Janssen Research & Development, LLC *

Clinical Protocol

A Phase 3b, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Guselkumab Versus Placebo for the Treatment of Low BSA Moderate Plaque Psoriasis With Special Site Involvement

Short Title: Study of guselkumab vs **P**lacebo safety and **E**ffi**C**acy for the **TRE**atment of low BSA **M**oderate plaque psoriasis
SPECTREM

Protocol CNTO1959PSO3017; Phase 3b
Version: Original

CNTO1959 (guselkumab)

*Janssen Research & Development is a global organization that operates through different legal entities in various countries. Therefore, the legal entity acting as the Sponsor for Janssen Research & Development studies may vary, such as, but not limited to Janssen Biotech, Inc.; Janssen Products, LP; Janssen Biologics, BV; Janssen-Cilag International NV; Janssen, Inc; Janssen Pharmaceutica NV; Janssen Sciences Ireland UC; Janssen Biopharma Inc.; or Janssen Research & Development, LLC. The term "sponsor" is used throughout the protocol to represent these various legal entities; the sponsor is identified on the Contact Information page that accompanies the protocol.

Studies conducted at sites in the United States (US) will be conducted under US Food and Drug Administration Investigational New Drug (IND) regulations (21 CFR Part 312).

IND: 105004

Status: Approved
Date: 15 February 2023
Prepared by: Janssen Research & Development, LLC
EDMS number: EDMS-RIM-844799, 2.0

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

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES AND FIGURES

TABLES

FIGURES

1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 3b, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Guselkumab Versus Placebo for the Treatment of Low BSA Moderate Plaque Psoriasis With Special Site Involvement

Guselkumab (Tremfya®) is a fully human immunoglobulin G1 (IgG1) lambda monoclonal antibody (mAb) that binds to the p19 subunit of human interleukin (IL)-23 with high specificity and affinity. The binding of guselkumab to the IL-23 p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor thus inhibiting IL-23-specific intracellular signaling and downstream activation and cytokine production.

OBJECTIVES AND ENDPOINTS AND/OR ESTIMANDS

OBJECTIVES AND ENDPOINTS	
Primary Objective	**Primary Endpoint**
The primary objective of the study is to evaluate the clinical efficacy of guselkumab compared to placebo in participants with low body surface area (BSA) moderate plaque psoriasis with special site involvement.	The proportion of participants who achieve an Investigator's Global Assessment (IGA) score of cleared (0) or minimal (1) at Week 16
Secondary Objectives **Efficacy** To evaluate the efficacy of guselkumab compared with placebo in improving the signs and symptoms of psoriasis and patient-reported outcomes (PROs)	**Major Secondary Efficacy Endpoints** (The final ordering of multiplicity controlled major secondary endpoints will be specified in the Statistical Analysis Plan [SAP]) 1. Change from baseline in BSA affected at Week 16 2. Change from baseline in total Psoriasis Area and Severity Index (PASI) score at Week 16 3. The proportion of participants who achieve an IGA score of cleared (0) at Week 16 4. The proportion of participants who achieve a PASI 90 response at Week 16 5. The proportion of participants who achieve a PASI 100 response at Week 16 6. The proportion of participants who achieve a scalp-specific IGA (ss-IGA) score of absence of disease (0) or very mild disease (1) at Week 16 among randomized participants with an ss-IGA score ≥3 at baseline 7. The proportion of participants who achieve a static Physician's Global Assessment of Genitalia (sPGA-G) score

	of clear (0) or minimal (1) at Week 16 among randomized participants with an sPGA-G score ≥3 at baseline 8. The proportion of participants who achieve an intertriginous IGA (i-IGA) score of clear (0) or minimal (1) at Week 16 among randomized participants with an i-IGA score ≥3 at baseline 9. The proportion of participants who achieve a facial IGA (f-IGA) score of clear (0) or minimal (1) at Week 16 among randomized participants with an f-IGA score ≥3 at baseline 10. The change from baseline in Psoriasis Symptom and Sign Diary (PSSD) total symptom score at Week 16 11. The proportion of participants who achieve ≥4-point reduction (improvement) in PSSD itch score from baseline at Week 16 among participants with a PSSD itch score ≥4 at baseline 12. The proportion of participants with PSSD Individual Symptom Scale Score = 0 at Week 16 among participants with PSSD >0 at baseline
Secondary Objectives **Safety** To evaluate the safety of guselkumab in participants with low BSA moderate plaque psoriasis with special site involvement	**Safety Endpoints** • The frequency and type of adverse events and serious adverse events

HYPOTHESIS

It is hypothesized that guselkumab is superior to placebo in the treatment of low BSA moderate plaque psoriasis with special site involvement as assessed by the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) at Week 16 (primary hypothesis).

OVERALL DESIGN

This is a Phase 3b, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of guselkumab versus placebo in participants with low BSA moderate plaque psoriasis with special site involvement.

Approximately 300 eligible participants will be randomized 2:1 to receive either guselkumab CCI CCI at Weeks 0 and 4 and then CCI CCI or placebo. Randomization will be stratified by qualifying special site (i.e., scalp, genital, intertriginous, and face), with approximately 25% of participants per each special site. If participants present with qualifying moderate psoriasis in multiple special sites, they will be allocated to the special site that is most severe, as determined by the participant. There will be 2 database locks (DBLs) in this study, at Weeks 16 and 56, to support reporting of short-and long-term efficacy and safety data, respectively. At the Week 16 DBL, unblinded data will only be made available to select Sponsor and Contract Research Organization (CRO) team members involved with analysis of the data and preparation of analyses for the Week 16 DBL. All other Sponsor, site, and CRO

personnel directly involved with study conduct will remain blinded to treatment assignments until the Week 56 DBL and related analyses have been completed.

NUMBER OF PARTICIPANTS

Approximately 300 eligible participants will be randomized 2:1 to receive either guselkumab CCI C at Weeks 0 and 4 and then CCI or placebo.

INTERVENTION GROUPS AND DURATION

There will be 2 treatment groups:

- A guselkumab group who will receive guselkumab CCI C at Weeks 0 and 4 and then CCI through Week 44. Placebo will be administered at Week 16 to maintain the blind.
- A placebo group who will receive placebo CC at Weeks 0, 4, and 12 after which they will cross over to receive guselkumab CCI at Weeks 16, 20, 28, 36, and 44.

EFFICACY EVALUATIONS

Efficacy assessments will include evaluation of body surface area (BSA), Investigator's Global Assessment (IGA), Psoriasis Area and Severity Index (PASI), scalp-specific IGA (ss-IGA), facial IGA (f-IGA), intertriginous IGA (i-IGA), static Physician's Global Assessment of Genitalia (sPGA-G), Palmoplantar IGA (pp-IGA), and Nail Psoriasis Severity Index (NAPSI).

In addition, patient-reported outcomes (PROs) will include Psoriasis Symptom and Sign Diary (PSSD), Dermatology Life Quality Index (DLQI), Psoriasis Epidemiology Screening Tool (PEST), Psoriatic Arthritis Impact of Disease score (PsAID-12), and a Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) questionnaire.

PHARMACOKINETIC AND IMMUNOGENICITY EVALUATIONS

Venous blood samples will be collected for measurement of serum concentrations of guselkumab and antibodies to guselkumab.

PHARMACODYNAMIC AND BIOMARKER EVALUATIONS

Biomarker samples will be collected to examine the biologic response associated with blocking IL-23 and to identify biomarkers associated with psoriasis. Serum will be collected from all participants; skin biopsies and tape strips will also be collected from participants who consent separately to this component of the study.

PHARMACOGENOMIC (DNA) EVALUATIONS

An optional pharmacogenomic blood sample will be collected from participants who consent separately to this component of the study to allow for pharmacogenomic research, as necessary where local regulations permit. The optional pharmacogenomic samples may be analyzed for identification of genetic factors that may be associated with psoriasis and/or the response to guselkumab.

SAFETY EVALUATIONS

Safety assessments will consist of adverse events (including serious adverse events), physical examinations, vital signs, height and weight, electrocardiograms, clinical safety laboratory assessments, suicidal ideation or behavior using the Columbia-Suicide Severity Rating Scale, and concomitant medication review. Injection site reactions, hypersensitivity reactions, infections, tuberculosis evaluations, and pregnancy testing will be performed or collected as specified in the Schedule of Activities.

STATISTICAL METHODS

A sample size of approximately 300 participants (200 participants on guselkumab and 100 participants on placebo) will allow at least 90% power to detect treatment effect differences of 45% between guselkumab (60%) and placebo (15%) for the primary endpoint with a 2-sided alpha level of 0.05. The sample size was also chosen to ensure an adequate number of participants with qualifying special site involvement (scalp, genital, intertriginous, and face). There will be approximately 25% of participants for each special site.

Descriptive statistics (e.g., mean, median, standard deviation [SD], interquartile [IQ] range, minimum, and maximum) will be used to summarize continuous variables. Counts and percentages will be used to summarize categorical variables. Graphical data displays (e.g., line plots) may also be used to summarize data.

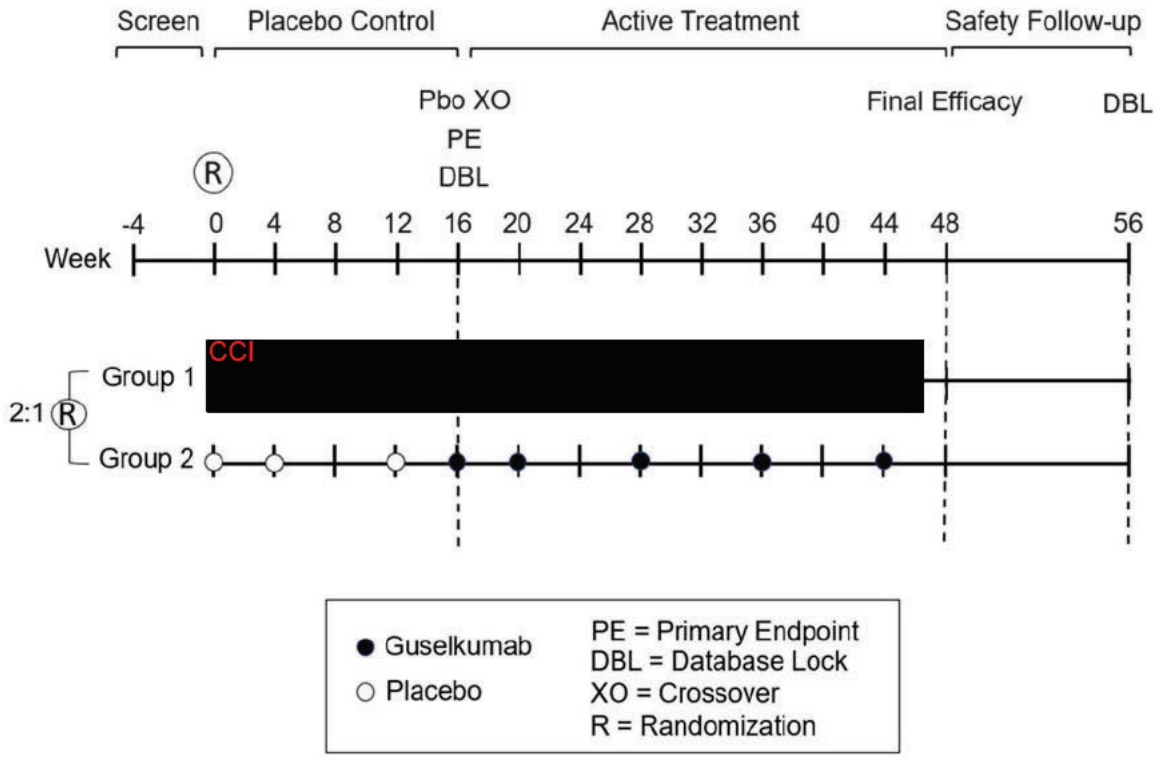
Analyses suitable for categorical data (e.g., chi-square tests, Cochran-Mantel-Haenszel [CMH] chi-square tests, or logistic regression, as appropriate) will be used to compare the proportions of participants achieving selected endpoints (e.g., clinical response). In cases of rare events, the Fisher's exact test will be used for treatment comparisons. Continuous response parameters will be compared using analysis of variance (ANOVA), analysis of covariance (ANCOVA), or a mixed model for repeated measures (MMRM), unless otherwise specified. If the normality assumption is in question, an ANOVA or ANCOVA on the van der Waerden normal scores will be used. For time to event endpoints, survival analysis techniques will be used.

The primary endpoint will be analyzed based on the estimands defined in Section 9. The overall Type I error rate will be controlled at the significance level of 0.05 (2-sided) for the primary and major secondary endpoints. In order to control the overall Type 1 error rate, the primary endpoint and major secondary endpoints will be tested in a hierarchical fashion. That is, the first major secondary endpoint will be tested only if the primary endpoint is positive, and the subsequent endpoint(s) will be tested only if the preceding endpoint in the hierarchy is positive. The final ordering of major secondary endpoints will be specified in the final SAP. No multiplicity control will be made for other endpoints, and nominal p-values will be reported.

To compare the guselkumab group versus the placebo group for the primary endpoint, the CMH chi-square test (2-sided) stratified by special site will be used. The study will be considered successful if the test of the primary endpoint is positive at the 0.05 significance level.

1.2. Schema

Figure 1: Study Design Schematic



1.3. Schedule of Activities (SoA)

Phase	Screening [a]	Placebo [b]				Active Treatment [b]								Follow-Up [b,c]		
Week		**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44 (last dose)**	**48 (Final Efficacy)**	**Early Term.**	**56 (Final Safety)**
Study Procedures [d]																
Screening																
Informed Consent [e]	X															
ICF for optional pharmacogenomics [e]	X															
ICF for optional skin biomarker substudy [e]	X															
Medical History	X															
Demographics	X															
Inclusion/exclusion criteria	X	X														
Study Intervention Administration																
Randomization		X														
IP administration		CCI														
Efficacy Assessments																
BSA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
IGA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PASI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
ss-IGA (scalp)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
f-IGA (facial)	X	X	X	X	X	X	X	X		X		X		X	X	
i-IGA (intertriginous)	X	X	X	X	X	X	X	X		X		X		X	X	
sPGA-G (genitals)	X	X	X	X	X	X	X	X		X		X		X	X	
pp-IGA (palmoplantar)	X	X	X	X	X	X	X	X		X		X		X	X	
NAPSI (all 10 fingernails)	X	X		X		X		X		X		X		X	X	
Clinical Photographs (half body + 1 special site or target lesion) [f]	X	X	X	X	X	X	X	X		X		X		X	X	
Patient-reported Outcomes																
PSSD (7-day version)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
DLQI		X		X		X		X		X		X		X	X	

Phase	Screening [a]	Placebo [b]				Active Treatment [b]								Follow-Up [b,c]		
Week		**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44 (last dose)**	**48 (Final Efficacy)**	**Early Term.**	**56 (Final Safety)**
PEST (no history of PsA and PEST negative at screening) [g]	X	X		X		X		X		X		X		X	X	
PsAID-12 (rheumatologist confirmed history of PsA or positive PEST at screening) [g]		X		X		X		X		X		X		X	X	
PROMIS-29		X		X		X		X		X		X		X	X	
Safety Assessments																
Full Physical Examination (including skin)	X													X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG	X															
TB evaluation	X	X	X		X		X		X		X		X	X	X	X
Chest X-ray [h]	X															
C-SSRS [i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine pregnancy test [j]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height		X						X						X	X	X
Weight		X						X						X	X	X
Clinical Laboratory Assessments																
Serum pregnancy test [j]	X															
TB IGRA [k]	X															
Hepatitis B and C serology [l]	X															
HIV Ab test	X															
Hematology	X	X	X			X		X		X				X	X	X
Chemistry	X	X	X			X		X		X				X	X	X
Lipid panel [n]		X						X						X	X	X
Hs-CRP		X	X			X		X		X				X	X	X
HbA1c		X						X						X	X	X

Phase	Screening [a]	Placebo [b]				Active Treatment [b]								Follow-Up [b,c]		
Week		0	4	8	12	16	20	24	28	32	36	40	44 (last dose)	48 (Final Efficacy)	Early Term.	56 (Final Safety)
Clinical Pharmacology and Biomarker Assessments [p]																
Serum guselkumab concentration		X	X			X				X				X	X	X
Anti-guselkumab antibodies		X	X			X				X				X	X	X
Serum biomarkers		X	X			X				X				X		
Optional Substudies [e]																
Skin biopsy [p]		X				X								X		
Tape stripping		X	X			X				X				X		
Whole blood (pharmacogenomics) [q]		X														
Ongoing Participant Review																
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

a: The screening visit should occur within approximately 4 weeks before the Week 0 visit.
b: All post-baseline visits will have a visit window of ±7 days counting from Week 0 as Day 1.
c: If a participant permanently discontinues study drug intervention prior to the Week 16 visit, they should be encouraged to return for all remaining study visits through Week 16, and the participant should also return for a final visit to perform assessments under the Week 56/final safety visit approximately 12 weeks after the last study intervention administration. If a participant permanently discontinues study drug at or after the Week 16 visit, they should complete the Week 48/final efficacy visit assessments at the time of discontinuation, or as soon as possible, and also return for a final safety visit to perform assessments under the Week 56/ final safety visit approximately 12 weeks after the last study intervention administration.
d: All study procedures and evaluations should be completed before administration of study drug.
e: ICFs must be signed before the first study-related activity. The optional skin biopsy, tape stripping, and pharmacogenomics substudies will use separate ICFs.
f: Details may be found in the Photography Manual.
g: Participants with no prior diagnosis of rheumatologist confirmed PsA will complete the PEST at screening. If screening PEST score ≥3, participants will complete PsAID-12 at Week 0 (baseline) and for the remainder of study visits as specified. If screening PEST score <3, participants will complete PEST at Week 0 (baseline) and for the remainder of study visits as specified. Participants with prior diagnosis of rheumatology confirmed PsA will complete the PsAID-12 starting at Week 0 (baseline) and for the remainder of study visits as specified.
h: Chest X-ray should be performed at screening if the participant does not have a chest X-ray within 12 weeks prior to the first administration of study intervention.
i: All participant questionnaires should be completed before any other tests, procedures, or evaluations on the day of the visit for baseline and post-baseline visits. The 'Baseline/Screening' version of the C-SSRS will be performed at the screening visit prior to all questionnaires. At Week 0 and all subsequent visits, the 'Since Last Visit' version of the C-SSRS will be performed after all other questionnaires.
j: Participants of childbearing potential must have a negative pregnancy test before randomization and before study drug administration at study visits.
k: Interferon gamma release assay testing includes either QuantiFERON-TB® or T-SPOT.TB®. Interferon gamma release assay testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB.

l: For details related to hepatitis B screening and eligibility, refer to Appendix 3. For details related to hepatitis C screening and eligibility, refer to Exclusion Criterion 32.
m: Laboratory tests are listed in Appendix 2 of the protocol.
n: Participants must fast (i.e., no food or beverages [except water]) for at least 8 hours before blood is drawn for lipid panel unless there is medical contradiction. All other visits can be non-fasting.
o: All blood samples must be collected before study agent administration at visits when a study agent administration is scheduled. Blood collected from 1 venipuncture will be divided into multiple aliquots of serum for the measurement of guselkumab concentration, antibodies to guselkumab, and a back-up sample. Biomarker blood collection will be divided into 3 aliquots. Details will be provided in the Laboratory Manual.
p: Biopsy collection is optional. At Week 0, lesional and non-lesional skin samples will be collected; only lesional samples will be collected at all later timepoints. Refer to the biopsy manual for further details.
q: The whole blood (pharmacogenomics) sample is optional and should be collected at the specified timepoint; however, if necessary, it may be collected at a later timepoint without constituting a protocol deviation.

Ab = antibodies; BSA = body surface area (affected); C-SSRS = Columbia-Suicide Severity Rating Scale; DLQI = Dermatology Life Quality Index; ECG = electrocardiogram; f-IGA = facial IGA; HbA1c = hemoglobin a1c; HIV = human immunodeficiency virus; Hs-CRP = high-sensitivity C-reactive protein; ICF = informed consent form; IGA = Investigator's Global Assessment; IGRA = interferon gamma release assay; i-IGA = intertriginous IGA; IP = investigational product; NAPSI = Nail Psoriasis Severity Index; PASI = Psoriasis Area and Severity Index; PEST = Psoriasis Epidemiology Screening Tool; pp-IGA = palmoplantar IGA; PROMIS-29 = Patient-Reported Outcomes Measurement Information System-29; PsA = psoriatic arthritis; PsAID-12 = Psoriatic Arthritis Impact of Disease score; PSSD = Psoriasis Symptom and Sign Diary; sPGA-G = static Physician's Global Assessment of Genitalia; ss-IGA = scalp-specific IGA; TB = tuberculosis; term. = termination

2. INTRODUCTION

Guselkumab (Tremfya®) is a fully human immunoglobulin G1 (IgG1) lambda monoclonal antibody (mAb) that binds to the p19 subunit of human interleukin (IL)-23 with high specificity and affinity. The binding of guselkumab to the IL-23 p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor thus inhibiting IL-23-specific intracellular signaling and downstream activation and cytokine production.

Guselkumab is currently approved for the treatment of adults with moderate-to-severe plaque psoriasis or moderate-to-severe psoriatic arthritis (PsA) in the United States (US), the European Union (EU), Canada, several countries in Latin America, and the Asia-Pacific region. Guselkumab has also been approved for the treatment of generalized pustular psoriasis, erythrodermic psoriasis, and palmoplantar pustulosis in Japan. In addition, guselkumab is being evaluated in both ulcerative colitis and Crohn's disease and in several other immune-mediated dermatologic and rheumatologic diseases globally.

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

The term "study intervention" throughout the protocol refers to study drug as defined in Section 6.1, Study Interventions Administered.

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

Psoriasis is a chronic, immune-mediated, multi-system disease resulting in skin symptoms that greatly impact a patient's quality of life (QoL). Traditionally, severity has been classified into 3 categories (mild, moderate, and severe) based largely on body surface area (BSA) involvement, Investigator's Global Assessment (IGA), and/or the Psoriasis Area and Severity Index (PASI) score (Langley 2004). However, these traditional severity categories erroneously assume a linear relationship with disease extent (e.g., higher BSA represents more severe disease, and lower BSA represents less milder disease), resulting in gross underestimation of the impact that low BSA (e.g., <10%) psoriasis can have on a patient's QoL and general well-being. This is particularly true if patients have low BSA psoriasis with special site involvement (e.g., scalp, genital, intertriginous, facial, nails, and palmoplantar), which can often have debilitating effects on daily functioning or can have significant impact on physical appearance and self-esteem (Lebwohl 2014; van de Kerkhof 2015; Augustin 2018). As a result, various treatment guidelines and consensus definitions have been developed to better characterize psoriasis severity that include a combination of both clinician- and patient-reported measures in an attempt to reduce the limitations of any singular measure that may not be representative of the impact low BSA psoriasis has on a patient.

To help define psoriasis disease severity in a practical manner useful to patients, clinicians, and researchers, both the International Psoriasis Council (IPC) and the American Academy of Dermatology (AAD)-National Psoriasis Foundation (NPF) have recently released publications that categorize patients as either (1) candidates for topical therapy or (2) candidates for phototherapy and systemic therapy including biologics (Strober 2020; Menter 2019). In clinical practice, dermatologists often use BSA and location of psoriasis as the main factors in deciding what type of treatment a patient should receive (Knuckles 2018). Thus, the IPC has proposed the following guidance in identifying patients who are candidates for systemic therapy: (1) BSA >10%, or (2) disease involving special areas (hands/feet, nails, face, scalp, and genitals), or (3) prior failure of topical therapy (Strober 2020).

Historically, pivotal clinical trials of biologic agents approved in the US for the treatment of moderate-to-severe psoriasis have included participants with BSA ≥10%, IGA ≥3, and PASI ≥12. Thus, efficacy of these agents in patients with lower BSA involvement with special sites involvement is lacking. This impacts the ability of providers to utilize biologics for patients with low BSA psoriasis as some health systems and payers decline reimbursement for patients who do not have ≥10% BSA involvement, based on the historical assumption that biologic treatments should be reserved only for patients with extensive (high) BSA psoriasis. Surveys of patients with psoriasis of lower BSA involvement have identified significant treatment dissatisfaction and substantial impact of their psoriasis on their general well-being (Vaidya 2015; Golbari 2021), advocating for further studies in this patient population with high unmet needs.

The objective of this study is to evaluate the efficacy and safety of guselkumab in the treatment of low BSA moderate plaque psoriasis with special site involvement, providing a potential new additional treatment option to this undertreated patient population.

2.2. Background

The clinical development program to support use of guselkumab in the US and globally for the treatment of moderate-to-severe plaque psoriasis includes 2 Phase 1 studies, 1 Phase 2 study, and 5 Phase 3 global studies (CNTO1959PSO3001 [VOYAGE 1], CNTO1959PSO3002 [VOYAGE 2], ECLIPSE, ORION, and NAVIGATE). Details about these studies are provided in the IB.

The Phase 3 VOYAGE 1 study (CNTO1959PSO3001) was a multicenter, randomized, double-blind, placebo- and active comparator-controlled study in participants with moderate-to-severe plaque psoriasis with 3 parallel treatment groups: placebo, guselkumab CCI and adalimumab. Participants in the placebo group crossed over to guselkumab CCI beginning at Week 16. In that study, 837 adult participants were randomized to receive guselkumab (n=329), adalimumab (n=334), or placebo (n=174). At Week 16, a significantly greater proportion of participants randomized to guselkumab achieved the co-primary endpoints of an IGA score of cleared (0) or minimal (1) and PASI 90 response (85.1% and 73.3%, respectively; $p < 0.001$ for both endpoints) compared with placebo (6.9% and 2.9%, respectively). Treatment with guselkumab was well tolerated through Week 48. The frequency of adverse events (AEs) was comparable between the treatment groups through Week 48. The most common AEs were nasopharyngitis and upper respiratory tract infection. Through Week 16, the percentage of

participants with 1 or more serious adverse events (SAEs) was 1.7% (n=3) in the placebo group and 2.4% (n=8) in the guselkumab group. The incidence of infections was comparable between the placebo, guselkumab, and adalimumab groups through Week 16. Through 5 years of follow-up, no opportunistic infections or active tuberculosis (TB) was reported.

The Phase 3 VOYAGE 2 study (CNTO1959PSO3002) was a multicenter, randomized, double-blind, placebo- and active comparator-controlled study in participants with moderate-to-severe plaque psoriasis with 3 treatment groups: placebo, guselkumab CCI and adalimumab. In that study, 992 adult participants were randomized to either the placebo (n=248), guselkumab (n=496), or adalimumab (n=248) treatment groups at Week 0. Participants in the placebo group crossed over to guselkumab CCI beginning at Week 16. This study evaluated the benefit of maintenance therapy using a randomized withdrawal design starting at Week 28. At Week 16, a significantly greater proportion of participants randomized to guselkumab achieved the co-primary endpoints of an IGA score of cleared (0) or minimal (1) and a PASI 90 response (84.1% and 70.0%, respectively; p <0.001 for both endpoints) compared with placebo (8.5% and 2.4%, respectively). Treatment with guselkumab was well tolerated. Through Week 16, the proportion of participants experiencing 1 or more AEs was comparable between treatment groups. Nasopharyngitis and upper respiratory tract infection were the most common AEs. The percentage of participants with 1 or more SAEs was comparable between the placebo and guselkumab groups. The incidence of infections was comparable between the placebo, guselkumab, and adalimumab groups through Week 16. Through 5 years of follow-up, no opportunistic infections or active TB was reported.

2.3. Benefit-Risk Assessment

A summary of the benefits and risks for study participation is summarized below. More detailed information about the known and expected benefits and risks of guselkumab may be found in the IB.

2.3.1. Risks of Study Participation

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
Potential risks due to study intervention (guselkumab)		
Serious infections and reactivation of latent infections	Available animal and human data suggest that blockade of IL-23 may be associated with an increased infection risk. Infections have been identified as adverse reactions of guselkumab, including respiratory infections, herpes simplex, tinea infections, and gastroenteritis.	• Participants with a history of, or ongoing, chronic, or recurrent infectious disease, including human immunodeficiency virus (HIV), or hepatitis B or C virus (HBV or HCV), will be excluded from the study. Similarly, participants with evidence of active or untreated TB will be excluded from the study (Section 5.2). • Participants who have received, or are expected to receive, any live virus or bacterial vaccination within 3 months prior to the first administration of study drug or plan to receive such vaccines during the study or within 4 weeks after the last administration of study intervention will be excluded from the study (Section 5.2). • Participants will be instructed to seek medical attention if they develop signs or symptoms suggestive of an infection, and investigators are instructed in the protocol to monitor for signs or symptoms of infections, including TB (Sections 8.2.10 and 8.2.11). • Discontinuation of a participant's study intervention must be strongly considered if the participant develops a serious infection, including, but not limited to, sepsis or pneumonia. In addition, any serious infection should be discussed with the medical monitor or designee, and the study intervention should be withheld until the clinical assessment is complete.
Hypersensitivity reactions, including serious hypersensitivity reactions	Hypersensitivity reactions including anaphylaxis have been identified as adverse reactions in post-marketing experience with guselkumab.	• Participants with known allergy, hypersensitivity, or intolerance to guselkumab or its excipients will be excluded from the study. • Sites are instructed that before any administration of study intervention, appropriately trained personnel and medications (e.g., injectable epinephrine,

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
		antihistamines) must be available to treat hypersensitivity reactions, including anaphylaxis. In addition, all participants must be observed carefully for signs and symptoms of a hypersensitivity reaction (e.g., urticaria, pruritis, angioedema, wheezing, dyspnea, or hypotension) (Section 8.2.9). • Any participant who develops a serious hypersensitivity reaction such as anaphylaxis must discontinue study intervention.
Malignancy	The preponderance of preclinical data suggests that blockade of endogenous IL-23 would not be detrimental and may in fact be beneficial in tumor immunosurveillance and host protection; however, a risk of malignancy cannot be excluded.	• Those participants who currently have a malignancy or have a history of malignancy within 5 years prior to screening (with exceptions noted in Section 5.2) will be excluded from the study. Additionally, participants who have 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, will be excluded from the study (Section 5.2). • During the conduct of the study, participants will undergo regular clinical monitoring including routine safety laboratory tests to assess for any changes in health status that may indicate a possible malignancy. • Participants who develop a malignancy during the study (with the exception of no more than 2 localized basal cell skin cancers that are treated with no evidence of recurrence or residual disease) will be discontinued from study intervention (Section 7.1).
Liver injury	An SAE of "toxic hepatitis" was reported in the ongoing Phase 2/3 guselkumab Crohn's disease (CD) program in a participant who received guselkumab 1200 mg intravenously (IV) at Weeks 0, 4, and 8 and 200 mg subcutaneously (CCI at Week 12. Based on the hepatocellular pattern of injury, temporal relationship of the event to guselkumab exposure, and the exclusion of alternative etiologies, this event may represent drug-	• During the conduct of the study, liver function tests will be monitored at regular intervals. The CCI C CCI dosage is approved in the major regions in which this study will be conducted. • Participants with marked liver enzyme elevations or symptoms or signs of liver dysfunction (e.g., jaundice) should undergo a thorough investigation for possible causes of liver injury. Participants must have their study intervention discontinued if the participant has severe liver test abnormalities that are not transient and

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
	induced liver injury (DILI) possibly related to guselkumab. Transaminase increases have been identified as an adverse reaction of guselkumab. In PsA studies, transaminase increases were observed with a higher incidence with a maintenance dose of CCI CCI (CCI compared to CCI CCI	are not explained by other etiologies (Section 7.1.1).
Risks due to study procedures		
Radiation	A chest X-ray will be performed at screening if the participant does not have a chest X-ray within 12 weeks prior to the first administration of study intervention. The exposure from 1 standard chest X-ray is 0.1 mSV, comparable to 10 days of exposure to natural background radiation (https://www.acr.org).	Exposure to radiation through radiographs is kept to a minimum by not requiring that a chest X-ray be performed at screening if one is available from within 12 weeks prior to the first administration of study intervention.

2.3.2. Benefits of Study Participation

Guselkumab has demonstrated benefit in improving the signs and symptoms of psoriasis in the Phase 3 studies (see Section 2.2), resulting in the registration of guselkumab in numerous countries globally. The demonstration of clinical benefit was observed in both participants who are biologic treatment naïve or experienced. The target population under study in this protocol are participants with low BSA moderate plaque psoriasis with special site involvement, who are intolerant of topical therapy or inadequate responders to topical therapy and eligible for systemic/phototherapy. Consistent with the established efficacy demonstrated in prior guselkumab studies, it is anticipated that individual participants may benefit from participation in the current study. Additionally, participation will help to obtain additional data on the impact of guselkumab on low BSA moderate psoriasis with special site involvement, which can greatly impact patients' QoL.

Participants may also experience some benefits from the participation in a clinical study irrespective of receiving study intervention, due to regular visits and assessments monitoring their overall health.

2.3.3. Benefit-Risk Assessment for Study Participation

The benefit-risk of guselkumab treatment in this target population of patients with low BSA moderate plaque psoriasis with special site involvement is further supported by additional data through 5 years of treatment from the PSO3001 and PSO3002 studies for guselkumab CCI CC

administered at Weeks 0 and 4 and then CCI in the moderate-to-severe psoriasis population and additional data through 2 years of treatment from the PSA3001 and PSA3002 studies for guselkumab CCI CC administered at Weeks 0 and 4 and then CCI in patients with active PsA, including a subset of participants who also has concurrent low BSA psoriasis (BSA ≥3%). The collective data across the psoriatic disease studies support an overall favorable benefit-risk profile for the use of guselkumab in the approved populations (moderate-to-severe plaque psoriasis, patients with active PsA with or without skin involvement) and in this study's target population with low BSA moderate plaque psoriasis with special site involvement. Potential risks of guselkumab, including those of clinically relevant infections and serious infections, malignancy, and liver injury, are being addressed via judicious inclusion/exclusion criteria, frequent study visits to allow for close monitoring of patient safety, guidelines for participant management (including monitoring of clinical laboratory tests and treatment discontinuation criteria), detailed description of allowed and prohibited concomitant medications, and comprehensive medical monitoring of data by the Sponsor/designee during the conduct of the studies.

The benefit-risk of placebo treatment, in a limited duration (16 weeks) in this study, is consistent with the pivotal studies conducted in the field of psoriasis. Patients will cross-over to active treatment at Week 16. Participants may also experience some benefits from the participation in a clinical study irrespective of receiving study intervention, due to regular visits and assessments monitoring their overall health.

In summary, considering the measures taken to minimize risk to participants in this study, the potential risks identified in association with the treatments under study in this protocol are justified by the benefits that may be provided to participants with low BSA moderate plaque psoriasis with special site involvement.

3. OBJECTIVES AND ENDPOINTS

The study objectives and endpoints are listed below.

OBJECTIVES AND ENDPOINTS	
Primary Objective	**Primary Endpoint**
The primary objective of the study is to evaluate the clinical efficacy of guselkumab compared to placebo in participants with low BSA moderate plaque psoriasis with special site involvement.	The proportion of participants who achieve an Investigator's Global Assessment (IGA) score of cleared (0) or minimal (1) at Week 16
Secondary Objectives **Efficacy** To evaluate the efficacy of guselkumab compared with placebo in improving the signs and symptoms of psoriasis and patient-reported outcomes (PROs)	**Major Secondary Efficacy Endpoints** (The final ordering of multiplicity controlled major secondary endpoints will be specified in the Statistical Analysis Plan) 1. Change from baseline in BSA affected at Week 16 2. Change from baseline in total Psoriasis Area Severity Index (PASI) score at Week 16

	3. The proportion of participants who achieve an IGA score of cleared (0) at Week 16 4. The proportion of participants who achieve a PASI 90 response at Week 16 5. The proportion of participants who achieve a PASI 100 response at Week 16 6. The proportion of participants who achieve a scalp-specific IGA (ss-IGA) score of absence of disease (0) or very mild disease (1) at Week 16 among randomized participants with an ss-IGA score ≥3 at baseline 7. The proportion of participants who achieve a static Physician's Global Assessment of Genitalia (sPGA-G) score of clear (0) or minimal (1) at Week 16 among randomized participants with an sPGA-G score ≥3 at baseline 8. The proportion of participants who achieve an intertriginous IGA (i-IGA) score of clear (0) or minimal (1) at Week 16 among randomized participants with an i-IGA score ≥3 at baseline 9. The proportion of participants who achieve a facial IGA (f-IGA) score of clear (0) or minimal (1) at Week 16 among randomized participants with an f-IGA score ≥3 at baseline 10. The change from baseline in Psoriasis Symptom and Sign Diary (PSSD) total symptom score at Week 16 11. The proportion of participants who achieve ≥4-point reduction (improvement) in PSSD itch score from baseline at Week 16 among participants with a PSSD itch score ≥4 at baseline 12. The proportion of participants with PSSD Individual Symptom Scale Score = 0 at Week 16 among participants with PSSD >0 at baseline
Secondary Objectives **Safety** To evaluate the safety of guselkumab in participants with low BSA moderate plaque psoriasis with special site involvement	**Safety Endpoints** • The frequency and type of AEs and SAEs

Other Objectives To evaluate the efficacy of additional clinical and patient-reported outcomes	**<u>Other Endpoints - Psoriasis Efficacy</u>** **The following endpoints will compare the guselkumab group with the placebo group:** • Change from baseline in BSA × IGA through Week 16 **The following endpoints relate to the guselkumab group only:** • Change from baseline in BSA × IGA over time through Week 48 • The proportion of participants who achieve National Psoriasis Foundation (NPF) target response (i.e., BSA ≤1%) over time through Week 48 • The proportion of participants who achieve NPF acceptable response (i.e., BSA ≤3%) over time through Week 48 among those with baseline BSA >3% • The proportion of participants who achieve PASI 75/90/100 over time through Week 48 • The proportion of participants who achieve IGA 0 over time through Week 48 • The proportion of participants who achieve IGA 0/1 over time through Week 48 • Median time to achievement of NPF target response (i.e., BSA ≤1%) • Median time to achievement of NPF acceptable response (i.e., BSA ≤3%) • The proportion of patients who achieve IGA 0/1 at Week 16 and who maintain IGA 0/1 response at Week 48 **<u>Other Endpoints – Special Site Efficacy</u>** **The following endpoints will compare the guselkumab group with the placebo group:** **Scalp** • Time to complete scalp psoriasis clearance (ss-IGA = 0) among randomized participants with scalp psoriasis at baseline • Proportion of participants with complete scalp psoriasis clearance (ss-IGA = 0) over time among randomized participants with scalp psoriasis at baseline over time through Week 16 • Proportion of participants who achieve an ss-IGA score of absence of disease (0) or very mild disease (1) with at least 2-grade improvement from baseline at Week 16 among randomized participants with an ss-IGA score ≥2 at baseline **Genital** • Time to complete genital psoriasis clearance (sPGA-G = 0) among randomized participants with genital psoriasis at baseline

	• Proportion of participants with complete genital psoriasis clearance (sPGA-G = 0) among randomized participants with genital psoriasis at baseline over time through Week 16 • Proportion of participants who achieve an sPGA-G score of clear (0) or minimal (1) with at least 2-grade improvement from baseline at Week 16 among randomized participants with an sPGA-G score ≥2 at baseline **Intertriginous** • Time to complete intertriginous psoriasis clearance (i-IGA = 0) among randomized participants with intertriginous psoriasis at baseline • Proportion of participants with complete intertriginous psoriasis clearance (i-IGA = 0) among randomized participants with intertriginous psoriasis at baseline over time through Week 16 • Proportion of participants who achieve an i-IGA score of clear (0) or minimal (1) with at least 2-grade improvement from baseline at Week 16 among randomized participants with an i-IGA score ≥2 at baseline **Face** • Time to complete facial psoriasis clearance (f-IGA = 0) among randomized participants with facial psoriasis at baseline • Proportion of participants with complete facial psoriasis clearance (f-IGA = 0) among randomized participants with facial psoriasis at baseline over time through Week 16 • Proportion of participants who achieve an f-IGA score of clear (0) or minimal (1) with at least 2-grade improvement from baseline at Week 16 among randomized participants with an f-IGA score ≥2 at baseline **These endpoints relate to the guselkumab group only:** • The proportion of participants achieving palmoplantar IGA (pp-IGA) of clear (0) or almost clear/minimal (1) with at least 2-point improvement over time through Week 48 among randomized participants with a pp-IGA score ≥2 at baseline • The proportion of participants achieving pp-IGA of clear (0) over time through Week 48 among randomized participants with palmoplantar psoriasis at baseline • The change from baseline in the Nail Psoriasis Severity Index (NAPSI) over time through Week 48 among randomized participants with nail psoriasis at baseline • The percent improvement from baseline in NAPSI over time through Week 48 among randomized participants with nail psoriasis at baseline • The proportion of participants achieving NAPSI 50/75/90/100 response over time through Week 48 among randomized participants with nail psoriasis at baseline

	• The proportion of participants achieving NAPSI 0 over time through Week 48 among randomized participants with nail psoriasis at baseline **Other Endpoints - Patient-Reported Outcomes** **The following endpoints will be summarized for each of the guselkumab and placebo treatment groups:** • The change from baseline in Psoriatic Arthritis Impact of Disease score (PsAID-12) over time through Week 48 • The proportion of participants with a score suggestive of PsA, i.e., ≥3 on the Psoriasis Epidemiology Screening Tool (PEST) over time through Week 48 among randomized participants with screening PEST score <3 **The following endpoints will compare the guselkumab group with the placebo group:** • The change from baseline in individual scale score of PSSD components at Week 16 • The proportion of participants who achieve a PSSD individual scale score of 0 at Week 16 among randomized participants with scale score ≥1 • The proportion of participants who achieve a PSSD symptom score = 0 at Week 16 among randomized participants with PSSD symptom score ≥1 • The proportions of participants who achieve a PSSD symptom score = 0 and a PSSD sign score = 0 and the proportion of participants who achieve a PSSD individual scale score of 0 for participants with a baseline symptom score, sign score, and each PSSD individual baseline scale score that is ≥1 over time through Week 16 • The proportion of participants with Dermatology Life Quality Index (DLQI) 0/1 at Week 16 • The change from baseline in patient-reported outcomes measurement information system-29 (PROMIS-29) score over time through Week 16 **These endpoints relate to the guselkumab group only:** • The change from baseline in PSSD symptom score over time through Week 48 • The proportion of participants who achieve ≥4-point reduction (improvement) in PSSD itch score from baseline over time through Week 48 among participants with a PSSD itch score ≥4 at baseline • The proportion of participants with PSSD Individual Symptom Scale Score = 0 over time through Week 48 among participants with PSSD >0 at baseline • The change from baseline in individual scale score of PSSD components over time through Week 48

	• The proportion of participants who achieve a PSSD individual scale score of 0 over time through Week 48 among randomized participants with scale score ≥1 • The proportion of participants who achieve a PSSD symptom score = 0 over time through Week 48 among randomized participants with PSSD symptom score ≥1 • The proportions of participants who achieve a PSSD symptom score = 0 and a PSSD sign score = 0 and the proportion of participants who achieve a PSSD individual scale score of 0 for participants with a baseline symptom score, sign score, and each PSSD individual baseline scale score that is ≥1 over time through Week 48 • The proportion of participants with Dermatology Life Quality Index (DLQI) 0/1 over time through Week 48 • The proportion of participants with DLQI 0 over time through Week 48 • The change from baseline in PROMIS-29 score over time through Week 48
Other Objectives	**Other Endpoints – Pharmacokinetics, Pharmacodynamics, Immunogenicity, and Pharmacogenomics**
To evaluate the pharmacokinetics (PK) and immunogenicity of guselkumab	• Serum guselkumab concentrations • Antibodies to guselkumab
To evaluate the pharmacodynamic (PD) effects of guselkumab	• Change from baseline in cellular and molecular biomarkers in skin and blood
To evaluate the pharmacogenomics of guselkumab	• Genetic factors associated with clinical response and PD effects

The ordering of endpoints, methods of analysis, and the approach to control the Type I error for multiplicity, as well as the data-handling rules for the major secondary endpoints, will be specified in the SAP.

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

HYPOTHESIS

It is hypothesized that guselkumab is superior to placebo in the treatment of low BSA moderate plaque psoriasis with special site involvement as assessed by the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) at Week 16 (primary hypothesis).

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 3b, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of guselkumab versus placebo in participants with low BSA moderate plaque psoriasis with special site involvement.

Approximately 300 eligible participants will be randomized in a 2:1 ratio to receive either guselkumab CCI CC at Weeks 0 and 4 and then CCI or placebo (Figure 1). Randomization will be stratified by special site. The study will aim to enroll no less than approximately 20% of participants from diverse racial-ethnic backgrounds (i.e., self-identify as non-white/non-Caucasian descent) to reflect the North American Census population.

There will be 2 treatment groups:

- A guselkumab group who will receive guselkumab CCI CC at Weeks 0 and 4 and then CCI through Week 44. Placebo will be administered at Week 16 to maintain the blind.
- A placebo group who will receive placebo at Weeks 0, 4, and 12 after which they will cross over to receive guselkumab at Weeks 16, 20, 28, 36, and 44.

Further details on active and blinding study intervention administrations for both treatment groups are provided in Section 6.

There will be 2 database locks (DBLs) in this study, at Weeks 16 and 56. After all participants have completed the Week 16 visit (or discontinued from the study), a Week 16 DBL will be performed, and unblinded data will only be made available to select Sponsor and Contract Research Organization (CRO) team members involved with analysis of the data and preparation of analyses for the Week 16 DBL. All other Sponsor, site, and CRO personnel directly involved with study conduct will remain blinded to treatment assignments until the Week 56 DBL and related analyses have been completed.

4.2. Scientific Rationale for Study Design

Blinding, Control, Study Phase/Periods, and Intervention Groups

A placebo-controlled design was chosen in order to provide a robust assessment of the efficacy of guselkumab CCI CC at Weeks 0 and 4 and then CCI in low BSA moderate plaque psoriasis with special site involvement. The placebo-controlled design is intended to minimize participant and investigator bias in evaluating the efficacy and safety of guselkumab in the selected patient population (Food and Drug Administration [FDA] Guidance for Industry E10).

DNA and Biomarker Collection

It is recognized that genetic variation can be an important contributory factor to interindividual differences in intervention distribution and response and can also serve as a marker for disease susceptibility and prognosis. Pharmacogenomic research may help to explain interindividual variability in clinical outcomes and may help to identify population subgroups that respond differently to an intervention. The goal of the pharmacogenomic component is to collect DNA to allow the identification of genetic factors that may influence the PK, PD, efficacy, or safety of guselkumab and to identify genetic factors associated with psoriasis.

Biomarker samples will be collected to evaluate mechanism of action of guselkumab, or help explain interindividual variability in clinical outcomes and may help to identify population subgroups that respond differently to an intervention. The goal of the biomarker analyses is to

evaluate the PD of guselkumab and aid in evaluating the intervention-clinical response relationship.

DNA and biomarker samples may be used to help address emerging issues and to enable the development of safer, more effective, and ultimately individualized therapies.

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 AEs of the study, and provide their consent voluntarily will be enrolled. Written consent/assent may be obtained through various sources (e.g., paper or electronic such as eConsent, eSignature, or digital signature) as determined by regulations as well as study and/or patient preferences.

The total blood volume to be collected is considered to be an acceptable amount of blood to be collected over this time period from the population in this study based upon the standard of the American Red Cross (www.redcrossblood.org).

The amount of radiation is within a safe range, with the exposure from 1 standard chest X-ray being comparable to 10 days of exposure to natural background radiation.

4.3. Justification for Dose

The current approved dose regimen of guselkumab of CCI CC at Week 0 and 4 and then CCI is the proposed dose regimen for this proposed study for the treatment of low BSA moderate plaque psoriasis with special site involvement.

Guselkumab doses ranging from CCI to CCI have been studied in the Phase 2/3 psoriasis and PsA development programs, with doses ranging from CCI to CCI CCI (CCI for psoriasis and CCI CCI or CCI for PsA. Results from these programs demonstrated the efficacy and safety of the CCI CC CCI dose regimen for participants with psoriasis and PsA, resulting in the approval of this dose regimen in the US and globally for both indications. The analyses of pooled safety data from the psoriasis and PsA studies demonstrated that guselkumab is safe and well tolerated through 5 years of treatment in psoriasis, and through 2 years of treatment in PsA. Post-marketing surveillance and safety experience accrued from additional clinical studies in psoriatic disease and in other immunology indication demonstrated a consistent safety profile, and no new safety signals have been identified.

Additional considerations in support of the proposed dose regimen are as follows:

1) The Phase 2b (CNTO1959PSO2001) and Phase 3 (CNTO1959PSO3001 and CNTO1959PSO3002) studies in participants with moderate-to-severe psoriasis demonstrated that CCI CC given at Weeks 0 and 4 followed by CCI resulted in optimal efficacy with an

adequate safety profile, and disease baseline severity was not found to be a significant covariate in the PK and exposure-response analyses.

2) Among participants in the combined Phase 3 psoriasis studies (CNTO1959PSO3001 and CNTO1959PSO3002), no exposure-response trend was observed in subjects with moderate-to-severe plaque psoriasis. In the PsA Phase 3 studies (CNTO1959PSA3001 and CNTO1959PSA3002), participants in the lowest guselkumab trough concentration quartile had lower clinical responses. Furthermore, CCI CCI showed incremental efficacy compared to CCI CCI indicating that a dose regimen lower than CCI CCI may result in suboptimal efficacy.

These findings indicate that the proposed guselkumab CCI CCI CCI dose regimen is appropriate for the low BSA moderate plaque psoriasis population with special site involvement to achieve optimal efficacy.

4.4. End of Study Definition

End of Study Definition

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 visit at that study site, in the time frame specified in the Clinical Trial Agreement.

Study Completion Definition

Participants who prematurely discontinue study drug for any reason prior to the Week 16 visit should complete the specified study visits and the Final Safety/Early Termination visit as outlined in Section 1.3 and Section 7.2.

A participant will be considered to have completed the study if he or she has completed assessments at the Final Safety/Early Termination visit.

5. STUDY POPULATION

Screening for eligible participants will be performed within approximately 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 or designee and resolve any issues before enrolling a participant in the study. Waivers are not allowed.

5.1. Inclusion Criteria

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

Age

1. At least 18 years of age.

Participant and Disease Characteristics

2. Have a diagnosis of plaque psoriasis (with or without PsA) for at least 6 months before the first administration of study intervention.

3. All participants must meet the following disease severity criteria at screening and at baseline:

    a) Overall IGA 3 (moderate) plaque psoriasis
    AND
    b) BSA 2-15% with at least 1 plaque outside of special sites
    AND
    c) Involvement of at least 1 special site with at least moderate severity. Qualifying sites include scalp with ss-IGA ≥3, face with f-IGA ≥3, intertriginous with i-IGA ≥3, or genital with sPGA-G ≥3.

4. Be inadequately controlled with or intolerant of at least 1 prior topical therapy (including, but not limited to, corticosteroids, retinoids, vitamin D, or vitamin D/steroid and retinoid/steroid combinations, tacrolimus, pimecrolimus, anthralin/dithranol, coal tar preparations, tapinarof, roflumilast, etc.) for the treatment of psoriasis at both screening and baseline.

5. Be a candidate for phototherapy or systemic treatment for psoriasis (either naïve or history of previous treatment; see Exclusion Criterion 6 for washout of prior treatments).

6. Be considered, in the opinion of the investigator, suitable candidates for guselkumab therapy according to their country's approved product labeling.

Sex and Contraceptive/Barrier Requirements

7. Before the first administration of study intervention, a participant must be either:
    a. Not of childbearing potential (Appendix 10.6): 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 sterile (e.g., hysterectomy, bilateral salpingectomy, or bilateral oophorectomy); or otherwise, incapable of pregnancy.
    b. Of childbearing potential and Practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) prior to receiving study intervention, and agrees to remain on a highly effective method while receiving

study intervention, and for at least 12 weeks after receiving the last administration of study intervention, the end of relevant systemic exposure, consistent with local regulations regarding the use of birth control methods for participants participating in clinical studies.

The investigator must evaluate the potential for contraceptive method failure (e.g., noncompliance, recently initiated) in relationship to the first dose of study intervention. Examples of highly effective methods of contraception are located in Appendix 10.6.

Note: If a participant's childbearing potential changes after the start of the study (e.g., 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.

8. A participant of childbearing potential must have a negative highly sensitive serum (β-human chorionic gonadotropin [β-hCG]) pregnancy test at screening and have negative pregnancy tests before receiving study intervention.

9. A participant of childbearing potential must agree not to be pregnant, breastfeeding, or planning to become pregnant while enrolled in this study or within 12 weeks after the last dose of study intervention.

10. A participant of childbearing potential must agree not to donate eggs (ova, oocytes) or freeze for future use for the purposes of assisted reproduction during the study and for at least 12 weeks after receiving the last administration of guselkumab.

11. A male participant must agree not to plan to father a child while enrolled in this study or within 12 weeks after the last dose of study intervention.

12. A male participant who is sexually active with a person of childbearing potential and has not had a vasectomy must agree to use a barrier method (i.e., condom) during the study and for at least 12 weeks after receiving the last administration of study intervention. Male participants must also be advised of the benefit for a female partner to use a highly effective method of contraception as condom may break or leak.

13. A male participant must agree not to donate sperm for the purpose of reproduction during the study and for at least 12 weeks after receiving the last administration of study intervention.

Screening Laboratory Tests

14. Have screening laboratory test results within the following parameters. If 1 or more of the laboratory parameters is out of range, a single retest of laboratory values is permitted:
    a. Hemoglobin ≥10 g/dL (≥100 g/L)
    b. White blood cells ≥3.5 x 10^3/μL (≥3.5 GI/L)
    c. Neutrophils ≥1.5 x 10^3/μL (≥1.5 GI/L)
    d. Platelets ≥100 x 10^3/μL (≥100 GI/L)

e. Serum creatinine ≤1.5 mg/dL (≤137 μmol/L)
f. Aspartate aminotransferase (AST) ≤2 x upper limit of normal (ULN)
g. Alanine aminotransferase (ALT) ≤2 x ULN
h. Alkaline phosphatase ≤2 x ULN

Other

15. Must sign an informed consent form (ICF) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.

16. Must sign a separate ICF for optional samples including:
a) For biomarkers, if the participant agrees to provide optional skin biopsy and tape strip samples
AND/OR
b) For pharmacogenomics, if the participant agrees to provide a DNA sample for research (where local regulations permit).

Refusal to give consent for any of the optional research samples does not exclude a participant from participation in the study.

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

5.2. Exclusion Criteria

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

Psoriasis related

1. Has a non-plaque form of psoriasis (e.g., erythrodermic, guttate, or pustular) at screening or randomization.

2. Has current drug-induced psoriasis (e.g., a new onset of psoriasis or an exacerbation of psoriasis from beta blockers, calcium channel blockers, or lithium).

3. For participants with palmoplantar involvement, confounding diagnoses, including, but not limited, to palmoplantar pustulosis, eczematous dermatitis, contact/irritant dermatitis, acquired keratoderma, etc., should be confirmed and excluded.

4. For participants with genital involvement, no pustules or vesicles should be present.

Psoriatic Disease Treatment-related

Participants will not be eligible if they have ever received OR if they have received any of the following treatments within the specified timeframe prior to the first administration of study intervention:

5. **Ever received:** Must be naïve to prior biologic (or biosimilars of) for the treatment of psoriasis, PsA, or any other indications that could impact the assessment of psoriasis.

   Prior biologics (or biosimilars of) may include, but not limited to, tumor necrosis factor (TNF)-inhibitors (e.g., adalimumab, etanercept, infliximab, or certolizumab or biosimilars), IL-17 inhibitors (e.g., secukinumab, ixekizumab, brodalumab, or bimekizumab), and IL-12/23 inhibitors (e.g., ustekinumab), or IL-23 inhibitor (e.g., guselkumab, risankizumab, or tildrakizumab).

6. **Within 4 weeks:**

   a) Any systemic immunosuppressants (e.g., methotrexate [MTX], azathioprine, cyclosporine, inhibitors of the JAK/TYK pathway, 6-thioguanine, mercaptopurine, mycophenolate mofetil, tacrolimus, acitretin, or anakinra).

   b) Any systemic medications that could affect psoriasis efficacy evaluations (including but not limited to oral or injectable corticosteroids, PDE4 pathway inhibitors [e.g., apremilast], retinoids [acitretin], 1, 25 dihydroxy vitamin D3 and analogs, psoralens, sulfasalazine, hydroxyurea, and fumaric acid derivatives etc.).

   c) Phototherapy or narrow band laser (e.g., Excimer or XTRAC).

   d) Lithium, antimalarials, or intramuscular (IM) gold.

7. **Within 2 weeks**:

   a) Any topical medications that could affect psoriasis efficacy evaluations (including but not limited to corticosteroids, retinoids, or vitamin D analog preparations, calcipotriene and betamethasone dipropionate ointment or foam, tacrolimus, pimecrolimus, anthralin/dithranol, coal tar preparations, PDE4 inhibitors, e.g., crisaborole, or other topicals used for the treatment of psoriasis, e.g., tapinarof, roflumilast, etc.).

   b) Any herbal or traditional medicines that could affect psoriasis efficacy evaluations (including but not limited to Chinese, Taiwanese, Korean, and other ethnic medicines).

Other Treatments or Experimental Treatments

8. **Within 12 weeks or 5 half-lives (whichever is longer)** of the first administration of study drug:

    a) Any other biologic therapy or experimental antibody.

    b) Any agent that modulates T-cells including but not limited to natalizumab, abatacept, visilizumab, etc.

9. **Within 4 weeks or 5 half-lives (whichever is longer)** of the first administration of study drug, any other non-biologic systemic therapy or experimental systemic therapy.

10. Is currently enrolled in another study using an investigational agent or procedure.

Coexisting Medical Conditions or History

11. Has evidence of skin conditions that would interfere with clinical assessments of psoriasis.

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

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

14. Currently has a known 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 drug administration or cervical carcinoma in situ that has been treated with no evidence of recurrence for at least 3 months before the first study drug administration).

15. 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.

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

17. Has known allergies, hypersensitivity, or intolerance to guselkumab or its excipients (refer to the IB).

18. 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.

19. Has unstable suicidal ideation or suicidal behavior, that may be defined as an electronic Columbia-Suicide Severity Rating Scale (C-SSRS) rating at screening of: Suicidal Ideation with Intention to Act ("4"), Suicidal Ideation with Specific Plan and Intent ("5"), or a suicide attempt (interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt) in the last 6 months and is confirmed to be at risk by the investigator based on an evaluation by a mental health professional. The final decision on excluding a participant will be made at the judgment of the investigator.

20. Has had major surgery (e.g., requiring general anesthesia and hospitalization) within 8 weeks before screening, or will not have fully recovered from such surgery, or has such surgery planned during the time the participant is expected to participate in the study (56 weeks).

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

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

Infections or Predisposition to Infections

22. Has a history of chronic or recurrent infectious disease, including, but not limited to, chronic renal infection, chronic chest infection (e.g., bronchiectasis), recurrent urinary tract infection (recurrent pyelonephritis or chronic non-remitting cystitis), fungal infection (mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.

23. Has or has had a serious infection (e.g., sepsis, pneumonia, or pyelonephritis), or has been hospitalized or received IV antibiotics for a clinically relevant infection during the 2 months before screening.

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

25. Has received, or is expected to receive, any live virus or bacterial vaccination within 3 months prior to the first administration of study drug, or plans to receive such vaccines during the study or within 4 weeks after the last administration of study

intervention. For Bacillus Calmette–Guérin (BCG) vaccine, see Exclusion Criterion 26.

26. Has received or is expected to receive a BCG vaccination within 12 months of screening, during the study, or within 12 weeks after the last administration of study intervention.

27. Meets **ANY** of the following TB screening criteria:

Note: Interferon gamma release assay (IGRA) testing includes either QuantiFERON-TB® or T-SPOT.TB®

a. Has a history of active TB or show signs or symptoms suggestive of active TB upon medical history and/or physical examination at screening.
b. Has a history of untreated latent TB prior to screening. An exception is made for participants who are currently receiving treatment or will initiate treatment for latent TB prior to first administration of study intervention.

Note: For participants with a history of treated latent TB, there must be documentation of appropriate treatment prior to the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous TB treatment and provide appropriate documentation. IGRA testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB.

c. Has had recent close contact with a person with active TB. An exception is made if such participants are referred to a physician specializing in TB to determine if treatment is warranted or not. This evaluation must be adequately documented and, if treatment is recommended, the participant must be receiving appropriate treatment prior to the first administration of study intervention.
d. Has a positive IGRA test result within 2 months prior to the first administration of study intervention. An exception is made for participants who:
    - have a history of adequately treated latent TB described above.
    - have a newly identified positive IGRA test result in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated prior to the first administration of study intervention.
    - have a false-positive IGRA test as determined by the following:
        - A suspected false-positive initial IGRA test must be repeated. If repeat testing is **NOT** positive, the participant must be referred to a physician specializing in TB to determine if the initial test can be considered a false-positive. This evaluation must be adequately documented prior to the first administration of study intervention. If repeat testing is positive, however, it will be considered a true-positive and the participant is only eligible if active TB has been ruled out and appropriate treatment for latent TB has been initiated as described above.

Note: Indeterminate/borderline results should be handled as outlined in Section 8.2.11.

28. Has a history of active granulomatous infection, including histoplasmosis or coccidioidomycosis, before screening. Refer to Exclusion Criterion 27 for information regarding eligibility with a history of latent TB.

29. Has had a nontuberculous mycobacterial infection or opportunistic infection (e.g., cytomegalovirus, pneumocystosis, aspergillosis).

30. Has a chest radiograph or computed tomography scan within 3 months before the first administration of study drug that shows an abnormality suggestive of a current active or inactive infection, including TB, or a malignancy.

31. Tests positive for HBV infection (see Appendix 3).

32. Is seropositive for antibodies to HCV, unless they satisfy 1 of the following conditions:
    a. Have a history of successful treatment (defined as being negative for HCV ribonucleic acid [RNA] at least 12 weeks after completing antiviral treatment) and have a negative HCV RNA test result at screening,

    OR

    b. While seropositive have a negative HCV RNA test result at least 12 weeks prior to screening and a negative HCV RNA test result at screening.

33. Is infected with human immunodeficiency virus.

General

34. Unable to avoid prolonged sun exposure or use of tanning booths or other ultraviolet light sources.

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

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

37. 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 must ensure that 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 the participant no longer meets all eligibility criteria, then the participant must be excluded from participation in the study.

5.3. Lifestyle Considerations

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

1. Agree to follow all requirements that must be met during the study as noted in the Inclusion and Exclusion Criteria (e.g., contraceptive requirements).

2. Must avoid prolonged sun exposure and avoid use of tanning booths or other ultraviolet (UV) light sources during the study.

3. Must refer to Section 6.8, Concomitant Therapy, for details regarding prohibited and restricted therapy during the study.

4. **Participants with facial psoriasis** should avoid any facial treatment that could worsen psoriasis or confound assessment, including, but not limited to, facials, peels, scrubs, lasers, microneedling, depilatory procedures, etc.

5. **Participants with scalp psoriasis** must attempt to keep a consistent hairstyle for all study visits. This includes the following recommendations:

    - While hair dye is permitted to be used during the study, participants are discouraged from undergoing any hair dying process or other hair treatments that may impact the scalp for 7 days prior to a study visit.
    - Hair prosthetics (e.g., wigs, hair extensions, etc.) are permitted but should be removed for clinical assessments of scalp psoriasis at all study visits. Hair extensions if not obscuring scalp can also be consistently left in place at all visits if preferred by investigator and participant.
    - Hair transplants and tattooing of scalp including procedures such as microblading are not permitted during the course of study and should not be performed within 3 months prior to screening.

6. **Participants with nail psoriasis** must avoid use of nail treatments that may affect the evaluation of nail psoriasis (including but not limited to acrylic nails, nail polish, gel nails, other nail treatments or nail extensions, etc.).

7. It is recommended that participants be up to date on all age-appropriate vaccinations prior to screening per routine local medical guidelines. It is strongly recommended that participants will have completed a locally approved (or emergency use-authorized) coronavirus disease 2019 (COVID-19) vaccination regimen at least 2 weeks prior to study-related visits or procedures. Study participants should follow applicable local vaccine labelling, guidelines, and standards-of-care for patients receiving immune-targeted therapy when determining an appropriate interval between vaccination and study enrolment (see also Section 6.8.4).

5.4. Screen Failures

If, during the screening phase, the participant has not met all inclusion criteria or met any exclusion criteria or is unable or unwilling to adhere to the prohibitions and restrictions of the study, the participant is considered to be a screen failure and is not eligible to be randomized at that time.

A participant will not be considered a screen failure if circumstances unrelated to the protocol (e.g., site closure due to COVID-19, or other unforeseen circumstances resulting in site closures or inability of participant to reach site, etc.) impact completion of screening and thus could be eligible for new screening and rescreening, if applicable.

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 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.

Rescreening

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened on 1 occasion only after consultation with the Sponsor or designee (i.e., study responsible physician, scientists).

Rescreened participants will be assigned a new participant number, undergo the informed consent process, and then start a new screening phase.

Previous TB evaluation results (including the IGRA test and chest X-ray), if done within the specified allowed time, are not required to be repeated.

Retesting

Retesting of abnormal laboratory values that may lead to exclusion will be allowed once. Retesting can occur at an unscheduled visit during the specified screening phase.

If a laboratory abnormality occurs, the site is encouraged to wait for all laboratory tests to be completed to ensure other laboratory tests do not need to be repeated, as only 1 retest of laboratory tests is allowed.

6. STUDY INTERVENTION AND CONCOMITANT THERAPY

6.1. Study Intervention(s) Administered

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

Guselkumab and placebo to match guselkumab will be manufactured and provided under the responsibility of the Sponsor. Refer to the guselkumab prescribing information for a list of excipients.

Detailed instructions on the administration of study intervention will be provided in the Site Investigational Product and Procedures Manual.

The 2 treatment groups will receive study intervention dosing and blinding administrations as below:

- Group 1 (guselkumab)
  - Guselkumab CCI CC at Weeks 0 and 4 and then CCI through Week 44
  - Placebo for guselkumab CC at Week 16

- Group 2 (placebo)
  - Placebo for guselkumab CC at Weeks 0, 4, 12
  - Cross-over to treatment with guselkumab CC at Weeks 16, 20, 28, 36, and 44

For a definition of study intervention overdose, refer to Section 6.7.

Guidelines for study intervention affected by the COVID-19 pandemic are provided in Appendix 8.

Description of Interventions

Group/Arm Name	Group 1	Group 2
Intervention Name	Guselkumab	Placebo
Dose Formulation	Liquid provided in a single-use prefilled syringe assembled with the UltraSafe PLUS™ Passive Needle Guard	Liquid provided in single-use prefilled syringe assembled with the UltraSafe PLUS™ Passive Needle Guard
Unit Dose Strength(s)	CCI	N/A
Dosage Level(s) and Frequency	CCI at Week 0, 4 and then CCI	N/A

Group/Arm Name	Group 1	Group 2
Route of Administration	☐ Oral ☐ IV infusion ☐ IV injection ☐ Intramuscular ☒ Other (CCI)	☐ Oral ☐ IV infusion ☐ IV injection ☐ Intramuscular ☒ Other (CCI)
Dosing Instructions	Group 1: CCI study agent will be administered by site personnel at specified dosing visits in the Schedule of Activities (SoA).	Group 2: CCI placebo agent will be administered by site personnel at specified dosing visits in the SoA.

6.2. Preparation/Handling/Storage/Accountability

Combination Products

For this protocol, the term combination product refers to the single integral drug-device combination.

The Sponsor-manufactured combination product for use in this study is the prefilled syringe (PFS) assembled with the UltraSafe PLUS™ Passive Needle Guard (PFS-U). Additional details on the PFS-U are provided in Section 6.1 and in the guselkumab IB.

All combination product deficiencies (including failure, malfunction, improper or inadequate design, manufacturer error, use error, and inadequate labeling) shall be documented and reported by the investigator throughout the study. For studies with combination products, these deficiencies will be reported as product quality complaints (PQC, see Appendix 10.5.6).

Preparation/Handling/Storage

Study intervention will be dispensed/administered at study visits as indicated in the SoA. If needed due to an emergency situation (see Appendix 8), the study intervention may be delivered directly to the participants from the site by a courier. Each courier will adhere to privacy requirements approved by the Independent Ethics Committee (IEC)/Institutional Review Board (IRB). The capability to utilize these direct-to-patient shipments will be assessed by the Sponsor to ensure that it is allowable per local regulations.

Guselkumab will be supplied as a CCI mL sterile liquid in a single-dose PFS assembled in a PFS-U. Placebo will be supplied as a 1 mL sterile liquid in a single-dose PFS-U. All guselkumab/placebo for guselkumab must be stored at controlled temperatures ranging from 36°F to 46°F (2°C to 8°C).

Guselkumab and placebo for guselkumab should be a clear and colorless to light yellow solution that may contain translucent particles. Do not use guselkumab or placebo for guselkumab if the liquid is cloudy, discolored, or has large particles. Protection from light is not required during the preparation and administration of the study intervention material but avoid direct exposure to

sunlight. Aseptic procedure must be used during the preparation and administration of the study intervention material.

Refer to the Site Investigational Product and Procedures Manual for additional guidance on study intervention preparation, handling, and storage.

Accountability

The investigator is responsible for ensuring that all study intervention received at the site is inventoried and accounted for throughout the study. The dispensing of study drug to the participant, and the return of study drug from the participant, must be documented on the drug accountability form. Participants must be instructed to return all original containers, whether empty or containing study drug. All study intervention will be stored and disposed of according to the Sponsor's instructions. Study site personnel must not combine contents of the study intervention containers.

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 intervention 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 intervention return form.

Potentially hazardous materials such as used ampules, needles, syringes, and vials should be disposed of immediately in a safe manner and therefore will not be retained for intervention accountability purposes.

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 individuals participating in the study. Returned study intervention must not be dispensed again, even to the same participant. Study intervention may not be relabeled or reassigned for use by other participants. The investigator agrees neither to dispense the study intervention from, nor store it at, any site other than the study sites agreed upon with the Sponsor. Further guidance and information for the final disposition of unused study interventions are provided in the Site Investigational Product and Procedures Manual.

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 2 intervention groups, based on a computer-generated randomization schedule prepared before the study by or under the supervision of the Sponsor. The randomization will use permuted block randomization with stratification by special site. If participants present with qualifying

moderate psoriasis in multiple special sites, they will be allocated to the special site that is most severe, as determined by the participant.

The interactive web response system (IWRS) will assign a unique intervention code, which will dictate the intervention assignment and matching intervention kit 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.

Blinding

To maintain the study blind, the study intervention container will have a label containing the study name, study intervention number, reference number, and storage instructions. The label will not identify the study intervention in the container. 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 study interventions 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 (i.e., study intervention serum concentrations, anti-drug antibody levels) 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.

After all participants have completed the Week 16 visit (or discontinued from the study), a Week 16 DBL will be performed, and unblinded data will only be made available to select Sponsor and CRO team members involved with analysis of the data and preparation of analyses for the Week 16 DBL. All other Sponsor, site, and CRO personnel directly involved with study conduct will remain blinded to treatment assignments until the Week 56 DBL and related analyses have been completed.

Under normal circumstances, the blind should not be broken until all participants have completed the study and the database is finalized. 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 by the IWRS, 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 should continue to return for scheduled evaluations and may not be eligible for further treatment.

6.4. Study Intervention Compliance

In this study, the CC investigational product (IP, guselkumab/placebo) will be administered at the study site.

Compliance will be assessed by direct questioning during the site visits and documented in the source documents and eCRF. Deviation(s) from the prescribed dosage regimen should be recorded in the eCRF.

During the study, the investigator or designated study research personnel will be responsible for providing additional instruction to reeducate any participant who is not compliant with taking the study intervention.

Compliance with the treatment schedule is strongly encouraged. It is understood that treatment may be interrupted for health-related or safety reasons.

- If, for any reason, a participant cannot receive the study intervention at the scheduled visit, the participant must make every effort to still come in for the scheduled assessments for that visit.
- In general, the dose should be administered within approximately 2 weeks of that scheduled visit.
- The participant should then resume the normal study schedule relative to the baseline visit (Week 0).

In the case when a participant does not come into the study site for a scheduled visit, the site will follow up with that participant. Due diligence could include telephone calls, certified letters, and email requests. Measures taken to obtain follow-up information must be documented.

- Study site personnel will keep a log of all study intervention dispensed and will compare the amount of study intervention dispensed with the amount returned.

All post-baseline visits will have a visit window of approximately ±7 days counting from Week 0 as Day 1. If a study visit occurs outside this window, the Sponsor should be consulted about how the participant should resume his or her normal dose schedule.

Information regarding study intervention administrations that are administered outside of the scheduled windows or missed will be recorded. Participant charts and worksheets may be reviewed and compared with the data entries on the eCRFs to ensure accuracy.

6.5. Dose Modification

Not applicable.

6.6. Continued Access to Study Intervention After the End of the Study

Participants will be instructed that study intervention will not be made available to them after they have completed/discontinued study intervention and that they should return to their primary physician to determine standard of care.

Local regulations on continued access will always take precedence. Plans for continued access stated in this protocol may change if new information on the benefit-risk profile of guselkumab becomes available during the study or program.

6.7. Treatment of Overdose

For this study, an overdose of the study intervention is any dose of study intervention greater than the highest protocol-specified dose at a single dosing visit (i.e., guselkumab CC CCI

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

- Contact the Medical Monitor (or designee) immediately.
- Evaluate the participant to determine, in consultation with the Medical Monitor (or designee), whether study intervention should be interrupted or whether the dose should be reduced.
- Closely monitor the participant for AE/SAE and laboratory abnormalities.
- Obtain a serum sample for PK analysis if requested by the Medical Monitor (or designee), determined on a case-by-case basis.
- Document the quantity of the excess dose as well as the duration of the overdosing in the eCRF.

6.8. Concomitant Therapy

Prestudy therapies that treat psoriatic disease and any vaccines including those authorized for emergency use (e.g., COVID-19) administered up to 30 days before first dose of study intervention must be recorded at screening as prior medications/treatments.

Medications/treatments taken after the first dose of study intervention has been administered will be documented as concomitant medications/treatments. Concomitant therapies, including any vaccinations or vaccines authorized for emergency use (e.g., COVID-19) must be recorded throughout the study beginning with the start of the first dose of study intervention to 12 weeks after the last dose of study intervention. Concomitant therapies must also be recorded beyond Week 56 only in conjunction with SAEs 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 (including prescription or [OTC] over-the-counter medicines, vitamins, and/or herbal supplements or teas) as well as all moisturizers or emollients that the participant is receiving at the time of enrollment or receives during the study must be recorded in the eCRF along with the following:

- Reason for use
- Dates of administration including start and end dates
- Dosage information including dose and frequency

Modification of an effective preexisting therapy should not be made for the explicit purpose of entering a participant into the study. The Medical Monitor should be contacted if there are any questions regarding concomitant or prior therapy.

6.8.1. Permitted Concomitant Medications

For the purposes of this protocol, dietary supplements are defined as vitamins, minerals, and purified food substances with pharmaceutical properties (e.g., garlic). Vitamins, minerals, and purified food substances are allowed in amounts not known to be associated with adverse effects (such as hypervitaminosis).

Any participant who is receiving a permitted concomitant medication for any reason must be on a locally approved medication and dose for the treated indication, and this must be documented in the eCRF. The Sponsor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered.

6.8.1.1. Topical Treatments

In general, topical moisturizers and emollients such as Vaseline, Aquaphor, coconut butter, Eucerin, Nivea, etc. are allowed throughout the study. Participants should not use any topical moisturizers and emollients on the day of study visits.

For intertriginous psoriasis, the use of drying and/or anti-fungal powders is allowed, including, but not limited to, Zeasorb and ZeasorbAF throughout the study. However, powders should not be used on the day of study visits.

6.8.2. Prohibited Concomitant Medications

6.8.2.1. Topical Treatments

All topical therapies, including prescription strength and active ingredient OTC shampoos, that could affect psoriasis or any efficacy evaluations are not permitted at any time during the study. These include, and are not limited to, corticosteroids, coal tar preparations, anthralin, calcipotriene, tazarotene, methoxsalen, pimecrolimus, tacrolimus, traditional ethnic medicines (Taiwanese, Korean, Chinese, etc.), tapinarof, roflumilast, etc.

6.8.2.2. Phototherapy or Systemic Therapy for Psoriasis

The use of phototherapy or systemic antipsoriatic medications that could affect psoriasis or any efficacy evaluation is not permitted at any time during the study. These treatments include but are not limited to the following:

- Those targeted for reducing TNF (including but not limited to infliximab, adalimumab, etanercept, or their biosimilars), drugs targeted for reducing IL-12, IL-17, or IL-23 (including but not limited to ustekinumab, tildrakizumab, risankizumab, secukinumab, ixekizumab, or brodalumab), alpha-4 integrin antagonists (including but not limited to natalizumab), and any other biological agent or other advanced systemic medications (including but not limited to apremilast, deucravacitinib, etc.).
- Steroids and any other conventional systemic therapy (including but not limited to MTX, cyclosporine, acitretin, etc.).
- Herbal treatments or traditional ethnic therapies (including but not limited to Taiwanese, Korean, Chinese, and other ethnic medicines etc.).

6.8.3. Concomitant Medications for Conditions Other Than Psoriasis

Every effort should be made to keep participants on stable concomitant medications. If the medication is temporarily discontinued because of abnormal laboratory values, side effects, concurrent illness, or the performance of a procedure, the change and reason for it should be clearly documented in the participant's medical record.

The use of stable doses of nonsteroidal anti-inflammatory drugs is allowed. However, disease-modifying agents such as MTX, sulfasalazine, or IM gold are prohibited during the study.

The use of corticosteroids for indications other than psoriasis 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.

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

6.8.4. Vaccinations (including COVID-19)

When considering use of locally approved non-live vaccines (including emergency use-authorized COVID-19 vaccines) in study participants, follow applicable local vaccine labelling, guidelines, and standards-of-care for participants receiving immune-targeted therapy.

For study participants receiving a locally approved (including emergency use-authorized) COVID-19 vaccine, in order to help identify acute reactions potentially related to COVID-19 vaccine, it is recommended where possible that vaccine and study intervention be administered on different days, separated by as large an interval as is practical within the protocol.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued if:

- The participant withdraws consent to receive study intervention
- The investigator believes that for safety reasons or tolerability reasons (e.g., AE) it is in the best interest of the participant to discontinue study intervention
- The participant becomes pregnant or plans to become pregnant within the study period. Refer to Section 8.3.5 and Appendix 6.
- A systemic opportunistic infection occurs
- The participant develops recurrent or chronic serious infection
- The participant is unable to adhere to study visit schedule or comply with protocol requirements including but not limited to noncompliance with study drug administration
- The participant meets **ANY** of the following TB-related 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 examinations or has had recent close contact with a person with active TB and cannot or will not continue to undergo additional evaluation.
  - A participant undergoing evaluation has chest imaging with evidence of current active TB and/or a positive IGRA test result, unless active TB can be ruled out and appropriate treatment for latent TB can be initiated prior to the next administration of study intervention and continued to completion. Indeterminate/borderline results should be handled as outlined in Section 8.2.11
  - A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy
- The participant has a serious adverse reaction that is temporally related to an injection, including a hypersensitivity reaction resulting in bronchospasm, wheezing and/or dyspnea that requires ventilatory support OR that results in symptomatic hypotension with a decrease in systolic blood pressure of 30% from a participant's baseline value
- 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 a malignancy, including squamous cell skin cancer. Consideration may be given to allowing participants who develop ≤2 basal cell skin cancers that are adequately treated with no evidence of residual disease to continue to receive study intervention
- The participant has severe liver test abnormalities that are not transient and are not explained by other etiologies, as described in Appendix 7

The Sponsor may elect to terminate the study at any time, and if the Sponsor decides not to continue development for any reason, the study medication/drug will no longer be provided to any participants.

Discontinuation of a participant's study intervention should be considered under the following conditions:

- If the participant initiates treatment with prohibited therapies, the Medical Monitor or designee should be notified for possible discontinuation of study intervention.
- The participant develops a serious infection, including but not limited to sepsis or pneumonia. Note: Any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete.
- Discontinuation of study treatment should be considered for participants who report Suicidal Ideation level 4 (some intent to act, no plan), Suicidal Ideation level 5 (specific plan and intent), or any suicidal behavior (e.g., actual suicide attempts, interrupted suicide attempts, aborted suicide attempts, or preparatory behaviors for making a suicide attempt) on a post-baseline (after Week 0) C-SSRS assessment. Discussion of such participants with the medical monitor or designee is required.
- The participant develops a severe injection site reaction but does not meet the criteria specified above.

If a participant discontinues study intervention for any reason before the end of the study, they should be encouraged to continue in the study to complete protocol-specified evaluations as outlined in the SoA and Section 7.2.

Study intervention assigned to a participant who discontinued study intervention may not be assigned to another participant. Additional participants may be entered to ensure the protocol-specified number of participants complete the study.

7.1.1. Liver Chemistry Stopping Criteria

Discontinuation of study intervention for abnormal liver tests is required by the investigator when a participant meets 1 of the conditions in Appendix 7A or in the presence of abnormal liver chemistries not meeting protocol-specified stopping rules, if the investigator believes that it is in the best interest of the participant.

7.1.2. Liver Chemistry Restart Criteria

Refer to Appendix 7B for study intervention restart guidelines following abnormal liver test results. The study Sponsor must provide written approval before study intervention is restarted.

7.2. Participant Discontinuation/Withdrawal From the Study

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

- Loss to follow-up
- Withdrawal of consent
- Death

When a participant withdraws before study completion, the reason for withdrawal is to be documented in the eCRF and in the source document. If the reason for withdrawal from the study is withdrawal of consent, then no additional assessments are allowed.

A participant will not be automatically withdrawn from the study if the participant discontinues study drug prior to the end of the planned treatment period (Week 44). Participants who discontinue study drug but do not terminate study participation will continue to return for protocol-specified procedures and evaluations per SoA and further guidance below.

Participants Who Discontinue Study Drug Prior to the Week 16 Visit

If a participant permanently discontinues study drug intervention prior to the Week 16 visit, they should be encouraged to return for all remaining study visits through Week 16. The participant should also return for a final safety visit to perform assessments under the Week 56/final safety visit approximately 12 weeks after the last study intervention administration.

Participants Who Discontinue Study Drug at or After the Week 16 Visit

If a participant permanently discontinues study drug at or after the Week 16 Visit, they should complete the Week 48 visit assessments at the time of discontinuation or as soon as possible. The participant should also return for a final safety visit to perform assessments under the Week 56/final safety visit approximately 12 weeks after the last study intervention administration.

Participants who Withdraw From Study Participation

Participants who withdraw from study participation prior to the Week 48 visit should complete the final safety/Early Termination visit at the time of early termination.

Withdrawal of Consent

A participant declining to return for scheduled visits does not necessarily constitute withdrawal of consent. Alternate follow-up mechanisms that the participant agreed to when signing the consent form apply as local regulations permit.

Withdrawal of consent should be an infrequent occurrence in clinical studies; therefore, prior to the start of the study, the Sponsor and the investigator should discuss and reach a clear understanding of what constitutes withdrawal of consent in the context of the available reduced follow-up mechanisms listed.

Circumstances for Reduced Follow-up

In the situation where a participant may be at risk for withdrawal of consent and is unable to return for scheduled visits at the protocol-defined frequency, the investigator may consider options for reduced follow-up with consultation of the Sponsor/designee and/or medical monitor. These may include the following (as local regulations permit):

- Less frequent clinical visits
- Telehealth visits: Telephone, video chat, email, letter, social media, fax, or other contact with the following:
  - Participant
  - Relatives of the participant
  - Participant's physicians (general or specialist)
- Review of any available medical records

Details regarding these contacts must be properly documented in source records including responses by participants.

7.2.1. Withdrawal From the Use of Research Samples

A participant who withdraws from the study will have the following options regarding the optional research samples:

- The collected samples will be retained and used in accordance with the participant's original separate informed consent for optional research samples.
- The participant may withdraw consent for optional research samples, in which case, the samples will be destroyed and no further testing will take place. To initiate the sample destruction process, the investigator must notify the Sponsor study site contact of withdrawal of consent for the optional research samples and request sample destruction. The Sponsor study site contact will, in turn, contact the biomarker representative to execute sample destruction. If requested, the investigator will receive written confirmation from the Sponsor that the samples have been destroyed.

Withdrawal From the Optional Research Samples While Remaining in the Main Study

The participant may withdraw consent for optional research samples while remaining in the study. In such a case, the optional research samples will be destroyed. The sample destruction process will proceed as described above.

Withdrawal From the Use of Samples in Future Research

The participant may withdraw consent for use of samples for future research (refer to Appendix 10.4.5). 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 and in the separate ICF for optional research samples.

7.3. Lost to Follow-up

To reduce the chances of a participant being deemed lost to follow-up, prior to randomization, attempts should be made to obtain contact information from each participant (e.g., home, work, and mobile telephone numbers and email addresses for both the participant as well as appropriate family members).

A participant will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site. A participant cannot be deemed lost to follow-up until all reasonable efforts made by the study site personnel to contact the participant are deemed futile. The following actions must be taken if a participant fails to return to the study site for a required study visit:

- The study site personnel must attempt to contact the participant to reschedule the missed visit as soon as possible, to counsel the participant on the importance of maintaining the assigned visit schedule, and to ascertain whether the participant wishes to or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee must make every reasonable effort to regain contact with the participant (where possible, 3 telephone calls, e-mails, fax, and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical records.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study.

Should a study site close (e.g., for operational, financial, or other reasons) and the investigator cannot reach the participant to inform them, their contact information will be transferred to another study site.

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

The SoA summarizes the frequency and timing of efficacy, PK, immunogenicity, PD, biomarker, pharmacogenomic, and safety measurements applicable to this study.

All PRO assessments should be conducted/completed before any tests, procedures, or other consultations to prevent influencing participant responses. Refer to the PRO completion guidelines for instructions on the administration of PROs.

Urine and blood collections for PK and PD assessments should be kept as close to the specified timepoints as possible. Other measurements may be done earlier than specified timepoints if needed. Actual dates and times of assessments will be recorded in the source documentation and eCRF.

The total blood volume to be collected from each participant will be no more than approximately 200 mL. However, additional repeat or unscheduled samples may be taken for safety reasons or due to technical issues with the samples.

Home Health Care and Telehealth Visits

As needed, home health care and telehealth visits may be implemented by or with approval from the Sponsor and per the clinical judgement of the investigator where feasible and permissible by local policy.

Participants for whom there is no safety concern may have home health care and telehealth (conducted via telephone or video chat, email, letter, social media, or fax) visits.

Study procedures may be performed with home health care and telehealth visits. Protocol-specified laboratory assessments (Section 1.3) for efficacy and safety may be collected during home health care visits.

Telehealth visits (conducted via telephone or video chat, email, letter, social media, or fax) may be implemented by or with approval from the Sponsor and per clinical judgement of the investigator for certain circumstances when warranted where feasible and permissible by local policy, regulations (as applicable) and for participants for whom there is no safety concern.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded in the eCRF or laboratory requisition form. Refer to the SoA (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 that will be provided. Collection, handling, storage, and shipment of samples must be under the specified, and where applicable, controlled temperature conditions as indicated in the Laboratory Manual.

Study-Specific Materials

The investigator will be provided with the following supplies:

- Investigator Site File (includes protocol and IB for guselkumab)
- Study site IP and procedures manual
- Laboratory Manual and laboratory supplies
- PRO device and user manual

- Clinician-reported outcome device and user manual
- Photography equipment, accessories, site guide, and manual
- IWRS manual
- Sample ICF
- eCRF completion instructions
- Participant recruitment materials

8.1. Efficacy Assessments

The Sponsor will provide training on the specified efficacy measures in this study. Documentation of this training will be maintained in the site's training files. Previous efficacy training by the Sponsor within the last 3 years with documentation (e.g., training certification) will be considered adequate for this study; however, repeat training prior to start of the study is strongly encouraged.

Every effort should be made to ensure that the physician or designee who performed the efficacy evaluations for a participant at baseline should also perform the efficacy evaluations for the same participant at all subsequent visits through Week 48.

8.1.1. Body Surface Area (BSA) Affected by Psoriasis

The BSA is a measurement of involved skin over the whole body. The overall BSA affected by psoriasis is estimated based on the participant's handprint (defined as the entire palmar surface of the hand including fingers; Long 1992; Rossiter 1996; Thomas 2007). The surface area of the whole body is made up of approximately 100 "handprints" (as 1 "handprint" equates to approximately 1% of total BSA).

8.1.2. Investigator's Global Assessment (IGA) of Psoriasis

The IGA documents the investigator's assessment of the participants psoriasis at a given timepoint (Langley 2015; Appendix 10.9). Overall lesions are graded for induration, erythema, and scaling. The participant's psoriasis is assessed using a 5-point scale: cleared (0), minimal (1), mild (2), moderate (3), or severe (4).

8.1.3. Psoriasis Area and Severity Index

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy (Fredriksson 1978; Appendix 10.10). The PASI produces a numeric score that can range from 0 to 72. A PASI 75 response is defined as ≥75% improvement in PASI score from baseline; PASI 50, PASI 90, and PASI 100 are similarly defined.

8.1.4. Scalp-Specific Investigator's Global Assessment (ss-IGA)

The ss-IGA is used to evaluate the disease severity of scalp psoriasis (Foley 2018; Appendix 10.11). The lesions are assessed in terms of the clinical signs of redness, thickness, and scaliness, which are scored using a 5-point scale: absence of disease (0), very mild disease (1), mild disease (2), moderate disease (3), and severe disease (4).

8.1.5. Facial Psoriasis Investigator's Global Assessment (f-IGA)

The same IGA used for the full body assessment will be adapted for use (Appendix 10.16), but only the face will be scored. The 5-point scale and associated severity categories are clear (0), minimal (1), mild (2), moderate (3), and severe (4).

It should be noted that erythema, and to an extent, scaling, are the more prominent features of facial psoriasis and less often elevation. Therefore, scoring may be predominantly driven by the severity of erythema and scaling if these are the dominant presenting features.

8.1.6. Intertriginous Psoriasis Investigator's Global Assessment (i-IGA)

The IGA used for the full body assessment has been adapted with descriptions of disease features that are more consistent with intertriginous psoriasis presentation (Appendix 15). The intertriginous areas affected to be scored include the axillary, sub-mammary, abdominal fold, inguinal, and intergluteal cleft/peri-anal region (distinct from genital/perineum involvement). The 5-point scale and associated severity categories are clear (0), minimal (1), mild (2), moderate (3), and severe (4).

It should be noted that erythema may be the predominant feature and there may or may not be the presence of elevation or scaling. Therefore, scoring may be predominantly driven by the severity of erythema if it is the dominant presenting feature.

8.1.7. Static Physician Global Assessment of Genitalia (sPGA-G)

The sPGA-G is used to evaluate the disease severity of genital psoriasis (Merola 2017). Severity is determined by a combination of 3 plaque characteristics (erythema, elevation, and scale) based on the descriptions of each characteristic as described in Appendix 10.12. The 6-point scale and associated severity categories are clear (0), minimal (1), mild (2), moderate (3), severe (4), and very severe (5). While the overall score represents a combination of all 3 features, it should primarily be determined by the degree of erythema, as erythema is the dominant feature in the majority of cases of genital psoriasis. Elevation and scaling are considered secondary. The assessment of genital psoriasis severity does not require all 3 characteristics to be present.

8.1.8. Nail Psoriasis Severity Index (NAPSI)

The NAPSI is an index used for assessing and grading the severity of nail psoriasis (Rich and Scher, 2003; Appendix 10.13). Each of the participant's 10 nails is divided into quadrants and is graded for nail matrix psoriasis (pitting, leukonychia, red spots in the lunula, and nail plate crumbling) and nail bed psoriasis (onycholysis, splinter hemorrhages, oil drop discoloration, and nail bed hyperkeratosis). Each quadrant is evaluated for the presence of any of the nail matrix and nail bed features, respectively, with scores ranging from 0 (none of the quadrants) to 4 (all 4 quadrants) impacted. The total individual nail score is the sum of the nail matrix and nail bed score and ranges from 0 to 8. The sum of these scores across all 10 nails represents the total NAPSI score (ranging from 0 to 80 for full hand nails).

8.1.9. Palmoplantar Investigator's Global Assessment (pp-IGA)

The pp-IGA is used to evaluate disease severity of palmoplantar psoriasis (Appendix 10.14). The lesions are assessed in terms of the clinical signs of coloration, thickening, and scaling, which are scored using a 5-point scale: clear (0), almost clear/minimal (1), mild (2), moderate (3), and severe (4) (Gottlieb 2017).

8.1.10. Clinical Photographs

Photographs of study participants will be obtained at various timepoints as per SoA. Photographic services will be provided through a central photography laboratory selected by the Sponsor. Detailed instructions and procedures to assure photographic quality and consistency will be provided separately in a central photography laboratory instruction manual.

Photographs will be used to support clinical evaluation and continued monitoring throughout the course of the trial.

If a participant is unable to attend an in-person clinic visit due to COVID-19 or other unforeseen situations, an alternative means of acquiring photographs may be implemented by or with approval from the Sponsor and per the clinical judgement of the investigator where feasible and permissible by local policy. Missing photographs due to COVID-19 illness or quarantine will be recorded in the eCRF as due to COVID-19.

8.1.11. Patient-reported Outcomes

The PRO instrument will be provided in the local language in accordance with local guidelines.

The PRO instrument will be available for regulators and for IRB/IEC submissions and will be provided separately in a companion manual with the instruments that will be submitted with the protocol.

The PRO and AE data will not be reconciled with one another.

8.1.11.1. Psoriasis Symptom and Sign Diary (PSSD)

The PSSD includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefits. The PSSD is self-administered and includes 11 items covering symptoms (itch, pain, stinging, burning, and skin tightness) and patient-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, and bleeding) using 0 to 10 numerical rating scales for severity. Two subscores will be derived: the psoriasis symptom score and the psoriasis sign score. A higher score indicates more severe disease. Participants will complete the 7-day recall version of the PSSD (see Appendix 10.17) at study visits as indicated in the SoA.

8.1.11.2. Dermatology Life Quality Index (DLQI)

The DLQI is a dermatology-specific QoL instrument designed to assess the impact of dermatologic disease on a participant's QoL (Finlay and Khan, 1994). It is a 10-item PRO questionnaire that, in addition to evaluating overall QoL, can be used to assess 6 different aspects that may affect QoL symptoms: 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 (see Appendix 10.18).

8.1.11.3. Psoriasis Epidemiology Screening Tool (PEST)

The PEST is a validated screening tool for PsA (Ibrahim 2009). It is a 5-item questionnaire developed to help identify PsA at an early stage (see Appendix 10.19). In this study, the PEST will be administered at screening to those who do not report a prior history of confirmed PsA. Those with scores ≥3 on the screening PEST may have undiagnosed PsA and will proceed with PsAID-12 at baseline (Week 0) and at all subsequent visits. Those who score <3 on PEST at screening will continue to receive PEST throughout the study.

8.1.11.4. Psoriatic Arthritis Impact of Disease Score (PsAID-12)

The PsAID-12 is made up of 0 to 10 numeric rating scale questions, with a final result included between 0 (no difficulty) to 10 (extreme difficulty). The 12 domains examine different perspectives, both physical and psychological, which are considered important in patients with PsA (see Appendix 10.20). Each domain has a different weight; pain, fatigue, and skin problems are those with a greater effect (Di Carlo, 2017). The PsAID-12 will be administered to all participants with known prior confirmed diagnosis of PsA as well as those who screen positive with a score ≥3 on PEST at the screening visit.

8.1.11.5. Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29)

The PROMIS-29 profile instrument is intended for adults (ages 18+). It is a collection of short forms containing 4 items for each of the 7 PROMIS domains (Depression, Anxiety, Physical Function, Pain Interference, Fatigue, Sleep Disturbance, and Ability to Participate in Social Roles and Activities; see Appendix 10.21). PROMIS-29 also includes an additional pain intensity 0 to 10 numeric rating scale. The PROMIS-29 profile is universal rather than disease specific. They assess all domains over the past 7 days except for Physical Function, which has no timeframe specified. The raw score of each domain is converted into a standardized score with a mean of 50 and a standard deviation (SD) of 10 (T-Score). The standardized T-score is reported as the final score for each participant. Pain Intensity is presented as raw responses (0 to 10). For PROMIS domains of Depression, Anxiety, Physical Function, Pain Interference, and Fatigue, a score of 50 is the average for the US general population with an SD of 10, because testing was performed on a large sample of the general population. However, the other 2 domains (Ability to Participate in Social Roles and Activities and Sleep Disturbance) were not centered in a national sample. For these 2 domains, a score of 50 represents the average of the calibration sample, which was generally more enriched for chronic illness, and a score of 50 likely represents somewhat sicker people than the general population. A higher PROMIS T-score represents more of the concept being measured. For negatively-worded concepts like Anxiety, a T-score of 60 is 1 SD worse than average. By comparison, an Anxiety T-score of 40 is 1 SD better than average. However, for positively-worded concepts like Physical Function, a T-score of 60 is better than average while a T-score of 40 is better.

8.2. Safety Assessments

Adverse events will be reported and followed by the investigator as specified in Section 8.3 and Appendix 5.

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 timepoints provided in the SoA (Section 1.3).

8.2.1. Physical Examinations

Complete physical examinations will include vital signs, weight, an examination of all major organ systems with an emphasis on assessing for active signs and symptoms of infection, and skin examinations for non-melanoma skin cancers. Complete physical examinations will be performed by the investigator or designated physician as specified in the SoA (Section 1.3). Any abnormalities or changes in severity noted during the review of body systems should be documented in the source document.

8.2.2. Vital Signs

Vital signs will be measured after the participant has been in a supine or semi-supine position for at least 5 minutes and will include blood pressure, pulse rate, respiratory rate, and temperature.

Pulse/heart rate and blood pressure will be assessed at each visit. Blood pressure and pulse/heart rate measurements will be assessed with a completely automated device. Manual techniques will be used only if an automated device is not available. If feasible, blood pressure and pulse/heart rate measurements should be preceded by at least 5 minutes of rest in a quiet setting without distractions (e.g., television or cell phones).

Weight will be measured per institutional standard of care. Participants should wear light clothing and remove shoes before weight is measured.

If any clinically significant changes in vital signs are noted, they must be reported as AEs and followed to resolution or until they reach a clinically stable condition.

8.2.3. Electrocardiograms

A 12-lead electrocardiogram (ECG) will be performed as specified in the SoA (Section 1.3).

During the collection of ECGs, participants should be in a quiet setting without distractions (e.g., television or cell phones). Participants should rest in a supine position for at least 5 minutes before ECG collection and should refrain from talking or moving arms or legs. If blood sampling or vital

sign measurement is scheduled for the same timepoint as the ECG recording, the procedures should be performed in the following order: ECG(s), vital signs, blood draw.

8.2.4. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology will be collected as noted in Appendix 2.

The investigator must review the laboratory result and document this review by signing and dating each report.

All clinical laboratory results that fall outside the reference range will be interpreted by the investigator as "abnormal, not clinically significant" or "abnormal, clinically significant." Laboratory results deemed "abnormal, clinically significant" will be recorded as AEs in the eCRF and should be fully investigated and repeated for verification. Clinically significant laboratory abnormalities requiring intervention should be discussed with the Medical Monitor. Additional tests and evaluations required to establish the significance or etiology of a clinically significant abnormal result or monitor the course of an AE should be obtained when clinically indicated. Whenever possible, the etiology of the clinically significant abnormal findings will be documented on the eCRF. The laboratory reports must be filed with the source documents.

Any significant laboratory abnormalities that are either serious or unexpected will be promptly reported to the Sponsor. Any additional relevant laboratory results obtained by the investigator during the course of this study will be reported to the Sponsor or designee.

8.2.5. Pregnancy Testing

Participants of childbearing potential must have a negative pregnancy test at screening and at baseline before randomization. Additionally, pregnancy testing is required for all participants of childbearing potential at every study intervention administration visit. Pregnancy tests must be completed, and the result must be negative before the administration of any intervention for that visit. All pregnancy test results must be recorded in study source documents.

8.2.6. Suicidal Ideation and Behavior Risk Monitoring (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 and will be conducted on the electronic clinical outcome assessment (eCOA) device provided to the site. Two versions of it will be used in this study: the "Baseline/Screening" version of the C-SSRS will be conducted during the screening visit and the "Since Last Visit" version of the C-SSRS will be completed at Week 0 and all other site visits through the end of the study. The investigator or trained study site personnel will interview the participant in a private place and complete the C-SSRS on the eCOA device. 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 (e.g., 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 (e.g., 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 to 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 is assessed; referral to a mental health professional.
  - Interruption or the discontinuation of study intervention should be considered for any participant who reports Suicidal Ideation with some intention to act, no plan ("Ideation level 4"), Suicidal Ideation with specific plan and intent ("Ideation level 5"), or suicidal behavior (e.g., 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 (Section 7.1).
- 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 as an AE.

8.2.7. Concomitant Medication Review

Concomitant therapies, including any vaccinations or vaccines authorized for emergency use, e.g., COVID 19 must be recorded throughout the study beginning with start of the first dose of study intervention to 12 weeks after the last dose of study intervention. Concomitant therapies must also be recorded beyond Week 56 only in conjunction with SAEs that meet the criteria outlined in Serious Adverse Events in Section 8.3.1.

8.2.8. Injection Site Reactions

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

8.2.9. Hypersensitivity Reactions

Before any administration of study intervention at the study site, appropriately trained personnel and medications (e.g., antihistamines or injectable epinephrine) must be available to treat hypersensitivity reactions, including anaphylaxis. All participants must be observed carefully for signs and symptoms of a hypersensitivity reaction (e.g., urticaria, pruritus, angioedema, wheezing, dyspnea, or hypotension).

8.2.10. Infections

Investigators are required to evaluate participants for any signs or symptoms of infection at scheduled visits. Study intervention administration should not be given to a participant with a clinically significant, active infection. If a participant develops a serious infection, including but not limited to sepsis or pneumonia, discontinuation of study intervention must be strongly considered (Section 7.1). Any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete.

8.2.11. Tuberculosis Evaluations

Initial Tuberculosis Evaluation

Participant 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 imaging results and responses to tuberculin skin or other TB testing. Investigators have the option to use the tuberculin skin test in addition to IGRA testing to screen for latent TB if preferred by local health authorities, or if they believe based on their judgment that both tests are clinically indicated to evaluate a participant at high risk for latent TB. Tuberculosis testing is not required at screening for participants with a history of treated latent TB.

Participants with a negative IGRA test result are eligible to continue with pre-randomization procedures. Participants with a newly identified positive IGRA test result must undergo an evaluation for active or latent TB or suspected false-positive initial testing and initiate appropriate treatment if needed. Appropriate treatment for latent TB is defined according to local country

guidelines for immunocompromised participants. If no local country guidelines for immunocompromised participants exist, US guidelines must be followed.

Participants with indeterminate/borderline IGRA test results should have the test repeated. Participants with persistently indeterminate/borderline IGRA test results may be randomized or continued in the trial without treatment for latent TB if active TB is ruled out, chest imaging shows no abnormality suggestive of TB (active or inactive), and the participant has no additional risk factors for TB as determined by the investigator. This determination must be promptly reported to the Sponsor's medical monitor and recorded in the participant's source documents and initialed by the investigator.

Ongoing Tuberculosis Evaluation

To aid in the early detection of TB infection or exposure during study participation, participants must be evaluated for TB signs, symptoms, and close contacts at scheduled visits (refer to Section 1.3) or by telephone approximately every 4 to 12 weeks. 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 for TB infection or the participant has had a close contact exposure to TB, study intervention must be withheld and an immediate and thorough investigation must be undertaken, including consultation with a physician specializing in TB to determine if treatment is warranted prior to any further study intervention. Participants should be encouraged to return for all subsequent scheduled study visits according to the protocol.

Note: Investigators should be aware that TB reactivation in immunocompromised participants may also present as extrapulmonary or disseminated disease.

8.3. Adverse Events, Serious Adverse Events, and Other Safety Reporting

Timely, accurate, and complete reporting and analysis of safety information, including AEs, SAEs, and PQCs 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.

Further details on AEs, SAEs, and PQCs can be found in Appendix 5.

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.

For the purposes of this Protocol, an AE is defined as the appearance of or worsening of any pre-existing undesirable sign, symptom, or medical condition that occurs after a participant provides informed consent. Abnormal laboratory values or test results occurring after informed consent constitute AEs only if they induce clinical signs or symptoms, are considered clinically meaningful, require therapy, or require changes in the study drug. Laboratory abnormalities that meet the criteria for AEs should be followed until they have returned to normal, or an adequate explanation of the abnormality is found. Adverse events (including laboratory abnormalities that constitute AEs) should be described using a diagnosis whenever possible rather than by individual underlying signs and symptoms (e.g., "anemia" instead of "low hemoglobin"). When a clear diagnosis cannot be identified, each sign or symptom should be reported as a separate AE.

All AEs with an onset date after the signing of the ICF and up to 30 days after study treatment discontinuation (up to the end of study for participants who enter a continued access program on the same day as the end of study visit) must be recorded on specific AE pages of the eCRF. Conditions that were already present at the time of informed consent should be recorded on the Medical History form in the eCRF.

All AEs should be treated appropriately. Concomitant medication or nondrug therapy used to treat an AE should be recorded in the eCRF. Once an AE is detected, it should be followed until it has resolved or until it is judged to be permanent; assessment should be made at each visit (or more frequently if necessary) of any changes in severity, the suspected relationship to the study drug, the interventions required to treat it, and the outcome.

Serious Adverse Events

All SAEs, as well as PQCs, 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.

A possible Hy's Law case is defined by the occurrence of ALT/AST ≥3 x ULN together with total bilirubin (Tbili) ≥2 x ULN or international normalized ratio (INR) >1.5 (if measured). Any possible Hy's Law case is considered an important medical event and must be reported to the Sponsor in an expedited manner, even before all other possible causes of liver injury have been excluded.

Information regarding SAEs will be transmitted to the Sponsor using the Serious Adverse Event Form, which must be completed and signed by a physician from the study site and transmitted to the Sponsor within 24 hours. The initial and follow-up reports of an SAE should be sent by secure transmission via encrypted email or fax. Telephone reporting **should be the exception** and the reporter should be asked to complete the appropriate form(s) first.

8.3.2. Method of Detecting Adverse Events and Serious Adverse Events

Care will be taken not to introduce bias when detecting AEs or SAEs. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrence.

Solicited Adverse Events

Solicited AEs are predefined local reactions at the injection site and systemic events for which the participant is specifically questioned. (see Section 8, Study Assessments and Procedures).

Unsolicited Adverse Events

Unsolicited AEs are all AEs for which the participant is not specifically questionedFollow-up of Adverse Events and Serious Adverse Events

The investigator is obligated to perform or arrange for the conduct of supplemental measurements and evaluations as medically indicated to elucidate the nature and causality of the AE, SAE, or PQC as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultations with other health care professionals.

Adverse events and the special reporting situation of pregnancy will be followed by the investigator as specified in Section 8.3.5.

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 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.

An anticipated event is an AE that commonly occurs in the study population independent of exposure to the drug under investigation. For the purposes of this study, the following SAE will be considered an anticipated event: Worsening of psoriasis.

These anticipated events will be periodically analyzed in aggregate by the Sponsor during study conduct. The Sponsor will prepare a safety report in narrative format if the aggregate analysis indicates that the anticipated event occurs more frequently in the intervention group than in the control group and the Sponsor concludes there is a reasonable possibility that the drug under investigation caused the anticipated event.

The plan for monitoring and analyzing the anticipated events is specified in a separate Anticipated Events Safety Monitoring Plan. The assessment of causality will be made by the Sponsor's unblinded safety assessment committee.

The Sponsor assumes responsibility for appropriate reporting of the listed anticipated events according to the requirements of the countries in which the studies are conducted.

8.3.4. Pregnancy

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 (e.g., spontaneous abortion, fetal death, stillbirth, congenital anomalies, or ectopic pregnancy) are considered SAEs and must be reported using an SAE reporting 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.

8.3.5. Adverse Events of Special Interest

Any newly identified malignancy or case of active TB occurring after the first administration of study intervention must be reported by the investigator according to the procedures in Appendix 10.5.5. 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. Pharmacokinetics

Serum samples will be used to evaluate the PK of guselkumab. Serum collected for PK 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.

8.4.1. Evaluations

Venous blood samples will be collected for the measurement of serum concentrations of guselkumab and antibodies to guselkumab at the timepoints shown in the SoA (Section 1.3). Serum samples will also be collected at the final visit from participants who discontinue study intervention or were withdrawn from the study. At visits where PK and immunogenicity will be evaluated, 1 blood draw of sufficient volume can be used. Each sample will be split into 3 aliquots (1 aliquot for serum guselkumab concentration, 1 aliquot for antibodies to study intervention, and 1 aliquot as a back-up). Samples must be collected before study intervention administration at visits when a study intervention administration is scheduled. The exact dates and times of blood sample collection must be recorded in the laboratory requisition form.

Additional information about the collection, handling, and shipment of biological samples can be found in the Laboratory Manual.

8.4.2. 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.

8.5. Immunogenicity Assessments

Serum samples for the detection of antibodies to guselkumab will be collected from all participants according to the SoA. Additionally, serum samples should also be collected at the final visit from participants who discontinued study intervention or were withdrawn from the study. 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.

Serum samples will be used to evaluate the immunogenicity of guselkumab. Serum samples will be screened for antibodies binding to guselkumab and the titer of confirmed positive samples will be reported. Serum samples that test positive for antibodies to guselkumab will be further characterized to determine if antibodies to guselkumab could neutralize the biological effects of guselkumab in vitro (i.e., neutralizing antibodies [NAbs] to guselkumab). Other analyses may be performed to verify the stability of antibodies to guselkumab and/or further characterize the immunogenicity of guselkumab.

Analytical Procedures

The detection and characterization of antibodies to guselkumab will be performed using a validated, specific, and sensitive immunoassay method by the Sponsor's bioanalytical facility or under the supervision of the Sponsor.

8.6. Pharmacogenomics

A pharmacogenomic blood sample will be collected from participants who consent separately to this component of the study to allow for pharmacogenomic research, as necessary where local regulations permit. Participant participation in pharmacogenomic research is optional.

Genetic (DNA) variation may be an important contributory factor to interindividual variability in drug response and associated clinical outcomes. Genetic and epigenetic factors may also serve as markers for disease susceptibility and prognosis and may identify population subgroups that respond differently to an intervention.

The optional pharmacogenomic samples may be analyzed for identification of genetic factors that may be associated with psoriasis and/or the response to treatment. This research may consist of the analysis of 1 or more candidate genes, of genetic markers throughout the genome, or of the entire genome (as appropriate) in relation to psoriasis and to treatment.

8.7. Biomarkers

Biomarker samples will be collected to examine the biologic response associated with treatment and to identify biomarkers that are relevant to psoriasis. Serum will be collected from all participants; skin biopsies and tape strips will also be collected in participants who consent to this optional part of the study. Biomarker sample collections will be conducted at the timepoints indicated in the SoA.

Data collected from these samples will be used for exploratory research that will include the following objectives:

- To understand the molecular/cellular PD effects of guselkumab in psoriasis patients
- To understand psoriasis disease pathogenesis
- To understand why an individual may respond differently to guselkumab

8.7.1. Skin Biomarkers

Punch biopsies and tape strips will be collected from participants that consent to this optional part of the study at the timepoints specified in the SoA. At baseline, skin sampling will be collected from both lesional and adjacent non-lesional areas; at subsequent weeks, only lesional areas will be sampled. Tape stripping allows for the measurement of gene expression as well as proteins or lipid biomarkers in the stratum corneum. Skin biopsy samples will be used to investigate differential gene expression during treatment compared with baseline to explore PD, mechanism of action, and differences in treatment response between individuals. In addition, skin biopsies may be analyzed for histological readouts and immunohistochemistry to explore the effects of study intervention on cellular composition in skin. Instructions for the collection and shipment of these samples can be found in the Laboratory Manual.

8.7.2. Serum Biomarkers

Serum biomarker analysis will include, but will not be limited to inflammatory mediators associated with the IL-23/Th17 axis (IL-17A, IL-17F, and IL-22) in psoriasis. Level of various anti-microbial peptides and cardiovascular disease-associated markers may also be measured.

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 that the study is terminated early or shows poor clinical efficacy, the completion of biomarker assessments is based on the justification and intended utility of the data.

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 is superior to placebo for the proportion of participants achieving an IGA score of cleared (0) or minimal (1) from baseline at Week 16.

9.2. Sample Size Determination

A sample size of approximately 300 participants (200 participants on guselkumab and 100 participants on placebo) will allow at least 90% power to detect treatment effect differences of 45% between guselkumab (60%) and placebo (15%) for the primary endpoint with a 2-sided alpha level of 0.05 (Table 1).

Table 1: Power for Primary Endpoint

Primary Endpoint	Placebo (N = 100)	Guselkumab (N = 200)	Delta	Power
Proportion of participants who achieve an IGA score of 0 or 1 from baseline at Week 16	15%	55% **60%**	40% **45%**	>99% **>99%**

IGA = Investigator's Global Assessment

The sample size is also chosen to ensure an adequate number of participants with low BSA moderate plaque psoriasis with each special site (scalp, genital, intertriginous, and face) involvement. The study will target to enroll approximately 25% of participants (i.e., 50 participants on guselkumab and 25 participants on placebo) for each special site. Fifty participants on guselkumab and 25 participants on placebo can achieve 90% power to detect a difference between the group proportions of 35% to 38% (Table 2). The test statistic used is the 2-sided CMH chi square test. The significance level of the test is 0.05.

Table 2: Treatment Difference (Delta) Detection for Each Special Site Involvement

Endpoint for Each Special Site	Placebo (n = 25)	Guselkumab (n = 50)	Delta
The proportion of participants who achieve a scalp-specific Investigator's Global Assessment (ss-IGA) score of absence of disease (0) or very mild disease (1) at Week 16 among randomized participants with an ss-IGA score ≥3 at baseline	15%	52%	37%
The proportion of participants who achieve a static Physician's Global Assessment of Genitalia (sPGA-G) of clear (0) or minimal (1) at Week 16 among randomized participants with an sPGA-G score ≥3 at baseline	10%	45%	35%

The proportion of participants who achieve a intertriginous IGA (i-IGA) score of clear (0) or minimal (1) at Week 16 among randomized participants with an i-IGA score ≥3 at baseline	10%	45%	35%
The proportion of participants who achieve a facial IGA (f-IGA) of clear (0) or minimal (1) at Week 16 among randomized participants with an f-IGA score ≥3 at baseline	25%	63%	38%

9.3. Populations for Analysis Sets

For purposes of analysis, the populations as defined in Table 3 will be used:

Table 3: Analysis populations

Population	Description
Enrolled	All participants who signed the ICF
Full Analysis Set (FAS)	All participants who were randomized in the study. This analysis set will be used for the efficacy analyses.
Scalp Special Site Analysis Set (SSSAS)	All participants who were randomized in the study within scalp special site involvement at baseline. This analysis set will be used for the efficacy analyses for the scalp special site.
Genital Special Site Analysis Set (GSSAS)	All participants who were randomized in the study within genital special site involvement at baseline. This analysis set will be used for the efficacy analyses for the genital special site.
Intertriginous Special Site Analysis Set (ISSAS)	All participants who were randomized in the study within intertriginous special site involvement at baseline. This analysis set will be used for the efficacy analyses for the intertriginous special site.
Facial Special Site Analysis Set (FSSAS)	All participants who were randomized in the study within facial special site involvement at baseline. This analysis set will be used for the efficacy analyses for the face special site.
Safety Analysis Set (SAS)	All participants who received at least 1 (complete or partial) administration of study intervention (i.e., the treated population).
Immunogenicity Analysis Set (IAS)	All participants who received at least 1 (complete or partial) administration of guselkumab and who had at least 1 sample obtained after their first administration of guselkumab
PK Analysis Set (PKAS)	All participants who received at least 1 complete administration of guselkumab and had at least 1 valid blood sample drawn for PK analysis
PD Analysis Set (PDAS)	All participants who received at least 1 (complete or partial) administration of study intervention

ICF = informed consent form; PD = pharmacodynamics; PK = pharmacokinetics

9.4. Statistical Analyses

The SAP will be finalized prior to the first DBL and unblinding and it will include a more technical and detailed description of the statistical analyses described in this section. This section is a summary of the planned statistical analyses of the most important endpoints, including the primary and key secondary endpoints.

9.4.1. General Considerations

Descriptive statistics (e.g., mean, median, SD, interquartile range, minimum, and maximum) will be used to summarize continuous variables. Counts and percentages will be used to summarize categorical variables. Graphical data displays (e.g., line plots) may also be used to summarize data.

Analyses suitable for categorical data (e.g., chi-square tests, Cochran-Mantel-Haenszel [CMH] chi-square tests, or logistic regression, as appropriate) will be used to compare the proportions of participants achieving selected endpoints (e.g., clinical response). In cases of rare events, the Fisher's exact test will be used for treatment comparisons. Continuous response parameters will be compared using an analysis of variance (ANOVA), analysis of covariance (ANCOVA), or a mixed model for repeated measures (MMRM), unless otherwise specified. If the normality assumption is in question, an ANOVA or ANCOVA on the van der Waerden normal scores will be used. Survival analysis techniques will be used for endpoints defined by time to an event.

The overall Type I error rate will be controlled at the significance level of 0.05 (2-sided). Hierarchical testing will be performed for primary and major secondary endpoints. That is, the

first major secondary endpoint will be tested only if the primary endpoint is positive, and the subsequent endpoint(s) will be tested only if the preceding endpoint in the hierarchy is positive. The final ordering of major secondary endpoints will be specified in the final SAP. Ordering as well as the data-handling rules for the primary and major secondary endpoints will be described in the SAP. No multiplicity control will be made for other endpoints, and nominal p-values will be reported.

9.4.2. Primary Endpoint

The primary endpoint is the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) at Week 16. The primary endpoint will be analyzed based on the estimands defined by the following 5 components:

Population: Participants with low BSA moderate plaque psoriasis with special site involvement defined as overall IGA 3 [moderate] and BSA 2-15% with at least 1 plaque outside special sites, with involvement of at least one special site (scalp, face, intertriginous, or genital) with moderate disease.

Treatment:

- Placebo
- Guselkumab

Variable (endpoints): The proportion of participants who achieve an IGA score of cleared (0) or minimal (1) at Week 16. Participants who have intercurrent events (ICEs) 1 or 2 (defined below) prior to Week 16 will be considered as non-responders for IGA score of cleared (0) or minimal (1) at Week 16, regardless of the observed data.

Intercurrent events (ICEs) and corresponding strategies:

The following are the ICEs considered for this trial:

1. Initiated protocol prohibited medications/therapies for psoriasis
2. Discontinued study intervention due to efficacy (e.g., lack of efficacy or an AE of worsening of psoriasis)
3. Treatment discontinuation due to reasons other than ICE 2.

ICEs in categories 1 and 2 will be handled with the composite strategy. The composite strategy assesses the treatment effects not only based on the variable measurements, but also based on ICEs. Under the composite strategy, participants with the ICE prior to Week 16 will be treated as non-responders for the IGA score of cleared (0) or minimal (1), regardless of the observed data.

ICE 3 will be handled with a treatment policy. The observed value will be used if available.

For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in category 3.

Population level summary: The difference in proportion of participants who achieve an IGA score of cleared (0) or minimal (1) between guselkumab and placebo at Week 16.

The analysis of the primary endpoint will be based on the Full Analysis Set. Participants will be analyzed according to the intervention group to which they were randomized regardless of the study intervention they actually received.

Participants with missing data, defined as those who terminated the study prior to the Week 16 visit or participants who have a missing value at the Week 16 visit, will be considered to not have achieved their primary efficacy endpoints.

To compare the guselkumab versus placebo group for the primary endpoint, a 2-sided CMH chi-square test stratified by special site will be used. The study will be considered successful if the test of the primary endpoint is positive at the 0.05 significance level.

Additional sensitivity/supplemental analyses which vary how ICEs (e.g., alternative estimand) are handled and how observed data are used will be specified in the SAP to further address the robustness of treatment effect of an IGA score of cleared (0) or minimal (1) with at least 2-grade improvement from baseline at Week 16.

9.4.3. Secondary Endpoints

Major secondary endpoints are provided in Section 3.

The ordering of endpoints, methods of analysis, and the approach to control the Type 1 error for multiplicity, as well as the data-handling rules for the major secondary endpoints will be specified in the SAP.

In addition to the primary and major secondary endpoints, all other secondary endpoints (Section 3) will be summarized over time by treatment groups. Treatment comparisons will be performed by visit through Week 48.

Descriptive statistics without formal hypothesis testing will be used for all other endpoints.

9.4.4. Subgroup Analyses

Subgroup analyses will be performed to evaluate consistency of the primary endpoint and selected major secondary endpoints by baseline demographics (including weight, gender, race/ethnicity, etc.), baseline disease characteristics (including BSA, special sites involved, etc.), and prior medications (including participants who had an inadequate response to, were intolerant to, or had a contraindication to previous anti-psoriatic systemic therapies, etc.).

9.4.5. Safety Analyses

All safety analyses will be made on the Safety Analysis Set.

Adverse Events

The verbatim terms used in the eCRF by investigators to identify AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). For each AE, the percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

The following analyses of AEs will be used to assess the safety of participants:

- The incidence and type of AEs
- The incidence and type of SAEs
- The incidence of AEs leading to study intervention discontinuation
- The incidence and type of injection site reactions

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 AE or an SAE.

Clinical Laboratory Tests

Laboratory data will be summarized by type of laboratory test. Descriptive statistics will be calculated for selected laboratory analytes at baseline and for observed values and changes from baseline at each scheduled timepoint. The number and percentage of participants by maximum National Cancer Institute–Common Terminology Criteria for Adverse Events (NCI-CTCAE) toxicity grades for laboratory analytes with NCI-CTCAE criteria defined will also be summarized, and participants with maximum NCI-CTCAE Grade ≥3 will also be presented in a listing.

Vital Signs

Vital signs including blood pressure, pulse rate, respiratory rate, and temperature will be summarized over time using descriptive statistics and/or graphically. The percentage of participants with values beyond clinically important limits will be summarized.

Physical Examinations

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

9.4.6. Other Analyses

9.4.6.1. Pharmacokinetic and Immunogenicity Analyses

Pharmacokinetic Analyses

The PK evaluable population (PK analysis set) is defined as all the participants who received at least 1 complete dose of guselkumab and had at least 1 valid blood sample drawn for PK analysis after their first dose of guselkumab.

Serum guselkumab concentrations over time will be summarized for each treatment group using descriptive statistics. All concentrations below the limit of quantitation (BQL) of the assay or missing data will be labeled as such in the concentration data listing or statistical analysis system dataset. The BQL concentrations will be treated as zero in the summary statistics.

Population PK modeling will be conducted when appropriate. The apparent total systemic clearance and apparent volume of distribution values will be estimated. The influence of important variables (such as body weight, antibodies to guselkumab, and concomitant medications) on the population PK parameter estimates may be evaluated. Details will be given in a population PK analysis plan and the results of the population PK analysis will be presented in a separate technical report.

Immunogenicity Analyses

The incidence and titers of antibodies to guselkumab will be summarized for all participants who receive at least 1 dose of guselkumab and have appropriate samples for detection of antibodies to guselkumab (i.e., 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 incidence of NAbs to guselkumab will be summarized for participants who are positive for antibodies to guselkumab and have samples evaluable for NAbs to guselkumab. Other immunogenicity analyses may be performed to further characterize the immune responses that are generated.

9.4.6.2. Biomarkers Analyses

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.

Any biomarker samples received by the contract vendor or Sponsor after the cutoff date will not be analyzed, and therefore, will be excluded from the biomarker analysis.

Changes in serum proteins and skin RNA/proteins/cellular composition over time will be summarized by treatment group. Associations between baseline levels and changes from baseline in select biomarkers and clinical response will be explored. Biomarker results will be reported in a separate report.

9.4.6.3. Pharmacogenomic Analyses

DNA samples will be analyzed if it is hypothesized that this may help resolve issues with the clinical data.

DNA samples will be used for research related to guselkumab or psoriasis. They may also be used to develop tests/assays related to guselkumab and psoriasis. Pharmacogenomic research may consist of the analysis of one or more candidate genes or of the analysis of genetic markers throughout the genome (as appropriate) in relation to guselkumab or psoriasis clinical endpoints.

Results will be presented in a separate report.

9.5. Interim Analysis

Not applicable.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Abbreviations

Abbreviation	Definition
β-hCG	β-human chorionic gonadotropin
AAD	American Academy of Dermatology
AE	adverse event
AIH	autoimmune hepatitis
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
ANOVA	analysis of variance
anti-HBc	hepatitis B core antibody
anti-HBs	hepatitis B surface antibody
AST	aspartate aminotransferase
BCG	Bacillus Calmette–Guérin
BQL	below the limit of quantitation
BSA	body surface area
BUN	blood urea nitrogen
CD	Crohn's disease
CMH	Cochran-Mantel-Haenszel
COVID-19	coronavirus disease 2019
CPK	creatine phosphokinase
CRF	case report form
CRO	Contract Research Organization
C-SSRS	Columbia-Suicide Severity Rating Scale
DBL	database lock
DILI	drug-induced liver injury
DLQI	Dermatology Life Quality Index
DNA	deoxyribonucleic acid
ECG	electrocardiogram
eCOA	electronic clinical outcome assessment
eCRF	electronic case report form
eDC	electronic data capture
EU	European Union
FDA	Food and Drug Administration
f-IGA	facial Investigator's Global Assessment
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
GGT	gamma-glutamyltransferase
GLDH	glutamate dehydrogenase
HbA1c	hemoglobin A1c
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
HRT	hormonal replacement therapy
Hs-CRP	high-sensitivity C-reactive protein
IB	Investigator's Brochure
ICE	intercurrent event
ICF	informed consent form
ICH	International Council on Harmonisation

ICMJE	International Committee of Medical Journal Editors
IEC	Independent Ethics Committee
IGA	Investigator's Global Assessment
IgG1	immunoglobulin G1
IgM	immunoglobulin M
IGRA	interferon gamma release assay
i-IGA	intertriginous Investigator's Global Assessment
IL	interleukin
IM	Intramuscular
INR	international normalized ratio
IP	investigational product
IPC	International Psoriasis Council
IRB	Institutional Review Board
IUD	intrauterine device
IUS	intrauterine hormone-releasing system
IV	intravenous(ly)
IWRS	interactive web response system
LAM	lactational amenorrhea method
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
mAb	monoclonal antibody
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed model for repeated measures
MTX	Methotrexate
NAbs	neutralizing antibodies
NAPSI	Nail Psoriasis Severity Index
NCI-CTCAE	National Cancer Institute - Common Terminology Criteria for Adverse Events
OTC	over-the-counter
PASI	Psoriasis Area and Severity Index
PCC	protocol clarification communication
PD	pharmacodynamic(s)
PEST	Psoriasis Epidemiology Screening Tool
PFS	prefilled syringe
PFS-U	PFS assembled with the UltraSafe PLUS™ Passive Needle Guard
PK	pharmacokinetic(s)
pp-IGA	palmoplantar Investigator's Global Assessment
PQC	product quality complaint
PRO	patient-reported outcome (paper or electronic as appropriate for this study)
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
PsA	psoriatic arthritis
PsAID-12	Psoriatic Arthritis Impact of Disease Score
PSSD	Psoriasis Symptom and Sign Diary
CCI	CCI
CCI	CCI
CCI	CCI
QoL	quality of life
RBC	red blood cell
SAE	serious adverse event
SAP	Statistical Analysis Plan
C	CCI
SD	standard deviation
sPGA-G	static Physician's Global Assessment of Genitalia
SoA	Schedule of Activities
ss-IGA	scalp-specific Investigator's Global Assessment

SUSAR	suspected unexpected serious adverse reaction
TB	tuberculosis
Tbili	total bilirubin
TNF	tumor necrosis factor
ULN	upper limit of normal
US	United States
UV	ultraviolet
WBC	white blood cell

10.2. Appendix 2: Clinical Laboratory Tests

The tests listed below will be performed according to the SoA by the central laboratory.

The actual date of assessment and, if required, the actual time of the assessment of laboratory samples will be recorded in the source documentation and in the eCRF or laboratory requisition form.

Protocol-Required Safety Laboratory Assessments

<table>
<tr><th>Laboratory Assessments</th><th colspan="3">Parameters</th></tr>
<tr><td rowspan="2">Hematology</td><td>Platelet count
Red blood cell count
Hemoglobin
Hematocrit</td><td><u>Red blood cell (RBC) indices:</u>
MCV
MCH
% reticulocytes</td><td><u>White blood cell (WBC) count with differential:</u>
Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils</td></tr>
<tr><td colspan="3">Note: A WBC evaluation may include any abnormal cells, which will then be reported by the laboratory. An RBC evaluation may include abnormalities in the RBC count, RBC parameters, or RBC morphology, which will then be reported by the laboratory. In addition, any other abnormal cells in a blood smear will also be reported.</td></tr>
<tr><td rowspan="2">Chemistry</td><td colspan="2">Sodium
Potassium
Calcium
Chloride
Bicarbonate
Blood urea nitrogen (BUN)
Creatinine
Glucose (non-fasting, acceptable)
Aspartate aminotransferase (AST)
Alanine aminotransferase (ALT)
Gamma-glutamyltransferase (GGT)</td><td>Total bilirubin
Alkaline phosphatase
Creatine phosphokinase (CPK)
Albumin
Total protein</td></tr>
<tr><td colspan="3">Note: Details of liver chemistry stopping criteria and required actions and follow-up are given in Appendix 7: Liver Safety.

Potential Hy's Law case (ALT or AST ≥3 x ULN and Tbili ≥2 x ULN or INR >1.5) reporting requirements are defined in Section 8.3.1.</td></tr>
<tr><td>Other</td><td colspan="3">• Lipid panel (fasting required): Total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides
• Pregnancy testing (serum, urine) for women of childbearing potential only
• High-sensitivity C-reactive protein (hsCRP)
• Serology (HIV antibody, hepatitis C virus antibody, and hepatitis B panel, which includes hepatitis B surface antigen [HBsAg], hepatitis B surface antibody [anti-HBs], and hepatitis B core antibody [anti-HBc total])</td></tr>
</table>

	• Interferon gamma release assay testing, which includes either QuantiFERON-TB® test or T-SPOT.TB® (for tuberculosis) • Follicle-stimulating hormone (screening only; to confirm potential post-menopausal status) • Hemoglobin A1c (HbA1c) • Hepatitis B DNA (screening only; for those whose hepatitis B serology results with HBsAg negative, anti-HBs negative and anti-Hbc total positive) • Hepatitis C RNA (screening only; for those who are hepatitis C antibody-positive or with history of Hepatitis C treatment) • Human immunodeficiency virus RNA (screening only; for those whose HIV screen is positive)

10.3. Appendix 3: Hepatitis B Virus (HBV) Screening with HBV DNA Testing

Participants must undergo screening for hepatitis B virus (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 (i.e., 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).
    - 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 that 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 the table below. For participants who are eligible with surface antigen (HBsAg-), core antibody (anti-HBc+) and/or surface antibody (anti-HBs+), and HBV DNA test negative, HBV DNA quantitation should be monitored according to local guidelines.

Eligibility Based on Hepatitis B Virus (HBV) Test Results			
Hepatitis B Test Result			**STATUS**
Hepatitis B Surface Antigen (HBs-Ag)	**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	(+)	Requires 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 this 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 HBV infection is recommended.

10.4. Appendix 4: Regulatory, Ethical, and Study Oversight Considerations

10.4.1. Regulatory and Ethical Considerations

Investigator Responsibilities

The investigator is responsible for ensuring that the study is performed in accordance with the protocol, current International Council 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 Clarification Communications

If text within a final approved protocol requires clarification (e.g., the current wording is unclear or ambiguous) that does not change any aspect of the current study conduct, a protocol clarification communication (PCC) may be prepared. The PCC document will be communicated to the investigational site, site monitors, local trial managers, clinical trial managers, and/or contract research organizations (CROs) who will ensure that the PCC explanations are followed by the investigators.

The PCC document may be shared by the sites with Independent Ethics Committees/Institutional Review Boards (IECs/IRBs) per local regulations.

The PCC documents must NOT be used in place of protocol amendments, but the content of the PCC document must be included in any future protocol amendments.

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 the 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.

In situations where a departure from the protocol is unavoidable during the study, 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 must 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 (e.g., Form FDA 1572), if applicable
- Documentation of investigator qualifications (e.g., 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 (e.g., 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 (e.g., 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 the 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).

Other Ethical Considerations

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

10.4.2. Financial Disclosure

Investigators and sub-investigators will provide the Sponsor with sufficient and 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 study and for 1 year after the completion of the study.

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

10.4.3. Informed Consent Process

Each participant (or a legally acceptable representative) must give consent according to local requirements after the nature of the study has been fully explained. The ICF(s) must be signed before the performance of any study-related activity. The ICF(s) that is/are used must be approved by both the Sponsor and the reviewing IEC/IRB and be in a language that the participant can read and understand. The informed consent must 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 or their legally acceptable representatives the aims, methods, reasonably anticipated benefits, and potential hazards of the study and any discomfort that 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 that the participant will receive for the treatment of his or her disease. 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 or legally acceptable representative is authorizing such access. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations and subsequent disease-related treatments, if needed.

The participant or legally acceptable representative 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 must be appropriately recorded by means of the participant's or his or her legally acceptable representative's personally dated signature. After having obtained the consent, a copy of the ICF must be given to the participant.

Participants who are rescreened are required to sign a new ICF.

Participants will be asked for consent to provide optional samples for research (where local regulations permit). After informed consent for the study is appropriately obtained, the participant or his or her legally acceptable representative will be asked to sign and personally date a separate ICF indicating agreement to participate in the optional research component. Refusal to participate in the optional research will not result in ineligibility for the study. A copy of this signed ICF will be given to the participant.

Where local regulations require, a separate ICF may be used for the required DNA component of the study.

10.4.4. 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 information, where required per applicable regulations, about 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. The informed consent also provides information to address the lawful 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 or make requests concerning his or her personal data in accordance with applicable data protection law. 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.

In the event of a data security breach, the Sponsor will apply measures to adequately manage and mitigate possible adverse effects taking into consideration the nature of the data security breach as necessary to address other obligations such as notifying appropriate authorities in accordance with applicable data protection law.

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.

10.4.5. 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 psoriasis, to understand differential intervention responders, and to develop tests/assays related to guselkumab and psoriasis. The research may begin at any time during the study or the post-study storage period.

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).

10.4.6. Publication Policy/Dissemination of Clinical Study Data

All information including but not limited to information regarding guselkumab or the Sponsor's operations (e.g., patent application, formulas, manufacturing processes, basic scientific data, prior clinical data, and formulation information) supplied by the Sponsor to the investigator and not

previously published and any data including pharmacogenomic or 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, use this information only to accomplish this study, and 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 pharmacogenomic or 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 substudy 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; 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 interim results of clinical studies as required by law. The disclosure of the study results will be performed after the end of study in order to ensure the statistical analyses are relevant.

10.4.7. 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 database. Written instructions will be provided for collection, handling, storage, and shipment of samples.

Guidelines for eCRF completion will be provided and reviewed with study site personnel before the start of the study.

The Sponsor may 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.

10.4.8. 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 electronic 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 must be available for review at the next scheduled monitoring visit.

All participative measurements (e.g., pain scale information or other questionnaires) will be completed by the same individual who made the initial baseline determinations whenever possible.

If necessary, queries will be generated in the electronic data capture (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).
- The Sponsor or Sponsor delegate can generate a query for resolution by the investigator and study site personnel.

10.4.9. 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 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 must be identifiable. Given that PROs are reports of a patient's health condition that come directly from the patient, without interpretation by a clinician or anyone else, the responses to PRO measures entered by study participants into source records cannot be overridden by site staff or investigators.

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 other equivalent document).

The following data will be recorded directly into the eCRF and will be considered source data:

- Race/ethnicity
- History of smoking (e.g., cigarettes [including e-cigarettes or the equivalent of e-cigarettes])
- Blood pressure and pulse/heart rate
- Height and weight
- Details of physical examination

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
- 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 (e.g., physical examination or laboratory assessment) and documented in the source documents.

An eSource system may be utilized, which contains data traditionally maintained in a hospital or clinic record to document medical care (e.g., 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.

10.4.10. Monitoring

The Sponsor will perform on-site monitoring visits as frequently as necessary. The monitor will record dates of the visits in a study site visit log that will be kept at the study site. The first post-initiation visit will be made as soon as possible after enrollment has begun. At these visits, the monitor may compare the data entered into the eCRF with the source documents (e.g., 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 can 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.

Central monitoring will take place for data identified by the Sponsor as requiring central review.

10.4.11. 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 must immediately notify the Sponsor if he or she has been contacted by a regulatory agency concerning an upcoming inspection.

10.4.12. 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 investigational product. 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.

10.4.13. Study and Site Start and Closure

First Act of Recruitment

The first participant screened is considered the first act of recruitment, and it becomes the study start date.

Study/Site 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 the following:

- 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

10.5. Appendix 5: Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

10.5.1. Adverse Event Definitions and Classifications

Adverse Event

An AE is any untoward medical occurrence in a clinical study participant administered a pharmaceutical (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. An AE 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)

For the purposes of this Protocol, an AE is defined as the appearance of or worsening of any pre-existing undesirable sign, symptom, or medical condition that occurs after a participant provides informed consent. Abnormal laboratory values or test results occurring after informed consent constitute AEs only if they induce clinical signs or symptoms, are considered clinically meaningful, require therapy, or require changes in the study drug. Laboratory abnormalities that meet the criteria for AEs should be followed until they have returned to normal, or an adequate explanation of the abnormality is found. Adverse events (including laboratory abnormalities that constitute AEs) should be described using a diagnosis whenever possible rather than by individual underlying signs and symptoms (e.g., “anemia” instead of “low hemoglobin”). When a clear diagnosis cannot be identified, each sign or symptom should be reported as a separate AE.

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 AE recording).

For combination products with a device constituent, AEs include those resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the device. It includes any AE resulting from use error or from intentional misuse of the investigational device.

Serious Adverse Event

An SAE 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 must 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.

If a serious and unexpected AE occurs for which there is evidence suggesting a causal relationship between the study intervention and the event (e.g., death from anaphylaxis), the event must be reported as a serious and unexpected suspected adverse reaction even if it is a component of the study endpoint (e.g., all-cause mortality).

For combination products with a device constituent, SAEs include adverse device effects that resulted in any of the consequences characteristic of an SAE. An unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report (see Section 2.3, Benefit-Risk Assessment).

Unlisted (Unexpected) Adverse Event/Reference Safety Information

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

10.5.2. Attribution Definitions

Assessment of Causality

The causal relationship to study intervention is assessed by the investigator. The following selection must be used to assess all AEs.

Related

There is a reasonable causal relationship between study intervention administration and the AE.

Not Related

There is not a reasonable causal relationship between study intervention administration and the AE.

The term “reasonable causal relationship” means that there is evidence to support a causal relationship.

10.5.3. 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 must use clinical judgment in assessing the severity of events not directly experienced by the participant (e.g., laboratory abnormalities).

10.5.4. 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
- Any failure of expected pharmacologic action (i.e., lack of effect if used according to the local label) of a Sponsor study intervention (to be reported as a PQC for marketed products)
- Unexpected therapeutic or clinical benefit from use of a Sponsor study intervention
- Medication error, intercepted medication error, or potential medication error involving a Johnson & Johnson medicinal product (with or without patient exposure to the Johnson & Johnson medicinal product, e.g., product name confusion, product label confusion, intercepted prescribing or dispensing errors)
- Exposure to a Sponsor study intervention from breastfeeding
- Reporting of participant pregnancy or participant partner(s) pregnancy

Special reporting situations should be recorded in the eCRF. Any special reporting situation that meets the criteria of an SAE should be recorded on the SAE page of the eCRF.

10.5.5. 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 (e.g., 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 AE to study therapy. All measures required for AE management must be recorded in the source document and reported according to Sponsor instructions.

For all studies with an outpatient phase, 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, which indicated 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 personnel 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 the participant's discontinuation from 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).

Any event requiring hospitalization (or prolongation of hospitalization) that occurs during participation in the study must be reported as an SAE, except hospitalizations for the following:

- Hospitalizations not intended to treat an acute illness or AE (e.g., 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 AE that results in a prolongation of the originally planned hospitalization is to be reported as a new SAE.

The cause of death of a participant in a study within 12 weeks of the last dose of study intervention, whether or not the event is expected or associated with the study intervention, is considered an SAE.

Information regarding SAEs will be transmitted to the Sponsor or designee using an SAE reporting form, which must be completed and signed by a physician from the study site and transmitted in a

secure manner to the Sponsor or designee within 24 hours. The initial and follow-up reports of an SAE should be made by encrypted email or facsimile (fax). Telephone reporting should be the exception, and the reporter should be asked to complete the appropriate form(s) first.

10.5.6. Product Quality Complaint Handling

Definition

A PQC is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, i.e., any dissatisfaction relative to the identity, quality, durability, reliability, or performance of a distributed product, including its labeling, drug delivery system, or package integrity. A PQC may have an impact on the safety and efficacy of the product. In addition, it includes any technical complaints, defined as any complaint that indicates a potential quality issue during manufacturing, packaging, release testing, stability monitoring, dose preparation, storage or distribution of the product or the drug delivery system.

This definition includes any PQC **related to a device constituent in a combination product, including those used in the administration of the study intervention or the comparator. A device deficiency is an inadequacy of a device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.**

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.

A sample of the suspected product should be maintained under the correct storage conditions until a shipment request is received from the Sponsor.

10.5.7. Contacting Sponsor Regarding Safety, Including Product Quality

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

10.6. Appendix 6: Contraceptive and Barrier Guidance

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 5, Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

Definitions

Participant of Childbearing Potential

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

Participant 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 female participants 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 female participants on HRT, the female participant will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if they wish to continue HRT during the study.
- **Permanently sterile (for the purpose of this study)**
  - Permanent sterilization methods include hysterectomy, or bilateral salpingectomy, or bilateral oophorectomy.
  - Has congenital abnormalities resulting in sterility.

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

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

Contraceptive (birth control) use by men or women must be consistent with local regulations regarding the acceptable methods of contraception for those participating in clinical studies.

Typical use failure rates may differ from those when used consistently and correctly. Use must be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.

EXAMPLES OF CONTRACEPTIVES[a] ALLOWED DURING THE STUDY INCLUDE FOR PARTICIPANTS OF CHILDBEARING POTENTIAL:
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
• Intrauterine device (IUD)
• Intrauterine hormone-releasing system (IUS)
• Tubal closure (e.g., bilateral tubal occlusion, bilateral tubal ligation)
• Azoospermic partner *(vasectomized or due to medical cause)* *(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 –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 FOR PARTICIPANTS OF CHILDBEARING POTENTIAL (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
• Cap, diaphragm, or sponge with spermicide
• A combination of male condom with either cap, diaphragm, or sponge with spermicide (double-barrier methods)
• Periodic abstinence (calendar, symptothermal, post-ovulation methods)
• Withdrawal (coitus-interruptus)
• Spermicides alone
• Lactational amenorrhea method (LAM)

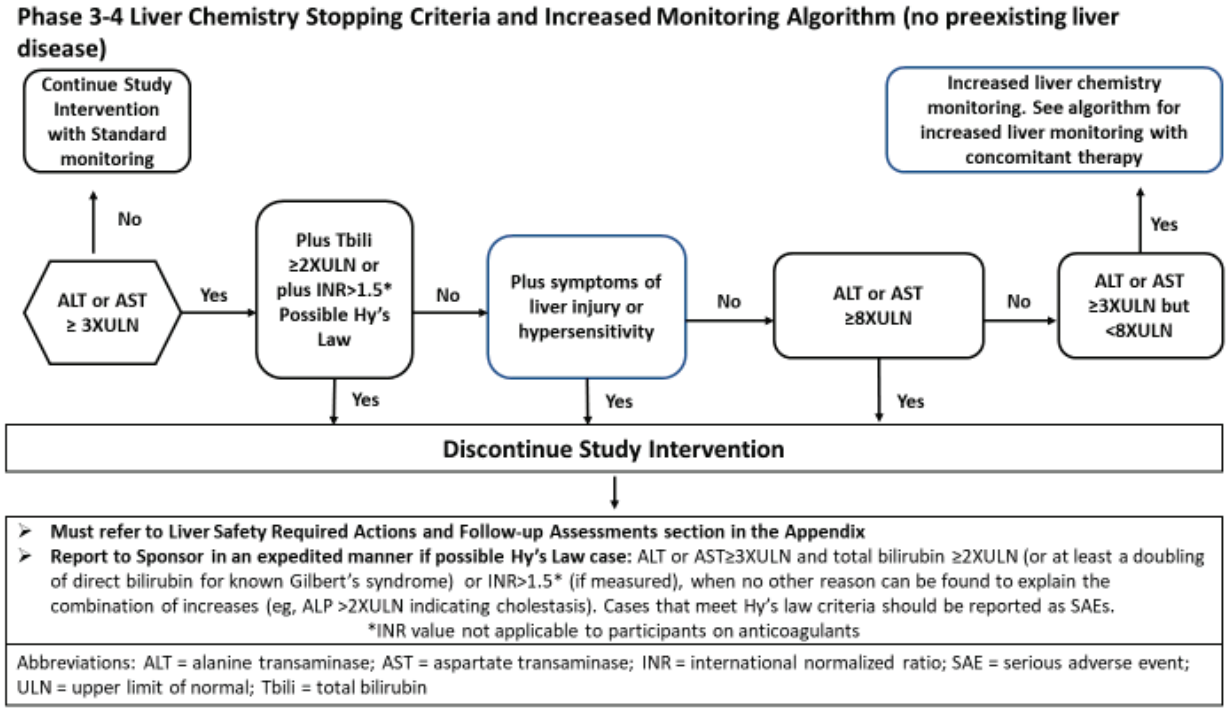
a) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.

10.7. Appendix 7: Liver Safety: Suggested Actions and Follow-up Assessments

10.7A. STOPPING CRITERIA AND INCREASED MONITORING ALGORITHMS

Liver Chemistry Stopping Criteria Algorithm

Study intervention will be discontinued for a participant if liver chemistry stopping criteria are met.

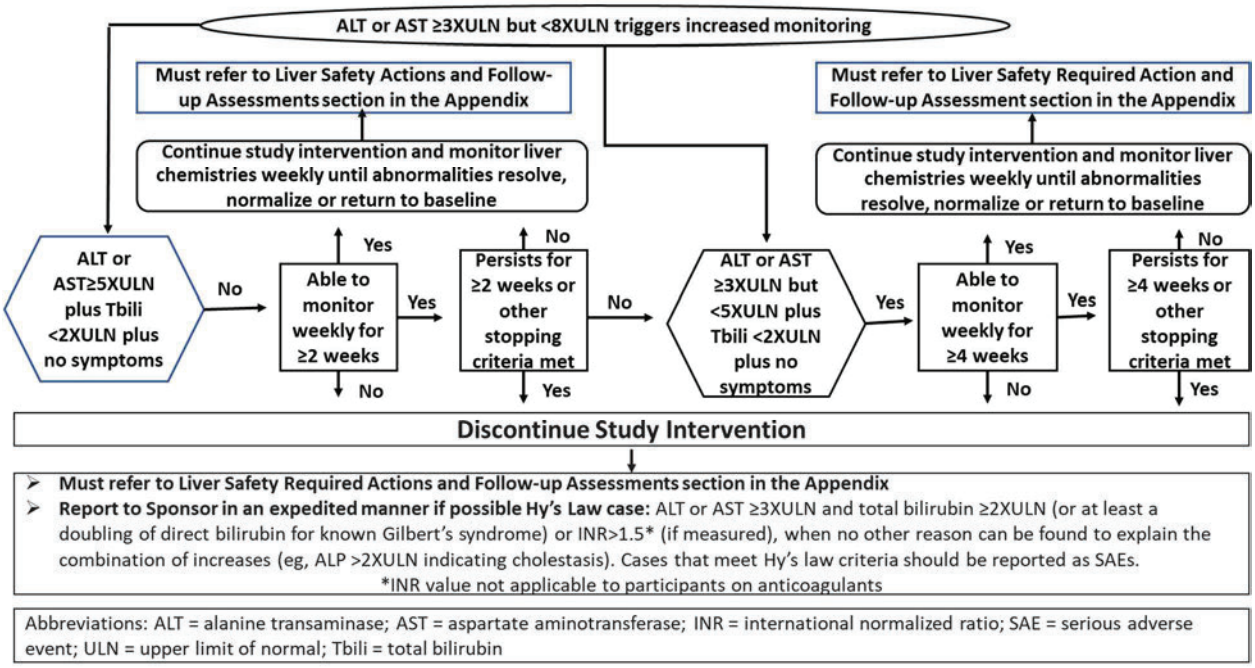


Refer to Appendix 7B, Liver Safety Required Actions and Follow-up Assessments

Increased Monitoring Algorithm

Study intervention discontinuation or continued participation will be decided based on the monitoring capability and laboratory results as outlined below. Study intervention will be discontinued for a participant if liver chemistry stopping criteria are met.

Phase 3-4 Liver Chemistry Increased Monitoring Algorithm with Continued Study Intervention for Participants with ALT or AST ≥3xULN but <8xULN (no preexisting liver disease)



Refer to Appendix 7B: Liver Safety Required Actions and Follow-up Assessments

B. LIVER SAFETY REQUIRED ACTIONS AND FOLLOW-UP ASSESSMENTS

Phase 3 to 4 liver chemistry stopping criteria are designed to assure participant safety and to evaluate liver event etiology.

Phase 3 to 4 Liver Chemistry Stopping Criteria and Follow-Up assessments

Liver Chemistry Stopping Criteria	
ALT or AST-absolute	ALT or AST ≥8 x ULN
ALT or AST-Increase	ALT or AST ≥5 x ULN but <8 x ULN persists for ≥2 weeks ALT or AST ≥3 x ULN but <5 x ULN persists for ≥4 weeks
Bilirubin[1, 2]	ALT or AST ≥3 x ULN **and** total bilirubin ≥2 x ULN
INR[2]	ALT or AST ≥3 x ULN **and** international normalized ratio (INR) >1.5
Cannot Monitor	ALT or AST ≥5 x ULN but <8 x ULN and cannot be monitored weekly for ≥2 weeks ALT or AST ≥3 x ULN but <5 x ULN and cannot be monitored weekly for ≥4 weeks
Symptomatic[3]	ALT or AST ≥3 x ULN associated with symptoms (new or worsening) believed to be related to liver injury or hypersensitivity

Suggested Actions, Monitoring, and Follow-up Assessments	
ACTIONS	**FOLLOW-UP ASSESSMENTS**
• **Immediately** stop study intervention • Report the event to the Sponsor **within 24 hours** • Complete the hepatic event form and complete an SAE eCRF if the event also met the criteria for an SAE[2] • Perform follow-up liver chemistry assessments as described in the **FOLLOW-UP ASSESSMENTS** column • Monitor the participant until liver chemistry test abnormalities resolve, stabilize, or return to baseline (see **MONITORING**) **MONITORING** **If ALT or AST ≥3 x ULN AND total bilirubin ≥2 x ULN(or at least a doubling of baseline direct bilirubin for known Gilbert's syndrome) or INR >1.5 (if measured):** • Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, total bilirubin, direct bilirubin, and INR[6]) and perform liver event **FOLLOW-UP ASSESSMENTS** within **24 hours** • Monitor participant twice weekly until liver chemistry test abnormalities resolve, stabilize, or return to baseline	• Viral hepatitis serology[4, 7] • Obtain blood sample for pharmacokinetic (PK)[5] analysis within 1 week of the event of ALT or AST ≥3×ULN. • Obtain serum creatine phosphokinase (CPK), lactate dehydrogenase (LDH), gamma-glutamyl transferase [GGT], and glutamate dehydrogenase [GLDH], and serum albumin[7] • Fractionate bilirubin • Obtain complete blood count with differential to assess eosinophilia • Record the appearance or worsening of clinical symptoms of liver injury, or hypersensitivity, on the CRF as per CRF completion guidelines • Record use of concomitant medications (including acetaminophen, herbal remedies, recreational drugs, and other over-the-counter medications) • Record alcohol use on the hepatic event form **<u>If ALT</u> or AST <u>≥3 x ULN AND total bilirubin ≥2 x ULN (or at least doubling of baseline direct bilirubin if known Gilbert's syndrome) or INR >1.5 (if measured):</u>** obtain the following in addition to the assessments listed above: • Anti-nuclear antibody, anti-smooth muscle antibody, Type 1 anti-liver kidney microsomal

• A specialist or hepatology consultation is recommended **If ALT or AST≥3 x ULN AND total bilirubin <2 x ULN and INR ≤1.5 (if measured):** • Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, total bilirubin, direct bilirubin, and INR[6]) and perform liver chemistry **FOLLOW-UP ASSESSMENTS** within **24 to 72 hours** • Monitor participants weekly until liver chemistry abnormalities resolve, stabilize, or return to baseline **RESTART** • **Do not restart** participant with study intervention unless allowed per protocol and Sponsor approval **is granted** • If restart is either **not allowed per protocol or not granted**, permanently discontinue study intervention. The participant may continue in the study for any protocol-specified follow-up assessments	antibodies, and quantitative total immunoglobulin G or gamma globulins[8] • Serum acetaminophen adduct assay, when available, to assess potential acetaminophen (paracetamol) contribution to liver injury in participants with definite or likely acetaminophen use in the preceding week • Liver imaging (ultrasound, magnetic resonance, or computerized tomography) to evaluate liver disease; complete liver Imaging form • Liver biopsy may be considered and discussed with local specialist if available, for instance: o In patients when serology raises the possibility of autoimmune hepatitis (AIH) o In patients when suspected DILI progresses or fails to resolve on withdrawal of study intervention o In patients with acute or chronic atypical presentation • If liver biopsy conducted record in eCRF

1. Serum bilirubin fractionation should be performed if testing is available. If serum bilirubin fractionation is not immediately available, discontinue study intervention if ALT or AST ≥3 x ULN **and** total bilirubin ≥2 x ULN. Additionally, if serum bilirubin fractionation testing is unavailable, **record the absence/presence of detectable urinary bilirubin on dipstick** which is indicative of direct bilirubin elevations suggesting liver injury.
2. All events of ALT or AST ≥3 x ULN **and** total bilirubin ≥2 x ULN or ALT or AST ≥3 x ULN **and** INR >1.5 (if measured), may indicate severe liver injury **(possible 'Hy's Law') and must be reported to sponsor in an expedited manner** using the SAE form, even before all other possible causes of liver injury have been excluded. A confirmed Hy's law case must be reported as an SAE. The INR stated threshold value will not apply to participants receiving anticoagulants.
3. New or worsening symptoms believed to be related to liver injury (such as fatigue, nausea, vomiting, right upper quadrant pain or tenderness, or jaundice) or hypersensitivity (such as fever, rash, or eosinophilia).
4. Includes hepatitis A immunoglobulin M (IgM) antibody, HBsAg; hepatitis C RNA, hepatitis C antibody, cytomegalovirus IgM antibody, Epstein-Barr viral capsid antigen IgM antibody (or if unavailable, heterophile antibody or monospot testing), and hepatitis E IgM antibody.
5. PK sample may not be required for participants known to be receiving placebo or non-comparator interventions. Record the date/time of the PK blood sample draw and the date/time of the last dose of study intervention prior to the PK blood sample draw on the eCRF. If the date or time of the last dose is unclear, provide the participant's best approximation. If the date/time of the last dose cannot be approximated OR a PK sample cannot be collected in the time period indicated above, do not obtain a PK sample. Instructions for sample handling and shipping are in the Laboratory Manual.
6. These are included in the Liver Safety kit. Verify laboratory selections with the Laboratory Manual.
7. These are included in the Liver Follow-Up Kit. Verify laboratory selections with the Laboratory Manual.
8. These are included in the DILI kit. Verify laboratory selections with the Laboratory Manual.

A participant who met liver chemistry stopping criteria cannot restart study intervention, unless all of the following conditions are met:

- Sponsor approval **is granted** (as described below).
- Institutional Review Board/Independent Ethics Committee (IRB/IEC) has been informed.
- The participant has been informed of the potential risks and has consented to resume study intervention.

If Sponsor approval to restart/rechallenge the participant with study intervention **is not granted**, then the participant must permanently discontinue study intervention and may continue in the study for protocol-specified follow-up assessments.

Restart Following Transient Resolving Liver Chemistry Events Not Related to Study Intervention

- Restart refers to resuming study intervention following liver chemistry events for which there are clear underlying causes (other than DILI) (e.g., biliary obstruction, pancreatic events, hypotension, and acute viral hepatitis). Furthermore, restart is not permitted following liver stopping event when the underlying cause was alcohol-related hepatitis. Approval by the Sponsor for study intervention restart can be considered when:
  - The investigator requests consideration for study intervention restart if liver chemistry events have a clear underlying cause (e.g., biliary obstruction, pancreatic events, hypotension, acute viral hepatitis) and liver chemistry tests have improved to normal or are within 1.5 x baseline and ALT or AST <3 x ULN.
  - The principal investigator requests consideration of rechallenge with study intervention for a participant who is receiving compelling benefit with study intervention that exceed risks and for whom no effective alternative therapy exists.
  - Possible DILI has been excluded by the investigator and the study team. This includes the absence of markers of hypersensitivity (otherwise unexplained fever, rash, eosinophilia). Where a study intervention has an identified genetic marker associated with liver injury (e.g., lapatinib, abacavir, and amoxicillin/clavulanate), the presence of the marker should be excluded.
  - There is no evidence of alcoholic-related hepatitis.
  - IRB/IEC has been informed regarding restart of study intervention.

If restart of study intervention is approved by the Sponsor in writing:

- The participant must be provided with a clear description of the possible benefits and risks of study intervention administration including the possibility of recurrent, more severe liver injury, liver transplantation, or death.
- The participant must provide signed informed consent specifically for the restart of study intervention. Documentation of informed consent must be recorded in the participant source documents.
- Study intervention must be administered at the dose specified by the Sponsor.

- Participants approved by the Sponsor for restart of study intervention must return to the clinic twice a week for liver chemistry tests until stable liver chemistry tests have been demonstrated and then standard laboratory monitoring may resume as per protocol.
- If the participant meets protocol-defined liver chemistry stopping criteria after study intervention restart, study intervention should be permanently discontinued.
- The Sponsor, Medical Monitor, and the IRB/IEC must be informed of the outcome for the participant following study intervention restart.
- The Sponsor must be notified of any AEs.

References:

Andrade RJ, Robles M, Lucena MI. Rechallenge in drug-induced liver injury: the attractive hazard. Expert Opin Drug Saf. 2009;8:709-714.

European Association for the Study of the Liver (EASL) Clinical Practice Guidelines: Drug-induced liver injury. Journal of Hepatology 2019;70:1222-1261.

Hunt, CM. Mitochondrial and immunoallergic injury increase risk of positive drug rechallenge after drug-induced liver injury: A systematic review. Hepatol. 2010;52:2216-2222.

James LP, Letzig L, Simpson PM, et al. Pharmacokinetics of acetaminophen-adduct in adults with acetaminophen overdose and acute liver failure. Drug Metab Dispos 2009;37:1779-1784.

Le Gal F, Gordien E, Affolabi D, et al. Quantification of hepatitis Delta virus RNA in serum by consensus real-time PCR indicates different patterns of virological response to interferon therapy in chronically infected patients. J Clin Microbiol. 2005;43:2363–2369.

Papay JI, Clines D, Rafi R, et al. Drug-induced liver injury following positive drug rechallenge. Regul Tox Pharm. 2009;54:84-90.

10.8. Appendix 8: Study Conduct During a Natural Disaster/Pandemic

GUIDANCE ON STUDY CONDUCT DURING PANDEMIC

It is recognized that the COVID-19 pandemic may have an impact on the conduct of this clinical study due to, for example, isolation or quarantine of participants and study site personnel; travel restrictions/limited access to public places, including hospitals; study site personnel being unavailable, isolated, or reassigned to critical tasks.

The Sponsor is providing options for study-related participant management in the event of disruption to the conduct of the study. This guidance does not supersede any local or government requirements or the clinical judgement of the investigator to protect the health and well-being of participants and site staff. If, at any time, a participant's travel to the study site is considered to be dangerous, study participation may be interrupted, and study follow-up conducted. If it becomes necessary to discontinue participation in the study, the procedures outlined in the protocol for discontinuing study intervention will be followed.

If, as a result of the COVID-19 pandemic, scheduled visits cannot be conducted in person at the study site, they will be performed to the extent possible remotely/virtually or delayed until such time that on-site visits can be resumed. At each contact, participants will be interviewed to collect safety data. Key efficacy endpoint assessments should be performed if required and as feasible. Participants will also be questioned regarding general health status to fulfill any physical examination requirement.

Every effort should be made to adhere to protocol-specified assessments for participants on study intervention, including follow-up. Modifications to protocol-required assessments may be permitted after consultation with the participant, investigator, and the Sponsor. Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the eCRF.

If the participant has tested positive for COVID-19, the investigator should contact the Sponsor's responsible medical officer or designee to discuss plans for administration of study intervention, performing study assessments, and follow-up. Modifications made to the study conduct as a result of the COVID-19 infection should be summarized in the clinical study report.

ADDITIONAL ELEMENTS, WHERE APPLICABLE:

- Certain protocol-mandated visits to the study site may not be possible during the COVID-19 pandemic. Therefore, temporary measures may be implemented if considered appropriate by the Sponsor and investigator to maintain continuity of patient care and study integrity. Certain measures, such as those listed below, may be necessary and should be instituted in accordance with applicable (including local) laws, regulations, guidelines, and procedures:
  - remote (e.g., by phone/telemedicine) or in-person, off-site (e.g., in-home) interactions between site staff (or designees) and patients for study procedures, e.g., those related to

safety monitoring/efficacy evaluation/study intervention storage and administration (including training where pertinent)

- procurement of study intervention by patients (or designee) or shipment of study intervention from the study site directly to patients for at-home administration (including the potential for patient self-administration of study intervention)
- laboratory assessments using a suitably accredited local laboratory; for selected measures (e.g., urine pregnancy), home testing may be employed

- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the eCRF.
  - other relevant study data elements impacted by the pandemic should also be documented as "COVID-19-related" in eCRFs and/or other study systems, as directed by detailed Sponsor guidance. These may include missed/delayed/modified study visits or assessments/dosing, and instances where temporary measures such as those above are implemented.
- The Sponsor will evaluate the totality of impact of COVID-19 on collection of key study data and additional data analyses will be outlined in study SAP(s).

10.9. Appendix 9: Investigator's Global Assessment (IGA)

Induration (I) (averaged over all lesions)
0 = no evidence of plaque elevation
1 = minimal plaque elevation, = 0.25 mm
2 = mild plaque elevation, = 0.5 mm
3 = moderate plaque elevation, = 0.75 mm
4 = severe plaque elevation, > 1 mm

Erythema (E) (averaged over all lesions)
0 = no evidence of erythema, hyperpigmentation may be present
1 = faint erythema
2 = light red coloration
3 = moderate red coloration
4 = bright red coloration

Scaling (S) (averaged over all lesions)
0 = no evidence of scaling
1 = minimal; occasional fine scale over less than 5% of the lesion
2 = mild; fine scale dominates
3 = moderate; coarse scale predominates
4 = severe; thick, scale predominates

Total Average = (I + E + S) / 3 (average will be calculated in the device but not displayed. Numeric result will be included in data transfer)
Investigator's Global Assessment based upon above Total Average
0 = Cleared, except for residual discoloration
1 = Minimal - majority of lesions have individual scores for I + E + S / 3 that averages 1
2 = Mild - majority of lesions have individual scores for I + E + S / 3 that averages 2
3 = Moderate - majority of lesions have individual scores for I + E + S / 3 that averages 3
4 = Severe - majority of lesions have individual scores for I + E + S / 3 that averages 4
Note: Scores should be rounded to the nearest whole number. If total ≤ 1.49, score = 1; if total ≥ 1.50, score = 2.

10.10. Appendix 10: Psoriasis Area and Severity Index (PASI)

PSORIASIS AREA AND SEVERITY INDEX (PASI)

Week _____

Symptom Score

Score	0	1	2	3	4
Erythema Induration Scaling	None	Slight	Moderate	Severe	Very Severe

Area of Psoriatic Involvement

Score	0	1	2	3	4	5	6
Area	0	1% - 9%	10% - 29%	30% - 49%	50% - 69%	70% - 89%	90% - 100%

To help with the area assessments, the following conventions should be noted:

a. The neck is considered part of the head
b. The axillae and groin are part of the trunk
c. The buttocks are part of the lower extremities

Symptom Score	Head (H)	Trunk (T)	Upper Limbs (UL)	Lower Limbs (LL)
Erythema (E)	☐	☐	☐	☐
Induration (I) (thickness)	☐	☐	☐	☐
Scaling (S)	☐	☐	☐	☐
Sum = E + I + S	☐☐	☐☐	☐☐	☐☐
Area of Psoriatic Involvement Score	☐	☐	☐	☐
Sum X Area =	☐☐	☐☐	☐☐	☐☐
	X 0.1 =	X 0.3 =	X 0.2 =	X 0.4 =

☐☐.☐
☐☐.☐
☐☐.☐
☐☐.☐
+

PASI = SUM ☐☐.☐

_____
Assessor's Signature

Date: ___ ___ - ___ ___ ___ - 2 0 ___ ___
day month year

10.11. Appendix 11: Scalp-Specific Investigator's Global Assessment (ss-IGA)

Participants with psoriasis of the scalp will be assessed using the 5-point ss-IGA presented below.

Score	Category	Description
0	Absence of Disease	No evidence of redness, no evidence of thickness, and no evidence of scaliness on the scalp.
1	Very Mild Disease	The overall clinical picture consists of flat lesions with barely perceptible erythema, with or without a trace of overlying fine scale
2	Mild Disease	The overall clinical picture consists of lesions with mild erythema, slight, but definite, thickness, and a thin scale layer
3	Moderate Disease	The overall clinical picture consists of lesions with moderate erythema, a moderate thickness, and a moderate scaled layer
4	Severe Disease	The overall clinical picture consists of lesions with bright erythema, severe thickness and a severe, coarse thick scale layer

10.12. Appendix 12: Static Physician's Global Assessment of Genitalia (sPGA-G)

The Static Physician Global Assessment of Genitalia		
Score[1]	Category	Category Description[2]
0	Clear	Erythema: residual or no erythema Plaque elevation: no elevation Scaling: no scale
1	Minimal	Erythema: faint, light pink erythema Plaque elevation: elevation is very slight and difficult to confirm Scaling: some fine, white surface dryness
2	Mild	Erythema: mild, pink erythema Plaque elevation: slight elevation with sloped edges Scaling: fine scale on some or most lesions
3	Moderate	Erythema: moderate, red erythema Plaque elevation: moderate elevation with definite edges that are either sloped or rough Scaling: coarse scale on most lesions
4	Severe	Erythema: severe, bright red erythema Plaque elevation: substantial elevation, hard or sharp edges Scaling: coarse, non-adherent scale on most to all lesions
5	Very Severe	Erythema: very severe, deep red erythema Plaque elevation: very significant elevation with hard and sharp edges Scaling: very coarse, thick, and adherent scale completely or nearly completely covering most or all lesions.

[1]The final sPGA-G score is on a 0-5 scale. Each score is associated with a severity category.

[2]Severity is determined by a combination of 3 plaque characteristics (erythema, elevation, and scale) based on descriptions of each characteristic. Erythema is the primary characteristic that should influence the rating, with plaque elevation and scaling considered secondarily. Assessment does not require all three characteristics to be present.

10.13. Appendix 13: Nail Psoriasis Severity Index (NAPSI)

All 10 fingernails will be scored using the NAPSI as described below.
The nail is divided with imaginary horizontal and longitudinal lines into quadrants.

Each nail is given a score for nail matrix psoriasis (0 to 4) and nail bed psoriasis (0 to 4) depending on the presence of ***any*** of the features of nail psoriasis in that quadrant.

1. **Evaluation 1: Nail matrix.** In each quadrant of the nail, nail matrix psoriasis is evaluated by presence of ***any*** of the nail matrix features (pitting, leukonychia red spots in the lunula, and nail plate crumbling): 0 for none, 1 if present in 1 quadrant of the nail, 2 if present in 2 quadrants of the nail, 3 if present in 3 quadrants of the nail, and 4 if present in 4 quadrants of the nail.

2. **Evaluation 2: Nail bed.** Nail bed psoriasis is evaluated by the presence of ***any*** of the nail bed features (onycholysis, splinter hemorrhages, oil drop (salmon patch) discoloration, and nail bed hyperkeratosis): 0 for none, 1 for 1 quadrant only, 2 for 2 quadrants, 3 for 3 quadrants, and 4 for 4 quadrants.

3. Each nail gets a matrix score and a nail bed score, the total of which is the score for that nail (0 to 8).

4. Each nail is evaluated, and the sum of all the nails is the total NAPSI score. The sum of the scores from all nails is 0 to 80.

Reference:

Rich P and Scher RK. Nail Psoriasis Severity Index: A useful tool for evaluation of nail psoriasis. J Am Acad Dermatol 2003; 49:206-212.

10.14. Appendix 14: Palmoplantar Investigator's Global Assessment (pp-IGA)

TABLE 1. Palmoplantar Investigator's Global Assessment (ppIGA)	
0 = Clear	No signs of psoriasis, postinflammatory hyperpigmentation may be present
1 = Almost clear/minimal	Coloration: normal to pink Thickening: none Scaling: none to minimal focal
2 = Mild	Coloration: pink to light red Thickening: just detectable to mild Scaling: predominantly fine scaling
3 = Moderate	Coloration: dull to bright red, clearly distinguishable Thickening: clearly distinguishable to moderate Scaling: moderate
4 = Severe	Coloration: bright to deep dark red Thickening: severe with hard edges Scaling: severe/coarse covering almost all/all lesions, numerous fissures

10.15. Appendix 15: Intertriginous Investigator's Global Assessment (i-IGA)

The IGA used for the full body assessment has been adapted with descriptions of disease features that are more consistent with intertriginous psoriasis presentation. The intertriginous areas affected to be scored include the axillary, sub-mammary, abdominal fold, inguinal, and intergluteal cleft/peri-anal region (distinct from genital/perineum involvement).

It should be noted that erythema may be the predominant feature, and there may or may not be the presence of elevation or scaling. Therefore, scoring may be predominantly driven by the severity of erythema if it is the dominant presenting feature.

Clear (0)	No evidence of elevation, papulation, or textural change to shiny, smooth No evidence of erythema, hyperpigmentation may be present No evidence of scaling
Minimal (1)	Minimal elevation and/or minimal textural change Faint erythema Minimal; occasional fine scale over less than 5% of the lesion, possibly only at edges/borders
Mild (2)	Mild elevation/papulation or mild textural change towards shiny, smooth Light red coloration Mild, fine scale dominates, possibly at borders, mild peeling, no fissuring
Moderate (3)	Moderate elevation and/or moderate textural change to shiny and smooth with partial loss of skin markings Moderate red coloration Moderate; coarse scale, possibly at borders, or moderate peeling, maceration, early fissures
Severe (4)	Severe elevation or severe textural difference from normal skin with complete/near complete loss of skin markings Bright red, dark red, violaceous Severe; thick, scale predominates if present at borders, or severe peeling, maceration, fissures, erosions/ulcerations

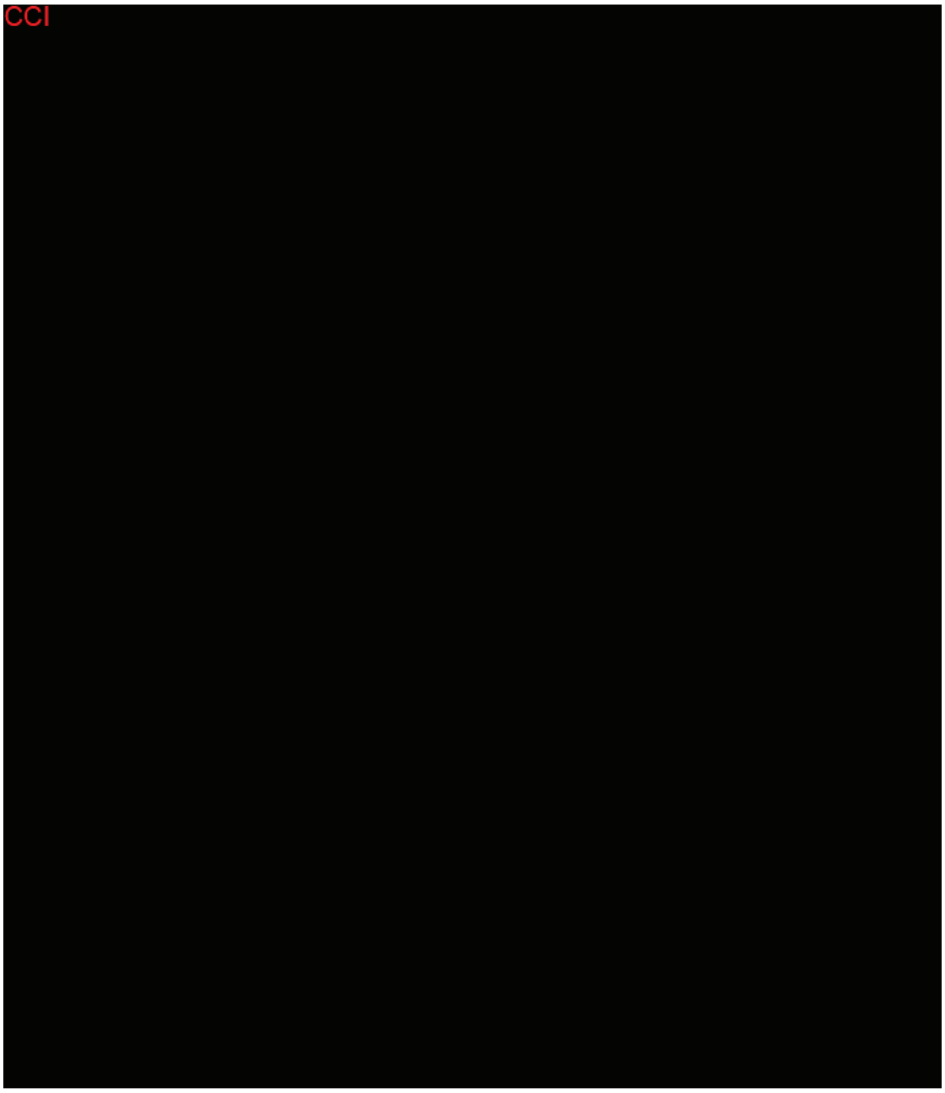
10.16. Appendix 16: Facial Investigator's Global Assessment (f-IGA)

The same IGA used for the full body assessment will be adapted for use, but only the face will be scored.

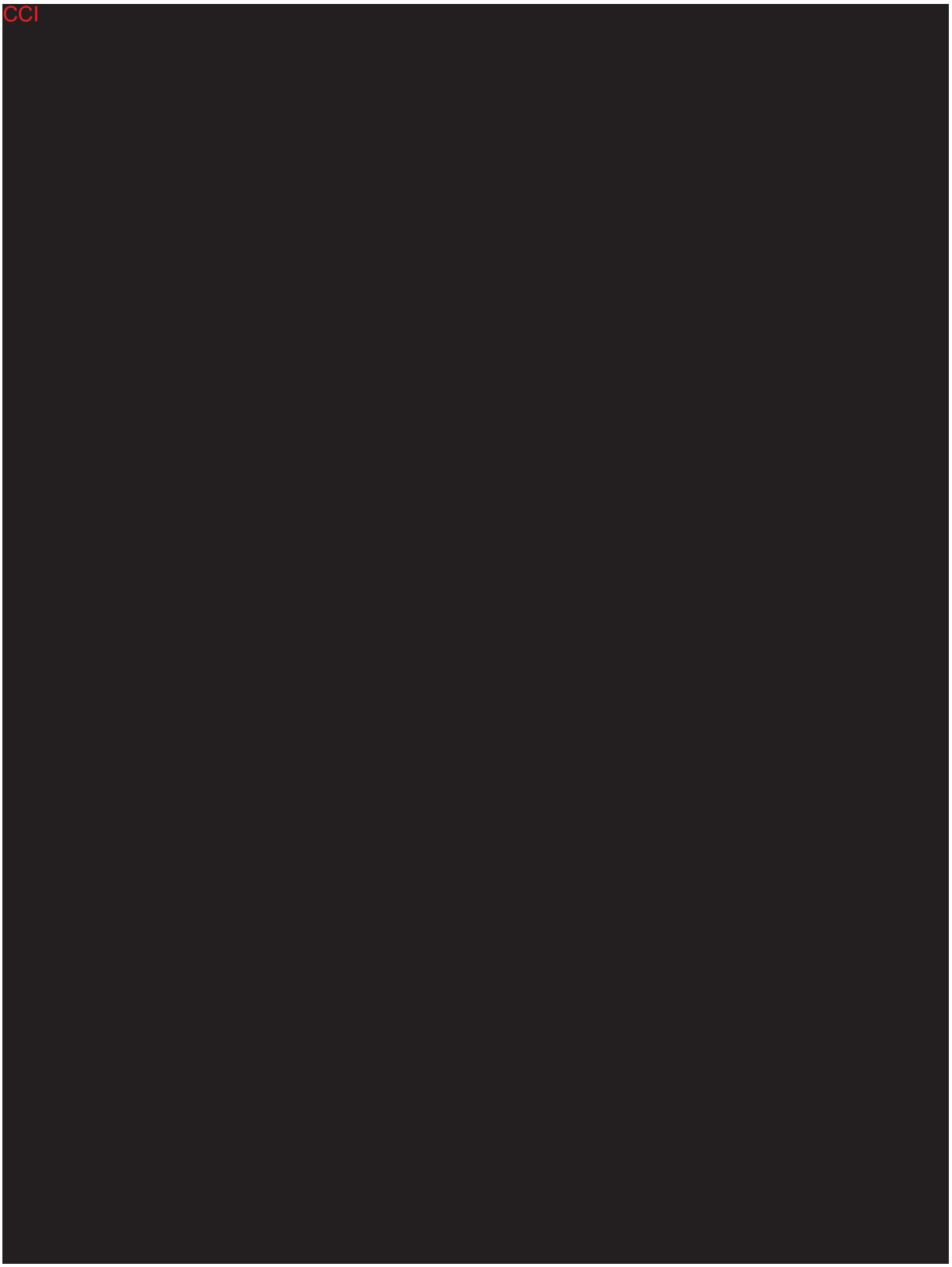
It should be noted that erythema and, to an extent, scaling are the more prominent features of facial psoriasis, and less often elevation. Therefore, scoring may be predominantly driven by the severity of erythema and scaling if these are the dominant presenting features.

Clear (0)	No evidence of plaque elevation No evidence of erythema, hyperpigmentation may be present No evidence of scaling
Minimal (1)	Minimal plaque elevation, = 0.25 mm Faint erythema Minimal; occasional fine scale over less than 5% of the lesion
Mild (2)	Mild plaque elevation, = 0.5 mm Light red coloration Mild, fine scale dominates
Moderate (3)	Moderate plaque elevation, = 0.75 mm Moderate red coloration Moderate; coarse scale predominates
Severe (4)	Severe plaque elevation, > 1 mm Bright red coloration Severe; thick, scale predominates

10.17. Appendix 17: Psoriasis Symptom and Sign Diary (PSSD) Based on 7-day Recall



10.18. Appendix 18: Dermatology Life Quality Index (DLQI)

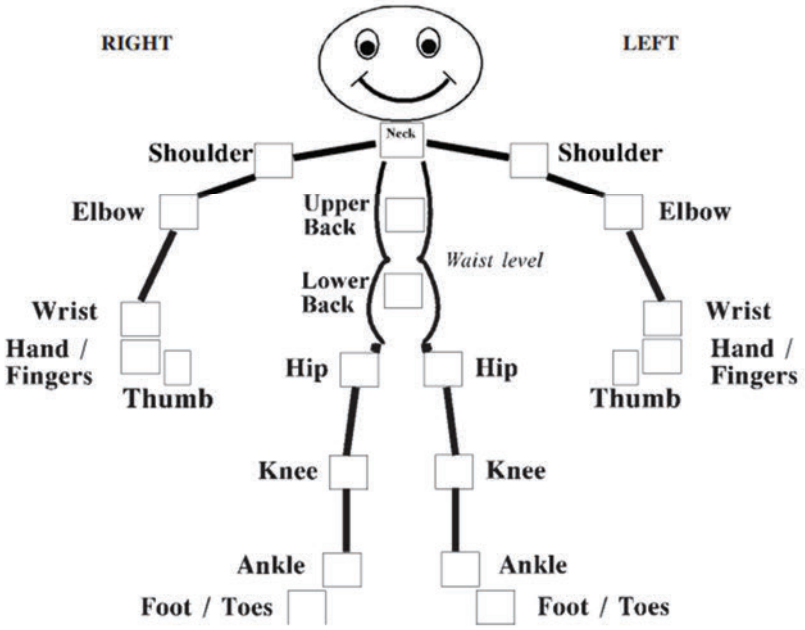


CCI

10.19. Appendix 19: Psoriasis Epidemiology Screening Tool (PEST)

Have you ever had a swollen joint (or joints)?
Has a doctor ever told you that you have arthritis?
Do your finger nails or toe nails have holes or pits?
Have you had pain in your heel?
Have you had a finger or toe that was completely swollen and painful for no apparent reason?

In the drawing below, please tick the joints that have caused you discomfort (*i.e.* stiff, swollen or painful joints).



10.20. Appendix 20: Psoriatic Arthritis Impact of Disease Score (PsAID-12)

The EULAR Psoriatic Arthritis Impact of Disease: PsAID12 for clinical practice

We want you to indicate how much your psoriatic arthritis impacts your health.
Please tell us how you have been feeling this last week.

1. Pain

Circle the number that best describes the pain you felt due to your psoriatic arthritis during the last week:

None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme

For office use only
Result x3 ☐

2. Fatigue

Circle the number that best describes the overall level of fatigue due to your psoriatic arthritis you have experienced during the last week:

No fatigue | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Totally exhausted

Result x2 ☐

3. Skin problems

Circle the number that best describes the skin problems including itching you felt due to your psoriatic arthritis during the last week:

None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme

Result x2 ☐

4. Work and/or leisure activities

Circle the number that best describes the difficulties you had to participate fully in work and/or leisure activities due to your psoriatic arthritis during the last week:

None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme

Result x2 ☐

5. Functional capacity

Circle the number that best describes the difficulty you had in doing daily physical activities due to your psoriatic arthritis during the last week:

No difficulty | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme difficulty

Result x2 ☐

6. Discomfort

Circle the number that best describes the feeling of discomfort and annoyance with everyday tasks due to your psoriatic arthritis during the last week:

None | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme

Result x2 ☐

7. Sleep disturbance

Circle the number that best describes the sleep difficulties (i.e., resting at night) you felt due to your psoriatic arthritis during the last week:

No difficulty | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Extreme difficulty

Result x2 ☐

1

8. Coping

Considering your psoriatic arthritis overall, how well did you cope (manage, deal, make do) with your psoriatic arthritis during the last week?

Very well	0	1	2	3	4	5	6	7	8	9	10	Very poorly

For office use only

Result x1 ☐

9. Anxiety, fear and uncertainty

Circle the number that best describes the level of anxiety, fear and uncertainty (for example about the future, treatments, fear of loneliness) due to your psoriatic arthritis you have experienced during the last week:

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

Result x1 ☐

10. Embarrassment and/or shame

Considering your psoriatic arthritis overall, circle the number that best describes the level of embarrassment and/or shame due to your appearance experienced during the last week:

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

Result x1 ☐

11. Social participation

Circle the number that best describes the difficulties you had to participate fully in social activities (including relationships with family and/or people very close to you) due to your psoriatic arthritis during the last week:

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

Result x1 ☐

12. Depression

Circle the number that best describes the level of depression due to your psoriatic arthritis you have experienced during the last week:

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

Result x1 ☐

THANK YOU FOR ANSWERING THIS QUESTIONNAIRE

PsAID12 SCORING AND CALCULATION RULES

The PsAID is calculated based on 12 Numerical rating scales (NRS) questions. Each NRS is assessed as a number between 0 and 10.

Calculation

PsAID final value =
(PsAID1 (pain) NRS value (range 0-10) x 3)
+ (PsAID2 (fatigue) NRS value (range 0-10) x 2)
+ (PsAID3 (skin) NRS value (range 0-10) x 2)
+ (PsAID4 (Work and/or leisure activities) NRS value (range 0-10) x 2)
+ (PsAID5 (function) NRS value (range 0-10) x 2)
+ (PsAID6 (discomfort) NRS value (range 0-10) x 2)
+ (PsAID7 (sleep) NRS value (range 0-10) x 2)
+ (PsAID8 (coping) NRS value (range 0-10) x 1)
+ (PsAID9 (anxiety) NRS value (range 0-10) x 1)
+ (PsAID10 (embarrassment) NRS value (range 0-10) x 1)
+ (PsAID11 (social life) NRS value (range 0-10) x 1)
+ (PsAID12 (depression) NRS value (range 0-10) x 1)

The total is divided by 20.

Thus, the range of the final PsAID value is 0-10 where higher figures indicate worse status.

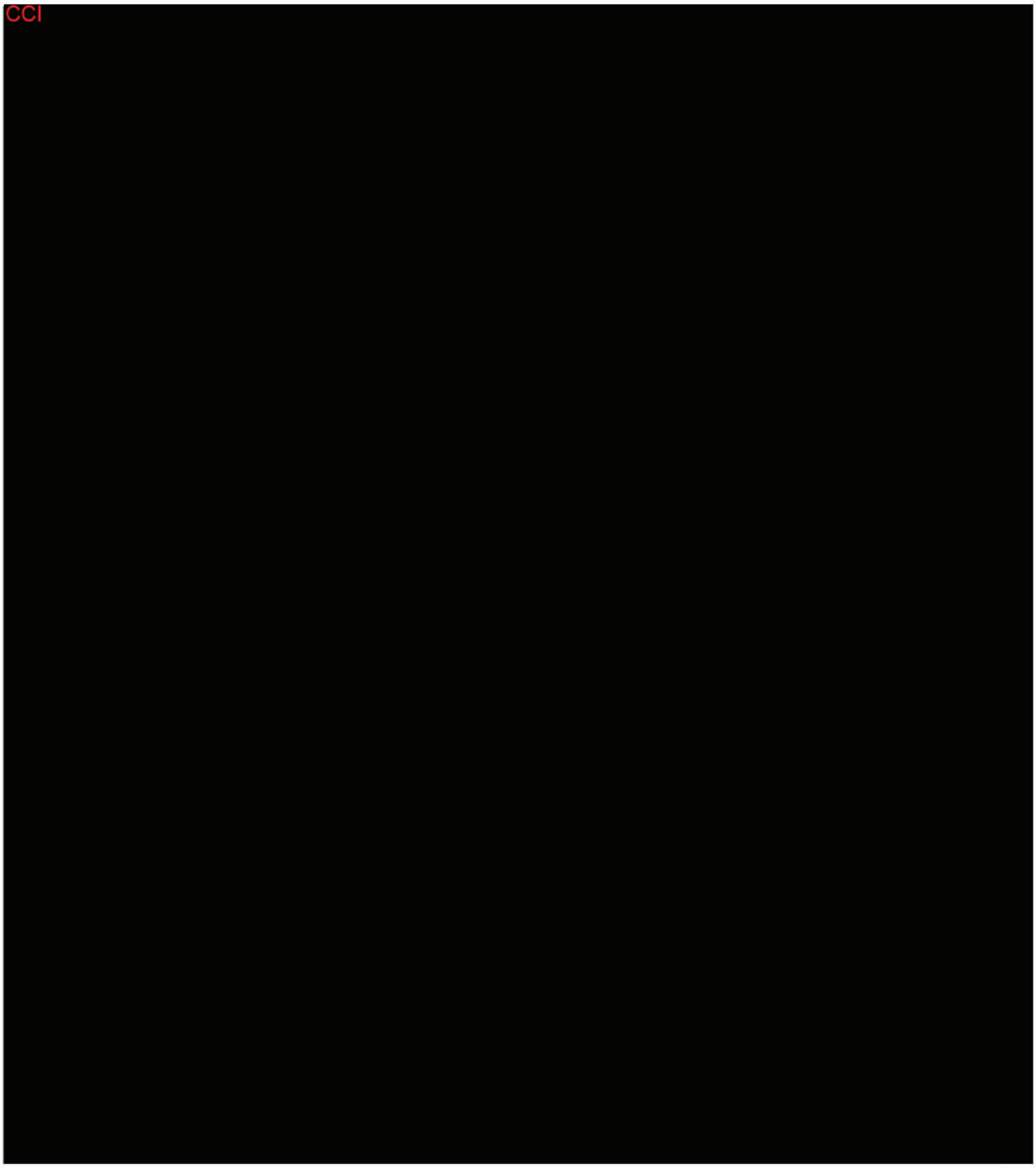
Missing data imputation

If one of the 12 NRS values composing the PsAID is missing, the imputation is as follows:
calculate the mean value of the 11 other (non-missing) NRS (range, 0-10)
impute this value for the missing NRS
Then, calculate the PsAID as explained above.

If 2 or more of the NRS are missing, the PsAID is considered as missing value (no imputation).

10.21. Appendix 21: PROMIS-29 Questionnaire (Version 2.0)

PROMIS–29 Profile v2.0



 Page 1 of 3

CCI

[redacted]

CCI

[redacted]

10.22. Appendix 22: Protocol Amendment History

This is an original protocol.

REFERENCES

Augustin M, Langenbruch A, Gutknecht M, et al. Definition of psoriasis severity in routine clinical care: current guidelines fail to capture the complexity of long-term psoriasis management. Br J Dermatol. 2018;179:1385-1391.

Di Carlo M, Becciolini A, Lato V, et al. The 12-item Psoriatic Arthritis Impact of Disease questionnaire: Construct validity, reliability, and interpretability in a clinical setting. J Rheumatol. 2017;44:279-285.

Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19:210-216.

Foley P, Gordon K, Griffiths CEM, et al. Efficacy of Guselkumab Compared With Adalimumab and Placebo for Psoriasis in Specific Body Regions: A secondary analysis of 2 randomized clinical trials. JAMA Dermatol. 2018;154:676–683.

Food and Drug Administration [FDA] Guidance for Industry E10. Choice of Control Group and Related Issues in Clinical Trials. May 2001.

Fredriksson T, Pettersson U. Severe psoriasis- oral therapy with a new retinoid. Dermatologica. 1978;157:238-244.

Golbari NM, van der Walt JM, Blauvelt A, et al. Psoriasis severity: commonly used clinical thresholds may not adequately convey patient impact. J Eur Acad Dermatol Venereol. 2021;35:417-421.

Gottlieb A, Sullivan J, van Doorn M, et al. Secukinumab shows significant efficacy in palmoplantar psoriasis: Results from GESTURE, a randomized controlled trial. J Am Acad Dermatol. 2017;76:70-80.

Ibrahim GH, Buch MH, Lawson C, et al. Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and the development of a new instrument: the Psoriasis Epidemiology Screening Tool (PEST) questionnaire. Clin Exp Rheumatol. 2009;27:469-474.

Knuckles MLF, Levi E, Soung J. Defining and treating moderate plaque psoriasis: a dermatologist survey. J Dermatolog Treat. 2018;29:658-663.

Langley RG, Ellis CN. Evaluating psoriasis with Psoriasis Area and Severity Index, Psoriasis Global Assessment, and Lattice System Physician's Global Assessment. J Am Acad Dermatol. 2004;51:563-569.

Langley RGB, Feldman SR, Nyirady J, et al. The 5-point Investigator's Global Assessment (IGA) Scale: A modified tool for evaluating plaque psoriasis severity in clinical trials. J Dermatol Treat. 2015;26:23-31.

Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. J Am Acad Dermtol. 2014; 70:871-881.

Long CC, Finlay AY, Averill RW. The rule of hand: 4 hand areas = 2 FTU = 1G. Arch Dermatol. 1992;128:1129-1130.

Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80:1029-1072.

Merola JF, Potts Bleakman A, Gottlieb AB, et al. The static Physician's Global assessment of genitalia: A clinical outcome measure for the severity of genital psoriasis. J Drugs Dermatol. 2017;16:793-799.

Rich P, Scher RK. Nail Psoriasis Severity Index: a useful tool for evaluation of nail psoriasis. J Am Acad Dermatol. 2003;49:206-212.

Rossiter ND, Chapman P, Haywood IA. How big is a hand? Burns. 1996;22:230-231.

Strober B, Ryan C, van de Kerkhof P, et al. Recategorization of psoriasis severity: Delphi consensus from the International Psoriasis Council. J Am Acad Dermatol. 2020;82:117-122.

Thomas CL, Finlay AY. The "handprint" approximates to 1% of the total body surface area whereas the "palm minus the fingers" does not. Br J Dermatol. 2007;157:1080-1081.

Vaidya TS, Anderson KL, Feldman SR. Even well-controlled psoriasis patients have unmet treatment needs regardless of disease severity. Dermatol Online J. 2015;21:13030.

van de Kerkhof PC, Reich K, Kavanaugh A, et al. Physician perspectives in the management of psoriasis and psoriastic arthritis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis survey. J Eur Acad Dermatol Venereal. 2015;29:2002-2010.

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): PPD, Senior Director, US Medical Affairs, Dermatology

Institution: Janssen Research & Development

Signature: electronic signature appended at the end of the protocol Date: _____

(Day Month Year)

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

Signature

User	Date	Reason
PPD	17-Feb-2023 22:04:04 (GMT)	Document Approval