Janssen EMEA*

Clinical Protocol

A Phase 3b, Multicenter, Interventional, Randomized, Placebo-controlled Study Investigating the Efficacy and Safety of Guselkumab for the Treatment of Palmoplantar-non-Pustular Psoriasis
G-PLUS

Efficacy and Safety of Guselkumab for the Treatment of Palmoplantar Psoriasis

Protocol CNTO1959PSO3013; Phase 3b
AMENDMENT 1
CNTO1959 (guselkumab)

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

PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

DOCUMENT HISTORY	
Document	**Date**
Amendment 1	12 July 2019
Original Protocol	19 December 2018

Amendment 1 (12 July 2019)

Overall Rationale for the Amendment: The primary reason for this amendment was to provide further clarification on the inclusion, exclusion and withdrawal criteria to provide specificity on the participants to be included in this study. The frequency of visits for tests and data collection have been changed, and minor edits and corrections have been made.

Section Number and Name	Description of Change	Brief Rationale
1.1 Synopsis, 1.3 Schedule of Activities, 4.1 Overall Design	• Occupational status of the participants will be collected at baseline (Week 0), Week 16, Week 24 and at the Final Efficacy Visit (Week 48).	Recording of occupational status at different time-points during the study will provide information on the impact of the study intervention on the quality of life and daily activities of participants.
	• The footnote for pregnancy testing was modified; Serum pregnancy tests will not be conducted in the study, rather urine pregnancy testing will be done at screening and all study visits.	Urine pregnancy tests are a reliable diagnostic tool and will be used as part of the safety follow-up for female participants, as detailed in the Schedule of Activities.
	• ppIGA and PASI scales will also be administered at screening.	The 2 scales administered at screening to ensure selection of patients with ppIGA scores ≥3 and PASI score ≥3 and <10 in accordance with the revised inclusion criteria.
	• Information on injection site reactions (ISR) will not be collected at the non-dosing visits.	Deleted as ISRs are not relevant at non-dosing visits.
	• Optional photographs of hands and feet of participants will also be collected at Week 8.	Added to be consistent with data collected in prior studies evaluating guselkumab for the treatment of palmoplantar psoriasis.
	• Rescue medication assessment has been deleted from the table.	Rescue medication will be assessed as part of the review of concomitant therapy throughout the study; the footnote has been modified accordingly.
1.1 Synopsis, 4.1 Overall Design, 5.1 Inclusion Criteria	The inclusion criteria were modified to accommodate the following changes:	These modifications were made to clarify the characteristics of the population within the scope of the study.
	• Should have a confirmed diagnosis of palmoplantar-non-pustular psoriasis with palm and/or sole involvement and at least one plaque at a body site other than the palms and soles for at least 6 months to confirm a diagnosis of chronic psoriasis.	The addition of "palms and/or soles" will ensure inclusion of participants who might have either, or both, palm and sole involvement. The addition of at least 6 months of disease ensures the enrollment of participants with chronic psoriasis.
	• Participants should have a ppIGA score ≥3 at screening and at baseline.	The ppIGA ≥3 criterion was added to define the inclusion of participants with moderate-to-severe palmoplantar

Section Number and Name	Description of Change	Brief Rationale
	• Aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase levels that would allow for inclusion in the study have been modified from <1.5 times the upper limit of normal (ULN) range to <2 ULN. • User-dependent methods of contraception: combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, and transdermal; progestogen-only hormone contraception associated with inhibition of ovulation: oral and injectable. • Participants must be compliant with the completion requirements for the PROs used in the study.	psoriasis and moderate psoriasis. The levels of AST, ALT and APH were amended for consistency with prior clinical trials (VOYAGE-1 and VOYAGE-2) which evaluated guselkumab for the treatment of psoriasis. The inclusion criteria were updated to include both user-independent and user-dependent methods of contraception aligned with the appendix. Both methods are considered highly effective. The PRO criterion was added to ensure the inclusion of participants who can comply with the completion requirements for the PROs used in the study.
1.1 Synopsis, 4.1 Overall Design, 5.2 Exclusion Criteria	The exclusion criteria were modified to accommodate the following changes: • Criterion 1: Currently has palmoplantar pustulosis, pustular psoriasis, or any other forms other than plaque-type psoriasis (eg, erythrodermic, guttate) or hyperkeratotic eczema. • Criterion 2 (has psoriasis with >10% BSA) was deleted. • Criterion 6 was modified to exclude pregnant, nursing, or planning a pregnancy (both men and women) while enrolled in this study, and for at least 12 weeks after the last administration of study intervention. • Criterion 7 was modified to include topical anti-psoriatic medication/treatments. • Criterion10: The washout period for methotrexate was specified as 2 weeks before the first administration of the study intervention. • Criterion 11: Apremilast, systemic immunosuppressive drugs, biologic agents, cytotoxic drugs and JAK inhibitors were added to the list of prohibited systemic treatments received by participants within 4 weeks of the first administration of the study intervention. • Criterion 32 was deleted. (Has any condition that, in the opinion of the investigator, would make participation	To ensure the homogeneity of the participants in the current study, and for consistency with prior studies evaluating the efficacy of guselkumab in palmoplantar psoriasis. Deleted due to redundancy since PASI score ⩾3 and <10 has been added as an inclusion criterion. Modified for consistency with previous protocols evaluating the efficacy of guselkumab in psoriasis. Participants who have received prior medications that could affect efficacy evaluations during the study will be excluded. This was a repetition of criterion 28.

Section Number and Name	Description of Change	Brief Rationale
	not be in the best interest (eg, compromise the well-being) of the participant or that could prevent, limit, or confound the protocol-specified assessments)	
6.5.1 Rescue Medication	• Marked disease worsening has been defined as a 25% increase in ppPASI score from baseline. • At the time any rescue medication is initiated by a participant, the study intervention will be stopped, and the participant will be considered a non-responder. Participants who are allowed to use a rescue medication are encouraged to continue in the study until Week 16 for further evaluation. Participants who start a rescue medication after Week 16 will have to stop the study intervention and will be encouraged to come for a safety follow up visit 12 weeks after the last study intervention administration.	The definition of disease worsening clarifies the time frame during which a rescue medication is permitted to be used in the study. Rescue medications could affect efficacy evaluations; therefore, these patients will be classified as non-responders and will stop the study intervention.
6.5.2.1 Systemic and Topical Therapy	Systemic therapies for psoriasis such as MTX, apremilast, systemic immunosuppressive drugs, biologic agents, cytotoxic drugs, JAK inhibitors, or investigational agents are not permitted. Agents that include salicylic acid, urea or any agents which have anti-psoriatic effects will not be permitted.	Systemic and topical medications could affect efficacy evaluations and confound outcomes attributable to the intervention (guselkumab) being used in the study.
6.5.3 Concomitant Medications for Conditions Other than Palmoplantar-non-pustular Psoriasis	Only the use of inhaled, otic or ophthalmic corticosteroids are permitted as a concomitant medication for indications other than palmoplantar-non-pustular psoriasis.	Medications that could affect efficacy evaluations for palmoplantar-non-pustular psoriasis will not be permitted during the study.
7.2 Participant Discontinuation/Withdrawal from the Study	The following criteria were added: • Initiation of rescue medication after Week 16. • Occurrence of pustules consistent with a diagnosis of palmoplantar pustulosis.	Rescue medication could affect the efficacy results when administered in conjunction with guselkumab; therefore, participants for whom they are prescribed will be withdrawn from the study. The study is not powered to evaluate the efficacy of guselkumab in participants with palmoplantar pustulosis.
8.1 Efficacy Assessments	The following text was added: The investigator-led assessments of efficacy (PASI, ppPASI, ppIGA, BSA) will be performed at the site by an assessor trained by the Sponsor, at the appropriate visits as outlined by the SOA. Efficacy assessments should preferably be done by a dermatologist; if a dermatologist is not available, a health care provider with at least 1 year of experience in performing	The text was added to provide guidance on the efficacy assessors experience and qualifications required by the Sponsor for the study.

Section Number and Name	Description of Change	Brief Rationale
	psoriasis efficacy assessments, after training by the Sponsor, may serve as an assessor. Health care providers with less than 1 year of experience may serve as an assessor after training by the Sponsor, based on the discretion and approval of the Sponsor.	
Section 1.1 Synopsis, Section 4.1 Overall Design, Section 8.1.3 Photographs of Palms and Soles	Overview photographs of palms and soles will be collected for publication purposes from a subset of participants who provide optional consent.	The text was added to clarify that the collection of optional photographs was not linked to efficacy evaluations of guselkumab in the study, but for publication purposes only.
8.3 Adverse Events and Serious Adverse Events	Anticipated adverse events will not be recorded or reported in this study. Consequently Appendix 7 Anticipated Events has also been deleted.	Since the reporting of anticipated adverse events is an FDA requirement, and the current study will be conducted only in Europe, the section on anticipated adverse events is not applicable.
9 Statistical Considerations	The following disclaimer was added: As guselkumab versus placebo comparisons for secondary endpoints are not based on pre-specified hypotheses, treatment effect estimates will be accompanied by 95% confidence intervals (CIs). Provided p-values will be considered nominal and are not to be interpreted as confirmatory.	Since p-values will be provided for the analysis of secondary endpoints, the disclaimer was added to reiterate the non-confirmatory nature of the secondary analysis.
10 Supporting Documentation and Operational Considerations	Sample clinician assessments, patient-reported outcomes questionnaires have been added as appendices.	Sample questionnaires and assessments were added for reference.
10.6 Appendix 6 Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting	The attribution definitions and assessment of causality of adverse events have been updated. The following criteria were deleted from Special Reporting Situations: • Medicinal product exposure during pregnancy (maternal and paternal). • Suspected transmission of any infectious agent via a medicinal product • Off-label use	These criteria have been updated and aligned with the current Janssen protocol template.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted and corrected accordingly.

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1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 3b, Multicenter, Interventional, Randomized, Placebo-controlled Study Investigating the Efficacy and Safety of Guselkumab for the Treatment of Palmoplantar-non-Pustular Psoriasis

Guselkumab is a fully human immunoglobulin G1 lambda monoclonal antibody that binds to the p19 protein subunit of human interleukin 23 (IL-23) with high specificity and affinity. Binding of guselkumab to the IL-23 p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23 specific intracellular signaling and subsequent activation and cytokine production. In this manner, guselkumab inhibits the biological activity of IL-23 in all in vitro assays examined. Guselkumab is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy.

OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate the efficacy of guselkumab for the treatment of palmoplantar psoriasis	Proportion of ppPASI75 responders in the guselkumab group versus the placebo group at Week 16
Secondary	
To evaluate the efficacy of guselkumab in improving general plaque psoriasis in participants with palmoplantar psoriasis	• Change from baseline in BSA and absolute PASI scores, and percentage change in PASI scores (PASI 75, 90 and 100) in the guselkumab group versus the placebo group at Week 16 • Change from baseline in BSA and absolute PASI scores, and percentage change in PASI scores (PASI 75, 90 and 100) in the guselkumab group at Weeks 24 and 48
To evaluate the efficacy of guselkumab in improving clinician assessments and disease-related patient-reported quality-of-life measures in participants with palmoplantar psoriasis	• Change from baseline in ppQLI, DLQI, EQ-5D-5L and ppIGA scores in the guselkumab group versus the placebo group at Week 16 • Change from baseline in f-PGA scores in the guselkumab group versus the placebo group at Week 16 • Change from baseline in ppQLI, DLQI, EQ-5D-5L and ppIGA scores in the guselkumab group at Weeks 24 and 48 • Change from baseline in f-PGA scores in the guselkumab group at Weeks 24 and 48
To evaluate the efficacy, patient-reported quality-of-life assessments and other scores in the placebo-crossover group at different timepoints	• BSA, PASI and ppPASI75 scores at Weeks 24 and 48 • DLQI, ppQLI, EQ-5D-5L, ppIGA, f-PGA, WPAI:PSO, NRS:P at Weeks 24 and 48

To evaluate the maintained efficacy of guselkumab for the treatment of palmoplantar psoriasis	Change from baseline in ppPASI scores in the guselkumab group at Weeks 24 and 48
To evaluate the efficacy of guselkumab in improving work productivity and limitations in participants with palmoplantar psoriasis	• Change from baseline in WPAI:PSO and NRS:P scores in the guselkumab group versus the placebo group at Week 16 • Change from baseline in WPAI:PSO and NRS:P scores in the guselkumab group at Weeks 24 and 48
To evaluate safety of guselkumab in participants with palmoplantar psoriasis	Rate of adverse events in the guselkumab and placebo/placebo-crossover groups

Abbreviations: BSA = Body Surface Area; DLQI = Dermatology Life Quality Index; EQ-5D-5L = European Quality of Life, 5-Dimension, 5-Level, f-PGA = Fingernails Physician Global Assessment; NRS:P = Numeric Rating Scale: Pain; PASI = Psoriatic Area and Severity Index; ppPASI = Palmoplantar Psoriatic Area and Severity Index; ppIGA = Palmoplantar Investigator's Global Assessment; ppQLI = Palmoplantar Quality-of-Life Index; WPAI:PSO = Work Productivity and Activity Index: Psoriasis
For endpoints related to Week 24 and Week 48 (and any analysis at Week 56), the placebo group will be termed the "placebo-crossover" group

HYPOTHESIS

The primary hypothesis is that guselkumab (administered as 100 mg at Weeks 0, 4 and 12) is superior to placebo as assessed by the proportion of participants achieving ppPASI75 response at Week 16.

OVERALL DESIGN

This is a Phase 3b, double-blind, prospective, placebo-controlled, multicenter study in participants aged ≥18 years who have a confirmed diagnosis of moderate-to-severe palmoplantar-non-pustular psoriasis with PASI score ≥3 and <10 and ppIGA ≥3, with palms and/or soles affected and at least 1 plaque at a body site other than the palms or soles (any size) for at least 6 months, to confirm a diagnosis of chronic psoriasis.

The study will be divided into 2 phases:

Double-blind Phase:

- Guselkumab group: Guselkumab (100 mg) subcutaneous (SC) injections at Weeks 0, 4, 12 and placebo injection at Week 16.
- Placebo group: Placebo SC injections at Weeks 0, 4, 12 and guselkumab (100 mg) SC injection 16.

Open-label Phase:

- Both guselkumab and placebo-crossover groups will receive guselkumab (100 mg) SC injections at Weeks 20, 28, 36, and 44.

The study will have an overall duration of 56 weeks. Key efficacy assessments include physician assessments (ppPASI, ppIGA, PASI, BSA, f-PGA) and patient-reported outcomes (PRO) questionnaires (WPAI-PSO, NRS:P, EQ-5D-5L, ppQLI, and DLQI) at Weeks 16, 24 and 48. Overview photographs of palms and soles will be collected for publication purposes from a subset of participants who provide optional consent. Safety and tolerability evaluations will include 12-lead electrocardiogram at baseline, pregnancy testing (for female participants) and monitoring of vital signs at all visits and recording of adverse events throughout the study. Biomarker assessments will include the evaluation of relevant markers in serum for all participants. For an optional pharmacogenomic assessment, it is the intention to collect whole blood samples from 50 participants enrolled in the study.

NUMBER OF PARTICIPANTS

The study will enroll a total of 105 participants. Following screening for inclusion into the study, eligible participants will be randomized (1:2 ratio) to receive either placebo or guselkumab (100 mg) SC, respectively.

INTERVENTION GROUPS AND DURATION

Participants in each study group will receive one injection of study intervention at each time-point detailed below:

- **Guselkumab group (guselkumab 100 mg):**
  - Guselkumab injection: Weeks 0, 4, 12, 20, 28, 36 and 44
  - Placebo injection: Week 16
- **Placebo group**:
  - Placebo injection: Weeks 0, 4 and 12
  - Guselkumab 100 mg injection: Weeks 16, 20, 28, 36, and 44

NOTE: The placebo group will be termed the placebo-crossover group for endpoints related to Week 24 and Week 48

Study intervention will always be administered at the site and by a health care professional (HCP), until the participant (or caregiver) is trained for self-administration. Study intervention will be administered by site personnel at Weeks 0 and 4. Beginning at Week 12, at the discretion of the investigator and participant and after appropriate and documented training, participants may self-administer study intervention at the investigative site under the supervision of an HCP. A caregiver may also be trained to administer study intervention. Participants unable or unwilling to self-administer will continue to have study intervention injections performed by an HCP.

EFFICACY EVALATIONS

Palmoplantar Psoriasis Response Evaluations

- Palmoplantar Psoriasis Area and Severity Index (ppPASI)
- Psoriasis Area and Severity Index (PASI)
- Palmoplantar Investigator Global Assessment Scale (ppIGA)
- Body Surface Area (BSA) percentage score
- Fingernail-Physician Global Assessment (f-PGA)

Patient-Reported Outcomes

- Dermatology Life Quality Index (DLQI)
- Work Productivity and Activity Impairment: Psoriasis (WPAI:PSO)
- Numeric Rating Scale: pain (NRS:P)
- Palmoplantar Quality-of-Life Instrument (ppQLI)
- European Quality of Life Group, 5-Dimension, 5-Level (EQ 5D-5L)

Photographs of the palms and soles will be collected for publication purposes.

PHARMACOGENOMIC (DNA) EVALUATIONS

A pharmacogenomic blood sample will be collected to allow for pharmacogenomic research, as necessary where local regulations permit. Participation in the pharmacogenomic research is optional.

SAFETY EVALUATIONS

The safety and tolerability of study intervention (guselkumab and placebo) will be monitored by collecting information on adverse events (including injection-site and allergic reactions), clinical laboratory tests, physical examinations, vital signs and concomitant medication review through Week 56.

STATISTICAL METHODS

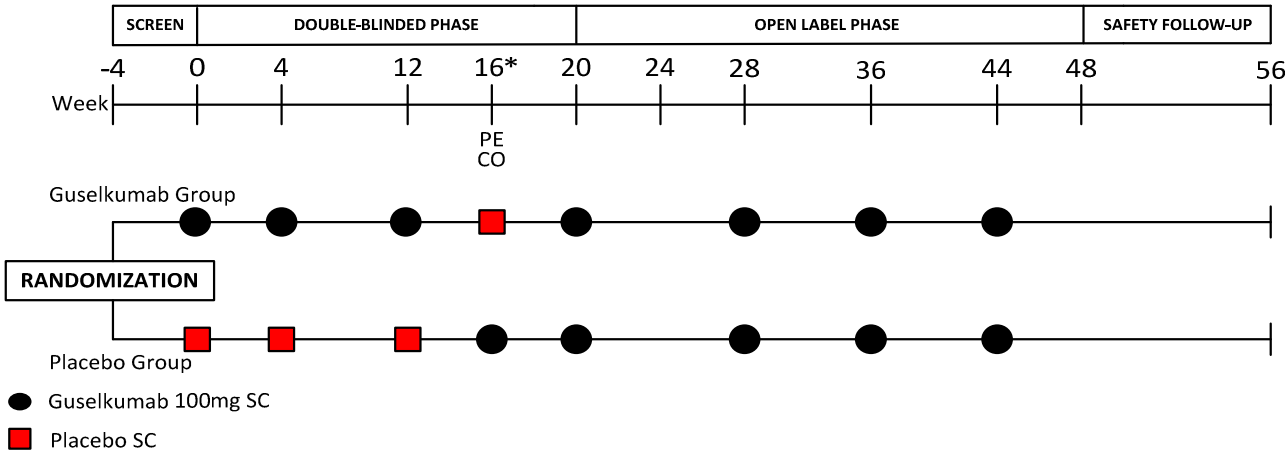
The assumptions for the sample size were based on results from a secondary analysis of palms and/or soles data in participants with psoriasis treated with guselkumab in two Phase 3 trials, and three Phase 3 trials in participants with palmoplantar psoriasis treated with ixekizumab. Based on these studies, it is assumed that the Week 16 ppPASI75 response rate in the placebo arm will not exceed 12.5%. With an assumed response rate of at least 45% in the guselkumab arm and maximally 12.5% in the placebo arm, sample sizes of 64 in the guselkumab arm and 32 in the placebo arm would achieve at least 90% power. The statistical test to be used is the two-sided Fisher's Exact test. The significance level of the test is targeted at 0.05. Participants will be randomized in a 2:1 ratio to the guselkumab and placebo arms.

To compensate for 8% non-evaluable participants, approximately 70 participants will be randomized to the guselkumab group and 35 participants to the placebo group. In total 105 participants will be randomized.

Simple descriptive summary statistics, such as n, mean, standard deviation (SD), median, interquartile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data. All statistical procedures will be performed 2-sided at a significance level of 0.05. In addition to statistical analyses, graphical summaries of the data may be used.

Database locks are planned at Week 16 and at End of Study. The analysis of the primary endpoint for Week 16 will be carried out at the first database lock after all randomized participants complete their assessments at Week 16 or discontinue the study before Week 16. The analysis of the secondary endpoints for Week 24 and Week 48 will be carried out after the second database lock at End of Study.

1.2. Schema



Abbreviations: CO = crossover; PE = primary endpoint; SC = subcutaneous.
Each symbol represents 1 injection.
*At Week 16, all participants in placebo group will crossover to receive guselkumab 100 mg SC at Weeks 16, 20, and then q8w through Week 44; Participants in the guselkumab group will remain on the dosing regimen they were randomized to at Week 0 through Week 44 and will receive a placebo injection at Week 16.
The placebo group will be termed the placebo-crossover group for endpoints related to Week 24 and Week 48

1.3. Schedule of Activities (SoA)

Period	Screening[a]	Placebo-controlled Treatment				Active Treatment							Safety Follow-up
Week	**–4 to 0**	**0[b]**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**36**	**44**	**48 or Final Efficacy Visit[c]**	**56 or Final Safety Visit**
Visit Window (Days)[d]			**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±14**
Screening/Administrative													
Informed consent form	X												
Review of inclusion/exclusion criteria	X	X											
Demography/medical history	X												
Occupational Status		X				X		X				X	
Planned surgery/procedure(s)	X												
Prior therapy review for eligibility	X	X											
Study Intervention Administration													
Randomization		X											
Study intervention administratione		X	X		X	X	X		X	X	X		
Safety Assessments													
Physical examination (including skin)	X					X							X
Vital signs[f]	X	X	X	X	X	X	X	X	X	X	X	X	X
Height		X											
Weight		X				X						X	
12-lead ECG[g]		X											
QFT test[h]	X												
Tuberculosis evaluation[i]		X	X	X	X	X	X	X	X	X	X	X	X
Chest radiograph[j]	X												
Pregnancy test[k]	X	X	X	X	X	X	X	X	X	X	X	X	X
Injection-site reaction evaluation		X	X		X	X	X		X	X	X		
Efficacy Assessments[l]													
ppPASI	X	X	X	X	X	X	X	X	X	X	X	X	
ppIGA	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	
BSA %		X				X		X			X	X	
f-PGA		X				X		X			X	X	
DLQI		X				X		X			X	X	
ppQLI		X				X		X			X	X	
EQ-5D-5L		X				X		X			X	X	

Period	Screening[a]	Placebo-controlled Treatment				Active Treatment							Safety Follow-up
Week	**–4 to 0**	**0[b]**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**36**	**44**	**48 or Final Efficacy Visit[c]**	**56 or Final Safety Visit**
Visit Window (Days)[d]			**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±7**	**±14**
WPAI:PSO		X				X		X			X	X	
NRS:P		X				X		X			X	X	
Photographs[m]		X	X	X	X	X	X	X	X	X	X	X	
Clinical Laboratory Tests[n]													
HBV/HCV serology	X												
HIV antibody test	X												
Hematology	X	X	X		X	X		X	X	X		X	X
Chemistry	X	X	X		X	X		X	X	X		X	X
Lipid panel[b]		X											
C-reactive protein	X	X	X	X	X	X	X	X	X	X	X	X	X
Follicle stimulating hormone[o]	X												
Biomarker Assessment													
Serum sample[p]		X				X		X				X	
Pharmacogenomic Assessment													
Whole Blood (DNA)[q]		X											
Ongoing Review													
Concomitant therapy[r]	X (throughout study)												
Adverse events	X (throughout study)												

Abbreviations: BSA = body surface area; DLQI = Dermatology Life Quality Index; ECG = electrocardiogram; EQ-5D-5L = European Quality of Life, 5-Dimension, 5-Level, f-PGA = Fingernails Physician Global Assessment; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; NRS:P = Numeric Rating Scale: Pain; PASI = Psoriatic Area and Severity Index; ppPASI = Palmoplantar Psoriatic Area and Severity Index; ppIGA = Palmoplantar Investigator's Global Assessment; ppQLI = Palmoplantar Quality-of-Life Index; QFT = QuantiFERON®-TB; WPAI:PSO = Work Productivity and Activity Index: Psoriasis

Footnotes:

a. The screening visit may be completed in a single visit or may be divided into more than 1 visit. It is recommended that after obtaining informed consent, the investigator completes the QFT test and all laboratory tests at the first visit. The participant may then return for the remainder of the screening procedures only if the participant is eligible for the study as determined by the central laboratory test results.

b. Participants must fast (ie, no food or beverages [except water]) for at least 8 hours before blood is drawn for lipid panel at Week 0. All other visits can be non-fasting because lipid panel will not be analyzed post-baseline.

c. If a participant permanently discontinues study intervention before Week 44, the Final Efficacy Visit should occur at the time of discontinuation or as soon as possible and all assessments scheduled for the Final Efficacy Visit should be performed. The participant should also return for a Final Safety Visit, 12 weeks after the last study intervention administration.

d. The study participants may receive notifications via a mobile app on their own device as per protocol scheduled events (eg, next clinical site visit, feedback on the use of the mobile app).

e. Always administered at the site by HCP at Weeks 0 and 4 and self-administered thereafter till Week 44 under supervision of HCP. Participants unable or unwilling to self-administer will continue to have study intervention injections performed by an HCP.
f. Vital signs include blood pressure, heart rate and axillary temperature.
g. 12-lead ECG must be done at Week 0 before administration of study intervention (for local assessment only).
h. The QFT test must be conducted within 8 weeks before initiating administration of study intervention. If QFT is not approved/registered in the country in which this study is being conducted, a tuberculin skin test is also required, with the exceptions noted in Inclusion Criterion 9 in Section 5.1.
i. After the screening visit, participants will be asked specific questions about a history of tuberculosis or known occupational or other personal exposure to individuals with active tuberculosis.
j. The chest radiograph may be taken within 3 months prior to the first administration of study intervention.
k. Women of childbearing potential who are dosed at the clinic must have a negative urine pregnancy test at screening and at all visits. The result must be negative before the administration of the study intervention at a dosing visit. Additional urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulations, to establish the absence of pregnancy at any time during the participation in the study.
l. All participant questionnaires should be completed before any other tests, procedures, evaluations, or study intervention administration on the day of the visit for baseline and post-baseline visits.
m. To be performed in a subset of participants who have provided optional consent for photography of palms and soles; see separate photography manual.
n. Laboratory tests are described in Appendix 4.
o. Prior to randomization, follicle stimulating hormone (FSH) is required for selected female participants to determine childbearing potential. This test is only required for a female participant of any age with amenorrhea for at least 6 months. This test should NOT be done for any female participant of childbearing potential or female participants >45 years of age with amenorrhea for at least 12 months. Refer to Inclusion Criterion 5 in Section 5.1 for details.
p. Biomarker assessments will include the evaluation of relevant markers in serum, including but not limited to markers associated with the IL-23/Th17 pathway (IL 17A, IL-17F and IL-22) and anti-microbial peptides.
q. Whole blood for genetic analyses will be collected (where local regulations permit) only from participants who sign a separate informed consent form (ICF) to participate in the optional pharmacogenomic sub-study. The pharmacogenomic (DNA) sample should be collected at the specified time-point; however, if necessary it may be collected later without constituting a protocol deviation.
r. Rescue medication received by participants will be documented along with concomitant medication at all the study visits.

2. INTRODUCTION

Psoriasis is a systemic, chronic, inflammatory disease affecting approximately 1% to 3% of the population worldwide.[23] The extent of skin involvement is very variable and ranges from discrete, localized areas to generalized body involvement.[30] Psoriasis may be resistant to treatment and shows frequent relapse. Additionally, some body areas such as hands, intertriginous areas, scalp and nails are more resistant to treatment, or are too sensitive to be treated with strong topical drugs, necessitating systemic drugs more frequently.[24]

Palmoplantar psoriasis is a clinical variant of plaque psoriasis, which may occur in isolation or in association with diffuse psoriasis vulgaris.[7] It is a chronic, debilitating disease affecting approximately 12% of psoriasis patients and is characterized by hyperkeratotic lesions along the palms and soles extending to the wrists and the margins of the soles and heels.[7,16] It has been observed that palmoplantar psoriasis is associated with greater impairment of skin-related quality-of-life and patients are more likely to report heavy use of topical prescriptions compared with patients with moderate-to-severe plaque psoriasis.[16]

A rapidly growing body of literature suggests that the interleukin (IL)-23/IL-17 pathway contributes to the chronic inflammation underlying the pathophysiology of many immune-mediated diseases, such as psoriasis, multiple sclerosis, rheumatoid arthritis (RA), inflammatory bowel disease, ankylosing spondylitis, psoriatic arthritis (PsA) and palmoplantar (small surfaces) pustulosis (PPP).[25,27]

Guselkumab (TREMFYA®) is a fully human immunoglobulin G1 lambda monoclonal antibody (mAb) that binds to the p19 protein subunit of human interleukin 23 (IL-23) with high specificity and affinity. Binding of guselkumab to the IL-23 p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23 specific intracellular signaling and subsequent activation and cytokine production. Guselkumab is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy. It is now being investigated for the treatment of a variety of immune-mediated diseases including PsA and Crohn's Disease. In a recent review, other therapies that also target mediators of inflammation in the IL-23/Th17 axis, such as ustekinumab and IL-17 inhibitors, have been shown to be effective in the treatment of palmoplantar psoriasis.[24] Guselkumab has demonstrated efficacy and was well tolerated in a Phase 2 proof-of-concept trial evaluating palmoplantar pustulosis in Japanese patients.[28] Furthermore, substantial improvements in psoriasis involving the hands and feet were reported in two large guselkumab Phase 3 randomized, controlled trials in moderate-to-severe psoriasis.[2,21] These results support further investigation of the efficacy and safety of guselkumab for the treatment of palmoplantar-non-pustular psoriasis in this Phase 3b clinical trial.

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[6] and the EU Summary of Product Characteristics.[26]

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.

The term "study intervention" throughout the protocol, refers to both guselkumab and placebo injections.

2.1. Study Rationale

Chronic plaque psoriasis is the most common form of psoriatic skin disease; however there is growing evidence that other variants including scalp, nail, inverse, and palmoplantar psoriasis are prevalent, undertreated, and are correlated with an increased risk of PsA.[29] Involvement of the scalp, nails, palms, soles and intertriginous areas including the genitalia, may result in significant morbidity with functional impairment and greater impairment in quality of life.[5]

Although biologics have been observed to be efficacious in the treatment of palmoplantar psoriasis, treatment algorithms have not been properly defined as there is a lack of large, placebo-controlled, randomized trials that have focused exclusively on this condition.[24] There remains an unmet need for effective treatment of palmoplantar-non-pustular psoriasis confirmed by randomized, controlled trials. Data from guselkumab Phase 3 trials in plaque psoriasis (CNTO1959PSO3001 [VOYAGE-1][2] and CNTO1959PSO3002 [VOYAGE-2][21]) demonstrated that a higher proportion of participants treated with guselkumab achieved hands-and-feet-Physician's Global Assessment (hf-PGA) scores of 0 and 0 or 1 after 16 and 24 weeks of treatment (compared with placebo or adalimumab, and adalimumab, respectively).' Treatment with guselkumab in a Phase 2 trial in palmoplantar pustulosis demonstrated that a significantly higher proportion of participants achieved higher Palmoplantar Pustulosis Severity Index (PPSI) and Palmoplantar Psoriatic Area and Severity Index (ppPASI) scores compared with placebo at Week 16, with the improvements maintained up to Week 24.[28] This study aims to bolster these results by providing robust efficacy and safety data on guselkumab treatment for palmoplantar-non-pustular psoriasis.

2.2. Background

Nonclinical Studies

Refer to the IB[6] for guselkumab for information about nonclinical studies.

Clinical Studies

Overall, the clinical development program for guselkumab includes trials in participants with psoriasis, palmoplantar pustulosis and PsA.

Efficacy

Psoriasis

Phase 3: In 2 large placebo- and active-controlled studies (VOYAGE-1 and VOYAGE-2),

- The proportion of participants who demonstrated improvements in psoriasis as assessed by all 4 PASI (PASI 100, PASI 90, PASI 75, and PASI 50) and IGA responses was higher among those receiving guselkumab 100 mg subcutaneously (SC) at Weeks 0, 4, and q8w compared with the placebo and adalimumab groups. Responses were observed beginning at Week 8 and maintained up to Week 100. Participants receiving adalimumab who crossed over to guselkumab at Week 52 showed rapid improvements in PASI and IGA scores, with the improvements maintained up to Week 100.
- In participants with baseline hf-PGA scores ≥2, guselkumab treatment produced a significantly higher proportion of participants with hf-PGA scores of clear (0) or almost clear (1), and at least a 2-grade improvement from baseline than placebo ($p<0.001$) at Week 16. At Week 24 and Week 48, guselkumab treatment produced a significantly higher proportion of participants with hf-PGA score of 0 or 1 and at least a 2-grade improvement from baseline than adalimumab ($p=0.001$ and $p=0.045$, respectively, at Week 24 and Week 48).
- Substantial, significant and clinically meaningful improvements were observed in skin, scalp, nail, hand and foot psoriasis, and patient-reported outcomes (PROs) compared with placebo through Week 16. Guselkumab demonstrated superior efficacy in the treatment of skin, scalp, hand and foot psoriasis, and PROs compared with adalimumab through Week 24.
- Most participants experienced clinically meaningful improvements in psoriasis symptoms (erythema, induration, and scaling) and involved body regions (head, trunk, upper extremities, and lower extremities) as measured by PASI 75 response. Following sustained treatment, the proportions of participants achieving a maximum PASI 90 response within 5 months after initiation, and a maximum PASI 100 response within 7 months were maintained through 1 year, with response rates for PASI and IGA response measures remaining stable for up to 2 years.
- Retreatment with guselkumab among PASI 90 responders withdrawn from treatment resulted in approximately 90% achieving a PASI 90 response within 6 months. Guselkumab was effective across all subpopulations, as defined by gender, baseline age, baseline weight, race, geographic region, baseline disease characteristics (including the comorbidity of PsA), and psoriasis treatment history.
- Participants receiving guselkumab demonstrated significant improvement in health-related quality-of-life and psoriasis symptoms and signs as measured by DLQI and Psoriasis Symptoms and Signs Diary measures, respectively, compared with those who received placebo and adalimumab.

- In a plaque psoriasis study (CNTO1959PSO3003: NAVIGATE), participants with an inadequate response to ustekinumab benefitted from switching to guselkumab, and approximately twice as many participants receiving guselkumab achieved clinical responses compared with participants receiving ustekinumab, with significant improvement in PASI and IGA scores as early as 4 weeks after switching.

- In an ongoing plaque psoriasis study in Japan (CNTO1959PSO3004), in general, clinical responses obtained at Week 16 in the guselkumab 50 mg and 100 mg groups either continued to improve or were maintained after Week 16 through Week 52 for all endpoints.
- Efficacy of guselkumab in the treatment of generalized pustular psoriasis (GPP) and erythrodermic psoriasis (EP) has been demonstrated (CNTO1959PSO3005). A majority of participants with GPP (77.8%) and EP (90.9%) achieved treatment success with guselkumab at Week 16, with results supported the efficacy of guselkumab through Week 52.
- In participants with moderate-to-severe plaque psoriasis (CNTO1959PSO3006: ORION), guselkumab treatment using a novel self-injection device gave rise to significantly higher proportions of participants achieving an IGA score of 0 or 1 (80.6% vs. 0.0%, p<0.001) and a PASI 90 response (75.8% vs. 0.0%, p<0.001), compared with placebo. In addition, significantly higher proportions of participants receiving guselkumab achieved an IGA score of 0 (56.5% vs 0.0, p<0.001) and a PASI 100 response (50.0% vs 0.0, p<0.001) at Week 16, compared with placebo.

Palmoplantar Pustulosis

In a Phase 2 study in Japan in participants with palmoplantar pustulosis, those receiving guselkumab demonstrated significantly better improvement from baseline in PPSI and Palmoplantar Pustulosis Area and Severity Index (ppPASI) total scores at Week 16 compared with placebo, with the numerical difference in PPSI generally maintained from Week 16 through Week 24 (CNTO1959PPP2001).

In a palmoplantar pustulosis Phase 3 study in Japan with a blinded treatment period up to Week 60 and observation period up to Week 84, results from the interim analysis demonstrated superior efficacy for guselkumab compared with placebo at Week 16 (p=0.017 for guselkumab 200 mg vs placebo and p<0.001 for guselkumab 100 mg vs placebo) and Week 24 with regards to change from baseline in the ppPASI total score. Efficacy observed in participants treated with guselkumab at Week 16 continued to improve through Week 52 (CNTO1959PPP3001).

Safety

Clinical data from the Phase 1 and Phase 2 studies in healthy participants, participants with psoriasis, participants with PsA, PPP and RA indicate that guselkumab administered intravenously (IV) or SC was generally well tolerated.

The safety of guselkumab was analyzed in a total of 1,721 participants from 2 placebo- and active-controlled Phase 3 studies (CNTO1959PSO3001 and CNTO1959PSO3002). Participants received guselkumab 100 mg SC at Weeks 0, 4, and q8w thereafter, or crossed over from placebo at Week 16, or from adalimumab treatment at Week 48 (CNTO1959PSO3001) and Week 28 (CNTO1959PSO3002).

- Participants receiving guselkumab demonstrated similar infrequent serious adverse event (SAE) rates compared with those receiving adalimumab through up to 2 years of therapy, with most SAEs being single occurrence, infection-related events.

- The rates of SAEs and AEs leading to discontinuation of guselkumab were similar following 3 years (Week 156) of treatment, suggesting no increased risk following prolonged exposure.
- No events of tuberculosis (TB) or opportunistic infection were reported with guselkumab treatment.
- The incidences of malignancies and major adverse cardiovascular events (MACE) through 1 and 2 years of treatment with guselkumab were low and generally comparable with adalimumab treatment and did not suggest any specific association with guselkumab treatment.
- A small proportion of participants reported injection-site reactions following guselkumab administration, almost all of which were mild and did not result in discontinuation of treatment. The frequency of injection-site reactions remained low through 2 years of treatment.
- In guselkumab clinical studies to date, no anaphylactic reactions or serum sickness-like reactions to guselkumab have been reported; however, anaphylactic reactions and serum sickness-like reactions (also known as delayed hypersensitivity reactions) have been associated with mAbs and may occur with guselkumab. Based on this evaluation, the Marketing Authorization Holder has concluded that serious hypersensitivity reactions are a newly identified risk that should be reflected in the label.

Overall, safety outcomes showed that the guselkumab 100 mg dosing regimen at Weeks 0 and 4 and q8w thereafter was well tolerated, with a favorable safety profile in participants with moderate-to-severe plaque psoriasis. A review of the cumulative safety data and risk-benefit analysis did not identify any change to the risk-benefit profile of guselkumab.

For the latest and most comprehensive information regarding safety and adverse drug reactions pertaining to guselkumab, refer to the latest version of the Investigator's Brochure.

2.3. Benefit/Risk Assessment

Guselkumab has undergone extensive nonclinical and clinical development, and available animal and human data strongly support the critical role of IL-23 in the pathogenesis of psoriasis and PPP.[14,18] A potential benefit therefore exists for an anti-IL-23 mAb in the treatment of palmoplantar-non-pustular psoriasis.

The lack of standardized outcome measures for palmoplantar-non-pustular psoriasis can be seen to limit the value of the clinical trial. However, the physician assessments and PRO questionnaires used in this study have been widely used and reported in clinical trials for the treatment of psoriasis and related conditions (Section 8), and will provide a substantial data set on the responsiveness to guselkumab, supporting the objectives of augmented health-related quality-of-life (HRQoL) and symptom benefit of the drug.

More detailed information about the known and expected benefits and risks of guselkumab may be found in the IB.[6]

3. OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate the efficacy of guselkumab for the treatment of palmoplantar psoriasis	Proportion of ppPASI75 responders in the guselkumab group versus the placebo group at Week 16
Secondary	
To evaluate the efficacy of guselkumab in improving general plaque psoriasis in participants with palmoplantar psoriasis	• Change from baseline in BSA and absolute PASI scores, and percentage change in PASI scores (PASI 75, 90 and 100) in the guselkumab group versus the placebo group at Week 16 • Change from baseline in BSA and absolute PASI scores, and percentage change in PASI scores (PASI 75, 90 and 100) in the guselkumab group at Weeks 24 and 48
To evaluate the efficacy of guselkumab in improving clinician assessments and disease-related patient-reported quality-of-life measures in participants with palmoplantar psoriasis	• Change from baseline in ppQLI, DLQI, EQ-5D-5L and ppIGA scores in the guselkumab group versus the placebo group at Week 16 • Change from baseline in f-PGA scores in the guselkumab group versus the placebo group at Week 16 • Change from baseline in ppQLI, DLQI, EQ-5D-5L and ppIGA scores in the guselkumab group at Weeks 24 and 48 • Change from baseline in f-PGA scores in the guselkumab group at Weeks 24 and 48
To evaluate the efficacy, patient-reported quality-of-life assessments and other scores in the placebo-crossover group at different timepoints	• BSA, PASI and ppPASI75 scores at Weeks 24 and 48 • DLQI, ppQLI, EQ-5D-5L, NRS:P, ppIGA, f-PGA, WPAI:PSO at Weeks 24 and 48
To evaluate the maintained efficacy of guselkumab for the treatment of palmoplantar psoriasis	Change from baseline in ppPASI scores in the guselkumab group at Weeks 24 and 48
To evaluate the efficacy of guselkumab in improving work productivity and limitations in participants with palmoplantar psoriasis	• Change from baseline in WPAI:PSO and NRS:P scores in the guselkumab group versus the placebo group at Week 16 • Change from baseline in WPAI:PSO and NRS:P scores in the guselkumab group at Weeks 24 and 48

To evaluate safety of guselkumab in participants with palmoplantar psoriasis	Rate of adverse events in the guselkumab and placebo/placebo-crossover groups

Abbreviations: BSA = Body Surface Area; DLQI = Dermatology Life Quality Index; EQ-5D-5L = European Quality of Life, 5-Dimension, 5-Level; f-PGA = Fingernails Physician Global Assessment; NRS:P = Numeric Rating Scale: Pain; PASI = Psoriatic Area and Severity Index; ppIGA = Palmoplantar Investigator's Global Assessment; ppPASI = Palmoplantar Psoriatic Area and Severity Index; ppQLI = Palmoplantar Quality-of-Life Index; WPAI:PSO = Work Productivity and Activity Index: Psoriasis
For endpoints related to Week 24 and Week 48 (and any analysis at Week 56), the placebo group will be termed the "placebo-crossover" group

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

HYPOTHESIS

The primary hypothesis is that guselkumab (administered as 100 mg at Weeks 0, 4 and 12) is superior to placebo as assessed by the proportion of participants achieving ppPASI75 response at Week 16.

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 3b, double-blind, prospective, placebo-controlled, multicenter study in participants ≥18 years of age with moderate-to-severe palmoplantar-non-pustular psoriasis with PASI score ≥3 and <10 and ppIGA score ≥3, with palms and/or soles affected and at least 1 plaque at a body site other than the palms or soles (any size) for at least 6 months, to confirm a diagnosis of chronic psoriasis. A total of 105 participants will be enrolled in this study, which has an overall duration of 56 weeks.

Following screening for inclusion into the study, eligible participants will be randomized (1:2 ratio) to receive either placebo or guselkumab (100 mg) SC, respectively. The study will be divided into 2 phases:

Double-blind Phase:

- Guselkumab group: Guselkumab (100 mg) SC injections at Weeks 0, 4, 12 and placebo injection at Week 16.
- Placebo group: Placebo SC injections at Weeks 0, 4, 12 and guselkumab (100 mg) SC injection at Week 16.

Open-label Phase:

- Both guselkumab and placebo-crossover groups will receive guselkumab (100 mg) SC injections at Weeks 20, 28, 36, and 44.

Key efficacy assessments include physician assessments (ppPASI, ppIGA, PASI, BSA, f-PGA) and PRO questionnaires (WPAI-PSO, ppQLI, EQ-5D-5L, NRS:P and DLQI) at Weeks 16, 24 and 48. Overview photographs of the palms and soles will be collected for publication purposes from a subset of participants who provide optional consent. Safety evaluations will include 12-lead electrocardiogram (ECG) at baseline, pregnancy testing and monitoring of vital signs at all visits, and recording of adverse events throughout the study. Biomarker assessments will include the evaluation of relevant markers in serum for all participants. For an optional pharmacogenomic assessment, it is the intention to collect whole blood samples from 50 participants enrolled in the study.

A diagram of the study design is provided in Section 1.2, Schema.

4.2. Scientific Rationale for Study Design

Blinding, Control, Study Phase/Periods, Intervention Groups

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

Biomarker and DNA Collection

Biomarker samples will be collected to evaluate the mechanism of action of guselkumab or help to explain interindividual variability in clinical outcomes. They may also help to identify population subgroups that respond differently to an intervention, and aid in evaluating the intervention-clinical response relationship. Biomarker samples may be used to address emerging issues and to enable the development of safer, more effective, and ultimately individualized therapies. Serum biomarkers will be collected in all participants to assess pharmacodynamic (PD) markers associated with the response to guselkumab, and anti-microbial peptides. The goal of the biomarker analyses is to further define the mechanism of action of the selective blockade of IL-23 with guselkumab in palmoplantar-non-pustular psoriasis.

Optional Pharmacogenomic Sub-study

The goal of the pharmacogenomic component is to collect DNA to allow for the identification of genetic factors that may influence the efficacy, safety, or tolerability of guselkumab and to identify genetic factors associated with palmoplantar-non-pustular psoriasis or the response to guselkumab treatment. The focus of this analysis will be the evaluation of genetic single nucleic polymorphisms associated with palmoplantar-non-pustular psoriasis and response to treatment with guselkumab. Whole blood for genetic analyses will be collected (where local regulations permit) only from participants who sign a separate informed consent form (ICF) to participate in the optional pharmacogenomic sub-study.

Rationale for PRO Assessments for Efficacy Evaluation

The severity of psoriasis has a significant effect on the quality of life of sufferers, and HRQoL is more indicative of its impact on patients' lives, rather than physical measures such as percentage of BSA affected by psoriasis.[15] Palmoplantar-non-pustular psoriasis has been known to cause greater impairment to HRQoL than moderate-to-severe plaque psoriasis, as measured by DLQI scores.[5] Patient-reported outcome assessments are therefore essential for the understanding of the full effect of this phenotype of plaque psoriasis. The current study will use the DLQI and other PRO questionnaires to quantify the limitations of the disease and efficacy of the intervention.

4.2.1. Study-Specific Ethical Design Considerations

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

The primary ethical concern is that participants with active disease may receive placebo for 16 weeks. However, the placebo control is necessary to capture the change in clinical

endpoints that may occur in the absence of active treatment. The placebo exposure is limited to 16 weeks, which is considered acceptable by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).[12] The randomization scheme has also been optimized (1:2) to reduce the number of participants receiving placebo.

4.3. Justification for Dose

A dose regimen of guselkumab 100 mg at Weeks 0 and 4 and q8w thereafter was selected for this study. This dosing regimen is the same dosing regimen that is approved for use in patients with moderate-to-severe plaque-type psoriasis based on the data from global Phase 3 studies (CNTO1959PSO3001 and CNTO1959PSO3002).

4.4. End of Study Definition

A participant will be considered to have completed the study if he or she has completed assessments at Week 56. Participants who prematurely discontinue study intervention for any reason before Week 56 will not be considered to have completed the study; for these participants, the last study visit will be the final safety visit 12 weeks after last study intervention administration.

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.

5. STUDY POPULATION

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

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

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

5.1. Inclusion Criteria

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

Participant population-related inclusion criteria

1. Male or female ≥18 years of age.

2. Criterion changed per Amendment 1:

2.1 Should have all the following:

- A confirmed diagnosis of moderate-to-severe palmoplantar-non-pustular psoriasis with palm and/or sole involvement and at least one plaque at a body site other than the palms and soles for at least 6 months, to confirm a diagnosis of chronic psoriasis.
- PASI score ≥3 and <10 at screening and at baseline.
- ppIGA score ≥3 at screening and at baseline.

3. Should be eligible to receive biological treatments; only participants who are naïve to biological treatments can be included.

4. Willing to participate in the study.

Reproduction-related inclusion criteria

5. Criterion changed per Amendment 1:

5.1 Before the first administration of guselkumab, a woman must be either:

- Not of childbearing potential defined as:
  - Postmenopausal: A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level (>40 IU/L or mIU/mL) in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy, however, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.

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

- Of childbearing potential and practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly). Examples of highly effective contraceptives include:
  - User-independent methods: implantable progestogen-only hormone contraception associated with inhibition of ovulation; intrauterine device; intrauterine hormone-releasing system; vasectomized partner; 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).
  - User-dependent methods: combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, and transdermal; progestogen-only hormone contraception associated with inhibition of ovulation: oral and injectable.
- Agree to remain on a highly effective method throughout the study and for at least 12 weeks after the last dose of study intervention.

  Note: If the childbearing potential changes after start of the study or the risk of pregnancy changes (eg, a woman who is not heterosexually active becomes active), a woman must begin a highly effective method of contraception as described throughout the inclusion criteria. If reproductive status is questionable, additional evaluation should be considered.

6. Criterion changed per Amendment 1:

6.1 A woman of childbearing potential must have a negative urine pregnancy test at screening and at Week 0.

7. A woman must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction from the first administration of study intervention through at least 12 weeks after receiving the last administration of guselkumab.

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

Infectious disease-related inclusion criteria

9. Is considered eligible according to the following TB screening criteria:

   a. Has no history of latent or active TB before screening. An exception is made for participants who have a history of latent TB and are currently receiving treatment for latent TB, will initiate treatment for latent TB before the first administration of study agent, or have documentation of having completed appropriate treatment for latent TB within 3 years before the first administration of study agent. It is the responsibility of the investigator to verify the adequacy of previous anti-tuberculous treatment and provide appropriate documentation.

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

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

   d. Within 2 months before the first administration of study agent, has a negative QuantiFERON-TB test result, or has a newly identified positive QuantiFERON-TB test result in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated before the first administration of study agent. Within 2 months before the first administration of study agent, a negative tuberculin skin test (Appendix 2: Tuberculin Skin Testing), or a newly identified positive tuberculin skin test in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated before the first administration of study agent, is additionally required if the QuantiFERON-TB test is not approved/registered in that country or the tuberculin skin test is mandated by local health authorities. A tuberculin skin test is recommended but not required for study centers in Ukraine if tuberculin is not available.

      A participant whose first QuantiFERON-TB test result is indeterminate should have the test repeated. In the event that the second QuantiFERON-TB test result is also indeterminate, the participant may be enrolled without treatment for latent TB, if active TB is ruled out, his/her chest radiograph shows no abnormality suggestive of TB (active or old, inactive TB), 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.

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

   e. Has a chest radiograph (posterior-anterior view), taken within 3 months before the first administration of study agent and read by a qualified

radiologist, with no evidence of current, active TB or old, inactive TB.

10. Agree not to receive a live virus or live bacterial vaccination during the study, or within 12 weeks after the last administration of study intervention. For Bacillus Calmette-Guérin (BCG) vaccination, see criterion 11.

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

Clinical laboratory-related inclusion criteria

12. Criterion changed per Amendment 1:

12.1 Have screening laboratory test results within the following parameters:

a.	Hemoglobin	≥8.5 g/dL	(SI: ≥85 g/L)
b.	White blood cells	≥3.5 x 10^3/µL	(SI: ≥3.5 GI/L)
c.	Neutrophils	≥1.5 x 10^3/µL	(SI: ≥1.5 GI/L)
d.	Platelets	≥100 x 10^3/µL	(SI: ≥100 GI/L)
e.	Serum creatinine	≤1.5 mg/dL	(SI: ≤133 µmol/L)

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase levels must be ≤2.0 times the upper limit of normal range for the central laboratory conducting the test.

NOTE: A one-time repeat of these screening laboratory tests is allowed during the 4-week screening phase and the Investigator may consider the participant eligible if the previously abnormal laboratory test result is within acceptable the range on repeat testing in the central laboratory.

Other inclusion criteria

13. Agree to avoid prolonged sun exposure and agree not to use tanning booths or other ultraviolet (UV) light sources from the first administration of study intervention through 12 weeks after the final dose of study intervention (Week 56).

14. Be willing to refrain from the use of complementary therapies for palmoplantar-non-pustular psoriasis or psoriasis including ayurvedic medicine, traditional Taiwanese, Korean, or Chinese medications and acupuncture within 2 weeks before the first study intervention administration and through Week 48.

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

16. Sign an ICF/eICF indicating that he or she understands the purpose of and procedures required for the study and is willing to participate in the study.

17. Criterion added per Amendment 1:
Be compliant with the completion requirements for the PROs used in the study.

5.2. Exclusion Criteria

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

Medical history-related exclusion criteria

1. Criterion changed per Amendment 1:
1.1 Currently has palmoplantar pustulosis, pustular psoriasis, or any other forms other than plaque-type psoriasis (eg, erythrodermic, guttate) or hyperkeratotic eczema.

2. Criterion deleted per Amendment 1.

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

4. Has had major surgery (eg, 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.
Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate.

5. 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.

6. Criterion changed per Amendment 1:
6.1 Is pregnant, nursing, or planning a pregnancy (both men and women) while enrolled in this study, and for at least 12 weeks after the last administration of study intervention.

Concomitant or previous medical therapies-related exclusion criteria

7. Criterion changed per Amendment 1:
7.1 Has used topical anti-psoriatic medications/treatments (including, but not limited to corticosteroids, vitamin D3 derivatives, tacrolimus, salicylic acid, urea, antibiotics or any agents with anti-psoriatic effects) that could affect efficacy evaluations within 2 weeks of the planned first administration of study intervention.

8. Has received prior treatment with biological agents for palmoplantar-non-pustular psoriasis.

9. Has had prior exposure, known and reported intolerance to guselkumab or excipients, or ineligible to treatment with biological agents.

10. Criterion changed per Amendment 1:
10.1 Has previously received MTX within 2 weeks, or any Disease-Modifying

Anti-Rheumatic Drugs (DMARDs) including cyclosporin, fumarates and Psoralen-UVA (PUVA)within 4 weeks of the planned first administration of the study intervention.

11. Criterion changed per Amendment 1:

11.1 Has received phototherapy or any systemic medications/treatments that could affect efficacy evaluations (including, but not limited to, apremilast, systemic immunosuppressive drugs, biologic agents, cytotoxic drugs, JAK inhibitors, oral or injectable corticosteroids, retinoids, 1,25-dihydroxy vitamin D3 and analogues, psoralens, sulfasalazine, hydroxyurea, fumaric acid derivatives, herbal treatments, or traditional Taiwanese, Korean, or Chinese medicines) within 4 weeks of the planned first administration of study intervention.

12. 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.

13. Received any other experimental therapy, including an investigational medical device within 90 days or 5 half-lives (whichever is longer) prior to the first administration of study intervention or is currently enrolled in another study using an investigational agent or procedure.

Infections or predisposition to infections

14. Has received, or is expected to receive, any live virus or bacterial vaccination within 3 months before the first administration of study intervention.

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

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

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

18. Has active TB or other serious infection (eg, sepsis, pneumonia or pyelonephritis), or has been hospitalized or received IV antibiotics for an infection during the 2 months before screening.

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

20. Has a history of active granulomatous infection, including histoplasmosis or coccidioidomycosis, before screening. Refer to Inclusion Criterion 9 for information regarding eligibility with a history of latent TB.

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

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

23. Has persistently indeterminate (indeterminate on repeat sampling) QuantiFERON-TB test results. Indeterminate results should be handled as described in Section 5.1.

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

25. Tests positive for hepatitis B virus (HBV) infection (refer Appendix 3: Hepatitis B Virus (HBV) Screening with HBV DNA) or who are seropositive for antibodies to hepatitis C virus (HCV), unless they have 2 negative HCV RNA test results 6 months apart after completing antiviral treatment and prior to screening, and have a third negative HCV RNA test result at screening.

Malignancy or increased potential for malignancy

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

27. 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.

Other exclusion criteria

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

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

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

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

32 Criterion deleted per Amendment 1.

33. 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.

34. Is an employee of the Sponsor.

NOTE: Investigators should 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 he or she no longer meets all eligibility criteria, then the participant should be excluded from participation in the study. Section 5.4, Screen Failures, describes options for retesting. The required source documentation to support meeting the enrollment criteria are noted in Appendix 5: Regulatory, Ethical, and Study Oversight Considerations.

5.3. Lifestyle Considerations

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

1. Refer to Section 6.5, Concomitant Therapy for details regarding prohibited and restricted therapy during the study.

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

5.4. Screen Failures

Participant Identification, Enrollment, and Screening Logs

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

The participant identification and enrollment log will be treated as confidential and will be filed by the investigator in the study file. To ensure participant confidentiality, no copy will be made. All reports and communications relating to the study will identify participants by participant identification 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.

Individuals who do not meet the criteria for participation in this study (screen failures) may be rescreened once.

6. STUDY INTERVENTION

6.1. Study Interventions Administered

Participants in both study groups will receive one injection of study intervention at each time-point detailed in the Schedule of Activities:

- **Guselkumab group (guselkumab 100 mg):**
  - Guselkumab injection: Weeks 0, 4, 12, 20, 28, 36 and 44
  - Placebo injection at Week 16
- **Placebo group (placebo)**:
  - Placebo injection: Weeks 0, 4 and 12
  - Guselkumab 100 mg injection: Weeks 16, 20, 28, 36 and 44

NOTE: The placebo group will be termed the placebo-crossover group for endpoints related to Week 24 and Week 48

Study intervention will always be administered at the site and by a health care professional (HCP), until the participant (or caregiver) is trained for self-administration. Study intervention will be administered by site personnel at Weeks 0 and 4. Beginning at Week 12, at the discretion of the investigator and participant and after appropriate and documented training, participants may self-administer study intervention at the investigative site under the supervision of an HCP. A caregiver may also be trained to administer study intervention. Participants unable or unwilling to self-administer will continue to have study intervention injections performed by an HCP.

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

Guselkumab and placebo will be manufactured and provided under the responsibility of the sponsor. Refer to the IB[6] for a list of excipients.

For a definition of study intervention overdose, refer to Section 8.3.6, Treatment of Overdose.

Guselkumab 100 mg will be provided in a single-use prefilled syringe (PFS) assembled with the UltraSafe PLUS™ Passive Needle Guard (PFS-U). Placebo for guselkumab will be supplied as a 1 mL sterile liquid in a single dose PFS assembled in a PFS-U. Malfunctions of the syringe must be detected, documented, and reported by the investigator throughout the study.

6.2. Preparation/Handling/Storage/Accountability

Guselkumab and placebo will be supplied to the study sites. Clinical sites may use scanning technology to manage clinical trial supplies and drug compliance activities. All study interventions must be stored according to the labeled storage conditions, at 2°C to 8°C (36ºF to 46ºF) and protected from exposure to light. Vigorous shaking of the product should be

avoided. The sterile product does not contain preservatives and is designed for single-use only. Protection from light is not required during administration.

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 intervention to the participant must be documented on the intervention accountability form. 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. 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 needles and syringes containing hazardous liquids, 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 participants in the study. Study intervention may not be relabeled or reassigned for use by other participants. The investigator agrees not to dispense the study intervention from, nor store it at, any site other than the study sites agreed upon with the sponsor. Refer to the pharmacy manual/study-site investigational product and procedures manual for additional guidance on study intervention preparation, handling, and storage.

6.3. Measures to Minimize Bias: Randomization and Blinding

Intervention Allocation

Procedures for Randomization

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 be balanced by using randomly permuted blocks. The interactive web response system (IWRS) will assign a unique intervention code, which will dictate the intervention assignment and matching study 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 other information on each part. The study intervention number will be available in the CRF.

The blinded 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 (ie, treatment accountability data, treatment allocation, biomarker or other specific laboratory data) 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 database lock and unblinding.

The investigator may in an emergency determine the identity of the intervention by using the IWRS. While the responsibility to break the blind 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, time, and reason for the unblinding must be documented by the IWRS, in the appropriate section of the CRF 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.

In general, randomization codes will be disclosed fully only if the study is completed and the clinical database is closed. However, for the database lock at Week 16, the randomization codes and, if required, the translation of randomization codes into intervention and control groups will be disclosed to those authorized and only for those participants included in the primary analysis. For guidance, please refer Appendix 5: Regulatory, Ethical, and Study Oversight Considerations.

6.4. Study Intervention Compliance

Study intervention will be administered at the investigational site throughout the study and study personnel will maintain a log of all study intervention administrations. Study intervention supplies for each participant will be inventoried and accounted for. All ongoing therapies administered at the time of screening must be recorded.

6.5. Concomitant Therapy

Concomitant therapies must be recorded throughout the study from screening and continuing until 12 weeks after the last dose of study intervention for randomized participants. Concomitant therapies should also be recorded beyond Week 56 only in conjunction with SAEs that meet the criteria outlined in Section 8.3.

All therapies (prescription or over-the-counter medications, including vaccines, vitamins, herbal supplements) different from the study intervention, as well as all moisturizers or emollients, must be recorded in the CRF. Modification of an effective pre-existing therapy should not be made for the explicit purpose of entering a participant into the study.

6.5.1. Rescue Medication

During the 16-week placebo-controlled period, participants in both groups will be allowed to use potent topical corticosteroids as rescue medication, in case of marked disease worsening (defined as 25% increase in ppPASI score from baseline). The decision to allow rescue medication will be at the judgment of the investigator. At the time any rescue medication is initiated by a participant, the study intervention will be stopped, and the participant will be considered a non-responder. Participants who are allowed to use a rescue medication are encouraged to continue in the study until Week 16 for further evaluation.

Participants who start a rescue medication after Week 16 will have to stop study intervention and will be encouraged to come for a Safety Follow-up Visit 12 weeks after the last study intervention administration.

6.5.2. Concomitant Medications for Treatment of Palmoplantar-non-pustular Psoriasis

6.5.2.1. Systemic and Topical Therapy

Systemic therapies for psoriasis such as MTX, apremilast, systemic immunosuppressive drugs, biologic agents, cytotoxic drugs, JAK inhibitors, or investigational agents are not permitted. Topical therapies that could affect palmoplantar-non-pustular psoriasis or efficacy evaluations (eg, corticosteroids, vitamin D3 derivatives, tacrolimus, and antibiotics) are not permitted. Agents which include salicylic acid, urea or any agents which have an anti-psoriatic effect are not permitted. Participants should not use moisturizers on the day of a study visit.

The only allowable concomitant treatments for palmoplantar-non-pustular psoriasis throughout the study are topical moisturizers including skin softener.

6.5.2.2. Complementary Therapies

The use of complementary therapies, including ayurvedic medicine, traditional Chinese medications or nonmedicinal therapy such as acupuncture for palmoplantar-non-pustular psoriasis, is not allowed from 2 weeks prior to the first administration of study intervention through Week 56.

6.5.3. Concomitant Medications for Conditions Other than Palmoplantar-non-pustular 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 illnesses, or the performance of a procedure, the change and reason for it should be clearly documented in the participant's medical records.

The use of nonsteroidal anti-inflammatory drugs is allowed. However, disease modifying agents such as MTX, sulfasala-zine, or intramuscular gold are prohibited during the study. Antimalarial agents, with the exception of chloroquine, may be used after Week 56.

Only the use of inhaled, otic or ophthalmic corticosteroids will be permitted as a concomitant medication for indications other than palmoplantar-non-pustular psoriasis.

6.6. Dose Modification

Dose or dosage adjustment is not permitted during the study.

6.7. Intervention After the End of the Study

Participants will be informed that guselkumab 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 their standard of care.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued for any of the following reasons:

- The investigator believes that for safety reasons or tolerability reasons (eg, adverse event) it is in the best interest of the participant to discontinue study intervention.
- The participant becomes pregnant or plans to become pregnant. Refer to Appendix 7.
- The participant is diagnosed with a malignancy (except 1-2 localized basal cell skin cancers that are treated with no evidence of recurrence or residual disease).
- The participant is deemed ineligible according to the following TB screening criteria:
  - A diagnosis of active TB is made.
  - A participant has symptoms suggestive of active TB based on follow-up assessment questions and/or physical examination or has had recent close contact with a person with active TB and cannot or will not continue to undergo additional evaluation.
  - A participant undergoing evaluation has a chest radiograph with evidence of current active TB and/or a positive QuantiFERON-TB test result (or a positive tuberculin skin test result in countries in which the QuantiFERON-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities), unless active TB can be ruled out and appropriate treatment for latent TB can be initiated before the next administration of study intervention and continued to completion. Participants who have an indeterminate result should have the test repeated. Participants with persistently indeterminate QuantiFERON-TB test results may continue without treatment for latent TB if active TB is ruled out, their chest radiograph shows no abnormality suggestive of TB (active or old, inactive TB) 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.
  - A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy.
- The participant initiates the following protocol prohibited medications: apremilast, systemic immunosuppressive drugs, biologic agents, cytotoxic drugs, JAK inhibitors, or investigational agents, and other systemic therapies for psoriasis.
- The participant withdraws consent for administration of study intervention.
- The participant is unable to adhere to the study visit schedule or comply with protocol requirements.
- The participant develops an allergic reaction such as bronchospasm with wheezing and/or dyspnea requiring ventilatory support, or symptomatic hypotension that occurs following a study intervention administration.
- 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.

Discontinuation of study treatment should be considered for participants for any of the following reasons:

- Participants who develop a serious or opportunistic infection. Discussion of such participants with the medical monitor or designee should also be considered.
- Participants who have shown no response with up to 28 weeks of treatment. These participants will be included in the primary analysis as non-responders.

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

If a participant permanently discontinues study intervention before Week 44, the Final Efficacy Visit should occur at the time of discontinuation or as soon as possible, and all assessments scheduled for the Final Efficacy Visit should be performed. The participant should also return for a Final Safety Visit, 12 weeks after the last study intervention administration.

If the reason for withdrawal from the study is withdrawal of consent, then no additional assessments are allowed. If a participant discontinues study treatment and starts another biologic treatment, an interval of at least 12 weeks between the last study intervention administration and the start of the new treatment is recommended.

7.2. Participant Discontinuation/Withdrawal from the Study

A participant will not be automatically withdrawn from the study if they have to discontinue study intervention before the end of the intervention regimen.

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

- Lost to follow-up
- Withdrawal of consent
- Initiation of rescue medication after Week 16.
- Occurrence of pustules consistent with a diagnosis of palmoplantar pustulosis.
- Death

- Discontinuation of study intervention for any reason. A participant's study intervention will be automatically discontinued if:
  - The investigator or sponsor believes (eg, that for safety or tolerability reasons, eg, adverse event) it is in the best interest of the participant to discontinue study intervention
  - The participant becomes pregnant. Refer to Appendix 7.

When a participant withdraws before completing the study, the reason for withdrawal is to be documented in the CRF and in the source document. Study intervention assigned to the withdrawn participant may not be assigned to another participant. Additional participants will not be entered.

7.3. Lost to Follow-up

If a participant is lost to follow-up, every reasonable effort must be made by the study-site personnel to contact the participant and determine the reason for discontinuation/withdrawal. The measures taken to follow-up must be documented. Refer to Section 7.2, Participant Discontinuation/Withdrawal from the Study.

7.4. Withdrawal from the Use of Research Samples

A participant who withdraws from the study will have the following options regarding the 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 (even if remaining in the study), 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 to 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.
- The participant may withdraw consent for use of samples for research. 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 ICF.

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

The Schedule of Activities summarizes the frequency and timing of efficacy, biomarker and safety measurements applicable to this study.

All PRO assessments should be conducted/completed before study intervention administration and any tests, procedures, or other consultations to prevent influencing participant perceptions. Other measurements may be done earlier than the specified timepoints if needed. Actual dates and times of assessments will be recorded in the source documentation and CRF.

Additional TB tests may be performed as determined necessary by the investigator or required by local regulation. For women of childbearing potential only, additional urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulations, to establish that a participant is not pregnant at any time during their participation in the study.

The total blood volume to be collected from each participant will be approximately 124.5 mL.

Type of Sample	Volume per Sample (mL)
Safety (including screening and posttreatment assessments)	
- Hematology	2.0
- Chemistry	2.5
- Serology (HBV, HCV, HIV)	10.0
- HBV DNA testing[a]	6.0
- TB testing	3.0
- Lipid panel and hsCRP	2.5
Biomarkers	
- Serum biomarkers	8.5
Pharmacogenomics	
- Whole blood (DNA)[b]	6
Approximate Total[c]	40.5

a. Performed only in participants who test positive for core HBV antibody.
b. Repeat or unscheduled samples may be taken for safety reasons or technical issues with the samples.
c. Whole blood for DNA is optional.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded in the CRF or laboratory requisition form. Refer to the Schedule of Activities for the timing and frequency of all sample collections.

Instructions for the collection, handling, storage, and shipment of samples are provided in the laboratory requisition form. Collection, handling, storage, and shipment of samples must be under the specified and, where applicable, controlled temperature conditions as indicated in the laboratory manual.

Repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.

Study-Specific Materials

The investigator will be provided with the following supplies:

- IB for guselkumab
- Study-site investigational product and procedures manual
- Laboratory manual and laboratory supplies
- Paper PROs and user manual
- Photography manual
- IWRS manual
- Electronic data capture (eDC) manual
- Sample ICF

8.1. Efficacy Assessments

The investigator-led assessments of efficacy (PASI, ppPASI, ppIGA, BSA) will be performed at the site by an assessor trained by the Sponsor, at the appropriate visits as outlined by the SOA.

Efficacy assessments should preferably be done by a dermatologist; if a dermatologist is not available, a health care provider with at least 1 year of experience in performing psoriasis efficacy assessments, after training by the Sponsor, may serve as an assessor. Health care providers with less than 1 year of experience may act as an assessor after training by the Sponsor, based on the discretion and approval of the Sponsor.

The following assessments will be carried out as detailed in the Schedule of Activities.

8.1.1. Palmoplantar-non-pustular Psoriasis Response Evaluations

8.1.1.1. Palmoplantar Pustular Psoriasis Area and Severity Index

The ppPASI is an assessment tool based on the PASI and is widely used for assessing PPP severity in participants with active disease.[1] The ppPASI assesses erythema, pustules and desquamation on a scale between 0 and 4 (0 = absent, and 4 = very severe) and the extent of the affection of the palms and/or soles on a scale between 0 and 6 (0 = absent, and 6 = 90–100%). For the current study population with palmoplantar-non-pustular psoriasis, the score for pustules will be considered 0, and the index will have a maximum score of 48. A sample ppPASI tool is provided in Appendix 8.

8.1.1.2. 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.[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 90 and PASI 100 are similarly defined.

The Sponsor will provide PASI training on assessment of PASI scores. Documentation of this training will be maintained in the site's training files. Previous PASI training by the Sponsor within the last 3 years with adequate documentation (eg, training certification) will be considered adequate for this study; however, repeat training prior to start of the study is encouraged. A sample PASI tool is provided in Appendix 9.

8.1.1.3. Palmoplantar Investigator Global Assessment Scale

The Food and Drug Administration (FDA) has recommended using a 5-point IGA scale for trials in psoriasis and other dermatologic conditions, arguing that the success criteria of achieving "clear" or "almost clear" status combined with a 2-point reduction from baseline is more clinically meaningful on a 5-point scale. The ppIGA scale is based on the version of the IGA modified in 2011, specifically applied to the palms and soles. The 5-point IGA has a more stringent definition for a score of 1 ("almost clear") compared with the 6-point IGA/PGA tools used in previous trials of other biologics in moderate-to-severe psoriasis.[17] A sample ppIGA tool is provided in Appendix 10.

8.1.1.4. Body Surface Area

The BSA score is the arithmetic mean of the affected skin surface based on the assumption that the head (H) presents 10%, the upper extremities (U) 20%, the trunk (T) 30%, and the lower extremities (L) 40% of the total body surface.[28] The formula for the calculation of BSA is provided in Appendix 11.

8.1.1.5. Fingernail-Physician Global Assessment

The f-PGA is a 5-point scale used to assess fingernails separately for nail bed and nail matrix for signs of disease.[11] A global score of between 0 (indicating clear) and 4 (indicating severe) is separately assigned for nail bed involvement and nail matrix involvement. A participant's overall global score is the worse of the nail bed and nail matrix scores. A sample f-PGA assessment tool is presented in Appendix 12.

8.1.2. Patient-Reported Outcomes

8.1.2.1. Dermatology Life Quality Index

The DLQI is a dermatology-specific quality-of-life instrument designed to assess the impact of the disease on quality of life.[8] It is a 10-item questionnaire that can be used to assess overall quality-of-life and 6 different aspects that may affect quality-of-life: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment. A sample DLQI assessment tool is provided in Appendix 13.

8.1.2.2. European Quality of Life (EuroQol) Group, 5-Dimension, 5-Level

The EQ-5D-5L is a standardized instrument for use as a measure of HRQoL, primarily designed for self-completion by respondents. It consists of 2 parts: the EQ-5D-5L descriptive system and the EQ visual analogue scale (EQ-VAS). The EQ-5D-5L descriptive system

comprises the following 5 dimensions: Mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each of the 5 dimensions is divided into 5 levels of perceived problems (Level 1 indicating no problem, Level 2 indicating slight problems, Level 3 indicating moderate problems, Level 4 indicating severe problems, and Level 5 indicating extreme problems).

The participant selects an answer for each of the 5 dimensions considering the response that best matches his or her health "today." The descriptive system can be represented as a health state. The EQ-VAS self-rating records the respondent's own assessment of his or her overall health status at the time of completion, on a scale of 0 to 100. A sample EQ-5D-5L assessment tool is provided in Appendix 14.

8.1.2.3. Numerical Rating Scale: Pain

In a Numerical Rating Scale (NRS), participants will be asked to circle the number between 0 and 10 that fits best to their pain intensity. The numbers themselves represent the answers. A score of 0 represents "no pain", a rating of 1-3 represents mild pain (nagging, annoying, interfering little in activities of daily living [ADLs]), a rating of 4-6 represents "moderate pain" (interfering significantly in ADLs) and a rating of 7-10 represents "severe pain" (disabling, unable to perform ADLs). The individual 0-10 pain intensity ratings have demonstrated sufficient psychometric strength to be used in the assessment of pain in chronic conditions, especially in studies that involves group comparison.[13] This scale should address skin (palms and soles) related pain only. A sample NRS-P scale is provided in Appendix 15.

8.1.2.4. Work Productivity and Activity Impairment: Psoriasis

The WPAI-PSO questionnaire is adapted from the WPAI-SHP (specific health problem).[22] The 6 questions in the WPAI are included to measure work productivity and activity impairment related to skin psoriasis. Following the standard methodology, the following 5 measures are constructed from the questions: current employment status; absenteeism (percentage of time missed from work), presenteeism (percentage reduced productivity while working), total activity impairment (percentage impairment in regular daily activities other than work) and total work productivity impairment, representing the total percentage of work impairment associated with psoriasis from both absenteeism and presenteeism. The percentage of impairment associated with psoriasis is self-attributed by each participant. A sample WPAI-PSO scale is provided in Appendix 16.

8.1.2.5. Palmoplantar Quality-of-Life Instrument

The ppQLI is specifically tailored to participants with palmoplantar psoriasis and assesses relevant dimensions affected by palmoplantar psoriasis: pain/discomfort, functionality, and social/activity limitations on a scale of 1 to 5 separately for hands and feet.[7] The scale was designed to measure the effect as far as possible of skin function as opposed to joint, muscle, or ligament function. The ppQLI makes it possible to quantitatively evaluate disease severity in participants with palmoplantar psoriasis, especially those with less than 10% BSA and, hence, responses to therapy over time. This will allow for evidence-based recommendations concerning systemic or biological therapies for adequate maintenance of clinical response. A sample PPQLI is provided in Appendix 17.

8.1.3. Photographs of Palms and Soles

Overview photographs of the palms and soles will be collected for publication purposes from a subset of participants who provide optional consent. See Trial Center File for photography instructions.

8.1.4. Pharmacogenomic Assessment

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. DNA samples will be analyzed for identification of genetic factors that may be associated with clinical response to guselkumab intervention and palmoplantar-non-pustular psoriasis. Participant participation in pharmacogenomic research is optional.

8.1.5. Biomarker Analysis

Biomarker assessments will be made to examine the biologic response to treatment and to identify biomarkers that are relevant to guselkumab treatment and/or palmoplantar-non-pustular psoriasis. Assessments will include the evaluation of relevant biomarkers in serum for all participants, including but not limited to markers associated with the IL-23/Th17 axis (IL-17A, IL-17F and IL-22) as specified in the Schedule of Activities. Data collected from these samples will be used for exploratory research that will include the following objectives:

- To understand the pharmacodynamic effects of guselkumab on serum proteins associated with the IL-23/Th17 pathway in participants with palmoplantar-non-pustular psoriasis.
- To understand palmoplantar-non-pustular psoriasis disease pathogenesis.
- To understand why an individual may respond differently to guselkumab.

Instructions for the collection and shipment of these samples can be found in the appropriate laboratory manual.

Biomarker analyses are dependent upon the availability of appropriate biomarker assays and clinical response rates. In the event the study is terminated early or shows poor clinical efficacy, biomarker assessments may not be evaluated. Biomarker analyses will be summarized in separate technical report.

8.1.5.1. Serum-based Biomarker Analysis

Blood samples for serum-based biomarker analysis will be collected from all participants. Analysis will include but not be limited to IL-17A, IL-17F and IL-22 and anti-microbial markers. Proprietary algorithms and standard statistical techniques, such as analysis of variance (ANOVA) and analysis of covariance (ANCOVA), will be used to identify individual proteins exhibiting statistically significantly different changes in their levels between samples and/or between groups of samples. This will enable the evaluation of changes in proteome profiles that may correlate with biological response relating to palmoplantar-non-pustular psoriasis or the mechanism of action of guselkumab.

8.2. Safety Assessments

Adverse events will be reported and followed by the investigator as specified in Section 8.3, Adverse Events and Serious Adverse Events and Appendix 6: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting. The investigator should make the decision whether there is a potential adverse event or not.

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

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

The study will include the following evaluations of safety and tolerability according to the time points provided in the Schedule of Activities.

8.2.1. Physical Examination

Physical examinations will be performed by the investigator or designated physician as specified in the Schedule of Activities. 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

Height, weight, blood pressure, axillary temperature and heart rate will be assessed as specified in the Schedule of Activities. If any clinically significant changes in vital signs are noted, they must be reported as adverse events and followed to resolution, or until reaching a clinically stable endpoint.

8.2.3. Electrocardiogram

A supine 12-lead ECG will be performed locally at Week 0 prior to administration of study intervention, as specified in the Schedule of Activities. A full 12-lead ECG will be recorded and the ECG data, including a copy of tracing as well as interpretation, should be stored in the participant's source document.

8.2.4. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology will be collected as noted in Appendix 4: Clinical Laboratory Tests. The investigator must review the laboratory results, document this review, and record any clinically relevant changes occurring during the study in the adverse event section of the CRF. The laboratory reports must be filed with the source documents.

8.2.5. Early Detection of Active Tuberculosis

To aid in the early detection of TB reactivation or new TB infection during study participation, participants must be evaluated for signs and symptoms of active TB at scheduled visits (or by telephone contact approximately every 8 to 12 weeks if a participant misses scheduled visits). The following series of questions is suggested for use during the evaluation:

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

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

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

Participants who experience close contact with an individual with active TB during the conduct of the study must have a repeat chest radiograph, a repeat QFT test, a repeat tuberculin skin test (Appendix 2: Tuberculin Skin Testing) in countries in which the QFT test is not approved/registered or the tuberculin skin test is mandated by local health authorities, and, if possible, referral to a physician specializing in TB to determine the participant's risk of developing active TB and whether treatment for latent TB is warranted. If the QFT test result is indeterminate, the test should be repeated. Participants should be encouraged to return for all subsequent scheduled study visits according to the protocol.

8.3. Adverse Events and Serious Adverse Events

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

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

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

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

All Adverse Events

All adverse events and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the participant's last study-related procedure, which may include contact for follow-up of safety. Serious adverse events, including those spontaneously reported to the investigator within 12 weeks after the last dose of study intervention, must be reported using the Serious Adverse Event Form and, where applicable, the Safety Report Form of the CRF, which must be completed and reviewed by a physician from the study-site and transmitted to the sponsor within 24 hours. The sponsor will evaluate any safety information that is spontaneously reported by an investigator beyond the time frame specified in the protocol.

Serious Adverse Events

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

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

8.3.2. Method of Detecting Adverse Events and Serious Adverse Events

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

Solicited Adverse Events

Solicited adverse events are predefined local and systemic events for which the participant is specifically questioned.

Unsolicited Adverse Events

Unsolicited adverse events are all adverse events for which the participant is not specifically questioned.

Injection-Site Reactions

An injection-site reaction is any unfavorable or unintended sign that occurs at the study intervention injection-site. All participants will be carefully observed at the study-site for at least 30 minutes after the SC injection of study intervention for symptoms of an injection-site reaction. If an injection-site reaction is observed, the participant should be treated at the investigator’s discretion.

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

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

8.3.4. Regulatory Reporting Requirements for Serious Adverse Events

The sponsor assumes responsibility for appropriate reporting of adverse events to the regulatory authorities. The sponsor will also report to the investigator (and the head of the investigational institute where required) all suspected unexpected serious adverse reactions (SUSARs). The investigator (or sponsor where required) must report SUSARs to the appropriate Independent Ethics Committee/Institutional Review Board (IEC/IRB) that approved the protocol unless otherwise required and documented by the IEC/IRB. A SUSAR will be reported to regulatory authorities unblinded. Participating investigators and IEC/IRB will receive a blinded SUSAR summary, unless otherwise specified.

8.3.5. Pregnancy

All initial reports of pregnancy in female participants or partners of male participants must be reported to the sponsor by the study-site personnel within 24 hours of their knowledge of the event using the appropriate pregnancy notification form. Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs and must be reported using the Serious Adverse Event Form and, where applicable, the Safety Report Form of the CRF, which must be completed and reviewed by a physician from the study-site and transmitted to the sponsor within 24 hours. 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.

Because the effect of the study intervention on sperm is unknown, pregnancies in partners of male participants included in the study will be reported as noted above. A male study participant is not required to discontinue study intervention if their partner becomes pregnant during the study.

8.3.6. Events of Special Interest

Any newly identified malignancy or case of active TB occurring after the participant's first study intervention administration must be reported within 24 hours by the investigator according to the procedures in Appendix 6 and Section 8.3.1. 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 a SAE.

8.4. Treatment of Overdose

No clinical studies in humans have been conducted to assess a toxic threshold for guselkumab. The highest single SC dose of guselkumab investigated in humans was 300 mg. The maximum IV dose (10 mg/kg) in humans was 987 mg.

In case of an overdose, it is recommended that the participant be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment be instituted immediately.

8.5. Medical Resource Utilization and Health Economics

Health Economics/Medical Resource Utilization and Health Economics parameters are not evaluated in this study.

9. STATISTICAL CONSIDERATIONS

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

Simple descriptive summary statistics, such as n, mean, standard deviation (SD), median, interquartile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data. All statistical procedures will be performed 2-sided at a significance level of 0.05. In addition to statistical analyses, graphical summaries of the data may be used.

Participant baseline data, demographics, and baseline disease characteristics, including prior palmoplantar-non-pustular psoriasis therapies, will be summarized. The baseline measurement is defined as the closest measurement before the Week 0 injection.

The study is designed to maintain a type I error of 0.05 or less for the primary analyses. As guselkumab versus placebo comparisons for secondary endpoints are not based on pre-specified hypotheses, treatment effect estimates will be accompanied by 95% confidence intervals (CIs). Provided p-values will be considered nominal and are not to be interpreted as confirmatory.

Database locks are planned at Week 16 and at End of Study. The analysis of primary and secondary endpoints for Week 16 will be carried out at the first database lock after all randomized participants have completed their assessments at Week 16 or have discontinued the study before Week 16. The second database lock for the final analysis will occur at End of Study.

9.1. Statistical Hypotheses

The primary hypothesis is that guselkumab (100 mg at Weeks 0, 4 and 12) is superior to placebo as assessed by the proportion of participants achieving ppPASI75 response at Week 16.

9.2. Sample Size Determination

The study is designed to evaluate the efficacy of guselkumab versus placebo in participants with moderate-to-severe palmoplantar-non-pustular psoriasis. Because guselkumab and placebo data are lacking for ppPASI75 response in the intended population, the assumptions for the sample size were based on results from a secondary analysis on participants with psoriasis of the palms and/or soles in 2 guselkumab studies (CNTO1959PSO3001 and CNTO1959PSO3002)[9], assessing the proportion of participants with hf-PGA score of 0 or 1 with at least a 2-grade improvement from baseline.[9] Additionally, results from secondary analysis on participants with palmoplantar psoriasis of 3 ixekizumab studies (UNCOVER-1, UNCOVER-2, UNCOVER-3)[19] were taken into consideration.

Since topical therapies which could affect palmoplantar psoriasis or efficacy evaluations (eg, corticosteroids, vitamin D3 derivatives, tacrolimus, and antibiotics) are not permitted, it is assumed that the Week 16 ppPASI75 response rate in the placebo arm will not exceed

12.5%. With an assumed response rate of at least 45% in the guselkumab arm and maximally 12.5% in the placebo arm, sample sizes of 64 in the guselkumab arm and 32 in the placebo arm would achieve at least 90% power. The statistical test to be used is the two-sided Fisher's Exact test. The significance level of the test is targeted at 0.05 (PASS version 11.0.9). Participants will be randomized in a 2:1 ratio to the guselkumab and placebo arms.

To compensate for 8% non-evaluable participants, approximately 70 participants will be randomized to the guselkumab group and 35 participants to the placebo group. In total 105 participants will be randomized.

9.3. Populations for Analyses

For purposes of analysis, the following populations are defined:

Population	Description
Screened	All participants who sign the ICF
Full Analysis Set	All randomized participants who receive at least 1 dose of study intervention. Participants will be analyzed according to the randomized treatment group, regardless of the intervention they actually received
Safety Analysis Set	All randomized participants who receive at least 1 dose of study intervention and complete at least 1 follow-up safety assessment. Participants will be analyzed according to the intervention they actually received

9.4. Statistical Analyses

9.4.1. Efficacy Analyses

Primary Endpoint Analysis

The primary endpoint to be analyzed in this study is the proportion of participants who achieve ppPASI75 response at Week 16. A participant who meets any of the following treatment failure criteria will be considered not to have achieved the primary endpoint, regardless of the observed ppPASI75 response status:

1. Discontinued study intervention injections due to lack of efficacy (non-responders).
2. Initiated protocol prohibited medications/therapies for palmoplantar-non-pustular psoriasis.

The treatment effect of the guselkumab group versus placebo will be tested using the Fisher exact test. The magnitude of the effect will be estimated by the difference in ppPASI75 response rates between the treatment groups with the 95% CI calculated based on Wald statistics. The study is designed to maintain a type I error of 0.05 or less for the primary analyses.

In the primary efficacy analysis, data from all randomized participants who received at least 1 administration of study treatment (full analysis set) will be analyzed according to their assigned treatment group regardless of their actual treatment received. Participants with missing data for ppPASI at Week 16 will be considered non-responders.

Further analysis of ppPASI data will be described in detail in the Statistical Analysis Plan.

Secondary Endpoint Analyses

For the major secondary analyses, the Fisher's exact test will be used to compare the proportion of participants responding to treatment. Continuous response parameters will be compared using ANOVA with treatment as a factor in the model will be used. Difference in means and 95% CI will be used for treatment comparisons versus placebo. All statistical testing will be performed at a two-sided alpha level of 0.05. No multiplicity adjustments will be made to control overall Type 1 error for secondary analyses.

The major secondary analyses are:

- The change from baseline in ppPASI score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in PASI score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in ppIGA score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in f-PGA score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in BSA score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in DLQI score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in ppQLI score at Week 16 will be compared between the guselkumab group and the placebo group
- The change from baseline in EQ-5D-5L score at Week 16 will be compared between the guselkumab group and the placebo group

Other Efficacy Analyses

In addition to the primary and major secondary analyses, the analyses for other efficacy endpoints will be performed and nominal p-values will be provided. The efficacy endpoints will also be summarized over time.

Biomarker Analyses

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

Changes in serum biomarkers over time will be summarized by intervention group. Associations between baseline levels and changes from baseline in select markers and clinical response will be explored. Biomarker analyses will be summarized in separate technical reports.

Pharmacogenomic Analyses

DNA samples will be analyzed for identification of genetic factors that may be associated with clinical response, safety and tolerability of guselkumab intervention and palmoplantar-non-pustular psoriasis.

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

The pharmacogenetic data generated from this study is planned to be integrated with genetic data from a subset of participants with palm-and-soles involvement from other dermatology trials owned by the sponsor. Results will be presented in a separate report.

9.4.2. Safety Analyses

Adverse Events

The verbatim terms used in the CRF by investigators to identify adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Intervention-emergent adverse events are adverse events with onset during the intervention phase or that are a consequence of a pre-existing condition that has worsened since baseline. All reported adverse events will be included in the analysis. For each adverse event, the percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group. In addition, comparisons between intervention groups will be provided if appropriate.

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

Clinical Laboratory Tests

Laboratory parameters, change from baseline in selected laboratory parameters (hematology and chemistry) and incidence of laboratory parameters that meet the criteria for Common Terminology Criteria for Adverse Events Grade 3 or Grade 4 will be summarized by treatment group.

Vital Signs

Descriptive statistics of body temperature, pulse/heart rate, respiratory rate, and blood pressure (systolic and diastolic) values and changes from baseline will be summarized at each scheduled time-point. The percentage of participants with values beyond clinically important limits will be summarized.

9.5. Interim Analysis

No interim analysis has been planned for this study.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Abbreviations and Trademarks

ADLs	Activities of daily living
AE	adverse event
ALT	alanine aminotransferase
AST	Aspartate aminotransferase
BCG	Bacillus Calmette-Guérin
BSA	body surface area
CRF	case report form(s) (paper or electronic as appropriate for this study)
DLQI	Dermatology Life Quality Index
DMARD	disease-modifying antirheumatic drug
DNA	Deoxyribonucleic acid
ECG	electrocardiogram
eDC	electronic data capture
EQ-5D-5L	European Quality of Life (EuroQol) Group, 5-Dimension, 5-Level
EU	European Union
f-PGA	Fingernail-Physicians Global Assessment
FSH	follicle stimulating hormone
Hf-PGA	hands/feet physician global assessment
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HRQoL	health-related quality-of-life
IB	investigator brochure
ICF	informed consent form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IGA	investigator global assessment
IL	interleukin
IRB	Institutional Review Board
IV	intravenous(ly)
IWRS	interactive web response system
mAb	Monoclonal antibody
MACE	major adverse cardiovascular events
MedDRA	Medical Dictionary for Regulatory Activities
MTX	methotrexate
NRS:P	Numerical Rating Scale: Pain
PASI	Psoriatic Area and Severity Index
PD	Pharmacodynamics
PFS	prefilled syringe
PK	pharmacokinetic(s)
ppIGA	Palmoplantar Investigator Global Assessment
PPP	Palmoplantar pustulosis
PPPASI	Palmoplantar Pustulosis Area and Severity Index
ppQLI	Palmoplantar Quality-of-Life Instrument
PPSI	Palmoplantar Pustulosis Severity Index
PRO	Patient-reported outcomes
PsA	psoriatic arthritis
PUVA	Psoralen-UVA
RA	rheumatoid arthritis
RNA	Ribonucleic acid
SAE	serious adverse event(s)
SC	subcutaneous(ly)
SUSAR	suspected unexpected serious adverse reaction
TB	tuberculosis
UV	ultraviolet
WPAI:Pso	Work Productivity and Activity Impairment: Psoriasis

Definitions of Terms

Clinical outcome assessment (COA)	Includes PROs, Clinician Reported Outcomes, Observer Reported Outcomes and Performance Reported Outcomes (PerfRO).
Electronic source system	Contains data traditionally maintained in a hospital or clinic record to document medical care or data recorded in a CRF as determined by the protocol. Data in this system may be considered source documentation.

10.2. Appendix 2: Tuberculin Skin Testing

Administering the Mantoux Tuberculin Skin Test

The Mantoux tuberculin skin test is the standard method of identifying persons infected with *Mycobacterium tuberculosis*.[4] Multiple puncture tests (Tine and Heaf) should not be used to determine whether a person is infected because the amount of tuberculin injected intradermally cannot be precisely controlled. Tuberculin skin testing is both safe and reliable throughout the course of pregnancy. The Mantoux tuberculin test is performed by placing an intradermal injection of 0.1 mL of tuberculin into the inner surface of the forearm. The test must be performed with tuberculin that has at least the same strength as either 5 tuberculin units (TU) of standard purified protein derivative (PPD)-S or 2 TU of PPD-RT 23, Statens Seruminstitut, as recommended by the World Health Organization. PPD strengths of 1 TU or 250 TU are not acceptable.[20] Using a disposable tuberculin syringe with the needle bevel facing upward, the injection should be made just beneath the surface of the skin. This should produce a discrete, pale elevation of the skin (a wheal) 6 mm to 10 mm in diameter. To prevent needle-stick injuries, needles should not be recapped, purposely bent or broken, removed from disposable syringes, or otherwise manipulated by hand. After they are used, disposable needles and syringes should be placed in puncture-resistant containers for disposal. Institutional guidelines regarding universal precautions for infection control (eg, the use of gloves) should be followed. A trained health care worker, preferably the investigator, should read the reaction to the Mantoux test 48 to 72 hours after the injection. Participants should never be allowed to read their own tuberculin skin test results. If a participant fails to show up for the scheduled reading, a positive reaction may still be measurable up to 1 week after testing. However, if a participant who fails to return within 72 hours has a negative test, tuberculin testing should be repeated. The area of induration (palpable raised hardened area) around the site of injection is the reaction to tuberculin. For standardization, the diameter of the induration should be measured transversely (perpendicular) to the long axis of the forearm. Erythema (redness) should not be measured. All reactions should be recorded in millimeters, even those classified as negative.

Interpreting the Tuberculin Skin Test Results

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

In the US and Canada, an induration of 5 mm or greater in response to the intradermal tuberculin skin test is considered to be a positive result and evidence for either latent or active TB.[3]

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

Treatment of Latent Tuberculosis

Local country guidelines **for immunocompromised participants** should be consulted for acceptable anti-tuberculous treatment regimens for latent TB. If no local country guidelines for immunocompromised participants exist, US guidelines must be followed.

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

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

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

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

Eligibility based on hepatitis B virus test results			
	Hepatitis B test result		
Action	**Hepatitis B surface antigen (HBsAg)**	**Hepatitis B surface antibody (anti-HBs)**	**Hepatitis B core antibody (anti-HBc total)**
Include	—	—	—
	—	+	—
	—	+	+
Exclude	+	— *or* +	— *or* +
Require testing for presence HBV DNA*	—	—	+
* If HBV DNA is detectable, exclude from the clinical study. If HBV DNA testing cannot be performed, or there is evidence of chronic liver disease, exclude from the clinical study.			

10.4. Appendix 4: Clinical Laboratory Tests

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

Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters	
Hematology	Platelet count Red blood cell count Hemoglobin Hematocrit	White Blood Cell (CBC) count with Differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils Bands
	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.	
Clinical Chemistry	Sodium Potassium Chloride Bicarbonate Blood urea nitrogen (BUN) Creatinine Glucose Aspartate aminotransferase (AST)/Serum glutamic-oxaloacetic Alanine aminotransferase (ALT)/Serum glutamic-oxaloacetic	Total bilirubin, with fractionation if hyperbilirubinemia Alkaline phosphatase Uric acid Calcium Albumin Total protein Cholesterol Triglycerides
	Note: All events of ALT ≥3 × upper limit of normal (ULN) and bilirubin ≥2 × ULN (>35% direct bilirubin) or ALT ≥3 × ULN and international normalized ratio (INR) >1.5, if INR measured which may indicate severe liver injury (possible Hy's Law), must be reported as a SAE (excluding studies of hepatic impairment or cirrhosis).	

Laboratory Assessments	Parameters
Other	• Serology: HBV, including HBV serology and HBV DNA (when indicated), antibody to HCV and HCV RNA (when indicated), and antibody to HIV • High sensitivity CRP • Lipid Panel • Serum Sample • FSH is optional. It is only needed for determining childbearing potential of a woman of any age with amenorrhea for less than 12 months. In the absence of 12 months of amenorrhea, 2 FSH measurements are needed. FSH is not needed for female participants with amenorrhea for at least 12 months or any woman of childbearing potential.
Pregnancy	Women of childbearing potential must have a negative urine pregnancy test at screening and at baseline before randomization. Additionally, urine pregnancy testing is required for all women of childbearing potential at every visit. Pregnancy tests must be completed, and the result must be negative before the administration of the study intervention at that visit. All pregnancy test results must be recorded in study source documents.

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

REGULATORY AND ETHICAL CONSIDERATIONS

Investigator Responsibilities

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

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

Protocol Amendments

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

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

Regulatory Approval/Notification

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

Required Prestudy Documentation

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

- Protocol and amendment(s), if any, signed and dated by the principal investigator.

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

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

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

Independent Ethics Committee or Institutional Review Board

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

- Final protocol and, if applicable, amendments
- Sponsor-approved ICF (and any other written materials to be provided to the participants)
- Investigator's Brochure (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.

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 adverse events that are serious, unlisted/unexpected, and associated with the study intervention
- New information that may adversely affect the safety of the participants or the conduct of the study
- Deviations from or changes to the protocol to eliminate immediate hazards to the participants
- Report of deaths of participants under the investigator's care
- Notification if a new investigator is responsible for the study at the site
- Development Safety Update Report and Line Listings, where applicable
- Any other requirements of the IEC/IRB

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

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

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

Country Selection

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

Other Ethical Considerations

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

FINANCIAL DISCLOSURE

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

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

INFORMED CONSENT PROCESS

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

Before enrollment in the study, the investigator or an authorized member of the study-site personnel must explain to potential participants or their legally acceptable representatives the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive for the treatment of his or her disease. Participants will be told that alternative treatments are available if they refuse to take part and that such refusal will not prejudice future treatment. 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 physician may also recontact the participant for the purpose of obtaining consent to collect information about his or her survival status.

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 should be appropriately recorded by means of either 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. An optional consent will be offered to participants for photography of palms and soles.

Participants who are rescreened are required to sign a new ICF, will be assigned a new participant number, and then start a new screening phase.

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.

If the participant or legally acceptable representative is unable to read or write, an impartial witness should be present for the entire informed consent process (which includes reading and explaining all written information) and should personally date and sign the ICF after the oral consent of the participant or legally acceptable representative is obtained.

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

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

Exploratory DNA, biomarker, and PK 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.

PUBLICATION POLICY/DISSEMINATION OF CLINICAL STUDY DATA

All information, including but not limited to information regarding guselkumab or the sponsor's operations (eg, patent application, formulas, manufacturing processes, basic scientific data, prior clinical data, formulation information) supplied by the sponsor to the investigator and not previously published, and any data, including 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 and use this information only to accomplish this study and will not use it for other purposes without the sponsor's prior written consent.

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

The results of the study will be reported in a Clinical Study Report generated by the sponsor and will contain data from all study sites that participated in the study as per protocol. Recruitment performance or specific expertise related to the nature and the key assessment parameters of the study will be used to determine a coordinating investigator for the study. Results of 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 sub-study approaches, secondary results generally should not be published before the primary endpoints of a study have been published. Similarly, investigators will recognize the integrity of a multicenter study by not submitting for publication data derived from the individual study-site until the combined results from the completed study have been submitted for publication, within 18 months after the study end date, or the sponsor confirms there will be no multicenter study publication. Authorship of publications resulting from this study will be based on the guidelines on authorship, such as those described in the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals, which state that the named authors must have made a significant contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of the data for the work; and drafted the work or revised it critically for important intellectual content; and given final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Registration of Clinical Studies and Disclosure of Results

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

DATA QUALITY ASSURANCE

Data Quality Assurance/Quality Control

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

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

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

CASE REPORT FORM COMPLETION

Case report forms are prepared and provided by the sponsor for each participant in electronic format. All data relating to the study must be recorded in CRF. All CRF 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 CRF are accurate and correct.

The study data will be transcribed by study-site personnel from the source documents onto an electronic CRF, 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 CRF. Any such worksheets will become part of the participant's source documents. Data must be entered into CRF in English. The CRF must be completed as soon as possible after a participant visit and the forms should be available for review at the next scheduled monitoring visit.

All participative measurements (eg, 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 eDC tool. If corrections to a CRF are needed after the initial entry into the CRF, this can be done in either of the following ways:

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

SOURCE DOCUMENTS

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

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

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

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

- Race
- Blood pressure, pulse/heart rate and temperature
- Height and weight

- Details of physical examination
- Investigator-completed scales and assessments (PROs will be completed on paper questionnaires and subsequently entered into the CRF)

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

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

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

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

MONITORING

The sponsor will use a combination of monitoring techniques: central, remote, or on-site monitoring to monitor this study.

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 will compare the data entered into the CRF with the source documents (eg, hospital/clinic/physician's office medical records). The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the CRF 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.

ON-SITE AUDITS

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

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

RECORD RETENTION

In compliance with the ICH/GCP guidelines, the investigator/institution will maintain all CRF 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.

STUDY AND SITE CLOSURE

Study Termination

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

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

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

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

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

ADVERSE EVENT DEFINITIONS AND CLASSIFICATIONS

Adverse Event

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

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

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

Serious Adverse Event

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

If a serious and unexpected adverse event occurs for which there is evidence suggesting a causal relationship between the study intervention and the event (eg, 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 (eg, all-cause mortality).

Unlisted (Unexpected) Adverse Event/Reference Safety Information

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

Adverse Event Associated with the Use of the Intervention

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

ATTRIBUTION DEFINITIONS

Assessment of Causality

The causal relationship to study treatment is determined by the Investigator. The following selection should be used to assess all adverse events (AE).

Related

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

Not Related

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

The term "reasonable causal relationship" means there is evidence to support a causal relationship.

SEVERITY CRITERIA

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

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

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

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

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

SPECIAL REPORTING SITUATIONS

Special Reporting Situations 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 (ie, lack of effect) of a sponsor study intervention
- 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, eg, product name confusion, product label confusion, intercepted prescribing or dispensing errors)
- Exposure to a sponsor study intervention from breastfeeding

Special reporting situations should be recorded in the CRF as adverse events. Any special reporting situation that meets the criteria of a SAE should be recorded on the SAE page of the CRF.

PROCEDURES

All Adverse Events

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

For all studies with an outpatient 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 indicating the following:

- Study number
- Statement, in the local language(s), that the participant is participating in a clinical study
- Investigator's name and 24-hour contact telephone number
- Local sponsor's name and 24-hour contact telephone number (for medical staff only)
- Site number
- Participant number
- Any other information that is required to do an emergency breaking of the blind

Serious Adverse Events

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

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

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

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

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 a SAE.

CONTACTING SPONSOR REGARDING SAFETY

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

PRODUCT QUALITY COMPLAINT HANDLING

A product quality complaint (PQC) is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, ie, any dissatisfaction relative to the identity, quality, durability, or reliability of a product, including its labeling or package integrity. A PQC may have an impact on the safety and efficacy of the product. Timely, accurate, and complete reporting and analysis of PQC information from studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies

worldwide. The sponsor has established procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of PQC information; all studies conducted by the sponsor or its affiliates will be conducted in accordance with those procedures.

Procedures

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

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

Contacting Sponsor Regarding Product Quality

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

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

Participants must follow contraceptive measures as outlined in Section 5.1, Inclusion Criteria. Pregnancy information will be collected and reported as noted in Section 8.3.5

Definitions

Woman of Childbearing Potential

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

Woman Not of Childbearing Potential

- **Premenarchal**
  A premenarchal state is one in which menarche has not yet occurred.
- **Postmenopausal**
  A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high FSH level (>40 IU/L or mIU/mL) in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy, however in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
- **Permanently sterile**
  Permanent sterilization methods include hysterectomy, bilateral salpingectomy, bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy.

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

Examples of Contraceptives

Contraceptive use by men or women should be consistent with local regulations regarding the use of contraceptive methods for participants participating in clinical studies. Examples of highly effective contraceptives include:

- User-independent methods: implantable progestogen-only hormone contraception associated with inhibition of ovulation; intrauterine device; intrauterine hormone-releasing system; vasectomized partner; 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).
- User-dependent methods: combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, and transdermal; progestogen-only hormone contraception associated with inhibition of ovulation: oral and injectable.

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 participating in clinical studies.

Study participants must agree to remain on a highly effective method throughout the study and for at least 12 weeks after the last dose of study intervention.

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

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

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

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

Pregnancy During the Study

A female 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.

Because the effect of the study intervention on sperm is unknown, pregnancies in partners of male participants included in the study will be reported. A male study participant is not required to discontinue study intervention if their partner becomes pregnant during the study.

Pregnancy Testing

A woman of childbearing potential must have a negative urine pregnancy test at screening and a negative urine pregnancy test at all study visits (the result must be negative before the administration of any agent at a dosing visit). Additional urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulation, to establish the absence of pregnancy at any time during the participation in the study.

10.8. Appendix 8: Palmoplantar Pustular Psoriasis Area and Severity Index (ppPASI)

Calculation of Palmoplantar Pustular Psoriasis Area and Severity Index (PPPASI)

Score	0	1	2	3	4	5	6
Erythema (E)	None	Slight	Moderate	Severe	Very severe		
Pustules (P)	None	Slight	Moderate	Severe	Very severe		
Desquamation (D)	None	Slight	Moderate	Severe	Very severe		
Area affected (%)	0	10	10 < 30	30 < 50	50 < 70	70 < 90	90-100

PPPASI = (E + P + D) Area x 0´2 (right palm) + (E + P + D) Area x 0´2 (left palm) + (E + P + D) Area x 0´3 (right sole) + (E + P + D) Area x 0´3 (left sole).

10.9. Appendix 9: Psoriasis Area and Severity Index (PASI)

The Psoriasis Area and Severity Index or PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy. The PASI produces a numeric score that can range from 0 to 72. The severity of disease is calculated as follows.

In the PASI system, the body is divided into 4 regions: the head (h), trunk (t), upper extremities (u), and lower extremities (l), which account for 10%, 30%, 20% and 40% of the total BSA, respectively. Each of these areas is assessed separately for erythema, induration and scaling, which are each rated on a scale of 0 to 4.

The scoring system for the signs of the disease (erythema, induration, and scaling) are: 0 = none,
1 = slight, 2 = moderate, 3 = severe, and 4 = very severe.

The scale for estimating the area of involvement for psoriatic lesions is outlined below.

0 = no involvement

1 = 1% to 9% involvement

2 = 10% to 29% involvement

3 = 30% to 49% involvement

4 = 50% to 69% involvement

5 = 70% to 89% involvement

6 = 90% to 100% involvement

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

The PASI formula is:

$$PASI = 0.1 (E_h + I_h + S_h) A_h + 0.3 (E_t + I_t + S_t) A_t + 0.2 (E_u + I_u + S_u) A_u + 0.4 (E_l + I_l + S_l) A_l$$

where E = erythema, I = induration, S = scaling, and A = area

Symptom Score

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

Symptom Score	**Head (H)**	**Trunk (T)**	**Upper Limbs (UL)**	**Lower Limbs (LL)**
Erythema (E)	☐	☐	☐	☐
Induration (I)	☐	☐	☐	☐
Scaling (S)	☐	☐	☐	☐

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

- **The neck is considered part of the head**
- **Axillae and groin are considered a part of the Trunk**
- **buttocks is considered part of the Lower extremities**

Area Score

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

Area Score	**Head (H)**	**Trunk (T)**	**Upper Limbs (UL)**	**Lower Limbs (LL)**
	☐	☐	☐	☐

NOTE: PASI score will be calculated by the eCRF, calculation is not required on this worksheet.

Efficacy Evaluator Signature: _____

Date: _____

10.10. Appendix 10: Palmoplantar Investigator Global Assessment

0 = Clear		No signs of psoriasis, post inflammatory 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

10.11. Appendix 11: Body Surface Area (BSA)

BSA:

- Area of the palm = unit of measure
- The palm of the hand represents approximately 1% of the BSA.

The regions are estimated using the rule of nice are as such
HEAD: 9%
ARMS: 19%
TRUNK: 38%
LEGS: 38%

Br J Dermatol. 1991 Jun;124(6):565-70.

10.12. Appendix 12: Fingernail-Physician Global Assessment (F-PGA)

Fingernail psoriasis will be assessed using a 5-point PGA scale. The assessor should select the category that best represents the condition of all of the fingernails.

0 = Clear	Normal fingernails with no signs of psoriasis in the nail plates or nail beds
1 = Minimal	Just perceptible nail plate pitting, crumbling, onycholysis, oil drop discoloration, and/or nail bed hyperkeratosis
2 = Mild.	Mild nail plate pitting, crumbling, onycholysis, oil drop discoloration, and/or nail bed hyperkeratosis
3 = Moderate	Moderate nail plate pitting, crumbling, onycholysis, oil drop discoloration, and/or nail bed hyperkeratosis
4 = Severe	Severe nail plate pitting, crumbling, onycholysis, oil drop discoloration, and/or nail bed hyperkeratosis

10.13. Appendix 13: Dermatology Life Quality Index (DLQI)

DERMATOLOGY LIFE QUALITY INDEX

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

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	☐ ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

10.14. Appendix 14: EQ-5D-5L

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

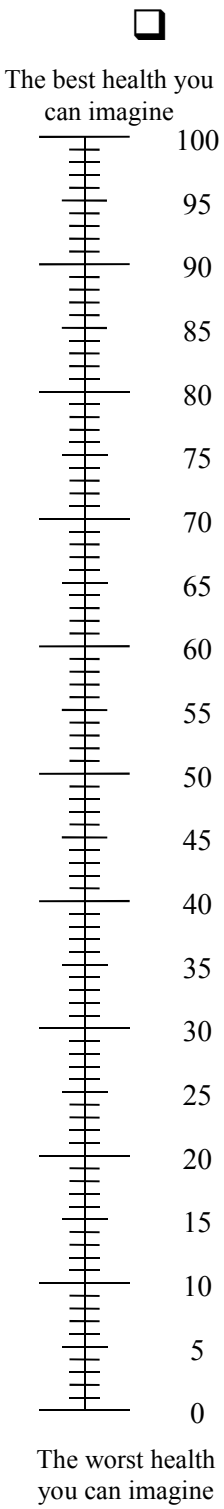
ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑

I am extremely anxious or depressed

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



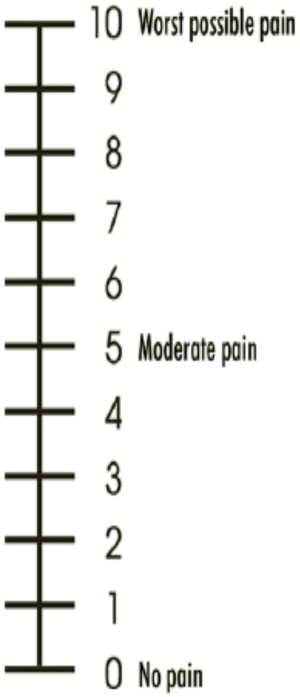
10.15. Appendix 15: Numerical Rating Scale: Pain

NUMERIC RATING SCALE (NRS)

- **Numeric Rating Scale Use**: Have the patient point to, or state the number that best shows how bad his or her pain is NOW
- **Numeric Rating Scale Scoring**: Document the numerical value indicated by the patient. Evaluate the pain intensity over time to determine the effectiveness of pain treatments, and need for changes in treatment.

Numeric Rating Scale

Point to the number that best represents the intensity of your pain NOW



0-10 Numeric Pain Intensity Scale

10.16. Appendix 16: Work Productivity and Activity Impairment: Psoriasis V2.0

The following questions ask about the effect of your psoriasis on your ability to work and perform normal daily activities. *Please fill in the blanks or circle a number, as indicated.*

1. Are you currently employed (working for pay)? _____NO _____YES
   If NO, tick "NO" and skip to question 6.

The next questions refer to the **past seven days**, not including today.

2. During the past seven days, how many hours did you miss from work because of problems associated with your psoriasis? *Include hours you missed on sick days, times you went in late, left early, etc., because of your psoriasis. Do not include time you missed to participate in this study.*

   _____HOURS

3. During the past seven days, how many hours did you miss from work because of any other reason, such as annual leave, holidays, time off to participate in this study?

   _____HOURS

4. During the past seven days, how many hours did you actually work?

   _____HOURS *(If "0", skip to question 6)*

5. During the past seven days, how much did your psoriasis affect your productivity while you were working?

Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If psoriasis affected your work only a little, choose a low number. Choose a high number if psoriasis affected your work a great deal.

Consider only how much psoriasis affected productivity while you were working.

Psoriasis had no effect on my work	0	1	2	3	4	5	6	7	8	9	10	Psoriasis completely prevented me from working

CIRCLE A NUMBER

6. During the past seven days, how much did your psoriasis affect your ability to perform your normal daily activities, other than work at a job?

By normal activities, we mean the usual activities you perform, such as working around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could perform and times you accomplished less than you would like. If psoriasis affected your activities only a little, choose a low number. Choose a high number if psoriasis affected your activities a great deal.

Consider only how much psoriasis affected your ability to do your normal daily activities, other than work at a job.

Psoriasis had no effect on my daily activities	0	1	2	3	4	5	6	7	8	9	10	Psoriasis completely prevented me from doing my daily activities

CIRCLE A NUMBER

Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993 Nov;4(5):353-65.

10.17. Appendix 17: Palmoplantar Quality-of-Life Instrument (PPQLI)

The Palmo-Plantar Quality of Life Instrument (PPQLI)

ID#_____ Date_____

(To be filled in by the research staff)

Hands:

	No Difficulty	Mild Difficulty	Moderate Difficulty	Severe Difficulty	Totally Unable
Open a tight or new jar	**1**	**2**	**3**	**4**	**5**
Heavy household chores	**1**	**2**	**3**	**4**	**5**
Carry shopping bag/briefcase	**1**	**2**	**3**	**4**	**5**
Use knife to cut food	**1**	**2**	**3**	**4**	**5**
Make a bed	**1**	**2**	**3**	**4**	**5**
Write	**1**	**2**	**3**	**4**	**5**
Wash/blow dry hair	**1**	**2**	**3**	**4**	**5**
Recreational activities (golf, tennis, knitting)	**1**	**2**	**3**	**4**	**5**
During the past month did your hands…	**Not at all**	**Slightly**	**Moderately**	**Quite a lot**	**Extremely**
Interfere with usual social activities?	**1**	**2**	**3**	**4**	**5**
Limit work/regular activities as a result of your hands?	**1**	**2**	**3**	**4**	**5**
During the past month did you have…	**None**	**Mild**	**Moderate**	**Severe**	**Extreme**
Hand pain	**1**	**2**	**3**	**4**	**5**
Hand burning/itching	**1**	**2**	**3**	**4**	**5**
Difficulty sleeping because of discomfort/pain in hands	**1**	**2**	**3**	**4**	**5**
I feel…	**Strongly disagree**	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
Embarrassed about my hands/will avoid handshakes and/or caressing	**1**	**2**	**3**	**4**	**5**
Less capable/confident/useful because of my hand problem	**1**	**2**	**3**	**4**	**5**

Feet

Disability	No difficulty	Mild difficulty	Moderate difficulty	Severe difficulty	Totally unable
Walking	1	2	3	4	5
Fast walking/running	1	2	3	4	5
Climbing stairs	1	2	3	4	5
Socks/tights on/off	1	2	3	4	5
In the last month, describe the pain from…	None	Mild	Moderate	Severe	Could not do
Walking	1	2	3	4	5
Fast walking/running	1	2	3	4	5
Climbing stairs	1	2	3	4	5
Standing barefoot	1	2	3	4	5
Standing wearing shoes	1	2	3	4	5
Activity Limitation:					
How often have you avoided pedicures/other activities that expose your feet, due to embarrassment? 1 not at all 2 rarely 3 sometimes 4 frequently 5 all the time					
How much did your feet interfere with normal work, including work outside the home and housework? 1 not at all 2 rarely 3 sometimes 4 frequently 5 all the time					
How much did your feet interfere with your life and ability to do what you want? 1 not at all 2 rarely 3 sometimes 4 frequently 5 all the time					
How much of the time did you use walking stick/crutches/walking frame to get around? 1 not at all 2 rarely 3 sometimes 4 frequently 5 all the time					
How much of the time did you stay indoors most of the day due to foot problems? 1 not at all 2 rarely 3 sometimes 4 frequently 5 all the time					

Hand and/or Feet Questionnaire

Thank you for completing this questionnaire! Please answer every question. Some questions may look like others but each is different. There is no right or wrong answer. If you are not sure how to answer a question, please respond with the best answer you can.

Please rate your ability to do the following activities with your **hands**, on average, over the **past month** by circling the number below the appropriate response.

HAND QUESTIONNAIRE

		No Difficulty	Mild Difficulty	Moderate Difficulty	Severe Difficulty	Totally Unable
1.	Open a tight or new jar	**1**	**2**	**3**	**4**	**5**
2.	Do heavy household chores such as cleaning the oven and floors	**1**	**2**	**3**	**4**	**5**
3.	Carry a shopping bag or briefcase	**1**	**2**	**3**	**4**	**5**
4.	Use a knife to cut food	**1**	**2**	**3**	**4**	**5**
5.	Make a bed	**1**	**2**	**3**	**4**	**5**
6.	Write	**1**	**2**	**3**	**4**	**5**
7.	Wash or blow dry your hair	**1**	**2**	**3**	**4**	**5**
8.	Recreational activities which require little effort such as card playing, knitting, etc.	**1**	**2**	**3**	**4**	**5**
9.	Recreational activities in which you receive some force or impact through your hand such as golf, hammering, tennis, etc.	**1**	**2**	**3**	**4**	**5**
		Not at all	**Slightly**	**Moderately**	**Quite a lot**	**Extremely**
10.	During the past month, *to what extent* have your hands interfered with your normal social activities with family, friends, neighbours?	**1**	**2**	**3**	**4**	**5**
		Not Limited At All	**Slightly Limited**	**Moderately Limited**	**Very Limited**	**Totally Unable**
11.	During the past month, were you limited in your work or other regular activities as a result of your hands?	**1**	**2**	**3**	**4**	**5**

Please rate the severity of the following symptoms in the last month	None	Mild	Moderate	Severe	Extreme
12. Hand Pain	1	2	3	4	5
13. Burning, itching of your hand	1	2	3	4	5
	No Difficulty	**Mild Difficulty**	**Moderate Difficulty**	**Severe Difficulty**	**So much difficulty I can't sleep**
14. During the past month, how much difficulty have you had sleeping because of discomfort/pain in your hands?	1	2	3	4	5
	Strongly Disagree	**Disagree**	**Neither Agree nor Disagree**	**Agree**	**Strongly Agree**
15. I feel embarrassed about my hands and will avoid handshakes and/or caressing	1	2	3	4	5
16. I feel less capable, less confident or less useful because of my hand problem	1	2	3	4	5

*Please rate your ability to do the following activities with your **feet**, on average, over the **past month** by circling the number below the appropriate response.

FEET QUESTIONNAIRE

Disability:					
	No Difficulty	**Mild Difficulty**	**Moderate Difficulty**	**Severe Difficulty**	**Totally Unable**
17. Walking?	1	2	3	4	5
18. Walking fast or running?	1	2	3	4	5
19. Going up or down stairs?	1	2	3	4	5
20. Putting on or taking off socks/tights	1	2	3	4	5
Pain:					
During the past month, please indicate how painful, on average, your foot/feet were during the following activities	**Not Painful**	**Mildly Painful**	**Moderately Painful**	**Extremely Painful**	**Could not do**
21. Walking?	1	2	3	4	5
22. Walking fast or running?	1	2	3	4	5
23. Going up or down stairs?	1	2	3	4	5
24. Standing barefoot?	1	2	3	4	5
25. Standing wearing shoes?	1	2	3	4	5

Activity Limitation:
26. How often have you avoided pedicures or other activities that allow your feet to be exposed because of embarrassment? **1** not at all **2** rarely **3** sometimes **4** frequently **5** all of the time
27. How much did your foot or feet interfere with your normal work, including work both outside the home and housework? **1** not at all **2** a little bit **3** moderately **4** extremely **5** unable to work due to feet
28. How much did your foot or feet interfere with your life and your ability to do what you want? **1** not at all **2** a little bit **3** moderately **4** extremely **5** totally unable to do what I want
29. How much of the time did you use a walking stick, crutches, or a walking frame to get around? **1** not at all **2** rarely **3** sometimes **4** frequently **5** all of the time
30. How much of the time did you stay indoors most of the day because of foot problems? **1** not at all **2** rarely **3** sometimes **4** frequently **5** all of the time

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INVESTIGATOR AGREEMENT

CNTO1959 (guselkumab)
Clinical Protocol CNTO1959PSO3013 Amendment 1

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): Bulent Ozturk

Institution: Janssen Pharmaceutica NV

Signature: _____ Date: 12/07/2019

(Day Month Year)

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

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Approved, Date: 12 July 2019