

Janssen Research & Development ***Clinical Protocol****Protocol Title**

A Phase 3b, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Safety and Efficacy of Guselkumab for the Treatment of Participants with Skin of Color who have Moderate-to-Severe Plaque Psoriasis and/or Moderate-to-Severe Scalp Psoriasis

VISIBLE [Varying Skin Tones in Body and Scalp Psoriasis: Guselkumab Efficacy and Safety]

Protocol CNTO1959PSO3018; Phase 3b**Version: Amendment 1****CNTO1959 (guselkumab)**

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

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

IND: 105004

Status: Approved

Date: 02 November 2022

Prepared by: Janssen Research & Development, LLC

EDMS number: EDMS-RIM-679103, 2.0

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

Confidentiality Statement

The information provided herein contains Company trade secrets, commercial or financial information that the Company customarily holds close and treats as confidential. The information is being provided under the assurance that the recipient will maintain the confidentiality of the information under applicable statutes, regulations, rules, protective orders or otherwise.

PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

Document	Date
Amendment 1	02 November 2022
Original Protocol	04 March 2022

Amendment 1 (02 November 2022)

Overall Rationale for the Amendment: The overall rationale for the changes in Amendment 1 is to correct or clarify errors in the Schedule of Events and clarify some descriptions and update statistics section to match current standards for protocols.

The changes made to the clinical protocol CNT01959PSO3018 as part of Protocol Amendment 1 are listed below, including the rationale of each change and a list of all applicable sections.

Section Number and Name	Description of Change	Brief Rationale
1.3 Schedule of Activities	A footnote was added to note those assessments not required for participants without psoriasis scalp involvement.	Clarification that participants without scalp psoriasis do not need to complete scalp-specific assessments.
	CCI	CCI
	Removed assessment of Skin Discoloration Impact Evaluation Questionnaire (SDIEQ) at Week 44.	The assessment at Week 44 was included erroneously.
	Clarified that a urine pregnancy test is not required for home administration visits.	Clarification.
	A footnote was added to note that screening photos can be used to confirm diagnosis of psoriasis and eligibility for study if needed.	Clarification.
1.3 Schedule of Activities; 8.1.9.5, PSSD; Appendix 18	Removed all references to 24-hour recall version of the Psoriasis Symptom and Sign Diary (PSSD).	The 24-hour version is not needed and has been removed.
1.3 Schedule of Activities; 8.2.11 Tuberculosis Evaluations; Appendix 2 Clinical Laboratory Tests, Other	Edited all QuantiFERON-Gold testing for tuberculosis (TB) to interferon gamma release assay (IGRA) that can also include T-SPOT.TB testing.	Per current Sponsor's TB testing instructions.
1.1 Synopsis	Removed all of the other prespecified endpoints	Updated per most recent Sponsor protocol template that lists other prespecified endpoints only in Section 3 Objectives and Endpoints

CCI

Section Number and Name	Description of Change	Brief Rationale
	CCI	

CCI

Section Number and Name	Description of Change	Brief Rationale
10.2 Appendix 2 Clinical Laboratory Tests, Other	Clarified that pregnancy testing can be done via serum and urine. Added human immunodeficiency virus RNA test (if screening HIV test is positive).	Clarification. Inadvertently omitted from original list.
10.6 Appendix 6 Contraceptive Guidance	Table of contraceptives, title edited to be clear is applicable for participants of childbearing potential.	Clarification.
10.7 Appendix 7 Liver Safety: Suggested Actions and Follow-up Assessments	Minor clarifications.	Updated to align with Sponsor's current protocol instructions.
10.12 Appendix 12: Scalp Specific Investigator Global Assessment (ss-IGA)	Corrected the title for the ss-IGA scale and replaced details with correct version.	An incorrect screenshot was erroneously included.

TABLE OF CONTENTS

PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE	2
TABLE OF CONTENTS	6
LIST OF IN-TEXT TABLES AND FIGURES	9
1. PROTOCOL SUMMARY	10
1.1. Synopsis	10
1.2. Schema	14
1.3. Schedule of Activities (SoA).....	15
2. INTRODUCTION.....	19
2.1. Study Rationale	19
2.2. Background	24
2.3. Benefit-Risk Assessment	25
2.3.1. Risks for Study Participation.....	25
2.3.2. Benefits for Study Participation	28
2.3.3. Benefit-Risk Assessment for Study Participation	28
3. OBJECTIVES AND ENDPOINTS	29
4. STUDY DESIGN	33
4.1. Overall Design.....	33
4.2. Scientific Rationale for Study Design	34
4.2.1. Study-Specific Ethical Design Considerations	35
4.3. Justification for Dose.....	35
4.4. End of Study Definition.....	36
5. STUDY POPULATION	36
5.1. Inclusion Criteria	36
5.2. Exclusion Criteria	39
5.3. Lifestyle Considerations	45
5.4. Screen Failures	46
6. STUDY INTERVENTION AND CONCOMITANT THERAPY.....	47
6.1. Study Intervention(s) Administered.....	47
6.2. Preparation/Handling/Storage/Accountability	48
6.3. Measures to Minimize Bias: Randomization and Blinding	50
6.4. Study Intervention Compliance	51
6.5. Dose Modification.....	52
6.6. Continued Access to Study Intervention After the End of the Study	52
6.7. Treatment of Overdose	53
6.8. Concomitant Therapy.....	53
6.8.1. Permitted Concomitant Medications	54
6.8.1.1. Topical treatments	54
6.8.2. Prohibited Concomitant Medications	54
6.8.2.1. Topical Treatments.....	54
6.8.2.2. Phototherapy or Systemic Therapy for Psoriasis	55
6.8.3. Concomitant Medications for Conditions Other than Psoriasis	55
7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL	56
7.1. Discontinuation of Study Intervention	56
7.1.1. Liver Chemistry Stopping Criteria	57
7.1.2. Liver Chemistry Restart Criteria	57
7.2. Participant Study Drug Discontinuation/Withdrawal From the Study.....	57
7.2.1. Withdrawal From the Use of Research Samples	59

7.3.	Lost to Follow-up	60
8.	STUDY ASSESSMENTS AND PROCEDURES	60
8.1.	Efficacy Assessments	62
8.1.1.	Psoriasis Area and Severity Index (PASI)	62
8.1.2.	Investigator's Global Assessment (IGA) of Psoriasis	62
8.1.3.	Scalp Specific Investigator Global Assessment (ss-IGA)	62
8.1.4.	Body or Scalp Surface Area Affected by Psoriasis	62
8.1.5.	Psoriasis Scalp Severity Index (PSSI)	63
8.1.6.	Clinical Photographs	63
8.1.7.	Post Inflammatory Dyspigmentation Area and Severity Index (PIDASI)	64
8.1.8.	Colorimeter or Mexameter Device	64
8.1.9.	Patient-reported Outcomes	64
8.1.9.1.	Skin Discoloration Impact Evaluation Questionnaire	64
8.1.9.2.	Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29)	64
8.1.9.3.	Scalp Itch Numeric Rating Scale (NRS)	65
8.1.9.4.	DLQI	65
8.1.9.5.	Psoriasis Symptom and Sign Diary (PSSD)	65
8.1.9.6.	Psoriasis Epidemiology Screening Tool (PEST)	65
8.1.9.7.	PsAID-12	66
8.2.	Safety Assessments	66
8.2.1.	Physical Examinations	66
8.2.2.	Vital Signs	66
8.2.3.	Electrocardiograms	67
8.2.4.	Clinical Safety Laboratory Assessments	67
8.2.5.	Pregnancy Testing	67
8.2.6.	Suicidal Ideation and Behavior Risk Monitoring	68
8.2.7.	Concomitant Medication Review	69
8.2.8.	Injection-Site Reactions	69
8.2.9.	Hypersensitivity Reactions	69
8.2.10.	Infections	69
8.2.11.	Tuberculosis Evaluations	69
8.3.	Adverse Events, Serious Adverse Events, and Other Safety Reporting	70
8.3.1.	Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information	71
8.3.2.	Method of Detecting Adverse Events and Serious Adverse Events	72
8.3.3.	Follow-up of Adverse Event and Serious Adverse Events	72
8.3.4.	Regulatory Reporting Requirements for Serious Adverse Events and Anticipated Events	72
8.3.5.	Pregnancy	73
8.3.6.	Adverse Events of Special Interest	73
8.4.	Pharmacokinetics	73
8.4.1.	Evaluations	74
8.4.2.	Analytical Procedures	74
8.5.	Pharmacogenomics	74
8.6.	Biomarkers	74
8.6.1.	Skin Biomarkers	75
8.6.2.	Serum Biomarkers	75
8.7.	Immunogenicity Assessments	76
9.	STATISTICAL CONSIDERATIONS	76
9.1.	Statistical Hypotheses	76
CCI		
9.3.	Populations for Analysis Sets	77
9.4.	Statistical Analyses	77
9.4.1.	General Considerations	78
9.4.2.	Primary Endpoint	78
9.4.3.	Secondary Endpoint(s)	79

9.4.4.	Safety Analyses	79
9.4.5.	Other Analyses	81
9.4.5.1.	Pharmacokinetic and Immunogenicity Analyses	81
9.4.5.2.	Biomarkers Analyses	81
9.4.5.3.	Pharmacogenomic Analyses	81
9.5.	Interim Analysis	82
10.	SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS	83
10.1.	Appendix 1: Abbreviations	83
10.2.	Appendix 2: Clinical Laboratory Tests	85
10.3.	Appendix 3: Hepatitis B Virus (HBV) Screening with HBV DNA Testing	87
10.4.	Appendix 4: Regulatory, Ethical, and Study Oversight Considerations	88
10.4.1.	Regulatory and Ethical Considerations	88
10.4.2.	Financial Disclosure.....	91
10.4.3.	Informed Consent Process	91
10.4.4.	Data Protection	92
10.4.5.	Long-Term Retention of Samples for Additional Future Research	93
10.4.6.	Publication Policy/Dissemination of Clinical Study Data	93
10.4.7.	Data Quality Assurance	95
10.4.8.	Case Report Form Completion	95
10.4.9.	Source Documents	96
10.4.10.	Monitoring	97
10.4.11.	On-Site Audits.....	98
10.4.12.	Record Retention.....	98
10.4.13.	Study and Site Start and Closure	98
10.5.	Appendix 5: Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.....	100
10.5.1.	Adverse Event Definitions and Classifications	100
10.5.2.	Attribution Definitions.....	101
10.5.3.	Severity Criteria	102
10.5.4.	Special Reporting Situations	102
10.5.5.	Procedures	102
10.5.6.	Product Quality Complaint Handling.....	104
10.5.7.	Contacting Sponsor Regarding Safety, Including Product Quality.....	104
10.6.	Appendix 6: Contraceptive Guidance	105
10.7.	Appendix 7: Liver Safety: Suggested Actions and Follow-up Assessments.....	108
10.8.	Appendix 8: Study Conduct During a Natural Disaster.....	114
10.9.	Appendix 9: Investigator Global Assessment (IGA).....	116
10.10.	Appendix 10: Psoriasis Area and Severity Index (PASI)	117
10.11.	Appendix 11: PSSI	118
10.12.	Appendix 12: Scalp Specific Investigator Global Assessment (ssIGA)	119
10.13.	Appendix 13: Post-inflammatory Dyspigmentation Area and Severity Score (PIDASI)	120
10.14.	Appendix 14: Skin Discoloration Impact Evaluation Questionnaire	121
10.15.	Appendix 15: PROMIS-29 Questionnaire (version 2.0)	122
10.16.	Appendix 16: Scalp Itch Numeric Rating Scale (NRS)	125
10.17.	Appendix 17: DLQI.....	126
10.18.	Appendix 18: Psoriasis Symptom and Sign Diary (PSSD) Based on 7-day Recall.....	128
10.19.	Appendix 19: PEST.....	129
10.20.	Appendix 20: PsAID-12.....	130
10.21.	Appendix 21: Protocol Amendment History	133
	REFERENCES.....	134
	INVESTIGATOR AGREEMENT	136

LIST OF IN-TEXT TABLES AND FIGURES

FIGURES

Figure 1: Schematic Overview of the Study	14
---	----

1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 3b, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Safety and Efficacy of Guselkumab for the Treatment of Participants with Skin of Color who have Moderate-to-Severe Plaque Psoriasis and/or Moderate-to-Severe Scalp Psoriasis

VISIBLE [Varying Skin Tones in Body and Scalp Psoriasis: Guselkumab Efficacy and Safety]

Guselkumab is a fully human immunoglobulin G1 lambda (IgG1lambda) monoclonal antibody (mAb) that binds to the p19 subunit of human interleukin (IL)-23 with high specificity and affinity. The binding of guselkumab to the IL-23p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, thus inhibiting IL-23 specific intracellular signaling and downstream activation and cytokine production. Guselkumab is approved in the United States (US) for moderate-to-severe plaque psoriasis (in patients who are candidates for systemic therapy or phototherapy), and for active psoriatic arthritis.

OBJECTIVES AND ENDPOINTS

Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
Primary		
To evaluate the efficacy of guselkumab treatment vs placebo in skin of color participants with predominant moderate-to-severe body psoriasis or predominant moderate-to-severe scalp psoriasis by assessing improvements in the signs and symptoms of psoriasis	The co-primary endpoints are proportions of participants who achieve an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) and the proportion of participants who achieve a Psoriasis Area and Severity Index (PASI) 90 response at Week 16, comparing the guselkumab group and the placebo group	The co-primary endpoints are proportions of participants who achieve a scalp specific (ss)-IGA score of absence of disease (0) or very mild disease (1) and the proportion of participants who achieve a Psoriasis Scalp Severity Index (PSSI) 90 response at Week 16, comparing the guselkumab group and the placebo group
Major Secondary (The final ordering of endpoints will be specified in the Statistical Analysis Plan [SAP])		
To evaluate the efficacy of guselkumab on additional measures of body and scalp psoriasis	- The proportion of participants who achieve an IGA score of cleared (0) at Week 16 - The proportion of participants who achieve a PASI 100 response at Week 16 - The change from baseline in PASI score at Week 16 - The change from baseline in body surface area (BSA) at Week 16 - The time to $\geq 90\%$ reduction in PASI through Week 16 - The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16 - The proportion of participants who achieve ≥ 4-point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants	- The change from baseline in PSSI score at Week 16 - The change from baseline in scalp surface area (SSA) at Week 16 - The proportion of participants who achieve a ss-IGA score of absence of disease (0) at Week 16 - The proportion of participants who achieve a PSSI 100 response at Week 16 - The time to $\geq 90\%$ reduction in PSSI through Week 16 - The change from baseline in DLQI score at Week 16 - The proportion of participants who achieve ≥ 4-point reduction (improvement) from baseline in the scalp itch numeric rating scale (NRS) score at Week 16, among participants with

Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
	with baseline PSSD itch ≥ 4 at baseline - The change from baseline in PSSD symptom score at Week 16 - The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score ≥ 1	baseline scalp itch ≥ 4 at baseline - The change from baseline in PSSD symptom score at Week 16 - The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score ≥ 1
Other Secondary Endpoint		
To evaluate the safety of guselkumab in participants with moderate to severe psoriasis	Frequency and type of adverse events (AEs) and serious adverse events (SAEs)	Frequency and type of AEs and SAEs

Hypothesis

Cohort A: It is hypothesized that guselkumab is superior to placebo in the treatment of skin of color participants with moderate-to-severe plaque psoriasis. This study is designed to show a difference between guselkumab and placebo in the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) and a PASI 90 response at Week 16.

Cohort B: It is hypothesized that guselkumab is superior to placebo in the treatment of skin of color participants with moderate-to-severe scalp psoriasis. This study is designed to show a difference between guselkumab and placebo in the proportion of participants who achieve a ss-IGA score of absence of disease (0) or very mild disease (1) and a PSSI 90 response at Week 16.

OVERALL DESIGN

This is a Phase 3b, multicenter, randomized, placebo-controlled, double-blind study designed to evaluate the efficacy and safety of guselkumab in participants of skin of color with predominant body moderate-to-severe plaque psoriasis (Cohort A) or predominant moderate-to-severe scalp psoriasis (Cohort B). Cohort A and B are independent and will have separate database locks (DBL) and analyses. There will be 3 DBLs in this study, at Week 16, Week 48, and Week 112 for each cohort. After all participants in the cohort have completed the Week 16 Visit (or discontinued from the study), a Week 16 DBL will be performed. The primary data analyses for each cohort will be conducted at Week 16.

NUMBER OF PARTICIPANTS

Approximately 200 participants (100 per cohort).

INTERVENTION GROUPS AND DURATION

Both Cohort A and Cohort B have guselkumab and placebo arms.

Intervention Name	Guselkumab	Placebo
Dose Formulation	Liquid provided in a single-use prefilled syringe (PFS) assembled with the UltraSafe PLUS™ Passive Needle Guard (PFS-U)	Placebo
Unit Dose Strength(s)	100 mg	N/A
Dosage Level(s) and Frequency	Guselkumab 100 mg will be administered at Week 0, 4 and then every 8 weeks (q8w) through Week 100 for those randomized to guselkumab. For those randomized to placebo and crossover to guselkumab at Week 16: Guselkumab 100 mg will be administered at Weeks 16 and 20 then q8w through Week 100	Placebo will be administered at Week 16 for those randomized to guselkumab to maintain the blind. Placebo will be administered at Week 0, 4 and 12 for those randomized to placebo.
Route of Administration	☐ Oral ☐ IV infusion ☐ IV injection ☐ Intramuscular ☒ Other [subcutaneous]	☐ Oral ☐ IV infusion ☐ IV injection ☐ Intramuscular ☒ Other [subcutaneous]

EFFICACY EVALUATIONS

There are a total of 8 efficacy evaluation measures to be completed by investigators: PASI, PSSI, IGA, ss-IGA, BSA, SSA, PIDASI, and skin pigmentation (by colorimeter or mexameter). Clinical photos will be taken to support efficacy evaluations.

There are a total of 6 patient-reported outcome (PRO) measures to be completed by participants: PROMIS-29, scalp itch NRS, DLQI, PSSD, SDIEQ, and PEST CCI or PsAID-12 CCI

PHARMACOKINETIC AND 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 samples will be collected to evaluate the mechanism of action of guselkumab and help to explain interindividual variability in clinical outcomes or may help to identify population subgroups that may respond differently to an intervention. Markers of metabolic syndrome (e.g., lipid panel and A1c), cardiovascular risk (e.g., high sensitivity C-reactive protein) and psoriasis will be analyzed in the study, along with the effect of guselkumab treatment on these markers over the treatment period.

PHARMACOGENOMIC (DNA) EVALUATIONS

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

SAFETY EVALUATIONS

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

STATISTICAL METHODS

A sample size of 100 participants for each cohort (75 to receive guselkumab and 25 to receive placebo) will have >90% power to detect differences between the guselkumab treatment group and placebo group in each cohort for the co-primary endpoints, assuming a 2-sided alpha level of 0.05.

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

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

The co-primary endpoints for the primary analyses are: **For Cohort A**, the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) and a PASI 90 response at Week 16; **For Cohort B**, the proportion of participants who achieve a ss-IGA score of absence of disease (0) or very mild disease (1) and a PSSI 90 response at Week 16.

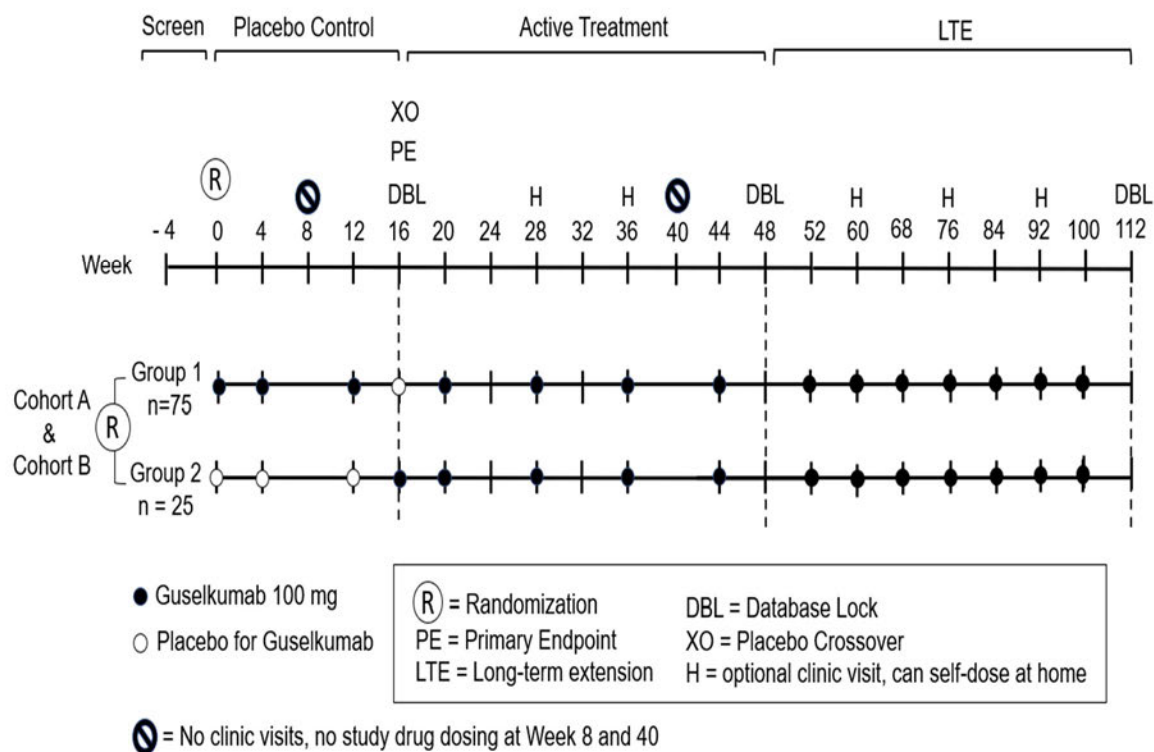
The co-primary endpoints will be analyzed based on the estimands defined in Section 9. The overall Type I error rate will be controlled at the significance level of 0.05 (2-sided) for the co-primary and major secondary endpoints within each cohort. No multiplicity control will be made for other endpoints and nominal p-values will be reported.

The study will be considered positive if the guselkumab group is significantly different from the placebo group for both co-primary endpoints within each cohort. Both co-primary endpoints will be tested at a 2-sided α -level of 0.05. If one of the comparisons is not significant at the 2-sided α -level of 0.05, the co-primary endpoints will be considered not significant.

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

Figure 1: Schematic Overview of the Study



Study drug for Weeks 28, 36, 60, 76, 92 (those denoted with H) will be dispensed at visits Weeks 24, 32, 52, 68, and 84 (all non-dosing visits) respectively for those who wish to home administer.

1.3. Schedule of Activities (SoA)

Phase	Screening ^a	Active Treatment ^{b,c}												Long-term follow-up ^{b,c}								
Week		0	4	12	16	20	24	28	32	36	44	48	52	60	68	76	84	92	100	112 - Final Safety/ Early Termination		
Screening/Administrative																						
Informed Consent	X																					
Medical & Psoriasis History	X																					
Demographics & Fitzpatrick skin type	X																					
Inclusion/exclusion criteria	X	X																				
Study Intervention Administration																						
Randomization		X																				
Study Drug Administration ^d		X	X	X	X	X		X		X	X		X	X	X	X	X	X	X			
Efficacy Assessments																						
BSA	X	X		X	X		X		X		X	X	X				X		X	X		
IGA	X	X	X	X	X	X	X		X		X	X	X				X		X	X		
PASI	X	X	X	X	X	X	X		X		X	X	X				X		X	X		
Scalp surface area ^e	X	X		X	X		X		X		X	X	X				X		X	X		
ss-IGA ^e	X	X	X	X	X	X	X		X		X	X	X				X		X	X		
PSSI ^e	X	X	X	X	X	X	X		X		X	X	X				X		X	X		
CCI																						
Patient reported outcomes																						
PROMIS-29 ^h		X			X		X		X			X					X		X	X		
Scalp itch NRS ^e		X			X		X		X			X					X		X	X		
DLQI ^h		X			X		X		X			X					X		X	X		
PSSD ⁱ		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
CCI																						

Phase	Screening ^a	Active Treatment ^{b,c}												Long-term follow-up ^{b,c}							
Week		0	4	12	16	20	24	28	32	36	44	48	52	60	68	76	84	92	100	112 - Final Safety/ Early Termination	
PEST CCI	X	X			X		X					X			X		X		X	X	
PsAID12 CCI		X			X		X					X			X		X		X	X	
Safety Assessments																					
Full Physical Exam (including skin)	X											X								X	
Vital signs	X	X	X	X	X	X	X		X		X	X	X		X		X		X	X	
12-lead ECG	X																				
Tuberculosis eval questions	X	X	X	X	X	X	X		X		X		X		X		X		X	X	
Chest X-ray	X																				
C-SSRS ^h	X	X	X	X	X	X	X		X		X	X	X		X		X		X	X	
Urine pregnancy test ^j		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Height		X					X					X					X			X	
Weight		X					X					X					X			X	
Clinical Laboratory Tests																					
Serum pregnancy test	X																				
FSH ^k	X																				
TB IGRA ^l	X																				
Hepatitis B & C serology	X																				
HIV Ab test	X																				
Hematology ^m	X	X	X	X	X		X		X			X			X		X		X	X	
Chemistry ^m	X	X	X	X	X		X		X			X			X		X		X	X	
Lipid panel ⁿ		X					X					X					X		X		
CCI																					

Phase	Screening ^a	Active Treatment ^{b,c}												Long-term follow-up ^{b,c}							
Week		0	4	12	16	20	24	28	32	36	44	48	52	60	68	76	84	92	100	112 - Final Safety/ Early Termination	
Clinical Pharmacology Assessments																					
Serum guselkumab concentration ^o		X	X	X		X			X			X			X		X		X	X	
Anti-guselkumab antibodies ^o		X	X	X		X			X			X			X		X		X	X	
Biomarkers																					
Serum biomarkers		X	X		X				X			X							X	X	
Optional																					
Skin biopsy ^p		X			X							X									
Tape stripping ^p		X			X							X									
Whole blood (Pharmacogenomics) ^q		X																			
Ongoing Participant Review																					
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

a: The screening visit should occur within approximately 4 weeks before the Week 0 visit.

b: Study visits will have a window of ± 7 days for visits during Weeks 0 through 48; study visits will have window of ± 14 days for visits during Weeks 52 through 112.

c: Participants who prematurely discontinue study intervention or terminate study participation for any reason prior to the Week 48 visit (if not participating in LTE) or the Week 100 visit (if participating in LTE) should complete the specified study visits and the Final Safety / Early Termination visit as outlined in Section 7.2.

d: All study procedures and evaluations should be completed before administration of study drug. Study drug may be administered at the study site or by the participant or their caregiver (without a study visit) at Weeks 28, 36, 60, 76 and 92.

e: Participants in Cohort A with no scalp involvement will not need to complete the following assessments/questionnaires: Scalp Surface Area, ss-IGA, PSSI, or Scalp Itch NRS.

f: Screening photos can be used to confirm diagnosis of psoriasis and eligibility for study if needed.

g: **CCI**

h: All participant questionnaires should be completed before any other tests, procedures, or evaluations on the day of the visit for baseline and post-baseline visits. The 'Baseline/Screening' version of the C-SSRS will be performed at the screening visit prior to all questionnaires. At Week 0 and all subsequent visits, the 'Since Last Visit' version of the C-SSRS will be performed after all other questionnaires. At visits with optional home administration C-SSRS will only be completed by participants who have study intervention administration at the investigative site.

- i: PSSD data will be collected at all site visits using a 7-day recall version; at visits with optional home administration, it will only be completed by participants who have study intervention administration at the investigative site.
- j: Women of childbearing potential must have a negative urine pregnancy test before randomization, and before study drug administration at all in-office visits. A urine pregnancy test is not required for participants who opt for at home administration visits occurring at Weeks 28, 36, 60, 76, and 92.
- k: Prior to randomization, FSH is required to confirm post-menopausal status for female participants of any age with amenorrhea present for at least 6 months. This test should not be done for any female participant of childbearing potential or female participants > 45 years of age with amenorrhea $\geq$ 12 months.
- l: Interferon gamma release assay (IGRA) testing includes either QuantiFERON-TB® or T-SPOT.TB®. IGRA testing is not required at screening for participants with a history of treated latent tuberculosis (TB) or ongoing treatment for latent TB.
- m: Laboratory tests will be listed in Section 10.2 (Appendix 2) of the protocol.
- n: Participants must fast (i.e., no food or beverages [except water]) for at least 8 hours before blood is drawn for visits that include a lipid panel (Weeks 0, 24, 48, 84, and 100). All other visits can be non-fasting.
- o: All blood samples must be collected before study agent administration at visits when a study agent administration is scheduled. Blood collected from one 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.
- p: The optional skin biopsy and tape stripping sub-studies will use a separate (biomarker) informed consent form (ICF). If participants opt into skin biopsy and/or tape stripping, both lesional and non-lesional skin will be sampled at Week 0 but only lesional skin will be sampled at Weeks 16 and 48.
- q: To participate in the optional pharmacogenomics (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.

Ab = antibodies; BSA = Body Surface Area (affected); C-SSRS = Columbia Suicide Severity Rating Scale; DLQI = Dermatology Life Quality Index; ECG = electrocardiogram; FSH = follicle stimulating hormone; FST = Fitzpatrick Skin Type; HbA1c = hemoglobin a1c; HIV = Human Immunodeficiency Virus; Hs-CRP = high sensitivity- C-Reactive Protein; IGA = Investigator's Global Assessment; IGRA = interferon gamma release assay; CCI [REDACTED]; T-SPOT.TB® = blood test for tuberculosis; IWRS = interactive web response system; LTE = long-term extension (follow-up); NRS = Numeric Rating Scale (itch); PASI = Psoriasis Area and Severity Index; PEST = Psoriasis Epidemiology Screening Tool; PIDASI = Post-Inflammatory Dyspigmentation Area and Severity score; PROMIS-29 = Patient-Reported Outcomes Measurement Information System-29; PsA = psoriatic arthritis; PsAID12 = Psoriatic Arthritis Impact of Disease 12; PSSD = Psoriasis Symptoms and Signs Diary; PSSI = Psoriasis Scalp Severity Index; ss-IGA = scalp specific IGA; term. = termination

2. INTRODUCTION

Guselkumab is a fully human immunoglobulin G1 lambda (IgG1lambda) monoclonal antibody (mAb) that binds to the p19 subunit of human interleukin (IL)-23 with high specificity and affinity. The binding of guselkumab to the IL-23p19 subunit blocks the binding of extracellular IL-23 to the cell surface IL-23 receptor, thus inhibiting IL-23 specific intracellular signaling and downstream activation and cytokine production. Guselkumab is approved in the United States (US) for moderate-to-severe plaque psoriasis (in patients who are candidates for systemic therapy or phototherapy), and for active psoriatic arthritis.

The clinical development program for guselkumab includes completed, ongoing, or planned studies in adult participants with psoriasis, psoriatic arthritis (PsA), 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 and the Prescribing Information.

The term “study intervention” throughout the protocol, refers to guselkumab or placebo administered using an UltraSafe PlusTM 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

Psoriasis is a common skin disease characterized by raised, well demarcated, erythematous scaly plaques that affects approximately 2% of the world population. In the US, the overall prevalence of psoriasis is estimated to be 3.7% based on the data from the National Health and Nutrition Examination Surveys (NHANES) in 2003-6 and 2009-10 with rates highest in white individuals (3.7%) followed by black (2.0%), and Hispanic and other individuals (1.6%) ([Kaufman and Alexis, 2018](#)). It is important to note that potential under-reporting, selection bias, and undiagnosed psoriasis in non-white individuals due to barriers to care and decreased healthcare utilization may result in underestimated prevalence in non-white individuals. There is precedence in other disease states such as hypertension, asthma, and atopic dermatitis where eventual research found differences in disease pathogenesis and treatment response as a result of racial/ethnic background, thus there is an unmet need to examine whether this difference also exists in psoriasis. While available small subgroup analyses suggest comparable efficacy and safety in psoriasis patients with skin of color ([Shah et al, 2011](#); [McMichael et al, 2012](#)), overall, there is limited data.

The term skin of color identifies individuals of particular racial and ethnic groups that share similar cutaneous characteristics and disorders as well as reaction patterns to those disorders ([Kelly et al, 2016](#)). Although the terms race and ethnicity are often used interchangeably, ethnicity refers to a group of people who share a common culture, language, religion, history, and other sources of

group identification without regard to race or ancestry. Because culture is related to behavior which then affects health and disease, it is important to consider ethnicity when studying skin of color (Kelly et al, 2016). In general, skin of color individuals possess darker skin tones than Caucasians and tend to fall into the following racial categories: Africans (e.g., African American, African, African Caribbean), Asians (e.g., Filipino, Thai, Malaysian, Chinese, Japanese, Korean, Vietnamese, Laotian, Hmong, Indian, Pakistani), Native Americans (e.g., Native American, Eskimo, Aleut), and Native Hawaiian or other Pacific Islander as well as those reporting Latino or Hispanic ethnicity. By this definition, people with skin of color are of various racial and ethnic backgrounds. It is important to recognize that race/ethnicity as a surrogate for biological or genetic inheritance is not ideal however there are cutaneous characteristics and disorders that disproportionately affect members of the same racial/ethnic group and to further study these there needs to be an easily understood categorization of these groups. This study will enroll 100% skin of color participants as defined by anyone who self-identifies as non-White.

In the clinical realm, the most widely used classification of skin types is the Fitzpatrick skin phototypes scale developed by Thomas B. Fitzpatrick in 1975. The Fitzpatrick scale is based on both a person's skin color and responses to sun exposure in terms of degree of burning and tanning. While the scale may be subjective, Fitzpatrick skin typing has demonstrated diagnostic and therapeutic value and has been validated in various studies. The current Fitzpatrick skin type classification (Pathak, 2004; Fitzpatrick, 1988) denotes 6 different skin types, skin color, and reaction to sun exposure which ranges from very fair (skin type I) to very dark (skin type VI) depending upon whether the patient burns or tans at the first average sun exposure. The 2 main factors found to influence skin type are genetic disposition and reaction to sun exposure and tanning habits. While Fitzpatrick skin type does not directly correlate with race/ethnicity, often times members of one race/ethnicity have a tendency towards a "most common" skin type because genetic disposition within a racial group is similar just as reaction to sun exposure and tanning habits may be cultural and reflected by one's ethnicity. The Fitzpatrick skin phototypes scale information is being used in this study to help ensure adequate representation across the entire spectrum of skin tones amongst skin of color participants.

Overall Study Rationale and Objectives

The primary objective of this study is to evaluate the efficacy and safety of guselkumab versus placebo in participants of skin of color with moderate-to-severe plaque psoriasis with extensive body involvement, or, predominant moderate-to-severe scalp psoriasis without extensive body involvement. There will be 2 cohorts based on the predominant area of psoriasis: **Cohort A**, with body psoriasis as the predominant form of psoriasis, will enroll participants with involved body surface area (BSA) $\geq 10\%$, Psoriasis Area and Severity Index (PASI) ≥ 12 , and Investigator's Global Assessment (IGA) ≥ 3 at baseline. **Cohort B**, with scalp psoriasis as the predominant form of psoriasis, will enroll participants with scalp specific IGA (ss-IGA) ≥ 3 , Psoriasis Scalp Severity Index (PSSI) ≥ 12 , and scalp surface area $\geq 30\%$, and one plaque outside of the scalp at baseline. The study will enroll a minimum of approximately 50% Fitzpatrick type IV-VI participants.

Secondary objectives of this study are safety, tolerability, pharmacokinetics, pharmacodynamics, and immunogenicity. Exploratory objectives of this study are to assess the impact of guselkumab on select biomarker changes in blood and skin. Pharmacogenomics assessment will explore genetic factors that may influence treatment response.

Psoriasis in Skin of Color

Multiple therapeutic options exist for the treatment of moderate-to-severe psoriasis; however, none of the currently approved agents, including biologic agents, can provide a meaningful response in all patients. Many factors influenced by genetics can impact treatment response. The presence of certain human leukocyte antigen (HLA) polymorphisms has been associated with response to biologic treatment ([Kaufman and Alexis, 2018](#)). Furthermore, presenting disease in Hispanic/Latino and Asian patients has been shown to be more severe than in Caucasian patients which may be partly due to genetic factors ([Abrouk et al, 2017](#); [Ashbaugh et al, 2020](#)). In a survey of US psoriasis experts, 66% of physicians reported clinical differences in psoriasis between black and white patients, with less erythema, increased risk of pigmentation, thicker plaques, more scaling, and greater body surface area involvement in black patients ([McMichael et al, 2012](#)). The majority of biomarker studies and pharmacogenomic studies have been in European American or Chinese populations ([Kaufman and Alexis, 2018](#)). Given that the diverse genetic background of skin of color patients ([Rawlings, 2006](#)) differs from Caucasians, it cannot be assumed that efficacy in this population will be identical.

Potential underlying genetic differences between populations, differences in access to care that impact time to diagnosis, and potential prior treatments tried before advancing to biologics may differ in the skin of color population and are several important factors that could impact response to treatment ([Fischer et al, 2018](#)). There is lower utilization of outpatient dermatology services by Hispanic patients (adjusted odds ratio [aOR]: 0.55) and Black (aOR:0.42) as compared to non-Hispanic white patients ([Tripathi et al, 2018](#)). These patients instead often utilize emergency room services for dermatology care ([Abokwidir et al, 2015](#)). Increased utilization of non-dermatology specialists by skin of color patients may contribute to differences in therapies prescribed. Additionally, even when these patients are able to see dermatologists, there are disparities in treatment. One survey of 29 dermatologists found that African American patients with moderate-to-severe psoriasis are primarily given either topicals or phototherapy first-line ([McMichael et al, 2012](#)). In fact, biologic use is 69% lower in African Americans compared to white patients ([Takeshita et al, 2015](#)). Racial disparities in biologic treatment for psoriasis in the US may be due in part to a greater level of unfamiliarity with biologics that may stem from having less exposure to the treatments (e.g., not being offered a biologic by a medical provider, not seeing advertisements for biologics, among other reasons) or lack of recognition or understanding of biologics as treatments for psoriasis ([Takeshita et al, 2019](#)).

Clinical studies have consistently demonstrated that guselkumab treatment leads to rapid, clinically significant improvement in participants with psoriasis; however, these studies had minimal representation of skin of color patients (and too few for any subgroup analysis). Results from VOYAGE 1 and 2 suggest no difference in efficacy based on race and ethnicity, however,

the number of non-white participants was too small for formal statistical analysis. There is precedence in other disease states such as hypertension, asthma, and atopic dermatitis where eventual research found differences in disease pathogenesis and treatment response as a result of racial/ethnic background, thus, there is an unmet need to examine whether this difference also exists in psoriasis. Furthermore, we know that various inflammatory skin diseases disproportionately affect populations of color for unclear reasons such as lupus, dermatomyositis and keloids in Asians and Africans and cutaneous T-cell lymphoma, sarcoidosis and hidradenitis in African Americans (Kelly et al, 2016). Cohort A is designed to fill this knowledge gap with regards to skin of color patients with psoriasis and to help better understand disease pathogenesis and treatment response. This study will enroll all Fitzpatrick types I-VI because, in particular, the Hispanic/Latino population can range across the entire spectrum; however, given historical disparities we will ensure at least 50% of the population is Fitzpatrick type IV-VI.

In summary, prior guselkumab trials in psoriasis enrolled 77-93% white participants, and data were limited for non-white racial/ethnic groups (VOYAGE 1 and 2, ECLIPSE, ORION, and NAVIGATE studies). Epidemiological, clinical, and therapeutic data pertaining to psoriasis in non-white racial/ethnic groups are currently limited (Alexis and Blackcloud, 2014). Most research that exists is in the form of post hoc analyses which have shown that baseline BSA is often higher in non-Caucasians (Shah et al, 2011). Disparities in access to care and ethnic differences in utilization of dermatology services partly contribute to these differences in baseline severity of disease. Research suggests that both genetic and environmental factors contribute to the observed epidemiological differences in psoriasis and that these factors may have implications on clinical presentation and responses to treatment (Alexis and Blackcloud, 2014). Thus, there is an unmet need to examine guselkumab efficacy in skin of color patients with moderate-to-severe plaque psoriasis.

Predominant Scalp Psoriasis

Scalp psoriasis can be a cause of great physical and social distress, with up to 97% of affected individuals reporting that the condition interferes with their daily life (Crowley et al, 2010). Scalp psoriasis is associated with intense pruritus, and scale is commonly shed as dandruff, creating significant social embarrassment for affected individuals. Quality of life is adversely affected by chronic itchy and painful symptoms from psoriasis which can lead to stress, interference with activities of daily living such as bathing and sleeping, depression, and suicidal ideation (Ferreira et al, 2016; Kimball et al, 2005). Furthermore, patients can experience feelings of shame, embarrassment, stigmatization, and poor self-esteem, particularly when a visible area such as the scalp is involved (Ferreira et al, 2016; Kimball et al, 2005). Moreover, scalp psoriasis can result in alopecia which, though reversible with appropriate treatment, has been increasingly linked to scarring alopecia due to chronic, relapsing episodes of the disease (George et al, 2015). In fact, both the National Psoriasis Foundation and International Psoriasis Council consider the scalp to be a sensitive area of the body so psoriasis on the scalp results in eligibility for systemic treatment. Thus, there remains a need to determine whether guselkumab provides benefit to those with predominantly moderate-to-severe scalp psoriasis, i.e., moderate-to-severe scalp psoriasis without

extensive body involvement in skin of color patients. Such patients may benefit from earlier biologic initiation.

Scalp psoriasis was chosen as the focus of Cohort B for several reasons. Scalp psoriasis is very prevalent, affecting ~80% of Asian, Hispanic, and African-American/Black patients with psoriasis. Furthermore, Asian and Black patients are more likely to present with scalp psoriasis (Kaufman and Alexis, 2018; Alexis and Blackcloud, 2014). Furthermore, hair characteristics such as hair follicle shape, density, and moisture content tend to differ in many populations of skin of color compared with Caucasians and skin reactivity to injury (an important factor when administering topical medications) differs by race thus meriting special consideration when evaluating and treating scalp psoriasis in skin of color. Due to clinical nuances, such as physical exam findings, patients who have scalp psoriasis may previously be diagnosed with chronic seborrheic dermatitis or sebopsoriasis, but in fact be suffering from true psoriasis. Clinically, one reason for this would be the difficulty in ascertaining visual erythema, and confounding visibility of extensive fine scale. Despite the vast array of treatment options available for psoriasis, psoriasis of the scalp remains a difficult treatment area in these populations. The presence of hair not only impacts the application and penetration of medications to affected areas, but also strongly influences treatment adherence (Crowley et al, 2010). Patients commonly complain of the greasy effect of medications in this area, and difficulty removing products from their hair. Topical corticosteroids, with or without the addition of the vitamin D analog calcipotriol, are the gold standard for the treatment of scalp psoriasis (Crowley et al, 2010). However, hair texture, hair styles, and hair care practices in skin of color patients may result in inability to utilize or tolerate topical treatments thus undertreating disease and resulting in increasing severity of scalp psoriasis. Separately, studies have demonstrated that the severity of patients' scalp lesions is a factor associated with reduced quality of life, irrespective of the severity of their psoriasis as a whole (Zampieron et al, 2015). Scalp psoriasis presents unique treatment challenges in the skin of color community due to hair texture variations and social/cultural hair styling practices thus there may be an unmet need in patients with isolated or predominant moderate-to-severe scalp psoriasis.

Guselkumab has previously been shown to be efficacious for scalp psoriasis in participants with concomitant extensive body involvement of moderate-to-severe plaque psoriasis, however, efficacy studies in patients with isolated moderate-to-severe scalp psoriasis or in conjunction with less extensive body psoriasis have not been performed. One biologic, secukinumab, has clinical trial data showing that it is a reasonable treatment option for patients with moderate-to-severe scalp psoriasis with or without plaque psoriasis elsewhere (Bagel et al, 2017). Data from the secukinumab study, in a predominantly Caucasian population (86%), did not report notable differences between patients of varying race/ethnicity, however, the limited subgroup of patients with skin of color precludes definite conclusions (Bagel et al, 2017). In summary, there is a significant unmet need to evaluate additional treatment options in patients with skin of color and psoriasis.

Post-inflammatory dyspigmentation

Psoriasis, like other inflammatory skin diseases, is commonly associated with post-inflammatory pigment alteration (PIPA). The pigment alteration in psoriasis patients is typically only observed in areas previously affected by psoriasis, and could manifest as both hyper- and hypopigmentation. While PIPA can occur in all skin types, it more frequently affects skin of color patients, including African Americans, Hispanics/Latinos, Asians, Native Americans, Pacific Islanders, and those of Middle Eastern descent (Davis and Callender, 2010). PIPA is underestimated in the literature and believed to be a frequent occurrence (Amico et al, 2020). Notably, in one survey of biologic-treated psoriasis patients, more than 80% of patients considered PIPA an important, neglected problem, and 73% thought this issue was an unmet need with regards to treatments available (Chiu et al, 2021). Disorders of dyspigmentation carry an associated psychological burden that must be addressed by health professionals when managing these conditions (Lakhan and Lynch, 2021). Hyperpigmentation has been significantly associated with darker Fitzpatrick skin type ($\geq$ IV) with an odds ratio of 3.99 (Amico et al, 2020) and can have a considerable impact on quality of life (Taylor et al, 2009). Furthermore, PIPA can have a significant psychosocial impact on Fitzpatrick skin type IV-VI patients, as these pigmentary changes occur with greater frequency and severity and are more obvious (Davis et al, 2010). In contrast, no significant association has been found between hypopigmentation and skin type but is significantly observed with younger age (Amico et al, 2020) and white hair (Chiu et al, 2021). Despite the high frequency of PIPA, little is known about timeline to resolution, repigmentation patterns and the literature remains speculative regarding the clinical factors associated with this phenomenon. The long-term portion of this study will use clinical photographs and other clinical measures to study PIPA which is an unmet need that disproportionately impacts skin of color patients and has not been assessed in prior psoriasis trials.

2.2. Background

Clinical Studies

The clinical development program to support use of guselkumab in the US and globally for the treatment of moderate-to-severe plaque psoriasis includes 2 Phase 1 studies, 1 Phase 2 study, and 5 Phase 3 global studies (CNT01959PSO3001 [VOYAGE 1], CNT01959PSO3002 [VOYAGE 2], ECLIPSE, ORION, and NAVIGATE). Details about these studies are provided in the Investigator's Brochure.

The Phase 3 VOYAGE 1 study (CNT01959PSO3001) was a multicenter, Phase 3, randomized, double-blind, placebo- and active-comparator-controlled study in participants with moderate-to-severe plaque psoriasis with 3 parallel treatment groups: placebo, guselkumab 100 mg, and adalimumab. Participants in the placebo group crossed over to guselkumab 100 mg beginning at Week 16. In that study, 837 adult participants were randomized to receive guselkumab (n=329) or adalimumab (n=334) or placebo (n=174). At Week 16, a significantly greater proportion of participants randomized to guselkumab achieved the co-primary endpoints of an IGA score of cleared (0) or minimal (1) and PASI 90 response (85.1% and 73.3%, respectively; $p < 0.001$ for both endpoints) compared with placebo (6.9% and 2.9%, respectively).

Treatment with guselkumab was well tolerated through Week 48. The frequency of adverse events (AEs) was comparable between the treatment groups through Week 48. The most common AEs were nasopharyngitis and upper respiratory tract infection. Through Week 16, the percentage of participants with 1 or more serious adverse events (SAEs) was 1.7% (n=3) in the placebo group and 2.4% (n=8) in the guselkumab group. The incidence of infections was comparable between the placebo, guselkumab, and adalimumab groups through Week 16. Through 5 years of follow-up, no opportunistic infections or active tuberculosis (TB) were reported.

The Phase 3 VOYAGE 2 study (CNTO1959PSO3002) was a multicenter, Phase 3, randomized, double-blind, placebo- and active-comparator-controlled study in participants with moderate-to-severe plaque psoriasis with 3 treatment groups: placebo, guselkumab 100 mg, and adalimumab. In that study, 992 adult participants were randomized to either the placebo (n=248), guselkumab (n=496), or adalimumab (n=248) treatment groups at Week 0. Participants in the placebo group crossed over to guselkumab 100 mg beginning at Week 16. This study evaluated the benefit of maintenance therapy using a randomized withdrawal design starting at Week 28.

At Week 16, a significantly greater proportion of participants randomized to guselkumab achieved the co-primary endpoints of an IGA score of cleared (0) or minimal (1) and a PASI 90 response (84.1% and 70.0%, respectively; $p < 0.001$ for both endpoints) compared with placebo (8.5% and 2.4%, respectively). Treatment with guselkumab was well tolerated. Through Week 16, the proportion of participants experiencing 1 or more AEs was comparable between treatment groups. Nasopharyngitis and upper respiratory tract infection were the most common AEs. The percentage of participants with 1 or more SAEs was comparable between the placebo and guselkumab groups. The incidence of infections was comparable between placebo, guselkumab, and adalimumab groups through Week 16. Through 5 years of follow-up, no opportunistic infections or active TB were reported.

2.3. Benefit-Risk Assessment

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

2.3.1. Risks for Study Participation

Potential Risks of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Potential risks due to study intervention (guselkumab)		
Serious infections and reactivation of latent infections	Available animal and human data suggest that blockade of IL-23 may be associated with an increased infection risk. Infections have been identified as adverse reactions of guselkumab, including respiratory infections, herpes simplex, tinea infections, and gastroenteritis.	Participants with a history of, or ongoing, chronic or recurrent infectious disease, including human immunodeficiency virus (HIV), or hepatitis B or C virus (HBV, 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 4 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 8.2.10 and 8.2.11). - Discontinuation of a participant's study intervention must be strongly considered if the participant develops a serious infection, including but not limited to sepsis or pneumonia. In addition, any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete.
Hypersensitivity reactions, including serious hypersensitivity reactions	Hypersensitivity reactions including anaphylaxis have been identified as adverse reactions in post-marketing experience with guselkumab.	- Participants with known allergy, hypersensitivity, or intolerance to guselkumab or its excipients will be excluded from the study. - Sites are instructed that before any administration of study intervention, appropriately trained personnel and medications (e.g., injectable epinephrine) must be available to treat hypersensitivity reactions, including anaphylaxis. In addition, all participants must be observed carefully for signs and symptoms of a hypersensitivity reaction (e.g., urticaria, pruritis, angioedema, wheezing, dyspnea, or hypotension) (Section 8.2.9). - Any participant who develops a serious hypersensitivity reaction such as anaphylaxis must discontinue study intervention.
Malignancy	The preponderance of preclinical data suggests that blockade of endogenous IL-23 would not be detrimental and may in fact be beneficial in tumor	Those participants who currently have a malignancy or have a history of malignancy within 5 years prior to screening (with exceptions noted in Section 7.1) will be excluded from the study. Additionally, participants who

	immunosurveillance and host protection; however, a risk of malignancy cannot be excluded.	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 subcutaneously (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, this event may represent drug-induced liver injury possibly related to guselkumab. Transaminase increases have been identified as an adverse reaction of guselkumab. In PsA studies transaminase increases were observed with a higher incidence with a maintenance dose of 100 mg every 4 weeks (q4w) compared to 100 mg every 8 weeks (q8w).	- During the conduct of the study, liver function tests will be monitored at regular intervals. The 100 mg SC q8w dosage is approved in the major regions in which this study will be conducted. - Participants with marked liver enzyme elevations or symptoms or signs of liver dysfunction (e.g., jaundice), should undergo a thorough investigation for possible causes of liver injury. 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 7.1.1).
Risks due to study procedures		
Radiation	A chest X-ray will be performed at screening if the participant does not have a chest X-ray within 12 weeks prior to the first administration of study intervention. The exposure from 1 standard chest X-ray is 0.1	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 12 weeks prior

	mSV, comparable to 10 days of exposure to natural background radiation (https://www.acr.org).	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 psoriasis in the Phase 2 and Phase 3 studies (see Section 2.2), resulting in the registration of guselkumab in numerous countries globally. The demonstration of clinical benefit was observed in participants who are biologic treatment naïve or experienced. The target population under study in this protocol are participants of skin of color who have active plaque psoriasis and are either biologic naïve or experienced. Consistent with the established efficacy demonstrated in prior guselkumab studies, it is anticipated that individual participants may benefit from participation in the current study. Additionally, participation will help to obtain additional data on the impact of guselkumab on post inflammatory pigment alteration, and in the general knowledge of the natural history and treatment of post inflammatory pigment alteration.

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. Furthermore, after Week 16, all participants will receive guselkumab through Week 100 (approximately a total of 2 years of treatment).

2.3.3. Benefit-Risk Assessment for Study Participation

Additional data through 5 years of treatment from the PSO3001 and PSO3002 studies for guselkumab 100 mg SC administered at Week 0, 4, and then q8w continue to support an overall favorable benefit-to-risk profile for the use of guselkumab in moderate-to-severe psoriasis.

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.

Considering 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 psoriasis.

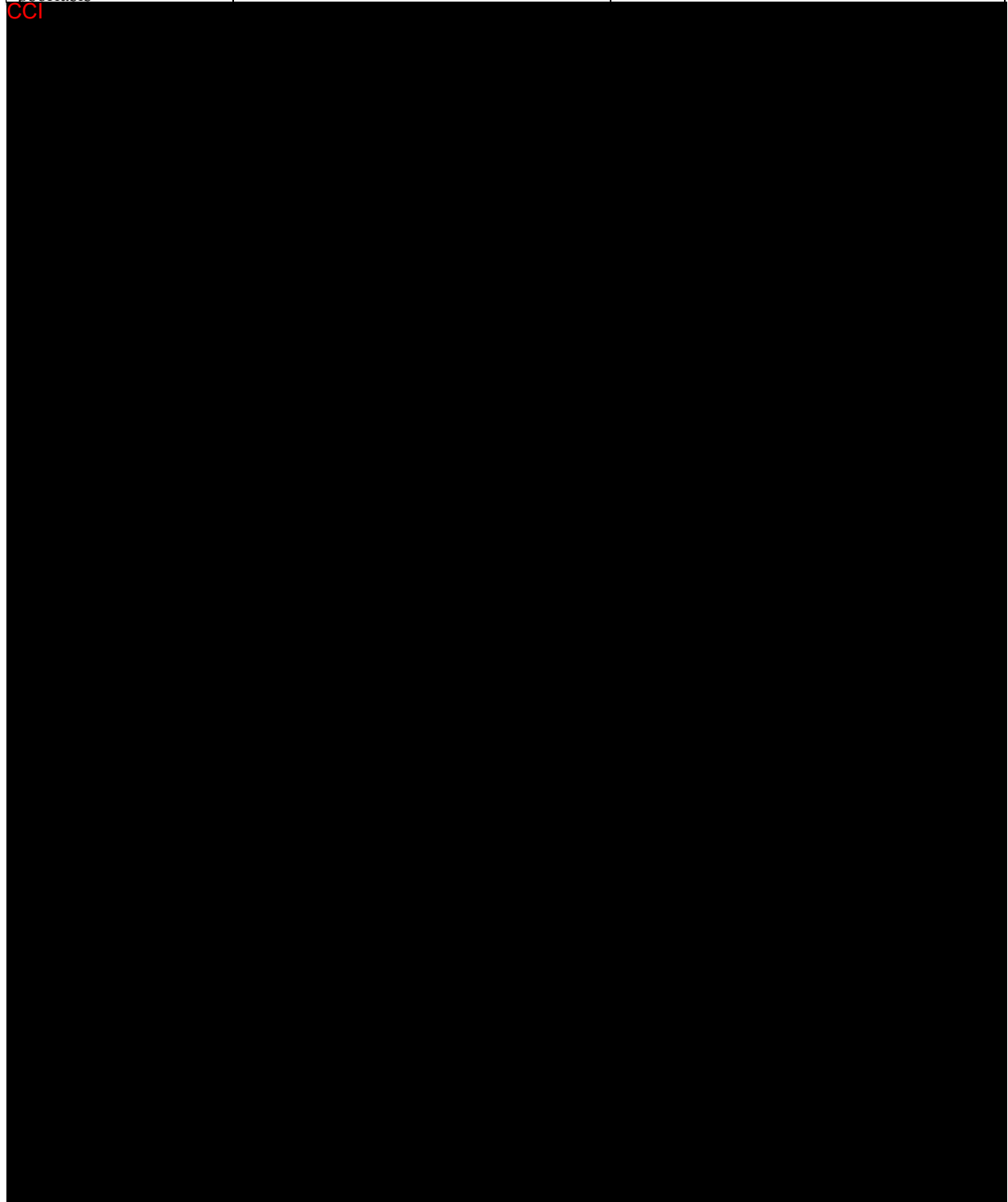
3. OBJECTIVES AND ENDPOINTS

The study objectives and endpoints are listed below.

Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
Primary		
To evaluate the efficacy of guselkumab treatment vs placebo in skin of color participants with predominant moderate-to-severe body psoriasis or predominant moderate-to-severe scalp psoriasis by assessing improvements in the signs and symptoms of psoriasis	The co-primary endpoints are proportions of participants who achieve an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) and the proportion of participants who achieve a Psoriasis Area and Severity Index (PASI) 90 response at Week 16, comparing the guselkumab group and the placebo group	The co-primary endpoints are proportions of participants who achieve a scalp specific (ss)-IGA score of absence of disease (0) or very mild disease (1) and the proportion of participants who achieve a Psoriasis Scalp Severity Index (PSSI) 90 response at Week 16, comparing the guselkumab group and the placebo group
Major Secondary (The final ordering of endpoints will be specified in the Statistical Analysis Plan [SAP])		
To evaluate the efficacy of guselkumab on additional measures of body and scalp psoriasis	• The proportion of participants who achieve an IGA score of cleared (0) at Week 16 • The proportion of participants who achieve a PASI 100 response at Week 16 • The change from baseline in PASI score at Week 16 • The change from baseline in body surface area (BSA) at Week 16 • The time to $\geq 90\%$ reduction in PASI through Week 16 • The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16 • The proportion of participants who achieve ≥ 4-point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch ≥ 4 at baseline • The change from baseline in PSSD symptom score at Week 16 • The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score ≥ 1	• The change from baseline in PSSI score at Week 16 • The change from baseline in scalp surface area (SSA) at Week 16 • The proportion of participants who achieve a ss-IGA score of absence of disease (0) at Week 16 • The proportion of participants who achieve a PSSI 100 response at Week 16 • The time to $\geq 90\%$ reduction in PSSI through Week 16 • The change from baseline in DLQI score at Week 16 • The proportion of participants who achieve ≥ 4-point reduction (improvement) from baseline in the scalp itch numeric rating scale (NRS) score at Week 16, among participants with baseline scalp itch ≥ 4 at baseline • The change from baseline in PSSD symptom score at Week 16 • The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score ≥ 1

Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
Other Secondary Endpoint		
To evaluate the safety of guselkumab in participants with moderate to severe psoriasis	Frequency and type of adverse events (AEs) and serious adverse events (SAEs)	Frequency and type of AEs and SAEs

CCI



Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
	CCI	

Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
	CCI	

Objectives	Cohort A (Predominant Body Psoriasis) Endpoints	Cohort B (Predominant Scalp Psoriasis) Endpoints
	CCI	
To evaluate pharmacokinetics and immunogenicity of guselkumab	- The serum concentrations of guselkumab - The incidence of antibodies to guselkumab	- The serum concentrations of guselkumab - The incidence of antibodies to guselkumab
To evaluate pharmacodynamic (PD) effects of guselkumab in psoriasis patients	The change from baseline in cellular and molecular biomarkers in skin and blood	The change from baseline in cellular and molecular biomarkers in skin and blood
To evaluate pharmacogenomic of guselkumab in psoriasis patients	The genetic factors associated with clinical response and PD	The genetic factors associated with clinical response and PD

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

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

HYPOTHESIS

Cohort A: It is hypothesized that guselkumab is superior to placebo in the treatment of skin of color participants with moderate-to-severe plaque psoriasis. This study is designed to show a difference between guselkumab and placebo in the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) and a PASI 90 response at Week 16.

Cohort B: It is hypothesized that guselkumab is superior to placebo in the treatment of skin of color participants with moderate-to-severe scalp psoriasis. This study is designed to show a difference between guselkumab and placebo in the proportion of participants who achieve a ss-IGA score of absence of disease (0) or very mild disease (1) and a PSSI 90 response at Week 16.

4. STUDY DESIGN

4.1. Overall Design

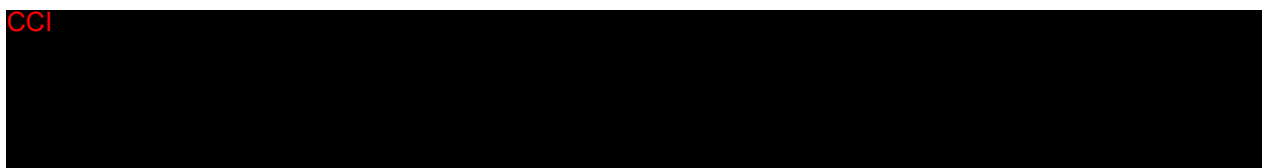
This is a Phase 3b, multicenter, randomized, placebo-controlled, double-blind study designed to evaluate the efficacy and safety of guselkumab in participants of skin of color with predominant body moderate-to-severe plaque psoriasis (Cohort A) or predominant moderate-to-severe scalp psoriasis (Cohort B). Cohort A and B are independent and will have separate database locks (DBLs) and analyses.

There will be 3 DBLs in this study, at Week 16, Week 48, and Week 112 for each cohort. After all participants in a cohort have completed the Week 16 Visit (or discontinued from the study), a Week 16 DBL will be performed. The primary data analysis for each cohort will be conducted at Week 16. However, unblinded data will only be made available to select Sponsor and Contract Research Organization (CRO) team members involved with analysis of the data and preparation of any Week 16 analyses. All other Sponsor, site, and CRO personnel directly involved with study conduct will remain blinded to treatment assignments until the Week 48 DBL and related analyses are completed.

Approximately 200 patients (~100 per cohort) will be enrolled and randomized 3:1 to receive either guselkumab 100 mg or placebo for the first 16 weeks. Participants will be separated into the following cohorts:

- Cohort A will be participants with predominant moderate-to-severe plaque psoriasis (at screening & baseline, BSA $\geq 10\%$, PASI ≥ 12 , IGA ≥ 3)
- Cohort B will be participants with predominant moderate-to-severe scalp psoriasis (at screening & baseline, ss-IGA ≥ 3 , scalp surface area $\geq 30\%$, PSSI ≥ 12 , and at least one psoriasis plaque outside of the scalp)
- Participants who meet criteria for both cohorts will be alternately randomized 1:1 between Cohort A and Cohort B. If and when one cohort is filled and closed, then all subsequent participants who meet criteria for both cohorts will be randomized to the remaining open cohort.

CCI



The study will consist of a screening phase of up to approximately 4 weeks; a blinded treatment period through Week 48; and a long-term extension (LTE) with treatment through Week 100 and a final follow-up visit at Week 112. The co-primary endpoints of IGA 0/1 and PASI 90 for participants in Cohort A or ss-IGA 0/1 and PSSI 90 for participants in Cohort B at baseline will be evaluated at Week 16. At Week 16, the participants who had been receiving placebo in each cohort will switch to guselkumab.

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

4.2. Scientific Rationale for Study Design

Blinding, Control, Study Phase/Periods, Intervention Groups

A placebo control will be used to establish the frequency and magnitude of changes in clinical endpoints that may occur in the absence of active intervention. Randomization will be used to minimize bias in the assignment of participants to intervention groups, to increase the likelihood that known and unknown participant attributes (e.g., 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

Comparisons are planned between guselkumab and placebo at Week 16, which is what has been used in prior trials (VOYAGE 1 & 2).

DNA and Biomarker Collection

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

Biomarker samples will be collected to help to explain interindividual 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 PD of guselkumab and aid in evaluating the intervention-clinical response relationship.

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

4.2.1. Study-Specific Ethical Design Considerations

Potential participants will be fully informed of the risks and requirements of the study and, during the study, participants will be given any new information that may affect their decision to continue participation. They will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only participants who are fully able to understand the risks, benefits, and potential AEs of the study, and provide their consent voluntarily will be enrolled. Written consent/assent may be obtained through various sources (e.g., paper or electronic such as eConsent, eSignature, or digital signature) as determined by regulations as well as study and/or patient preferences.

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

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

4.3. Justification for Dose

The current approved dose regimen for guselkumab for the treatment of moderate-to-severe plaque psoriasis will be used in this study.

The dose regimen of guselkumab 100 mg at Weeks 0 and 4 and q8w thereafter was used for the global Phase 3 studies of guselkumab for the treatment of moderate-to-severe plaque psoriasis. This dose regimen was chosen based on results of the guselkumab dose-ranging study (CNT01959PSO2001) in participants with moderate-to-severe plaque-type psoriasis and PK/ PD modeling based on the data from the PSO2001 study. A population PK analysis for guselkumab in psoriasis (Summary of Clinical Pharmacology, Guselkumab Psoriasis Biologic Licensing Application [BLA]) did not identify race as a covariate, thus, no differences in PK by race are expected and the approved dose is appropriate for this population of participants with skin of color.

4.4. End of Study Definition

End of Study Definition

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

Study Completion Definition

Participants who prematurely discontinue study drug for any reason prior to the Week 48 visit (if not participating in LTE) or the Week 100 visit (if participating in LTE) should complete the specified study visits and the Final Safety / Early Termination visit as outlined in Section 1.3 and Section 7.2.

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

5. STUDY POPULATION

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

Age

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

Type of Participant and Disease Characteristic

2. Be non-white, as per self-reported race/ethnicity.
3. Have a diagnosis of plaque psoriasis (with or without PsA) for at least 6 months before the first administration of study drug **OR** expert panel confirmed psoriasis diagnosis (based on clinical photos) **OR** biopsy confirmed psoriasis.
4. Be a candidate for phototherapy or systemic treatment for psoriasis.
5. a. Have moderate to severe plaque psoriasis defined by an involved BSA $\geq 10\%$, PASI ≥ 12 , and IGA ≥ 3 at screening and at baseline (Cohort A)

OR

- b. Have moderate to severe scalp psoriasis defined by scalp surface area $\geq 30\%$, PSSI ≥ 12 , and ss-IGA ≥ 3 , and at least one plaque outside of the scalp at screening and at baseline (Cohort B).

Sex and Contraceptive/Barrier Requirements

6. A woman of childbearing potential must have a negative highly sensitive serum β -human chorionic gonadotropin [β -hCG] at screening and agree to urine pregnancy testing before receiving study intervention administration.
7. Before the first administration of study drug, a woman must be either:
 - a. Not of childbearing potential: premenarchal; postmenopausal (>45 years of age with amenorrhea for at least 12 months or any age with amenorrhea for at least 6 months and a serum follicle-stimulating hormone level >40 IU/L); permanently sterilized (e.g., hysterectomy, bilateral salpingectomy, or bilateral oophorectomy); or otherwise incapable of pregnancy.
 - b. Of childbearing potential and practicing a highly effective method of birth control, consistent with local regulations regarding the use of birth control methods for participants participating in clinical studies: e.g., established use of oral, injected, or implanted hormonal methods of contraception; placement of an intrauterine device or intrauterine system; male partner sterilization (the vasectomized partner should be the sole partner for that participant); true abstinence (when this is in line with the preferred and usual lifestyle of the participant).

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

8. 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 guselkumab.
9. 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 (e.g., either a condom [condom plus spermicidal foam/gel/film/cream/suppository; or a partner with an occlusive cap [diaphragm or cervical/vault caps] plus spermicidal foam/gel/film/cream/suppository), during the study and for at least 12 weeks after receiving the last administration of guselkumab.
10. All men must agree to not donate sperm during the study and for at least 12 weeks after receiving the last administration of guselkumab.

Infectious disease-related

11. Agree not to receive a live virus or live bacterial vaccination during the study, or within 4 weeks after the last administration of study intervention.
12. Agree not to receive a Bacillus Calmette-Guérin (BCG) vaccination during the study, and within 12 weeks after the last administration of study intervention.
13. 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.
14. Have screening laboratory test results within the following parameters, if one or more of the laboratory parameters is out of range, a single retest of laboratory values is permitted:
 - a. Hemoglobin ≥ 10 g/dL (SI: ≥ 100 g/L)
 - b. White blood cells $\geq 3.5 \times 10^3/\mu\text{L}$ (SI: ≥ 3.5 GI/L)
 - c. Neutrophils $\geq 1.5 \times 10^3/\mu\text{L}$ (SI: ≥ 1.5 GI/L)
 - d. Platelets $\geq 100 \times 10^3/\mu\text{L}$ (SI: ≥ 100 GI/L)
 - e. Serum creatinine ≤ 1.5 mg/dL (SI: ≤ 137 $\mu\text{mol/L}$)
 - f. Aspartate aminotransferase $\leq 2 \times$ upper limit of normal (ULN)
 - g. Alanine aminotransferase $\leq 2 \times$ ULN
 - h. Alkaline phosphatase $\leq 2 \times$ ULN

Informed Consent

15. Must sign an informed consent form (ICF) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.
16. Must sign a separate ICF for optional samples including:
 - a) For biomarkers if the participant agrees to provide an optional biopsy and/or tape stripAND/OR
 - b) For pharmacogenomics, if participant agrees to provide a DNA sample for research (where local regulations permit).

Refusal to give consent for any of the optional research samples does not exclude a participant from participation in the study.
17. Be willing and able to adhere to the prohibitions and restrictions specified in this protocol.

5.2. Exclusion Criteria

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

Psoriasis/Psoriasis Treatments

1. Received any of the following treatment regimens specified in the timeframes below:
 - a. **Has previously received at any time** any therapeutic agent directly targeted to IL-23 including but not limited to guselkumab, risankizumab, tildrakizumab, or mirikizumab
 - b. **Within 26 weeks** of first dose of study drug: any agent that depletes B-cells including but not limited to rituximab, belimumab, ofatumumab, ocrelizumab, etc.
 - c. **Within 12 weeks or 5 half lives, whichever is longer** of first dose of study drug: any agent that modulates T-cells including but not limited to natalizumab, abatacept, visilizumab, etc.
 - d. **Within 12 weeks** of first dose of study drug: ustekinumab, ixekizumab, secukinumab, or brodalumab

- e. **Within 8 weeks** of first dose of study drug: infliximab or golimumab (IV)
 - f. **Within 6 weeks** of first dose of study drug: adalimumab or certolizumab
 - g. **Within 4 weeks** of first administration of study drug:
 - i. Etanercept
 - ii. Phototherapy (e.g., ultraviolet B [UVB], psoralen ultraviolet A [PUVA] or other phototherapy)
 - iii. Any other systemic medications or treatments that could affect psoriasis evaluations (including but not limited to apremilast, retinoids e.g., acitretin, psoralens, fumaric acid derivatives, and 1,25-dihydroxy vitamin D3 and analogs)
 - iv. Any systemic immunosuppressants including but not limited to methotrexate (MTX), azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, JAK/TYK2 pathway inhibitors, tacrolimus or anakinra
 - h. **Within 2 weeks** of first administration of study drug
 - i. Topical medications/treatments that could affect psoriasis including, but not limited to topical corticosteroids, topical retinoids, or Vitamin D analog preparations, e.g., calcipotriene, tacrolimus, pimecrolimus, crisaborole, anthralin/dithranol, experimental topicals (including but not limited to taparinoof or roflumilast), and coal tar or its derivatives
 - ii. Traditional Taiwanese, Korean, or Chinese medicines or other herbal or ethnic treatments
- 2. Has a nonplaque form of psoriasis (e.g., erythrodermic, guttate, or pustular).
 - 3. Has current drug-induced psoriasis (e.g., a new onset of psoriasis or an exacerbation of psoriasis from beta blockers, calcium channel blockers, or lithium).
 - 4. Is currently receiving lithium, antimalarials, or intramuscular (IM) gold, or have received lithium, antimalarials, or IM gold within 4 weeks of the first administration of study drug.

Coexisting Medical Conditions or Past History

5. Has received an experimental antibody or biologic therapy within the previous 12 weeks or 5 half-lives (whichever is longer) of any study drug administration or is currently enrolled in another study using an investigational agent or procedure.
6. Has a history or current signs or symptoms of severe, progressive, or uncontrolled renal, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances.
7. Has unstable cardiovascular disease, defined as a recent clinical deterioration (e.g., unstable angina, rapid atrial fibrillation) in the last 3 months or a cardiac hospitalization within the last 3 months.
8. Currently has a known malignancy or has a history of malignancy within 5 years before screening (with the exception of a nonmelanoma skin cancer that has been adequately treated with no evidence of recurrence for at least 3 months before the first study drug administration or cervical carcinoma in situ that has been treated with no evidence of recurrence for at least 3 months before the first study drug administration).
9. 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.
10. Has a transplanted organ (with exception of a corneal transplant >3 months before the first administration of study drug).
11. 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.
12. Has unstable suicidal ideation or suicidal behavior in the last 6 months, that may be defined as a Columbia-Suicide Severity Rating Scale (C-SSRS) rating at screening of:
 - 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.

13. Participant has known allergies, hypersensitivity, or intolerance to guselkumab or its excipients (refer to Investigator's Brochure).
14. Is pregnant, nursing, or planning a pregnancy (both men and women) while enrolled in this study or within 12 weeks following the last administration of study drug.
15. Has had major surgery (e.g., requiring general anesthesia and hospitalization) within 8 weeks before screening, or will not have fully recovered from such surgery, or has such surgery planned during the time the participant is expected to participate in the study.

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

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

Infections or Predisposition to Infection

17. Has or has had a serious infection (e.g., sepsis, pneumonia or pyelonephritis), or has been hospitalized or received intravenous antibiotics for an infection during the 2 months before screening.
18. Has a history of active granulomatous infection, including histoplasmosis or coccidioidomycosis, before screening. Refer to Exclusion Criterion 25 for information regarding eligibility with a history of latent TB.
19. Has ever had a nontuberculous mycobacterial infection or opportunistic infection (e.g., cytomegalovirus, pneumocystosis, aspergillosis).
20. Has a chest radiograph within 3 months before the first administration of study drug that shows an abnormality suggestive of a malignancy or current active infection, including TB.
21. Has a history of chronic or recurrent infectious disease, including but not limited to chronic renal infection, chronic chest infection (e.g., bronchiectasis), recurrent urinary tract infection (recurrent pyelonephritis or chronic non-remitting cystitis), fungal infection (mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.

22. Has or has had herpes zoster within the 2 months of screening.
23. Has received, or is expected to receive, any live virus or bacterial vaccination within 12 weeks before the first administration of study drug, or plans to receive such vaccines during the study, or within 4 weeks after last administration of study drug. For BCG vaccine, see Exclusion Criterion 24.
24. Has had a BCG vaccination within 12 months of screening.
25. Meet **ANY** of the following tuberculosis (TB) screening criteria:

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

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

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

ruled out and appropriate treatment for latent TB has been initiated as described above.

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

- e. Have a chest radiograph or chest computed tomography within 3 months prior to the first administration of study intervention that shows abnormalities suggestive of active or inactive TB.
26. Is infected with human immunodeficiency virus (HIV, positive serology for HIV antibody).
27. Tests positive for hepatitis B virus (HBV) infection ([Appendix 3](#)).
28. Is seropositive for antibodies to hepatitis C virus (HCV), unless they satisfy one of the following conditions:
- a. Have a history of successful treatment (defined as being negative for HCV RNA at least 12 weeks after completing antiviral treatment) and have a negative HCV RNA test result at screening,
- OR**
- b. While seropositive have a negative HCV RNA test result at least 12 weeks prior to screening and a negative HCV RNA test result at screening.
29. During the 6 weeks prior to baseline, have had ANY of the following:
- 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 –CoV – 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, e.g., 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.

Other Exclusions

30. Is unable or unwilling to undergo multiple venipunctures because of poor tolerability or lack of easy access to veins.
31. Lives in an institution on court or authority order.
32. Has any condition that, in the opinion of the investigator, would make participation not be in the best interest (e.g., compromise the well-being) of the participant or that could prevent, limit, or confound the protocol-specified assessments.
33. Is an employee of the investigator or study site with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.

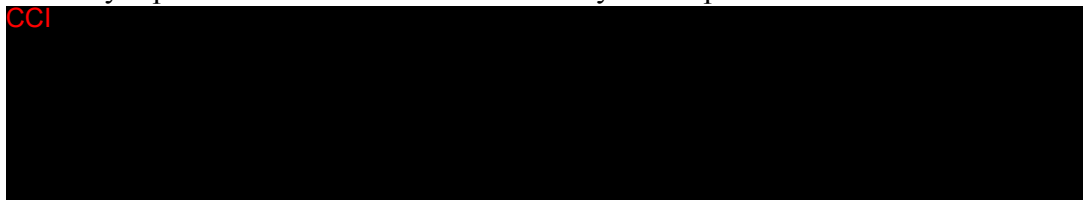
NOTE: Investigators must ensure that all study enrollment criteria have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after screening but before the first dose of study intervention is given such that the participant no longer meets all eligibility criteria, then the participant must be excluded from participation in the study. The required source documentation to support meeting the enrollment criteria are noted in [Appendix 4: Regulatory, Ethical, and Study Oversight Considerations](#).

5.3. Lifestyle Considerations

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

1. Refer to Section 6.8, Concomitant Therapy for details regarding prohibited and restricted therapy during the study. Briefly, key prohibited and restricted therapies during the study:
 - Any increased use or new start of medicated shampoo (e.g., ketoconazole, coal-tar, etc.) for the scalp; stable use (defined as stable and regular frequency of use for at least 3 months prior to first study drug administration) will be allowed
 - Any class of topical steroids through Week 48
 - Any topical vitamin D derivatives on body or scalp

CCI



CCI

2. Participants must avoid prolonged sun exposure and avoid use of tanning booths or other UV light sources during the study.
3. Following the Week 0 visit, participants in Cohort B must attempt to keep a consistent hairstyle for all study visits. This includes the following recommendations:
 - While hair dye is permitted to be used during the study, participants are discouraged from undergoing any hair dying process or other hair treatments that may impact the scalp for 7 days prior to a study visit
 - Hair prosthetics (e.g., wigs, hair extensions, etc.) are permitted but should be removed for clinical assessments of scalp psoriasis at all study visits. Hair extensions if not obscuring scalp can also be consistently left in place at all visits if preferred by investigator and participant.
 - Hair transplants and tattooing of scalp including procedures such as microblading are not permitted during the course of study but may be performed prior to screening
4. Agree to follow all requirements that must be met during the study as noted in the Inclusion and Exclusion Criteria (e.g., contraceptive requirements).

5.4. Screen Failures

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

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

Participant Identification, Enrollment, and Screening Logs

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

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

Rescreening

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

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

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

Retesting

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

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

6. STUDY INTERVENTION AND CONCOMITANT THERAPY

6.1. Study Intervention(s) Administered

Study intervention administration must be captured in the source documents and the electronic case report form (eCRF). 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 8.

Intervention Name	Guselkumab	Placebo
Dose Formulation	Liquid provided in a single-use prefilled syringe (PFS) assembled with the UltraSafe PLUS™ Passive Needle Guard (PFS-U)	Liquid provided in a single-use prefilled syringe (PFS) assembled with the UltraSafe PLUS™ Passive Needle Guard (PFS-U)
Unit Dose Strength(s)	100 mg	N/A for placebo

Dosage Level(s) and Frequency	Guselkumab 100 mg will be administered at Week 0, 4 and then every 8 weeks (q8w) through Week 100 for those randomized to guselkumab. For those randomized to placebo and crossover to guselkumab at Week 16: Guselkumab 100 mg will be administered at Weeks 16 and 20 then q8w through Week 100	Placebo will be administered at Week 16 for those randomized to Guselkumab to maintain the blind. Placebo will be administered at Week 0, 4 and 12 for those randomized to placebo.
Route of Administration	☐ Oral ☐ IV infusion ☐ IV injection ☐ Intramuscular ☒ Other [subcutaneous]	☐ Oral ☐ IV infusion ☐ IV injection ☐ Intramuscular ☒ Other [subcutaneous]
Dosing instructions	Study agent will be administered by site personnel at Weeks 0, 4, 12, 16, 20 then q8w through Week 100. Beginning at Week 20, at the discretion of the investigator and participant (or caregiver), and after appropriate and documented training, participants (or caregivers) may self-administer study agent at the investigative site under the supervision of a Health Care Provider. Study drug may be administered at the study site or by the participant or their caregiver (without a study visit) at Weeks 28, 36, 60, 76 and 92.	
Use	☒ Experimental ☐ Background intvn. ☐ Challenge agent ☐ Diagnostic ☐ Other	☐ Experimental ☒ Placebo comparator ☐ Active comparator ☐ Sham comparator ☐ Rescue medication ☐ Background intvn. ☐ Challenge agent ☐ Diagnostic ☐ Other
Investigational Medicinal Product (IMP)	☒ Yes ☐ No	☒ Yes ☐ No
Non-Investigational Medicinal Product (NIMP)	☐ Yes ☒ No	☐ Yes ☒ No

6.2. Preparation/Handling/Storage/Accountability

Combination Products

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

The Sponsor-manufactured combination product for use in this study is the pre-filled syringe (PFS) assembled in an UltraSafe Plus™ PFS-U. Additional details on the PFS-U are provided in Section 6.1 and the guselkumab Investigator Brochure.

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

Preparation/Handling/Storage

The study intervention may be delivered directly to the participants from the site by a courier, if needed. Each courier will adhere to privacy requirements approved by the Independent Ethics Committee (IEC)/Institutional Review Board (IRB). The capability to utilize these direct-to-patient shipments will be assessed by the sponsor to ensure that it is allowable per local regulations.

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. All study intervention must be stored at controlled temperatures ranging from 36°F to 46°F (2°C to 8°C).

Guselkumab and placebo for guselkumab should be a clear and colorless to light yellow solution that may contain translucent particles. Do not use guselkumab or placebo for guselkumab if the liquid is cloudy 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.

Study drug may be administered at the study site or at home by the trained participant or their caregiver (without a study visit) at Weeks 28, 36, 60, 76 and 92. 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. The dispensing of study drug to the participant, and the return of study drug from the participant, must be documented on the drug accountability form. Participants must be instructed to return all original containers, whether empty or containing study drug. All study intervention will be stored and disposed of according to the Sponsor's instructions. Study site personnel must not combine contents of the study intervention containers.

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

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

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

Since participants may potentially be self-administering study drug at home between Weeks 28 and 110, they will receive detailed instructions for study drug storage and disposal of used syringes and handling of unused study material. Participants will receive a sharps container to dispose of used syringes. Participants will be instructed to return the sharps container and/or unused cartons with syringes. Participants will record study drug administrations with time and date information in their participant diary.

6.3. Measures to Minimize Bias: Randomization and Blinding

Intervention Allocation

Procedures for Randomization and Stratification

Central randomization will be implemented in this study. In each cohort, participants will be randomly assigned to 1 of 2 intervention groups, based on a computer-generated randomization schedule prepared before the study by or under the supervision of the Sponsor. CCI

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

Blinding

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

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

Data that may potentially unblind the intervention assignment (i.e., study intervention serum concentrations, anti-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.

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 16 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 participant-level data will be documented prior to unblinding. Investigative study sites and participants will remain blinded to initial treatment assignment until after the Week 48 database lock.

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 16 will have a visit window of ± 7 days counting from Week 0 as Day 1. After Week 48, all visits will have a visit window of ± 14 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

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

Medications/treatments taken after the first dose of study intervention has been administered will be documented as concomitant medications/treatments. Concomitant therapies, including any vaccinations or vaccines authorized for emergency use, e.g., COVID-19, must be recorded throughout the study beginning with start of the first dose of study intervention to 12 weeks after the last dose of study intervention. Concomitant therapies must also be recorded beyond Week 112 only in conjunction with SAEs that meet the criteria outlined in Serious Adverse Events in Section 8.3.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information.

All therapies (including prescription or over-the-counter or prescription medicines, vitamins and/or herbal supplements or teas) as well as all moisturizers or emollients, that the participant is receiving at the time of enrollment or receives during the study must be recorded in eCRF along with:

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

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

6.8.1. Permitted Concomitant Medications

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

Any participant who is receiving a permitted concomitant medication for any reason must be on a locally approved medication and dose for the treated indication and this must be documented in the eCRF.

After the Week 48 visit, the medication rules outlined below still apply except that most topical therapies are permitted for treatment of psoriasis; however, Class I and II corticosteroids are still prohibited during the long-term extension period. CCI

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

6.8.1.1. Topical treatments

- All non-medicated shampoos are allowed. Nonmedicated shampoos may be used on the day of the study visit.
- Stable use (defined as dose and regimen are held stable for at least 3 months prior to the Week 0 Visit of the study) of medicated shampoos containing tar, salicylic acid, selenium sulfide or ketoconazole as their active ingredient are allowed throughout the study. Participants should not use any medicated shampoos on the day of a study visit.
- Topical moisturizers such as Vaseline, coconut butter, Eucerin, Nivea, etc. are allowed throughout the study. Participants should not use any topical agents on the day of a study visit.

6.8.2. Prohibited Concomitant Medications

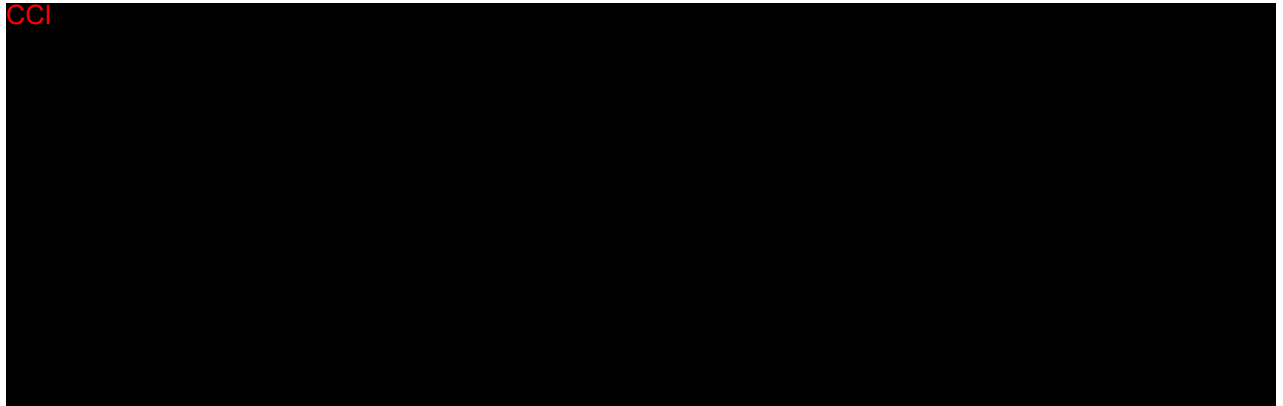
6.8.2.1. Topical Treatments

Topical therapies that could affect psoriasis or any efficacy evaluations like IGA or PASI (e.g., corticosteroids, tar [except shampoos containing tar], anthralin, calcipotriene, tazarotene, methoxsalen, pimecrolimus, tacrolimus, and traditional Taiwanese, Korean, or Chinese medicines) are not permitted.

Any increased frequency of use or new start of medicated shampoo or topical for the scalp is prohibited; stable use (defined as regular frequency of use for at least 3 months prior to first study drug administration) will be allowed.

Any class of topical steroids used on the scalp, trunk, extremities, genitals, or face is prohibited through Week 48 after which only Class I and II steroids are prohibited.

CCI



6.8.2.2. Phototherapy or Systemic Therapy for Psoriasis

The use of phototherapy or systemic antipsoriatic medications is not permitted at any time during the study. These medications include those targeted for reducing tumor necrosis factor (including but not limited to infliximab, adalimumab or etanercept), drugs targeted for reducing IL-12, IL-17, or IL-23 (including but not limited to ustekinumab, tildrakizumab [MK3222], secukinumab [AIN457], ixekizumab [LY2439821], or brodalumab [AMG827]), alpha-4 integrin antagonists (including but not limited to natalizumab), steroids, any conventional systemic therapy that could affect psoriasis or the IGA evaluation (including but not limited to MTX, cyclosporine, apremilast, acitretin), herbal treatments, or traditional Taiwanese, Korean, or Chinese medicines, and any other biological agent or other systemic medication that could affect psoriasis or the IGA evaluation.

6.8.3. Concomitant Medications for Conditions Other than Psoriasis

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

Disease-modifying agents such as MTX, sulfasalazine, or IM gold are prohibited during the study.

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

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

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued if:

- The participant withdraws consent to receive study intervention.
- The investigator believes that for safety reasons or tolerability reasons (e.g., AE) it is in the best interest of the participant to discontinue study intervention.
- The participant becomes pregnant or plans to come pregnant within the study period. Refer to Appendix 6.
- A systemic opportunistic infection occurs.
- Participant develops recurrent or chronic serious infection.
- The participant is unable to adhere to the study visit schedule or comply with protocol requirements.
- The participant meets **ANY** of the following TB related conditions:
 - 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 chest imaging with evidence of current active TB and/or a positive IGRA test result, unless active TB can be ruled out and appropriate treatment for latent TB can be initiated prior to the next administration of study intervention and continued to completion. Indeterminate/borderline results should be handled as outlined in Section 8.2.11.
 - A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy.
- The participant has a serious adverse reaction that is temporally related to an injection including a hypersensitivity reaction resulting in bronchospasm, wheezing and/or dyspnea that requires ventilatory support OR that results in symptomatic hypotension with a decrease in systolic blood pressure of 30% from a participant's baseline value or systolic blood pressure <90 mm Hg.
- The participant has a reaction resulting in myalgia and/or arthralgia with fever and/or rash (suggestive of serum sickness and not representative of signs and symptoms of other recognized clinical syndromes) occurring 1 to 14 days after an injection of study intervention. These may be accompanied by other events including pruritus, facial, hand, or lip edema, dysphagia, urticaria, sore throat, and/or headache.
- The participant has a malignancy including squamous cell skin cancer. Consideration may be given to allowing participants who develop ≤ 2 basal cell skin cancers that are adequately treated with no evidence of residual disease to continue to receive study intervention.

- The participant has severe liver test abnormalities that are not transient and are not explained by other etiologies, as described in Appendix 7.

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

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

- If the participant initiates treatment with prohibited therapies, the medical monitor or designee should be notified for possible discontinuation of study intervention.
- The participant develops a serious infection, including but not limited to sepsis or pneumonia.
Note: Any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete.
- Discontinuation of study treatment should be considered for participants who report suicidal ideation level 4 (some intent to act, no plan), 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) C-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 10.7A 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 10.7B for study intervention restart guidelines following abnormal liver test results. Study Sponsor must provide written approval before study intervention is restarted.

7.2. Participant Study Drug Discontinuation/Withdrawal From the Study

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

- Loss to follow-up

- Withdrawal of consent
- Death

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

A participant will not be automatically withdrawn from the study if the participant discontinues study drug prior to the end of the planned treatment period (Week 100). Participants who discontinue study drug but do not terminate study participation will continue to return for protocol-specified procedures and evaluations per SoA and further guidance below.

Participants who Discontinue Study Drug Prior to or at the Week 48 Visit

If a participant permanently discontinues study drug prior to, or at the Week 48 visit, they should complete the Week 48 visit assessments at the time of discontinuation, or as soon as possible. The participant should also return for a Final Safety / Early Termination visit and complete all specified assessments approximately 12 weeks after the last study intervention administration.

Participants who Discontinue Study Drug after the Week 48 Visit

If a participant discontinues study drug after the Week 48 visit, they should complete the specified assessments for the Week 100 visit at the time of discontinuation, or as soon as possible. The participant should also return for a Final Safety / Early Termination visit and complete all specified assessments approximately 12 weeks after the last study intervention administration.

Participants who Withdraw from Study Participation

Participants who withdraw from study participation prior to the Week 48 visit (if not participating in LTE) or the Week 100 visit (if participating in LTE) should complete the Final Safety / Early Termination visit at the time of early termination.

Withdrawal of Consent

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

Withdrawal of consent should be an infrequent occurrence in clinical studies ([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, video chat, 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 [10.4.5](#)). In such a case, samples will be destroyed after they are no longer needed for the clinical study. Details of the sample retention for research are presented in the main ICF and in the separate ICF for optional research samples.

7.3. Lost to Follow-up

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

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

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

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

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

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

All 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 approximately 250 mL. However, additional repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.

Home Health Care and Telehealth Visits

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

Participants for whom there is no safety concern may have home health care and telehealth (conducted via phone or video conference) visits.

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

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

Sample Collection and Handling

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

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

Study-Specific Materials

The investigator will be provided with the following supplies:

- Investigator Site File (includes protocol and Investigator Brochure [IB] for guselkumab)
- Study site investigational product and procedures manual
- Laboratory manual and laboratory supplies
- PRO device and user manual
- Clinician-reported outcome device and user manual
- IWRS Manual
- Sample ICF
- eCRF completion instructions
- Participant recruitment materials
- Participant diary cards
- Camera and associated accessories for clinical photos

- Colorimeter or Mexameter Device & associated accessories/documents/site guide
- Photography site guide

8.1. Efficacy Assessments

8.1.1. 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](#); [Appendix 10](#)). The PASI produces a numeric score that can range from 0 to 72. A PASI 75 response is defined as $\geq 75\%$ improvement in PASI score from baseline; PASI 50, 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 (e.g., training certification) will be considered adequate for this study; however, repeat training prior to start of the study is highly recommended as this training will specifically include PASI evaluation on skin of color.

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

The IGA documents the investigator's assessment of the participants psoriasis at a given timepoint ([Appendix 9](#)). Overall lesions are graded for induration, erythema, and scaling. 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 (e.g., training certification) will be considered adequate for this study; however, repeat training prior to start of the study is encouraged.

8.1.3. Scalp Specific Investigator Global Assessment (ss-IGA)

The Scalp Specific IGA (ss-IGA) is used to evaluate the disease severity of scalp psoriasis ([Appendix 12](#)). The lesions are assessed in terms of the clinical signs of redness, thickness, and scaliness which are scored as: clear (0), almost clear (1), mild disease (2), moderate disease (3), and severe disease (4).

8.1.4. Body or Scalp Surface Area Affected by Psoriasis

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

The Scalp Surface Area (SSA) is a measurement of involved skin on the scalp. The adult SSA is 520-705 cm², meaning that 1% SSA is 5.2-7.1 cm². The thumbprint has an average surface area of 5.5 cm² ± 1.3 cm². Hence, the thumb (in particular, the thumb projection) can be used as a tool for accurate measurement of 1% SSA ([Wambier and King, 2019](#)). The overall SSA affected by psoriasis can thus be estimated based on the participant's thumb.

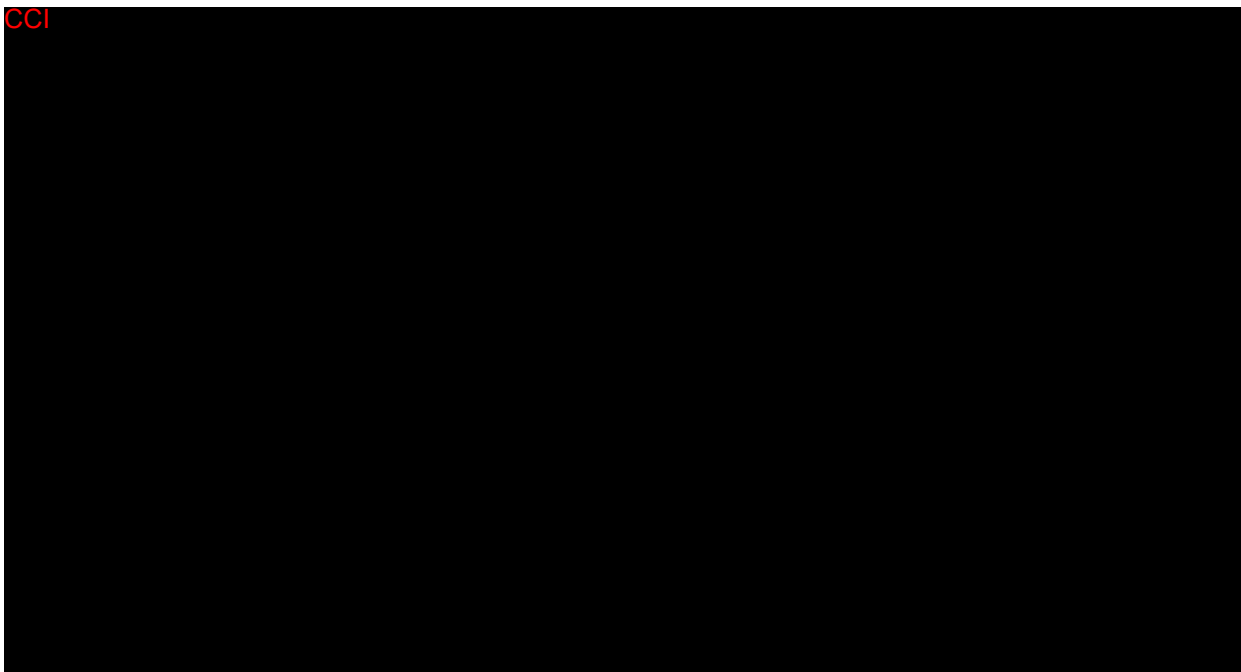
8.1.5. Psoriasis Scalp Severity Index (PSSI)

The Psoriasis Scalp Severity Index (PSSI) measures the extent of psoriasis involvement and the severity of erythema, infiltration, and desquamation of the scalp. Involvement and severity of psoriasis for the PSSI is scored by physicians using a scale from 0 to 72, where 0 = no psoriasis, and higher scores indicating more severe disease ([Appendix 11](#)). The PSSI calculation does not include the face or neck area.

8.1.6. Clinical Photographs

Photographs of study participants will be obtained (according to the separately provided Photography Instructions) at various time points as per Schedule of Activities. Photographic services will be provided through a central photography lab selected by the sponsor. Detailed procedures to assure photographic quality and consistency will be provided separately in a central photography laboratory instruction manual.

CCI



Photographs of the lesions will be used to support screening eligibility, clinical evaluation, rater training and continued monitoring throughout the course of the trial.

If a participant is unable to attend an in-person clinic visit due to COVID-19 or other unforeseen situation, alternative means of acquiring photographs may be implemented by or with approval from the sponsor and per the clinical judgement of the investigator, where feasible and permissible

by local policy. Missing photographs due to COVID-19 illness or quarantine, will be recorded in the eCRF as due to COVID-19.

8.1.7. Post Inflammatory Dyspigmentation Area and Severity Index (PIDASI)

The PIDASI includes 2 characteristics of dyspigmentation (intensity and heterogeneity) and the area involved ([Chiu et al, 2021](#)). The sum of the rating for intensity and heterogeneity is multiplied by the numerical value of the areas involved and weighted for each respective area. This scale was validated by 4 independent raters using both the PIDASI and global severity score as well as MX 18 Mexameter to measure differences in pigmentation of 3 representative lesions within 1 randomly selected body area (face and neck, upper limb, trunk, or lower limb; see [Appendix 13](#)).

8.1.8. Colorimeter or Mexameter Device

Colorimeter or Mexameter Device will be used to help quantify erythema and pigmentation changes. Colorimeter or Mexameter user guide and specific instructions pertaining to this study will be provided separately.

8.1.9. Patient-reported Outcomes

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

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

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

8.1.9.1. Skin Discoloration Impact Evaluation Questionnaire

This 5-question patient-reported outcome questionnaire was initially developed and used in the PIGMENT trial for facial melasma ([Balkrishnan et al, 2004](#); see [Appendix 14](#)). Items from this questionnaire were validated and included as part of the MELASQOL ([Balkrishnan et al, 2004](#)). This PRO was also described in the paper that developed the PIDASI clinician reported outcome that will be utilized in this trial ([Chiu et al, 2021](#)).

8.1.9.2. 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; [Appendix 15](#)). 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

8.1.9.3. Scalp Itch Numeric Rating Scale (NRS)

The Scalp Itch NRS, which closely mirrors the Whole Body Itch NRS, is a single-item scale that asks participants to rate the severity of their scalp itching due to psoriasis by considering their worst level of itching over the past 24 hours ([Wang et al, 2019](#)). The 11-point Scalp Itch NRS ranges from 0 (no scalp itch) to 10 (worst scalp itch imaginable). The Scalp Itch NRS has been validated among patients with moderate to severe plaque psoriasis (see [Appendix 16](#)).

8.1.9.4. DLQI

The DLQI is a dermatology specific quality of life instrument designed to assess the impact of dermatologic disease on a participant's quality of life. It is a 10-item PRO questionnaire that, in addition to evaluating overall quality of life, can be used to assess 6 different aspects that may affect quality of life symptoms: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment. The DLQI produces a numeric score that can range from 0 to 30. A higher score indicates more severe disease (see [Appendix 17](#)).

8.1.9.5. Psoriasis Symptom and Sign Diary (PSSD)

The PSSD includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefits. The 7-day recall version asks the participant to answer the PRO questions thinking about the last 7 days. The PSSD is a self-administered PRO instrument and includes 11 items covering symptoms (itch, pain, stinging, burning and skin tightness) and patient observable signs (skin dryness, cracking, scaling, shedding or flaking, redness and bleeding) using 0 to 10 numerical rating scales for severity. Two subscores will be derived: the psoriasis symptom score and the psoriasis sign score. A higher score indicates more severe disease. For the entire study, from the screening visit through Week 112, participants will complete the 7-day recall version of the PSSD (see [Appendix 18](#)) at study visits as indicated in the Schedule of Activities.

8.1.9.6. Psoriasis Epidemiology Screening Tool (PEST)

The Psoriasis Epidemiology Screening Tool (PEST) is a validated screening tool for psoriatic arthritis ([Ibrahim et al, 2009](#)). It is a 5-item questionnaire developed to help identify PsA at an early stage (see [Appendix 19](#)). CCI

[REDACTED]

[REDACTED]

[REDACTED]

CCI

8.1.9.7. PsAID-12

The PsAID-12 is made up of 0-10 numeric rating scale (NRS) 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 ([Appendix 20](#)). Each domain has a different weight: pain, fatigue, and skin problems are those with a greater effect ([DiCarlo, 2017](#)). CCI

8.2. Safety Assessments

Adverse events will be reported and followed by the investigator as specified in [Section 8.3](#) and [Appendix 5](#).

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

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

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

8.2.1. Physical Examinations

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

8.2.2. Vital Signs

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

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

Weight will be measured per institution standard of care. Patients should wear light clothing and remove his/her shoes before weight is measured.

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

8.2.3. Electrocardiograms

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

During the collection of ECGs, participants should be in a quiet setting without distractions (e.g., television, 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.

8.2.4. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology will be collected as noted in [Appendix 2](#).

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

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

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

8.2.5. Pregnancy Testing

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.

8.2.6. Suicidal Ideation and Behavior Risk Monitoring

The C-SSRS defines 5 subtypes of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior and completed suicide. It will be used as a screening tool to prospectively evaluate suicidal ideation and behavior in this study, as part of a comprehensive evaluation of safety.

The C-SSRS is an investigator-administered questionnaire and will be conducted on the electronic clinical outcomes assessment (eCOA) device provided to the site. Two versions of it will be used in this study: the ‘Baseline/Screening’ version of the C-SSRS will be conducted during the screening visit and the ‘Since Last Visit’ version of the C-SSRS (will be completed at Week 0 and all other site visits through the end of the study. The investigator or trained study-site personnel will interview the participant in a private place and complete the C-SSRS on the eCOA device. At the conclusion of each assessment, the trained personnel administering the C-SSRS will determine the level of suicidal ideation or behavior, if any. They will then determine the next course of action if any level of suicidal ideation or behavior is reported. The participant should not be released from the site until the C-SSRS has been reviewed by the investigator and the participant’s risk has been assessed and follow-up determined, as appropriate.

At screening (within the last 6 months) and Week 0, participants with a C-SSRS rating of Suicidal Ideation with Intention to Act (“Ideation level 4”), Suicidal Ideation with Specific Plan and Intent (“Ideation level 5”), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt), must be determined to not be at risk by the investigator based on an evaluation by a mental health professional (e.g., psychiatrist, psychologist, or appropriately trained social worker or nurse) in order to be randomized. Participants with C-SSRS ratings of Wish to be Dead (“Ideation level 1”), Non-Specific Active Suicidal Thoughts (“Ideation level 2”), Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act (“Ideation level 3”) or non-suicidal self-injurious behavior must be determined not to be at risk by the investigator in order to be randomized. Any questions regarding eligibility of such participants should be discussed with the medical monitor or designee.

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

- No suicidal ideation or behaviors (including self-injurious behavior without suicidal intent): No further action is needed.
- Suicidal ideation levels 1-3 or non-suicidal self-injurious behavior: Participant risk is assessed by the investigator.
- Suicidal ideation levels 4 or 5 or any suicidal behavior: Participant risk assessed and referral to a mental health professional. Interruption or the discontinuation of study intervention should be considered for any participant who reports Suicidal Ideation with Intention to Act (“Ideation level 4”), Suicidal Ideation with Specific Plan and Intent (“Ideation level 5”), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt) on a post-baseline C-SSRS assessment and who is deemed to be at risk

by the investigator based upon evaluation by a mental health professional. If a participant can be adequately treated with psychotherapy and/or pharmacotherapy then the participant, at the discretion of the investigator, may be continued with treatment if agreed to by the medical monitor or designee. Discussion of such participants with the medical monitor or designee is required (Section 7.1).

Any C-SSRS finding, which in the opinion of the investigator is new or considered to be a worsening and clinically significant, should be reported on the AE eCRF.

8.2.7. Concomitant Medication Review

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

8.2.8. 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.

8.2.9. Hypersensitivity Reactions

Before any administration of study intervention at the study site, appropriately trained personnel and medications (e.g., 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 (e.g., urticaria, pruritus, angioedema, wheezing, dyspnea, or hypotension).

8.2.10. Infections

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

8.2.11. Tuberculosis Evaluations

Initial Tuberculosis Evaluation

Participant medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB. The participant should be asked about past testing for TB, including chest imaging results and responses to tuberculin skin or other TB testing. Investigators have the option to use the tuberculin skin test in addition to IGRA testing to screen for latent TB if preferred by local health authorities, or if they believe based on their judgment that both tests are clinically indicated to evaluate a participant at high risk for latent TB.

Participants with a negative IGRA test result are eligible to continue with prerandomization procedures. Participants with a newly identified positive IGRA test result must undergo an evaluation for active or latent TB, or suspected false-positive initial testing, and initiate appropriate treatment if needed (see Section 5.2). Appropriate treatment for latent TB is defined according to local country guidelines for immunocompromised patients. If no local country guidelines for immunocompromised patients exist, US guidelines must be followed.

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

Ongoing Tuberculosis Evaluation

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

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

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

Timely, accurate, and complete reporting and analysis of safety information, including AEs, SAEs, and PQCs, from clinical studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established

Standard Operating Procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of safety information; all clinical studies conducted by the sponsor, or its affiliates will be conducted in accordance with those procedures.

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

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 PQCs can be found in [Appendix 5](#).

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

All Adverse Events

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

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

All AEs with an onset date after the signing of the ICF and up to 30 days after study treatment discontinuation (up to the end of study for participants who enter a continued access program [see [Section 6.6](#)] on the same day as the end of study visit) must be recorded on specific AE pages of the eCRF. Conditions that were already present at the time of informed consent should be recorded on the Medical History form in the eCRF.

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

Serious Adverse Events

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

A possible Hy's law Case is defined by the occurrence of alanine transaminase (ALT)/aspartate transaminase (AST) $\geq 3 \times$ ULN together with Tbili $\geq 2 \times$ ULN or INR > 1.5 (if measured). Any possible Hy's Law case is considered an important medical event and must be reported to the sponsor in an expedited manner, even before all other possible causes of liver injury have been excluded.

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

8.3.2. Method of Detecting Adverse Events and Serious Adverse Events

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

Solicited Adverse Events

Solicited AEs are predefined local 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 Event 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 and the special reporting situation of pregnancy will be followed by the investigator as specified in [Appendix 5: 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 AEs to the regulatory authorities. The Sponsor will also report to the investigator (and the head of the investigational institute where

required) all suspected unexpected serious adverse reactions (SUSARs). The investigator (or Sponsor where required) must report SUSARs to the appropriate IEC/IRB that approved the protocol unless otherwise required and documented by the IEC/IRB. A SUSAR will be reported to regulatory authorities unblinded. Participating investigators and IEC/IRB will receive a blinded SUSAR summary, unless otherwise specified.

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

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

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

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

8.3.5. 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 (e.g., 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 administration of study intervention must be reported by the investigator according to the procedures in Section 10.5.5. Investigators are also advised that active TB is considered a reportable disease in most countries. These events are to be considered serious only if they meet the definition of a serious adverse event.

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 factors that may be associated with psoriasis and/or the response guselkumab. This research may consist of the analysis of 1 or more candidate genes, or the analysis of genetic markers throughout the genome, or analysis of the entire genome (as appropriate) in relation to the psoriasis and guselkumab.

8.6. Biomarkers

Biomarker assessments will be made to examine the biologic response to treatment and to identify biomarkers that are relevant to guselkumab treatment and psoriasis. Assessments will include the evaluation of relevant biomarkers in serum for all participants. Skin biopsies and tape strips will also be collected in participants that consent to this optional part of the study.

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

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

8.6.1. Skin Biomarkers

Skin sampling by tape strips and/or punch biopsies will be collected from participants that consent to this part of the study at sites with the capabilities at time points specified in the SoA. At baseline, skin sampling will be collected from both lesional and adjacent non-lesional areas; at Weeks 16 and 48, only lesional areas will be sampled. Tape stripping allows for the measurement of gene expression as well as levels of proteins or other biomarkers in the stratum corneum. Skin biopsy samples will be performed to investigate differential gene expression during treatment compared with baseline to explore PD, mechanism of action, and differences in treatment response between individuals. In addition, the tissue biopsies may be analyzed for histological readouts and immunohistochemistry to explore the effects of study intervention on cellular composition in skin. Instructions for the collection and shipment of these samples can be found in the laboratory manual.

Participants may consent to participate in either collection of skin biopsies or tape strips (which is a less invasive collection method than a biopsy), or both of these methods for skin sampling.

8.6.2. Serum Biomarkers

Guselkumab has been shown to selectively inhibit IL-23 in psoriasis and produce substantial clinical responses ([Gordon et al, 2019](#)). Serum biomarker analysis will include, but not limited to inflammatory mediators associated with the IL-23/Th17 axis (IL-17A, IL-17F and IL-22), anti-microbial peptides, cardiovascular disease associated markers.

The association between IL-23 and disease progression in patients with carotid atherosclerosis has been previously shown, with a potential involvement of IL-17-related mechanisms ([Abbas et al, 2015](#)). High-sensitivity C-reactive protein (hsCRP) levels will be analyzed in the study, as they are related to the prevention of cardiovascular events and death, independent of lowering serum lipids ([Ridker et al, 2018](#)).

Psoriasis is a chronic inflammatory disease that has been associated with metabolic syndrome (a constellation of cardiovascular risk factors including obesity, hypertension, dyslipidemia, and insulin resistance) due to overlapping inflammatory pathways and genetic susceptibility ([Gelfand and Yeung, 2012](#)). Multiple epidemiologic studies have consistently demonstrated higher prevalence of metabolic syndrome in patients with psoriasis ([Gelfand and Yeung, 2012](#)). Furthermore, the prevalence of metabolic syndrome varies between racial/ethnic groups and in the United States, the prevalence of metabolic syndrome is highest in Hispanics ([Lear and Gasevic, 2019](#)). CCI

CCI

Vitamin D, which has been shown to play a role in metabolic syndrome and improve psoriatic skin lesions, will be measured ([Fu and Vender, 2021](#); [Ames et al, 2021](#)).

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.

8.7. 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 (i.e., 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.

9.1. Statistical Hypotheses

In Cohort A the primary hypotheses of this study are that guselkumab treatment is superior to placebo for the proportion of participants achieving an IGA score of 0/1 and a PASI 90 response at Week 16.

In Cohort B the primary hypotheses of this study are that guselkumab treatment is superior to placebo for the proportion of participants achieving a ss-IGA score of 0/1 and a PSSI 90 response at Week 16.

CCI

9.3. Populations for Analysis Sets

For purposes of analysis, the following populations are defined:

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 one (complete or partial) administration of study intervention. This analysis set will be used for the efficacy analyses.
Safety Analysis Set	All participants who received at least one (complete or partial) administration of study intervention, i.e., the treated population
Immunogenicity Analysis Set (IAS)	All participants who received at least one (complete or partial) administration of guselkumab and who had at least 1 sample obtained after their first administration of guselkumab.
PK Analysis Set (PKAS)	All participants who received at least one complete administration of guselkumab and had at least one valid blood sample drawn for PK analysis.
PD Analysis Set (PDAS)	All participants who received at least one (complete or partial) administration of study intervention.

9.4. Statistical Analyses

The SAP will be finalized prior to the first DBL and unblinding and it will include a more technical and detailed description of the statistical analyses described in this section. This section is a

summary of the planned statistical analyses of the most important endpoints including primary and key secondary endpoints.

9.4.1. General Considerations

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

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

The overall Type I error rate will be controlled at the significance level of 0.05 (2-sided) for each cohort.

9.4.2. Primary Endpoint

For Cohort A, the co-primary endpoints are the proportion of participants achieving an IGA score of 0/1 and a PASI 90 response at Week 16.

For Cohort B, the co-primary endpoints are the proportion of participants achieving a ss-IGA score of 0/1 and a PSSI 90 response at Week 16.

These endpoints will be analyzed based on the estimands defined by the 5 components:

- **Population:** Cohort A: participants with moderate-to-severe plaque psoriasis with extensive body involvement. Cohort B: participants with predominant moderate-to-severe scalp psoriasis without extensive body involvement.
- **Treatment:**
 - Placebo
 - Guselkumab
- **Variable (Endpoints):** For Cohort A, proportion of participants who achieve PASI90 response at Week 16 and Proportion of participants who achieve IGA 0/1 at Week 16. Participants who have intercurrent events (ICEs) 1-3 (defined below) prior to Week 16 will have a zero for PASI90 response and IGA 0/1 response, regardless of the observed data. For Cohort B, Proportion of participants who achieve PSSI90 response at Week 16 and proportion of participants who achieve ss-IGA 0/1 at Week 16. Participants who have intercurrent events ICE 1-3 (defined below) prior to the Week 16 will have a zero for PSSI 90 response and ss-IGA 0/1 response, regardless of the observed data.
- **Intercurrent Events (ICEs):**

The following are the ICEs considered for this trial:

1. Initiated protocol prohibited medications/therapies for psoriasis.
2. Discontinued study intervention due to efficacy (lack of efficacy or AE of worsening of psoriasis).
3. Treatment discontinuation due to trial conduct affected by COVID-19 or other major disruption.
4. Severe treatment non-compliance due to trial conduct affected by COVID-19 or other major disruption (e.g., due to treatment interruption, inability to attend study evaluation visits, etc.).

ICEs in categories 1-2 will be handled with the composite strategy. The composite strategy assesses the treatment effects not only based on the variable measurements, but also based on ICEs. Under the composite strategy, participants with the ICE prior to Week 16 will be treated as non-responders for PASI90 response, IGA cleared (0) or minimal (1) response, PSSI 90 response, and ss-IGA cleared (0) or minimal (1) response for the primary analysis, regardless of the observed data.

ICEs 3-4 will be handled with a treatment policy. Observed value will be used if available. For participants experiencing multiple ICEs, an ICE in categories 1-2 will supersede an ICE in category 3-4.

- **Population level summary:** Difference in proportion of achieving 90% reduction in Psoriasis Area and Severity Index (PASI 90) response and IGA of cleared or minimal (IGA 0/1) at Week 16 between guselkumab and placebo for Cohort A, and a 90% reduction in Psoriasis Scalp Severity Index (PSSI 90) response and ss-IGA of absence of disease or very mild disease (ss-IGA 0/1) at Week 16 between guselkumab and placebo for Cohort B.

CCI

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 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 100.

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.

Physical Examinations

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

9.4.5. Other Analyses

9.4.5.1. Pharmacokinetic and Immunogenicity 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 (i.e., participants with at least 1 sample obtained after their first dose of guselkumab).

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

The incidence of 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.

9.4.5.2. Biomarkers Analyses

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

9.4.5.3. Pharmacogenomic Analyses

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

DNA samples will be used for research related to guselkumab or psoriasis. They may also be used to develop tests/assays related to guselkumab and psoriasis. Pharmacogenomic research may

consist of the analysis of one or more candidate genes or of the analysis of genetic markers throughout the genome (as appropriate) in relation to guselkumab or psoriasis clinical endpoints.

Results will be presented in a separate report.

9.5. Interim Analysis

No interim analyses are planned for this study.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Abbreviations

Abbreviation	Definition
AE	adverse event
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
ANOVA	analysis of variance
aOR	adjusted odds ratio
AST	aspartate aminotransferase
BCG	Bacillus Calmette-Guérin
β-HCG	beta-human chorionic gonadotropin
BLA	Biologic Licensing Application
BQL	below the limit of quantitation
BSA	body surface area
CD	Crohn's disease
CMH	Cochran-Mantel Haenszel
CRF	case report form(s) (paper or electronic as appropriate for this study)
CRP	C-reactive protein
CRO	contract research organization
C-SSRS	Columbia Suicide Severity Rating Scale
DBL	database lock
DILI	drug-induced liver injury
DLQI	Dermatology Life Quality Index
eCOA	electronic clinical outcomes assessment
ECG	electrocardiogram
eDC	electronic data capture
FDA	Food and Drug Administration
FOIA	Freedom of Information Act
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
HBV	hepatitis B virus
HCV	hepatitis C virus
HBsAg	hepatitis B surface antigen
HIV	human immunodeficiency virus
HRT	hormone replacement therapy
hsCRP	high sensitivity C-Reactive Protein
IB	Investigator Brochure
ICE	Intercurrent Events
ICF	informed consent form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IEC	Independent Ethics Committee
IGA	Investigator Global assessment
IgG	immunoglobulin G
IGRA	interferon gamma release assay
IL	interleukin
IM	intra-muscular
IMP	Investigational Medicinal Product
INR	international normalized ratio
IQ	interquartile
IRB	Institutional Review Board

IV	intravenous(ly)
IWRS	interactive web response system
LTE	long-term extension
mAb	monoclonal antibody
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed model for repeated measures
MTX	methotrexate
Nabs	neutralizing antibodies
NCI-CTCAE	National Cancer Institute – Common Terminology Criteria for Adverse Events
NIMP	Non-Investigational Medicinal Product
NRS	numeric rating scale
PASI	Psoriasis Area and Severity Index
PCC	protocol clarification communication
PD	pharmacodynamic(s)
PEST	Psoriasis Epidemiology Screening Tool
PFS	pre-filled syringe
PFS-U	Ultrasafe Passive Needle Guard
PIDASI	Post-inflammatory Dyspigmentation Area and Severity Score
PIPA	Post-inflammatory Pigment Alteration
PK	pharmacokinetic(s)
PQC	Product Quality Complaint
PRO	patient-reported outcome
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
PsA	psoriatic arthritis
PsAID12	Psoriatic Arthritis Impact of Disease 12
PSSD	Psoriasis Symptoms and Signs Diary
PSSI	Psoriasis Scalp Severity Index
q4w/q8w	every 4 weeks/every 8 weeks
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	subcutaneous(ly)
SD	standard deviation
SDIEQ	Skin Discoloration Impact Evaluation Questionnaire
SI	International System of Units
SSA	scalp surface area
ss-IGA	Scalp-specific – Investigator Global Assessment
SoA	Schedule of Activities
SUSAR	suspected unexpected serious adverse reaction
TB	tuberculosis
Tbili	total bilirubin
ULN	upper limit of normal
US	United States

10.2. Appendix 2: Clinical Laboratory Tests

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

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

Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters		
Hematology	Platelet count Red blood cell count Hemoglobin Hematocrit	<u>Red Blood Cell (RBC) Indices:</u> MCV MCH % Reticulocytes	<u>White Blood Cell (WBC) count with Differential:</u> Neutrophils Lymphocytes Monocytes Eosinophils Basophils
	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.		
Clinical Chemistry	Sodium Potassium Calcium Chloride Bicarbonate Blood urea nitrogen (BUN) Creatinine Glucose (non-fasting, acceptable) Aspartate aminotransferase (AST) Alanine aminotransferase (ALT) Gamma-glutamyltransferase (GGT)	Total bilirubin Alkaline phosphatase Creatine phosphokinase (CPK) Albumin Total protein	
	Note: Details of liver chemistry stopping criteria and required actions and follow-up are given in Appendix 7: Liver Safety . Potential Hy’s Law case (ALT or AST ≥3 x ULN and Tbili ≥2 x ULN) reporting requirements are defined in Section 8.3.1.		
Other	- Lipid Panel (fasting required): Total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides - Pregnancy Testing (serum, urine) for women of childbearing potential only - High-sensitivity C-reactive protein (hsCRP) - Serology (HIV antibody, Hepatitis C virus antibody, and Hepatitis B panel which includes: hepatitis B surface antigen [HBsAg], hepatitis B surface antibody [anti-HBs], and hepatitis B core antibody [anti-HBc total])		

	• Interferon gamma release assay (IGRA) testing includes either QuantiFERON-TB® Gold in Tube Test or T-SPOT.TB®(for tuberculosis) • Follicle-stimulating hormone (screening only to confirm potential post-menopausal status) • Vitamin D (1,25 Dihydroxy Blood Test) CCI [REDACTED] • Hemoglobin A1c (HbA1c) • Hepatitis B DNA (screening only for those whose Hepatitis B serology results with HbsAg negative, anti-HBs negative and anti-Hbc total positive) • Hepatitis C RNA (screening only for those who are Hepatitis C antibody positive or with history of Hepatitis C treatment) • Human immunodeficiency virus RNA (screening only for those whose HIV screen is positive)
--	--

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

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

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

These eligibility criteria based on HBV test results are also represented in table below. For participants who are eligible with surface antigen (HBsAg) negative, core antibody (anti-HBc) and/or surface antibody (anti-HBs) positive, and HBV DNA test is negative, HBV DNA quantitation should be monitored according to local guidelines.

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

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

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

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

10.4.1. Regulatory and Ethical Considerations

Investigator Responsibilities

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

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

Protocol Clarification Communications

If text within a final approved protocol requires clarification (e.g., 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.

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

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

Regulatory Approval/Notification

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

Required Pre-study Documentation

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

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

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

- Completed investigator financial disclosure forms from all sub-investigators
- Documentation of sub-investigator qualifications (e.g., curriculum vitae)
- Name and address of any local laboratory conducting tests for the study, and a dated copy of current laboratory normal ranges for these tests, if applicable

Local laboratory documentation demonstrating competence and test reliability (e.g., accreditation/license), if applicable

Independent Ethics Committee or Institutional Review Board

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

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

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

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

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

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

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

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

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

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

Other Ethical Considerations

For study-specific ethical design considerations, refer to Section [4.2.1](#).

10.4.2. Financial Disclosure

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

Refer to Required Pre-study Documentation (above) and contracts for details on financial disclosure.

10.4.3. Informed Consent Process

Each participant (or a legally acceptable representative) must give consent according to local requirements after the nature of the study has been fully explained. The ICF(s) must be signed before 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 or their legally acceptable representatives the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive for the treatment of his or her disease. Finally, they will be told that the investigator will maintain a participant identification register for the purposes of long-term follow up if needed and that their records may be accessed by health authorities and authorized sponsor personnel without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations. By signing the ICF the participant or legally acceptable representative is authorizing such access. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed.

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

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

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

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

10.4.4. Data Protection

Privacy of Personal Data

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

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures

or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of participants confidential.

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

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

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

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

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

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

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

10.4.6. Publication Policy/Dissemination of Clinical Study Data

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

previously published, and any data, including pharmacogenomic or biomarker research data, generated as a result of this study, are considered confidential and remain the sole property of the sponsor. The investigator agrees to maintain this information in confidence and use this information only to accomplish this study and will not use it for other purposes without the sponsor's prior written consent.

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

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

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

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

state that the named authors must have made a significant contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of the data for the work; and drafted the work or revised it critically for important intellectual content; and given final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Registration of Clinical Studies and Disclosure of Results

The sponsor will register and disclose the interim results of clinical studies as required by law. The disclosure of the study results will be performed after the end of study in order to ensure the statistical analyses are relevant.

10.4.7. Data Quality Assurance

Data Quality Assurance/Quality Control

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

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

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

10.4.8. Case Report Form Completion

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

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

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

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

If necessary, queries will be generated in the electronic data capture (eDC) tool. If corrections to a CRF are needed after the initial entry into the CRF, this can be done in either of the following ways:

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

10.4.9. Source Documents

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

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

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

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

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

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
- Pathology report (for those seeking inclusion through route of biopsy proven psoriasis)

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

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

10.4.10. Monitoring

The sponsor will perform on-site monitoring visits as frequently as necessary. The monitor will record dates of the visits in a study site visit log that will be kept at the study site. The first post-initiation visit will be made as soon as possible after enrollment has begun. At these visits, the monitor may compare the data entered into the CRF with the source documents (e.g., hospital/clinic/physician's office medical records). The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the CRF are known to the sponsor and study site personnel and are accessible for verification by the sponsor study site contact. If electronic records are maintained at the study site, the method of verification must be discussed with the study site personnel.

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

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

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

10.4.11. On-Site Audits

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

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

10.4.12. Record Retention

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

Essential documents must be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

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

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

10.4.13. Study and Site Start and Closure

First Act of Recruitment

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

Study/Site Termination

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

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

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

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

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

10.5.1. Adverse Event Definitions and Classifications

Adverse Event

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

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

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

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

Serious Adverse Event

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

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

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

Unlisted (Unexpected) Adverse Event/Reference Safety Information

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

10.5.2. Attribution Definitions

Assessment of Causality

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

Related

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

Not Related

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

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

10.5.3. Severity Criteria

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

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

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

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

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

10.5.4. Special Reporting Situations

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

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

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

10.5.5. Procedures

All Adverse Events

All AEs, regardless of seriousness, severity, or presumed relationship to study intervention, must be recorded using medical terminology in the source document and the CRF. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (e.g., cough, runny nose, sneezing, sore throat, and head congestion should be reported as "upper respiratory infection"). Investigators must record in the CRF 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 (e.g., social reasons such as pending placement in long-term care facility)
- Surgery or procedure planned before entry into the study (must be documented in the eCRF). Note: Hospitalizations that were planned before the signing of the ICF, and where the underlying condition for which the hospitalization was planned has not worsened, will not be considered SAEs. Any AE that results in a prolongation of the originally planned hospitalization is to be reported as a new SAE.

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

Information regarding SAEs will be transmitted to the sponsor 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.

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

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

Procedures

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

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

10.5.7. Contacting Sponsor Regarding Safety, Including Product Quality

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

10.6. Appendix 6: Contraceptive 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 10.5.4, Pregnancy and Appendix 5.

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 >45 years of age with amenorrhea for at least 12 months or any age with amenorrhea for at least 6 months and a serum follicle-stimulating hormone [FSH] level >40 IU/L. If there is a question about menopausal status in women on hormone replacement therapy (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, or bilateral salpingectomy, or bilateral oophorectomy.
 - Has congenital abnormalities resulting in sterility.

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

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

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

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

Examples of Contraceptives

EXAMPLES OF CONTRACEPTIVES^a ALLOWED DURING THE STUDY FOR PARTICIPANTS OF CHILDBEARING POTENTIAL INCLUDE:
USER INDEPENDENT Highly Effective Methods That Are User Independent <i>Failure rate of <1% per year when used consistently and correctly.</i>
• Implantable progestogen-only hormone contraception associated with inhibition of ovulation^b • Intrauterine device (IUD) • Intrauterine hormone-releasing system (IUS) • Bilateral tubal occlusion • Azoospermic partner (<i>vasectomized or due to medical cause</i>) <i>(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.)</i>
USER DEPENDENT Highly Effective Methods That Are User Dependent <i>Failure rate of <1% per year when used consistently and correctly.</i>
• 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 <i>(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.)</i>
NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION DURING THE STUDY (not considered to be highly effective - failure rate of $\geq 1\%$ 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)

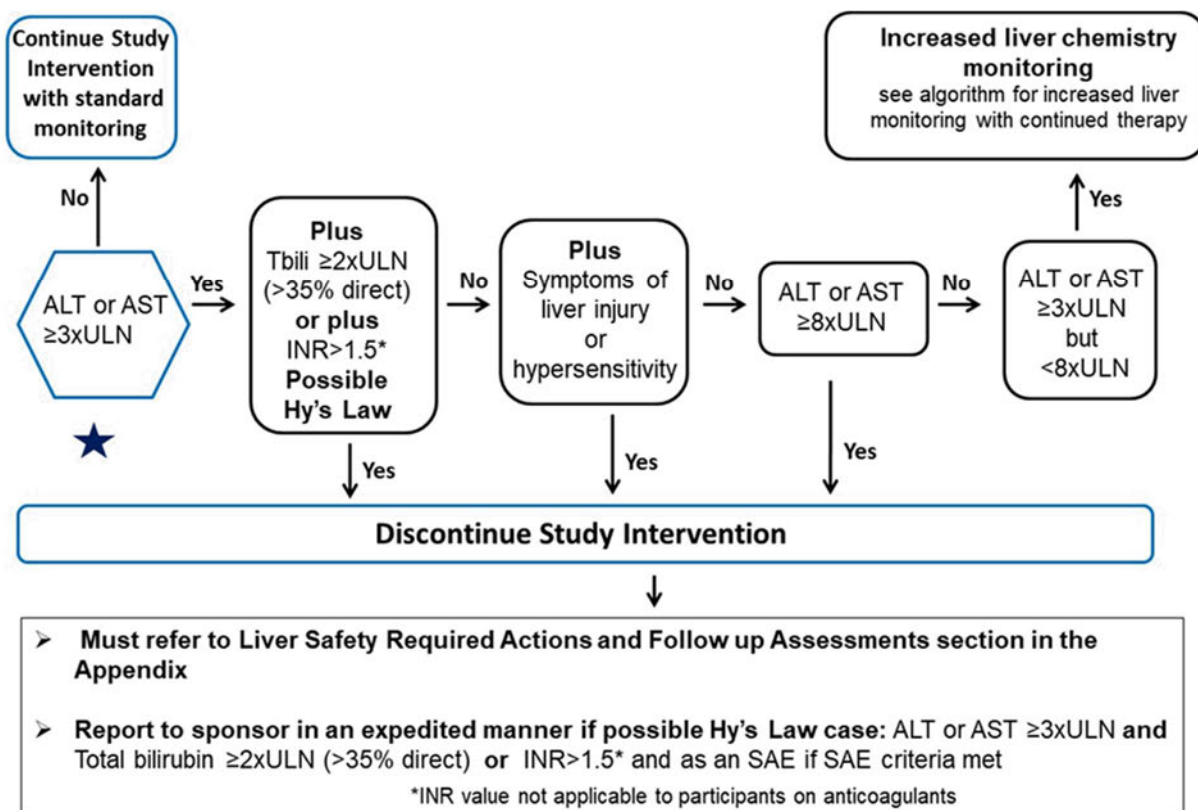
- a) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.
- b) Hormonal contraception may be susceptible to interaction with the study intervention, 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).

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

10.7A. STOPPING CRITERIA AND INCREASED MONITORING ALGORITHMS

Liver Chemistry Stopping Criteria Algorithm

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



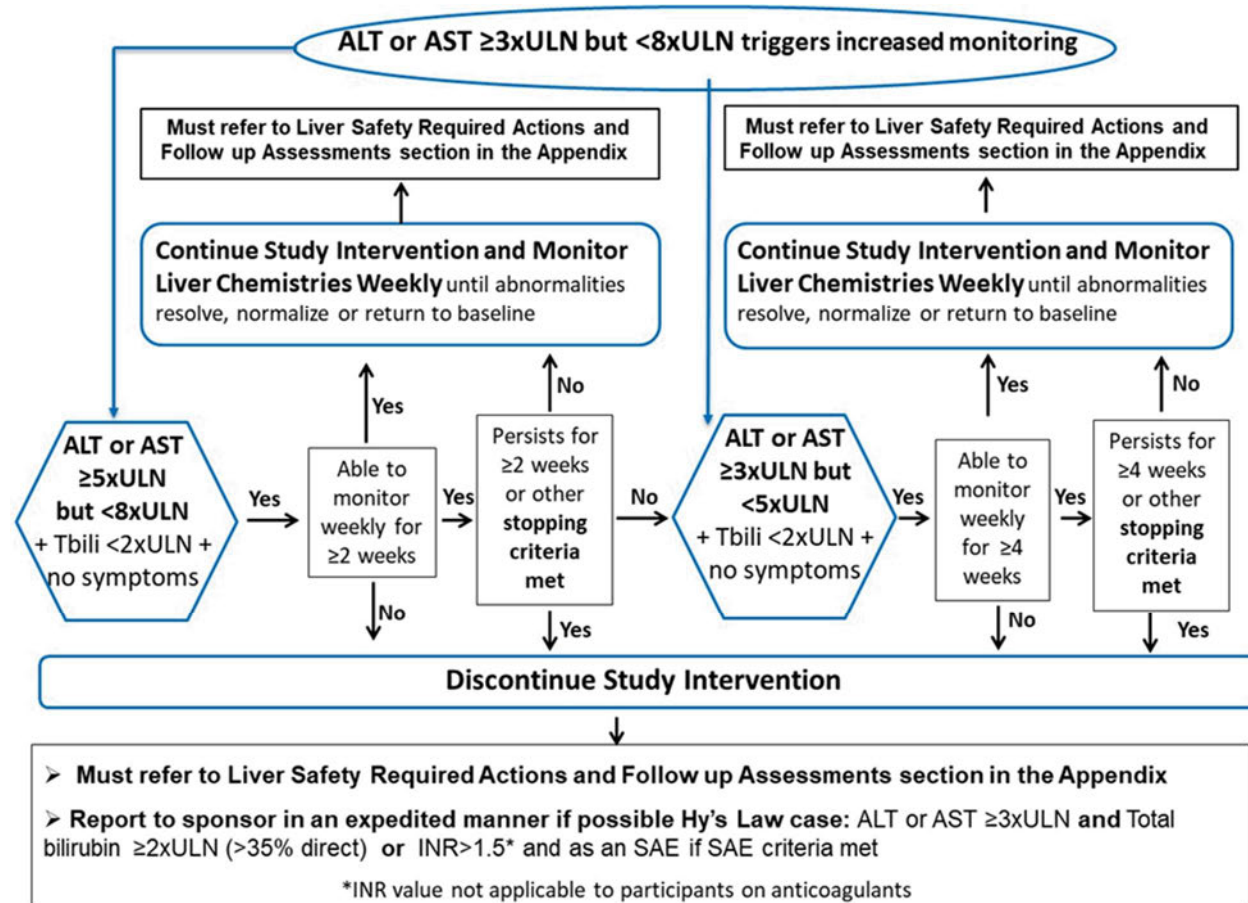
Abbreviations: ALT = alanine transaminase; AST = aspartate transaminase, INR = international normalized ratio; SAE = serious adverse event; Tbili = Total bilirubin; ULN = upper limit of normal.

Refer to [Appendix 7B](#): Liver Safety Required Actions and Follow-up Assessments

Increased Monitoring Algorithm

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

Liver Chemistry Increased Monitoring Algorithm with Continued Study Intervention for Participants with ALT or AST $\geq 3 \times \text{ULN}$ but $< 8 \times \text{ULN}$



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

Refer to [Appendix 7B](#): Liver Safety Required Actions and Follow-up Assessments

B. LIVER SAFETY REQUIRED ACTIONS AND 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 $\geq 8 \times \text{ULN}$
ALT or AST-Increase	ALT or AST $\geq 5 \times \text{ULN}$ but $< 8 \times \text{ULN}$ persists for ≥ 2 weeks ALT or AST $\geq 3 \times \text{ULN}$ but $< 5 \times \text{ULN}$ persists for ≥ 4 weeks
Bilirubin^{1,2}	ALT or AST $\geq 3 \times \text{ULN}$ and total bilirubin $\geq 2 \times \text{ULN}$
INR²	ALT or AST $\geq 3 \times \text{ULN}$ and international normalized ratio (INR) > 1.5
Cannot Monitor	ALT or AST $\geq 5 \times \text{ULN}$ but $< 8 \times \text{ULN}$ and cannot be monitored weekly for ≥ 2 weeks ALT or AST $\geq 3 \times \text{ULN}$ but $< 5 \times \text{ULN}$ and cannot be monitored weekly for ≥ 4 weeks
Symptomatic³	ALT or AST $\geq 3 \times \text{ULN}$ associated with symptoms (new or worsening) believed to be related to liver injury or hypersensitivity
Suggested Actions, Monitoring, and Follow up Assessments	
ACTIONS • Immediately stop study intervention • Report the event to the Sponsor within 24 hours • Complete the hepatic event form and complete an SAE eCRF if the event also met the criteria for an SAE² • Perform follow-up assessments as described in the FOLLOW UP ASSESSMENTS column • Monitor the participant until liver chemistry test abnormalities resolve, stabilize, or return to baseline (see MONITORING) MONITORING If ALT or AST $\geq 3 \times \text{ULN}$ AND total bilirubin $\geq 2 \times \text{ULN}$ or INR > 1.5: • Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, total bilirubin, direct bilirubin, and INR⁶) and perform liver event FOLLOW UP ASSESSMENTS within 24 hours • Monitor participant twice weekly until liver chemistry test abnormalities resolve, stabilize, or return to baseline • A specialist or hepatology consultation is recommended If ALT or AST $\geq 3 \times \text{ULN}$ AND total bilirubin $< 2 \times \text{ULN}$ and INR ≤ 1.5:	FOLLOW UP ASSESSMENTS • Viral hepatitis serology^{4, 7} • Obtain blood sample for pharmacokinetic (PK)⁵ analysis within 1 week of the event of ALT or AST $\geq 3 \times \text{ULN}$. • Obtain serum creatine phosphokinase (CPK), lactate dehydrogenase (LDH), gamma-glutamyltransferase [GGT], and glutamate dehydrogenase [GLDH], and serum albumin⁷ • Fractionate bilirubin, if total bilirubin $\geq 2 \times \text{ULN}$ • Obtain complete blood count with differential to assess eosinophilia • Record the appearance or worsening of clinical symptoms of liver injury, or hypersensitivity, on the CRF as per CRF completion guidelines • Record use of concomitant medications (including acetaminophen, herbal remedies, recreational drugs, and other over-the-counter medications) • Record alcohol use on the hepatic event form <u>If ALT or AST $\geq 3 \times \text{ULN}$ AND total bilirubin $\geq 2 \times \text{ULN}$ or INR > 1.5</u> 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 or gamma globulins⁸ • Serum acetaminophen adduct assay, when available, to assess potential acetaminophen

- Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, total bilirubin, direct bilirubin, and INR⁶) 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	(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
--	--

- 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 $\geq 3 \times \text{ULN}$ **and** total bilirubin $\geq 2 \times \text{ULN}$. Additionally, if serum bilirubin fractionation testing is unavailable, **record the absence/presence of detectable urinary bilirubin on dipstick** which is indicative of direct bilirubin elevations suggesting liver injury.
- All events of ALT or AST $\geq 3 \times \text{ULN}$ **and** total bilirubin $\geq 2 \times \text{ULN}$ or ALT or AST $\geq 3 \times \text{ULN}$ **and** INR > 1.5 (if measured), may indicate severe liver injury (**possible 'Hy's Law'**) **and must be reported to sponsor in an expedited manner** using the SAE form, even before all other possible causes of liver injury have been excluded. A confirmed Hy's law case must be reported as an SAE. The INR stated threshold value will not apply to participants receiving anticoagulants.
- 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).
- Includes hepatitis A immunoglobulin M (IgM) antibody; HBsAg; hepatitis C RNA; hepatitis C antibody, cytomegalovirus IgM antibody; Epstein-Barr viral capsid antigen IgM antibody (or if unavailable, heterophile antibody or monospot testing); and hepatitis E IgM antibody.
- 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.
- These are included in the Liver Safety kit. Verify lab selections with study lab manual.
- These are included in the Liver Follow Up Kit. Verify lab selections with study lab manual.
- These are included in the DILI kit. Verify lab selections with the study lab manual.

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

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

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

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

- Restart refers to resuming study intervention following liver chemistry events for which there are clear underlying causes (other than DILI) (e.g., biliary obstruction, pancreatic events, hypotension, acute viral hepatitis). Furthermore, restart is not permitted following liver stopping event when the underlying cause was alcohol-related hepatitis. Approval by the Sponsor for study intervention restart can be considered when:
 - The investigator requests consideration for study intervention restart if liver chemistry events have a clear underlying cause (e.g., biliary obstruction, pancreatic events, hypotension, acute viral hepatitis) and liver chemistry tests have improved to normal or are within 1.5 x baseline and ALT or AST <3xULN.
 - The principal 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 (e.g., lapatinib, abacavir, amoxicillin/clavulanate), the presence of the marker should be excluded.
 - There is no evidence of alcoholic-related hepatitis.
 - IRB/IEC has been informed regarding restart of study intervention.

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

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

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

References:

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

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

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

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

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

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

10.8. Appendix 8: Study Conduct During a Natural Disaster

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 it becomes necessary to discontinue participation in the study, the procedures outlined in the protocol for discontinuing study intervention will be followed.

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

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

If the participant has tested positive for COVID-19, the investigator should contact the sponsor's responsible medical officer 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 infection should be summarized in the clinical study report.

ADDITIONAL ELEMENTS, WHERE APPLICABLE:

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

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

- procurement of study intervention by patients (or designee) or shipment of study intervention from the study site directly to patients for at-home administration (including the potential for patient self-administration of study intervention)
- laboratory assessments using a suitably accredited local laboratory; for selected measures (e.g., urine pregnancy), home testing may be employed
- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented with the prefix “COVID-19-related” in the eCRF.
 - other relevant study data elements impacted by the pandemic should also be documented as “COVID-19-related” in eCRFs and/or other study systems, as directed by detailed Sponsor guidance. These may include missed/delayed/modified study visits or assessments/dosing, and instances where temporary measures such as those above are implemented.
- The Sponsor will evaluate the totality of impact of COVID-19 on collection of key study data and additional data analyses will be outlined in study SAP(s).

Precaution: for those who may carry a higher risk for severe COVID-19 illness (e.g., 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.

10.9. Appendix 9: Investigator Global Assessment (IGA)

Induration (I) (averaged over all lesions; use the National Psoriasis Foundation Reference card for measurement)

0 = no evidence of plaque elevation

1 = minimal plaque elevation, = 0.25 mm

2 = mild plaque elevation, = 0.5 mm

3 = moderate plaque elevation, = 0.75 mm

4 = severe plaque elevation, > 1 mm

Erythema (E) (averaged over all lesions)

0 = no evidence of erythema, hyperpigmentation may be present

1 = faint erythema

2 = light red coloration

3 = moderate red coloration

4 = bright red coloration

Scaling (S) (averaged over all lesions)

0 = no evidence of scaling

1 = minimal; occasional fine scale over less than 5% of the lesion

2 = mild; fine scale predominates

3 = moderate; coarse scale predominates

4 = severe; thick, scale predominates

Total Average = $(I + E + S) / 3$ (average will be calculated in the device but not displayed. Numeric result will be included in data transfer)

Investigator's Global Assessment based upon above Total Average

0 = Cleared, except for residual discoloration

1 = Minimal - majority of lesions have individual scores for $I + E + S / 3$ that averages 1

2 = Mild - majority of lesions have individual scores for $I + E + S / 3$ that averages 2

3 = Moderate - majority of lesions have individual scores for $I + E + S / 3$ that averages 3

4 = Severe - majority of lesions have individual scores for $I + E + S / 3$ that averages 4

Note: Scores should be rounded to the nearest whole number. If total ≤ 1.49 , score = 1; if total ≥ 1.50 , score = 2.

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

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

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

The scoring system for the signs of the disease (erythema, induration, and scaling) are:

0 = none,

1 = slight,

2 = moderate,

3 = severe, and

4 = very severe.

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

0 = no involvement

1 = 1% to 9% involvement

2 = 10% to 29% involvement

3 = 30% to 49% involvement

4 = 50% to 69% involvement

5 = 70% to 89% involvement

6 = 90% to 100% involvement

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

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

The PASI formula is: $PASI = 0.1 (E_h + I_h + S_h) A_h + 0.3 (E_t + I_t + S_t) A_t + 0.2 (E_u + I_u + S_u) A_u + 0.4 (E_l + I_l + S_l) A_l$ Where E = erythema, I = induration, S = scaling, and A = area

10.11. Appendix 11: PSSI

The PSSI is the result of a modified area score with the severity score, which is equivalent to the PASI severity score.

Assessment of extent of scalp psoriasis

1	<10%
2	10–29%
3	30–49%
4	50–69%
5	70–89%
6	90–100%

Assessment of clinical symptoms (erythema, induration and desquamation)

0	absent
1	slight
2	moderate
3	severe
4	severest possible

PSSI = Sum of scores for erythema, induration and desquamation × involved area (range 0–72).

Thaçi D, Daiber W, Boehncke WH, Kaufmann R. Calcipotriol solution for the treatment of scalp psoriasis: evaluation of efficacy, safety and acceptance in 3,396 patients. *Dermatology*. 2001;203(2):153-6. doi: 10.1159/000051731. PMID: 11586015.

10.12. Appendix 12: Scalp Specific Investigator Global Assessment (ssIGA)

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

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

10.13. Appendix 13: Post-inflammatory Dyspigmentation Area and Severity Score (PIDASI)

Postinflammatory Dyspigmentation Area and Severity Score (PIDASI)

Characteristic	Lesion score	Face and Neck	Upper Limbs	Trunk	Lower Limbs
Intensity	Intensity: [‡] -9: Significantly lighter -6: Moderately lighter -3: Slightly lighter 0: similar to 3: Slightly darker 6: Moderately darker 9: Significantly darker than surrounding skin				
Heterogeneity	Heterogeneity [‡] 0: minimal 1/-1: slight 2/-2: mild 3/-3: marked 4/-4: maximum (negative value indicated hypopigment)				
Add together each of the 2 scores for each body region to give 4 separate sums (A).					
Lesion Score Sum (A)					
Percentage area	Area score	Face and Neck	Upper Limbs	Trunk	Lower Limbs
Area Score (B)	0 = 0%				
<i>Degree of involvement as a</i>	1 = 1% - 9%				
<i>percentage for each body</i>	2 = 10% - 29%				
<i>region affected (score each</i>	3 = 30% - 49%				
<i>region with score between 0-</i>	4 = 50% - 69%				
<i>6)</i>	5 = 70% - 89%				
	6 = 90% - 100%				
Multiply Lesion Score Sum (A) by Area Score (B), for each body region, to give 4 individual subtotals (C).					
Subtotals (C)					
Multiply each of the Subtotals (C) by amount of body surface area represented by that region, i.e. x 0.4 for head, x 0.3 for upper body, x 0.1 for trunk, and x 0.2 for lower limbs. [†]					
Body Surface Area		x 0.4	x 0.3	x 0.1	x 0.2
Totals (D)					
Add together each of the scores for each body region to give the final PASI Score (from -78 to 78)					

PIDASI score = (0.4*H (A)*H(B)) + (0.3*UL(A)*UL (B)) + (0.2*LL(A)* LL(B)) + (0.1*T(A)*T(B)); H: face and neck, UL: upper limb, LL: lower limb, T: trunk

[†]The weighting for each variable was arbitrarily assigned based on feedback from patients, who were asked to rank these variables in order of importance.

[‡]High positive intensity and heterogeneity scores indicate more severe hyperpigmentation and higher heterogeneity within hyperpigmented lesions, respectively. In contrast, low negative values suggest more severe hypopigmentation and higher heterogeneity within hypopigmented lesions.

Investigator: _____

PIDASI Score=

Date: _____

10.14. Appendix 14: Skin Discoloration Impact Evaluation Questionnaire

Question	Response
“Over the last week... ...how embarrassed or self-conscious have you been because of your skin?”	Very much A lot A little Not at all
...how much have people focused on your skin discoloration rather than on what you are saying or doing?”	Very much A lot A little Not at all
...how much has your skin discoloration made you feel unattractive to others?”	Very much A lot A little Not at all
...how much effort have you put into hiding your skin discoloration from others?”	Very much A lot A little Not at all
...how much has your skin affected any of your social or leisure activities?”	Very much A lot A little Not at all

10.15. Appendix 15: PROMIS-29 Questionnaire (version 2.0)**PROMIS–29 Profile v2.0**

Please respond to each question or statement by marking one box per row.

<u>Physical Function</u>		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
PFA11 1	Are you able to do chores such as vacuuming or yard work?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA21 2	Are you able to go up and down stairs at a normal pace?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA23 3	Are you able to go for a walk of at least 15 minutes?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA53 4	Are you able to run errands and shop?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
<u>Anxiety</u>						
In the past 7 days...		Never	Rarely	Sometimes	Often	Always
EDANX01 5	I felt fearful	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX40 6	I found it hard to focus on anything other than my anxiety	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX41 7	My worries overwhelmed me	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX53 8	I felt uneasy	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
<u>Depression</u>						
In the past 7 days...		Never	Rarely	Sometimes	Often	Always
EDDEP04 9	I felt worthless	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP06 10	I felt helpless	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP29 11	I felt depressed	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP41 12	I felt hopeless	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
<u>Fatigue</u>						
During the past 7 days...		Not at all	A little bit	Somewhat	Quite a bit	Very much
HI7 13	I feel fatigued	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
AN3 14	I have trouble <u>starting</u> things because I am tired	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

<u>Fatigue</u>						
In the past 7 days...		Not at all	A little bit	Somewhat	Quite a bit	Very much
FATEXP41 15	How run-down did you feel on average? ...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP40 16	How fatigued were you on average?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
<u>Sleep Disturbance</u>						
In the past 7 days...		Very poor	Poor	Fair	Good	Very good
Sleep109 17	My sleep quality was.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
In the past 7 days...		Not at all	A little bit	Somewhat	Quite a bit	Very much
Sleep116 18	My sleep was refreshing.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep20 19	I had a problem with my sleep	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep44 20	I had difficulty falling asleep	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
<u>Ability to Participate in Social Roles and Activities</u>						
		Never	Rarely	Sometimes	Usually	Always
SRPPER11 _CaPS 21	I have trouble doing all of my regular leisure activities with others	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER18 _CaPS 22	I have trouble doing all of the family activities that I want to do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER23 _CaPS 23	I have trouble doing all of my usual work (include work at home)	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER46 _CaPS 24	I have trouble doing all of the activities with friends that I want to do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
<u>Pain Interference</u>						
In the past 7 days...		Not at all	A little bit	Somewhat	Quite a bit	Very much
PAININ9 25	How much did pain interfere with your day to day activities?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ22 26	How much did pain interfere with work around the home?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ31 27	How much did pain interfere with your ability to participate in social activities? ..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ34 28	How much did pain interfere with your household chores?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Pain Intensity**In the past 7 days...**

Global07 29	How would you rate your pain on average?.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
		0	1	2	3	4	5	6	7	8	9	10
		No pain										Worst imaginable pain

10.16. Appendix 16: Scalp Itch Numeric Rating Scale (NRS)**SCALP ITCH NUMERIC RATING SCALE**

Please rate the itching severity of your scalp due to your psoriasis by circling the number that best describes your worst level of itching in the past 24 hours.

0	1	2	3	4	5	6	7	8	9	10
0 = No scalp itch									10 = Worst scalp itch imaginable	

10.17. Appendix 17: DLQI

Hospital No:

Date:

Name:

Score:

Address:

Diagnosis:

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

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

- | | | | |
|-----|---|--------------|--------------------------|
| | | Not relevant | ☐ |
| 9. | Over the last week, how much has your skin caused any sexual difficulties ? | Very much | ☐ |
| | | A lot | ☐ |
| | | A little | ☐ |
| | | Not at all | ☐ |
| | | Not relevant | ☐ |
| 10. | Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time? | Very much | ☐ |
| | | A lot | ☐ |
| | | A little | ☐ |
| | | Not at all | ☐ |
| | | Not relevant | ☐ |

Please check you have answered EVERY question. Thank you.

©AY Finlay, GK Khan, April 1992 www.dermatology.org.uk, this must not be copied without the permission of the authors.

10.18. Appendix 18: Psoriasis Symptom and Sign Diary (PSSD) Based on 7-day Recall

Psoriasis Symptom and Sign Diary (7-day version)

Please answer each question to the best of your ability. There are no right or wrong answers. Please pay close attention to the time period of interest. These questions ask you to think about the **past 7 days**.

Individuals with psoriasis may experience a range of symptoms. Please indicate how severe each of the following skin symptoms was in the **past 7 days**. Please select only one number for each item on the 0 to 10 scale (0=Absent and 10= Worst imaginable).

1. Rate the severity of itch in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
2. Rate the severity of dryness in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
3. Rate the severity of cracking in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
4. Rate the severity of skin tightness in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
5. Rate the severity of scaling (build-up of skin) in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
6. Rate the severity of shedding or flaking in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
7. Rate the severity of redness in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
8. Rate the severity of bleeding in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
9. Rate the severity of burning in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
10. Rate the severity of stinging in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable
11. Rate the severity of pain from your psoriasis lesions in the past 7 days.	0 Absent	1	2	3	4	5	6	7	8	9	10 Worst imaginable

10.19. Appendix 19: PEST

Have you ever had a swollen joint (or joints)?

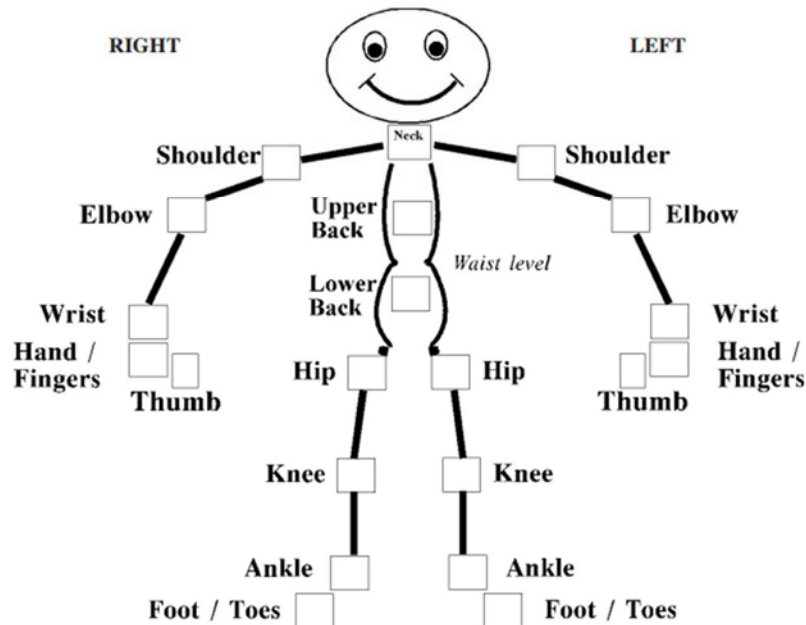
Has a doctor ever told you that you have arthritis?

Do your finger nails or toe nails have holes or pits?

Have you had pain in your heel?

Have you had a finger or toe that was completely swollen and painful for no apparent reason?

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



10.20. Appendix 20: PsAID-12

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

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

1. Pain

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

For
office
use only

Result
x3

☐

2. Fatigue

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

No

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Totally exhausted

Result
x2

☐

3. Skin problems

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result
x2

☐

4. Work and/or leisure activities

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result
x2

☐

5. Functional capacity

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

No

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme difficulty

Result
x2

☐

6. Discomfort

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result
x2

☐

7. Sleep disturbance

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

No

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme difficulty

Result
x2

☐

8. Coping

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

Very well

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Very poorly

For office use only

Result x1

☐
9. Anxiety, fear and uncertainty

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result x1

☐
10. Embarrassment and/or shame

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result x1

☐
11. Social participation

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result x1

☐
12. Depression

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

None

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 Extreme

Result x1

☐

THANK YOU FOR ANSWERING THIS QUESTIONNAIRE

PsAID12 SCORING AND CALCULATION RULES

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

Calculation

PsAID final value =

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

The total is divided by 20.

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

Missing data imputation

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

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

10.21. Appendix 21: Protocol Amendment History

This is an original protocol.

REFERENCES

- Abbas A, Gregersen I, Holm S, et al. Interleukin 23 levels are increased in carotid atherosclerosis: possible role for the interleukin 23/interleukin 17 axis. *Stroke*. 2015;46:793-799.
- Abokwidir M, Davis SA, Fleischer AB, et al. Use of the Emergency Department for dermatologic care in the United States by ethnic group. *J of Derm Treatment*. 2015;26:1-14.
- Abrouk M, Lee K, Brodsky M, et al. Ethnicity affects the presenting severity of psoriasis. *J Am Acad Dermatol*. 2017;77:180-182.
- Alexis AF, Blackcloud P. Psoriasis in skin of color: epidemiology, genetics, clinical presentation, and treatment nuances. *J Clin Aesthet Dermatol*. 2014;7:16-24.
- Ames BN, Grant WB, Willett WC. Does the high prevalence of vitamin D deficiency in African Americans contribute to health disparities? *Nutrients*. 2021;13:499.
- Amico S, Barnette T, Dequidt L, et al. Characteristics of postinflammatory hyper- and hypopigmentation in patients with psoriasis: A survey study. *J Am Acad Dermatol*. 2020;83:1188-1191.
- Ashbaugh AG, Ekelem C, Landaverde Y, et al. Psoriatic Disease in the US Latino Population: A Comprehensive Review. *Am J Clin Dermatol*. 2020;21:265-274.
- Bagel J, Callis Duffin C, Moore A, et al. The effect of secukinumab on moderate-to-severe scalp psoriasis: Results of a 24-week, randomized, double-blind, placebo-controlled phase 3b study. *J Am Acad Dermatol*. 2017;77:667-674.
- Balkrishnan R, Kelly AP, McMichael A, Torok H. Improved quality of life with effective treatment of facial melasma: the pigment trial. *J Drugs Dermatol*. 2004;3:377-381.
- Chiu HY, Chang Liao NF, Hui RC, et al. Measurement and prediction of the severity of postinflammatory dyspigmentation after resolution of psoriatic plaques in patients treated with biologic therapy. *J Am Acad Dermatol*. 2021:S0190-9622(21)00333-9.
- Crowley J. Scalp psoriasis: an overview of the disease and available therapies. *J Drugs Dermatol*. 2010;9:912-918.
- Davis EC, Callender VD. Postinflammatory hyperpigmentation: a review of the epidemiology, clinical features, and treatment options in skin of color. *J Clin Aesthet Dermatol*. 2010;3:20-31.
- DiCarlo M, Becciolini A, Lato V, et al. The 12-item Psoriatic Arthritis Impact of Disease Questionnaire: construct validity, reliability, and interpretability in a clinical setting. *J Rheumatol*. 2017;44:279-285.
- Ferreira BI, Abreu JL, Dos Reis APG, et al. Psoriasis and associated psychiatric disorders: A systematic review on etiopathogenesis and clinical correlation. *J Clin Aesthet Dermatol*. 2016;9:36-43.
- Fischer AH, Shin GB, Gelfand JM, et al. Health care utilization for psoriasis in the United States differs by race: An analysis of the 2001-2013 Medical Expenditure Panel Surveys. *J Am Acad Dermatol*. 2018;78:200-203.
- Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. *Arch Dermatol*. 1988;124:869-871.
- Fredriksson T, Pettersson U. Severe psoriasis—oral therapy with a new retinoid. *Dermatologica*. 1978;157:238-244.
- Fu LW, Vender R. Systemic role for vitamin D in the treatment of psoriasis and metabolic syndrome. *Dermatol Res Pract*. 2021;2011:276-279.
- Gelfand JM, Yeung H. Metabolic syndrome in patients with psoriatic disease. *J Rheumatol Suppl*. 2012;89:24-28.
- George SMC, Taylor MR, Farrant PBJ. Psoriatic alopecia. *Clin Exp Dermatol*. 2015; 40:717-721.
- Gordon KB, Armstrong AW, Foley P, et al. Guselkumab efficacy after withdrawal is associated with suppression of serum IL-23-regulated IL-17 and IL-22 in psoriasis: VOYAGE 2 Study. *J Invest Dermatol*. 2019;139:2437-2446.
- Ibrahim GH, Buch MH, Lawson C, Waxman R, Helliwell PS. Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and the development of a new instrument: the Psoriasis Epidemiology Screening Tool (PEST) questionnaire. *Clin Exp Rheumatol*. 2009;27:469-474.

Kaufman BP, Alexis AF. Psoriasis in skin of color: Insights into the epidemiology, clinical presentation, genetics, quality-of-life impact, and treatment of psoriasis in non-white racial/ethnic groups. *Am J Clin Dermatol*. 2018;19:405-423.

Kelly AP, et al. 2016 Taylor and Kelly's Dermatology for Skin of Color, McGraw-Hill Education.

Kimball AB, Jacobson C, Weiss S, et al, The psychosocial burden of psoriasis. *Am J Clin Dermatol*. 2005;6:383-392.

Lakhan MK, Lynch M. Skin pigmentation. *Medicine*. 2021;49:447-452.

Lear SA, Gasevic D. Ethnicity and Metabolic Syndrome: Implications for Assessment, Management and Prevention. *Nutrients*. 2019;12:15.

CCI

McMichael AJ, Vachiramon V, Guzman-Sanchez DA, et al. Psoriasis in African-Americans: a caregivers' survey. *J Drug Dermatol*. 2012;11:478-482.

Pathak MA. In memory of Thomas Bernhard Fitzpatrick. *J Invest Dermatol*. 2004;122:20-21.

Rawlings AV. Ethnic skin types: are there differences in skin structure and function? *International J Cosmetic Science*. 2006;28:79-93.

Ridker PM, MacFadyen JG, Everett BM, et al. Relationship of C-reactive protein reduction to cardiovascular event reduction following treatment with canakinumab: a secondary analysis from the CANTOS randomised controlled trial. *Lancet*. 2018;391:319-328.

Rodriguez F, Harrison RW, Wojdyla D, et al. Lost to follow-up and withdrawal of consent in contemporary global cardiovascular randomized clinical trials. *Crit Pathways in Cardiol*. 2015;14:150-153.

Shah SK, Arthur A, Yang YC, et al, A retrospective study to investigate racial and ethnic variations in the treatment of psoriasis with etanercept. *J Drugs Dermatol*. 2011;10:866-872.

Takeshita J, Gelfand JM, Li P, et al. Psoriasis in the US Medicare Population: Prevalence, treatment, and factors associated with biologic use. *J Invest Dermatol*. 2015;135:2955-2963.

Takeshita J, Eriksen WT, Raziano VT, et al. Racial differences in perceptions of psoriasis therapies: implications for racial disparities in psoriasis treatment. *J Invest Dermatol*. 2019;139:1672-1679.

Taylor S, Grimes P, Lim J, et al. Postinflammatory hyperpigmentation. *J Cutaneous Med Surg*. 2009;13:183-191.

Tripathi R, Knusel KD, Ezaldein HH, et al. Association of demographic and socioeconomic characteristics with differences in use of outpatient dermatology services in the United States. *JAMA Dermatol*. 2018;154:1286-1291.

Wambier CG, King BA. Rule of thumb: A simple tool to estimate 1% scalp surface area. *J Am Acad Dermatol*. 2019;81:630-631.

Wang Y, Coyne K, Sofen H, et al. Qualitative analysis and reproducibility assessment of the Scalp Itch Numeric Rating Scale among patients with moderate to severe plaque psoriasis of the scalp. *J Dermatolog Treat*. 2019;30:775-783.

Zampieron A, Buja A, Fusco M, et al. Quality of life in patients with scalp psoriasis. *G Ital Dermatol Venereol*. 2015;150:309-316.

INVESTIGATOR AGREEMENT

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

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

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

Signature: _____ Date: _____

(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

Telephone Number: _____

Signature: _____ Date: _____

(Day Month Year)

Sponsor's Responsible Medical Officer:Name (typed or printed): PPD, Senior Director, US Medical Affairs, DermatologyInstitution: Janssen Research & DevelopmentSignature: [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	03-Nov-2022 21:16:53 (GMT)	Document Approval