Janssen Research & Development *

Clinical Protocol

Protocol Title

A Phase 3B, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Guselkumab Administered Subcutaneously in Participants with Active Psoriatic Arthritis who had an Inadequate Response and/or Intolerance to One Prior Anti-Tumor Necrosis Factor α Agent

SOLSTICE

Short Title

Guselkumab versus Placebo for the Treatment of Active Psoriatic Arthritis in Participants with Inadequate Response and/or Intolerance to One Prior Anti-Tumor Necrosis Factor α Agent

Protocol CNTO1959PSA3005; Phase 3b
AMENDMENT 2

Guselkumab (Tremfya)

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

Studies conducted at sites in the European Economic Area (EEA) will be conducted under Regulation [EU] No 536/2014.

IND: 124177
EU TRIAL NUMBER: 2023-504715-33

Status: Approved
Date: 04 September 2024
Prepared by: Janssen Research & Development, LLC
EDMS number: EDMS-RIM-394927, 3.0

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 2	04 September 2024
Amendment 1	12 May 2022
Original Protocol	13 April 2021

Amendment 2 (04 September 2024)

Overall Rationale for the Amendment: The overall reason for this amendment is to update the protocol to comply with the European Union /European Economic Area Clinical Trial Regulations (EU CTR) requirements. In addition, revisions were made to correct errors and to improve clarity and consistency in the protocol.

The changes made to the clinical protocol CNTO1959PSA3005 as part of Protocol Amendment 2 are listed below, including the rationale of each change and a list of all applicable sections. Changes made in previous protocol amendments are listed in Section 10.10 Appendix 10: Protocol Amendment History.

Section Number and Name	Description of Change	Brief Rationale
Title Page; 1.1. Synopsis	Added text on EU regulation, and EU trial number per EU CTR requirement.	For compliance with EU CTR.
1.1 Synopsis	Added Benefit-Risk Assessment section to protocol synopsis.	
8.3.4 Regulatory Reporting Requirements for Serious Adverse Events and Anticipated Events	Text in this section was updated.	
10.5.7. Publication Policy/Dissemination of Clinical Study Data	Text added to specify timing of submission of Week 24 results to the EU database.	
10.5.13. Record Retention	Text added to specify length of time the content of the trial master file will be archived after study completion.	
1.2. Schema	Study visits removed from Weeks 60 and 92.	Schema corrected to indicate Weeks 60 and 92 are not required site visits.
1.3. Schedule of Activities	Study intervention administration added at Week 52.	Added study intervention administration at Week 52, which was accidentally omitted previously.
1.3. Schedule of Activities	Footnote m. updated to indicate pregnancy tests administration is optional for participants who dose at home during at-home administration visits.	Clarification of use of pregnancy test(s) during at-home administration visits.
1.3. Schedule of Activities	Physical examination at Week 80 was removed from schedule.	Removed physical examination at Week 80 to correct previous addition error.
5.1. Inclusion Criteria	Note regarding acceptability of a condom or occlusive cap as the sole method of contraception	Note was incorrectly located in criterion regarding male

Section Number and Name	Description of Change	Brief Rationale
	moved from Inclusion Criteria 21 (removed) to Inclusion Criteria 17 (added).	contraception. Note moved to correct location in criteria regarding female contraception.
6.8.3. Nonsteroidal Anti-Inflammatory Drugs and Other Analgesics	Interval of maintenance of stable dose of NSAIDs and other analgesics, including topical analgesics from baseline updated from “through Week 52” to “through Week 24”.	Updated for consistency within section regarding initiation or increase of NSAIDs or other analgesics after Week 24.
6.8.5. Complementary Therapies	Length of prohibition of use of complementary therapies corrected to through Week 112.	The use of complementary therapies is prohibited through the end of study.
8. Study Assessments and Procedures, Overview	Maximum total volume of blood to be collected from each participant updated to 625 mL.	Updated maximum blood draw volume due to change in lab tubes used for the study.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted

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1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 3B, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Guselkumab Administered Subcutaneously in Participants with Active Psoriatic Arthritis who had an Inadequate Response and/or Intolerance to One Prior Anti-Tumor Necrosis Factor α Agent

IND: 124177
EU TRIAL NUMBER: 2023-504-715-33

Short Title: Guselkumab versus Placebo for the Treatment of Active Psoriatic Arthritis in Participants with Inadequate Response and/or Intolerance to One Prior Anti-Tumor Necrosis Factor α Agent

Guselkumab (TREMFYA®, CNTO1959) is a fully human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody (mAb) that binds to the p19 protein subunit of interleukin (IL)-23 with high affinity. By binding to the p19 protein subunit of IL-23, guselkumab blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23-mediated intracellular signaling, activation, and cytokine production.

Benefit-Risk Assessment for Study Participation

Additional data through 1 year of treatment from the PSA3001 and PSA3002 studies for both guselkumab doses (ie, 100 mg SC q8w and q4w) under study in this protocol continue to support an overall favorable benefit-to-risk profile for the use of guselkumab in active PsA.

Potential risks of guselkumab are being addressed via judicious inclusion/exclusion criteria, frequent study visits to allow for close monitoring of patient safety, guidelines for participant management (including monitoring of clinical laboratory tests and treatment discontinuation criteria), detailed description of allowed and prohibited concomitant medications, and comprehensive medical monitoring of data by the Sponsor/designee during the conduct of the studies.

Taking into account the measures taken to minimize risk to participants in this study, the potential risks identified in association with guselkumab are justified by the benefits that may be provided to participants with PsA.

OBJECTIVES AND ENDPOINTS

Objective	Endpoint
Primary	
• To evaluate the efficacy of guselkumab treatment in participants with active PsA and IR and/or intolerance to a prior anti-TNF by assessing the reduction in signs and symptoms of PsA.	• Proportion of participants who achieve an ACR20 response at Week 24
Major Secondary	
• To evaluate the efficacy of guselkumab on additional measures of signs and symptoms of PsA, psoriasis, and patient well-being.	• Proportion of participants who achieve a psoriasis response of IGA psoriasis score of 0 (cleared) or 1 (minimal) AND ≥2-grade reduction from baseline at Week 24 among the participants with ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at baseline • Proportion of participants who achieve PASI 90 response at Week 24 among the participants

	with ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at baseline • Change from baseline in HAQ-DI at Week 24 • Change from baseline in the SF-36 PCS at Week 24 • Change from baseline in Functional Assessment of Chronic Illness Therapy – fatigue (FACIT-F) score at Week 24 • Proportion of participants achieving minimal disease activity (MDA) at Week 24 • Proportion of participants who achieve ACR20 response at Week 16 • Proportion of participants who achieve ACR50 response at Week 16 • Proportion of participants who achieve ACR50 response at Week 24 • Proportion of participants who achieve ACR70 response at Week 24 The ordering of endpoints, methods of analysis and the approach to control the Type I error for multiplicity, as well as the data-handling rules for the major secondary endpoints will be specified in the Statistical Analysis Plan (SAP).
Other Secondary	
• To evaluate the safety of guselkumab in participants with active PsA.	Other secondary: • Frequency and type of AEs, SAEs, reasonably related AEs, AEs leading to discontinuation of study intervention, infections, and injection-site reactions • Laboratory abnormalities (chemistry, hematology) maximum toxicity (Common Terminology Criteria for Adverse Events [CTCAE 5.0]) grades
• To evaluate the pharmacokinetics (PK) and immunogenicity of guselkumab in participants with active PsA.	• Serum guselkumab concentration over time • Incidence of antibodies to guselkumab
CCI [redacted]	

CCI

[redacted]

CCI

Hypothesis

The primary hypothesis of this study is that guselkumab is superior to placebo as assessed by the proportion of participants who had an IR and/or intolerance to one prior anti-TNF achieving an ACR 20 response at Week 24.

OVERALL DESIGN

This is a Phase 3b, multicenter, randomized, double-blind, placebo-controlled interventional study in participants who had IR and/or intolerance to one prior anti-TNF. Stable doses of concomitant non-steroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids (≤ 10 mg/day prednisone equivalent), selected non-biologic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate (MTX), sulfasalazine (SSZ), hydroxychloroquine (HCQ), or leflunomide (LEF) are not required but will be allowed if participants are on stable doses.

There will be a screening phase of up to 6 weeks, a blinded treatment phase of approximately 2 years that will include a placebo-controlled period from Week 0 to Week 24 and an active-controlled treatment phase from Week 24 to Week 100, and a safety follow-up at Week 112 (approximately 12 weeks after the last intended dose at Week 100 per protocol).

Database locks (DBLs) are scheduled at Week 24, Week 52, and the end of the study (Week 112). The end of study is considered as the last visit for the last participant in the study.

STUDY POPULATION

The target study population is participants with active PsA who had an IR and/or intolerance to one prior anti-TNF. This population is appropriate to provide relevant efficacy and safety information given that the likely intended use of guselkumab for active PsA in pragmatic clinical settings would be as an alternative mechanism of action after anti-TNF utilization.

NUMBER OF PARTICIPANTS

A target of 450 participants will be randomly assigned in this study with 150 participants planned per intervention group: Guselkumab every 8 weeks (n=150), guselkumab every 4 weeks (n=150), or placebo (n=150).

INTERVENTION GROUPS AND DURATION

At Week 0, participants who satisfy all inclusion and exclusion criteria will be randomly assigned to 1 of the following 3 treatment groups in a 1:1:1 ratio using permuted block randomization stratified by baseline non-biologic DMARD use (yes/no).

- **Group I (n=150), guselkumab 100 mg subcutaneously (SC) every 8 weeks (q8w):** Participants will receive guselkumab 100 mg SC at Weeks 0, 4, then q8w at Weeks 12, 20, 28, 36, 44, 52, 60, 68, 76, 84, 92, and 100. Participants will receive placebo at Weeks 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, and 96 to maintain the blind.
- **Group II (n=150), guselkumab 100 mg SC every 4 weeks (q4w):** Participants will receive guselkumab 100 mg SC at Weeks 0, 4, then q4w at Weeks 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, and 100.

- **Group III (n=150), placebo and placebo cross-over to guselkumab 100 mg SC q4w:** Participants will receive placebo SC at Weeks 0, 4, 8, 12, 16 and 20, and will cross over at Week 24 to receive guselkumab 100 mg SC at Weeks 24, 28, then q4w at Weeks 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, and 100.

At Week 16, all participants in Groups I, II, and III with <20% improvement from baseline in both tender and swollen joint counts will qualify for early escape and will be allowed to initiate or increase the dose of one of the permitted concomitant medications up to the maximum allowed dose as specified in Table 3, as selected by the investigator.

At Week 24, all participants in the placebo group (Group III) will cross over in a blinded fashion to receive guselkumab 100 mg SC q4w through Week 100; this will allow for collection of additional safety data for the 100 mg SC q4w dose. Participants in the guselkumab groups (Groups I and II) will remain on the dosing regimen they were randomized to at Week 0, through Week 100.

Description of Interventions

Group/Arm Name	Group I (q8w)	Group II (q4w)	Group III
Intervention Name	Guselkumab	Guselkumab	Placebo
Dose Formulation	Guselkumab 100 mg and matching liquid placebo for guselkumab will be provided in a single-use prefilled syringe (PFS) assembled with the Ultrasafe PLUS™ Passive Needle Guard (PFS-U).	Guselkumab 100 mg will be provided in a single-use PFS assembled with the PFS-U.	Placebo
Unit Dose Strength(s)	100 mg	100 mg	
Dosage Level(s)	100 mg at Weeks 0, 4, then q8w through Week 100 (placebo at alternate visits)	100 mg q4w through Week 100	Placebo q4w through Week 20, then guselkumab 100 mg q4w through Week 100
Route of Administration	subcutaneous	subcutaneous	subcutaneous

EFFICACY EVALUATIONS

Efficacy assessments of arthritis: Joint count (tender and swollen), nonevaluable joints, ACR Responses, dactylitis score, enthesitis assessments, Health Assessment Questionnaire-Disability Index (HAQ-DI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in participants with spondylitis with peripheral arthritis as their primary arthritic presentation of PsA at baseline, Disease Activity index for PSoriatic Arthritis (DAPSA), Minimal Disease Activity (MDA), Very Low Disease Activity (VLDA), and Psoriatic ArthritiS Disease Activity Score (PASDAS) will be performed at visits according to the Schedule of Activities.

Efficacy assessments of psoriasis: Psoriasis Area and Severity Index (PASI) and Investigator's Global Assessment (IGA), will be performed at visits according to the Schedule of Activities.

Patient-reported outcomes: PsA Impact of Disease (PsAID)-12, Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, Patient-Reported Outcomes Measurement Information System (PROMIS)-29, and 36-item Short Form Health Survey (SF-36) will be performed at visits according to the Schedule of Activities.

PHARMACOKINETIC/IMMUNOGENICITY EVALUATIONS

Venous blood samples will be collected for measurement of serum concentrations of guselkumab and antibodies to guselkumab at the timepoints shown in the Schedule of Activities. Serum collected for PK

and immunogenicity analyses may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period.

PHARMACODYNAMIC AND BIOMARKER EVALUATIONS

Biomarker assessments will be made to examine the biologic response to treatment and to identify biomarkers that are relevant to guselkumab treatment and/or PsA, where local regulations permit. Assessments may include the evaluation of relevant biomarkers in serum, plasma, whole blood, and (optional) skin biopsy collected as specified in the Schedule of Activities, where local regulations permit.

PHARMACOGENOMIC (DNA) EVALUATIONS

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

SAFETY EVALUATIONS

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

STATISTICAL METHODS

A sample size of 150 participants per group for each of the guselkumab treatment groups and placebo will have >90% power to detect differences between each guselkumab treatment group and placebo for the primary endpoint assuming a 2-sided alpha level of 0.05.

In general, descriptive statistics, such as mean, standard deviation (SD), median, interquartile (IQ) range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data. For binary response efficacy endpoints, treatment comparisons will generally be performed using a Chi-square test or a Cochran-Mantel-Haenszel (CMH) test. For continuous endpoints of efficacy data, treatment comparisons will be performed using an analysis of covariance (ANCOVA), a mixed model for repeated measures (MMRM) or a constrained longitudinal data analysis (cLDA) model.

In general, statistical testing will be performed using 2-sided tests. The overall type I error will be controlled among the primary and major secondary endpoints at 5%.

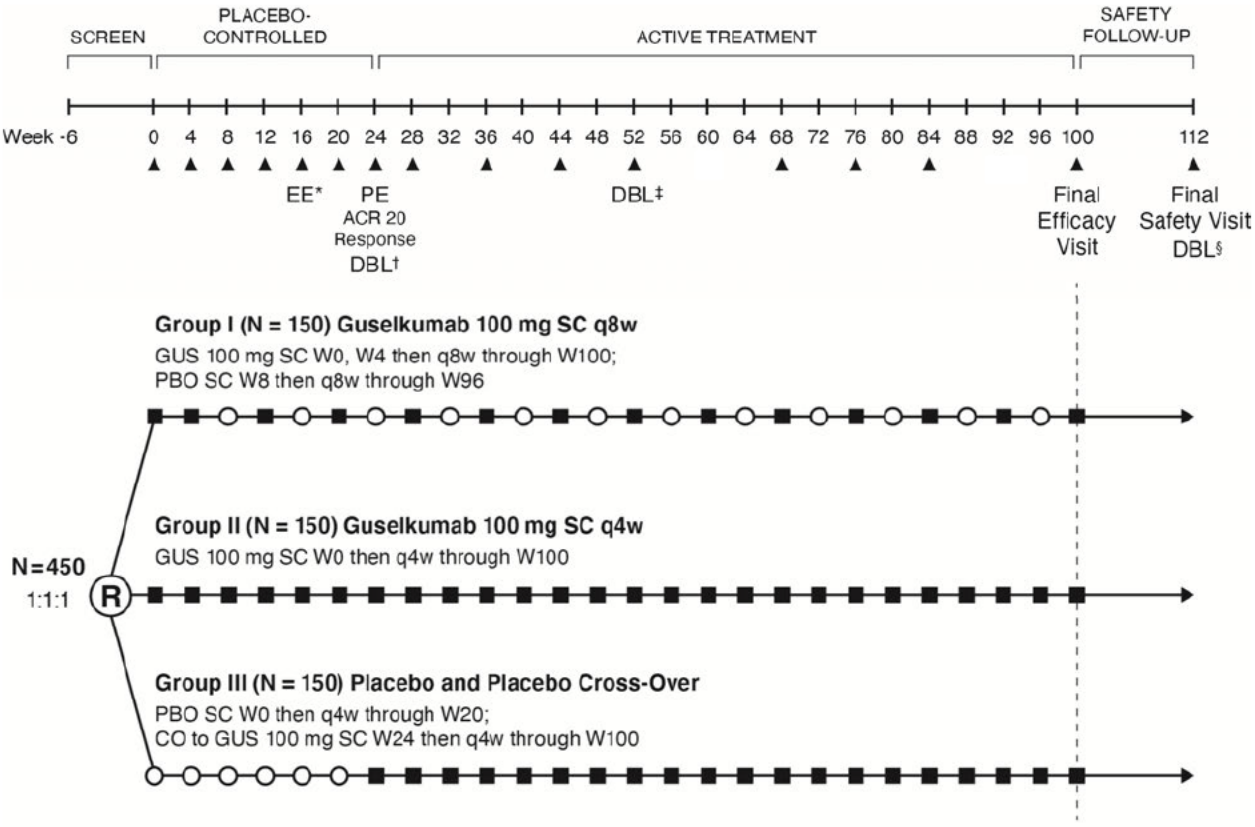
The primary endpoint to be analyzed for the primary analysis is the proportion of participants who achieved an ACR 20 response at Week 24. This endpoint will be analyzed based on the estimands defined in Section 9. Participants with missing data at Week 24 will be considered non-responders.

The Type 1 error will be multiplicity controlled for the primary and major secondary endpoints. All other secondary endpoints will be summarized over time by treatment groups. Treatment comparisons will be performed by visit through Week 24.

For safety analyses, for each AE, the percentage of participants who experience at least 1 occurrence of the given event will be summarized by treatment group. The analyses of AEs will be performed for safety measures including but not limited to, AEs, SAEs, infections, and injection site reactions. Descriptive statistics will be calculated for selected laboratory analytes at baseline and for observed values and changes from baseline at each scheduled timepoint.

1.2. Schema

Schematic Overview of the Study



Ⓡ = Randomization ■ = Guselkumab 100 mg SC ○ = Placebo SC ▲ = Study visit

DBL = Database Lock EE = Early Escape CO = Placebo Crossover PE = Primary Endpoint SC = subcutaneous
GUS = guselkumab PBO = placebo q4w = every 4 weeks q8w = every 8 weeks

* Early Escape: At Week 16, all participants in Groups I, II, and III with <20% improvement from baseline in both tender and swollen joint counts will qualify for early escape and will be allowed to initiate or increase the dose of one of the permitted concomitant medications up to the maximum allowed dose, as selected by the investigator.

† The first DBL will occur when all randomized participants have either completed the Week 24 assessments or terminated study participation prior to the Week 24 visit.

‡ The second DBL will occur when all randomized participants have either completed the Week 52 assessments or terminated study participation prior to the Week 52 visit.

§ The third DBL will occur when all participants have either completed their final safety visit or have terminated study participation.

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1.3. Schedule of Activities (SoA)

Through Week 52

Phase	Screening	Blinded Placebo-controlled [b]							Blinded Active-controlled [b]						
Week	**Screening [a]**	**0 [c]**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**	**52**
Study Procedures [d]															
Screening/Administrative															
Informed Consent (ICF/eICF [e])	X														
Review of Inclusion/Exclusion Criteria	X	X													
Demography/Medical History	X														
Pre-planned Surgery/Procedure(s)	X														
Pre-study Therapy Review for Eligibility	X	X													
Pelvic X-ray	X [f]														
Study Intervention Administration															
Randomization		X													
Study Intervention		X	X	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]	X [g]
Safety Assessments															
Physical Examination (including skin)	X							X							X
eC-SSRS [h]	X	X	X	X	X	X	X	X	X	X [h]	X	X [h]	X	X [h]	X
Vital Signs [i]	X	X	X	X	X	X	X	X	X	X [i]	X	X [i]	X	X [i]	X
Height		X													
Weight		X						X							X
Local 12-lead ECG [j]		X [j]													
Tuberculosis Evaluation [k]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chest Radiograph [l]	X														
Pregnancy Test [m]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Injection Site Reaction		X	X	X	X	X	X	X	X	X	X	X	X	X	

Phase	Screening	Blinded Placebo-controlled [b]							Blinded Active-controlled [b]						
Week	**Screening [a]**	**0 [c]**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**	**52**
Study Procedures [d]															
Screening/Administrative															
Early Escape						X [n]									
Efficacy Assessments															
Joint Assessments [o]	X	X	X	X	X	X	X	X	X		X		X		X
HAQ-DI [p]		X	X	X	X	X	X	X	X		X		X		X
Physician Global Assessment of Disease Activity [o]		X	X	X	X	X	X	X	X		X		X		X
Patient's Global Assessment of Disease Activity (Arthritis) [p]		X	X	X	X	X	X	X	X		X		X		X
Patient's Global Assessment of Disease Activity (Arthritis and Psoriasis) [p]		X	X	X	X	X	X	X	X		X		X		X
Patient's Assessment of Pain [p]		X	X	X	X	X	X	X	X		X		X		X
Dactylitis assessments		X	X	X		X		X	X		X		X		X
Enthesitis assessments (LEI, SPARCC)		X	X	X		X		X	X		X		X		X
BASDAI [f,p,q]		X		X		X		X							X
PsAID-12 [p]		X		X		X		X							X
FACIT-fatigue [p]		X		X		X		X							X
PROMIS-29 [p]		X		X		X		X							X
SF-36 [p]		X		X		X		X							X
BSA % Involvement of Psoriasis		X													
IGA-Psoriasis		X				X		X							X
PASI		X				X		X							X
Clinical Laboratory Tests															
QuantiFERON-TB test [r]	X														
Hepatitis B and C Serologies [s]	X														
HIV Antibody Test [s]	X														
Hematology, Chemistry [s]	X	X	X	X	X	X	X	X	X		X		X		X
Lipid Panel [s]		X													X
C-reactive Protein [s]	X	X	X	X	X	X	X	X	X		X		X		X
Rheumatoid Factor [s,t]	X														
Follicle Stimulating Hormone [s,u]	X														

Phase	Screening	Blinded Placebo-controlled [b]							Blinded Active-controlled [b]						
Week	**Screening [a]**	**0 [c]**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**	**52**
Study Procedures [d]															
Screening/Administrative															
PK/Antibodies/Biomarkers															
PK sampling [v]		X	X	X	X	X	X	X			X		X		X
Antibodies to study agent [v]		X	X		X			X							X
Serum biomarkers		X	X			X		X							X
Plasma biomarkers		X	X			X		X							X
Whole Blood (RNA)		X	X			X		X							X
Pharmacogenomics DNA collection (optional, whole blood/EDTA) [w]		X													
PBMC [x]		X	X			X		X							X
Skin biopsy (optional) [y]		X						X							
Ongoing															
Device deficiencies		X----------													X
Prior and Concomitant therapy		X----------													X
Adverse events		X----------													X

a. The screening visit is to occur within approximately 6 weeks before administration of study intervention at Week 0. 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 complete 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. All post-baseline visits up to and including Week 24 will have a visit window of ± 4 days counting from Week 0 as Day 1. After Week 24, study visits will have a visit window of ± 7 days. Week 112 or the final safety visit (12 weeks after the last dose in participants who discontinued study treatment) will have a visit window of ±14 days.

c. Participants must fast (ie, no food or beverages [except water]) for at least 8 hours before blood is drawn for lipid panel (Week 0). All other visits can be non-fasting.

d. If a participant discontinues study drug intervention prior to the Week 24 visit, they should be encouraged to return for all remaining study visits through Week 24. The participant should also return for a final safety visit to perform assessments under the Week 112/final safety visit approximately 12 weeks after the last study intervention administration. If a participant permanently discontinues study intervention administration at or after the Week 24 and before the Week 100 visit, the final efficacy visit should occur at the time of discontinuation or as soon as possible and all assessments under the Week 100/final efficacy visit should be performed. Fasting is not required for the final efficacy visit. The participant should also return for a final safety visit to perform assessments under the Week 112/final safety visit approximately 12 weeks after the last study intervention administration.

e. Must be signed before first study-related activity.

f. Participants with spondylitis with peripheral arthritis as their primary arthritic presentation of PsA will have confirmation of sacroiliitis during screening by a centrally read pelvic X-ray (ie, anteroposterior views of the sacrum). An existing X-ray done within 3 months of screening may be sent for central reading in lieu

of a screening X-ray (and if not of sufficient quality, a new screening X-ray would then be performed and centrally read). Participants who have confirmed sacroiliitis will complete the BASDAI at specified visits in the SoA.

g. Study intervention will be administered SC q4w by a healthcare professional during visits to the site 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 8, at the discretion of the investigator and participant, and after appropriate and documented training, participants (or caregiver) may administer study intervention at the investigative site under the supervision of a health care professional. After appropriate training, beginning at Week 32, participants (or caregiver) may administer study intervention at home and on-site visits are only required at Weeks 36, 44, and 52. Safety and efficacy assessments, including blood samples for clinical laboratory and pharmacokinetics/immunogenicity, as specified in the SoA should be performed prior to study intervention administration.
h. At the screening visit (after signing informed consent), the eC-SSRS should be performed after the joint assessment. At Week 0/baseline and at all post-baseline visits, the eC-SSRS should be completed after all PRO, but before other tests, procedures or other consultations. At Weeks 32, 40, 48, the eC-SSRS is only completed by participants who have study intervention administration at the investigative site. See Section 8.2.7 for more details.
i. Vital signs include blood pressure and heart rate. At Weeks 32, 40, 48, vital signs are only assessed for participants who have study intervention administration at the investigative site.
j. 12-lead ECG must be done prior to first administration of study intervention.
k. Participants (as outlined in Inclusion Criterion 13) must undergo testing for TB (Appendix 10.2) and their medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB.
l. The chest radiograph may be taken within 3 months prior to the first administration of study intervention.
m. Females of childbearing potential will have a serum pregnancy test at screening. Those who are dosed at the clinic must have a negative urine pregnancy test at all dosing visits prior to administration of study intervention. For those who choose to dose at home during the at-home administration visits (Weeks 32, 40, 48, 56, 60, 64, 72, 80, 88, 92, and 96), pregnancy test(s) are not required.
n. At Week 16, all participants who qualify for early escape will continue on the dosing regimen to which they were randomized and will be allowed to initiate or increase the dose of a permitted concomitant medication intervention up to the maximum dose as specified in Table 3, at the discretion of the investigator. Titration to a stable dose of the medication should be completed for participants qualifying for early escape by the Week 24 visit.
o. These efficacy evaluations should be performed prior to study intervention administration at each visit, as applicable.
p. All patient questionnaires should be completed before any other tests, procedures, or evaluations on the day of the visit for baseline and post-baseline visits.
q. The BASDAI will be completed only in participants with spondylitis with peripheral arthritis as their primary arthritic presentation of PsA based on confirmation of sacroiliitis by a centrally read pelvic X-ray (ie, anteroposterior views of the sacrum) during screening (see footnote f).
r. A tuberculin skin test is additionally required if the QuantiFERON®-TB test is not approved/registered in the country in which this study is being conducted, with the exception noted in Inclusion Criterion 13. All participants will undergo QuantiFERON-TB testing. The frequency of TB testing can be increased depending on local health authority requirements. In Ukraine, while the QuantiFERON-TB test is not approved/registered, it is accepted, and a tuberculin skin test is not required.
s. Laboratory tests are listed in Appendix 10.2.
t. This test is optional. It can be done only if needed to confirm whether CASPAR criteria are met.
u. Prior to randomization, FSH is required for female participants with amenorrhea for less than 12 months. A second FSH measurement may be needed to confirm amenorrhea in these participants. This test should not be done for any female participant of childbearing potential or female participants with amenorrhea for at least 12 months.
v. All blood samples must be collected before study intervention administration at visits when a study intervention administration is scheduled. Blood collected from 1 venipuncture will be divided into multiple aliquots of serum for the measurement of guselkumab concentration, antibodies to guselkumab, and a back-up sample. Details will be provided in the Laboratory Manual.
w. To participate in the optional DNA research component of this study, participants must sign the DNA research ICF indicating willingness to participate.

Blood samples for pharmacogenomic and epigenetic research will be collected only from participants who give informed consent for DNA research. The pharmacogenomic (DNA) sample should be collected at the specified timepoint; however, if necessary, it may be collected at a later timepoint without constituting a protocol deviation.

x. PBMCs will be collected at sites where logistically feasible.

y. Optional skin biopsies may be collected at select sites, if feasible. Samples from a lesional and a non-lesional region will be collected at Week 0 and only a sample from a lesional region will be collected at Week 24.

Abbreviations: BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BSA = body surface area; CASPAR = ClASsification criteria for Psoriatic Arthritis; DNA = deoxyribonucleic acid; ECG = electrocardiogram; eC-SSRS=electronic Columbia-Suicide Severity Rating Scale; EDTA = ethylenediaminetetraacetic acid; FACIT = Functional Assessment of Chronic Illness Therapy; FSH = follicle stimulating hormone; HAQ-DI = Health Assessment Questionnaire- Disability Index; HIV = human immunodeficiency virus; ICF = informed consent form; IGA = Investigator's Global Assessment; LEI = Leeds Enthesitis Index; PASI = Psoriatic Area and Severity Index; PBMC = peripheral blood mononuclear cell; PsAID-12 = psoriatic arthritis impact of disease score; PROMIS = Patient-Reported Outcome Measure Information System; q4w =every 4 weeks; RNA = ribonucleic acid; SC=subcutaneous; SF-36 = 36-item short form health survey; SPARCC = Spondyloarthritis Research Consortium of Canada; TB = tuberculosis.

Long-term Extension: Week 56 through Week 112

Phase	Blinded Active-controlled											Final efficacy visit [b]	Safety follow-up [b]
Week	**56**	**60**	**64**	**68**	**72**	**76**	**80**	**84**	**88**	**92**	**96**	**100**	**112**
Study Procedures [a]													
Study Intervention Administration													
Study Intervention [c]	X	X	X	X	X	X	X	X	X	X	X	X	
Safety Assessments													
Physical Examination (including skin)												X	X
eC-SSRS [d]				X		X		X				X	X
Vital Signs [e]				X		X		X				X	X
Height												X	
Weight												X	
Tuberculosis Evaluation				X		X		X				X	X
Pregnancy Test				X		X		X				X	X
Injection Site Reaction				X		X		X				X	
Efficacy Assessments													
Joint Assessments [f]				X		X		X				X	
HAQ-DI [g]				X		X		X				X	
Physician Global Assessment of Disease Activity [f]				X		X		X				X	
Patient's Global Assessment of Disease Activity (Arthritis) [g]				X		X		X				X	
Patient's Global Assessment of Disease Activity (Arthritis and Psoriasis) [g]				X		X		X				X	
Patient's Assessment of Pain [g]				X		X		X				X	
Dactylitis assessments				X		X		X				X	
Enthesitis assessments (LEI, SPARCC)				X		X		X				X	
BASDAI [f,g,h]						X						X	
PsAID-12 [g]						X						X	
FACIT-fatigue [g]						X						X	
PROMIS-29 [g]						X						X	
SF-36 [g]						X						X	
BSA % Involvement of Psoriasis						X						X	

Phase	Blinded Active-controlled											Final efficacy visit [b]	Safety follow-up [b]
Week	**56**	**60**	**64**	**68**	**72**	**76**	**80**	**84**	**88**	**92**	**96**	**100**	**112**
Study Procedures [a]													
IGA-Psoriasis						X						X	
PASI						X						X	
Clinical Laboratory Tests													
Hematology, Chemistry [i]				X		X		X				X	X
Lipid Panel												X	
C-reactive Protein				X		X		X				X	
PK/Antibodies/Biomarkers													
PK sampling [j]						X						X	X
Antibodies to study agent [j]						X						X	X
Serum biomarkers												X	
Plasma biomarkers												X	
Whole Blood (RNA)												X	
PBMC [k]												X	
Ongoing													
Device deficiencies	X----------											X	
Prior and Concomitant therapy	X----------											X	X
Adverse events	X----------											X	X

a. After Week 24, study visits will have a visit window of ± 7 days. Week 112 or the final safety visit (12 weeks after the last dose in participants who discontinued study treatment) will have a visit window of ±14 days.
b. If a participant discontinues study drug intervention prior to the Week 100 visit, they should be encouraged to return for all remaining study visits through Week 100. The participant should also return for a final safety visit to perform assessments under the Week 112/final safety visit approximately 12 weeks after the last study intervention administration. If a participant permanently discontinues study intervention administration before the Week 100 visit, the final efficacy visit should occur at the time of discontinuation or as soon as possible and all assessments under the Week 100/final efficacy visit should be performed. Fasting is not required for the final efficacy visit. The participant should also return for a final safety visit to perform assessments under the Week 112/final safety visit approximately 12 weeks after the last study intervention administration.
c. Participants (or caregiver) may administer study intervention at home and on-site visits are only required at Weeks 68, 76, 84 and 100. Safety and efficacy assessments, including blood samples for clinical laboratory and pharmacokinetics/immunogenicity, as specified in the SoA should be performed prior to study intervention administration.
d. The eC-SSRS should be performed after the joint assessment. The eC-SSRS should be completed after all PRO, but before other tests, procedures or other consultations. At Weeks 56, 60, 64, 72, 80, 88, 92 and 96, the eC-SSRS is only completed by participants who have study intervention administration at the investigative site. See Section 8.2.7 for more details.
e. Vital signs include blood pressure and heart rate. At Weeks 56, 60, 64, 72, 80, 88, 92 and 96 vital signs are only assessed for participants who have study intervention administration at the investigative site.

f. These efficacy evaluations should be performed prior to study intervention administration at each visit, as applicable.
g. All patient questionnaires should be completed before any other tests, procedures, or evaluations on the day of the visit for post-baseline visits.
h. The BASDAI will be completed only in participants with spondylitis with peripheral arthritis as their primary arthritic presentation of PsA based on confirmation of sacroiliitis by a centrally read pelvic X-ray (ie, anteroposterior views of the sacrum) during screening.
i. Laboratory tests are listed in Appendix 10.2.
j. All blood samples must be collected before study intervention administration at visits when a study intervention administration is scheduled. Blood collected from 1 venipuncture will be divided into multiple aliquots of serum for the measurement of guselkumab concentration, antibodies to guselkumab, and a back-up sample. Details will be provided in the Laboratory Manual.
k. PBMCs will be collected at sites where logistically feasible.

2. INTRODUCTION

Guselkumab (TREMFYA®, CNTO1959) is a fully human immunoglobulin (IgG)1λ monoclonal antibody (mAb) that binds to the p19 protein subunit of interleukin (IL)-23 with high affinity. By binding to the p19 protein subunit of IL-23, guselkumab blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23-mediated intracellular signaling, activation, and cytokine production.

The clinical development program for guselkumab includes completed, ongoing, or planned studies in adult participants with psoriatic arthritis (PsA), psoriasis, lupus nephritis, inflammatory bowel disease, rheumatoid arthritis, palmoplantar pustulosis, generalized pustular psoriasis, erythrodermic psoriasis and familial adenomatous polyposis, giant cell arteritis, Hidradenitis Suppurativa as well as an ongoing study in pediatric participants with psoriasis.

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

The term “study intervention” throughout the protocol, refers to guselkumab or placebo administered using an UltraSafe Plus™ Passive Needle Guard (PFS-U) device as defined in Section 6.1, Study Interventions Administered.

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

2.1. Study Rationale

Despite recent advances in treatment options for PsA, there remains an unmet medical need for novel therapeutic agents that address the heterogeneous clinical manifestations of PsA and offer an improved benefit/risk profile. Although anti-tumor necrosis factor (TNF) agents are frequently chosen as the first biologic therapy for patients with PsA, a substantial proportion of patients assessed in clinical trials do not achieve meaningful American College of Rheumatology (ACR)-defined responses, and some patients may not tolerate or may have medical contraindications to these agents. In addition, patients who have had an inadequate response (IR) to an anti-TNF may be more difficult to treat and may require dose flexibility to attain improved efficacy.

Guselkumab is the first IL-23 inhibitor to be approved for the treatment of active PsA in numerous countries globally, offering an alternative to currently used biologics and conventional and targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs). The guselkumab PsA clinical development program evaluated guselkumab subcutaneous (SC) dose regimens of 100 mg at Weeks 0, 4 followed by every 8 weeks (q8w) or every 4 weeks (q4w) dosing thereafter.

As of March 2021, guselkumab 100 mg at Weeks 0 and 4 then q8w is now the approved dose regimen in the US, Canada, Australia, Taiwan, and Japan for both psoriasis and PsA, while both guselkumab q8w and q4w dose regimens have been approved in Brazil, Ecuador, and the European Union (EU) for PsA.

While both guselkumab dose regimens produced clinically meaningful benefit on the improvement in the signs and symptoms of PsA compared with placebo, there may be incremental benefit of higher dosing in a more treatment refractory population, therefore, the current study is intended to provide additional data on the impact of the 2 guselkumab dose regimens on signs and symptoms in patients with active PsA who have previously failed or been intolerant to one prior anti-TNF.

2.2. Background

Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory disease characterized by peripheral joint inflammation, enthesitis, dactylitis, axial disease and the skin lesions associated with psoriasis. Psoriatic arthritis affects approximately 0.02% to 0.25% of the general population (Setty, 2007). In patients with psoriasis, the prevalence of PsA ranges from 6% to 48%; however, arthritis is not correlated with extent of psoriasis skin disease (Gladman, 2009).

In addition to joint disease, PsA is also associated with a number of metabolic co-morbidities, including cardiovascular disease, diabetes and obesity as well as psychological co-morbidities, including depression and anxiety (Ogdie, 2015). Early clinic-based studies suggested an increased risk of mortality, although this risk improved over time (Gladman, 2008). However, recent studies suggest no increased risk of mortality among patients with PsA (Ogdie, 2014; Buckley, 2010).

Clinical Studies

The clinical development program for guselkumab in the treatment of active PsA includes a Phase 2 global Study CNTO1959PSA2001 (hereafter referred to as PSA2001) and 2 Phase 3 global Studies, PSA3001 (DISCOVER 1) and PSA3002 (DISCOVER 2). These studies evaluated the efficacy and safety of the guselkumab 100 mg q8w and q4w dose regimens in a broad population, including both participants who had IR and/or intolerance to conventional DMARDs, and participants who had IR and/or intolerance also to anti-TNFs.

A Phase 3b study, PSA3003 (COSMOS), evaluated the efficacy and safety of the guselkumab 100 mg q8w dose regimen in participants with PsA who had IR and/or intolerance to DMARDs and up to 2 prior anti-TNFs.

A high level summary of the study design, and efficacy and safety results for Studies PSA3001, PSA3002, and PSA3003 are provided in Section 2.2.1.1. For the most comprehensive clinical information regarding guselkumab, refer to the latest version of the guselkumab IB.

2.2.1.1. Phase 3 Studies: CNTO1959PSA3001 (DISCOVER 1) and CNTO1959PSA3002 (DISCOVER 2)

2.2.1.1.1. Study design

The PSA3001 and PSA3002 studies are global, multicenter, randomized, double-blind, placebo-controlled, 3-arm studies of guselkumab in participants with active PsA who had inadequate response to standard therapies (eg, non-biologic DMARDs, apremilast, or nonsteroidal anti-inflammatory drug [NSAIDs]). Both studies included a screening phase of up to 6 weeks and a treatment period including a placebo-controlled period from Week 0 to Week 24, and both have

an active treatment period that began at Week 24 and a safety follow-up period of 12 weeks after the last administration of study treatment. Stable doses of concomitant NSAIDs, oral corticosteroids, and selected DMARDs (limited to methotrexate [MTX], sulfasalazine [SSZ], hydroxychloroquine [HCQ], and leflunomide [LEF]) were allowed but not required.

PSA3001 and PSA3002 had similar study designs. Some differences in study population, sample size, and study duration reflected the additional study objective in PSA3002 to assess the progression of radiographic structural damage.

The PSA3001 study allowed approximately 30% of participants who had prior anti-TNF exposure to enroll, ie, participants who had been previously treated with up to 2 anti-TNFs. In the PSA3002 study, however, participants were required to be naïve to biologic agents. Additionally, the higher C-reactive protein (CRP) and joint count requirements in PSA3002, listed below, were intended to enrich the population for participants at greater risk for structural damage progression so that the impact of guselkumab on radiographic parameters could be assessed:

- **PSA3001: ≥3** swollen joints and **≥3** tender joints at screening and baseline, and CRP **≥0.3 mg/dL** at screening.
- **PSA3002: ≥5** swollen joints and **≥5** or more tender joints at screening and baseline, and CRP **≥0.6 mg/dL** at screening.

2.2.1.1.2. Efficacy results

Refer to the latest version of the guselkumab IB for detailed efficacy results of PSA3001 and PSA3002.

Through Week 24

In both PSA3001 and PSA3002, both guselkumab dose regimens (100 mg SC q4w or 100 mg SC q8w) demonstrated efficacy and produced clinically meaningful benefit on the improvement in the signs and symptoms of PsA and psoriasis, physical function, enthesitis, dactylitis and health-related quality of life (HRQoL). In addition, in PSA3002, inhibition of radiographic progression as measured by mean change in total modified van der Heijde-Sharp (vdH-S) score was observed in both guselkumab dose groups compared to placebo, however, only the q4w dose demonstrated a statistically significant change in vdH-S score compared with placebo at Week 24.

Through Week 52

The results of PSA3001 and PSA3002 (from Week 24 through Week 52) demonstrated that guselkumab 100 mg SC q8w and guselkumab 100 mg SC q4w were both effective in the maintenance of clinical responses through 1 year in the 3 major manifestations of psoriatic disease (joint, soft tissue, and skin), and physical function and HRQoL improvement in adults with active PsA. In addition, in PSA3002, inhibition of radiographic progression as measured by mean change in total modified vdH-S was also maintained post Week 24 through Week 52 (0.62) compared to baseline to Week 24 (0.46) in the guselkumab 100 mg q4w group.

2.2.1.1.3. Safety results

Refer to the latest version of the guselkumab IB for detailed safety results of PSA3001 and PSA3002.

Overall, the guselkumab safety profile in the PsA population was generally comparable with that established in the psoriasis population.

Through 1 year, the pooled safety data from PSA3001 (through Week 60) and PSA 3002 (through Week 52) indicated that both guselkumab dose regimens (ie, 100 mg SC administered at Weeks 0 and 4 and then q8w or q4w) were well tolerated in participants with active PsA. Similar proportions of participants in the guselkumab q8w and q4w groups experienced adverse events (AEs), serious adverse events (SAEs), AEs leading to study discontinuation, AEs with severe intensity, infections, serious infections, and injection-site reactions through 1 year of follow-up. Frequencies of events of suicidal ideation, malignancy, and major adverse cardiovascular events were low and comparable in the guselkumab q8w and q4w groups. There were no events of opportunistic infections, active tuberculosis (TB), anaphylaxis or serum sickness reactions, or suicidal behavior or self-injurious behavior without suicidal intent in guselkumab-treated participants in either of the PSA3001 or PSA3002 studies through 1 year. The proportion of participants experiencing increases in transaminases was slightly higher in the guselkumab q4w group compared with the q8w group. In addition, the number of participants with AEs, SAEs, AEs leading to discontinuation of study intervention, infections, and serious infections per 100 subject-years of follow-up were generally comparable between the guselkumab 100 mg q8w and q4w groups through 1 year and the placebo-controlled period through Week 24.

2.2.1.2. Phase 3b Study: CNTO1959PSA3003 (COSMOS)

The COSMOS study is an ongoing Phase 3b study in participants with PsA who had an IR and/or intolerance to up to 2 anti-TNFs. Treatment with guselkumab 100 mg at Week 0 and Week 4 and then q8w demonstrated superiority of guselkumab over placebo with respect to the primary endpoint of ACR 20 response at Week 24, and superiority of guselkumab over placebo with respect to all 4 key secondary endpoints at Week 24, based on a predefined hierarchical testing procedure: Health Assessment Questionnaire – Disability Index (HAQ-DI), ACR 50 response, 36-item short form health survey (SF-36) PCS, and Psoriasis Area and Severity Index (PASI) 100. The results were robust and generally consistent across the primary and supplementary analyses.

Overall, guselkumab demonstrated robust efficacy on signs and symptoms of the joints and skin psoriasis, improved physical function, and improvement in the physical component of health-related quality of life.

The guselkumab dosing regimen was safe and well tolerated through Week 24 in this study. The safety profile of guselkumab through Week 24 in this population of patients with PsA who were refractory to anti-TNF therapy is generally consistent with that demonstrated in the psoriasis and the bionaïve PsA indications.

2.3. Benefit-Risk Assessment

More detailed information about the known and expected benefits and risks of guselkumab may be found in the Package Insert and Summary of Product Characteristics.

2.3.1. Risks for Study Participation

Table 1: Potential Study Risks

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
Potential risks due to study intervention (guselkumab)		
Serious infections and reactivation of latent infections	Available animal and human data suggest that blockade of IL-23 may be associated with an increased infection risk.	• Participants with a history of, or ongoing, chronic or recurrent infectious disease, including human immunodeficiency virus (HIV), or hepatitis B or C virus (HBV, HCV), will be excluded from the study. Similarly, participants with evidence of active or untreated TB will be excluded from the study (Section 5.2). • Participants who have received a live viral or bacterial vaccination within 12 weeks of baseline will be excluded from the study. In addition, participants must agree not to receive a live viral or live bacterial vaccination during the study and for 12 weeks after receiving the last dose of study intervention (Section 5.2). • Participants will be instructed to seek medical attention if they develop signs or symptoms suggestive of an infection, and investigators are instructed in the protocol to monitor for signs or symptoms of infections, including TB (Sections 8.2.11 and 8.2.12). • Discontinuation of a participant's study intervention must be strongly considered if the participant develops a serious infection, including but not limited to sepsis or pneumonia. In addition, any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete.
Hypersensitivity reactions, including serious hypersensitivity reactions	Serious hypersensitivity reactions including anaphylaxis have been reported in postmarketing experience with guselkumab in psoriasis patients.	• Participants with known allergy, hypersensitivity, or intolerance to guselkumab or its excipients will be excluded from the study. • Sites are instructed that before any administration of study intervention,

		appropriately trained personnel and medications (eg, injectable epinephrine) must be available to treat hypersensitivity reactions, including anaphylaxis. In addition, all participants must be observed carefully for signs and symptoms of a hypersensitivity reaction (eg, urticaria, pruritis, angioedema, wheezing, dyspnea, or hypotension) (Section 8.2.10). • Any participant who develops a serious hypersensitivity reaction such as anaphylaxis must discontinue study intervention (Section 7.1).
Malignancy	The preponderance of preclinical data suggests that blockade of endogenous IL-23 would not be detrimental and may in fact be beneficial in tumor immunosurveillance and host protection; however, a risk of malignancy cannot be excluded.	• Those participants who currently have a malignancy or have a history of malignancy within 5 years prior to screening (with exceptions noted in Section 5.2) will be excluded from the study. Additionally, participants who have a history of lymphoproliferative disease, including lymphoma; a history of monoclonal gammopathy of undetermined significance or signs and symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy or splenomegaly will be excluded from the study (Section 5.2). • During the conduct of the study, participants will undergo regular clinical monitoring including routine safety labs to assess for any changes in health status that may indicate a possible malignancy. • Participants who develop a malignancy during the study (with the exception of no more than 2 localized basal cell skin cancers that are treated with no evidence of recurrence or residual disease) will be discontinued from study intervention (Section 7.1).
Liver injury	An SAE of 'toxic hepatitis' was reported in the ongoing Phase 2/3 guselkumab Crohn's disease (CD) program in a participant who received guselkumab 1200 mg intravenously (IV) at Weeks 0, 4, and 8, and 200 mg SC at Week 12. Based on the hepatocellular pattern of injury, temporal relationship of the event to guselkumab exposure, and the exclusion of alternative etiologies,	• During the conduct of the study, liver function tests will be monitored at regular intervals. In addition, the doses included in this study will be lower and will not exceed 100 mg SC q4w. The 100 mg SC q8w dosage is approved in the major regions in which this study will be conducted and the 100 mg SC q4w dosage is approved in the EU, Australia, Taiwan, Brazil, Ecuador and Japan.

	this event may represent drug-induced liver injury possibly related to guselkumab. A review of available guselkumab Phase 2 and 3 clinical trial data across multiple indications (psoriasis, PsA, rheumatoid arthritis [RA], palmoplantar pustulosis [PPP], and CD) was performed by the Sponsor - demonstrated previously noted association between guselkumab exposure and mild (≤3 x upper limit of normal [ULN]) elevations in liver transaminases at exposures of 100 mg q4w or higher - significant elevations of alanine aminotransferase [ALT] (>5 x ULN) or cases satisfying the biochemical criteria for Hy's Law during guselkumab exposure have been infrequent. These cases have been confounded by concomitant medications, alcohol use, medical history, and/or concurrent diagnoses.	• Participants with marked liver enzyme elevations or symptoms or signs of liver dysfunction (eg, jaundice), should undergo a thorough investigation for possible causes of liver injury. A participant must have their study intervention discontinued if the participant has severe liver test abnormalities that are not transient and are not explained by other etiologies (Section 7.1).
Immunosuppression	Although guselkumab has been studied with other immunosuppressives in other diseases, there may be an increased risk of infection or malignancy.	In order to minimize the theoretical increased risk of infection or malignancy with the combination of guselkumab with immunosuppressive therapy, the baseline dose of oral glucocorticoids on study entry is limited to a dose equivalent to ≤10 mg of prednisone/day. Additionally, participants are also excluded from the study if they have received any systemic immunosuppressants (eg, azathioprine, cyclosporine, 6 thioguanine, mercaptopurine, mycophenolate mofetil, hydroxyurea, tacrolimus within 4 weeks of the first administration of study intervention or are receiving 2 or more non-biologic DMARDs specified in Table 3 at baseline. Further detail regarding concomitant medications is provided in Section 6.8.
Risks due to study procedures		
Radiation	A chest X-ray will be performed at screening if the participant does not have a chest X-ray within 12 weeks prior to the first administration of study intervention. The exposure from 1 standard chest X-ray is	Exposure to radiation through radiographs is kept to a minimum by not requiring a chest X-ray be performed at screening if one is available from within

	0.1 mSV, comparable to 10 days of exposure to natural background radiation (https://www.acr.org). A subset of participants with spondylitis with peripheral arthritis at baseline will have a pelvic X-ray, approximately 0.7 mSV, comparable to 3 months of exposure to natural background radiation (https://hps.org/physicians/document/ doses_from_Medical_X-Ray_Procedures.pdf)	12 weeks prior to the first administration of study intervention.

2.3.2. Benefits for Study Participation

Guselkumab has demonstrated benefit in improving the signs and symptoms of PsA in the Phase 2 and Phase 3 studies (see Section 2.1), resulting in the registration of guselkumab in numerous countries to date; and ongoing regulatory reviews for approval globally. The demonstration of clinical benefit was observed in participants who are biologic treatment naïve or experienced. The target population under study in this protocol are participants who have had IR and/or intolerance to one prior anti-TNF. These patients may be more difficult to treat and may require higher dosing to achieve optimal efficacy. Consistent with prior studies, it is anticipated that individual participants may benefit from participation in the current study. Additionally, participation will help to obtain additional data on the impact of guselkumab on joint damage, and in the general knowledge of the treatment and natural history of PsA.

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

2.3.3. Benefit-Risk Assessment for Study Participation

Additional data through 1 year of treatment from the PSA3001 and PSA3002 studies for both guselkumab doses (ie, 100 mg SC q8w and q4w) under study in this protocol continue to support an overall favorable benefit-to-risk profile for the use of guselkumab in active PsA.

Potential risks of guselkumab, including those of clinically relevant infections and serious infections, malignancy, and liver injury; are being addressed via judicious inclusion/exclusion criteria, frequent study visits to allow for close monitoring of patient safety, guidelines for participant management (including monitoring of clinical laboratory tests and treatment discontinuation criteria), detailed description of allowed and prohibited concomitant medications, and comprehensive medical monitoring of data by the Sponsor/designee during the conduct of the studies.

Taking into account the measures taken to minimize risk to participants in this study, the potential risks identified in association with guselkumab are justified by the benefits that may be provided to participants with PsA.

3. OBJECTIVES AND ENDPOINTS

Objective	Endpoint
Primary	
• To evaluate the efficacy of guselkumab treatment in participants with active PsA and IR and/or intolerance to a prior anti-TNF by assessing the reduction in signs and symptoms of PsA.	• Proportion of participants who achieve an ACR 20 response at Week 24
Major Secondary	
• To evaluate the efficacy of guselkumab on additional measures of signs and symptoms of PsA, psoriasis, and patient well-being.	• Proportion of participants who achieve a psoriasis response of IGA psoriasis score of 0 (cleared) or 1 (minimal) AND ≥2-grade reduction from baseline at Week 24 among the participants with ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at baseline • Proportion of participants who achieve PASI 90 response at Week 24 among the participants with ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at baseline • Change from baseline in HAQ-DI at Week 24 • Change from baseline in the SF-36 PCS at Week 24 • Change from baseline in Functional Assessment of Chronic Illness Therapy – fatigue (FACIT-F) score at Week 24 • Proportion of participants achieving minimal disease activity (MDA) at Week 24 • Proportion of participants who achieve ACR 20 response at Week 16 • Proportion of participants who achieve ACR 50 response at Week 16 • Proportion of participants who achieve ACR 50 response at Week 24 • Proportion of participants who achieve ACR 70 response at Week 24 The ordering of endpoints, methods of analysis and the approach to control the Type I error for multiplicity, as well as the data-handling rules for the major secondary endpoints will be specified in the Statistical Analysis Plan (SAP).

Other Secondary	
• To evaluate the safety of guselkumab in participants with active PsA.	• Frequency and type of AEs, SAEs, reasonably related AEs, AEs leading to discontinuation of study intervention, infections, and injection-site reactions • Laboratory abnormalities (chemistry, hematology) maximum toxicity (Common Terminology Criteria for Adverse Events [CTCAE 5.0]) grades
• To evaluate the pharmacokinetics (PK) and immunogenicity of guselkumab in participants with active PsA.	• Serum guselkumab concentration over time • Incidence of antibodies to guselkumab

CCI

[redacted]

CCI

[redacted]

HYPOTHESIS

The primary hypothesis of this study is that guselkumab is superior to placebo as assessed by the proportion of anti-TNF-IR and/or intolerant participants achieving an ACR 20 response at Week 24.

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 3b, multicenter, randomized, double-blind, placebo-controlled interventional study in participants with active PsA who had an IR and/or intolerance to one prior anti-TNF.

A target of 450 participants will be randomly assigned in this study with 150 participants planned per intervention group: Guselkumab q8w (n=150), guselkumab q4w (n=150), or placebo (n=150). Participants impacted by major disruptions may be replaced. Stable doses of concomitant NSAIDs, oral corticosteroids (≤ 10 mg/day prednisone equivalent), selected non-biologic DMARDs (MTX, SSZ, HCQ, LEF) will be allowed but are not required.

There will be a screening phase of up to 6 weeks, a treatment phase of approximately 2 years that will include a double-blind placebo-controlled period from Week 0 to Week 24 and an active-controlled treatment phase from Week 24 to Week 100, and a safety follow-up at Week 112 (approximately 12 weeks after the last intended dose at Week 100 per protocol).

At Week 0, participants who satisfy all inclusion and exclusion criteria will be randomly assigned to 1 of the following 3 treatment groups in a 1:1:1 ratio using permuted block randomization stratified by baseline non-biologic DMARD use (yes/no).

- **Group I (n=150), guselkumab 100 mg SC every 8 weeks (q8w):** Participants will receive guselkumab 100 mg SC at Weeks 0, 4, then q8w at Weeks 12, 20, 28, 36, 44, 52, 60, 68, 76, 84, 92, and 100. Participants will receive placebo SC at Weeks 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, and 96 to maintain the blind.
- **Group II (n=150), guselkumab 100 mg SC every 4 weeks (q4w):** Participants will receive guselkumab 100 mg SC at Weeks 0, 4, then q4w at Weeks 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, and 100.
- **Group III (n=150), placebo and placebo crossover to guselkumab 100 mg SC q4w:** Participants will receive placebo SC at Weeks 0, 4, 8, 12, 16 and 20, and will cross over at Week 24 to receive guselkumab 100 mg SC at Weeks 24, 28, then q4w at Weeks 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, and 100.

At Week 16, all participants in Groups I, II, and III with <20% improvement from baseline in both tender and swollen joint counts will qualify for early escape and will be allowed to initiate or increase the dose of one of the permitted concomitant medications up to the maximum allowed dose as specified in Table 3, as selected by the investigator.

At Week 24, all participants in the placebo group (Group III) will cross over in a blinded fashion to receive guselkumab 100 mg SC q4w through Week 100; this will allow for collection of additional safety data for the guselkumab 100 mg SC q4w dose. Participants in the guselkumab groups (Groups I and II) will remain on the dosing regimen they were randomized to at Week 0, through Week 100.

Database locks (DBLs) are scheduled at Week 24, Week 52 and the end of the study (Week 112). The first DBL will occur when all randomized participants have either completed the Week 24 assessments or terminated study participation prior to the Week 24 visit (referred to as Week 24 DBL). The second DBL will occur when all randomized participants have either completed the Week 52 assessments or terminated study participation prior to the Week 52 visit (referred to as Week 52 DBL). The third DBL will occur when all participants have either completed their final safety visit or have terminated study participation (referred to as Final DBL).

The end of study is considered as the last visit for the last participant in the study.

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

4.2. Scientific Rationale for Study Design

Study population

The target study population is participants with active PsA who have had an IR and/or intolerance to one prior anti-TNF. This population is appropriate to provide relevant efficacy and safety information given that the likely intended use of guselkumab for active PsA in real world pragmatic clinical settings would be as an alternative mechanism of action after anti-TNF utilization.

In PSA3001 and PSA3002, both the guselkumab 100 mg q8w and q4w dose regimens produced clinically meaningful benefit on the improvement in the signs and symptoms of PsA in the overall population. While the studies were not designed nor powered to evaluate relative benefit between the guselkumab q8w and q4w dose regimens, potential incremental benefit of higher guselkumab dosing (ie, q4w) in PsA was observed for certain efficacy outcomes, and especially in the anti-TNF treatment experienced and IR population.

Potential incremental benefit with higher dosing in the overall population

In PSA3002 (in participants with IR to prior DMARDs only, and biologic naïve), while there was not a significant dose response noted for changes in signs and symptoms of PsA as assessed by ACR responses and other relevant joint and skin endpoints, analysis of radiographic data demonstrated that the guselkumab 100 mg q4w dose regimen significantly inhibited structural damage progression compared to the placebo group while the guselkumab 100 mg q8w dose regimen did not reach statistical significance. In high-risk participants (ie, those with baseline risk factors), there appeared to be a dose-response trend with the guselkumab 100 mg q4w dose regimen showing greater benefit than the 100 mg q8w dose regimen in inhibiting structural damage progression.

In PSA3001 (in patients with IR to prior DMARDs and/or prior TNF), the ACR 20/50/70 response rates compared with placebo (22.2%, 8.7%, 5.6%), were modestly numerically higher in the guselkumab 100 mg q4w group (59.4%, 35.9%, 20.3%) than those in the guselkumab100 mg q8w group (52.0%, 29.9%, 11.8%) at Week 24, and also generally numerically higher at each timepoint evaluated between Week 4 through Week 24.

Potential incremental benefit with higher dosing in the anti-TNF IR population

Results from PSA3001 also provide some evidence, though limited, to suggest there may be potential to achieve better efficacy with a guselkumab dose of 100 mg q4w than with q8w in a subset of participants with IR to an anti-TNF (Deodhar, 2020). In PSA3001, 118 treated participants across the 3 treatment groups (approximately 30% of all participants) were anti-TNF-experienced. Among these, a total of 44 participants were anti-TNF-IR. A dose response between the q4w and q8w guselkumab dose regimens was not evident for the anti-TNF-naïve population, but a potential dose response may exist for the anti-TNF-IR population, especially driven by the greater treatment effects vs placebo observed for ACR50 and ACR 70 responses. However, this

observation was based on a very small number of patients (17 in the q4w group and 15 in the q8w group).

A recent Phase 3b study, PSA3003 (COSMOS), in which participants with PsA who had an IR to up to 2 prior anti-TNFs were treated with guselkumab 100 mg q8w, demonstrated the efficacy of guselkumab compared with placebo for signs and symptoms of peripheral arthritis, soft tissue inflammation, skin psoriasis, improved physical function, and improvement in the physical component of health-related quality of life (at Week 24). However, as a consequence of only the q8w dosing regimen being studied vs placebo in PSA3003, the need exists to determine whether a guselkumab q4w dosing regimen provides additional benefit with respect to clinical efficacy in anti-TNF-IR patients, which is the primary objective of this present study.

Consistent with the studies of guselkumab in participants with PsA, other previous studies in overlapping mechanisms of actions (targeting the IL-17 pathway) have also suggested that anti-TNF-IR patients are harder to treat than anti-TNF-naïve patients. In the FUTURE-1 study of secukinumab for the treatment of PsA, a higher proportion of participants who were anti-TNF-naïve achieved an ACR 20 response versus participants who were anti-TNF-IR. Sustained efficacy through Week 104 was shown in participants naive to prior anti-TNF therapy as well as in those with prior incomplete response, although it was more marked in the former population (Kavanaugh, 2017). In the FUTURE-2 study, data have demonstrated greater clinical improvements with secukinumab 300 mg versus 150 mg in psoriasis symptoms and ACR scores in anti-TNF-IR patients, indicating that a higher dose of secukinumab seems appropriate for these patients (McInnes, 2017).

In summary, based on the overall evidence to date, the hypothesis that more frequent dosing, or higher doses, that result in higher serum drug concentrations, especially during the early course of treatment may result in better efficacy for TNF-IR patients is clinically relevant to study and represents an unmet need for a sizable population of patients with PsA.

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.

While guselkumab has been approved in a number of countries and is expected to be approved in more, the use of a placebo control is still necessary in the context of this study because the primary objective is to establish the efficacy of guselkumab in the anti-TNF population for which there is a paucity of data. In addition, the potential incremental relative benefit of the higher vs the lower guselkumab dose, each compared with placebo, is being evaluated. For these reasons, having a placebo control is appropriate in this trial.

DNA and Biomarker Collection

Optional pharmacogenomic samples may be obtained from participants only when specific consent is provided by signing the optional genetic research informed consent form (ICF). It is recognized that genetic variation can be an important contributory factor to inter-individual differences in intervention distribution and response and can also serve as a marker for disease susceptibility and prognosis. Pharmacogenomic research may help to explain inter-individual variability in clinical outcomes and may help to identify population subgroups that respond differently to an intervention. The goal of the pharmacogenomic component is to collect DNA to allow the identification of genetic factors that may influence the pharmacokinetics (PK), PD, efficacy, safety, or tolerability of guselkumab and to identify genetic factors associated with PsA.

Biomarker samples will be collected to evaluate the mechanism of action of guselkumab or help to explain inter-individual variability in clinical outcomes or may help to identify population subgroups that respond differently to an intervention. The goal of the biomarker analyses is to evaluate the pharmacodynamics of guselkumab and aid in evaluating the intervention-clinical response relationship.

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

Collection of biomarker samples, including samples from the optional pharmacogenomic collection, will only occur where local regulations permit and may not occur at all clinical sites.

4.2.1. Study-Specific Ethical Design Considerations

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

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

The amount of radiation is within a safe range, with the exposure from 1 standard chest X-ray being comparable to 10 days of exposure to natural background radiation, and the exposure to a pelvic X-ray (in a subset of participants), approximately 0.7 mSV, comparable to 3 months of exposure to natural background radiation (www.acr.org).

4.3. Justification for Dose

The 2 dose regimens which were evaluated in the Phase 3 PSA3001 and PSA3002 studies (100 mg at Weeks 0 and 4 then q8w and 100 mg q4w) and which demonstrated clinically meaningful benefits across domains of PsA were selected to be evaluated in this study. As of March 2021,

guselkumab 100 mg at Weeks 0 and 4 then q8w is now the approved dose regimen in the US, Canada, Australia, Taiwan, and Japan for both psoriasis and PsA, while both guselkumab q8w and q4w dose regimens have been approved in Brazil, Ecuador, and the EU for PsA.

Efficacy results from PSA3001/3002 demonstrated that both guselkumab q8w and q4w dose regimens were generally similarly effective in treating the signs and symptoms of PsA, as measured by ACR responses, DAS28 with CRP, dactylitis, enthesitis, IGA and PASI responses, improving overall physical function measured by HAQ-DI and health-related quality of life as measured by the SF-36 PCS. The magnitude of treatment effects for both guselkumab dose regimens in treating signs and symptoms compared to placebo were consistent among all major endpoints across the individual Phase 3 studies and for the pooled data from both studies.

Consistent with the biological plausibility that more treatment refractory patients could benefit from higher dosing and drug exposure, a potential greater benefit of the q4w regimen compared with the q8w regimen was observed in PSA3001, especially among patients with prior anti-TNF treatment experience including prior inadequate response (see Section 4.2). Specifically, in anti-TNF-IR patients in PSA3001, a greater proportion of participants in the guselkumab q4w group compared with the q8w group achieved ACR 50 (29% vs 13%) and ACR 70 (18% vs 7%) responses at Week 24. In addition, analysis of guselkumab serum concentration vs ACR response data at Week 24 from PSA3001 indicated a potential exposure-response relationship in patients with prior anti-TNF treatment experience (ie, a greater proportion of participants with guselkumab serum concentration above the median achieved higher ACR 50 and ACR 70 response compared with patients who had guselkumab serum concentration below the median concentration).

Overall, the 2 proposed dose regimens demonstrated clinically meaningful efficacy and were well tolerated with an acceptable safety profile in participants with active PsA. Including both dose regimens in this study will provide additional data to support an evaluation of the relative efficacy and safety of the q8w and q4w dosing regimens vs placebo in treating the signs and symptoms of PsA in anti-TNF IR patients.

4.4. End of Study Definition

End of Study Definition

The end of study is considered as the last visit for the last participant in the study. The final data from the study site will be sent to the Sponsor (or designee) after completion of the final participant visit at that study site, in the time frame specified in the Clinical Trial Agreement.

Study Completion Definition

A participant will be considered to have completed the main study if he or she has completed assessments at the 12-week safety follow-up visit at Week 112.

Participants who prematurely discontinue study intervention for any reason prior to Week 100 should complete the specified study visits and the final safety follow-up visit as outlined in Section 1.3 and Section 7.2. Participants will not be considered to have completed the study unless they complete the safety follow-up.

5. STUDY POPULATION

Screening for eligible participants will be performed within approximately 6 weeks before administration of the study intervention. Refer to Section 5.4, Screen Failures for conditions under which the repeat of any screening procedures may be 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.

5.1. Inclusion Criteria

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

PsA and psoriasis

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

2. Have a diagnosis of PsA for at least 6 months prior to the first administration of study intervention and meet ClASsification criteria for Psoriatic ARthritis (CASPAR) criteria at screening.

3. Have active PsA as defined by:

    a. At least 3 swollen joints and at least 3 tender joints at screening and at baseline

    -AND-

    b. CRP ≥0.3 mg/dL at screening from the central laboratory.

    NOTE: A 1-time repeat assessment of CRP level is allowed during the 6-week screening phase and the investigator may consider the participant eligible if the test result is within acceptable range on repeat testing in the central laboratory.

4. Have at least 1 of the following PsA subsets: distal interphalangeal joint involvement, polyarticular arthritis with absence of rheumatoid nodules, asymmetric peripheral arthritis, or spondylitis with peripheral arthritis.

5. Have an inadequate response and/or intolerance to anti-TNFα therapy, defined as presence of active PsA despite previous treatment with one prior anti-TNFα agent. Participants may meet either one or both of the following criteria:

    a. Lack of benefit of no more than one prior anti-TNFα therapy, as documented in the patient history by the treating physician, after at least 12 weeks of etanercept, adalimumab, golimumab, or certolizumab pegol therapy (or their biosimilars) or at least a 14-week dosage regimen (ie, at least 4 doses) of infliximab (or its biosimilars). Documented lack of benefit may include inadequate improvement in joint counts, physical function, or disease activity

AND/OR

b. Intolerance to no more than one prior anti-TNFα therapy, as documented in the patient history by the treating physician, to etanercept, adalimumab, golimumab, certolizumab pegol, or infliximab (or their biosimilars).

6. Participants are permitted to enter the study on a stable dose of 1 non-biologic DMARD (limited to MTX, SSZ, HCQ, or LEF). If currently using non-biologic DMARDs, participants should have started treatment for at least 3 months and the dose must be stable for at least 4 weeks before first administration of study intervention and should have no serious toxic side effects attributable to the non-biologic DMARD. If currently not using MTX, SSZ, or HCQ, must not have received for at least 4 weeks before first administration of study intervention. If currently not using LEF, must not have received for at least 12 weeks before first administration of study intervention.

   In addition, the following stable dose criteria must be met:

   a. If using MTX, the route of administration and dose must be stable and the dose must be ≤25 mg/week.
   b. If receiving SSZ, the dose must be ≤3g/day.
   c. If receiving HCQ, the dose must be ≤400 mg/day.
   d. If receiving LEF, the dose must be ≤20 mg/day

7. If using NSAIDs or other analgesics for PsA at baseline, participants must be on a stable dose for at least 2 weeks prior to the first administration of study intervention. If currently not using NSAIDs or other analgesics for PsA, must not have received NSAIDs or other analgesics for PsA within 2 weeks prior to the first administration of study intervention.

8. If using oral corticosteroids at baseline, participants must be on a stable dose equivalent to ≤10 mg of prednisone/day for at least 2 weeks prior to the first administration of study intervention. If not currently using oral corticosteroids, the participant must not have received oral corticosteroids within 2 weeks prior to the first administration of study intervention.

9. Have active plaque psoriasis, with at least 1 psoriatic plaque of ≥2 cm diameter and/or nail changes consistent with psoriasis, or documented history of plaque psoriasis.

10. Agree to avoid prolonged sun exposure and agree not to use tanning booths or other ultraviolet (UV) light sources during study (for participants with skin lesions or with documented history of psoriasis).

11. Are willing to refrain from the use of complementary therapies for PsA or psoriasis including ayurvedic medicine, traditional Taiwanese, Korean, or Chinese medication(s)

and acupuncture within 2 weeks prior to the first study intervention administration and through Week 52

Screening laboratory tests and vaccinations

12. 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)

f. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase levels must be ≤1.5 times the upper limit of normal (ULN) range for the central laboratory conducting the test.

NOTE: A 1-time repeat of screening laboratory tests (a-e) is allowed during the 6-week screening phase and the investigator may consider the participant eligible if the previously abnormal laboratory test result is within an acceptable range on repeat testing in the central laboratory. **No rescreening for ineligible ALT or AST levels is permitted.**

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

a. Have no history of latent or active TB before screening. An exception is made for participants who have a history of latent TB and:
   - are currently receiving treatment for latent TB, **OR**
   - will initiate treatment for latent TB before the first administration of study intervention, **OR**
   - have documentation of having completed appropriate treatment (as per local guidelines) for latent TB within 5 years before the first dose of study intervention. It is the responsibility of the investigator to verify the adequacy of previous anti-tuberculous treatment and provide appropriate documentation. Participants with a history and documentation of having completed appropriate treatment for latent TB more than 5 years before the first dose of study intervention are not eligible.

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

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

d. Within 8 weeks before the first administration of study intervention, have a negative QuantiFERON®-TB test result, or have 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 intervention.

NOTE: A negative tuberculin skin test result is required if the QuantiFERON-TB test is not approved/registered in the country in which this protocol is being conducted. The frequency of TB testing can be increased depending on local health authority requirements. In Ukraine, while the QuantiFERON-TB test is not approved/registered, it is acceptable, and an additional tuberculin skin test is not required. The QuantiFERON-TB test and the tuberculin skin test are not required at screening for participants with a history of latent TB, if active TB has been ruled out, and if appropriate treatment has been initiated/completed as described above in Inclusion Criterion 13a.

e. Have a chest radiograph (both posterior-anterior and lateral views, or per country regulations where applicable), taken within 12 weeks before the first administration of study intervention and read by a radiologist or qualified pulmonologist, with no evidence of current, active TB or old, inactive TB. A chest CT scan is also acceptable if already available or obtained outside of the study protocol. 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 medical monitor or designee and recorded in the participant's source documents and initialed by the investigator.

14. Agree not to receive a live virus or live bacterial vaccination during the study, or within 12 weeks after the last administration of study intervention.

15. Agree not to receive a Bacillus Calmette-Guérin (BCG) vaccination during the study, and within 12 weeks after the last administration of study intervention.

16. It is recommended that patients are up-to-date on age-appropriate vaccinations prior to screening as per routine local medical guidelines. For study patients who received locally approved (and including emergency use-authorized) COVID-19 vaccines recently prior to study entry, follow applicable local vaccine labelling, guidelines, and standards of care for patients receiving immune-targeted therapy when determining an appropriate interval between vaccination and study enrolment (see also Section 6.8.7).

Pregnancy and contraception

17. Criterion modified per Amendment 2.

17.1 Before randomization, a woman must be

- Not of childbearing potential **OR**

- Of childbearing potential and practicing (if heterosexually active) a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) and agrees to remain on a highly effective method while receiving study intervention and until 12 weeks after last dose - the end of relevant systemic exposure. The investigator should evaluate the potential for contraceptive method failure (eg, noncompliance, recently initiated) in relationship to the first dose of study intervention. Examples of highly effective methods of contraception are provided in Appendix 10.7.

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

  A condom or occlusive cup with spermicidal foam/gel/film/cream/suppository is not acceptable if used as the sole method of contraception in this study. For examples of acceptable and unacceptable methods of contraception, please refer to Appendix 10.7.

18. A woman of childbearing potential must have a negative serum (β-human chorionic gonadotropin [β-hCG]) pregnancy test at screening and a negative urine pregnancy test at Week 0.

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

20. All men must agree not to donate sperm from the first administration of study intervention through at least 12 weeks after receiving the last administration of study intervention.

21. Criterion modified per Amendment 2.

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

General

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

23. Must sign an ICF indicating that he or she understands the purpose of and procedures required for the study and is willing to participate in the study.

24. Must sign a separate ICF if he or she agrees to provide an optional DNA sample for research (where local regulations permit). Refusal to provide consent for the optional DNA research sample does not exclude a participant from study participation.

5.2. Exclusion Criteria

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

PsA and Psoriasis

1. Has other inflammatory diseases that might confound the evaluations of benefit of guselkumab therapy in the treatment of PsA, including but not limited to rheumatoid arthritis, ankylosing spondylitis/non-radiographic axial spondyloarthritis (note: this does not include a primary diagnosis of PsA with spondylitis), systemic lupus erythematosus, or Lyme disease (confirmed by Western blot).

2. Has received more than 1 prior anti-TNFα agent (or biosimilars).

3. Has received an anti-TNFα agent within the following timeframes:

   - Infliximab (or its biosimilars) or golimumab (IV), within 8 weeks prior to the first administration of study intervention.

   - Golimumab SC, adalimumab or certolizumab pegol (or their biosimilars), within 6 weeks prior to the first administration of study intervention.

   - Etanercept (or its biosimilars) within 4 weeks prior to the first administration of study intervention.

4. Has previously received any biologic treatment other than an anti-TNFα agent including, but not limited to, guselkumab, ustekinumab, secukinumab, tildrakizumab, ixekizumab,brodalumab, risankizumab or other investigative biologic treatment.

5. Has ever received Janus kinase (JAK) inhibitor including but not limited to tofacitinib, baricitinib, filgotinib, peficitinib, decernotinib, upadacitinib or any other investigational JAK inhibitor.

6. Has received any systemic immunosuppressants (eg, azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, hydroxyurea, tacrolimus) within 4 weeks prior to the first administration of study intervention.

7. Has received apremilast within 4 weeks prior to the first administration of study intervention.

8. Has received non-biologic DMARDs other than MTX, SSZ, HCQ, LEF, within 4 weeks prior to the first administration of study intervention.

9. Is receiving 2 or more non-biologic DMARDs specified in Table 3 at baseline.

10. Has a nonplaque form of psoriasis (eg, erythrodermic, guttate, or pustular).

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

12. Has received phototherapy or any systemic medications/treatments that could affect psoriasis evaluations (including, but not limited to, retinoids, 1,25-dihydroxy vitamin D3 and analogues, psoralens, fumaric acid derivatives, with the exception of those in Table 3) within 4 weeks of the first administration of study intervention.

13. Has used topical medications/treatments that could affect psoriasis evaluations (including, but not limited to, topical or intralesional injection of corticosteroids, anthralin, calcipotriene, topical vitamin D derivatives, retinoids, tazarotene, methoxsalen, trimethylpsoralens, pimecrolimus, tacrolimus, or topical traditional Taiwanese, Korean, or Chinese medicines) within 2 weeks of the first administration of any study intervention. Low potency topical corticosteroids on the face or groin are allowed at any time.

14. Has received epidural, intra-articular, intramuscular (IM), or IV corticosteroids, including adrenocorticotropic hormone during the 4 weeks prior to the first administration of study intervention.

15. Has received lithium within 4 weeks of the first administration of study intervention.

16. Has received an experimental antibody or biologic therapy (other than those listed everywhere else in this section) within 6 months prior to the first administration of study intervention, or received any other experimental therapy, including an investigational medical device, or new investigational agent within 3 months 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 intervention or procedure.

Coexisting medical conditions or past medical history

17. Has a history or current signs or symptoms of severe, progressive, or uncontrolled renal, hepatic, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic (with the exception of PsA), psychiatric, genitourinary, or metabolic disturbances.

18. Has unstable cardiovascular disease, defined as a recent clinical deterioration (eg, unstable angina, rapid atrial fibrillation, or transient ischemic attack) in the last 3 months prior to screening or a cardiac hospitalization within the last 3 months prior to screening.

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

20. 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.

21. Is currently undergoing or has previously undergone allergy immunotherapy for a history of anaphylactic reactions.

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

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

24. Has unstable suicidal ideation or suicidal behavior in the last 6 months, that may be defined as an electronic Columbia-Suicide Severity Rating Scale (eC-SSRS) rating at screening of:

    - Ideation level 4: Some intent to act, no plan; OR
    - Ideation level 5: Specific plan and intent; OR
    - Any of the following suicidal behaviors:
        - Actual suicide attempts
        - Interrupted attempts
        - Aborted attempts
        - Preparatory actions

      AND

    is confirmed to be at risk by the investigator based on an evaluation by a mental health professional. The final decision on excluding a participant will be made at the judgment of the investigator.

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

26. Is pregnant, nursing, or planning a pregnancy (both men and women) within 12 weeks after receiving the last administration of study intervention.

27. Has had major surgery (eg, requiring general anesthesia and hospitalization) within 8 weeks prior to 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 (52 weeks). Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate.

28. Is known to have had a substance abuse (drug or alcohol) problem within the previous 12 months prior to the first administration of study intervention.

Infections or predisposition to infections

29. 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 (eg, recurrent pyelonephritis or chronic non-remitting cystitis), fungal infection (eg, mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.

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

31. Has or has had a serious infection (eg, sepsis, pneumonia, or pyelonephritis) or has been hospitalized or received IV antibiotics for an infection within 2 months prior to screening.

32. Has or has had a herpes zoster infection within 2 months before screening.

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

34. Has had a BCG vaccination within 12 months of first administration of study intervention.

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

36. Has a chest radiograph within 3 months prior to the first administration of study intervention that shows an abnormality suggestive of a malignancy, significant cardiovascular or pulmonary disease or current active infection, including TB.

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

38. Has persistently indeterminate (indeterminate on repeat sampling) QuantiFERON-TB test results. Indeterminate results should be handled as described in Section 8.2.12.

39. Is infected with HIV (a confirmed positive serology for HIV antibody).

40. During the 6 weeks prior to baseline, have had ANY of

    a) confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/COVID 19 infection (test positive), **OR**

    b) suspected SARS – CoV – 2 infection (clinical features without documented test results), **OR**

    c) close contact with a person with known or suspected SARS –SoV – 2 infection.

    An exception to this criterion maybe granted if a participant has a documented negative result for a validated SARS-CoV-2 test:

    – Obtained at least 2 weeks after conditions (a), (b), (c) above (timed from resolution of key clinical features if present, eg, fever, cough, dyspnea)

    AND

    – with absence of ALL conditions (a), (b), (c) above during the period between the negative test result and the baseline study visit.

    NOTES on COVID-related exclusion:

    - The field of COVID-related testing (for presence of, and immunity to, the SARS-CoV-2 virus) is rapidly evolving. Additional testing may be performed as part of screening and/or during the study if deemed necessary by the investigator and in accordance with current regulations / guidance from authorities / standards of care.

    Precaution: for those who may carry a higher risk for severe COVID-19 illness, follow guidance from local health authorities when weighing the potential benefits and risks of enrolling in the study, and during participation in the study.

41. Tests positive for hepatitis B virus (HBV) infection (see Appendix 4 in Section 10) or is seropositive for antibodies to hepatitis C virus (HCV) at screening, unless the participant meets 1 of the following conditions:

i. Has a history of successful treatment (defined as being negative for HCV RNA at least 12 weeks after completing antiviral treatment) and has a negative HCV RNA test result at screening, OR

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

General

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

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

44. 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.

45. 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.

46. 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 prior to the first dose of study intervention is given such that the participant no longer meets all eligibility criteria, then the participant should be excluded from participation in the study, Section 5.4, describes options for retesting. The required source documentation to support meeting the enrollment criteria are noted in Appendix 10.5.

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 6.8, 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).

3. Must not receive guselkumab outside of this protocol or participate in any other clinical study with an investigational agent while in this study and must terminate study participation if they do.

5.4. Screen Failures

If, during the screening phase, the participant has not met all inclusion criteria or met any exclusion criteria or is unable or unwilling to adhere to the prohibitions and restrictions of the study, the participant is considered to be a screen failure and is not eligible to be randomized at that time. A participant who might be considered a screen failure due to circumstances unrelated to the protocol (eg, site closure due to COVID-19, other unforeseen circumstances resulting in site closure, etc) could be eligible for screening and rescreening if applicable.

Participant Identification, Enrollment, and Screening Logs

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

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

Rescreening

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

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

Chest x-rays, if done within the specified allowed time, are not required to be repeated.

If the QuantiFERON-TB test and/or the tuberculin skin test were positive in the first screening, these tests should not be repeated. Also, if the QuantiFERON-TB test and tuberculin skin test were done within the specified allowed time, they should not be repeated.

Retesting

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

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

5.5. Criteria for Temporarily Delaying Administration of Study Intervention

Guidelines for study intervention administration affected by the COVID-19 pandemic are found in Appendix 10.9.

6. STUDY INTERVENTION AND CONCOMITANT THERAPY

6.1. Study Intervention(s) Administered

Study intervention administration must be captured in the source documents and the electronic case report form (eCRF). Study site personnel will instruct participants on how to store study intervention for at-home use as indicated for this protocol.

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

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

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

Guidelines for study intervention affected by the COVID-19 pandemic are provided in Appendix 10.9.

Description of Interventions

Table 2: Study Interventions (Treatment Groups)

Group/Arm Name	Group I (q8w)	Group II (q4w)	Group III (placebo)
Intervention Name	Guselkumab	Guselkumab	Placebo
Dose Formulation	Guselkumab 100 mg and matching liquid placebo for guselkumab will be provided in a single-use prefilled syringe (PFS) assembled with the Ultrasafe PLUS™ Passive Needle Guard (PFS-U).	Guselkumab 100 mg will be provided in a single-use PFS assembled with the PFS-U.	Placebo
Unit Dose Strength(s)	100 mg	100 mg	
Dosage Level(s)	100 mg at Weeks 0, 4, then q8w through Week 100 (placebo at alternate visits)	100 mg q4w through Week 100	Placebo q4w through Week 20, then guselkumab 100 mg q4w through Week 100
Route of Administration	subcutaneous	subcutaneous	subcutaneous

6.1.1. Combination Products

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

The Sponsor-manufactured combination product for use in this study is the pre-filled syringe (PFS) assembled in an UltraSafe Plus™ PFS-U. Additional details on the PFS-U are provided in Section 6.2 and the guselkumab IB.

All combination product deficiencies (including failure, malfunction, improper or inadequate design, manufacturer error, use error, and inadequate labeling) shall be documented and reported by the investigator throughout the study. For studies with combination products, these deficiencies will be reported as product quality complaints (PQC, see Appendix 10.6).

6.2. Preparation/Handling/Storage/Accountability

Preparation/Handling/Storage

For SC administration, guselkumab will be supplied as a 100 mg/mL sterile liquid in a single-dose PFS assembled in a PFS-U. For SC administration, placebo will be supplied as a 1 mL sterile liquid in a single-dose PFS-U.

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

After Week 28 (ie, starting at the Week 32 visit), participants (or caregivers) who are able and who have been appropriately trained in the administration of study intervention may administer study intervention at home, as per the schedule of Activities (SoA). Study personnel will instruct participants on how to transport, store, and administer study intervention for at-home use as indicated for this protocol.

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

Accountability

The investigator is responsible for ensuring that all study intervention received at the site is inventoried and accounted for throughout the study. All study intervention will be stored and disposed of according to the Sponsor's instructions. Study site personnel must not combine contents of the study intervention containers.

Study intervention must be handled in strict accordance with the protocol and the container label and must be stored at the study site in a limited-access area or in a locked cabinet under appropriate environmental conditions. Unused study intervention must be available for verification by the

Sponsor's study site monitor during on-site monitoring visits. The return to the Sponsor of unused study intervention will be documented on the intervention return form. When the study site is an authorized destruction unit and study intervention supplies are destroyed on-site, this must also be documented on the intervention return form.

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

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

6.3. Measures to Minimize Bias: Randomization and Blinding

Intervention Allocation

Procedures for Randomization and Stratification

Central randomization will be implemented in this study. Participants will be randomly assigned to 1 of 3 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 and will be stratified at the study level by baseline non-biologic DMARD use (yes/no).

The interactive web response system (IWRS) will assign a unique intervention code, which will dictate the intervention assignment and matching intervention kit for the participant. The requestor must use his or her own user identification and personal identification number when contacting the IWRS and will then give the relevant participant details to uniquely identify the participant.

Blinding

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

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

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

The results of the post-baseline CRP measurements performed by the central laboratory will be blinded to the investigative sites.

Under normal circumstances, the blind should not be broken until all participants have completed the study and the database is finalized. The investigator may in an emergency determine the identity of the intervention by contacting the IWRS. While the responsibility to break the intervention code in emergency situations resides solely with the investigator, it is recommended that the investigator contact the Sponsor or its designee if possible, to discuss the particular situation, before breaking the blind. Telephone contact with the Sponsor or its designee will be available 24 hours per day, 7 days per week. In the event the blind is broken, the Sponsor must be informed as soon as possible. The date and reason for the unblinding must be documented by the IWRS, in the appropriate section of the eCRF, and in the source document. The documentation received from the IWRS indicating the code break must be retained with the participant's source documents in a secure manner.

Participants who have had their intervention assignment unblinded should continue to return for scheduled evaluations and may not be eligible for further treatment.

At the Week 24 database lock, the data will be unblinded for analysis to some Sponsor personnel while participants are still participating in the study. Identification of Sponsor personnel who will have access to the unblinded subject-level data will be documented prior to unblinding. Investigative study sites and participants will remain blinded to initial treatment assignment until after the final database is locked.

6.4. Study Intervention Compliance

When participants have self- (or caregiver-) administration of study intervention at home, compliance with study intervention will be assessed at each visit. Compliance will be assessed by direct questioning during the site visits and documented in the source documents and eCRF. Deviation(s) from the prescribed dosage regimen should be recorded in the eCRF.

Participants will receive instructions on compliance with study treatment when they begin self-administration of study intervention at home. When participants begin self-administration at home, the investigator or designated study personnel will maintain a log of all study intervention dispensed and returned.

When study intervention is self-administered by participants (or caregivers) at home, participants will record all study intervention administrations on a diary card.

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

Compliance with the treatment schedule is strongly encouraged. It is understood that treatment may be interrupted for health-related or safety reasons. Therefore, if for any reason a participant cannot receive a dose of study intervention at the scheduled visit, the participant must make every effort to still come in for the scheduled assessments for that visit. In general, the dose should be administered within approximately 2 weeks of that scheduled visit. The participant should then resume the normal study schedule relative to the baseline visit (Week 0). In the case when a participant does not come into the investigational site for a scheduled visit, the site will follow-up with that participant. Due diligence could include telephone calls, certified letters, and email requests. Measures taken to obtain follow-up information must be documented.

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

All post-baseline visits up to and including Week 24 will have a visit window of ±4 days counting from Week 0 as Day 1. After Week 24, all visits will have a visit window of ±7 days. The final safety visit (12 weeks after the last dose in participants who discontinued study treatment) will have a visit window of ±14 days. If a study visit occurs outside this window, the Sponsor should be consulted about how the participant should resume his or her normal dose schedule.

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

6.5. Dose Modification

Not applicable.

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

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

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

6.7. Treatment of Overdose

For this study, any dose of guselkumab greater than the highest dose at a single dosing visit will be considered an overdose. The Sponsor does not recommend specific treatment for an overdose.

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

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

6.8. Concomitant Therapy

Therapies administered up to 30 days before first dose of study intervention must be recorded at screening.

Concomitant therapies must be recorded throughout the study beginning with start of the first dose of study intervention to after the last dose of study intervention. Concomitant therapies should also be recorded beyond that point only in conjunction with SAEs that meet the criteria outlined in Serious Adverse Events in Section 8.3.1.

All therapies (prescription or over-the-counter medications, including vaccines, vitamins, herbal supplements; non-pharmacologic therapies such as electrical stimulation, acupuncture, special diets, exercise regimens, or other specific categories of interest) different from the study intervention must be recorded in the eCRF.

Recorded information will include a description of the type of therapy, treatment period, dosage, route of administration and indication. Modification of an effective preexisting therapy should not be made for the explicit purpose of entering a participant into the study.

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

Every effort should be made to keep participants' concomitant medications for PsA stable through Week 112 or as specified in the following sections. The concomitant medication dose may be reduced or temporarily discontinued because of abnormal laboratory values, adverse effects or intolerance, concurrent illness, or the performance of a surgical procedure but the change and reason for the change should be clearly documented in the participant's medical record.

Permitted concomitant medications for PsA and the maximum allowed doses during the study as specified in the following sections are summarized in Table 3.

Table 3: Permitted Concomitant Medications for PsA and the Maximum Allowed Doses During the Study	
Permitted Concomitant Medications for Psoriatic Arthritis (PsA)[a]	**Maximum Allowed Dose**
NSAIDs and other analgesics	Marketed dose approved in in the country where the study is being conducted
Oral corticosteroids	Equivalent to 10 mg/day of prednisone
Methotrexate (MTX)[b]	25 mg/week
Sulfasalazine (SSZ)	3 g/day
Hydroxychloroquine (HCQ)	400 mg/day
Leflunomide (LEF)	20 mg/day

[a] Permitted concomitant medications are not supplied by the Sponsor.
[b] It is recommended that all participants taking MTX in this study receive at least 5 mg oral folate or 5 mg folinic acid weekly. Guidelines for dose adjustment in the event of MTX toxicity are included in the Trial Center File.

- Participants should not initiate any new treatment for PsA through Week 52 except at Week 16 for those participants who have <20% improvement from baseline in both tender and swollen joint counts (early escape criteria). Participants who meet early escape criteria will be allowed to initiate or increase the dose of 1 of the permitted concomitant medications up to the maximum allowed dose as specified in Table 3, as selected by the investigator. Titration to a stable dose of the medication should be completed for participants qualifying for early escape by the Week 24 visit.

- Participants may not be receiving more than 1 non-biologic DMARD from baseline through Week 52 (with the exception of participants who are eligible for early escape at Week 16, who may receive up to 2 non-biologic DMARDs, see further details in Section 6.8.1). At baseline, participants are permitted to enter the study on a stable dose of 1 non-biologic DMARD (limited to MTX, SSZ, HCQ, or LEF) up to the maximum allowed dose specified in Table 3. At Week 16, participants who meet criteria for early escape may initiate or increase the dose of non-biologic DMARD depending on status of baseline use (see Table 4). Note: participants cannot be on concomitant MTX and LEF. After Week 52 and through the end of the study, participants may receive another non-biologic DMARD.

- Beginning at Week 52, the treatment options in Table 3 are allowed to be initiated or dose increased up to the maximum allowed dose specified in Table 4 for participants with ongoing PsA disease activity at the investigator's judgment; the rationale should be clearly documented in the participants medical record.

The concomitant medication review will occur at study visits identified in the SoA (Section 1.3).

6.8.1. Non-biologic DMARDs

6.8.1.1. Permitted Non-biologic DMARDs

Participants are permitted to enter the study on a stable dose of 1 non-biologic DMARD (limited to MTX, SSZ, HCQ, or LEF) up to the maximum allowed dose specified in Table 3. Only 1 of these non-biologic DMARDs is allowed from baseline through Week 52 (with the exception of participants who are eligible for early escape at Week 16, who may receive up to 2 non-biologic DMARDs). Note: participants cannot be on concomitant MTX and LEF. Participants receiving 2 or more non-biologic DMARDs at baseline are excluded from study participation.

At any time during the study, the dose of the permitted non-biologic DMARD may be reduced or temporarily discontinued due to abnormal laboratory values, side effects, concurrent illness, or the performance of a surgical procedure.

Refer to Table 4 for protocol requirements of the permitted non-biologic DMARDs, including allowances at early escape. Note: participants cannot be on concomitant MTX and LEF.

Table 4: Protocol Requirements of the Permitted Non-biologic Disease-Modifying Antirheumatic Drugs				
Permitted Non-biologic DMARDs	**Baseline Usage**	**Prior to Week 0**	**Week 0 through Week 52**	**Week 52 through Week 112**
Methotrexate (MTX)	Used	Treatment should have started at least 3 months prior to the first administration of study intervention. MTX routes of administration and doses should be stable for at least 4 weeks prior to the first administration of the study intervention, and must be ≤25 mg/week.	Stable dose and route of administration (oral, intramuscular, or subcutaneous permitted) required unless early escape or unacceptable side effects	Dose changes allowed up to the maximum dose specified in Table 3 or changes of the route of administration, at the investigator's discretion
	Not Used	Discontinued at least 4 weeks prior to the first administration of study intervention.	Not allowed unless early escape	Allowed up to the maximum dose specified in Table 3 at investigators discretion
Sulfasalazine (SSZ) or Hydroxychloroquine (HCQ)	Used	Treatment should have started at least 3 months prior to the first administration of study intervention. Dose should be stable for at least 4 weeks prior to the first administration of the study intervention and must be ≤3 g/day (SSZ) or ≤400mg/day (HCQ).	Stable dose required unless early escape or unacceptable side effects	Dose changes allowed up to the maximum dose specified in Table 3 at the investigator's discretion
	Not Used	Discontinued at least 4 weeks prior to the first administration of study intervention.	Not allowed unless early escape	Allowed up to the maximum dose specified in Table 3 at investigators discretion
Leflunomide (LEF)	Used	Treatment should have started at least 3 months prior to the first administration of study intervention. Dose should be stable for at least 4 weeks prior to the first administration of the study intervention and must be ≤20 mg/day.	Stable dose required unless early escape or unacceptable side effects	Dose changes allowed up to the maximum dose specified in Table 3 at the investigator's discretion
	Not Used	Discontinued at least 12 weeks prior to the first administration of study intervention.	Not allowed unless early escape	Allowed up to the maximum dose specified in Table 3 at investigators discretion

6.8.1.2. Prohibited Non-biologic DMARDs and Apremilast

All other non-biologic DMARDs (including, but not limited to chloroquine, gold preparations, penicillamine) and apremilast must be discontinued at least 4 weeks prior to the first administration of study intervention and remain prohibited through Week 112.

6.8.1.3. Systemic Immunosuppressive Drugs

Systemic immunosuppressants (including, but not limited to azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, hydroxyurea, or tacrolimus) must be discontinued at least 4 weeks prior to the first administration of study intervention and remain prohibited through Week 112. If any of these systemic immunosuppressants is initiated during the study, study intervention must be permanently discontinued.

Systemic immunosuppressants do not refer to corticosteroids; see Section 6.8.2 for restrictions regarding the use of corticosteroids.

6.8.2. Corticosteroids

6.8.2.1. Oral Corticosteroids

Participants not using oral corticosteroids at baseline for PsA must have discontinued oral corticosteroids at least 2 weeks prior to the first administration of study intervention and must not receive oral corticosteroids through Week 52 of the study for PsA. An exception is made for participants who qualify for early escape at Week 16.

Participants using oral corticosteroids at baseline for PsA must be on a stable dose equivalent to ≤10 mg prednisone per day for at least 2 weeks prior to the first administration of study intervention and continue on this dose through Week 52 unless early escape at Week 16.

After Week 24 and through Week 52, a one-time dose decrease in oral corticosteroids is allowed; otherwise, throughout the study, the dose and type of oral corticosteroid may be changed at the discretion of the investigator only if the participant develops unacceptable side effects.

6.8.2.2. Corticosteroids – Intravenous, Intramuscular, or Epidural Administration

Intravenous, intramuscular, or epidural administration of corticosteroids for the treatment of PsA are not allowed through Week 112.

Long-term (>2 weeks) oral, IV, intramuscular, or epidural corticosteroid use for indications other than PsA or psoriasis are not allowed through Week 112. Short-term (≤2 weeks) oral, IV, intramuscular, or epidural corticosteroid used for indications other than PsA should be limited to situations where, in the opinion of the investigator, there are no adequate alternatives.

6.8.2.3. Corticosteroids – Intra-articular Injection

Attempts should be made to avoid intra-articular corticosteroid injections for PsA, especially during the first 24 weeks of the study. However, if necessary, participants may receive up to 2 intra-articular, tendon sheath, or bursal corticosteroid injections in no more than 2 affected sites within any 24-week period of the study. In the case of severe tenderness or swelling in a single joint, it is suggested that the participant be evaluated for infection prior to receiving an intra-articular corticosteroid injection.

6.8.2.4. Corticosteroids – Other Routes of Administration

Inhaled, otic, ophthalmic, intranasal, and other routes of mucosal delivery of corticosteroids for indications other than PsA and psoriasis are allowed throughout the course of the study.

6.8.3. Nonsteroidal Anti-inflammatory Drugs and Other Analgesics

For participants receiving NSAIDs, including aspirin and selective cyclooxygenase 2 inhibitors, or other analgesics for PsA at baseline, treatment with a stable dose of NSAIDs or other analgesics should have been initiated at least 2 weeks prior to the first administration of study intervention and continue through Week 24 unless early escape at Week 16. The dose administered should be the usual marketed dose approved in the country where the study is being conducted.

The use of topical analgesics including capsaicin and diclofenac is allowed and should be recorded in the eCRF. For topical and analgesic patches, the dose should be stable through Week 24 and may be changed only if the participant develops unacceptable side effects.

Participants not receiving NSAIDs or other analgesics for PsA at baseline must have discontinued NSAIDs or other analgesics at least 2 weeks prior to the first administration of study intervention and must not receive NSAIDs or other analgesics for PsA through Week 24 of the study. An exception is made for participants who qualify for early escape at Week 16.

After Week 24, participants with ongoing PsA disease activity can initiate or increase the dose of NSAIDs or other analgesics based on the investigator's clinical judgment.

At any time during the study, the dose of NSAIDs or other analgesics may be reduced or temporarily discontinued due to abnormal laboratory values, side effects, concurrent illness, or the performance of a surgical procedure.

Use of NSAIDs and other analgesics for indications other than PsA are permitted throughout the study.

In this study, aspirin is considered an NSAID, except for low-dose aspirin prescribed for cardiovascular or cerebrovascular disease.

6.8.4. Biologic Agents, Cytotoxic Drugs, JAK Inhibitors, or Investigational Agents

The concomitant use of biologic agents, cytotoxic agents, JAK inhibitors, and/or investigational drugs is not allowed, with the exception of limited emergency use for treatment of COVID-19 infection. Biologic agents include, but are not limited to golimumab, anakinra, etanercept, adalimumab, infliximab, ustekinumab, alefacept, efalizumab, rituximab, natalizumab, certolizumab pegol, bimekizumab, tildrakizumab, secukinumab, ixekizumab, brodalumab, and respective biosimilars as applicable. Cytotoxic agents include, but are not limited to chlorambucil, cyclophosphamide, nitrogen mustard, and other alkylating agents. JAK inhibitors include, but are not limited to tofacitinib, baricitinib, filgotinib, peficitinib, upadacitinib and decernotinib. If any of these medications are used, study intervention must be permanently discontinued, with the exception of limited emergency use for treatment of COVID-19 infection. Continuation of study intervention in such cases should be discussed with the Sponsor's medical monitor

6.8.5. Complementary Therapies

The use of complementary therapies, including ayurvedic medicine, traditional Chinese, Taiwanese, or Korean medications or non-medicinal therapy such as acupuncture for PsA or psoriasis, is not allowed from 2 weeks prior to the first administration of study intervention through Week 112.

6.8.6. Topical Therapy and Ultraviolet B Light

Concurrent use of topical medications/treatments for psoriasis (eg, topical or intralesional corticosteroids, keratolytics (with the exception of salicylic acid shampoos, which are allowed throughout the study), coal tar (with the exception of coal tar shampoos, which are allowed throughout the study), anthralin, vitamin D3 analogues, or topical tacrolimus, and retinoids) are not permitted through Week 24.

Use of salicylic acid- and tar-containing shampoos is not permitted on the morning prior to a study visit; non-medicated shampoos may be used on the day of a study visit.

Low-potency topical corticosteroids may be used on the face and groin only. Low and mid-potency topical or intralesional corticosteroids (Class III-VII) may be used after Week 24 for psoriasis. High and ultra-high potency corticosteroids (Class I and II) are prohibited through Week 112.

Phototherapy including UVB or tanning beds are not permitted during the study through Week 112. Participants should be encouraged to avoid prolonged sun exposure during the study.

6.8.6.1. Systemic Therapy for Psoriasis

Concurrent use of systemic therapy for psoriasis (eg, psoralen with ultraviolet light A, systemic retinoids, cyclosporine or tacrolimus, with the exception of those in Table 3) must be discontinued at least 4 weeks prior to the first administration of study intervention and is not permitted during the study through Week 112; if a systemic antipsoriatic treatment (except those in Table 3) is initiated during the study, study intervention must be permanently discontinued.

Participants must not receive any biologic outside of the protocol or participate in any other clinical study with an investigational agent while in this study and must terminate study participation if they do. Prior to termination of study participation, participants should complete evaluations for a study intervention discontinuation visit.

6.8.7. Vaccinations (Including for COVID-19)

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

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

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued if:

- The participant withdraws consent to receive study intervention.
- The investigator believes that for safety reasons or tolerability reasons (eg, AE) it is in the best interest of the participant to discontinue study intervention.
- The participant becomes pregnant or plans to come pregnant within the study period. Refer to Appendix 10.7.
- A systemic opportunistic infection.
- The participant is unable to adhere to the study visit schedule or comply with protocol requirements.
- 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, and/or 2 indeterminate QuantiFERON-TB test results on repeat testing (refer to Section 8.2.12.) (and/or a positive tuberculin skin test result in countries in which the QuantiFERON-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities).

    Note: In Ukraine, while the QuantiFERON-TB test is not approved/registered, it is acceptable, and an additional tuberculin skin test is not required.

The frequency of TB testing can be increased depending on local health authority requirements.

– A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy.

- The participant has a serious adverse reaction that is temporally related to an injection including a hypersensitivity reaction resulting in bronchospasm, wheezing and/or dyspnea that requires ventilatory support OR that results in symptomatic hypotension with a decrease in systolic blood pressure of 30% from a participant's baseline value or systolic blood pressure <90 mm Hg (Sampson, 2006). In general, discontinuation of study intervention administration must be considered for participants who develop a severe injection-site reaction.
- The participant has a reaction resulting in myalgia and/or arthralgia with fever and/or rash (suggestive of serum sickness and not representative of signs and symptoms of other recognized clinical syndromes) occurring 1 to 14 days after an injection of study intervention. These may be accompanied by other events including pruritus, facial, hand, or lip edema, dysphagia, urticaria, sore throat, and/or headache.
- The participant has a malignancy including squamous cell skin cancer. Consideration may be given to allowing participants who develop ≤2 basal cell skin cancers that are adequately treated with no evidence of residual disease to continue to receive study intervention.
- The participant has severe liver test abnormalities that are not transient and are not explained by other etiologies, as described in Appendix 10.8.
- The Sponsor may elect to terminate the study at any time, and if the Sponsor decides not to continue development for any reason, study medication/drug will no longer be provided to any participants.

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

- If the participant initiates treatment with prohibited therapies, the medical monitor or designee should be notified for possible discontinuation of study intervention.
- Recurrent or chronic serious infection.
- The participant develops a serious infection, including but not limited to sepsis or pneumonia.

  Note: Any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete.

- Discontinuation of study treatment should be considered for participants who report suicidal Ideation level 4 (some intent to act, no plan), Ideation level 5 (specific plan and intent), or any suicidal behavior (actual suicide attempts, interrupted attempts, aborted attempts, or preparatory actions) on a postbaseline (after Week 0) electronic Columbia-Suicide Severity Rating Scale (eC-SSRS) assessment. Discussion of such participants with the medical monitor or designee is required.
- The participant develops a severe injection-site reaction, but not meeting criteria specified above.

If a participant discontinues study intervention for any reason before the end of the study, they should be encouraged to continue in the study to complete protocol specified evaluations as outlined in the SoA (Section 1.3) and Section 7.2.

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

7.1.1. Liver Chemistry Stopping Criteria

Discontinuation of study intervention for abnormal liver tests is required by the investigator when a participant meets 1 of the conditions in Appendix 10.8A or in the presence of abnormal liver chemistries not meeting protocol-specified stopping rules if the investigator believes that it is in best interest of the participant.

7.1.2. Liver Chemistry Restart Criteria

Refer to Appendix 10.8B for study intervention restart guidelines following abnormal liver test results. Study Sponsor must provide written approval before study intervention is restarted.

7.2. Participant Discontinuation/Withdrawal From the Study

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

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

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

Participants who Discontinue Study Intervention Prior to the Week 24 Visit

If a participant permanently discontinues study drug intervention prior to the Week 24 visit, they should be encouraged to return for all remaining study visits through Week 24. The participant should also return for a final safety visit to perform assessments under the Week 112/final safety visit approximately 12 weeks after the last study intervention administration.

Participants who Discontinue Study Intervention at or after Week 24 and Prior to the Week 100 Visit

If a participant discontinues study intervention at or after Week 24, the final efficacy visit should occur at the time of discontinuation or as soon as possible and all assessments under the Week 100 final efficacy visit should be performed with the exception of study intervention administration.

The participant should also return for a final safety visit to perform assessments under the Week 112/final safety visit approximately 12 weeks after the last study.

Withdrawal of Consent

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

Withdrawal of consent should be an infrequent occurrence in clinical studies (Rodriguez, 2015), therefore, prior to the start of the study the Sponsor and the investigator should discuss and reach a clear understanding of what constitutes withdrawal of consent in the context of the available reduced follow-up mechanisms listed.

Circumstances for Reduced Follow-up

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

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

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

7.2.1. Withdrawal from the Use of Research Samples

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

- The collected samples will be retained and used in accordance with the participant's original separate informed consent for optional research samples.
- The participant may withdraw consent for optional research samples, in which case the samples will be destroyed and no further testing will take place. To initiate the sample destruction process, the investigator must notify the Sponsor study site contact of withdrawal of consent for the optional research samples and 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.

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

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

Withdrawal from the Use of Samples in Future Research

The participant may withdraw consent for use of samples for research (refer to Appendix 10.5.3). In such a case, samples will be destroyed after they are no longer needed for the clinical study. Details of the sample retention for research are presented in the main ICF and in the separate ICF for optional research samples.

7.3. Lost to Follow-up

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

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

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

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

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

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

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

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

The total blood volume to be collected from each participant will be no more than 625 mL. Repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded in the eCRF or laboratory requisition form. Refer to the SoA (Section 1.3) for the timing and frequency of all sample collections.

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

Study-Specific Materials

The investigator will be provided with the following supplies:

- Investigator Site File (includes protocol and IB for guselkumab)
- Study site investigational product and procedures manual
- Laboratory manual and laboratory supplies
- PRO device and user manual
- IWRS Manual
- Sample ICF
- eCRF completion instructions
- Participant recruitment materials
- Participant diary cards
- Imaging manual

8.1. Efficacy Assessments

8.1.1. Psoriatic Arthritis Response Evaluations

8.1.1.1. Joint count (tender and swollen)

Each of 68 joints will be evaluated for tenderness, and each of 66 joints will be evaluated for swelling (hips are excluded for swelling).

An independent joint assessor (IJA) with adequate training and experience in performing joint assessments will be designated at each study site to perform all joint assessments. The IJA should preferably be a rheumatologist but if a rheumatologist is not available, it should be a health care provider with at least 1 year of experience in performing joint assessments. Health care providers with less than 1 year of experience may serve as an IJA based upon the discretion and approval of the Sponsor. It is strongly recommended that the designated IJA identify an appropriate back-up IJA for coverage in the event of absences of the designated IJA. It is strongly recommended that the same IJA who performs the baseline joint assessments for a participant should also perform the joint assessments for that participant at every subsequent visit.

Through Week 112, the IJA should have no other contact (other than joint assessments) with the participant once the participant is randomized, should not be the treating physician, should not discuss the participant's clinical status with the participant or other site personnel during the joint assessment, and will not be permitted to review the participants medical records or the eCRFs, or any of the previous joint assessments. The IJA should maintain a neutral attitude during joint assessment and should limit interactions with the participant only to activities associated with performing joint assessment or enthesitis or dactylitis assessments.

The IJA will perform only joint assessments and enthesitis and dactylitis assessments; this individual will not perform or assist in any other assessments in this study such as but not limited to administering participant and/or performing physician global assessments or administering study intervention.

The Sponsor will provide training for each site's designated IJA prior to the screening of the first participant at each site. A back-up IJA must complete training before performing a joint assessment for a participant's study visit.

If an IJA was trained by the Sponsor (with joint assessments) in a previous Janssen clinical study within the last 3 years and there is adequate documentation of this training (certification), that training will be considered adequate for this study; however, repeat training prior to start of the study is encouraged. Training documentation of each IJA should be maintained at the study site.

All IJA performing the joint evaluation at a site must be listed on the Delegation Log at the study site.

8.1.1.2. Non-evaluable Joints

Joints should only be designated as "non-evaluable" by the IJA if it is physically impossible to assess the joint (ie, joint inaccessible due to a cast, joint not present due to an amputation, artificial joint, or a recent wound near or at the joint so as to make it impossible to assess). In all other cases, the IJA should assess each joint for tenderness and swelling (hips are excluded for swelling). This should be completed regardless of any visual indications of prior surgeries (eg, scars) or knowledge they may have of a participant's prior joint procedures/injections (eg, if the participant was the IJA's patient prior to study participation).

8.1.1.3. American College of Rheumatology Response

American College of Rheumatology (ACR) responses are presented as the numerical measurement of improvement in multiple disease assessment criteria. For example, an ACR 20 response (Felson 1995) is defined as:

1. ≥20% improvement from baseline in both swollen joint count (66 joints) and tender joint count (68 joints),

AND

2. ≥20% improvement from baseline in 3 of the following 5 assessments:

- Patient's assessment of pain Visual Analogue Scale (VAS)
- Patient's Global Assessment of Disease Activity (arthritis, VAS)
- Physician's Global Assessment of Disease Activity (VAS)
- Patient's assessment of physical function as measured by HAQ-DI
- CRP

ACR 50 and ACR 70 are similarly defined except improvement threshold from baseline is 50% and 70% for all endpoints, respectively.

The assessments (other than joint counts) that are used to calculate ACR responses are described below.

8.1.1.4. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

The BASDAI was developed as a participant self-assessment for ankylosing spondylitis that consists of 6 questions relating to the 5 major symptoms of ankylosing spondylitis (Garrett, 1994). Only participants with spondylitis with peripheral arthritis as their primary arthritic presentation of PsA will complete the BASDAI using a 10-unit VAS to indicate the degree of their symptoms over the past week on the following criteria:

A. Fatigue
B. Spinal pain
C. Joint pain
D. Enthesitis
E. Qualitative morning stiffness

F. Quantitative morning stiffness

The BASDAI score = 0.2 (A + B + C + D + 0.5[E + F]). Higher scores indicate greater disease severity and a score decrease of 50% or 2 points is considered clinically meaningful (Zochling, 2006).

8.1.1.5. Dactylitis Score

Presence and severity of dactylitis will be assessed by the IJA in both hands and feet using a scoring system from 0 to 3 (0 – no dactylitis, 1 – mild dactylitis, 2 – moderate dactylitis, and 3 – severe dactylitis) (Gladman, 2007; Gladman, 2013).

The Sponsor will provide dactylitis assessment training. Documentation of this training will be maintained in the study site's training files. Previous dactylitis assessment 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.

It is strongly recommended that the same person who performs the baseline dactylitis assessments for a participant should also perform the dactylitis assessments for that participant at every subsequent visit through Week 100.

8.1.1.6. Enthesitis Assessments

Enthesitis will be assessed by the IJA using the LEI (Healy, 2008) and the SPARCC.

The LEI was developed to assess enthesitis in participants with PsA, and evaluates the presence or absence of pain by applying local pressure to the following entheses:

- Lateral epicondyle humerus, left and right
- Medial femoral condyle, left and right
- Achilles tendon insertion, left and right

The SPARCC developed a measure for enthesitis in general spondyloarthritis (ie, not limited to PsA or ankylosing spondylitis) which evaluates the presence or absence of pain by applying local pressure to the following entheses:

- Supraspinatus insertion, left and right
- Medial epicondyle humerus, left and right
- Lateral epicondyle humerus, left and right
- Greater trochanter, left and right
- Quadriceps–to-Patella, left and right
- Patellar-to-tibia, left and right
- Achilles tendon insertion, left and right
- Plantar fascia, left and right

The Sponsor will provide enthesitis assessment training. Documentation of this training will be maintained in the study site's training files. Previous enthesitis assessment 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.

It is strongly recommended that the same person who performs the baseline enthesitis assessments for a participant should also perform the enthesitis assessments for that participant at every subsequent visit.

8.1.1.7. Physician's Global Assessment of Disease Activity

The physician is asked to assess the patient's arthritis on a 100 mm VAS, with the left end indicating "No arthritis activity" and the right end indicating "Extremely active arthritis".

8.1.1.8. Health Assessment Questionnaire – Disability Index (HAQ-DI)

The functional status of the participant will be assessed by the Health Assessment Questionnaire – Disability Index (HAQ-DI) (Fries, 1980). This 20-question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area (ie, lower scores are indicative of better functioning). Properties of the assessment have been evaluated and its validity in PsA has been demonstrated (Husted, 1998). It has also been shown to be responsive to changes in a participant's disease (Mease, 2015). In PsA, a decrease in score of 0.35 has been determined to indicate a meaningful improvement (Mease, 2011).

8.1.1.9. Minimal Disease Activity

The PsA minimal disease activity (MDA) criteria are a composite of 7 outcome measures used in PsA. Participants are classified as achieving MDA if they fulfill 5 of 7 outcome measures: tender joint count ≤1; swollen joint count ≤1; psoriasis activity and severity index ≤1; patient pain VAS score of ≤15; patient global disease activity VAS (arthritis and psoriasis) score of ≤20; HAQ score ≤0.5; and tender entheseal points ≤1 (Coates, 2010).

8.1.1.10. Very Low Disease Activity

Remission or very low disease activity (VLDA) is achieved when 7 of the 7 MDA cutoffs are met.

8.1.1.11. Disease Activity Index for Psoriatic Arthritis (DAPSA)

Disease Activity index for PSoriatic Arthritis (DAPSA) is calculated as the sum of the following components: tender joint count (0–68), swollen joint count (0–66), CRP level (mg/dL), patient assessment of pain (0–10 VAS), and patient global assessment of disease activity (arthritis, 0 –10 VAS) (Helliwell, 2014b). The cutoffs for disease activity are 18.5 (low) to 45.1 (high) (Helliwell, 2014a).

8.1.1.12. Psoriatic Arthritis Disease Activity Score (PASDAS)

The PASDAS is calculated using the following variables: patient global VAS (arthritis and psoriasis, to 0–100), physician global VAS (range 0–100), swollen joint count (0-66), tender joint count (0-68), CRP level (mg/L), enthesitis (measured by the LEI), dactylitis count (using 2 different counts [1] scoring each digit from 0–3 and recoding to 0–1, where any score >0 equaled 1, and [2] scoring each digit for tenderness, 0-1), and the PCS scale of the SF-36 health survey (Helliwell 2013; Helliwell 2014b).

The formula to calculate PASDAS = {[(0.18 × √Physician global VAS) + (0.159 × √Patient global VAS) – (0.253 × √SF36 – PCS) + (0.101 × LN (Swollen joint count + 1)) + (0.048 × LN (Tender joint count + 1)) + (0.23 × LN (Leeds Enthesitis Count + 1)) + (0.377 × LN (Dactylitis count + 1)) + (0.102 × LN (CRP + 1))] +2} ×1.5

The cutoffs for disease activity are 3.2 (low) to 5.4 (high) (Helliwell, 2014a).

8.1.2. Psoriasis Response Evaluations

8.1.2.1. Psoriasis Area and Severity Index (PASI)

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy (Fredriksson, 1978). 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.

Every effort should be made to ensure that the physician or designee who performed the PASI evaluations for a participant at baseline should also perform the PASI evaluations for the participant at all subsequent visits through Week 100. The Sponsor will provide PASI training. 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.

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

The IGA documents the investigator's assessment of the participants psoriasis at a given timepoint. Overall lesions are graded for induration, erythema, and scaling using 0 (no evidence), 1 (minimal), 2 (mild), 3 (moderate) and 4 (severe) scale. The IGA score of psoriasis is based upon the average of induration, erythema and scaling scores. The patient's psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4).

Every effort should be made to ensure that the physician or designee who performed the IGA evaluations for a participant at baseline should also perform the IGA evaluations for the participant at all subsequent visits through Week 100. The Sponsor will provide IGA training. Documentation of this training will be maintained in the site's training files. Previous IGA 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.

8.1.3. Patient Reported Outcomes

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

The PRO instruments must be available for regulators and for IRB/ERC submissions, therefore the PRO instrument or screen shots need to be attached to the protocol or provided in a companion manual with the instruments that will be submitted with the protocol.

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

8.1.3.1. PsA Impact of Disease (PSAID)-12

The PsAID-12 is made up of 0-10 questions, with a final result included between 0 (no difficulty)-10 (extreme difficulty). The 12 domains examine different perspectives, both physical and psychological, that are considered important in patients with PsA. Each domain has a different weight: pain, fatigue, and skin problems are those with a greater effect (DiCarlo, 2017).

8.1.3.2. Functional Assessment of Chronic Illness Therapy (FACIT) - Fatigue

Fatigue has been identified as an important symptom and a unique concept in addition to the core disease measures of patients with PsA (Chandran, 2007). The Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue questionnaire consists of 13 questions that assess a participant's level of fatigue and tiredness over the last 7 days. Each question is graded on a 5-point scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; 4 = very much); accordingly, scores can range from 0 to 52. Lower scores reflect more severe fatigue. Although not developed for PsA, FACIT-Fatigue has demonstrated strong internal consistency and test-test reliability. It distinguishes between healthy and PsA patients and is correlated with swollen joint count and actively inflamed joint count. In rheumatology, a change of 4 points is considered meaningful and has been used in the PsA population (Cella, 2005).

8.1.3.3. Patient's Global Assessment of Disease Activity

Patient's global assessment of disease activity (arthritis and psoriasis): Participants will be asked to rate how they felt during the prior week regarding their psoriasis and arthritis on a 100 mm VAS, with the left end indicating "Excellent" and the right end indicating "Poor".

Patient's global assessment of disease activity (arthritis): Participants will be asked to rate how they felt during the prior week regarding their arthritis on a 100 mm VAS, with the left end indicating "Very Well" and the right end indicating "Very Poor".

8.1.3.4. Patient's Assessment of Pain

Patient's assessment of pain: Participants will be asked to assess their average pain during the prior week on a 100 mm VAS, with the left end indicating "no pain" and the right end indicating "the worst possible pain".

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

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

8.1.3.6. Short-Form 36 (SF-36)

The SF-36 questionnaire was developed as part of the Rand Health Insurance Experiment and consists of 8 multi-item domain scales:

- Limitations in physical functioning due to health problems
- Limitations in usual role activities due to physical health problems
- Bodily pain
- General mental health (psychological distress and well-being)
- Limitations in usual role activities due to emotional problems
- Limitations in social functioning due to physical or mental health problems
- Vitality (energy and fatigue)
- General health perception.

These scales are scored from 0 to 100 with higher scores indicating better health. Another algorithm yields 2 summary scores, the PCS and the MCS. These summary scores are also scaled with higher scores indicating better health but are scored using a norm-based system where linear transformations are performed to transform scores to a mean of 50 and standard deviations of 10, based upon general US population norms (Ware et al, 1994). It has been demonstrated in a study of patients with RA that a change of 4.4 in PCS and 4.7 in MCS was the minimally important

change (Kosinski et al, 2000). There is no specific cut-off for a clinically meaningful change in patients with PsA and a conservative threshold of ≥5 points change in both PCS and MCS have been used in the clinical studies to define clinically meaningful improvement for various diseases. The concepts measured by the SF-36 are not specific to any age, disease, or treatment group, allowing comparison of relative burden of different diseases and the relative benefit of different treatments (Ware et al, 1992).

8.2. Safety Assessments

Adverse events will be reported and followed by the investigator as specified in Section 8.3 and Appendix 10.6.

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

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

The study will include the following evaluations of safety and tolerability according to the timepoints provided in the SoA (Section 1.3).

8.2.1. Physical Examinations

Physical examinations will be performed by the investigator or designated physician as specified in the SoA (Section 1.3). Any abnormalities or changes in severity noted during the review of body systems should be documented in the source document.

8.2.2. Vital Signs

Pulse/heart rate and blood pressure will be assessed at each visit.

Blood pressure and pulse/heart rate measurements will be assessed with a completely automated device. Manual techniques will be used only if an automated device is not available.

If feasible, blood pressure and pulse/heart rate measurements should be preceded by at least 5 minutes of rest in a quiet setting without distractions (eg, television, cell phones).

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

8.2.3. Height and Weight

Height and weight will be measured as specified in the SoA (Section 1.3).

8.2.4. Electrocardiograms

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

During the collection of ECGs, participants should be in a quiet setting without distractions (eg, television, cell phones). Participants should rest in a supine position for at least 5 minutes

before ECG collection and should refrain from talking or moving arms or legs. If blood sampling or vital sign measurement is scheduled for the same timepoint as ECG recording, the procedures should be performed in the following order: ECG(s), vital signs, blood draw.

8.2.5. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology will be collected as noted in Appendix 10.2. The investigator must review the laboratory results, document this review, and record any clinically relevant changes occurring during the study in the AE section of the eCRF. The laboratory reports must be filed with the source documents.

The tests that will be performed by the central laboratory unless otherwise specified or approved by the medical monitor/designee are specified in Appendix 10.2.

8.2.6. Pregnancy Testing

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

8.2.7. Suicidal Ideation and Behavior Risk Monitoring

No signal of suicidal ideation and behavior has been observed in the clinical trials of guselkumab to date. However, in light of reports concerning suicidal ideation and behavior in patients with plaque psoriasis treated with an IL-17R antagonist (brodalumab), the eC-SSRS will be used as a screening tool to prospectively evaluate suicidal ideation and behavior among study participants. The eC-SSRS measures 5 possible levels of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior. The assessment is a fully structured, participant self-report eC-SSRS-questionnaire, including standardized questions, follow-up prompts, error handling routines, and scoring conventions (Mundt, 2013; Posner, 2011).

Two versions of the eC-SSRS will be used in this study, the Lifetime version and the Since Last Contact version. The Lifetime version will be conducted during the screening visit and the Since Last Contact version will be conducted at all other visits. Participants will complete the eC-SSRS questionnaire using the Sponsor-provided electronic device. Study site personnel will train the participants on how to use the electronic device. The eC-SSRS will be provided in the local languages in accordance with local guidelines.

The eC-SSRS will be performed during each evaluation visit according to the SoA (Section 1.3). During a visit, participants will be directed to a private, quiet place with the electronic device to complete the assessment. Participants who do not have suicidal behavior or ideation will answer a limited number of questions and will usually complete the assessment in about 3 minutes. Participants with significant suicidal ideation and behavior may require up to 10 minutes to answer all relevant questions.

At the screening visit, the eC-SSRS should be completed as the first assessment after signing informed consent and joint assessment, but before any other tests, procedures, or other consultations. For subsequent visits, the eC-SSRS should be completed after all PROs and before any other tests, procedures, or other consultations. At the conclusion of each assessment, the eC-SSRS Findings Report can be viewed electronically. At screening ("In the last 6 months") and Week 0, participants with an Ideation level (1-5) or any suicidal behaviors or with a response of "YES" for non-suicidal, self-injurious behavior must be determined to be not at risk by the investigator based on an evaluation by a mental health professional in order to be randomized. Participants with an Ideation level (1-5) on the eC-SSRS or any suicidal behaviors or with a response of "YES" for non-suicidal, self-injurious behavior at any postbaseline visit will also be referred to an appropriate mental health professional for evaluation. If a participant's psychiatric disorder can be adequately treated with psychotherapy and/or pharmacotherapy then the participant, at the discretion of the investigator, should be continued with treatment. Ultimately, the determination of suicidality and risk is up to the investigator's clinical judgment following evaluation by a mental health professional (eg, psychiatrist, psychologist, or appropriately trained social worker or nurse).

Positive reports are generated from the eC-SSRS vendor for ANY of the following findings:

- Ideation level 4: Some intent to act, no plan
- Ideation level 5: Specific plan and intent
- Behaviors: Actual suicide attempts
- Behaviors: Interrupted attempts
- Behaviors: Aborted attempts
- Behaviors: Preparatory actions.

Negative suicidality indication reports are generated from the eC-SSRS vendor when there are NO indications of the above.

The participant should not leave the site at screening or be dosed at dosing visits before the eC-SSRS Findings Report (both for negative and positive reports) is reviewed by the investigator and the participant's risk has been assessed and follow-up determined, as appropriate. For each Ideation level and Behavior, the following actions and associated alerts will be generated, if applicable:

- No ideation with No Behaviors: No further action is needed.
- Ideation Levels (1-5) or suicidal behavior: Participant risk assessed and referral to a mental health professional.
  - Ideation level of a 1, 2, or 3 with No Behaviors: Negative findings report will be generated.
  - Ideation level of a 4 or 5 or any suicidal behavior: Positive findings report will be generated. When the system reports that the participant has a positive suicidal indication

(including for an incomplete-positive assessment), the site can immediately see the outcome via the electronic device.

- Non-suicidal, self-injurious behavior = YES: Participant risk assessed and referral to a mental health professional. Negative findings report will be generated.

Interruption or the discontinuation of study treatment should be considered for any participant who reports suicidal Ideation level 4 (some intent to act, no plan), Ideation level 5 (specific plan and intent), or any suicidal behavior (actual suicide attempts, interrupted attempts, aborted attempts, or preparatory actions) on a postbaseline (after Week 0) eC-SSRS assessment and who is deemed to be at risk by the investigator based upon evaluation by a mental health professional. Discussion of such participants with the medical monitor or designee is required (see Section 7.1). The final decision on suitability for continuing in the study will be made by the investigator. Any eC-SSRS findings, which in the opinion of the investigator are new or considered to be a worsening and clinically significant, should be reported on the AE eCRF.

8.2.8. Concomitant Medication Review

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

8.2.9. Injection-Site Reactions

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

8.2.10. Hypersensitivity Reactions

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

8.2.11. Infections

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

8.2.12. Tuberculosis Evaluations

8.2.12.1. Initial Tuberculosis Evaluation

Participants must undergo testing for TB (refer to Appendix 10.3) and their medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB. The participant should be asked about past testing for TB, including chest radiograph results and responses to tuberculin skin or other TB testing. Investigators have the option to use both the QuantiFERON-TB test and the tuberculin skin test to screen for latent TB if they believe, based on their judgment, that the use of both tests is clinically indicated to evaluate a participant who is high risk of having latent TB. If either the QuantiFERON-TB test or the tuberculin skin test is positive, the participant is considered to have latent TB infection for the purposes of eligibility for this study.

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

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, 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 or designee's medical monitor and recorded in the participant's source documents and initialed by the investigator.

8.2.12.2. Ongoing Tuberculosis Evaluation

Early Detection of Active Tuberculosis

To aid in the early detection of TB reactivation or new TB infection during study participation, participants must be evaluated for signs and symptoms of active TB at scheduled visits (refer to the SoA in Section 1.3) or by telephone contact approximately every 8 to 12 weeks. The following series of questions is suggested for use during the evaluation:

- "Have you had a new cough of >14 days' duration or a change in a chronic cough?"
- "Have you had any of the following symptoms:
  - Persistent fever?
  - Unintentional weight loss?
  - Night sweats?"

- "Have you had close contact with an individual with active TB?" (If there is uncertainty as to whether a contact should be considered "close," a physician specializing in TB should be consulted.)

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

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

Participants who experience close contact with an individual with active TB during the conduct of the study must have a repeat chest radiograph, a repeat QuantiFERON-TB test, a repeat tuberculin skin test in countries in which the QuantiFERON-TB test is not approved/registered or the tuberculin skin test is mandated by local health authorities, and, if possible, referral to a physician specializing in TB to determine the participant's risk of developing active TB and whether treatment is warranted. Study intervention administration should be interrupted during the investigation. A positive QuantiFERON-TB test or tuberculin skin test result should be considered detection of latent TB. Participants with a newly identified positive QuantiFERON-TB test result must undergo an evaluation to rule out active TB and initiate appropriate treatment for latent TB. Appropriate treatment for latent TB is defined according to local country guidelines for immunocompromised patients. If no local country guidelines for immunocompromised patients exist, US guidelines should be followed, or the participant will be excluded from the study. If the QuantiFERON-TB 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. Participants who discontinue treatment for latent TB prematurely or who are noncompliant with therapy must immediately discontinue further administration of study intervention and be encouraged to return for all subsequent scheduled study visits according to the SoA (Section 1.3).

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

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

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

For study intervention that meets the definition of a combination product, malfunctions or deficiencies of a device constituent will be reported as a PQC.

Further details on AEs, SAEs, and PQC can be found in Appendix 10.6.

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

All Adverse Events

All AEs and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the participant's last study-related procedure, which may include contact for follow-up of safety.

Serious Adverse Events

All SAEs, as well as PQCs, occurring during the study must be reported to the appropriate Sponsor contact person by study site personnel within 24 hours of their knowledge of the event.

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

Possible Hy's law case

Any possible Hy's law case (ALT or AST ≥3 x the upper limit of normal [ULN] together with bilirubin ≥2 x ULN or INR >1.5 is considered an important medical event and must be reported to the sponsor in an expedited manner using the Serious Adverse Event form, even before all other possible causes of liver injury have been excluded (INR criterion is not applicable to participants receiving anticoagulants). A confirmed Hy's law case must be reported as an SAE.

8.3.2. Method of Detecting Adverse Events and Serious Adverse Events

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

Solicited Adverse Events

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

Unsolicited Adverse Events

Unsolicited AEs are all AEs for which the participant is not specifically questioned in the participant diary.

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

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

Adverse events, including pregnancy, will be followed by the investigator as specified in Appendix 10.6, Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

8.3.4. Regulatory Reporting Requirements for Serious Adverse Events and Anticipated Events

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

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

- Worsening of psoriasis
- Worsening of PsA

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

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

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

8.3.5. Pregnancy

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

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

8.3.6. Adverse Events of Special Interest

Any newly identified malignancy or case of active TB occurring after the first study intervention administration(s) in participants in this clinical study must be reported by the investigator to the Sponsor or designee within 24 hours after being made aware of the event, according to the procedures in Appendix 10.6.4. Investigators are also advised that active TB is considered a reportable disease in most countries. These events are to be considered serious only if they meet the definition of an SAE.

8.4. Pharmacokinetics

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

8.4.1. Evaluations

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

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

8.4.2. Analytical Procedures

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

8.5. Pharmacogenomics

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

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

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

8.6. Biomarkers

Samples for serum biomarkers will be collected for all participants as indicated in the SoA (Section 1.3).

Biomarker assessments will be made to examine the biologic response to treatment and to identify biomarkers that are relevant to guselkumab treatment and/or PsA, where local regulations permit. Assessments (detailed below) will include the evaluation of relevant biomarkers in serum, plasma, and whole blood collected as specified in the SoA, where local regulations permit.

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

1. To understand the molecular effects of guselkumab.

2. To understand PsA pathogenesis.

3. To understand why individual participants may respond differently to guselkumab.

4. To develop diagnostic tests to identify PsA populations that may be responsive or non-responsive to treatment with guselkumab.

Stopping Analysis

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

8.6.1. Pharmacodynamics

Samples for the analysis of pharmacodynamic biomarkers will be collected. Serum level of T helper (Th)-17 cytokines, including but not limited to IL-17A, IL-17F, and IL-22, may be measured to assess the pharmacodynamic effect of guselkumab.

8.6.2. Serum and Plasma Biomarkers

Blood samples will be collected from all participants for serum and plasma-based biomarker analyses, where local regulations permit. Serum level of Th17 cytokines, such as IL-17A, IL-17F, and IL-22, may be measured to assess the pharmacodynamic effect of guselkumab. Serum and

plasma may be analyzed for other inflammation-related molecules, and/or broad panel of analytes relevant to PsA pathogenesis and guselkumab treatment.

8.6.3. Whole Blood Gene Expression Profile

Whole blood will be collected by venipuncture from participants for RNA expression analysis, where local regulations permit. Total RNA will be isolated and used for differential gene expression analyses to identify gene expression patterns that are relevant to guselkumab treatment and/or PsA, and to evaluate markers that can predict clinical response. Transcriptomic studies may be conducted using microarray, and/or alternative equivalent technologies, which facilitate the simultaneous measurement of the relative abundances of multiple RNA species resulting in a transcriptome profile for each blood sample. The samples may also be used for targeted assessment of genes relevant to the disease and/or the treatment. These analyses may be used to evaluate the changes in gene expression profiles that may correlate with biological response relating to PsA and/or the action of guselkumab, and may also be used to identify population subgroups that respond differently to an intervention.

8.6.4. Peripheral Blood Mononuclear Cells

Whole blood will also be collected and processed for peripheral blood mononuclear cells (PBMC) isolation and cryopreserved for later analysis. Analysis may include but is not limited to flow cytometric assessment of cell populations, single cell transcriptomics, or functional assessment of cells in response to guselkumab treatment and/or related to PsA pathogenesis. These analyses may not be performed if cryopreserved PBMC samples do not meet the quality or quantity standard required for the assessments.

8.6.5. Tissue Biomarkers

Biopsies from lesional and non-lesional skin may be collected from participants who meet additional eligibility criteria and consent to this optional substudy component of the study (with a separate ICF), as fixed blocks, slides, or fresh samples, where local regulations permit. Tissue samples may be analyzed for levels of proteins, transcripts, and other inflammation-related molecules and/or soluble factors relevant to PsA pathogenesis and guselkumab treatment. Analysis may include, but is not limited to, tissue proteomic and transcriptomic assessment of cell populations to identify cellular biomarkers associated with PsA pathogenesis and/or guselkumab treatment as permitted by relevant and advancing technologies.

8.7. Immunogenicity Assessments

Serum samples for detection of antibodies to guselkumab will be collected from all participants according to the SoA. Additionally, serum samples should also be collected at the final visit from participants who discontinued study intervention or were withdrawn from the study. Samples collected for immunogenicity analyses may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period. Genetic analyses will not be performed on these serum samples. Participant confidentiality will be maintained.

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

Analytical Procedures

The detection and characterization of antibodies to guselkumab will be performed using a validated immunoassay method by or under the supervision of the Sponsor.

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 (SAP).

9.1. Statistical Hypotheses

The primary hypothesis of this study is that guselkumab is superior to placebo as assessed by the proportion of participants achieving an ACR 20 response at Week 24.

The method of addressing the multiplicity of hypotheses to keep the family-wise type I error controlled at the 0.05 level will be specified in the SAP.

9.2. Sample Size Determination

The planned enrollment in the study is approximately 450 participants. Participants impacted by major disruptions may be replaced. The sample size selection was determined based on the primary endpoint of proportion of participants who achieve an ACR 20 response at Week 24. The assumptions are based on the PSA3001 and PSA3003 studies.

9.2.1. Primary Endpoint – ACR 20 Response at Week 24

In the PSA3001 study, the ACR 20 response rates in the overall efficacy population at Week 24 were 22.2%, 52.0%, and 59.4%, for the placebo, guselkumab SC 100 mg q8w, and guselkumab 100 mg q4w treatment groups, respectively.

In the PSA3003 study which included participants who have an inadequate response or intolerance to up to 2 prior anti-TNFs, the ACR 20 response rates at Week 24 were 19.8% and 44.4%, for placebo and guselkumab SC 100 mg q8w, respectively.

For this study, assuming an ACR 20 response rate comparable to those in PSA3001 and PSA3003 in each of the guselkumab groups and the placebo group, a sample size of 150 participants per group for each of the guselkumab treatment groups and placebo will have >90% power to detect differences between each guselkumab treatment group and placebo for the primary endpoint assuming a 2-sided alpha level of 0.05 (Table 5). The sample size calculations assume that 100%

of the effect observed in PSA3001 and PSA3003 will be observed. If only 70 or 80% of the effect seen in PSA3001 and PSA3003 is observed, the power will still exceed 90% for the Primary endpoint.

Table 5: Power Calculations for Primary and Major Secondary Endpoints Based on 150 per Treatment Group

Endpoint	Source	Mean or proportion			p=0.05
		Placebo	Gus Q8W/Q4W	Effect size/diff	Q8W/Q4W
Primary: ACR 20 at Week 24					
	PSA3001	22%	52%	30%	>99%
	PSA3001		59%	37%	>99%
	PSA3003[a]	19.8%	44.4%	24.6%	>99%
[a:] PSA3003 (COSMOS) data is for Q8W only					

9.3. Populations for Analysis Sets

For purposes of analysis, the populations defined in Table 6 will be used:

Table 6: Analysis Populations

Population	Description
Enrolled	All participants who signed the informed consent form (ICF).
Full Analysis Set	All participants who were randomized in the study and received at least 1 (complete or partial) administration of study intervention. This analysis set will be used for the efficacy analyses.
Modified Full Analysis Set	All participants who were randomized, excluding participants from sites rendered unable to support key study operations due to major disruptions (eg, Natural Disaster or Other Major Disruption). Details will be provided in the SAP.
Safety Analysis Set	All participants who received at least 1 (complete or partial) administration of study intervention, ie, the treated population.
Immunogenicity Analysis Set	All participants who received at least 1 (complete or partial) administration of guselkumab and who had at least 1 sample obtained after their first administration of guselkumab.
PK Analysis Set	All participants who received at least 1 complete administration of guselkumab and had at least 1 valid blood sample drawn for PK analysis.
PD Analysis Set	All participants who received at least 1 (complete or partial) administration of study intervention.

9.4. Statistical Analyses

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

9.4.1. General Considerations

In general, descriptive statistics, such as mean, SD, median, interquartile (IQ) range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data.

For binary response efficacy endpoints, treatment comparisons will generally be performed using a Chi-square test or a Cochran-Mantel-Haenszel (CMH) test. For continuous endpoint of efficacy data, treatment comparisons will be performed using an analysis of covariance (ANCOVA), a mixed model for repeated measures (MMRM) or a constrained longitudinal data analysis (cLDA) model.

In general, statistical testing will be performed using 2-sided tests. The overall type I error will be controlled among the primary and major secondary endpoints at 5%.

9.4.2. Primary Endpoint(s)

The primary endpoint is the proportion of participants who achieved an ACR 20 response at Week 24. This endpoint will be analyzed based on the adjusted **estimand** defined by the 5 components:

- Population: Participants with active PsA who have inadequate response and/or intolerance to 1 prior anti-TNF, and were randomized and treated with study intervention
- Treatment:
  - Placebo
  - Guselkumab
- Variable: ACR 20 at Week 24, where a responder is defined as a participant who achieves ACR20 response at Week 24 and does not experience Intercurrent Events categories 1 to 3.
- Intercurrent events (ICEs): Participants with an ICE in categories 1-3 will follow the composite strategy, where participants who experience them prior to Week 24 will be considered as non-responders regardless of the observed ACR 20 response status. Participants with an ICE in categories 4 or 5 will follow the hypothetical strategy postulating a scenario where the major disruption (eg, Natural Disaster or Other Major Disruption) and ICEs directly resulting from them, did not occur, and observed data through Week 24 after meeting these ICEs will not be used and will be assumed to be Missing at Random (MAR). For participants experiencing multiple ICEs, an ICE in categories 1 to 3 will supersede an ICE in categories 4 and 5. Additional details for the ICEs below will be further defined in the SAP as applicable.
  1. Discontinued study intervention injections due to any reason except due to Natural Disaster or Major Disruption.
  2. Initiated or increased the dose of non-biologic DMARDs (MTX, SSZ, HCQ, LEF) or oral corticosteroids over baseline for PsA.
  3. Initiated protocol prohibited medications/therapies for PsA.
  4. Discontinued study intervention injections due to Natural Disaster or Major Disruption.
  5. Severe treatment non-compliance due to Natural Disaster or Major Disruption.
- Population level summary: difference in proportion of responders between guselkumab group and placebo group.

Data from all participants in the modified full analysis set (mFAS) will be analyzed according to randomized treatment group regardless of the treatment actually received. Participants with missing data for any reason other than due to major disruptions (eg, Natural Disaster or Other Major Disruption) will be considered nonresponders, while missing data due to major disruptions (eg, Natural Disaster or Other Major Disruption) or data not used due to ICE categories 4 or 5 will be assumed to be MAR and imputed using multiple imputation (MI). The treatment effect of each guselkumab group versus placebo will be tested using a CMH test stratified by baseline non-biologic DMARD use (yes/no). The magnitude of the effect will be estimated by the difference in ACR 20 response rates between the guselkumab and placebo groups with the 95% confidence interval calculated based on Wald statistics.

To evaluate the robustness of the primary endpoint analysis results, the exhaustive scenario tipping point sensitivity analyses will be performed by varying the amount of non-responder imputation for missing data.

Additional sensitivity/supplemental analyses which vary how ICEs (eg, alternative estimand) are handled, how observed data are used, and how missing data are treated will be specified in the SAP to further address the robustness of treatment effect of ACR 20 at Week 24.

Subgroup Analyses

Subgroup analysis will be performed to evaluate consistency in the primary efficacy endpoint by demographic characteristics, baseline disease characteristics, and baseline medications. Interaction test between the subgroups and treatment group will also be provided if appropriate.

9.4.3. Secondary Endpoint(s)

Major secondary endpoints are provided in Section 3.

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

In addition to the primary and major secondary endpoints, all other secondary endpoints (Section 3) will be summarized over time by treatment groups. Treatment comparisons will be performed by visit through Week 24.

The estimand, analysis method, and data handling rules for major secondary endpoints, as well as the approach to control the type I error for multiplicity will be specified in the SAP.

9.4.4. Safety Analyses

All safety analyses will be made on the Safety Population.

Adverse Events

The verbatim terms used in the eCRF by investigators to identify AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). For each AE, the percentage of

participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

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

- The incidence and type of AEs.
- The incidence and type of SAEs.
- The incidence and type of infections.
- The incidence and type of injection site reactions.

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

Clinical Laboratory Tests

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

Vital Signs

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

9.4.5. Other Analyses

Pharmacokinetic Analyses

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

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

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

analysis plan and the results of the population PK analysis will be presented in a separate technical report.

Immunogenicity Analyses

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

A listing of participants who are positive for antibodies to guselkumab will be provided.

The incidence of neutralizing antibodies (NAbs) to guselkumab will be summarized for participants who are positive for antibodies to guselkumab and have samples evaluable for NAbs to guselkumab. Other immunogenicity analyses may be performed to further characterize the immune responses that are generated.

Biomarker and Pharmacodynamic Analyses

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

The biomarker analyses will be used to understand PsA, characterize the effects of guselkumab to identify PD markers and biomarkers relevant to treatment, and to determine if these markers can predict response to guselkumab. The biomarker analysis may include but are not limited to serum Th17 cytokines, inflammatory markers, whole blood RNA profile, and other categories of biomarkers potentially involved in the development and the progression of PsA.

Changes in biomarkers over time may be summarized by intervention group. Associations between baseline levels and changes from baseline in select markers and clinical response may be explored.

Results of biomarker analyses may be presented in a separate report.

Pharmacokinetic/Pharmacodynamic Analyses

If data permit, the relationships between serum guselkumab concentrations and efficacy and/or relevant PD endpoints may be analyzed graphically. If a relationship is observed, a suitable PK/PD model may be developed to describe the exposure-response relationship and will be presented in a separate technical report.

Pharmacogenomic Analyses

Genetic (DNA) analyses may be conducted only in participants who sign the consent form to participate in the pharmacogenomic sampling. These analyses are considered exploratory. DNA samples may be used for research related to guselkumab and/or PsA. They may also be used to develop tests/assays related to guselkumab and PsA. Pharmacogenomic research may consist of

the analysis of candidate genes or of the analysis of genetic markers throughout the genome or analysis of the entire genome (as appropriate) in relation to guselkumab or PsA clinical endpoints.

Results may be presented in a separate report.

9.5. Interim Analysis

Not applicable.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Abbreviations

Abbreviation	Definition
ACR	American College of Rheumatology
AE	adverse event
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
AS	ankylosing spondylitis
AST	aspartate aminotransferase
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BCG	Bacillus Calmette-Guérin
BQL	below the limit of quantitation
BSA	body surface area
CASPAR	ClASsification criteria for Psoriatic Arthritis
CD	Crohn's disease
cLDA	constrained longitudinal data analysis
CMH	Cochran Mantel Haenszel
CRF	case report form
CRP	C-reactive protein
CTCAE	Common Terminology Criteria for Adverse Events
DAPSA	Disease Activity index for PSoriatic Arthritis
DBL	database lock
DMARD	disease modifying anti-rheumatic drug
ECG	electrocardiogram
eC-SSRS	electronic Columbia-Suicide Severity Rating Scale
eCRF	electronic CRF
eDC	electronic data capture
EEA	European Economic Area
EU	European Union
FACIT-F	Functional Assessment of Chronic Illness Therapy – fatigue
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
HAQ-DI	Health Assessment Questionnaire – Disability Index
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCQ	hydroxychloroquine
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HRQoL	health related quality of life
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IEC	Independent Ethics Committee
Ig	immunoglobulin
IGA	Investigator's Global Assessment
IJA	independent joint assessor
IL	interleukin
IM	intramuscular
IQ	interquartile
IRB	Institutional Review Board

IR	inadequate response
IV	intravenous(ly)
IWRS	interactive web response system
JAK	Janus kinase
LEF	leflunomide
LEI	Leeds Enthesitis Index
mAb	monoclonal antibody
MCS	Mental Component Score
MDA	Minimal Disease Activity
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed model for repeated measures
MTX	methotrexate
NAbs	neutralizing antibodies
NCI	National Cancer Institute
NSAID	nonsteroidal anti-inflammatory drug
PASDAS	Psoriatic ArthritiS Disease Activity Score
PASI	Psoriasis Area and Severity Index
PBMC	peripheral blood mononuclear cells
PCS	Physical Component Score
PD	pharmacodynamic(s)
PFS-U	prefilled syringe with the Ultrasafe PLUS™ passive needle guard
PK	pharmacokinetic(s)
PQC	Product Quality Complaint
PRO	patient-reported outcome(s) (paper or electronic as appropriate for this study)
PsA	psoriatic arthritis
PsAID12	psoriatic arthritis impact of disease score
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
q4w, q8w	every 4 weeks, every 8 weeks
RA	rheumatoid arthritis
SAE	serious adverse event
SAP	Statistical Analysis Plan
SARS-COV-2	Severe Acute Respiratory Syndrome Coronavirus 2 (Coronavirus disease 2019)
SC	subcutaneous
SD	standard deviation
SF-36	36-item short form survey
SPARCC	Spondyloarthritis Research Consortium of Canada
SSZ	sulfasalazine
SoA	Schedule of Activities
SUSAR	suspected unexpected serious adverse reaction
TB	tuberculosis
TNF	tumor necrosis factor
ULN	upper limit of normal
UV	ultraviolet
VAS	visual analog scale
vdH-S	van der Heijde-Sharp score
VLDA	very low disease activity

10.2. Appendix 2: Clinical Laboratory Tests

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

Protocol-Required Safety Laboratory Assessments

<table>
<tr><th>Laboratory Assessments</th><th colspan="3">Parameters</th></tr>
<tr><td rowspan="2">Hematology</td><td>Platelet count
Red blood cell count
Hemoglobin
Hematocrit</td><td><u>Red Blood Cell (RBC) Indices:</u>
Mean corpuscular volume
Mean corpuscular hemoglobin
% Reticulocytes</td><td><u>White Blood Cell (WBC) count with Differential:</u>
Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils</td></tr>
<tr><td colspan="3">Note: A WBC evaluation may include any abnormal cells, which will then be reported by the laboratory. A RBC evaluation may include abnormalities in the RBC count, RBC parameters, or RBC morphology, which will then be reported by the laboratory. In addition, any other abnormal cells in a blood smear will also be reported.</td></tr>
<tr><td rowspan="2">Clinical Chemistry</td><td colspan="2">Sodium
Potassium
Chloride
Bicarbonate
Blood urea nitrogen (BUN)
Creatinine
Glucose (see SoA [Section 1.3])
Aspartate aminotransferase (AST)
Alanine aminotransferase (ALT)</td><td>Total bilirubin (direct only if total elevated)
Alkaline phosphatase
Calcium
Albumin
Total protein</td></tr>
<tr><td colspan="3">Note: Details of liver chemistry stopping criteria and required actions and follow-up are given in Appendix 10.8.</td></tr>
<tr><td>Other</td><td colspan="3">• Total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (Week 0 only)
• Serum Pregnancy Testing for women of childbearing potential only
• High-sensitivity C-reactive protein (CRP)
• Serology (HIV antibody, hepatitis B surface antigen [HBsAg], and hepatitis C virus antibody)
• QuantiFERON -tuberculosis (TB) test
• TB skin test (where applicable; performed locally)
• Rheumatoid factor (screening only)
• Follicle-stimulating hormone (screening only)</td></tr>
</table>

10.3. Appendix 3: Tuberculin Skin Testing

The Mantoux tuberculin skin test (CDC, 2000) is a method of identifying persons infected with *Mycobacterium tuberculosis*. Multiple puncture tests (Tine and Heaf) should not be used to determine whether a person is infected because the amount of tuberculin injected intradermally cannot be precisely controlled. Tuberculin skin testing is both safe and reliable throughout the course of pregnancy.

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

Interpreting the Tuberculin Skin Test Results

In the US and many other countries, the most conservative definition of positivity for the tuberculin skin test is reserved for immunocompromised patients, and this definition is to be applied in this study to maximize the likelihood of detecting latent TB, even though the participants may not be immunocompromised at baseline. In the US and Canada, an induration of 5 mm or greater in response to the intradermal tuberculin skin test is considered to be a positive result and evidence for either latent or active TB. In countries outside the US and Canada, country-specific guidelines for immunocompromised patients should be consulted for the interpretation of tuberculin skin test results. If no local country guidelines for immunocompromised patients exist, US guidelines must be followed.

Treatment of Latent Tuberculosis

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

References

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

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

10.4. Appendix 4: Hepatitis B Virus (HBV) Screening with HBV DNA Testing

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

- Participants who test negative for all HBV screening tests (ie, HBsAg-, anti-HBc-, and anti-HBs-) are eligible for this protocol.
- Participants who test negative for surface antigen (HBsAg-) and test positive for core antibody (antiHBc+) and surface antibody (anti-HBs+) are eligible for this protocol.
- Participants who test positive only for surface antibody (anti-HBs+) are eligible for this protocol.
- Participants who test positive for surface antigen (HBsAg+) are NOT eligible for this protocol, regardless of the results of other hepatitis B tests.
- Participants who test positive only for core antibody (anti-HBc+) are NOT eligible for this protocol.

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

Eligibility Based on the Hepatitis B Virus (HBV) Test Results			
Test Result			STATUS
Hepatitis B surface antigen (HBs-Ag)	Hepatitis B surface antibody (anti-HBs)	Hepatitis B core antibody (anti-HBc total)	
negative	negative	negative	ELIGIBLE
negative	positive	negative	
negative	positive	positive	
positive	negative or positive	negative or positive	NOT ELIGIBLE
negative	negative	positive	Requires testing for presence of HBV DNA*

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

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

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

10.5.1. Regulatory and Ethical Considerations

Investigator Responsibilities

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

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

Protocol Clarification Communications

If text within a final approved protocol requires clarification (eg, current wording is unclear or ambiguous) that does not change any aspect of the current study conduct, a protocol clarification communication (PCC) may be prepared. The PCC Document will be communicated to the Investigational Site, Site Monitors, Local Trial Managers (LTMs), Clinical Trial Managers (CTMs), and/or Contract Research Organizations (CROs) who will ensure that the PCC explanations are followed by the investigators.

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

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

Protocol Amendments

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

During the course of the study, in situations where a departure from the protocol is unavoidable, the investigator or other physician in attendance will contact the appropriate Sponsor representative listed in the Contact Information page(s), which will be provided as a separate document. Except in emergency situations, this contact should be made before implementing any departure from the protocol. In all cases, contact with the Sponsor must be made as soon as possible

to discuss the situation and agree on an appropriate course of action. The data recorded in the eCRF and source documents will reflect any departure from the protocol, and the source documents will describe this departure and the circumstances requiring it.

Regulatory Approval/Notification

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

Required Prestudy Documentation

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

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

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

- Completed investigator financial disclosure forms from all 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)
- IB (or equivalent information) and amendments/addenda
- Sponsor-approved participant recruiting materials
- Information on compensation for study-related injuries or payment to participants for participation in the study, if applicable
- Investigator's curriculum vitae or equivalent information (unless not required, as documented by the IEC/IRB)
- Information regarding funding, name of the Sponsor, institutional affiliations, other potential conflicts of interest, and incentives for participants
- Any other documents that the IEC/IRB requests to fulfill its obligation

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

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

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

- Protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct)
- Revision(s) to ICF and any other written materials to be provided to participants
- If applicable, new or revised participant recruiting materials approved by the Sponsor
- Revisions to compensation for study-related injuries or payment to participants for participation in the study, if applicable
- New edition(s) of the IB and amendments/addenda

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

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

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

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

Country Selection

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

Other Ethical Considerations

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

10.5.2. 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) and contracts for details on financial disclosure.

10.5.3. Informed Consent Process

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

Before enrollment in the study, the investigator or an authorized member of the study site personnel must explain to potential participants the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive Finally, they will be told that the investigator will maintain a participant identification register for the purposes of long-term follow up (if needed) and that their records may be accessed by health authorities and authorized Sponsor personnel without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations.

By signing the ICF the participant is authorizing such access, which includes permission to obtain information about his or her survival status. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed.

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

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

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

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

10.5.4. Data Protection

Privacy of Personal Data

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

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

The informed consent obtained from the participant includes 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.

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

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

10.5.5. Long-Term Retention of Samples for Additional Future Research

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

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

10.5.6. Committees Structure

Not applicable

10.5.7. 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 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 biomarker analyses performed after the Clinical Study Report has been issued may 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.

The summary of the results from the Week 24 Database Lock (DBL), will be submitted to the EU database within one year of the data analysis date.

The disclosure of the final study results will be performed after the end of study in order to ensure the statistical analyses are relevant.

10.5.8. Data Quality Assurance

Data Quality Assurance/Quality Control

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

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

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

10.5.9. 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 eCRF. All eCRF entries, corrections, and alterations must be made by the investigator or authorized study site personnel. The investigator must verify that all data entries in the eCRF are accurate and correct.

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

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

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 electronic data capture (eDC) tool. If corrections to an eCRF are needed after the initial entry into the eCRF, this can be done in either of the following ways:

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

10.5.10. Source Documents

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

The author of an entry in the source documents should be identifiable. Given that PROs are reports of a patient's health condition that come directly from the patient, without interpretation by a clinician or anyone else, the responses to PRO measures entered by trial participants into source records cannot be overridden by site staff or investigators.

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

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

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

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

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

10.5.11. 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 eCRF with the source documents (eg, hospital/clinic/physician's office medical records). The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the eCRF are known to the Sponsor and study site personnel and are accessible for verification by the Sponsor study site contact. If electronic records are maintained at the study site, the method of verification must be discussed with the study site personnel.

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

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

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

10.5.12. 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.

10.5.13. Record Retention

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

Essential documents must be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or by an agreement with the Sponsor. It is the responsibility of the Sponsor to inform the investigator/institution as to when these documents no longer need to be retained. For trials performed under Regulation [EU] No. 536/2014, the Sponsor and the investigator shall archive the content of the clinical trial master file for at least 25 years after the end of the clinical trial.

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

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

10.5.14. Study and Site Start and Closure

First Act of Recruitment

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

Study/Site Termination

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

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

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

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

10.6.1. Adverse Event Definitions and Classifications

Adverse Event

An AE is any untoward medical occurrence in a clinical study participant administered a pharmaceutical (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. (Definition per 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 AEs starting with the signing of the ICF (refer to All Adverse Events under Section 8.3.1, Time Period and Frequency for Collecting Adverse Events and Serious Adverse Events Information, for time of last AE recording).

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

Serious Adverse Event

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 AE 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).

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

Unlisted (Unexpected) Adverse Event/Reference Safety Information

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

10.6.2. Attribution Definitions

Assessment of Causality

The causal relationship to study intervention is determined by the Investigator. The following selection should be used to assess all AEs.

Related

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

Not Related

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

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

10.6.3. Severity Criteria

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

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

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

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

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

10.6.4. Special Reporting Situations

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

- Overdose of a Sponsor study intervention
- Suspected abuse/misuse of a Sponsor study intervention
- Accidental or occupational exposure to a Sponsor study intervention
- Any failure of expected pharmacologic action (ie, lack of effect if used according to the local label) of a Sponsor study intervention (to be reported as a PQC for marketed products)
- Unexpected therapeutic or clinical benefit from use of a Sponsor study intervention
- Medication error, intercepted medication error, or potential medication error involving a Johnson & Johnson medicinal product (with or without patient exposure to the Johnson & Johnson medicinal product, eg, product name confusion, product label confusion, intercepted prescribing or dispensing errors)
- Exposure to a Sponsor study intervention from breastfeeding
- Participant pregnancy or participant partner(s) pregnancy

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

10.6.5. Procedures

All Adverse Events

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

For all studies with an outpatient phase, including open-label studies, the participant must be provided with a "wallet (study) card" and instructed to carry this card with them for the duration of the study 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 personnel only)
- Site number
- Participant number
- Any other information that is required to do an emergency breaking of the blind

Serious Adverse Events

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

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

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

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

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

Information regarding SAEs will be transmitted to the sponsor using an SAE reporting form, which must be completed and signed by a physician from the study site, and transmitted in a secure manner to the sponsor within 24 hours. The initial and follow-up reports of an SAE should be made by facsimile (fax). Telephone reporting should be the exception and the reporter should be asked to complete the appropriate form(s) first.

10.6.6. Product Quality Complaint Handling

Definition

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

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

Procedures

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

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

10.6.7. Contacting Sponsor Regarding Safety, Including Product Quality

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

10.7. Appendix 7: Contraceptive and Barrier Guidance

Participants must follow contraceptive measures as outlined in Section 5.1, Inclusion Criteria. Pregnancy information will be collected and reported as noted in Section 8.3.5, Pregnancy and Appendix 6 Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

Definitions

Woman of Childbearing Potential (WOCBP)

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

Woman Not of Childbearing Potential

- **premenarchal**
  A premenarchal state is one in which menarche has not yet occurred.
- **postmenopausal**
  A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high 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 (HRT), however in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient. If there is a question about menopausal status in women on HRT, the woman will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if she wishes to continue HRT during the study.
- **permanently sterile (for the purpose of this study)**
  Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. Has congenital abnormality resulting in sterility.

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.

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

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

Examples of Contraceptives for Female Participants

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

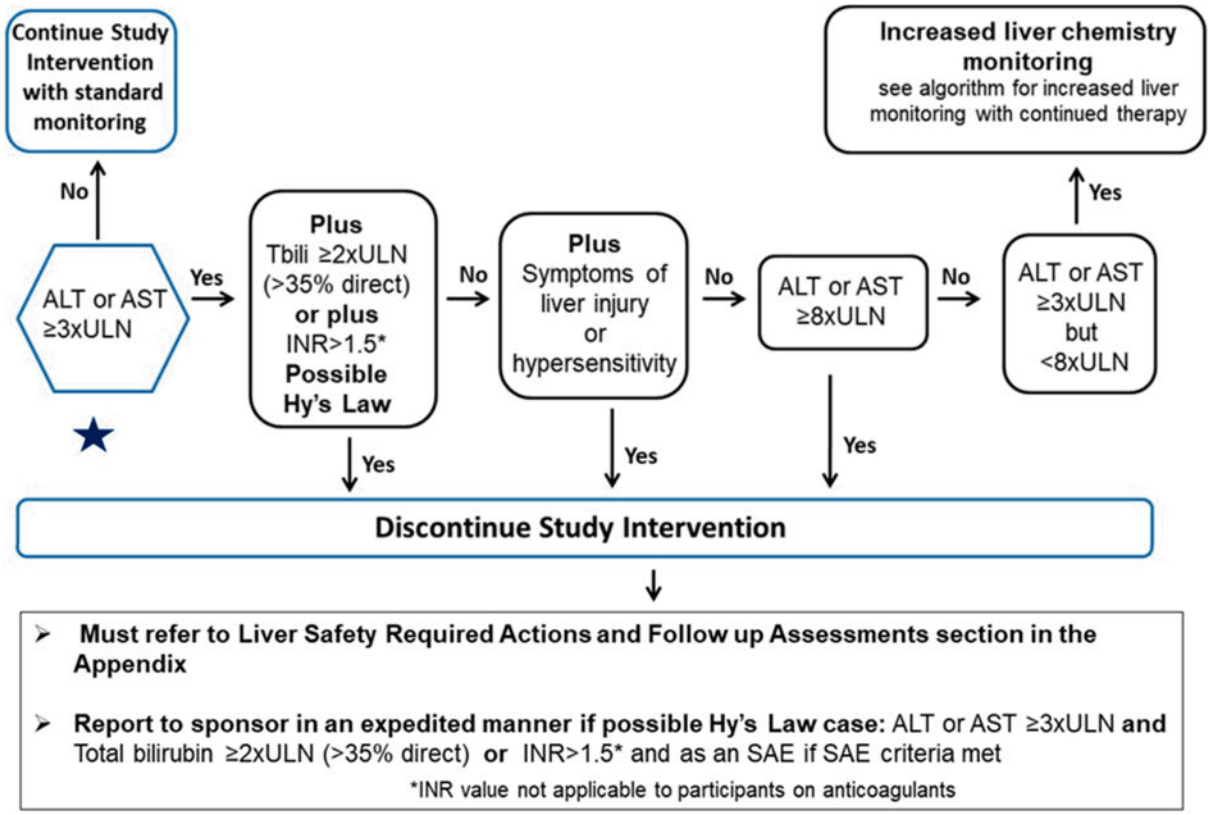
a) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.
b) Hormonal contraception may be susceptible to interaction with the study intervention,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

10.8. Appendix 8: Liver Safety: Suggested Actions and Follow-up Assessments

10.8A. STOPPING ALGORITHM

Liver Chemistry Stopping Criteria and Increased Monitoring Algorithm

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

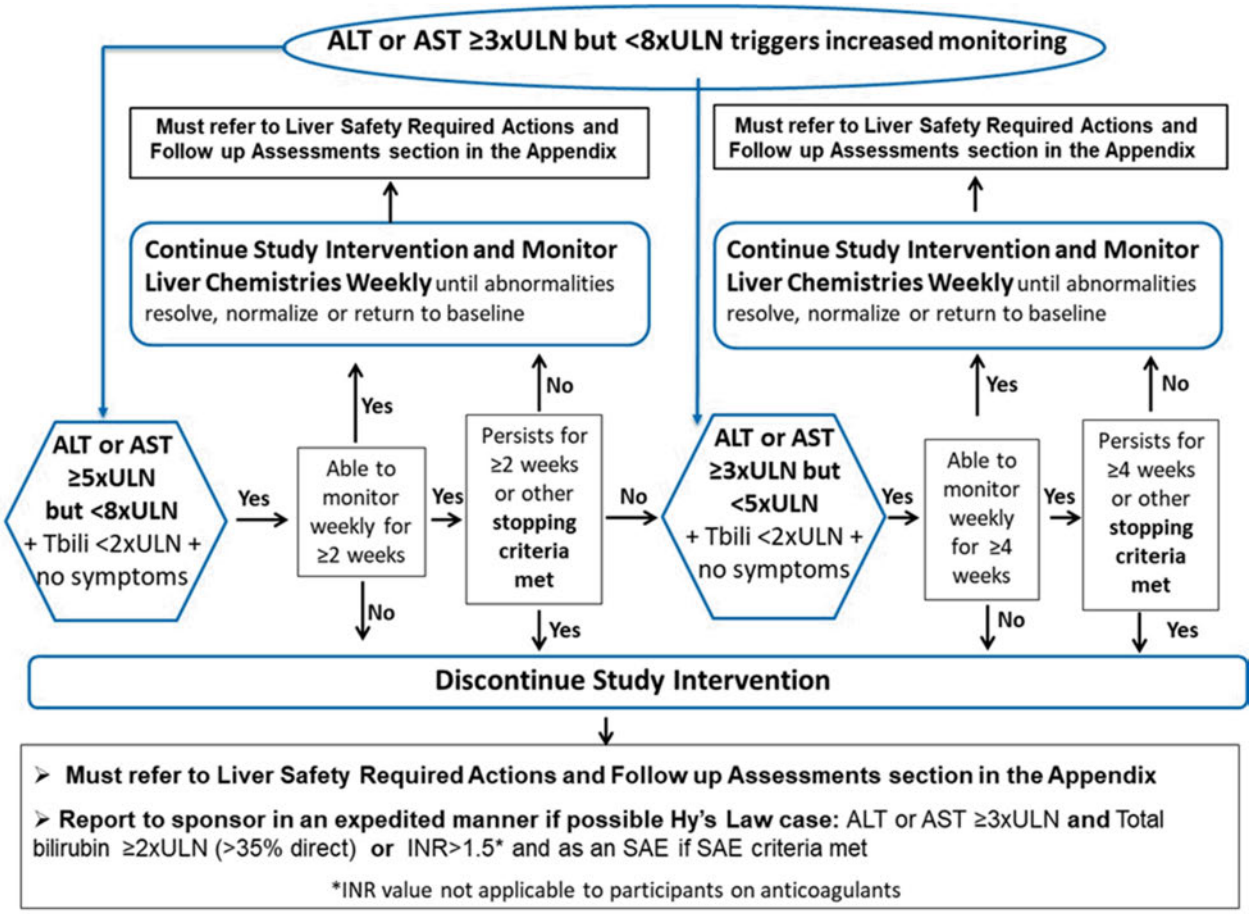


Abbreviations: ALT = alanine transaminase; AST = aspartate transaminase, INR = international normalized ratio; SAE = serious adverse event; ULN = upper limit of normal, Tbili = Total bilirubin.

Refer to Appendix [8B]: Follow-up Assessments.

Liver Chemistry Increased Monitoring Algorithm with Continued Study Intervention for Participants with ALT or AST ≥3xULN but <8xULN

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



Abbreviations: ALT = alanine transaminase; AST = aspartate transaminase, INR = international normalized ratio; SAE = serious adverse event; ULN = upper limit of normal, Tbili = Total bilirubin.

Refer to Appendix [8B]: Follow-up Assessments.

B. FOLLOW-UP ASSESSMENTS

Liver Safety: Follow-up assessments

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

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

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

Suggested Actions, Monitoring, and Follow up Assessments	
Actions	**Follow Up Assessments**
• **Immediately** discontinue study intervention • Report the event to the Sponsor within **24 hours** • Complete the hepatic event form and complete an SAE eCRF if the event also met the criteria for an SAE[2] • Perform follow-up assessments as described in the Follow up Assessment column • Monitor the participant until liver chemistry test abnormalities resolve, stabilize, or return to baseline **MONITORING:** **If ALT or AST ≥3xULN AND total bilirubin ≥2xULN or INR >1.5:** • Repeat liver chemistry tests (include ALT, aspartate transaminase [AST], alkaline phosphatase, total bilirubin, direct bilirubin, and INR) and perform	• Viral hepatitis serology[4] • Obtain blood sample for pharmacokinetic (PK)[5] analysis within 1 week of the event of ALT or AST ≥3×ULN. • Obtain serum creatine phosphokinase (CPK), lactate dehydrogenase (LDH), gamma-glutamyltransferase [GGT], and glutamate dehydrogenase [GLDH], and serum albumin • Fractionate bilirubin, if total bilirubin ≥2xULN • Obtain complete blood count with differential to assess eosinophilia • Record the appearance or worsening of clinical symptoms of liver injury, or hypersensitivity, on hepatic event form • Record use of concomitant medications (including acetaminophen, herbal remedies, recreational drugs, and other over-the-counter medications) • Record alcohol use on the hepatic event form

liver event follow-up assessments within **24 hours** • Monitor participant twice weekly until liver chemistry test abnormalities resolve, stabilize, or return to baseline • A specialist or hepatology consultation is recommended **If ALT or AST≥3xULN AND total bilirubin <2xULN and INR ≤1.5:** • Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, total bilirubin, direct bilirubin, and INR) and perform liver chemistry follow-up assessments within **24 to 72 hours** • Monitor participants weekly until liver chemistry abnormalities resolve, stabilize, or return to baseline **RESTART** • **Do not restart** participant with study intervention unless allowed per protocol and Sponsor approval **is granted** • If restart is either **not allowed per protocol or not granted**, permanently discontinue study intervention. The participant may continue in the study for any protocol specified follow up assessments	**If ALT or AST ≥3xULN AND total bilirubin ≥2xULN or INR >1.5** obtain the following in addition to the assessments listed above: • Anti-nuclear antibody, anti-smooth muscle antibody, Type 1 anti-liver kidney microsomal antibodies, and quantitative total immunoglobulin G (IgG) or gamma globulins • Serum acetaminophen adduct assay, when available, to assess potential acetaminophen (paracetamol) contribution to liver injury in participants with definite or likely acetaminophen use in the preceding week • Liver imaging (ultrasound, magnetic resonance, or computerized tomography) to evaluate liver disease; complete liver Imaging form • Liver biopsy may be considered and discussed with local specialist if available, for instance: – In patients when serology raises the possibility of autoimmune hepatitis (AIH) – In patients when suspected drug-induced liver injury (DILI) progresses or fails to resolve on withdrawal of study intervention – In patients with acute or chronic atypical presentation • If liver biopsy conducted record in eCRF

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

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

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

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

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

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

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

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

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

10.9. Appendix 9: Study Conduct During a Natural Disaster

GUIDANCE ON STUDY CONDUCT DURING THE COVID-19 PANDEMIC

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

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

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

Every effort should be made to adhere to protocol-specified assessments for participants on study intervention, including follow up. Modifications to protocol-required assessments may be permitted using the examples contained in this appendix, after consultation with the participant, investigator, and the sponsor.

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

ADDITIONAL ELEMENTS, WHERE APPLICABLE:

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

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

- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the eCRF.
  - other relevant study data elements impacted by the pandemic should also be documented as "COVID-19-related" in eCRFs and/or other study systems, as directed by detailed Sponsor guidance. These may include missed/delayed/modified study visits or assessments/dosing, and instances where temporary measures such as those above are implemented.
- The Sponsor will evaluate the totality of impact of COVID-19 on collection of key study data and additional data analyses will be outlined in study SAP(s).
- Precaution: for those who may carry a higher risk for severe COVID-19 illness (eg, those aged over 65 years), follow guidance from local health authorities when weighing the potential benefits and risks of enrolling in the study, and during participation in the study.

10.10. Appendix 10: Protocol Amendment History

The Protocol Amendment Summary of Changes Table for the current amendment is located directly before the Table of Contents.

Amendment 1 (12 May 2022)

Overall Rationale for the Amendment: The overall rationale for the amendment is to add a long-term extension to this study. Additional changes are related to sites impacted by Natural Disaster or Major Disruption, clarifications, and updates to align with current sponsor study conventions.

Section Number and Name	Description of Change
Rationale: A one-year long-term extension is being added for this study to evaluate longer term improvements in signs and symptoms of psoriatic arthritis (PsA).	
Schedule of Activities and anywhere study period is mentioned	The final study visit is now to occur at Week 112, after treatment through Week 100. Study assessments were added through Week 112.
Rationale: Due to major disruptions in some countries where the study is being conducted, replacing participants who are forced to discontinue from the study due to such major disruptions (eg, Natural Disaster or Other Major Disruption) is being allowed.	
4.1 Overall Design 9.2 Sample Size Determination 9.3. Population for Analysis Sets 9.4.2 Primary Endpoint	Participants impacted by major disruptions may be replaced. Modified Full Analysis Set: All participants who were randomized, excluding participants from sites rendered unable to support key study operations due to major disruptions (eg, Natural Disaster or Other Major Disruption). Details will be provided in the SAP. Details for intercurrent events and missing data due to major disruptions (eg, Natural Disaster or Other Major Disruption) are added.
Rationale: Clarifying the inclusion criterion regarding prior treatment failure.	
5.1, Inclusion criteria, #5a	Lack of benefit ….after at least 12 weeks of etanercept, adalimumab, golimumab, or certolizumab pegol therapy (or their biosimilars) ~~**and**~~/or at least a 14-week dosage regimen (ie, at least 4 doses) of infliximab
Rationale: Correcting exclusion criterion that was worded incorrectly; it was only meant to address hypersensitivity (and not intolerance which is covered in the inclusion criteria).	
5.2, Exclusion Criteria, #23	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
Rationale: The exclusion criterion regarding hepatitis C virus screening has been clarified to be consistent with current practice guidelines (bold text added).	
5.2 Exclusion Criteria, #41	Tests positive for hepatitis B virus (HBV) infection (see Appendix 4 in Section 10) **or is seropositive for antibodies to hepatitis C virus (HCV) at screening, unless the participant meets 1 of the following conditions:** **i. Has a history of successful treatment (defined as being negative for HCV RNA at least 12 weeks after completing**

Section Number and Name	Description of Change
	antiviral treatment) and has a negative HCV RNA test result at screening, OR ii. **While seropositive has a negative HCV RNA test result at least 12 weeks prior to screening and a negative HCV RNA test result at screening.**
Rationale: The emergency use of treatment for COVID-19 is now allowed.	
6.8.4 Biologic Agents, Cytotoxic Drugs, JAK Inhibitors, or Investigational Agents	The concomitant use of …is not allowed, **with the exception of limited emergency use for treatment of COVID-19 infection. Continuation of study intervention in such cases should be discussed with the Sponsor's medical monitor**.
Rationale: Clarification for when the eC-SSRS assessment should be performed is being added as the timing was not described consistently in the original protocol.	
8.2.7, Suicidal Ideation and Behavior Risk Monitoring	At the screening visit, the eC-SSRS should be completed as the first assessment after signing informed consent **and joint assessment**, but before any other tests, procedures, or other consultations. For subsequent visits, the eC-SSRS should be completed after all PROs and before any other tests, procedures, or other consultations.
Schedule of Activities, footnote h	At the screening visit (after signing informed consent), the eC-SSRS should be performed after the joint assessment. At Week 0/baseline and at all post-screening baseline visits, the **eC-SSRS should be** ~~the first assessment/questionnaire the patient completes~~ **completed after all PRO, but before other tests**, procedures or other consultations.
Rationale: Correction that measuring C-reactive Protein (CRP) is not optional.	
Schedule of Assessments, footnote t	Removing footnote t for CRP assessment.
Rationale: Adding a physical examination at Week 52, which was accidentally omitted.	
Schedule of Assessments	Adding physical examination at Week 52
Rationale: For the primary endpoint, language referring to "treatment failure" has been updated.	
1.1 Synopsis, Statistical Methods 9.4.2 Primary Endpoint	….This endpoint will be analyzed based on the estimand**s defined in Section 9** ~~under which the intercurrent event of treatment failure prior to Week 24 will be treated as non-response for the primary analysis, regardless of the observed ACR 20 response status~~. Participants with an ICE in categories 1-3 will follow the composite strategy, where participants who experience them prior to Week 24 will be considered ~~treatment failures and will be treated~~ as non-responders
Rationale: The timepoint for recommended changes for certain concomitant medications was revised from Week 60 to Week 52, since Week 52 is the final efficacy visit for Year 1 of this 2-year study.	
Inclusion Criteria, #11	Use of complementary therapies
Rationale: Correcting administrative information.	
Cover page	Correcting the IND # on cover page from 105044 to 124177; also adding a version number to the document identifier on the cover page which was accidentally omitted in the prior version.
Rationale: Several updates were made to align with Janssen's current protocol language, including clarifications in the instructions for tuberculosis (TB) testing and guidance for enrollment of participants with prior TB infection, and expedited reporting of a participant pregnancy or participant partner(s) pregnancy. These updates are necessary to gain alignment with updated CDC guidelines and continue to ensure optimal participant safety is maintained.	

Section Number and Name	Description of Change
5.4 Screen Failures	A participant **who might be** ~~is~~ considered a screen failure due to circumstances unrelated to the protocol (eg, site closure due to COVID-19, **other unforeseen circumstances resulting in site closure, etc**) could be eligible ~~to be~~ **for screening and** rescreen**inged** ~~**if applicable**~~.
7.2 Participant Discontinuation/Withdrawal From the Study	(added as reason for withdrawal) Sponsor decision
10.6.4 Special Reporting Situations	(added) • Participant pregnancy or participant partner(s) pregnancy
Appendix 7: Contraceptive and Barrier Guidance	(added, under definition of permanently sterile)Has congenital abnormality resulting in sterility.
Appendix 8: Liver Safety: Suggested actions and Follow-up Assessments	Updates made to clarify steps for restarting of study intervention.
Appendix 9: Study Conduct During a Natural Disaster	Updates made to align with current COVID-19-related recommendations.

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INVESTIGATOR AGREEMENT

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

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

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Signature: _____ Date: _____

(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____

(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): PPD

Institution: Janssen Research & Development

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

(Day Month Year)

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

Signature

User	Date	Reason
PPD	09-Sep-2024 14:13:35 (GMT)	Document Approval