlusive cap [diaphragm or cervical/vault caps] plus spermicidal foam/gel/film/cream/suppository if available in their locale), during the study and for at least 12 weeks after receiving the last administration of study intervention.

12. All men must also agree to not donate sperm during the study and for at least 12 weeks after receiving the last administration of study intervention.

13. Are considered eligible according to the following tuberculosis (TB) screening criteria:

    a. Have no history of latent or active TB before screening. An exception is made for participants who have a history of latent TB and
        - are currently receiving treatment for latent TB,
        - will initiate treatment for latent TB before the first administration of study intervention,
        - or have documentation of having completed appropriate treatment for latent TB within 5 years before the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous anti-TB treatment and provide appropriate documentation.

    b. Have no signs or symptoms suggestive of active TB upon medical history and/or physical examination.

    c. Have had no recent close contact with a person with active TB or, if there has been such contact, will be referred to a physician specializing in TB to undergo additional evaluation and, if warranted, receive appropriate treatment for latent TB before the first administration of study intervention.

    d. Within 2 months before the first administration of study intervention, have a negative QuantiFERON®-TB test result, or have a newly identified positive QuantiFERON®-TB test result (see laboratory manual) in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated before the first administration of study intervention. Within 2 months before the first administration of study intervention, a negative tuberculin skin test, or a newly identified positive tuberculin skin test in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated before the first administration of study intervention, is additionally required if the QuantiFERON®-TB test is not approved/registered in that country or the tuberculin skin test is mandated by local health authorities.

       NOTE: The QuantiFERON®-TB test and the tuberculin skin test are not required at screening for participants with a history of latent TB and ongoing treatment for latent TB or documentation of having completed adequate treatment as described above; participants with documentation of having completed adequate treatment as described above are not required to initiate additional treatment for latent TB.

    e. Have a chest radiograph (both posterior-anterior and lateral views, or per country regulations where applicable), taken within 3 months before the first administration of study intervention and read by a qualified radiologist, with no evidence of current, active TB or old, inactive TB.

14. Agree not to receive a live virus or live bacterial vaccination during the study, or within 12 weeks after the last administration of study intervention. For information on Bacille Calmette-Guérin (BCG) vaccination, see Inclusion Criterion 15.

15. Agree not to receive a BCG vaccination during the study, or within 12 months after the last administration of study intervention.

16. Have screening laboratory test results within the following parameters, if one or more of the laboratory parameters is out of range, a single retest of laboratory values is permitted:

    a. Hemoglobin ≥10 g/dL (SI: ≥100 mmol/L)
    b. White blood cells ≥3.5 x 10^3/µL (SI: ≥3.5 GI/L)
    c. Neutrophils ≥1.5 x 10^3/µL (SI: ≥1.5 GI/L)
    d. Platelets ≥100 x 10^3/µL (SI: ≥100 GI/L)
    e. Serum creatinine ≤1.5 mg/dL (SI: ≤137 µmol/L)
    f. Aspartate aminotransferase ≤2 × upper limit of normal (ULN)
    g. Alanine aminotransferase ≤2 × ULN
    h. Alkaline phosphatase ≤2 × ULN

17. Be willing and able to adhere to the prohibitions and restrictions specified in this protocol.

18. Must sign an informed consent form (ICF) indicating that he or she understands the purpose of and procedures required for the study and is willing to participate in the study.

5.2. Exclusion Criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the study:

1. Any other active skin disease or condition (eg, bacterial, fungal or viral infection) that could have interfered with assessment of HS.

2. Has a draining fistula count of >20 at the baseline visit.

3. Receipt of prescription topical therapies for the treatment of HS within 14 days prior to the baseline visit.

4. Receipt of systemic non-biologic therapies for the treatment of HS <4 weeks prior to the baseline visit.

5. Receipt of immunomodulatory biologic therapies (eg monoclonal antibodies) within 3 months or 5 half-lives prior to the baseline visit, whichever is longer (refer to Section 6.5.5).

6. Receipt of any oral antibiotic treatment for HS or inflammatory disorders within 4 weeks prior to the baseline visit.

7. Receipt of opioid analgesics (including tramadol) within 14 days prior to the baseline visit, or if it is anticipated that the participant will require initiation of opioid analgesics (excluding tramadol) for any reason during the study period.

8. Receipt of oral concomitant analgesics (including opioids) for HS-related pain within 14 days prior to the baseline visit.

9. Receipt of "PRN" or "as needed" non-opioid analgesics for treatment of a chronic pain condition other than HS within 14 days prior to the baseline visit (participants may be receiving non-opioid analgesics for treatment of chronic non-HS-related pain but must be on a stable dose for at least 14 days prior to the baseline visit and be expected to continue use throughout the study).

10. Has a current diagnosis or signs or symptoms of severe, progressive, or uncontrolled renal, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances.

11. Has unstable cardiovascular disease, defined as a recent clinical deterioration (eg, unstable angina, rapid atrial fibrillation) in the last 3 months or a cardiac hospitalization within the last 3 months.

12. Currently has a malignancy or has a history of malignancy within 5 years before screening (with the exception of a non-melanoma skin cancer that has been adequately treated with no evidence of recurrence for at least 3 months before the first study intervention administration or cervical carcinoma in situ that has been treated with no evidence of recurrence for at least 3 months before the first study intervention administration).

13. Has a history of lymphoproliferative disease, including lymphoma; a history of monoclonal gammopathy of undetermined significance; or signs and symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy or splenomegaly.

14. Has a history of chronic or recurrent infectious disease, including but not limited to chronic renal infection, chronic chest infection (eg, bronchiectasis), recurrent urinary tract infection (recurrent pyelonephritis or chronic nonremitting cystitis), fungal infection (mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.

15. Has a transplanted organ (with exception of a corneal transplant >3 months before the first administration of study intervention).

16. Has a history of an infected joint prosthesis or has received antibiotics for a suspected infection of a joint prosthesis, if that prosthesis has not been removed or replaced.

17. Has or has had a serious infection (eg, sepsis, pneumonia, or pyelonephritis), or has been hospitalized or received IV antibiotics for an infection during the 2 months before screening.

18. Has or has had herpes zoster within the 2 months before screening.

19. Is pregnant, nursing, or planning a pregnancy (both men and women) while enrolled in the study or within 12 weeks following the last administration of study intervention.

20. Has previously received guselkumab.

21. Has received any therapeutic agent directly targeted to IL-17 or IL-23 within 6 months of the first administration of study intervention (including but not limited to ustekinumab, tildrakizumab, risankizumab, secukinumab, ixekizumab, or brodalumab).

22. Has received natalizumab, belimumab, or agents that modulate B cells or T cells (eg, rituximab, alemtuzumab, abatacept, or visilizumab) within 12 months of the first administration of study intervention.

23. Has received any systemic immunosuppressants (eg, methotrexate [MTX], azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, tacrolimus) or anakinra within 4 weeks of the first administration of study intervention.

24. Has received an experimental antibody or biologic therapy within the previous 6 months or received any other experimental therapy or new investigational agent within 30 days or 5 half-lives (whichever is longer) of any study intervention administration or is currently enrolled in another study using an investigational agent, device, or procedure.

25. Has received, or is expected to receive, any live virus or bacterial vaccination within 12 weeks before the first administration of study intervention. For BCG vaccine, see Exclusion Criterion 26.

26. Has had a BCG vaccination within 12 months of screening.

27. Has suicidal ideation or suicidal behavior in the last 6 months that may be defined as a Columbia-Suicide Severity Rating Scale (C-SSRS) rating at screening of: Suicidal Ideation with Intention to Act ("Ideation level 4"), Suicidal Ideation with Specific Plan and Intent ("Ideation level 5"), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt), and is considered to be at risk by the investigator based on an evaluation by a mental health professional. In addition, participants with C-SSRS ratings of Wish to be Dead ("Ideation level 1"), Non-Specific Active Suicidal Thoughts ("Ideation level 2"), Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act ("Ideation level 3") or non-suicidal self-injurious behavior who are determined to be at risk by the investigator may not be randomized.

28. Has known intolerance or hypersensitivity to any biologic medication, or known allergies or clinically significant reactions to murine, chimeric, or human proteins, mAbs, or antibody fragments.

29. Participant has known allergies, hypersensitivity, or intolerance to guselkumab or its excipients (refer to IB).

30. Has a history of active granulomatous infection, including histoplasmosis or coccidioidomycosis before screening. Refer to Inclusion Criterion 13 for information regarding eligibility with a history of latent TB.

31. Has a chest radiograph within 3 months before the first administration of study intervention that shows an abnormality suggestive of a malignancy or current active infection, including TB.

32. Has ever had a nontuberculous mycobacterial infection or opportunistic infection (eg, cytomegalovirus, pneumocystosis, aspergillosis).

33. Has two indeterminate (on repeat sampling) QuantiFERON®-TB test results.

34. Is infected with human immunodeficiency virus (HIV), positive serology for HIV antibody).

35. Tests positive for hepatitis B virus (HBV) infection (see Appendix 9, [Section 10.9]) or who are seropositive for antibodies to hepatitis C virus (HCV) at screening.

36. Has had major surgery (eg, requiring general anesthesia and hospitalization) within 8 weeks before screening, or has not fully recovered from such surgery, or has such surgery planned during the time the participant is expected to participate in the study (48 weeks).

    Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate.

37. Is known to have had a substance abuse (drug or alcohol) disorder within the previous 12 months.

38. Is unable or unwilling to undergo multiple venipunctures because of poor tolerability or lack of easy access to veins.

39. Lives in an institution on court or authority order.

40. Has any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

41. Is an employee of the investigator or study-site, with direct involvement in the proposed study or other studies under the direction of that investigator or study-site, as well as family members of the employees or the investigator.

NOTE: Investigators should ensure that all screening assessments have been completed and all study enrollment criteria have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after screening but before the first dose of study intervention is given such that he or she no longer meets all eligibility criteria, then the participant should be excluded from participation in the study. Section 5.4, Screen Failures, describes options for retesting. The required source documentation to support meeting the enrollment criteria are noted in Appendix 5 (Section 10.5), Regulatory, Ethical, and Study Oversight Considerations.

5.3. Lifestyle Considerations

Potential participants must be willing and able to adhere to the following lifestyle restrictions during the course of the study to be eligible for participation:

1. A woman of childbearing potential who is heterosexually active must remain on a highly effective method of birth control (Inclusion Criterion 8) during the study and for at least 12 weeks after receiving the last administration of study intervention.

2. A woman must agree not to donate eggs (ova, oocytes) during the study and for a period of at least 12 weeks following the last administration of study intervention.

3. A man who is sexually active with a female of childbearing potential and has not had a vasectomy must agree to use a barrier method of birth control (See Inclusion Criterion 11) during the study and for at least 12 weeks after receiving the last administration of study intervention.

4. A man must agree to not donate sperm during the study and for at least 12 weeks after receiving the last administration of study intervention.

5. Participants must not receive a live virus or bacterial vaccination during the study and for 3 months after the last administration of any study intervention. See Lifestyle Consideration 6 for information regarding BCG vaccination.

6. Participants must not receive a BCG vaccination during the study and for 12 months after the last administration of any study intervention.

7. Participants must comply with restrictions on concomitant medications and therapies specified in the protocol (refer to Section 6.5, Concomitant Therapy, for details).

8. Participants must agree to follow all requirements that must be met during the study as noted in the Inclusion and Exclusion Criteria (eg, contraceptive requirements).

5.4. Screen Failures

Participant Identification, Enrollment, and Screening Logs

The investigator agrees to complete a participant identification and enrollment log to permit easy identification of each participant during and after the study. This document will be reviewed by the sponsor study-site contact for completeness.

The participant identification and enrollment log will be treated as confidential and will be filed by the investigator in the study file. To ensure participant confidentiality, no copy will be made. All reports and communications relating to the study will identify participants by participant identification number and age at initial informed consent. In cases where the participant is not randomized into the study, the date seen and age at initial informed consent will be used.

Completion of screening and randomization procedures within the specified screening window of approximately 4 weeks is required.

Retesting

Retesting of abnormal laboratory values that may lead to exclusion will be allowed once. Retesting can occur at an unscheduled visit during the screening period, as long as this is done within the specified screening window of approximately 4 weeks.

Rescreening

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened 1 time. Rescreened participants will be assigned a new participant number, undergo the informed consent process, and then start a new screening period.

6. STUDY INTERVENTION

6.1. Study Interventions Administered

All participants will receive 1 IV infusion at Weeks 0, 4, and 8 (either active or placebo).

All participants will receive 2 SC injections at each visit (either active, active and placebo, or placebo) every 4 weeks from Weeks 0 to 36.

Intravenous study intervention should be administered over a period of not less than 1 hour, and not more than 2 hours. The infusion should be completed within 6 hours of preparation.

Since 2 SC injections will be administered at each administration visit, each SC injection should be given at a different location of the body.

Detailed instructions on the administration of IV and SC study intervention will be provided in the Site Investigational Product (IP) Binder.

Study intervention administration must be captured in the source documents and the electronic case report form (eCRF).

Guselkumab and placebo will be manufactured and provided under the responsibility of the sponsor. Refer to the IB for a list of excipients.

For details on rescue medications, refer to Section 6.5.1. For a definition of study intervention overdose, refer to Section 8.4, Treatment of Overdose.

6.2. Preparation/Handling/Storage/Accountability

Study intervention labels will contain information to meet the applicable regulatory requirements.

All study intervention must be stored at controlled temperatures ranging from 36°F to 46°F (2°C to 8°C), not frozen, and protected from light. Vigorous shaking of the product should be avoided. The sterile product does not contain preservatives and is designed for single use only. Prior to administration, the product should be inspected visually for particulate matter and discoloration. If discoloration (other than a slight yellow color), visible opaque particles, or other foreign particles are observed in the solution, the product should not be used. Study intervention in prefilled syringe assembled with the UltraSafe PLUS™ Passive Needle Guard (PFS-U) format will be ready to use for SC administration and will need to be prepared for IV administration. Aseptic procedures must be used during the preparation and administration of the study material.

Protection from ambient light is not required during dose preparation or administration; however, exposure to sunlight should be avoided.

Further details regarding the preparation and storage of IV and SC guselkumab and placebo will be provided in the Site IP Binder. The investigator is responsible for ensuring that all study intervention received at the site is inventoried and accounted for throughout the study. The study intervention administered to the participant must be documented on the drug accountability form. All study intervention will be stored and disposed of according to the sponsor's instructions.

Study intervention must be handled in strict accordance with the protocol and the container label and must be stored at the study-site in a limited-access area or in a locked cabinet under appropriate environmental conditions. Unused study intervention must be available for verification by the sponsor's study-site monitor during on-site monitoring visits. The return to the sponsor of unused study intervention will be documented on the drug return form. When the study-site is an authorized destruction unit and study intervention supplies are destroyed on-site, this must also be documented on the drug return form.

Potentially hazardous materials such as used ampules, needles, syringes and vials containing hazardous liquids, should be disposed of immediately in a safe manner and therefore will not be retained for drug accountability purposes. The study intervention boxes will be retained for inventory by the sponsor.

Study intervention should be dispensed under the supervision of the investigator or a qualified member of the study-site personnel, or by a hospital/clinic pharmacist. Study intervention will be supplied only to participants participating in the study. Study intervention may not be relabeled or reassigned for use by other participants. The investigator agrees to neither dispense the study intervention from, nor store it at, any site other than the study sites agreed upon with the sponsor.

6.3. Measures to Minimize Bias: Randomization and Blinding

Intervention Allocation

Procedures for Randomization and Stratification

Central randomization will be implemented in this study. Participants will be randomly assigned to 1 of 3 intervention groups based on a computer-generated randomization schedule prepared under the supervision of the sponsor. Permuted block randomization with stratification by baseline weight (≤ 95 kg, > 95 kg) and baseline Hurley stage (I, II, and III) will be used. The number of participants in Hurley stage I should be limited to approximately 30% of the total planned number of participants. Additionally, the number of participants in Hurley stage III should be limited to approximately 50% of the total planned number of participants. The interactive web response system (IWRS) will assign a unique intervention code, which will dictate the intervention assignment and matching study intervention kits for the participant. The requestor must use his or her own user identification and personal identification number when

contacting the IWRS and will then give the relevant participant details to uniquely identify the participant.

At Week 16, participants randomized to placebo at Week 0 will be rerandomized using the IWRS either to guselkumab 200 mg SC q4w or guselkumab 100 mg SC at Weeks 16, 20, and q8w thereafter (participants will receive placebo SC at Weeks 24 and 32) in a 1:1 ratio using permuted block randomization and the randomization and will be stratified by baseline weight (≤95 kg, >95 kg) and baseline Hurley stage (I, II, and III).

Blinding

To maintain the study blind, the study intervention container will have a label containing the study name, study intervention number, and reference number. The blinded label will not identify the specific study intervention in the container (ie, guselkumab or placebo). However, if it is necessary for a participant's safety, the study blind may be broken, and the identity of the study intervention ascertained. The study intervention number will be entered in the eCRF when the study intervention is administered. The guselkumab and placebo will be identical in appearance and will be packaged in identical containers.

The investigator will not be provided with randomization codes. The codes will be maintained within the IWRS, which has the functionality to allow the investigator to break the blind for an individual participant.

Data that may potentially unblind the intervention assignment (ie, study intervention serum concentrations, anti-guselkumab antibodies, and intervention allocation) will be handled with special care to ensure that the integrity of the blind is maintained and the potential for bias is minimized. This can include making special provisions, such as segregating the data in question from view by the investigators, clinical team, or others as appropriate until the time of DBL and unblinding.

Under normal circumstances, the blind should not be broken until all participants have completed the study and the database is finalized. However, selected sponsor personnel will be unblinded for analysis after the Week 16 DBL has occurred. All site personnel and participants will remain blinded to the treatment assignments until the last participant completes Week 48 evaluations and the database has been locked. The investigator may, in an emergency, determine the identity of the intervention by contacting the IWRS. While the responsibility to break the intervention code in emergency situations resides solely with the investigator, it is recommended that the investigator contact the sponsor or its designee if possible to discuss the particular situation, before breaking the blind. Telephone contact with the sponsor or its designee will be available 24 hours per day, 7 days per week. In the event the blind is broken, the sponsor must be informed as soon as possible. The date and reason for the unblinding must be documented in the appropriate section of the eCRF, and in the source document. The documentation received from the IWRS indicating the code break must be retained with the participant's source documents in a secure manner.

Participants who have had their intervention assignment unblinded by the investigator will not be eligible to receive further study intervention but should continue complete evaluations specified in the Schedule of Activities (Section 1.3).

For the planned interim analyses and the DMC, the randomization codes and the translation of randomization codes into intervention and control groups will be disclosed to those authorized and only for those participants included in the interim analysis.

6.4. Study Intervention Compliance

Because study intervention will be administered at the investigational site for all randomized participants, intervention compliance will be ensured by site personnel.

When study intervention is administered as an IV infusion or SC injection by qualified staff, the details of each administration will be recorded in the eCRF. For IV infusions, these will include date and start and stop times of the IV infusion and volume infused; for SC injections, these will include date, body location and time of SC injection.

All visits through Week 36 should occur within ±7 days of the scheduled visit. If a study visit occurs outside this window, the sponsor should be consulted about how the participant should resume his/her normal dosing schedule relative to the baseline visit (Week 0).

Information regarding study intervention administrations that are administered outside of the scheduled windows or missed will be recorded. Source data will be reviewed and compared with the data entries on the eCRFs to ensure accuracy. Although it is understood that intervention may be interrupted for many reasons, compliance with the intervention schedule is strongly encouraged.

6.5. Concomitant Therapy

Concomitant therapies must be recorded throughout the study from Week 0 through Week 48 or continuing until 12 weeks after the last dose of study intervention. Concomitant therapies on randomized participants should also be recorded beyond that point only in conjunction with serious adverse events (SAE) that meet the criteria outlined in Serious Adverse Events in Section 8.3.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information.

All therapies (prescription or over-the-counter medications, including vaccines, vitamins, herbal supplements; non-pharmacologic therapies such as electrical stimulation) different from the study intervention must be recorded in the eCRF. Modification of an effective pre-existing therapy should not be made for the explicit purpose of entering a participant into the study.

The sponsor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered.

6.5.1. Rescue Therapy

In the event that a particularly painful HS lesion occurs that necessitates an acute intervention, investigators will have the option to perform protocol-allowed interventions.

Two types of interventions are allowed:

- Injection with intralesional triamcinolone acetonide suspension (at a concentration of up to 5 mg/mL, up to 1 cc)
- Incision and drainage of the lesion

If incision and drainage is performed, the required over-the-counter soap and water or antiseptic wash should continue to be used. New systemic and topical therapies following incision and drainage (including antibiotics) are prohibited. Concomitant use of wound care dressings is allowed; however, options are limited to alginates, hydrocolloids, and hydrogels. Participants should continue using any ongoing oral and topical therapies (as described in Section 6.5, Concomitant Therapy) during the study.

Concomitant therapies associated with the lesion intervention(s) must be captured in the source documentation and on the appropriate eCRF.

A total of 2 protocol-allowed interventions are permissible through Week 16. An intervention can occur maximally on 2 different lesions at the same visit or on the same lesion at 2 different study visits. The same lesion cannot be treated 2 times at the same visit. If a participant requires more than 2 interventions within the first 16 weeks, then he or she must be discontinued from study interventions but continued for follow-up for approximately 12 weeks after last administration of study intervention.

After Week 16, interventions will not be permitted since all participants will receive active guselkumab treatment. If a participant requires an intervention after Week 16, he or she must be discontinued from study interventions, but continued for follow-up for approximately 12 weeks after last administration of study intervention.

All study visit evaluations must occur before any interventions are performed. Any lesion that undergoes an intervention will be documented in the source.

6.5.2. Antiseptic Therapy

Participants are required to use a daily antiseptic wash on their HS lesions. Allowable antiseptic washes are limited to one of the following: soap and water, a topical antiseptic wash containing chlorhexidine gluconate, triclosan, or benzoyl peroxide, or a dilute bleach bath.

6.5.3. Wound Care

Concomitant use of wound care dressings on HS wounds is allowed; however, options are limited to alginates, hydrocolloids, and hydrogels.

6.5.4. Analgesic Therapy

Use of opioid analgesics is prohibited for 14 days prior to the baseline visit regardless of HS or non-HS reasons. During the study, concomitant use of opioid analgesics is also prohibited, with the exception of tramadol as detailed below.

Oral analgesics for HS-related pain are prohibited 14 days prior to the baseline visit. If a participant is on a stable dose of a non-opioid analgesic (PRN is not considered stable) for a non-HS medical condition (eg, osteoarthritis), the participant may continue the analgesic, provided the dose is stable for 14 days prior to baseline and is anticipated to remain stable throughout study participation.

If a participant's pain (HS-related or non-HS-related) worsens after baseline, they may initiate analgesic therapy at any time as follows:

For HS-related pain, permitted analgesics are limited to:

- Ibuprofen (at a dose of up to 800 mg by mouth every 6 hours) not to exceed 3.2 grams/24 hours; AND/OR
- Acetaminophen as per local labeling; AND/OR
- If HS-related pain is uncontrolled with ibuprofen and/or acetaminophen at the above dosing regimens after the baseline visit, participants can be prescribed tramadol (at a dose of up to 100 mg by mouth every 4 hours), not to exceed 400 mg/24 hours.

Dose adjustments of ibuprofen, acetaminophen, or tramadol, and use of these analgesics on an "as needed" (PRN) basis for HS-related pain up to the maximum permitted dose and frequency, are allowed during the study.

From Screening through Week 40, participants will not be permitted to use any analgesics related to HS pain within 24 hours of a scheduled study visit. All analgesics and dose adjustments will be captured in the source and on the appropriate eCRF.

For non-HS-related pain:

- All other non-opioid analgesics and tramadol are allowed at the recommended or prescribed dose.

6.5.5. Prohibited Therapy

Participants who initiate the following treatments during study participation must have their study intervention discontinued:

- Phototherapy (PUVA and/or UVB)
- All biologic therapy with a potential therapeutic impact on the disease being studied, including but not limited to the following:
  - Adalimumab (Humira®)
  - Anakinra (Kineret®)

- Abatacept (Orencia®)
- Natalizumab (Tysabri®)
- Ustekinumab (STELARA)
- Etanercept (Enbrel®)
- Infliximab (REMICADE®)
- Rituximab (Rituxan®)
- Tocilizumab (Actemra®)
- Efalizumab (Raptiva®)
- Golimumab (SIMPONI®)
- Certolizumab (Cimzia®)
- Belimumab (Benlysta®)
- Secukinumab (Cosentyx®)
- Ixekizumab (Taltz®)
- Brodalumab (Siliq®)
- Tildrakizumab (Ilumya®)

- Any investigational agents for the treatment of HS.
- Any other systemic drug therapies for HS, including but not limited to MTX, cyclosporine, and retinoids.
- Concomitant use of oral antibiotic therapy for HS or inflammatory disorders. Systemic antibiotic use (including oral) is allowed for the treatment of acute infections such as bacterial, viral, or fungal.
- Oral or injectable corticosteroids for the treatment of HS, except for protocol allowed intralesional rescue therapy as outlined in Section 6.5.1.
- Surgical or laser intervention for an HS lesion except as outlined in Section 6.5.1, Rescue Therapy.

6.5.6. Concomitant Corticosteroid use for Conditions Other than HS

The use of systemic corticosteroids for indications other than HS should be limited to situations for which, in the opinion of the treating physician, there are no adequate alternatives. They should be used on a short-term basis, preferably for ≤2 weeks. Longer-term use of corticosteroids should be discussed with the medical monitor or designee and may require discontinuation of study drug. Inhaled, otic, ocular, nasal or other routes of mucosal delivery of corticosteroids are allowed throughout the study.

6.6. Dose Modification

No treatment/dose adjustment will be permitted through the study

6.7. Intervention After the End of the Study

No LTE is provided in this Phase 2 POC study. Participants and investigators will be informed that study intervention will not be made available to them beyond this protocol and that they should return to their treating physician for guidance.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

A participant will be considered to have completed the study if he or she has completed assessments through Week 48 as specified in the Schedule of Activities (Section 1.3).

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued if any of the following occur:

- The investigator believes that for safety reasons or tolerability reasons (eg, AE) it is in the best interest of the participant to discontinue study intervention.
- The participant has a serious adverse reaction that is temporally related to an injection or an infusion including an injection-site or infusion reaction, resulting in bronchospasm with wheezing and/or dyspnea that requires ventilatory support OR that results in symptomatic hypotension with a decrease in systolic blood pressure >40 mm Hg or blood pressure <90/60 mm Hg. This may include events of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) toxicity grade ≥3. In general, discontinuation of study intervention administration must be considered for participants who develop a severe injection-site or infusion reaction.
- The participant or their legally acceptable representative withdraws consent/assent for administration of study intervention.
- The participant becomes pregnant or plans a pregnancy during the study period. Refer to Appendix 7 (Section 10.7), Contraceptive and Barrier Guidance and Collection of Pregnancy Information.
- The initiation of protocol-prohibited medications, treatments, or interventions (outlined in Section 6.5, Concomitant Therapy) that have an impact on HS efficacy evaluations.
- The participant has a malignancy including squamous cell skin cancer. Consideration may be given to allow participants, who develop ≤2 basal cell skin cancers and who are adequately treated with no evidence of residual disease, to continue to receive study intervention.
- A systemic opportunistic infection.
- A recurrent or chronic serious infection.
- The participant is deemed ineligible according to the following TB screening criteria:
  - A diagnosis of active TB is made.
  - A participant has symptoms suggestive of active TB based on follow-up assessment questions and/or physical examination or has had recent close contact with a person with active TB and cannot or will not undergo additional evaluation.

  - A participant undergoing evaluation has a chest radiograph with evidence of current active TB and/or a positive QuantiFERON®-TB test result and/or 2 indeterminate QuantiFERON®-TB test results on repeat testing (refer to Section 8.2.11, Tuberculosis Evaluations) (and/or a positive tuberculin skin test result in countries in which the QuantiFERON®-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities).
  - A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy.

- The participant is unable to adhere to the study visit schedule or comply with protocol requirements.
- The participant has a reaction resulting in myalgia and/or arthralgia with fever and/or rash (suggestive of serum sickness and not representative of signs and symptoms of other recognized clinical syndromes) occurring 1 to 14 days after an injection of study intervention. These may be accompanied by other events including pruritus, facial, hand, or lip edema, dysphagia, urticaria, sore throat, and/or headache.
- The participant has his/her treatment assignment unblinded by the investigator.
- Sponsor decision.

Discontinuation of a participant's study intervention should be considered for:

- Participants with any type of suicidal ideation or behavior, or any self-injurious behavior, who are deemed to be at risk by the investigator. Discussion of such participants with the medical monitor or designee is required. For participants who report Suicidal Ideation with Intention to Act ("Ideation level 4"), suicidal ideation with specific plan and intent ("Ideation level 5"), suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt) or any self-injurious behavior on a post-baseline C-SSRS assessment, the investigator risk assessment must be based upon evaluation by a mental health professional (see Section 8.2.5).

Participants who decide to discontinue study intervention administration for reasons other than those outlined above must be interviewed by the investigator to determine if a specific reason for discontinuing study intervention can be identified. Participants should be explicitly asked about the possible contribution of AEs to their decision to discontinue study intervention; investigators should confirm that any AE information elicited has been documented. If a participant elects to discontinue study intervention due to an AE, the event should be recorded as the reason for study intervention discontinuation, even if the investigator's assessment is that the AE would not require study intervention discontinuation. The reason for study intervention discontinuation must be documented in the eCRF and in source documents. Study intervention assigned to a participant who discontinues may not be assigned to another participant.

A participant will not be automatically withdrawn from the study if he or she must discontinue treatment before the end of the treatment regimen. Participants who discontinue study intervention but do not terminate study participation will continue to return for protocol-specified procedures and evaluations for approximately 12 weeks following the last dose of study intervention. The procedures and evaluations listed for the Early Termination Visit should also be performed approximately 12 weeks after the last dose of study intervention.

All procedures and evaluations must be conducted prior to a participant's withdrawal of consent.

7.2. Participant Discontinuation/Withdrawal from the Study

A participant will be withdrawn from the study for any of the following reasons:

- Lost to follow-up (Refer to Section 7.3)
- Withdrawal of consent
- Death

To ensure access for participant follow-up, study sites should try to obtain both primary and secondary telephone contact numbers from participants (eg, home, work, and mobile phones), as well as other contact information such as email addresses, and emphasize the importance of follow-up information to the participant, before randomization. For participants who withdraw from study participation, every effort should be made to conduct the Early Termination Visit assessments, as indicated in the Schedule of Activities (Section 1.3). If the reason for withdrawal from the study is withdrawal of consent, then no additional assessments are allowed.

Withdrawal of consent should be a very unusual occurrence in a clinical trial; the investigator should make every effort to maintain good participant relationships to avoid withdrawals of consent. For participants who truly request withdrawal of consent, it is recommended that the participant withdraw consent in writing; if the participant or the participant's representative refuses to do so or is physically unavailable, the study-site should document the reason for the participant's failure to withdraw consent in writing, sign the documentation, and maintain it with the participant's source records. When a participant withdraws before completing the study, the reason for withdrawal is to be documented in the eCRF and in the source document. Study intervention assigned to the withdrawn participant may not be assigned to another participant. Participants who withdraw will not be replaced.

7.2.1. Withdrawal from the Use of Research Samples

The participant may withdraw consent for use of samples for research (refer to Long-Term Retention of Samples for Additional Future Research in Appendix 5 [Section 10.5], Regulatory, Ethical, and Study Oversight Considerations). In such a case, samples will be destroyed after they are no longer needed for the clinical study. Details of the sample retention for research are presented in the main ICF.

7.3. Lost to Follow-up

If a participant fails to return for study visits (and thus is considered lost to follow-up), study-site personnel must make all reasonable efforts to contact the participant to determine the participant's reason for discontinuation/withdrawal before considering the participant to be lost to follow-up. Such efforts should include repeated telephone calls, certified letters, email requests, etc. Measures taken to obtain follow-up information must be documented. Refer to Section 7.2, Participant Discontinuation/Withdrawal from the Study.

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

The Schedule of Activities (Section 1.3) summarizes the frequency and timing of efficacy, PK, immunogenicity, biomarker, and safety measurements applicable to this study.

All PRO assessments should be conducted/completed before any tests, procedures, or other consultations, with the exception of a urine pregnancy test, to prevent influencing participant perceptions.

Blood collections for PK and biomarker assessments should be kept as close to the specified time as possible. Actual dates of all assessments will be recorded in the source documentation; in addition, times of all blood collections will be recorded in the source documentation (laboratory requisition form).

Additional serum or urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulation, to establish the absence of pregnancy at any time during the participation in the study. Results of all pregnancy testing should be documented in the participants' source documents.

Blood Sample Collection

The total blood volume to be collected from each participant through Week 48 of the study will be approximately 181.5 mL. In addition, repeat or unscheduled samples may be collected for safety reasons or for technical issues with the samples.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded on the laboratory requisition form. Refer to the Schedule of Activities (Section 1.3) for the timing and frequency of all sample collections.

Instructions for the collection, handling, storage, and shipment of samples are found in the laboratory manual.

Study-Specific Materials

The investigator will be provided with the following supplies:

- Protocol
- Investigator's Brochure for guselkumab
- Site Investigational Product Binder
- Laboratory manual
- IWRS Manual
- Sample ICF

- PFS-U Instructions for Use
- Participant Study Participation Card
- Investigative Site File
- IV Ancillary Supplies
- Laboratory Kits
- Recruitment materials, as needed

8.1. Efficacy Assessments

Efficacy evaluations are consistent with those used to evaluate other therapies for HS and will include the following:

8.1.1. Hidradenitis Suppurativa Investigator's Global Assessment

The HS-IGA (Appendix 10 [Section 10.10]) documents the investigator's assessment of the participant's HS at a given timepoint. The anatomic region with the most severe HS activity at the baseline visit should be evaluated for erythema, drainage, and pain and/or tenderness to palpation for each participant. For each participant, the same anatomic site selected for evaluation at the baseline visit should be re-evaluated at each subsequent visit. The participant's HS is assessed as inactive (0), almost inactive (1), mild activity (2), moderate activity (3), or severe activity (4). A higher score indicates more severe disease.

8.1.2. Lesion Counts

Lesion counts are defined as the counting of abscesses, inflammatory nodules, non-inflammatory nodules, draining fistulas, and non-draining fistulas. Lesions will be counted during each visit.

8.1.3. Hurley Staging

Hurley staging consists of 3 stages of disease that will be used to determine stratification:

- Stage I: Abscess formation, single or multiple, without sinus tracts and scarring
- Stage II: One or more widely separated recurrent abscesses with tract formation and scarring
- Stage III: Multiple interconnected tracts and abscesses across the entire area, with diffuse or near diffuse involvement

8.1.4. Hidradenitis Suppurativa Symptom Diary

The HSSD (Appendix 11 [Section 10.11]) is a 7-item patient self-reported questionnaire that assesses 5 HS-related symptoms including pain, tenderness, hot skin feeling, odor, and itchiness. The participants are asked to rate the severity of each symptom on a 0 to 10 numerical rating scale, with 0 indicating no symptom experience and 10 indicating the worst possible symptom experience. All 5 symptoms have a recall period of the past 7 days, except for 2 additional questions on pain which evaluate current pain and pain in the past 24 hours. Each individual symptom scale score, ranging from 0-10, will be summarized. A total symptom score, which will

also range from 0-10, will be derived by averaging the 5 individual scale scores that utilize the past 7-day recall period.

8.1.5. Dermatological Life Quality Index

The DLQI (Appendix 12 [Section 10.12]) is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a participant's quality of life. It is a 10-item PRO questionnaire that, in addition to evaluating overall quality of life, can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment. The DLQI produces a numeric score that can range from 0 to 30. A higher score indicates more severe disease.

8.1.6. Hospital Anxiety and Depression Scale

The HADS (Appendix 13 [Section 10.13]) consists of 2 subscales, one measuring anxiety (A-scale) and one measuring depression (D scale), which are scored separately. A higher score indicates more severe disease.

8.1.7. Patient Global Impression of Change of Hidradenitis Suppurativa Severity

The Patient Global Impression of Change (PGIC) of HS Severity (Appendix 14 [Section 10.14]) is a questionnaire that measures participants' perceived change (improvement or deterioration) in severity of their HS. Participants will rate how his/her HS has changed since the beginning of the study using a 7-point scale ranging from "a lot better now" to "a lot worse now" with a neutral center point ("neither better nor worse"). PGIC will be used as an anchor to test reliability and establish a clinical response criterion of other patient or physician reported outcomes for future reference.

8.1.8. Photographs of Skin Lesions

Photographs of selected HS lesions will be taken at a subset of study sites in participants who provide additional consent. Consult the Trial Center File for photography instructions.

8.2. Safety Assessments

Details regarding the DMC are provided in Committees Structure in Section 9.6, Data Monitoring Committee.

Adverse events will be reported and followed by the investigator as specified in Section 8.3, Adverse Events and Serious Adverse Events and Appendix 6 (Section 10.6), Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting.

Any clinically relevant changes occurring during the study must be recorded on the Adverse Event section of the eCRF.

Any clinically significant abnormalities persisting at the end of the study/early withdrawal will be followed by the investigator until resolution or until a clinically stable condition is reached.

The study will include the following evaluations of safety and tolerability according to the time points provided in the Schedule of Activities (Section 1.3):

8.2.1. Physical Examination

Physical Examination

Physical examinations will be performed by the investigator or designated physician, nurse practitioner or physician assistant as specified in the Schedule of Activities (Section 1.3). Any new, clinically significant finding (in the opinion of the investigator) must be captured as an AE. In addition, resolution of any abnormal findings during the study will be noted in the source document and in the eCRF.

Height and Weight

Height and weight will be measured as specified in the Schedule of Activities (Section 1.3). Participants will be instructed to remove shoes and outdoor apparel and gear prior to these measurements.

Waist Circumference

Waist Circumference will be measured as specified in the Schedule of Activities (Section 1.3).

8.2.2. Vital Signs

Vital signs (including temperature, pulse/heart rate, respiratory rate, and blood pressure) will be obtained before and approximately every 30 minutes during every IV infusion, and at approximately 30 minutes after completion of the final IV infusion.

8.2.3. Electrocardiogram

A single 12-lead electrocardiogram (ECG) will be performed during screening to serve as a baseline reference for comparison, should a subsequent cardiovascular related safety event occur.

8.2.4. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology will be collected as noted in Section 8 and Appendix 3 (Section 10.3). The investigator must review the laboratory results, document this review, and record any clinically relevant changes occurring during the study in the AE section of the eCRF. The laboratory reports must be filed with the source documents.

The tests that will be performed by the central laboratory unless otherwise specified or approved by the medical monitor are specified in Appendix 3 (Section 10.3), Clinical Laboratory Tests.

Female participants of childbearing potential will undergo a urine pregnancy test at screening, before each study intervention administration, and at the Week 48 or early termination visit.

A medical monitor or delegate and the clinical site will be notified if prespecified abnormal laboratory values defined in the laboratory manual are identified in any participant during the conduct of the study.

8.2.5. Columbia-Suicide Severity Rating Scale (C-SSRS)

The C-SSRS defines 5 subtypes of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior and completed suicide. It will be used as a screening tool to prospectively evaluate suicidal ideation and behavior in this study, as part of a comprehensive evaluation of safety. The C-SSRS is an investigator-administered questionnaire.[13,15]Two versions of it will be used in this study: the 'Baseline/Screening' version of the C-SSRS (see Appendix 15, [Section 10.15])will be conducted during the screening visit and the 'Since Last Visit' version of the C-SSRS (see Appendix 16, [Section 10.16]) will be completed at all other visits through the end of the study.

The investigator or trained study-site personnel will interview the participant and complete the C-SSRS. The C-SSRS will be provided in the local languages in accordance with local guidelines.

At screening and after obtaining informed consent, the C-SSRS will be the first assessment performed, before any other study procedure. At all subsequent visits, the C-SSRS will be performed according to the Schedule of Activities (Section 1.3) and should be performed before any tests, procedures, or other consultations, with the exception of the urine pregnancy test, to prevent influencing participant perceptions. Participants will be interviewed by the investigator or trained study-site personnel in a private, quiet place.

At the conclusion of each assessment, the trained personnel administering the C-SSRS will determine the level of suicidal ideation or behavior, if any. They will then determine the next course of action if any level of suicidal ideation or behavior is reported. The participant should not be released from the site until the C-SSRS has been reviewed by the investigator and the participant's risk has been assessed and follow-up determined, as appropriate.

At screening (within the last 6 months) and Week 0, participants with a C-SSRS rating of Suicidal Ideation with Intention to Act ("Ideation level 4"), Suicidal Ideation with Specific Plan and Intent ("Ideation level 5"), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt), must be determined to not be at risk by the investigator based on an evaluation by a mental health professional (eg, psychiatrist, psychologist, or appropriately trained social worker or nurse) in order to be randomized.

Participants with C-SSRS ratings of Wish to be Dead ("Ideation level 1"), Non-Specific Active Suicidal Thoughts ("Ideation level 2"), Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act ("Ideation level 3") or non-suicidal self-injurious behavior must be determined not to be at risk by the investigator in order to be randomized. Any questions

regarding eligibility of such participants should be discussed with the medical monitor or designee.

For each assessment after Week 0, the following actions should be taken, if applicable:

- No suicidal ideation or behaviors (including self-injurious behavior without suicidal intent): No further action is needed.
- Suicidal ideation levels 1-3 or non-suicidal self-injurious behavior: Participant risk is assessed by the investigator.
- Suicidal ideation levels 4 or 5 or any suicidal behavior: Participant risk assessed and referral to a mental health professional.

Interruption or the discontinuation of study intervention should be considered for any participant who reports Suicidal Ideation with Intention to Act ("Ideation level 4"), Suicidal Ideation with Specific Plan and Intent ("Ideation level 5"), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt) on a post-baseline C-SSRS assessment and who is deemed to be at risk by the investigator based upon evaluation by a mental health professional. If a participant can be adequately treated with psychotherapy and/or pharmacotherapy then the participant, at the discretion of the investigator, may be continued with treatment if agreed to by the medical monitor or designee. Discussion of such participants with the medical monitor or designee is required (see Section 7.1, Discontinuation of Study Intervention).

Any C-SSRS finding, which in the opinion of the investigator is new or considered to be a worsening and clinically significant, should be reported on the AE eCRF (see Appendix 6 [Section 10.6], Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting).

8.2.6. Immunogenicity Assessments

Anti-guselkumab antibodies will be evaluated in serum samples collected from all participants according to the Schedule of Activities (Section 1.3). Additionally, serum samples should also be collected at the final visit or at the Early Termination Visit from participants who are discontinued from intervention or withdrawn from the study. These samples will be tested by the sponsor or sponsor's designee.

Serum samples will be screened for antibodies binding to guselkumab and the titer of confirmed positive samples will be reported as applicable. Other analyses may be performed to further characterize the immunogenicity of guselkumab.

Samples collected for immunogenicity analyses may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period. Genetic analyses will not be performed on these serum samples. Participant confidentiality will be maintained.

Evaluations

At visits where antibodies to study intervention will be evaluated in addition to serum concentration of study intervention, 1 venous blood sample of sufficient volume should be collected. Each serum sample will be divided into 3 aliquots (1 each for serum concentration of study intervention, antibodies to study intervention, and a back-up).

Immunogenicity Analytical Procedures

The detection and characterization of anti-guselkumab antibodies will be performed using a validated assay method by or under the supervision of the sponsor. All samples collected for detection of anti-guselkumab antibodies will also be evaluated for guselkumab serum concentration to enable interpretation of the antibody data.

8.2.7. Concomitant Medication

Concomitant medications will be reviewed at each visit and recorded in the source documents and eCRF.

8.2.8. Allergic Reactions

Before any SC injection or IV infusion, appropriately trained personnel and medications must be available to treat allergic reactions, including anaphylaxis. All participants must be observed carefully for symptoms of an allergic reaction (eg, urticaria, itching, hives). If a mild or moderate allergic reaction is observed, acetaminophen, non-steroidal anti-inflammatory drugs, and/or diphenhydramine may be administered.

In the case of a severe allergic reaction (eg, anaphylaxis), SC aqueous epinephrine, corticosteroids, respiratory assistance, and other proper resuscitative measures may be essential and must be available at the location where the injections or infusions are being administered.

Participants who experience serious adverse reactions related to an injection or infusion should be discontinued from further study intervention administrations.

Participants who experience reactions following an injection or infusion that result in bronchospasm with wheezing and/or dyspnea that requires ventilatory support, or symptomatic hypotension with a decrease in systolic blood pressure >40 mm Hg or blood pressure <90/60 mm Hg will not be permitted to receive additional study intervention.

Participants who experience reactions suggestive of serum sickness-like reactions (resulting in symptoms such as myalgia and/or arthralgia with fever and/or rash that are not representative of signs and symptoms of other recognized clinical syndromes) occurring 1 to 14 days after an injection of study intervention, should be discontinued from further study intervention administrations. Note that these symptoms may be accompanied by other events including pruritus, facial, hand, or lip edema, dysphagia, urticaria, sore throat, and/or headache.

8.2.9. Adverse Events Temporarily Related to Infusion

Any AE that occurs during or within 1 hour after the IV infusion of study intervention will be carefully evaluated. Minor infusion-related AEs may be managed by slowing the rate of the IV infusion and/or treating with antihistamines and/or acetaminophen (paracetamol) as clinically indicated. If an IV infusion of study intervention is stopped because of an AE that, in the opinion of the investigator, is not severe or does not result in a SAE, the infusion may be restarted with caution.

8.2.10. Injection-site Reactions

A study intervention injection-site reaction is any adverse reaction at an SC study intervention injection-site. The injection sites will be evaluated for reactions and any injection-site reactions will be recorded as an AE.

8.2.11. Tuberculosis Evaluation(s)

8.2.11.1. Initial Tuberculosis Evaluation

Participants must undergo testing for TB (refer to laboratory manual for QuantiFERON®-TB test or Appendix 4 [Section 10.4] for tuberculin skin test) and their medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB. The participant should be asked about past testing for TB, including chest radiograph results and responses to tuberculin skin or other TB testing. Investigators have the option to use both the QuantiFERON®-TB test and the tuberculin skin test to screen for latent TB if they believe, based on their judgment, that the use of both tests is clinically indicated in order to evaluate a participant who has high risk of having latent TB. If either the QuantiFERON®-TB test or the tuberculin skin test is positive, the participant is considered to have latent TB infection for the purposes of eligibility for this study.

Participants with a negative QuantiFERON®-TB test result (and a negative tuberculin skin test result in countries in which the QuantiFERON®-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities) are eligible to continue with pre-randomization procedures. Participants with a newly identified positive QuantiFERON®-TB (or tuberculin skin) test result must undergo an evaluation to rule out active TB and initiate appropriate treatment for latent TB. Appropriate treatment for latent TB is defined according to local country guidelines for immunocompromised patients. If no local country guidelines for immunocompromised patients exist, US guidelines must be followed, or the participant will be excluded from the study.

8.2.11.2. Ongoing Tuberculosis Evaluation

Early Detection of Active Tuberculosis

To aid in the early detection of TB reactivation or new TB infection during study participation, participants must be evaluated for signs and symptoms of active TB at scheduled visits (refer to the Schedule of Activities in Section 1.3). The following series of questions is suggested for use during the evaluation:

- "Have you had a new cough of >14 days' duration or a change in a chronic cough?"
- "Have you had any of the following symptoms:
  - Persistent fever?
  - Unintentional weight loss?
  - Night sweats?"
- "Have you had close contact with an individual with active TB?" (If there is uncertainty as to whether a contact should be considered "close," a physician specializing in TB should be consulted.)

If the evaluation raises suspicion that a participant may have TB reactivation or new TB infection, an immediate and thorough investigation should be undertaken, including, where possible, consultation with a physician specializing in TB.

Investigators should be aware that TB reactivation in immunocompromised participants may present as disseminated disease or with extrapulmonary features. Participants with evidence of active TB should be referred for appropriate treatment.

Participants who experience close contact with an individual with active TB during the conduct of the study must have a repeat chest radiograph, a repeat QuantiFERON®-TB test, a repeat tuberculin skin test in countries in which the QuantiFERON®-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities, and, if possible, referral to a physician specializing in TB to determine the participant's risk of developing active TB and whether treatment for latent TB is warranted.

Study intervention administration should be interrupted during the investigation. A positive QuantiFERON®-TB test or tuberculin skin test result should be considered for the detection of latent TB. If the QuantiFERON®-TB test result is indeterminate, the test should be repeated as outlined in the laboratory manual. Participants should be encouraged to return for all subsequent scheduled study visits according to the protocol. Participants who discontinue treatment for latent TB prematurely or who are noncompliant with therapy must immediately discontinue further administration of study intervention and be encouraged to return for all subsequent scheduled study visits according to the Schedule of Activities (Section 1.3).

8.3. Adverse Events and Serious Adverse Events

Timely, accurate, and complete reporting and analysis of safety information from clinical studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established Standard Operating Procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of safety information; all clinical studies conducted by the sponsor or its affiliates will be conducted in accordance with those procedures.

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally acceptable representative) for the duration of the study.

Anticipated events will be recorded and reported as described in Appendix 2 (Section 10.2), Anticipated Events.

For further details on AEs and SAEs (Definitions and Classifications; Attribution Definitions; Severity Criteria; Special Reporting Situations; Procedures) as well as product quality complaints (PQCs), refer to Appendix 6 (Section 10.6), Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting.

8.3.1. Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information

All Adverse Events

All AEs and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the participant's last study-related procedure, which may include contact for follow-up of safety. Serious adverse events, including those spontaneously reported to the investigator within 12 weeks after the last dose of study intervention, must be reported using the Serious Adverse Event Form. The sponsor will evaluate any safety information that is spontaneously reported by an investigator beyond the time frame specified in the protocol.

Serious Adverse Events

All SAEs occurring during the study must be reported to the appropriate sponsor contact person by study-site personnel within 24 hours of their knowledge of the event.

Information regarding SAEs will be transmitted to the sponsor using the Serious Adverse Event Form and Safety Report Form of the eCRF, which must be completed and reviewed by a physician from the study-site and transmitted to the sponsor within 24 hours. The initial and follow-up reports of a serious adverse event should be transmitted electronically or by facsimile (fax).

8.3.2. Follow-up of Adverse Events and Serious Adverse Events

Adverse events, including pregnancy, will be followed by the investigator as specified in Appendix 6 (Section 10.6), Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

8.3.3. Regulatory Reporting Requirements for Serious Adverse Events

The sponsor assumes responsibility for appropriate reporting of AEs to the regulatory authorities. The sponsor will also report to the investigator (and the head of the investigational institute where required) all suspected unexpected serious adverse reactions (SUSARs). The investigator (or sponsor where required) must report SUSARs to the appropriate Independent Ethics

Committee/Institutional Review Board (IEC/IRB) that approved the protocol unless otherwise required and documented by the IEC/IRB. A SUSAR will be reported to regulatory authorities unblinded. Participating investigators and IEC/IRB will receive a blinded SUSAR summary, unless otherwise specified.

8.3.4. Pregnancy

All initial reports of pregnancy in female participants or partners of male participants must be reported to the sponsor by the study-site personnel within 24 hours of their knowledge of the event using the appropriate pregnancy notification form. Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs and must be reported using the Serious Adverse Event Form. Any participant who becomes pregnant during the study must discontinue further study intervention (see Section 7, Discontinuation of Study Intervention).

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required

8.3.5. Events of Special Interest

Any newly identified malignancy or case of active TB occurring after the first study intervention administration(s) in participants participating in this clinical study must be reported by the investigator according to the procedures in Appendix 6 (Section 10.6). Investigators are also advised that active TB is considered a reportable disease in most countries. These events are to be considered serious only if they meet the definition of an SAE.

8.4. Treatment of Overdose

For this study, any dose of study intervention greater than the highest dose at a single dosing visit specified in this protocol will be considered an overdose. The sponsor does not recommend specific intervention for an overdose.

In the event of an overdose, the investigator or treating physician should:

- Contact the medical monitor immediately.
- Closely monitor the participant for AE/SAE and laboratory abnormalities.
- Document the quantity of the excess dose in the eCRF.

Decisions regarding dose interruptions or modifications will be made by the investigator in consultation with the medical monitor based on the clinical evaluation of the participant.

8.5. Pharmacokinetics

Blood samples will be collected for the measurement of serum guselkumab concentrations at the timepoints presented in the Schedules of Activities. Serum samples should also be collected at the final visit or at the Early Termination Visit from participants who are discontinued from

intervention or withdrawn from the study. Blood samples collected for serum guselkumab concentrations may also be used for exploratory biomarker analyses.

Evaluations

At visits in which only serum concentration of guselkumab will be evaluated (ie, no antibodies to guselkumab will be evaluated), 1 venous blood sample of sufficient volume should be collected, and each serum sample should be divided into 2 aliquots: 1 for serum concentration of guselkumab and a back-up. At visits where serum concentration of guselkumab and antibodies to guselkumab will be evaluated, 1 venous blood sample of sufficient volume should be collected. Each serum sample will be divided into 3 aliquots: 1 for serum concentration of guselkumab, 1 for antibodies to guselkumab, and 1 back-up. The exact dates and times of blood sample collection must be recorded in the laboratory requisition form. See the laboratory manual for further information regarding collection, handling, and shipment of biological samples. Genetic analyses will not be performed on these serum samples. Participant confidentiality will be maintained.

Pharmacokinetic Analytical Procedures

Serum samples will be analyzed to determine serum guselkumab concentrations using a validated, specific, and sensitive immunoassay method by the sponsor's bioanalytical facility or under the supervision of the sponsor. The sponsor, or its designee, under conditions in which the participants' identity remains blinded, will assay these samples.

8.6. Genetics

Samples for DNA analysis will not be collected in this study.

8.7. Biomarkers

Biomarker assessments will include the evaluation of relevant markers in serum for all participants. The samples will be used to better understand the biology of HS in the following ways: to provide mechanistic assessment of the pharmacodynamic response of participants to treatment with guselkumab, to analyze differences between responders and nonresponders, and to determine if the markers can be used to classify participants as potential responders prior to treatment. Samples will be collected pre-dose at Week 0, and at Weeks 4, 16, 40, and 48 for serum biomarkers. Instructions for the collection and shipment of these samples are found in the laboratory manual.

Serum samples will be analyzed for circulating factors such as cytokines and other inflammatory markers (eg, IL-17A, IL-17F, IL-23, TNFα, IL-6, IL-22), and other categories of biomarkers potentially associated with the development and progression of HS or related to the guselkumab mechanism of action.

Stopping Analysis

Biomarker analyses are dependent upon the availability of appropriate biomarker assays and clinical response rates. Biomarker analysis may be deferred or not performed, if during or at the end of the study, it becomes clear that the analysis will not have sufficient scientific value for biomarker evaluation, or if there are not enough samples or responders to allow for adequate biomarker evaluation. In the event the study is terminated early or shows poor clinical efficacy, completion of biomarker assessments is based on justification and intended utility of the data.

8.8. Health Economics

Health Economics parameters are not evaluated in this study.

9. STATISTICAL CONSIDERATIONS

Statistical analysis will be done by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be used to analyze the efficacy and safety data is outlined below. Specific details will be provided in the SAP.

9.1. Statistical Hypotheses

The primary hypothesis is that guselkumab treatment is superior to placebo as assessed by the proportion of participants achieving HiSCR at Week 16. More specifically, considering 2 guselkumab treatment arms in the study, the study will be considered positive if one of the following hypotheses are true:

- Guselkumab Regimen 1 (1200 mg IV q4w x3 → 200 mg SC q4w) demonstrates superior efficacy compared with placebo as measured by HiSCR at Week 16
- Guselkumab Regimen 2 (200 mg SC q4w x3 → 200 mg SC q4w) demonstrates superior efficacy compared with placebo as measured by HiSCR at Week 16

The major secondary hypotheses are that guselkumab treatment is:

- Superior to placebo as assessed by the change from baseline in total AN count at Week 16.
- Superior to placebo as assessed by the improvement in PROs as measured by:
- The change from baseline in DLQI score at Week 16.
- The change from baseline in HS-related pain in the past 24 hours based on HSSD at Week 16.

9.2. Sample Size Determination

This study is designed to enroll approximately 180 participants, primarily in order to provide adequate information to have sufficient power for the primary efficacy endpoint. The rationale for the study sample size is based on the hypothesis tests for the primary efficacy endpoint.

Two adalimumab (Humira®) Phase 3 clinical studies have been conducted to evaluate the safety and efficacy of adalimumab in the treatment of adult participants with moderate to severe HS. The response rates observed in Study M11-313 (PIONEER I) and M11-810 (PIONEER II) for HiSCR at Week 12 were 42% vs 26% and 59% vs 28% in the adalimumab weekly group and placebo group, respectively.

Therefore, the assumptions to calculate sample size and power shown in Table 1 are:

- The proportion of placebo participants achieving HiSCR at Week 16 is approximately 25%
- The difference between guselkumab treatment group and placebo group on proportion of participants achieving HiSCR at Week 16 is approximately 30%

Based on the above assumptions, with 60 participants in each of the guselkumab treatment group and 60 participants in the placebo group, there will be more than 90% power to detect a treatment difference of 30% with a significance level of 0.05.

Table 1: Statistical Power for the HiSCR Response Rate Comparing to Placebo at Week 16					
	Treatment group	**Sample size**	**HiSCR**	**Δ (difference)**	**Power**
1	Placebo	60	20%	25%	85%
	Guselkumab	60	45%		
2	Placebo	60	20%	30%	94%
	Guselkumab	60	50%		
3	Placebo	60	20%	35%	98%
	Guselkumab	60	55%		
4	Placebo	60	25%	25%	82%
	Guselkumab	60	50%		
5	Placebo	60	25%	30%	93%
	Guselkumab	60	55%		
6	Placebo	60	25%	35%	98%
	Guselkumab	60	60%		
HiSCR=Hidradenitis Suppurativa Clinical Response					

9.3. Populations for Analyses

For the efficacy analyses in this study, the full analysis set (FAS) will be used according to the participants' assigned treatment to which they were randomized, regardless of the treatment they actually received. The FAS includes all randomized participants who receive at least one administration of study intervention. The FAS will be used for all primary and secondary efficacy analyses.

Safety analyses will include all participants who received at least 1 dose (complete or partial) of study intervention and participants will be analyzed based on the treatment they actually received, regardless of the treatment groups to which they were assigned.

Pharmacokinetics analyses for guselkumab will include participants who receive at least one complete dose of guselkumab and have at least one post-dose sample collection. Antibodies to guselkumab will be analyzed for participants who receive at least one dose of guselkumab and have at least one post-dose sample collection.

9.4. Statistical Analyses

9.4.1. Statistical Method

Statistical analysis will be done by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be used to analyze the efficacy and safety data is outlined below. Specific details will be provided in the SAP.

In general, efficacy and participant information analyses will include all randomized participants who received at least 1 dose (complete or partial) of study intervention and will be analyzed based on the randomized treatment groups, regardless of the treatment they actually received.

Simple descriptive summary statistics, such as n, mean, standard deviation (SD), median, inter quantile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data.

In general, for response efficacy endpoints, treatment comparisons will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by the baseline weight (≤95 kg, >95 kg) and baseline Hurley stage (I, II, and III). For continuous efficacy endpoints, treatment comparisons will be performed using either a Mixed-Effect Model Repeated Measure (MMRM) model or an analysis of covariance (ANCOVA) model. All of the models will have treatment group, baseline weight (≤95 kg, >95 kg), baseline Hurley stage (I, II, and III), and baseline value as explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. In addition, treatment differences and their associated 95% confidence intervals will be presented.

In case the number of subjects that are Hurley Stage I at baseline is much less than was expected, subjects that were Hurley Stage I will be pooled with subjects that were Hurley Stage II at baseline when baseline Hurley Stage is adjusted for in analyses.

In general, all statistical tests will be performed at a 2-sided significance level of α=0.05. In addition, graphical data displays (eg, line plots) and participant listings may also be used to summarize/present the data.

Participants who discontinue study intervention due to lack of efficacy or an AE of worsening of HS, or who started a protocol-prohibited medication or therapy during the study that could improve HS are considered treatment failures. The baseline values will be assigned regardless of the observed data for continuous endpoints, zero will be assigned to improvement and percent improvement, and nonresponders status will be assigned to binary response variables. Lesions that received intervention will be counted as present after the visit of intervention. After applying the treatment failure rules, the remaining missing data will be assigned nonresponders status for binary variables. For the longitudinal analyses, missing data handling rules will not be applied.

9.4.2. Efficacy Analyses

9.4.2.1. Primary Analysis

The primary efficacy endpoint is the proportion of patients with a clinical response at Week 16, defined according to the HiSCR measure as at least a 50% reduction from baseline in the total abscess and inflammatory- nodule count, with no increase in the abscess or draining fistula count.

In the primary efficacy analysis, data from all randomized participants who received at least 1 administration of study intervention will be analyzed according to their assigned treatment group. Participants who meet treatment failure criteria prior to Week 16 will be considered nonresponders for the primary endpoint at Week 16. In addition, participants who do not return for evaluation at Week 16 will be considered nonresponders at Week 16.

In this primary analysis, the number and proportion of participants who achieve a HiSCR at Week 16 will be summarized for each treatment group. To address the primary objective, a CMH chi-squared statistic stratified by baseline weight (≤95 kg, >95 kg) and baseline Hurley stage at an alpha level of 0.05 will be used for each of the following hypotheses:

1. Guselkumab Regimen 1 (1200 mg IV q4w x 3 → 200 mg SC q4w) versus placebo in HiSCR at Week 16.
2. Guselkumab Regimen 2 (200 mg SC q4w x 3 → 200 mg SC q4w) versus placebo in HiSCR at Week 16.

The study is considered positive if at least one of the hypotheses is tested as significant.

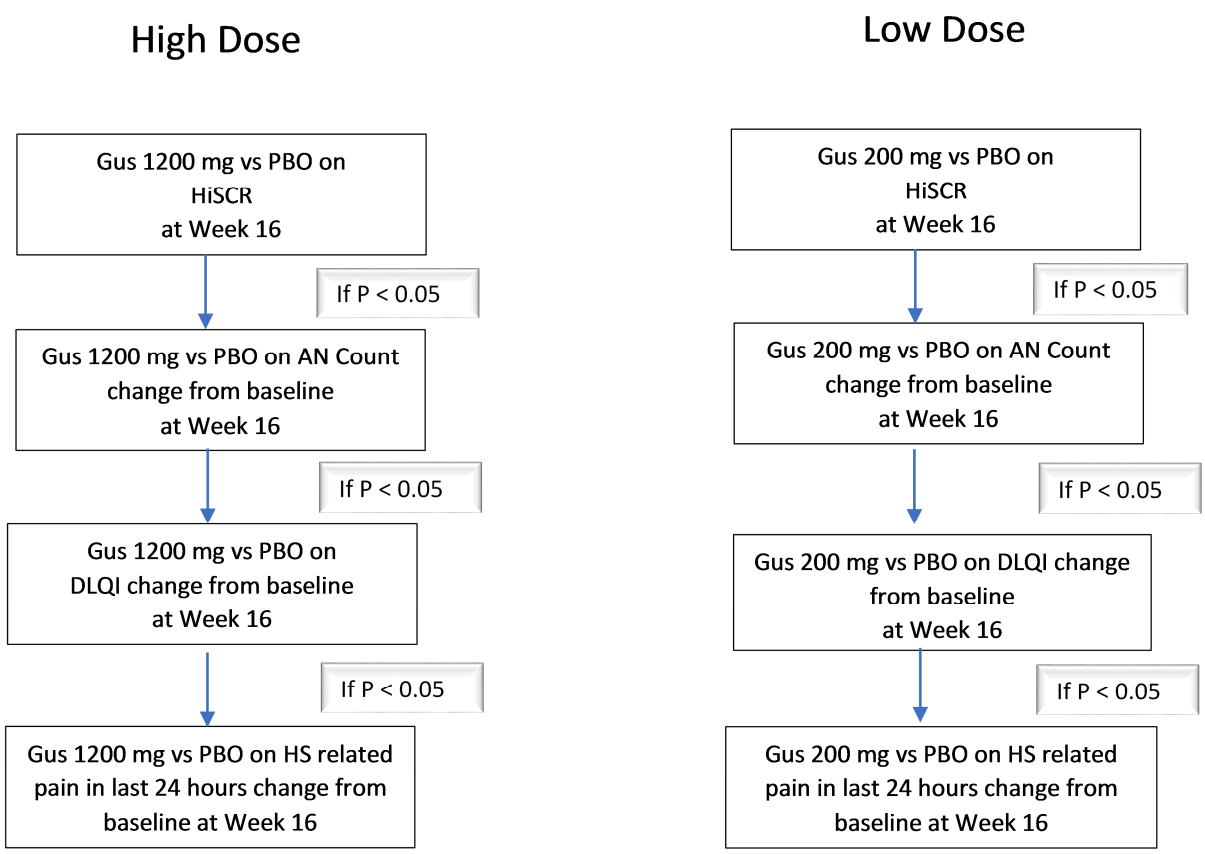
9.4.2.2. Major Secondary Analyses

The major secondary analyses are:

- The change from baseline in total AN count at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in DLQI at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in HS-related skin pain in the past 24 hours based on HSSD at Week 16 will be compared between each of the guselkumab groups and the placebo group.

The primary and major secondary hypotheses will be tested in the specified order and the order and procedure are shown in Figure 2.

Figure 2: Diagram for Multiple Testing Procedure for Primary and Secondary Hypotheses



With the sequential analyses specified above within each dose group vs placebo, each of the hypotheses will be tested at a 2-sided α-level of 0.05 provided that the significance is achieved for the preceding hypothesis test in the specified order shown in Figure 2. If a given comparison is not significant at the 2-sided α-level of 0.05, nominal p values will be provided for the subsequent treatment group comparisons and the subsequent treatment group comparisons will be considered as supportive.

9.4.2.3. Other Efficacy Analyses

In addition to the primary and major secondary analyses, the analyses for other efficacy endpoints will be performed and nominal p-values will be provided. The efficacy endpoints (including primary and major secondary endpoints) will also be summarized over time. Additional efficacy analyses may be performed and will be documented in the SAP.

- The proportion of participants achieving at least 50%, 75%, 90%, and 100% reduction in total AN count at Week 16 will be compared between each of the guselkumab groups and the placebo group.

- The proportion of participants achieving an AN count of 1 and 2, respectively at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants who achieved complete elimination of abscesses at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in number of abscesses at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants who achieved complete elimination of draining fistulas at Week 16 will be compared between each of the guselkumab groups and the placebo group among those with draining fistulas at baseline.
- The change from baseline in number of draining fistulas at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants who achieved complete elimination of inflammatory nodules at Week 16 will be compared between each of the guselkumab groups and the placebo group among those with inflammatory nodules at baseline.
- The change from baseline in number of inflammatory nodules at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants with HS-IGA score of inactive (0), almost inactive (1), or mild activity (2) and with at least 2-grade improvement relative to baseline at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants with HS-IGA score of inactive (0), almost inactive (1) at Week 16 among participants with HS-IGA score of moderate activity (3) or severe activity (4) at baseline will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in HSSD symptom scale score (other than pain in the past 24 hours) at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in HSSD total symptom score at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in HADS at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in high-sensitivity-C-reactive protein (hs-CRP) at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The distribution of the PGIC at Week 16 will be compared between each of the guselkumab groups and the placebo group.

9.4.3. Safety Analyses

Safety data, including but not limited to, AEs, SAEs, infections, serious infections, mortality, changes in laboratory assessments, and changes in vital signs will be summarized. Intervention-emergent AEs will be summarized by treatment group and Medical Dictionary for Regulatory

Activities (MedDRA) system organ class and preferred terms. Details will be specified in the SAP.

Safety Definition

Injection-Site Reactions

An injection-site reaction is any unfavorable or unintended sign that occurs at an injection-site and will be recorded as an AE. Detailed instructions for the evaluation of injection-site reactions are in the Trial Center File.

Adverse Events

The verbatim terms used in the eCRF by investigators to identify AEs will be coded using the MedDRA. Intervention-emergent AEs are AEs with onset during the intervention period or that are a consequence of a pre-existing condition that has worsened since baseline. All intervention-emergent AEs will be included in the analysis. For each AE, the percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group. In addition, comparisons between intervention groups will be provided if appropriate.

Summaries, listings, datasets, or participant narratives may be provided, as appropriate, for those participants who die, who discontinue intervention due to an AE, or who experience a severe or a SAE.

The following analyses will also be used to assess the safety of participants in the study:

- The incidence and type of AEs.
- The incidence and type of SAEs.
- The incidence and type of infections.
- The incidence and type of reasonably related AEs.
- The incidence and type of injection-site reactions.
- The incidence and type of AEs temporally associated with infusion (defined as an AE that occurred on the same day of infusion, with a start time during infusion or ≤ 60 minutes after the end of infusion).
- The laboratory parameters and change from baseline in selected laboratory parameters (hematology and chemistry).
- The incidence of abnormal laboratory parameters (hematology and chemistry).

Listings of participants with SAEs and anaphylactic reaction/serum sickness reactions will also be provided. All safety analyses will be based on the population of participants who received at least 1 administration of study intervention; participants will be summarized by the intervention they received.

Clinical Laboratory Tests

Laboratory data will be summarized by type of laboratory test (eg, hematology, clinical chemistry). Selected laboratory parameters will be summarized by treatment groups. Common Terminology Criteria (CTC) will be used to identify abnormal laboratory test results, and the incidence and severity of abnormal laboratory parameters (hematology and chemistry) will be summarized by treatment group.

In addition, a listing of participants with grade 3 or higher laboratory test results (based on the CTC criteria) will also be provided.

Vital Signs

Descriptive statistics of heart rate and blood pressure (systolic and diastolic) values and changes from baseline will be summarized at each scheduled time point.

Weight and Waist Circumference

Descriptive statistics of changes from baseline will be summarized at selected scheduled time points.

9.4.4. Other Analyses

Pharmacokinetic Analyses

Serum guselkumab concentrations over time will be summarized for treated participants. Descriptive statistics, including arithmetic mean, SD, median, interquartile range, minimum, and maximum will be calculated at each nominal sampling timepoint. All concentrations below the lowest quantifiable concentration of the assay (BQL) or missing data will be labeled as such in the concentration data listing or statistical analysis dataset. The BQL concentrations will be treated as zero in the summary statistics.

Population PK modeling may be conducted when appropriate. The analysis will be presented in a separate technical report when applicable.

Pharmacokinetic/Pharmacodynamic Analyses

The relationship between serum guselkumab concentrations and PD and/or efficacy measures may be examined when appropriate.

Immunogenicity Analyses

The incidence and titers of anti-guselkumab antibodies will be summarized for all participants who receive at least 1 dose of guselkumab and have appropriate samples for detection of antibodies to guselkumab (ie, participants with at least 1 sample obtained after their first dose of guselkumab). A listing of participants who are positive for antibodies to guselkumab will be provided. The maximum titers of antibodies to guselkumab will be summarized for participants who are positive for antibodies to guselkumab.

The incidence of neutralizing antibodies (NAbs) to guselkumab will be summarized for participants who are positive for antibodies to guselkumab and have samples evaluable for NAbs to guselkumab.

Biomarker Analyses

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information. Any biomarker samples received by the contract vendor or sponsor after the cutoff date will not be analyzed, and therefore, excluded from the biomarker analysis.

Changes in serum analytes obtained over time will be summarized by treatment group. Associations between baseline levels and changes from baseline in select markers and response to treatment will be explored. The analyses will aim to identify biomarker relevant to treatment. Results of serum biomarker analyses will be reported in separate technical reports.

9.5. Interim Analysis

Before the first DBL at Week 16, an interim analysis will be conducted when a subset of the participants has completed the Week 16 visit. Details of the plan for the interim analysis will be specified in a separate interim analysis plan before the time at which the interim analysis is performed. The interim analysis will be used to determine whether the efficacy of guselkumab 1200 mg IV and guselkumab 200 mg SC doses, as measured by the primary endpoint, is sufficiently low to consider terminating the study based on prespecified criteria from the data accrued up to the interim analysis. Interim analysis results will not be disseminated to investigators or individuals associated with the conduct of the study.

A sponsor's committee otherwise not involved in the study conduct will be responsible for reviewing the results of this interim analysis. The interim analysis plan will define the organization and roles and responsibilities of the committee, possible recommendations or requests, and the communication following this review.

9.6. Data Monitoring Committee

An independent DMC will be responsible for monitoring safety data on an ongoing basis to ensure the continuing safety of the participants enrolled in this study. The committee will meet regularly to review unblinded safety data. After the review, the DMC will make recommendations to the sponsor regarding the conduct of the study. The details will be provided in the DMC charter. The DMC will consist of at least one clinical physician with relevant therapeutic expertise (dermatology) and one statistician. DMC responsibilities, authorities, and procedures will be documented in the DMC charter.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Abbreviations and Trademarks

AE	Adverse Events
AN	Abscess and inflammatory nodule
ANCOVA	Analysis of covariance
ARC	Anticipated Event Review Committee
AUC	area under the serum concentration versus time curve
BCG	Bacille Calmette-Guérin
BQL	Below the lowest quantifiable concentration of the assay
CMH	Cochran-Mantel-Haenszel
CTC	Common Terminology Criteria
DBL	Database Lock
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EP	Erythrodermic psoriasis
FAS	Full analysis set
FSH	Follicle-stimulating hormone
GCP	Good Clinical Practice
GPP	Generalized pustular psoriasis
HADS	Hospital Anxiety and Depression Scale
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human immunodeficiency virus
HiSCR	Hidradenitis Suppurativa Clinical Response
HRT	Hormonal replacement therapy
HS	Hidradenitis suppurativa
HSSD	Hidradenitis Suppurativa Symptom Diary
IB	Investigator's Brochure
ICF	Informed consent form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IGA	Investigator's global assessment
IP	Investigational Product
IWRS	Interactive Web Response System
IV	Intravenous
LTE	Long-term extensions
mAb	Monoclonal antibody
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-Effect Model Repeated Measure
MTX	Methotrexate
NAb	Neutralizing antibody
NOAEL	No-observed-adverse-effect level
PD	Pharmacodynamics
PFS-U	Prefilled syringe with an UltraSafe PLUS™ Passive Needle Guard
PGIC	Patient Global Impression of Change
PK	Pharmacokinetics
POC	Proof-of-concept
PPD	Purified protein derivative
PPP	Palmoplantar pustular psoriasis
PQC	Product quality complaint
PRO	Patient-reported outcomes
PsA	Psoriatic arthritis

SAE	Serious adverse event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard deviation
SUSAR	Suspected unexpected serious adverse reactions
TB	Tuberculosis
TU	Tuberculin units

Definitions of Terms

Electronic source system	Contains data traditionally maintained in a hospital or clinic record to document medical care or data recorded in a CRF as determined by the protocol. Data in this system may be considered source documentation.

10.2. Appendix 2: Anticipated Events

Anticipated Event

An anticipated event is an adverse event (serious or non-serious) that commonly occurs as a consequence of the underlying disease or condition under investigation (disease-related) or background regimen.

For the purposes of this study the following events will be considered anticipated events:

- Worsening of HS

Reporting of Anticipated Events

All AEs will be recorded in the eCRF regardless of whether considered to be anticipated events and will be reported to the sponsor as described under All Adverse Events in Section 8.3.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information. Any anticipated event that meets serious adverse event criteria will be reported to the sponsor as described under Serious Adverse Events in Section 8.3.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information. These anticipated events are exempt from expedited reporting as individual single cases to health authorities. However, if based on an aggregate review, it is determined that an anticipated event is possibly related to study intervention, the sponsor will report these events in an expedited manner.

Anticipated Event Review Committee

An Anticipated Event Review Committee (ARC) will be established to perform reviews of prespecified anticipated events at an aggregate level. The ARC is a safety committee within the sponsor's organization that is independent of the sponsor's study team. The ARC will meet to aid in the recommendation to the sponsor's study team as to whether there is a reasonable possibility that an anticipated event is related to the study intervention.

Statistical Analysis

Details of statistical analysis of anticipated events, including the frequency of review and threshold to trigger an aggregate analysis of anticipated events will be provided in a separate Anticipated Events Safety Monitoring Plan.

10.3. Appendix 3: Clinical Laboratory Tests

The following tests will be performed according to the Schedule of Activities (Section 1.3) by the central laboratory:

Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters		
Hematology	Platelet count Red blood cell count Hemoglobin Hematocrit	RBC Indices: MCV MCH	White Blood Cell (WBC) count with Differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils Bands
Clinical Chemistry	Sodium Potassium Chloride Blood urea nitrogen (BUN) Creatinine Glucose Aspartate aminotransferase (AST)/Serum glutamic-oxaloacetic Alanine aminotransferase (ALT)/Serum glutamic-oxaloacetic	Total bilirubin Indirect bilirubin Alkaline phosphatase Calcium Phosphate Albumin Total protein	
Other Laboratory Tests	• Urine pregnancy testing for women of childbearing potential only • Lipids (Week 0 only) • High-sensitivity C-reactive protein • Serology (HIV antibody, hepatitis B surface antigen [HBsAg], hepatitis B surface antibody [anti-HBs], hepatitis B core antibody [anti-HBc], and hepatitis C virus antibody		

10.4. Appendix 4: Tuberculin Skin Testing

Administering the Mantoux Tuberculin Skin Test

The Mantoux tuberculin skin test (CDC, 2000) is the standard method of identifying persons infected with *Mycobacterium tuberculosis*. Multiple puncture tests (Tine and Heaf) should not be used to determine whether a person is infected because the amount of tuberculin injected intradermally cannot be precisely controlled. Tuberculin skin testing is both safe and reliable throughout the course of pregnancy. The Mantoux tuberculin test is performed by placing an intradermal injection of 0.1 mL of tuberculin into the inner surface of the forearm. The test must be performed with tuberculin that has at least the same strength as either 5 tuberculin units (TU) of standard purified protein derivative (PPD)-S or 2 TU of PPD-RT 23, Statens Seruminstitut, as recommended by the World Health Organization. PPD strengths of 1 TU or 250 TU are not acceptable (Menzies, 2000). Using a disposable tuberculin syringe with the needle bevel facing upward, the injection should be made just beneath the surface of the skin. This should produce a discrete, pale elevation of the skin (a wheal) 6 mm to 10 mm in diameter. To prevent needle-stick injuries, needles should not be recapped, purposely bent or broken, removed from disposable syringes, or otherwise manipulated by hand. After they are used, disposable needles and syringes should be placed in puncture-resistant containers for disposal. Institutional guidelines regarding universal precautions for infection control (eg, the use of gloves) should be followed. A trained health care worker, preferably the investigator, should read the reaction to the Mantoux test 48 to 72 hours after the injection. Participants should never be allowed to read their own tuberculin skin test results. If a participant fails to show up for the scheduled reading, a positive reaction may still be measurable up to 1 week after testing. However, if a participant who fails to return within 72 hours has a negative test, tuberculin testing should be repeated. The area of induration (palpable raised hardened area) around the site of injection is the reaction to tuberculin. For standardization, the diameter of the induration should be measured transversely (perpendicular) to the long axis of the forearm. Erythema (redness) should not be measured. All reactions should be recorded in millimeters, even those classified as negative.

Interpreting the Tuberculin Skin Test Results

In the US and many other countries, the most conservative definition of positivity for the tuberculin skin test is reserved for immunocompromised patients, and this definition is to be applied in this study to maximize the likelihood of detecting latent TB, even though the participants may not be immunocompromised at baseline.

In the US and Canada, an induration of 5 mm or greater in response to the intradermal tuberculin skin test is considered to be a positive result and evidence for either latent or active TB.

In countries outside the US and Canada, country-specific guidelines **for immunocompromised patients** should be consulted for the interpretation of tuberculin skin test results. If no local country guidelines for immunocompromised patients exist, US guidelines must be followed.

Treatment of Latent Tuberculosis

Local country guidelines **for immunocompromised patients** should be consulted for acceptable antituberculous treatment regimens for latent TB. If no local country guidelines for immunocompromised patients exist, US guidelines must be followed.

References

Centers for Disease Control and Prevention. Core curriculum on tuberculosis: What the clinician should know (Fourth Edition). Atlanta, GA: Department of Health and Human Services; Centers for Disease Control and Prevention; National Center for HIV, STD, and TB Prevention; Division of Tuberculosis Elimination; 2000:25-86.

Menzies RI. Tuberculin skin testing. In: Reichman LB, Hershfield ES (eds). *Tuberculosis, a comprehensive international approach*. 2nd ed. New York, NY: Marcel Dekker, Inc; 2000:279-322.

10.5. Appendix 5: Regulatory, Ethical, and Study Oversight Considerations

REGULATORY AND ETHICAL CONSIDERATIONS

Investigator Responsibilities

The investigator is responsible for ensuring that the study is performed in accordance with the protocol, current International Conference on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP), and applicable regulatory and country-specific requirements.

Good Clinical Practice is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and well-being of study participants are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the study data are credible.

Protocol Amendments

Neither the investigator nor the sponsor will modify this protocol without a formal amendment by the sponsor. All protocol amendments must be issued by the sponsor and signed and dated by the investigator. Protocol amendments must not be implemented without prior IEC/IRB approval, or when the relevant competent authority has raised any grounds for non-acceptance, except when necessary to eliminate immediate hazards to the participants, in which case the amendment must be promptly submitted to the IEC/IRB and relevant competent authority. Documentation of amendment approval by the investigator and IEC/IRB must be provided to the sponsor. When the change(s) involve only logistic or administrative aspects of the study, the IEC/IRB (where required) only needs to be notified.

During the course of the study, in situations where a departure from the protocol is unavoidable, the investigator or other physician in attendance will contact the appropriate sponsor representative listed in the Contact Information page(s), which will be provided as a separate document. Except in emergency situations, this contact should be made before implementing any departure from the protocol. In all cases, contact with the sponsor must be made as soon as possible to discuss the situation and agree on an appropriate course of action. The data recorded in the eCRF and source documents will reflect any departure from the protocol, and the source documents will describe this departure and the circumstances requiring it.

Regulatory Approval/Notification

This protocol and any amendment(s) must be submitted to the appropriate regulatory authorities in each respective country, if applicable. A study may not be initiated until all local regulatory requirements are met.

Required Prestudy Documentation

The following documents must be provided to the sponsor before shipment of study intervention to the study-site:

- Protocol and amendment(s), if any, signed and dated by the principal investigator.
- A copy of the dated and signed (or sealed, where appropriate per local regulations), written IEC/IRB approval of the protocol, amendments, ICF, any recruiting materials, and if applicable, participant compensation programs. This approval must clearly identify the specific protocol by title and number and must be signed (or sealed, where appropriate per local regulations) by the chairman or authorized designee.
- Name and address of the IEC/IRB, including a current list of the IEC/IRB members and their function, with a statement that it is organized and operates according to GCP and the applicable laws and regulations. If accompanied by a letter of explanation, or equivalent, from the IEC/IRB, a general statement may be substituted for this list. If an investigator or a member of the study-site personnel is a member of the IEC/IRB, documentation must be obtained to state that this person did not participate in the deliberations or in the vote/opinion of the study.
- Regulatory authority approval or notification, if applicable.
- Signed and dated statement of investigator (eg, Form FDA 1572), if applicable.
- Documentation of investigator qualifications (eg, curriculum vitae).
- Completed investigator financial disclosure form from the principal investigator, where required.
- Signed and dated clinical trial agreement, which includes the financial agreement.
- Any other documentation required by local regulations.

The following documents must be provided to the sponsor before enrollment of the first participant:

- Completed investigator financial disclosure forms from all sub-investigators
- Documentation of sub-investigator qualifications (eg, curriculum vitae)
- Name and address of any local laboratory conducting tests for the study, and a dated copy of current laboratory normal ranges for these tests, if applicable
- Local laboratory documentation demonstrating competence and test reliability (eg, accreditation/license), if applicable

Independent Ethics Committee or Institutional Review Board

Before the start of the study, the investigator (or sponsor where required) will provide the IEC/IRB with current and complete copies of the following documents (as required by local regulations):

- Final protocol and, if applicable, amendments
- Sponsor-approved ICF (and any other written materials to be provided to the participants)
- IB (or equivalent information) and amendments/addenda
- Sponsor-approved participant recruiting materials

- Information on compensation for study-related injuries or payment to participants for participation in the study, if applicable
- Investigator's curriculum vitae or equivalent information (unless not required, as documented by the IEC/IRB)
- Information regarding funding, name of the sponsor, institutional affiliations, other potential conflicts of interest, and incentives for participants
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after the IEC/IRB has given full approval of the final protocol, amendments (if any, excluding the ones that are purely administrative, with no consequences for participants, data or study conduct, unless required locally), the ICF, applicable recruiting materials, and participant compensation programs, and the sponsor has received a copy of this approval. This approval letter must be dated and must clearly identify the IEC/IRB and the documents being approved.

Approval for the collection of optional samples for research and for the corresponding ICF must be obtained from the IEC/IRB. Approval for the protocol can be obtained independent of this optional research component.

During the study the investigator (or sponsor where required) will send the following documents and updates to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct)
- Revision(s) to ICF and any other written materials to be provided to participants
- If applicable, new or revised participant recruiting materials approved by the sponsor
- Revisions to compensation for study-related injuries or payment to participants for participation in the study, if applicable
- New edition(s) of the IB and amendments/addenda
- Summaries of the status of the study at intervals stipulated in guidelines of the IEC/IRB (at least annually)
- Reports of AEs that are serious, unlisted/unexpected, and associated with the study intervention
- New information that may adversely affect the safety of the participants or the conduct of the study
- Deviations from or changes to the protocol to eliminate immediate hazards to the participants
- Report of deaths of participants under the investigator's care
- Notification if a new investigator is responsible for the study at the site

- Development Safety Update Report and Line Listings, where applicable
- Any other requirements of the IEC/IRB

For all protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct), the amendment and applicable ICF revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).

At least once a year, the IEC/IRB will be asked to review and reapprove this study, where required.

At the end of the study, the investigator (or sponsor where required) will notify the IEC/IRB about the study completion (if applicable, the notification will be submitted through the head of investigational institution).

Country Selection

This study will only be conducted in those countries where the intent is to launch or otherwise help ensure access to the developed product if the need for the product persists, unless explicitly addressed as a specific ethical consideration in Section 4.2.1, Study-Specific Ethical Design Considerations.

Other Ethical Considerations

For study-specific ethical design considerations, refer to Section 4.2.1.

FINANCIAL DISCLOSURE

Investigators and sub-investigators will provide the sponsor with sufficient, accurate financial information in accordance with local regulations to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

Refer to Required Prestudy Documentation (above) for details on financial disclosure.

INFORMED CONSENT PROCESS

Each participant must give written consent according to local requirements after the nature of the study has been fully explained. The ICF(s) must be signed before performance of any study-related activity. The ICF(s) that is/are used must be approved by both the sponsor and by the reviewing IEC/IRB and be in a language that the participant can read and understand. The informed consent should be in accordance with principles that originated in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy.

Before enrollment in the study, the investigator or an authorized member of the study-site personnel must explain to potential participants the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive. Finally, they will be told that the investigator will maintain a participant identification register for the purposes of long-term follow-up if needed and that their records may be accessed by health authorities and authorized sponsor personnel without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations. By signing the ICF the participant is authorizing such access. It also denotes that the participant agrees to allow his or her study physician to re-contact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed.

The participant will be given sufficient time to read the ICF and the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by means of the participant's personally dated signature. After having obtained the consent, a copy of the ICF must be given to the participant.

A participant may be rescreened 1 time. Participants who are rescreened are required to sign a new ICF.

Completion of screening and randomization procedures within the specified approximately 4-week window is required. If a participant is approaching the completion of that period, the medical monitor can be contacted to discuss eligibility.

If any delay leads to the expiration of time-specific assessments (eg, TB, chest radiograph), the participant will be considered a screen failure because he/she will not meet eligibility criteria, and the expired assessments (along with the non-time-specific laboratory tests) will have to be repeated on rescreening.

DATA PROTECTION

Privacy of Personal Data

The collection and processing of personal data from participants enrolled in this study will be limited to those data that are necessary to fulfill the objectives of the study.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of participants confidential.

The informed consent obtained from the participant includes explicit consent for the processing of personal data and for the investigator/institution to allow direct access to his or her original medical records (source data/documents) for study-related monitoring, audit, IEC/IRB review, and regulatory inspection. This consent also addresses the transfer of the data to other entities and to other countries.

The participant has the right to request through the investigator access to his or her personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps will be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Exploratory biomarker, PK, and immunogenicity research is not conducted under standards appropriate for the return of data to participants. In addition, the sponsor cannot make decisions as to the significance of any findings resulting from exploratory research. Therefore, exploratory research data will not be returned to participants or investigators, unless required by law or local regulations. Privacy and confidentiality of data generated in the future on stored samples will be protected by the same standards applicable to all other clinical data.

LONG-TERM RETENTION OF SAMPLES FOR ADDITIONAL FUTURE RESEARCH

Samples collected in this study may be stored for up to 15 years (or according to local regulations) for additional research. Samples will only be used to understand guselkumab, to understand HS, to understand differential intervention responders, and to develop tests/assays related to guselkumab and HS. The research may begin at any time during the study or the post-study storage period. The start of the storage period will be the time at which the Clinical Study Report is issued.

Stored samples will be coded throughout the sample storage and analysis process and will not be labeled with personal identifiers. Participants may withdraw their consent for their samples to be stored for research (refer to Section 7.2.1, Withdrawal from the Use of Research Samples).

COMMITTEES STRUCTURE

Data Monitoring Committee

Details regarding the DMC are presented in Section 9.6

PUBLICATION POLICY/DISSEMINATION OF CLINICAL STUDY DATA

All information, including but not limited to information regarding guselkumab or the sponsor's operations (eg, patent application, formulas, manufacturing processes, basic scientific data, prior clinical data, formulation information) supplied by the sponsor to the investigator and not previously published, and any data, including exploratory biomarker research data, generated as a result of this study, are considered confidential and remain the sole property of the sponsor. The investigator agrees to maintain this information in confidence and use this information only

to accomplish this study, and will not use it for other purposes without the sponsor's prior written consent.

The investigator understands that the information developed in the study will be used by the sponsor in connection with the continued development of guselkumab, and thus may be disclosed as required to other clinical investigators or regulatory agencies. To permit the information derived from the clinical studies to be used, the investigator is obligated to provide the sponsor with all data obtained in the study.

The results of the study will be reported in a Clinical Study Report generated by the sponsor and will contain data from all study sites that participated in the study as per protocol. Recruitment performance or specific expertise related to the nature and the key assessment parameters of the study will be used to determine a coordinating investigator for the study. Results of exploratory biomarker analyses performed after the Clinical Study Report has been issued will be reported in a separate report and will not require a revision of the Clinical Study Report.

Study participant identifiers will not be used in publication of results. Any work created in connection with performance of the study and contained in the data that can benefit from copyright protection (except any publication by the investigator as provided for below) shall be the property of the sponsor as author and owner of copyright in such work.

Consistent with Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines, the sponsor shall have the right to publish such primary (multicenter) data and information without approval from the investigator. The investigator has the right to publish study-site-specific data after the primary data are published. If an investigator wishes to publish information from the study, a copy of the manuscript must be provided to the sponsor for review at least 60 days before submission for publication or presentation. Expedited reviews will be arranged for abstracts, poster presentations, or other materials. If requested by the sponsor in writing, the investigator will withhold such publication for up to an additional 60 days to allow for filing of a patent application. In the event that issues arise regarding scientific integrity or regulatory compliance, the sponsor will review these issues with the investigator. The sponsor will not mandate modifications to scientific content and does not have the right to suppress information. For multicenter study designs and sub-study approaches, secondary results generally should not be published before the primary endpoints of a study have been published. Similarly, investigators will recognize the integrity of a multicenter study by not submitting for publication data derived from the individual study-site until the combined results from the completed study have been submitted for publication, within 18 months after the study end date, or the sponsor confirms there will be no multicenter study publication. Authorship of publications resulting from this study will be based on the guidelines on authorship, such as those described in the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals, which state that the named authors must have made a significant contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of the data for the work; and drafted the work or revised it critically for important intellectual content; and given final approval of the version to be published; and

agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Registration of Clinical Studies and Disclosure of Results

The sponsor will register and disclose the existence of and the results of clinical studies as required by law.

DATA QUALITY ASSURANCE

Data Quality Assurance/Quality Control

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study sites, review of protocol procedures with the investigator and study-site personnel before the study, periodic monitoring visits by the sponsor, and direct transmission of clinical laboratory data from a central laboratory into the sponsor's data base. Written instructions will be provided for collection, handling, storage, and shipment of samples.

The sponsor or designee will review the eCRF for accuracy and completeness during on-site monitoring visits and after transmission to the sponsor; any discrepancies will be resolved with the investigator or designee, as appropriate. After upload of the data into the study database they will be verified for accuracy and consistency with the data sources.

CASE REPORT FORM COMPLETION

Case report forms are prepared and provided by the sponsor for each participant in electronic format. All data relating to the study must be recorded in the eCRF. All eCRF entries, corrections, and alterations must be made by the investigator or authorized study-site personnel. The investigator must verify that all data entries in the eCRF are accurate and correct.

The study data will be transcribed by study-site personnel from the source documents onto an eCRF, if applicable. Study-specific data will be transmitted in a secure manner to the sponsor.

Worksheets may be used for the capture of some data to facilitate completion of the eCRF. Any such worksheets will become part of the participant's source documents. Data must be entered into the eCRF in English. The eCRF must be completed as soon as possible after a participant visit and the forms should be available for review at the next scheduled monitoring visit.

If necessary, queries will be generated in the eDC tool. If corrections to an eCRF are needed after the initial entry into the eCRF, this can be done in either of the following ways:

- Investigator and study-site personnel can make corrections in the eDC tool at their own initiative or as a response to an auto query (generated by the eDC tool).
- Sponsor or sponsor delegate can generate a query for resolution by the investigator and study-site personnel.

SOURCE DOCUMENTS

At a minimum, source documents consistent in the type and level of detail with that commonly recorded at the study-site as a basis for standard medical care must be available for the following: participant identification, eligibility, and study identification; study discussion and date and time of signed informed consent; dates of visits; results of safety and efficacy parameters as required by the protocol; record of all AEs and follow-up of AEs; concomitant medication; intervention receipt/dispensing/return records; study intervention administration information; and date of study completion and reason for early discontinuation of study intervention or withdrawal from the study, if applicable.

The author of an entry in the source documents should be identifiable.

Specific details required as source data for the study and source data collection methods will be reviewed with the investigator before the study and will be described in the monitoring guidelines (or another equivalent document).

The minimum source documentation requirements for Section 5.1, Inclusion Criteria and Section 5.2, Exclusion Criteria that specify a need for documented medical history are as follows:

- Referral letter from treating physician or
- Complete history of medical notes at the site
- Discharge summaries

Inclusion and exclusion criteria not requiring documented medical history must be verified at a minimum by participant interview or other protocol-required assessment (eg, physical examination, laboratory assessment) and documented in the source documents.

An electronic source (eSource) system may be utilized, which contains data traditionally maintained in a hospital or clinic record to document medical care (eg, electronic source documents) as well as the clinical study-specific data fields as determined by the protocol. This data is electronically extracted for use by the sponsor. If eSource is utilized, references made to the eCRF in the protocol include the eSource system but information collected through eSource may not be limited to that found in the eCRF.

MONITORING

The sponsor designee will perform on-site monitoring visits as frequently as necessary. This will include blinded site monitors who will perform source data verification and review drug preparation and dispensation. The monitor will record dates of the visits in a study-site visit log that will be kept at the study-site, as allowed by local regulation. The first post-initiation visit will be made as soon as possible after enrollment has begun. At these visits, the monitor will compare the data entered into the eCRF (as defined in the monitoring guidelines) with the source documents (eg, hospital/clinic/physician's office medical records). The nature and location of all

source documents will be identified to ensure that all sources of original data required to complete the eCRF are known to the sponsor and study-site personnel and are accessible for verification by the sponsor study-site contact. If electronic records are maintained at the study-site, the method of verification must be discussed with the study-site personnel.

Direct access to source documents (medical records) must be allowed for the purpose of verifying that the recorded data are consistent with the original source data. Findings from this review will be discussed with the study-site personnel. The sponsor expects that, during monitoring visits, the relevant study-site personnel will be available, the source documents will be accessible, and a suitable environment will be provided for review of study-related documents. The monitor will meet with the investigator on a regular basis during the study to provide feedback on the study conduct.

In addition to on-site monitoring visits, remote contacts will occur. It is expected that during these remote contacts, study-site personnel will be available to provide an update on the progress of the study at the site.

ON-SITE AUDITS

Representatives of the sponsor's clinical quality assurance department may visit the study-site at any time during or after completion of the study to conduct an audit of the study in compliance with regulatory guidelines and company policy. These audits will require access to all study records, including source documents, for inspection. Participant privacy must, however, be respected. The investigator and study-site personnel are responsible for being present and available for consultation during routinely scheduled study-site audit visits conducted by the sponsor or its designees.

Similar auditing procedures may also be conducted by agents of any regulatory body, either as part of a national GCP compliance program or to review the results of this study in support of a regulatory submission. The investigator should immediately notify the sponsor if he or she has been contacted by a regulatory agency concerning an upcoming inspection.

RECORD RETENTION

In compliance with the ICH/GCP guidelines, the investigator/institution will maintain all eCRF and all source documents that support the data collected from each participant, as well as all study documents as specified in ICH/GCP Section 8, Essential Documents for the Conduct of a Clinical Trial, and all study documents as specified by the applicable regulatory requirement(s). The investigator/institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the IP. These documents will be retained for a longer

period if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

If the responsible investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the investigator relocate or dispose of any study documents before having obtained written approval from the sponsor.

If it becomes necessary for the sponsor or the appropriate regulatory authority to review any documentation relating to this study, the investigator/institution must permit access to such reports.

STUDY AND SITE CLOSURE

Study Termination

The sponsor reserves the right to close the study-site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study-site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study-site by the sponsor or investigator may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IEC/IRB or local health authorities, the sponsor's procedures, or GCP guidelines
- Inadequate recruitment of participants by the investigator
- Discontinuation of further study intervention development

10.6. Appendix 6: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

ADVERSE EVENT DEFINITIONS AND CLASSIFICATIONS

Adverse Event

An adverse event is any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An adverse event does not necessarily have a causal relationship with the intervention. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. (Definition per ICH)

This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

Note: The sponsor collects AEs starting with the signing of the ICF (refer to All Adverse Events under Section 8.3.1, Time Period and Frequency for Collecting Adverse Events and Serious Adverse Events Information, for time of last adverse event recording).

Serious Adverse Event

A serious adverse event based on ICH and EU Guidelines on Pharmacovigilance for Medicinal Products for Human Use is any untoward medical occurrence that at any dose:

- Results in death
- Is life-threatening
  (The participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is a suspected transmission of any infectious agent via a medicinal product
- Is Medically Important*

*Medical and scientific judgment should be exercised in deciding whether expedited reporting is also appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above. These should usually be considered serious.

Unlisted (Unexpected) Adverse Event/Reference Safety Information

An adverse event is considered unlisted if the nature or severity is not consistent with the applicable product reference safety information. For guselkumab, the expectedness of an adverse event will be determined by whether or not it is listed in the IB.

Adverse Event Associated with the Use of the Intervention

An adverse event is considered associated with the use of the intervention if the attribution is possible, probable, or very likely by the definitions listed below (see Attribution Definitions).

ATTRIBUTION DEFINITIONS

Not Related

An adverse event that is not related to the use of the intervention.

Doubtful

An adverse event for which an alternative explanation is more likely, eg, concomitant treatment(s), concomitant disease(s), or the relationship in time suggests that a causal relationship is unlikely.

Possible

An adverse event that might be due to the use of the intervention. An alternative explanation, eg, concomitant treatment(s), concomitant disease(s), is inconclusive. The relationship in time is reasonable; therefore, the causal relationship cannot be excluded.

Probable

An adverse event that might be due to the use of the intervention. The relationship in time is suggestive (eg, confirmed by dechallenge). An alternative explanation is less likely, eg, concomitant treatment(s), concomitant disease(s).

Very Likely

An adverse event that is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation, eg, concomitant treatment(s), concomitant disease(s). The relationship in time is very suggestive (eg, it is confirmed by dechallenge and rechallenge).

SEVERITY CRITERIA

An assessment of severity grade will be made using the following general categorical descriptors:

Mild: Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with everyday activities.

Moderate: Sufficient discomfort is present to cause interference with normal activity.

Severe: Extreme distress, causing significant impairment of functioning or incapacitation. Prevents normal everyday activities.

The investigator should use clinical judgment in assessing the severity of events not directly experienced by the participant (eg, laboratory abnormalities).

SPECIAL REPORTING SITUATIONS

Safety events of interest on a sponsor study intervention in an interventional study that may require expedited reporting or safety evaluation include, but are not limited to:

- Overdose of a sponsor study intervention
- Suspected abuse/misuse of a sponsor study intervention
- Accidental or occupational exposure to a sponsor study intervention
- Medication error involving a sponsor product (with or without participant/patient exposure to the sponsor study intervention, eg, name confusion)
- Exposure to a sponsor study intervention from breastfeeding

Special reporting situations should be recorded in the eCRF. Any special reporting situation that meets the criteria of a serious adverse event should be recorded on the serious adverse event page of the eCRF.

PROCEDURES

All Adverse Events

All AEs, regardless of seriousness, severity, or presumed relationship to study intervention, must be recorded using medical terminology in the source document and the eCRF. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (eg, cough, runny nose, sneezing, sore throat, and head congestion should be reported as "upper respiratory infection"). Investigators must record in the eCRF their opinion concerning the relationship of the adverse event to study therapy. All measures required for adverse event management must be recorded in the source document and reported according to sponsor instructions.

For all studies with an outpatient period, including open-label studies, the participant must be provided with a "wallet (study) card" and instructed to carry this card with them for the duration of the study indicating the following:

- Study number
- Statement, in the local language(s), that the participant is participating in a clinical study
- Investigator's name and 24-hour contact telephone number
- Local sponsor's name and 24-hour contact telephone number (for medical staff only)
- Site number

- Participant number
- Any other information that is required to do an emergency breaking of the blind

Serious Adverse Events

All SAEs that have not resolved by the end of the study, or that have not resolved upon discontinuation of the participant's participation in the study, must be followed until any of the following occurs:

- The event resolves
- The event stabilizes
- The event returns to baseline, if a baseline value/status is available
- The event can be attributed to agents other than the study intervention or to factors unrelated to study conduct
- It becomes unlikely that any additional information can be obtained (participant or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts)

Suspected transmission of an infectious agent by a medicinal product will be reported as a serious adverse event. Any event requiring hospitalization (or prolongation of hospitalization) that occurs during the course of a participant's participation in a study must be reported as a serious adverse event, except hospitalizations for the following:

- Hospitalizations not intended to treat an acute illness or adverse event (eg, social reasons such as pending placement in long-term care facility).
- Surgery or procedure planned before entry into the study (must be documented in the eCRF). Note: Hospitalizations that were planned before the signing of the ICF, and where the underlying condition for which the hospitalization was planned has not worsened, will not be considered SAEs. Any adverse event that results in a prolongation of the originally planned hospitalization is to be reported as a new serious adverse event.

The cause of death of a participant in a study within 16 weeks of the last dose of study intervention, whether or not the event is expected or associated with the study intervention, is considered a serious adverse event.

CONTACTING SPONSOR REGARDING SAFETY

The names (and corresponding telephone numbers) of the individuals who should be contacted regarding safety issues or questions regarding the study are listed in the Contact Information page(s), which will be provided as a separate document.

PRODUCT QUALITY COMPLAINT HANDLING

A PQC is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, ie, any dissatisfaction relative to the identity, quality, durability, or reliability of a product, including its labeling or package integrity. A PQC may have an impact on the safety and

efficacy of the product. Timely, accurate, and complete reporting and analysis of PQC information from studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of PQC information; all studies conducted by the sponsor or its affiliates will be conducted in accordance with those procedures.

Procedures

All initial PQCs must be reported to the sponsor by the study-site personnel within 24 hours after being made aware of the event.

If the defect is combined with a serious adverse event, the study-site personnel must report the PQC to the sponsor according to the serious adverse event reporting timelines (refer to Section 8.3.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information). A sample of the suspected product should be maintained for further investigation if requested by the sponsor.

Contacting Sponsor Regarding Product Quality

The names (and corresponding telephone numbers) of the individuals who should be contacted regarding product quality issues are listed in the Contact Information page(s), which will be provided as a separate document.

10.7. Appendix 7: Contraceptive and Barrier Guidance and Collection of Pregnancy Information

Participants must follow contraceptive measures as outlined in Section 5.1, Inclusion Criteria. Pregnancy information will be collected and reported as noted in Section 8.3.4, Pregnancy and Appendix 6 (Section 10.6), Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

Definitions

Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

Woman Not of Childbearing Potential

- **premenarchal**

  A premenarchal state is one in which menarche has not yet occurred.

- **postmenopausal**

  A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high FSH level (>40 IU/L or mIU/mL) in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT), however in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient. If there is a question about menopausal status in women on HRT, the woman will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if she wishes to continue HRT during the study.

- **permanently sterile**

  Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy.

Note: If the childbearing potential changes after start of the study (eg, a premenarchal woman experiences menarche) or the risk of pregnancy changes (eg, a woman who is not heterosexually active becomes active), a woman must begin a highly effective method of contraception, as described throughout the inclusion criteria.

If reproductive status is questionable, additional evaluation should be considered.

As noted in Inclusion Criterion 8, study participants who are women of childbearing potential must be practicing a highly effective method of contraception and remain on a highly effective method while receiving study intervention and until 12 weeks after last dose. Examples of highly effective methods of contraception are provided below; however, the method selected must meet local/regional regulations/guidelines for highly effective contraception.

Examples of Contraceptives

EXAMPLES OF CONTRACEPTIVES[a] ALLOWED DURING THE STUDY INCLUDE:
USER-INDEPENDENT **Highly Effective Methods That Are User-Independent** *Failure rate of ≤1% per year when used consistently and correctly.*
• Implantable progestogen-only hormone contraception associated with inhibition of ovulation[b]
• Intrauterine device (IUD)
• Intrauterine hormone-releasing system (IUS)
• Bilateral tubal occlusion
• Vasectomized partner *(Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the woman of childbearing potential and the absence of sperm has been confirmed. If not, additional highly effective method of contraception should be used. Spermatogenesis cycle is approximately 74 days.)*
USER-DEPENDENT **Highly Effective Methods That Are User-Dependent** *Failure rate of <1% per year when used consistently and correctly.*
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation[b] – oral – intravaginal – transdermal – injectable
• Progestogen-only hormone contraception associated with inhibition of ovulation[b] – oral – injectable
• Sexual abstinence *(Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.)*
NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION DURING THE STUDY (not considered to be highly effective - failure rate of >1% per year).
• Progestogen-only oral hormonal contraception where inhibition of ovulation is not the primary mode of action.
• Male or female condom with or without spermicide[c]
• Cap, diaphragm, or sponge with spermicide
• A combination of male condom with either cap, diaphragm, or sponge with spermicide (double-barrier methods)[c]
• Periodic abstinence (calendar, symptothermal, post-ovulation methods)
• Withdrawal (coitus-interruptus)
• Spermicides alone

• Lactational amenorrhea method (LAM)
a) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies. b) Hormonal contraception may be susceptible to interaction with the study intervention, which may reduce the efficacy of the contraceptive method. In addition, consider if the hormonal contraception may interact with the study intervention. c) Male condom and female condom should not be used together (due to risk of failure with friction).

Pregnancy During the Study

All initial reports of pregnancy in female participants or partners of male participants must be reported to the sponsor or designee by the study-site personnel within 24 hours of their knowledge of the event using the appropriate pregnancy notification form. Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs and must be reported using the Serious Adverse Event Form. Any participant who becomes pregnant during the study must discontinue further study intervention.

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

10.8. Appendix 8: Guselkumab Predicted Exposure Margins

Parameters	Mean C_{max} (µg/mL)	Mean AUC (µg.day/mL)
(a) 1200 mg IV Loading Dosing at Weeks 0, 4 and 8		
Cynomolgus Monkey Exposure at the NOAEL (50 mg/kg/week) Following 4 Weekly IV Doses	1432[a]	4817[b]
Human Predicted IV Exposure	250[c]	1070[d]
Predicted Exposure Margin[e]	***5.7***	***4.5***
(b) 200 mg SC q4w Dosing		
Cynomolgus Monkey Exposure at the NOAEL (50 mg/kg/week) Following 24 Weekly SC Doses	993[a]	5412[b]
Human Predicted SC Exposure	19.5[c]	92.8[d]
Predicted Exposure Margin[e]	***50.9***	***58.3***

[a] Highest observed concentration following the fourth 50 mg/kg IV dose or the twenty-fourth 50 mg/kg SC dose, respectively

[b] For IV, AUC from Day 21 through 28 (one week after the last 50 mg/kg dose); for SC, AUC from Day 161 through 168 (one week after the last 50 mg/kg dose)

[c] Highest predicted concentration after the third 1200 mg IV guselkumab dose, or at steady-state following the 200 mg q4w SC regimen

[d] Predicted human AUC after the third 1200 mg IV guselkumab dose (from Week 8 through Week 12), or at steady-state following 200 mg SC administration. Each value was divided by 4 to obtain the AUC over one week, which in turn corresponds to the AUC interval for cynomolgus monkeys.

[e] Exposure margins represent the ratio between guselkumab exposure metrics in the cynomolgus monkey compared to those predicted in humans.

Abbreviations: AUC= area under the curve; C_{max}= maximum serum concentration; IV = intravenous; NOAEL = non-observed adverse effect level; SC= subcutaneous.

10.9. Appendix 9: Hepatitis B Virus (HBV) Screening With HBV DNA Testing

Participants must undergo screening for HBV. At a minimum, this includes testing for HBsAg (HBV surface antigen), anti-HBs (HBV surface antibody), and anti-HBc total (HBV core antibody total):

- Participants who test negative for all HBV screening tests (ie, HBsAg-, anti-HBc-, and anti-HBs-) ***are eligible*** for this protocol.
- Participants who test **negative** for surface antigen (HBsAg-) and test **positive** for core antibody (anti-HBc+) ***and*** surface antibody (anti-HBs+) ***are eligible*** for this protocol.
- Participants who test **positive only** for **surface antibody** (anti-HBs+) ***are eligible*** for this protocol.
- Participants who test **positive** for surface antigen (HBsAg+) ***are NOT eligible*** for this protocol, regardless of the results of other hepatitis B tests.
- Participants who test **positive only** for **core antibody** (anti-HBc+) must undergo further testing for the presence of hepatitis B virus deoxyribonucleic acid (HBV DNA) test. If the HBV DNA test is **negative**, the participant ***is eligible*** for this protocol. If the HBV DNA test is **positive**, the participant ***is NOT eligible*** for this protocol. In the event the HBV DNA test cannot be performed, the participant ***is NOT eligible*** for this protocol.

These eligibility criteria based on HBV test results are also represented in Table 2 below.

Table 2: Eligibility Based on Hepatitis B Virus Test Results

HEPATITIS B TEST RESULT			STATUS
Hepatitis B surface antigen (HBsAg)	**Hepatitis B surface antibody (anti-HBs)**	**Hepatitis B core antibody (anti-HBc total)**	
negative	negative	negative	**Eligible**
negative	(+)	negative	
negative	(+)	(+)	
(+)	negative *or* (+)	negative *or* (+)	**Not eligible**
negative	negative	(+)	**(Require testing for presence of HBV DNA*)**

* If HBV DNA is detectable, the participant is not eligible for this protocol. If HBV DNA testing cannot be performed, or there is evidence of chronic liver disease, the participant is not eligible for the protocol.

For participants who **are not eligible for this protocol due to HBV test results**, consultation with a physician with expertise in the treatment of hepatitis B virus infection is recommended.

10.10. Appendix 10: Hidradenitis Suppurativa Investigator's Global Assessment

HS-IGA

0=Inactive – no erythema, hypopigmentation or hyperpigmentation may be present; no drainage, areas are dry following palpation; no pain and/or tenderness with palpation.

1=Almost inactive – faint, barely perceptible erythema; scant amount of drainage or discharge with palpation; slight pain and/or tenderness with palpation.

2=Mild activity – light red color; mild spontaneous drainage; mild pain and/or tenderness with palpation.

3=Moderate activity - moderate red color; moderate amount of spontaneous drainage; moderate pain and/or tenderness with palpation, participant winces.

4= Severe activity - bright red coloration; severe spontaneous drainage occurring over broad area(s); severe pain and/or tenderness with palpation, participant winces and attempts to withdraw

Erythema

0=no erythema, hypopigmentation or hyperpigmentation may be present

1= faint, barely perceptible erythema

2= light red color

3= moderate red color

4= bright red coloration

Drainage

0= no drainage, areas are dry following palpation

1= scant amount of discharge with palpation

2= mild spontaneous drainage

3= moderate amount of spontaneous drainage

4= severe spontaneous drainage occurring over broad area(s)

Pain and/or tenderness to gentile palpation (excluding scarring area)

0=no pain and/or tenderness with palpation

1= slight pain and/or tenderness with palpation

2= mild pain and/or tenderness with palpation

3= moderate pain and/or tenderness with palpation, participant winces

4= severe pain and/or tenderness with palpation, participant winces and attempts to withdraw

10.11. Appendix 11: Hidradenitis Suppurativa Symptom Diary

Hidradenitis Suppurativa Symptoms Diary

Individuals with Hidradenitis Suppurativa (HS) may experience a range of symptoms. Please indicate the severity of each symptom, paying close attention to the timeframe for each question. Please select only one number for each item on a scale of 0 to 10 (0 = None, and 10 = Worst possible).

1. What is the severity of pain from your HS affected area(s) right now?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

2. What was the severity of the worst pain from your HS affected area(s) in the past 24 hours?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

3. What was the severity of the worst pain from your HS affected area(s) in the past 7 days?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

4. What was the severity of the worst tenderness (pain when touching) from your HS affected area(s) in the past 7 days?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

5. What was the severity of itch from your HS affected area(s) in the past 7 days?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

6. What was the severity of hot feelings from your HS affected area(s) in the past 7 days?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

7. What was the severity of odor coming from your HS affected area(s) in the past 7 days?

0	1	2	3	4	5	6	7	8	9	10
None										Worst possible

10.12. Appendix 12: Dermatology Life Quality Index

DERMATOLOGY LIFE QUALITY INDEX DLQI

Hospital No: Date: Score:

Name: Diagnosis:

Address:

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please check one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **yard?**	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	☐ ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	

8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

10.13. Appendix 13: Hospital Anxiety and Depression Scale

GL assessment
the measure of potential

Hospital Anxiety and Depression Scale (HADS)

Name: _____ Date: _____

FOLD HERE

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings he or she will be able to help you more.

This questionnaire is designed to help your clinician to know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

FOLD HERE

A	D		A	D
		I feel tense or 'wound up'		
3		Most of the time		
2		A lot of the time		
1		From time to time, occasionally		
0		Not at all		
		I still enjoy the things I used to enjoy		
	0	Definitely as much		
	1	Not quite so much		
	2	Only a little		
	3	Hardly at all		
		I get a sort of frightened feeling as if something awful is about to happen		
3		Very definitely and quite badly		
2		Yes, but not too badly		
1		A little, but it doesn't worry me		
0		Not at all		
		I can laugh and see the funny side of things		
	0	As much as I always could		
	1	Not quite so much now		
	2	Definitely not so much now		
	3	Not at all		
		Worrying thoughts go through my mind		
3		A great deal of the time		
2		A lot of the time		
1		Not too often		
0		Very little		
		I feel cheerful		
	3	Never		
	2	Not often		
	1	Sometimes		
	0	Most of the time		
		I can sit at ease and feel relaxed		
0		Definitely		
1		Usually		
2		Not often		
3		Not at all		
		I feel as if I am slowed down		
		Nearly all the time		3
		Very often		2
		Sometimes		1
		Not at all		0
		I get a sort of frightened feeling like 'butterflies' in the stomach		
		Not at all	0	
		Occasionally	1	
		Quite often	2	
		Very often	3	
		I have lost interest in my appearance		
		Definitely		3
		I don't take as much care as I should		2
		I may not take quite as much care		1
		I take just as much care as ever		0
		I feel restless as if I have to be on the move		
		Very much indeed	3	
		Quite a lot	2	
		Not very much	1	
		Not at all	0	
		I look forward with enjoyment to things		
		As much as I ever did		0
		Rather less than I used to		1
		Definitely less than I used to		2
		Hardly at all		3
		I get sudden feelings of panic		
		Very often indeed	3	
		Quite often	2	
		Not very often	1	
		Not at all	0	
		I can enjoy a good book or radio or television programme		
		Often		0
		Sometimes		1
		Not often		2
		Very seldom		3

Now check that you have answered all the questions

	A	D
TOTAL		

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10.14. Appendix 14: Patient Global Impression of Change of Hidradenitis Symptom Severity

Patient's Global Impression of Change (PGIC)
of Hidradenitis Suppurativa Severity

Compared to when you received the first treatment in this study, how has your Hidradenitis Suppurativa changed? (Please select one response)

- ☐ 1. A lot better now
- ☐ 2. Moderately better now
- ☐ 3. A little better now
- ☐ 4. Neither better, nor worse (no change)
- ☐ 5. A little worse now
- ☐ 6. Moderately worse now
- ☐ 7. A lot worse now

PGIC_HS_v1.0

10.15. Appendix 15: Columbia-Suicide Severity Rating Scale (Baseline/Screening)

COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Baseline/Screening Version

Version 1/14/09

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

Disclaimer:

This scale is intended to be used by individuals who have received training in its administration. The questions contained in the Columbia-Suicide Severity Rating Scale are suggested probes. Ultimately, the determination of the presence of suicidal ideation or behavior depends on the judgment of the individual administering the scale.

Definitions of behavioral suicidal events in this scale are based on those used in ***The Columbia Suicide History Form****, developed by* PPD *, MD and* PPD *, MD, Conte Center for the Neuroscience of Mental Disorders (CCNMD), New York State Psychiatric Institute,* PPD *(Oquendo M. A., Halberstam B. & Mann J. J., Risk factors for suicidal behavior: utility and limitations of research instruments. In M.B. First [Ed.]* Standardized Evaluation in Clinical Practice*, pp. 103 -130, 2003.)*

For reprints of the C-SSRS contact PPD *Ph.D., New York State Psychiatric Institute,* PPD PPD *: inquiries and training requirements contact* PPD

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C-SSRS Baseline Screening - United States/English - Mapi.
C-SSRS-BaselineScreening_AU5.1_eng-USori.doc

SUICIDAL IDEATION		
Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.	**Lifetime: Time He/She Felt Most Suicidal**	**Past 6 Months**
1. Wish to be Dead Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. ***Have you wished you were dead or wished you could go to sleep and not wake up?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
2. Non-Specific Active Suicidal Thoughts General non-specific thoughts of wanting to end one's life/commit suicide (e.g., *"I've thought about killing myself"*) without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period. ***Have you actually had any thoughts of killing yourself?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g., thought of method to kill self but not a specific plan). Includes person who would say, *"I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it… and I would never go through with it."* ***Have you been thinking about how you might do this?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to *"I have the thoughts but I definitely will not do anything about them."* ***Have you had these thoughts and had some intention of acting on them?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
5. Active Suicidal Ideation with Specific Plan and Intent Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out. ***Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
INTENSITY OF IDEATION		
The following features should be rated with respect to the most severe type of ideation (i.e.,1-5 from above, with 1 being the least severe and 5 being the most severe). Ask about time he/she was feeling the most suicidal. Lifetime - ***Most Severe Ideation:*** ___ ***Type # (1-5)*** ___ ***Description of Ideation*** Past X Months - ***Most Severe Ideation:*** ___ ***Type # (1-5)*** ___ ***Description of Ideation***	Most Severe	Most Severe
Frequency ***How many times have you had these thoughts?*** (1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day	___	___
Duration ***When you have the thoughts how long do they last?*** (1) Fleeting - few seconds or minutes (2) Less than 1 hour/some of the time (3) 1-4 hours/a lot of time (4) 4-8 hours/most of day (5) More than 8 hours/persistent or continuous	___	___
Controllability ***Could/can you stop thinking about killing yourself or wanting to die if you want to?*** (1) Easily able to control thoughts (2) Can control thoughts with little difficulty (3) Can control thoughts with some difficulty (4) Can control thoughts with a lot of difficulty (5) Unable to control thoughts (0) Does not attempt to control thoughts	___	___
Deterrents ***Are there things - anyone or anything (e.g., family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?*** (1) Deterrents definitely stopped you from attempting suicide (2) Deterrents probably stopped you (3) Uncertain that deterrents stopped you (4) Deterrents most likely did not stop you (5) Deterrents definitely did not stop you (0) Does not apply	___	___
Reasons for Ideation ***What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?*** (1) Completely to get attention, revenge or a reaction from others (2) Mostly to get attention, revenge or a reaction from others (3) Equally to get attention, revenge or a reaction from others and to end/stop the pain (4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (0) Does not apply	___	___

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SUICIDAL BEHAVIOR *(Check all that apply, so long as these are separate events; must ask about all types)*	**Lifetime**	**Past 6 Months**
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, *as a result of act*. Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is ***any*** intent/desire to die associated with the act, then it can be considered an actual suicide attempt. ***There does not have to be any injury or harm***, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g., gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. ***Have you made a suicide attempt?*** ***Have you done anything to harm yourself?*** ***Have you done anything dangerous where you could have died?*** ***What did you do?*** ***Did you_____as a way to end your life?*** ***Did you want to die (even a little) when you_____?*** ***Were you trying to end your life when you_____?*** ***Or did you think it was possible you could have died from_____?*** ***Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)?*** (Self-Injurious Behavior without suicidal intent) If yes, describe:	Yes ☐ No ☐ Total # of Attempts _____	Yes ☐ No ☐ Total # of Attempts _____
Has subject engaged in Non-Suicidal Self-Injurious Behavior?	Yes ☐ No ☐	Yes ☐ No ☐
Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act *(if not for that, actual attempt would have occurred).* Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. ***Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything?*** If yes, describe:	Yes ☐ No ☐ Total # of interrupted _____	Yes ☐ No ☐ Total # of interrupted _____
Aborted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. ***Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything?*** If yes, describe:	Yes ☐ No ☐ Total # of aborted _____	Yes ☐ No ☐ Total # of aborted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g., buying pills, purchasing a gun) or preparing for one's death by suicide (e.g., giving things away, writing a suicide note). ***Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
Suicidal Behavior: Suicidal behavior was present during the assessment period?	Yes ☐ No ☐	Yes ☐ No ☐

Answer for Actual Attempts Only	Most Recent Attempt Date:	Most Lethal Attempt Date:	Initial/First Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g., surface scratches). 1. Minor physical damage (e.g., lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g., conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; *medical* hospitalization and likely intensive care required (e.g., comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; *medical* hospitalization with intensive care required (e.g., comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	*Enter Code* _____	*Enter Code* _____	*Enter Code* _____
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	*Enter Code* _____	*Enter Code* _____	*Enter Code* _____

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10.16. Appendix 16: Columbia-Suicide Severity Rating Scale (Since Last Visit)

COLUMBIA-SUICIDE SEVERITY RATING SCALE (C-SSRS)

Since Last Visit

Version 1/14/09

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

Disclaimer:

This scale is intended to be used by individuals who have received training in its administration. The questions contained in the Columbia-Suicide Severity Rating Scale are suggested probes. Ultimately, the determination of the presence of suicidal ideation or behavior depends on the judgment of the individual administering the scale.

Definitions of behavioral suicidal events in this scale are based on those used in ***The Columbia Suicide History Form****, developed by* PPD *, MD and* PPD *MD, Conte Center for the Neuroscience of Mental Disorders (CCNMD), New York State Psychiatric Institute,* PPD
Halberstam B. & Mann J. J., Risk factors for suicidal behavior: utility and limitations of research instruments. In M.B. First [Ed.] Standardized Evaluation in Clinical Practice*, pp. 103 -130, 2003.)*

For reprints of the C-SSRS contact PPD *Ph.D., New York State Psychiatric Institute,* PPD
PPD *; inquiries and training requirements contact* PPD

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C-SSRS Since Last Visit - United States/English - Mapi.
C-SSRS-SinceLastVisit_AU5.1_eng-USori.doc

SUICIDAL IDEATION

Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.

Since Last Visit

1. Wish to be Dead
Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up.
Have you wished you were dead or wished you could go to sleep and not wake up?

If yes, describe:

Yes ☐ No ☐

2. Non-Specific Active Suicidal Thoughts
General non-specific thoughts of wanting to end one's life/commit suicide (e.g., *"I've thought about killing myself"*) without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period.
Have you actually had any thoughts of killing yourself?

If yes, describe:

Yes ☐ No ☐

3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act
Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g., thought of method to kill self but not a specific plan). Includes person who would say, *"I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it.....and I would never go through with it".*
Have you been thinking about how you might do this?

If yes, describe:

Yes ☐ No ☐

4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan
Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to *"I have the thoughts but I definitely will not do anything about them".*
Have you had these thoughts and had some intention of acting on them?

If yes, describe:

Yes ☐ No ☐

5. Active Suicidal Ideation with Specific Plan and Intent
Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out.
Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?

If yes, describe:

Yes ☐ No ☐

INTENSITY OF IDEATION

The following features should be rated with respect to the most severe type of ideation (i.e.,1-5 from above, with 1 being the least severe and 5 being the most severe).

Most Severe Ideation: _____ _____

Type # (1-5) ***Description of Ideation***

Most Severe

Frequency
How many times have you had these thoughts?
(1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day

____

Duration
When you have the thoughts how long do they last?
(1) Fleeting - few seconds or minutes
(2) Less than 1 hour/some of the time
(3) 1-4 hours/a lot of time
(4) 4-8 hours/most of day
(5) More than 8 hours/persistent or continuous

____

Controllability
Could/can you stop thinking about killing yourself or wanting to die if you want to?
(1) Easily able to control thoughts
(2) Can control thoughts with little difficulty
(3) Can control thoughts with some difficulty
(4) Can control thoughts with a lot of difficulty
(5) Unable to control thoughts
(0) Does not attempt to control thoughts

____

Deterrents
Are there things - anyone or anything (e.g., family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?
(1) Deterrents definitely stopped you from attempting suicide
(2) Deterrents probably stopped you
(3) Uncertain that deterrents stopped you
(4) Deterrents most likely did not stop you
(5) Deterrents definitely did not stop you
(0) Does not apply

____

Reasons for Ideation
What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?
(1) Completely to get attention, revenge or a reaction from others
(2) Mostly to get attention, revenge or a reaction from others
(3) Equally to get attention, revenge or a reaction from others and to end/stop the pain
(4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling)
(5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling)
(0) Does not apply

____

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C-SSRS—Since Last Visit (Version 1/14/09)

Page 1 of 2

SUICIDAL BEHAVIOR *(Check all that apply, so long as these are separate events; must ask about all types)*	**Since Last Visit**
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, *as a result of act*. Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is ***any*** intent/desire to die associated with the act, then it can be considered an actual suicide attempt. ***There does not have to be any injury or harm***, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g., gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. ***Have you made a suicide attempt?*** ***Have you done anything to harm yourself?*** ***Have you done anything dangerous where you could have died?*** ***What did you do?*** ***Did you_____as a way to end your life?*** ***Did you want to die (even a little) when you_____?*** ***Were you trying to end your life when you_____?*** ***Or Did you think it was possible you could have died from_____?*** ***Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)?*** (Self-Injurious Behavior without suicidal intent) If yes, describe: **Has subject engaged in Non-Suicidal Self-Injurious Behavior?**	**Yes** ☐ **No** ☐ Total # of Attempts _____ **Yes** ☐ **No** ☐
Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act *(if not for that, actual attempt would have occurred)*. Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. ***Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything?*** If yes, describe:	**Yes** ☐ **No** ☐ Total # of interrupted _____
Aborted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. ***Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything?*** If yes, describe:	**Yes** ☐ **No** ☐ Total # of aborted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g., buying pills, purchasing a gun) or preparing for one's death by suicide (e.g., giving things away, writing a suicide note). ***Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)?*** If yes, describe:	**Yes** ☐ **No** ☐
Suicidal Behavior: Suicidal behavior was present during the assessment period?	**Yes** ☐ **No** ☐
Suicide:	**Yes** ☐ **No** ☐
Answer for Actual Attempts Only	Most Lethal Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g., surface scratches). 1. Minor physical damage (e.g., lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g., conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; *medical* hospitalization and likely intensive care required (e.g., comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; *medical* hospitalization with intensive care required (e.g., comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	*Enter Code* _____
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	*Enter Code* _____

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10.17. Appendix 17: Protocol Amendment History

This is the first amendment to the original protocol.

11. REFERENCES

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INVESTIGATOR AGREEMENT

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the study intervention, the conduct of the study, and the obligations of confidentiality.

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Signature: _____ Date: _____
(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____
(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): Bruce Randazzo, MD

Institution: Janssen Research & Development

Signature: PPD Date: 03-May-2019
(Day Month Year)

Note: If the address or telephone number of the investigator changes during the course of the study, written notification will be provided by the investigator to the sponsor, and a protocol amendment will not be required.

110

Approved, Date: 2 May 2019