

## Statistical Analysis Plan

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**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**

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**Protocol CNTO1959PSO3018; Phase 3b**

**CNTO1959 (guselkumab)**

**Status:** Approved  
**Date:** 23 June 2023  
**Prepared by:** Janssen Research & Development, LLC  
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**Compliance:** The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

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**VERSION HISTORY****Table 1 – SAP Version History Summary**

| <b>SAP Version</b> | <b>Approval Date</b> | <b>Change</b>  | <b>Rationale</b> |
|--------------------|----------------------|----------------|------------------|
| 1                  | 23 June 2023         | Not Applicable | Initial release  |
|                    |                      |                |                  |
|                    |                      |                |                  |
|                    |                      |                |                  |
|                    |                      |                |                  |

## 1. INTRODUCTION

This statistical analysis plan contains definitions of analysis sets, derived variables, and statistical methods for the analysis of efficacy, safety, pharmacokinetics (PK), and pharmacodynamics (PD), and Immunogenicity in the CNTO1959PSO3018 study. Guselkumab (CNTO 1959) is a fully human immunoglobulin G1 lambda (IgG1 $\lambda$ ) monoclonal antibody (mAb) that inhibits the biological activity of interleukin (IL)-23 for the treatment of psoriasis.

### 1.1. Objectives and Endpoints

#### Primary Objective

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 with or 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)  $\geq 12$ , and Investigator's Global Assessment (IGA)  $\geq 3$  at baseline.

**Cohort B**, with scalp psoriasis as the predominant form of psoriasis, will enroll participants with scalp-specific IGA (ss-IGA)  $\geq 3$ , Psoriasis Scalp Severity Index (PSSI)  $\geq 12$ , and scalp surface area (SSA)  $\geq 30\%$ , and at least one psoriasis plaque outside of the scalp at baseline.

#### Secondary Objectives

Secondary objectives of this study are to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and immunogenicity for guselkumab treatment in participants with Cohort A and Cohort B.

**Table 2: The study objectives and endpoints are listed below.**

| Objectives                                                                                                                                                                                                                                                       | Cohort A (Predominant Body Psoriasis)<br>Endpoints                                                                                                                                                                                                                                                                                     | Cohort B (Predominant Scalp Psoriasis)<br>Endpoints                                                                                                                                                                                                                                                                               |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Primary</b>                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                   |
| 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 <ol style="list-style-type: none"> <li>Proportions of participants who achieve an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) response at Week 16,</li> <li>Proportion of participants who achieve a Psoriasis Area and Severity Index (PASI) 90 response at Week 16.</li> </ol> | The co-primary endpoints <ol style="list-style-type: none"> <li>Proportions of participants who achieve a scalp specific (ss)-IGA score of absence of disease (0) or very mild disease (1) at Week 16.</li> <li>Proportion of participants who achieve a Psoriasis Scalp Severity Index (PSSI) 90 response at Week 16.</li> </ol> |
| <b>Major Secondary</b>                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                   |
| To evaluate the efficacy of guselkumab on                                                                                                                                                                                                                        | 1. The proportion of participants who achieve an IGA score of cleared (0) at Week 16.                                                                                                                                                                                                                                                  | 1. The change from baseline in PSSI score at Week 16.                                                                                                                                                                                                                                                                             |

| Objectives                                                                             | Cohort A (Predominant Body Psoriasis)<br>Endpoints                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Cohort B (Predominant Scalp Psoriasis)<br>Endpoints                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| additional measures of body and scalp psoriasis.                                       | <ol style="list-style-type: none"> <li>2. The proportion of participants who achieve a PASI 100 response at Week 16.</li> <li>3. The change from baseline in PASI score at Week 16.</li> <li>4. The change from baseline in body surface area (BSA) at Week 16.</li> <li>5. The time to <math>\geq 90\%</math> reduction in PASI through Week 16.</li> <li>6. The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16.</li> <li>7. The proportion of participants who achieve <math>\geq 4</math>-point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch <math>\geq 4</math> at baseline.</li> <li>8. The change from baseline in PSSD symptom score at Week 16.</li> <li>9. The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score <math>\geq 1</math>.</li> </ol> | <ol style="list-style-type: none"> <li>2. The change from baseline in scalp surface area (SSA) at Week 16.</li> <li>3. The proportion of participants who achieve a ss-IGA score of absence of disease (0) at Week 16.</li> <li>4. The proportion of participants who achieve a PSSI 100 response at Week 16.</li> <li>5. The time to <math>\geq 90\%</math> reduction in PSSI through Week 16.</li> <li>6. The change from baseline in DLQI score at Week 16.</li> <li>7. The proportion of participants who achieve <math>\geq 4</math>-point reduction (improvement) from baseline in the scalp itch numeric rating scale (NRS) score at Week 16, among participants with baseline scalp itch <math>\geq 4</math> at baseline.</li> <li>8. The change from baseline in PSSD symptom score at Week 16.</li> <li>9. The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score <math>\geq 1</math>.</li> </ol> |
| <b>Other Secondary Endpoint</b>                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 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)<br>Endpoints | Cohort B (Predominant Scalp Psoriasis)<br>Endpoints |
|------------|----------------------------------------------------|-----------------------------------------------------|
|            | CCI                                                |                                                     |

| Objectives | Cohort A (Predominant Body Psoriasis)<br>Endpoints | Cohort B (Predominant Scalp Psoriasis)<br>Endpoints |
|------------|----------------------------------------------------|-----------------------------------------------------|
|            | CCI                                                |                                                     |

| Objectives                                                                   | Cohort A (Predominant Body Psoriasis)<br>Endpoints                                                                                                  | Cohort B (Predominant Scalp Psoriasis)<br>Endpoints                                                                                                |
|------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                              | CCI                                                                                                                                                 |                                                                                                                                                    |
| To evaluate pharmacokinetics and immunogenicity of guselkumab                | <ol style="list-style-type: none"> <li>1. The serum concentrations of guselkumab.</li> <li>2. The incidence of antibodies to guselkumab.</li> </ol> | <ol style="list-style-type: none"> <li>1. The serum concentrations of guselkumab</li> <li>2. The incidence of antibodies to guselkumab.</li> </ol> |
| To evaluate pharmacodynamic (PD) effects of guselkumab in psoriasis patients | <ol style="list-style-type: none"> <li>1. The change from baseline in cellular and molecular biomarkers in skin and blood.</li> </ol>               | <ol style="list-style-type: none"> <li>1. The change from baseline in cellular and molecular biomarkers in skin and blood.</li> </ol>              |
| To evaluate pharmacogenomic of guselkumab in psoriasis patients              | <ol style="list-style-type: none"> <li>1. The genetic factors associated with clinical response and PD.</li> </ol>                                  | <ol style="list-style-type: none"> <li>1. The genetic factors associated with clinical response and PD.</li> </ol>                                 |

## 1.2. Study 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). The co-primary endpoints of IGA 0/1 and PASI 90 for participants in Cohort A or the co-primary endpoints of ss-IGA 0/1 and PSSI 90 for participants in Cohort B at baseline will be evaluated at Week 16. Comparisons are planned between guselkumab and placebo at Week 16.

Approximately 200 patients (~100 per cohort) will be enrolled and randomized 3:1 in each cohort to receive either guselkumab 100 mg or placebo for the first 16 weeks. The two cohorts are:

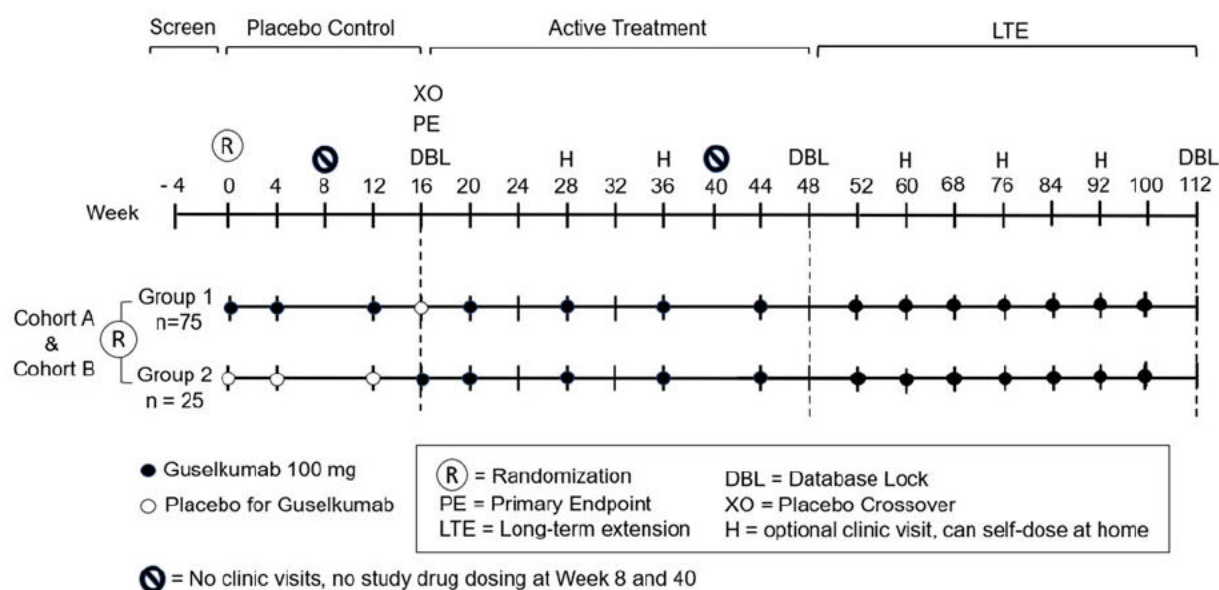
- Cohort A will be participants with predominant moderate-to-severe plaque psoriasis (at screening & baseline, BSA  $\geq 10\%$ , PASI  $\geq 12$ , IGA  $\geq 3$ )
- Cohort B will be participants with predominant moderate-to-severe scalp psoriasis (at screening & baseline, ss-IGA  $\geq 3$ , SSA  $\geq 30\%$ , PSSI  $\geq 12$ , 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 one cohort is filled and closed, then all subsequent participants who meet criteria for both cohorts will be randomized to the remaining open cohort. In each cohort,

participants will be randomized to guselkumab or placebo in a 3:1 ratio CCI

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 Week 16 DBL 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. A diagram of the study design is provided in Figure 1.

**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.

### Week 0 through Week 16 (Placebo Controlled Period)

- Group I (n=75): guselkumab 100 mg at Weeks 0, 4 and 12. Placebo will be administered at Week 16 to maintain the blind.
- Group II (n=25): placebo at Weeks 0, 4, and 12 followed by guselkumab 100 mg at Weeks 16.

### Week 0 through Week 48 (Placebo Controlled and Active Treatment Period)

- Group I (n=75): guselkumab 100 mg at Weeks 0, 4, 12, and every 8 weeks (q8w) thereafter through Week 48
- Group II (n=25): placebo at Weeks 0, 4, and 12 followed by guselkumab 100 mg at Weeks 16, 20, and q8w thereafter through Week 48.

**From Week 52 through Week 112 (Long-Term Extension Treatment Period)**

- Groups I and II: Participants will continue to receive guselkumab 100 mg q8w at Week 52 and through Week 100 and a final follow-up visit at Week 112.

A placebo control will be used to establish the frequency and magnitude of changes in clinical endpoints that may occur in the absence of active intervention. Randomization will be used to minimize bias in the assignment of participants to intervention groups, to increase the likelihood that known and unknown participant attributes (eg, demographic and baseline characteristics) are evenly balanced across intervention groups, and to enhance the validity of statistical comparisons across intervention groups. Blinded intervention will be used to reduce potential bias during data collection and evaluation of clinical endpoints. Comparisons are planned between guselkumab and placebo at Week 16.

**2. STATISTICAL HYPOTHESES****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 (**primary hypothesis**).

If the primary hypothesis of the co-primary endpoints for cohort A achieves the statistical significance at 2-sided  $\alpha$ -level of 0.05, the cohort A of the study will be considered positive.

**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 (**primary hypothesis**).

If the primary hypothesis of the co-primary endpoints for cohort B achieves the statistical significance at 2-sided  $\alpha$ -level of 0.05, the cohort B of the study will be considered positive.

**3. SAMPLE SIZE DETERMINATION****Co-Primary Endpoints**

The co-primary endpoints for Cohort A are:

1. Proportions of participants who achieve an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) response at Week 16
2. Proportion of participants who achieve a Psoriasis Area and Severity Index (PASI) 90 response at Week 16.

The co-primary endpoints for Cohort B are:

1. Proportions of participants who achieve a scalp specific (ss)-IGA score of absence of disease (0) or very mild disease (1) at Week 16.
2. Proportion of participants who achieve a Psoriasis Scalp Severity Index (PSSI) 90 response at Week 16.

A total sample size of approximately 200 participants across the two cohorts, based on a 3:1 guselkumab:placebo randomization ratio in each of the 100-participant cohort (ie, with approximately 75 participants assigned to guselkumab and 25 assigned to placebo in each cohort), will provide at least 90% power

CCI

CCI

### Major Secondary Endpoints

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CCI

#### 4. POPULATIONS (ANALYSIS SETS) FOR ANALYSIS

The analysis sets and the descriptions are defined below in [Table 5](#).

**Table 5: Analysis Sets**

| Analysis Sets                                   | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Enrolled                                        | All participants who signed the informed consent form (ICF). This analysis set will be used for summarizing the overall study completion/withdrawal information.                                                                                                                                                                                                                                                                                                          |
| Full Analysis Set (FAS) - Efficacy Analysis Set | All participants who were randomized in the study. This analysis set will be used for the efficacy analyses.                                                                                                                                                                                                                                                                                                                                                              |
| CCI                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Per Protocol Analysis Set (PPAS)                | <p>The per protocol analysis set includes a subset of participants in the FAS CCI who were in compliance with the protocol. Specifically, the per-protocol population includes all randomized participants except those:</p> <ol style="list-style-type: none"> <li>Who did not meet the inclusion criteria 2, 5a or 5b in the protocol as listed below: <ul style="list-style-type: none"> <li>Be non-white, as per self-reported race/ethnicity.</li> </ul> </li> </ol> |

| Analysis Sets | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|               | <ul style="list-style-type: none"> <li>○ Have moderate to severe plaque psoriasis defined by an involved BSA <math>\geq 10\%</math>, PASI <math>\geq 12</math>, and IGA <math>\geq 3</math> at screening and at baseline (Cohort A) or have moderate to severe scalp psoriasis defined by scalp surface area <math>\geq 30\%</math>, PSSI <math>\geq 12</math>, and ss-IGA <math>\geq 3</math>, and at least one plaque outside of the scalp at screening and at baseline (Cohort B).</li> </ul> <p>2. Who violated the exclusion diagnosis criteria 2 and 3 in the protocol as listed below:</p> <ul style="list-style-type: none"> <li>○ Has a nonplaque form of psoriasis (eg, erythrodermic, guttate, or pustular)</li> <li>○ Has current drug-induced psoriasis (eg, a new onset of psoriasis or an exacerbation of psoriasis from beta blockers, calcium channel blockers, or lithium).</li> </ul> <p>3. Who violated the exclusion criteria (EC) pertaining to prior psoriasis medication criteria (EC# 1,4, 5) in the protocol as listed below:</p> <ul style="list-style-type: none"> <li>○ Received any of the following treatment regimens specified in the timeframes below: <ul style="list-style-type: none"> <li>(a) Has previously received at any time any therapeutic agent directly targeted to IL-23 including but not limited to guselkumab, <u>risakizumab</u>, tildrakizumab, or mirikizumab</li> <li>(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.</li> <li>(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.</li> <li>(d) Within 12 weeks of first dose of study drug: ustekinumab, ixekizumab, secukinumab, or brodalumab.</li> <li>(e) Within 8 weeks of first dose of study drug: infliximab or golimumab (IV).</li> <li>(f) Within 6 weeks of first dose of study drug: adalimumab or certolizumab</li> <li>(g) Within 4 weeks of first administration of study drug: <ul style="list-style-type: none"> <li>i. Etanercept</li> </ul> </li> </ul> </li> </ul> |

| Analysis Sets | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|               | <ul style="list-style-type: none"> <li>ii. Phototherapy (e.g., ultraviolet B [UVB], psoralen ultraviolet A [PUVA] or other phototherapy)</li> <li>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).</li> <li>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.</li> </ul> <p>(h) Within 2 weeks of first administration of study drug</p> <ul style="list-style-type: none"> <li>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 taparino or roflumilast), and coal tar or its derivatives.</li> <li>ii. Traditional Taiwanese, Korean, or Chinese medicines or other herbal or ethnic treatments</li> </ul> <ul style="list-style-type: none"> <li>○ 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.</li> <li>○ 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.</li> </ul> <p>4. Who did not complete the specified exposure to study agent as outline below:</p> <ul style="list-style-type: none"> <li>○ Participants randomized to placebo who received guselkumab prior to Week 16</li> </ul> |

| Analysis Sets                        | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|--------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                      | <ul style="list-style-type: none"> <li>○ Participants randomized to guselkumab at Week 0 but did not receive all scheduled guselkumab administrations or received one or more placebo administrations prior to Week 16.</li> </ul> <p>5. Participants who discontinued the study agent due to unsatisfactory therapeutic effect or an adverse event (AE) of worsening of psoriasis, or participants who started prohibited medications and continued receiving study agents prior to the timepoint of per-protocol analysis will be included in the per-protocol analysis and ICE rules specified will apply. Participants who had a major protocol deviation as specified above and were excluded from the per protocol analysis will also be summarized.</p> |
| Safety Analysis Set (SAS)            | The safety analysis set will include all participants who received at least 1 (partial or complete) dose of study agent (the treated population). In the safety analyses, participants will be analyzed per the treatment they received, regardless of the treatments they are randomized.                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Immunogenicity Analysis Set (IAS)    | The immunogenicity analysis set will include all participants who received at least 1 (partial or complete) dose of guselkumab and who have appropriate samples for detection of antibodies to guselkumab (ie, Participants with at least 1 sample obtained after their first dose of guselkumab). In the immunogenicity analyses, participants will be analyzed per the treatment they received, regardless of the treatments they are randomized.                                                                                                                                                                                                                                                                                                            |
| Pharmacokinetics Analysis Set (PKAS) | The PK analysis set will include all participants who received at least 1 guselkumab injection and had at least 1 PK sample evaluated for serum guselkumab concentration. In the PK analyses, participants will be analyzed according to the treatment they actually received, regardless of the treatments they are randomized to.                                                                                                                                                                                                                                                                                                                                                                                                                            |
| PD Analysis Set (PDAS)               | All participants received at least one (complete or partial) administration of study intervention.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |

## 5. STATISTICAL ANALYSES

### 5.1. General Considerations

In general, descriptive statistics will include counts and percentages for categorical variables, and mean, standard deviation (SD), median, interquartile (IQ) range, minimum, and maximum for continuous variables. Graphical data displays may also be used to summarize the data.

In this study, efficacy will be primarily evaluated through Week 100. Evaluation of PK, immunogenicity, PD, biomarker, safety, selected participant information data, as well as selected additional efficacy measures will be conducted through Week 112.

Analyses and summaries (including overtime summaries) in general will be carried out during the following study periods when appropriate:

1. From Week 0 through Week 16 (Placebo Controlled Period)
2. From Week 0 through Week 48 (Placebo Controlled and Active Treatment Period)
3. From Week 52 through Week 112 (Long-Term Extension Treatment Period)
4. From Week 0 through Week 112

### **Binary Response Efficacy Endpoints**

For binary response efficacy endpoints, treatment comparisons will generally be performed using a Cochran-Mantel-Haenszel (CMH) test CCI

■ Difference in response rates between guselkumab and placebo groups at Week 16 with 95% confidence interval (CI) will be calculated.

In case of rare events, the Fisher's Exact test will be used for treatment comparisons in binary response endpoints. The proportion difference between guselkumab group and placebo and the exact confidence interval will be calculated. In these analyses, participants with missing data will be imputed as not achieving the response.

### **Continuous Efficacy Endpoints**

For continuous efficacy endpoints, treatment comparisons will be performed using a Mixed Effects Model for Repeated Measures (MMRM), which relies on the Missing at Random (MAR) assumption for the missing responses. Under the assumption of MAR, the missing data will be accounted for through correlation of repeated measures in the model.

The explanatory variables of the MMRM model will include treatment group, visit, baseline efficacy endpoint score, CCI an interaction term of visit with treatment group, and an interaction term of visit with baseline efficacy endpoint score. An unrestricted (UN) variance-covariance matrix for repeated measures within a participant will be used. If the model with unstructured covariance structure does not converge, alternative covariance structures will be tried in the following order, with the first structure that converges being used in the analysis: heterogeneous Toeplitz (TOEPH) or autoregressive of order 1 (AR (1)).

ANCOVA model will be used when there is only one post baseline efficacy endpoint collected from baseline through Week 16. The ANCOVA model will include treatment group, baseline efficacy endpoint score CCI as explanatory factors. In the ANCOVA model, participants with missing data will not be imputed.

The baseline measurement is defined as the closest measurement taken prior to or at the time of the first study agent administration date unless otherwise specified. The treatment difference between a guselkumab group and the placebo group will be estimated by the difference in the Least Square (LS) means. The 95% CIs for the differences in LS means and p-values will be calculated.

## **Time to an Event Efficacy Endpoints**

Survival analysis techniques such as life-table estimates will be calculated for time to event endpoints for Cohort A and Cohort B for the 2 treatment groups. CCI

### **5.1.1. Visit Windows**

#### **5.1.1.1. Visit Windows for Dosing and PK Analysis**

All post-baseline visits from Baseline through Week 16 will have a visit window of  $\pm 7$  days counting from week 0 as Day 1. After Week 48 will have a visit window of  $\pm 14$  days. The final safety visit (12 weeks after the last dose in participants who discontinued study treatment) will have a visit window of  $\pm 14$  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.

For PK analyses, if a participant has an administration outside the visit window at a visit, the concentration data collected at and after that visit will be excluded from the by-visit data analyses.

### **5.2. Participant Dispositions**

The number of participants screened will be summarized overall by each cohort.

Disposition will include tabulations, by randomized treatment group, of the number of participants who discontinued study agent administration, the primary reasons for discontinuation of study agent administration, the number of participants who discontinued study participation, and the primary reason for discontinuation of study participation.

Tabulations by randomized treatment group will also be provided for participants who met 1 or more ICE criteria as defined in Section 5.3.2.

Disposition data will be summarized for each cohort through the study periods that include but are not limited to the following:

1. From Week 0 through Week 16 (Placebo Controlled Period)
2. From Week 0 through Week 48 (Placebo Controlled and Active Treatment Period)
3. From Week 16 through Week 48 (Active Treatment Period)
4. From Week 52 through Week 112 (Long-Term Extension Treatment Period)
5. From Week 0 through Week 112 (Overall Study)

In addition, participants who were randomized but never treated and participants who were unblinded during the study will be presented in data listings.

### 5.3. Primary Endpoint(s) Analysis

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 analyses will be compared between the guselkumab treatment and the placebo treatment group for each of the cohort and tested at a 2-sided  $\alpha$ -level of 0.05. Within the cohort if one of the comparisons is not significant at the 2-sided  $\alpha$ -level of 0.05, the co-primary endpoints will be considered not significant.

#### Composite Strategy

The Composite Strategy assesses the treatment effects not only based on the variable measurements, but also based on intercurrent events (ICE) defined in Section 5.4.2.1.

If a participant met any of the ICEs in categories 1-2, then it will be handled with the composite strategy. 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.

#### Treatment Policy Strategy

If a participant met any of the ICEs 3-4, then it 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.

#### 5.3.1. Definition of Endpoint(s)

##### 5.3.1.1. Investigator's Global Assessment (IGA)

The Investigator's Global Assessment (IGA) documents the investigator's assessment of the Participant's psoriasis at a given time point. 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). The analysis for IGA will be based on participants randomized at week 0 with baseline IGA score  $\geq 3$ . Primary efficacy endpoints related to the IGA score is defined below:

**IGA Cleared or Minimal Responder.**

Participants who achieve an IGA score of cleared (0) or minimal (1) will be considered IGA cleared or minimal responders.

**5.3.1.2. 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. In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities. Each of these areas is assessed separately for erythema, induration, and scaling, which are each rated on a scale of 0 to 4. The PASI produces a numeric score that can range from 0 (no psoriasis) to 72. A higher score indicates more severe disease. The analysis for PASI will be based on participants randomized at week 0 with baseline PASI score  $\geq 12$ . Primary efficacy endpoint related to the PASI score is defined below:

**PASI 90 Responder**

Participants with  $\geq 90\%$  improvement in PASI from baseline will be considered PASI 90 responders.

**5.3.1.3. Evaluation of Regional Psoriasis Disease****5.3.1.3.1. Scalp-Specific Investigator's Global Assessment (ss-IGA)**

The ss-IGA instrument is used to evaluate the disease severity of scalp psoriasis. The lesions are assessed in terms of the clinical signs of redness, thickness, and scaliness which are scored as: absence of disease (0), very mild disease (1), mild disease (2), moderate disease (3), or severe disease (4). The analysis for ss-IGA will be based on participants randomized at week 0 with baseline ss-IGA score  $\geq 3$ . Primary efficacy endpoints related to the ss-IGA score is defined below:

**ss-IGA Absence of Disease or Very Mild Disease Responder**

Participants who achieve ss-IGA score of absence of disease (0) or very mild disease (1) will be consider ss-IGA absence of disease or very mild disease responders.

**5.3.1.3.2. 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. The PSSI calculation does not include the face or neck area. The analysis for PSSI will be based on participants randomized at week 0 with baseline PSSI score  $\geq 12$ . Primary efficacy endpoints related to the PSSI score is defined below:

**PSSI 90 Responder**

Participants with  $\geq 90\%$  improvement in PSSI from baseline will be considered PSSI 90 responders.

### 5.3.2. Estimand

#### 5.3.2.1. Primary Estimand (Estimand 1)

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 following 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) 1-2 (defined below) prior to Week 16 will be considered as not achieved 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 1-2 (defined below) prior to the Week 16 will be considered as not achieved for PSSI 90 response and ss-IGA 0/1 response, regardless of the observed data.

- **Intercurrent Events (ICEs): ICE categories 1 to 4 are presented below.** ICE categories 1 to 2 will follow the composite strategy, where participants who meet them prior to Week 16 will be considered nonresponders 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. ICE categories 3 to 4 will follow the treatment policy strategy, where participants who meet them prior to week 16, will used the observed values. For participants experiencing multiple ICEs, an ICE in categories 1 to 2 will supersede an ICE in categories 3 to 4.

1. Initiated protocol prohibited medications/therapies for psoriasis, except for the following
  - a) If the prohibited medication is a corticosteroid and was used for an indication other than psoriasis and for  $\leq 2$  weeks (short term use)
  - b) If the prohibited medication is a corticosteroid and the mode of delivery is inhaled, otic, ocular, nasal or other route of mucosal delivery.
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 (eg, due to treatment interruption, inability to attend study evaluation visits, etc.).
  4. Severe treatment and/or study visit non-compliance due to trial conduct affected by COVID-19 or other major disruption (eg, due to treatment interruption, inability to attend study evaluation visits, etc.).
- **Population level summary:** Difference in proportion of participants achieving 90% reduction in PASI 90 response and IGA of cleared or minimal (IGA 0/1) at Week 16 between guselkumab and placebo for Cohort A. Difference in proportion of participants achieving 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.

### 5.3.2.2. Supplementary Estimand (Estimand 2)

In this supplementary estimand, all intercurrent events are addressed by the **composite strategy**. The components of the supplementary estimand and variable (endpoint) are the same as those for the primary estimand.

Under Estimand 2, participants who have intercurrent events ICE 1-4 prior to Week 16 will have non-response for the primary endpoint response, regardless of the observed data.

### 5.3.3. Analysis Methods

The co-primary endpoints within each cohort will be analyzed at Week 16 DBL based on the primary estimand. If a participant experiences ICE of 1 or 2 prior to Week 16, they 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. If a participant experiences ICE of 3 or 4 then observed value will be used if available.

This primary analysis will include all data collected up to and including Week 16 for all participants in the primary efficacy analysis set. In these primary efficacy analyses, data from all randomized participants will be analyzed according to their assigned treatment group.

For each of the cohort the co-primary endpoints at Week 16 will be summarized for each treatment group respectively.

To address the primary objective, a 2-sided ( $\alpha=0.05$ ) CMH chi-squared test CCI [REDACTED] will be used for the co-primary endpoints.

Statistical analysis for both primary (Estimand 1) and supplementary estimand (Estimand 2) are the same.

The overall Type I error rate will be controlled at the significance level of 0.05. The study will be considered positive if the guselkumab group is significantly different from the placebo group for both co-primary endpoints for each cohort.

Both co-primary endpoints will be tested at a 2-sided  $\alpha$ -level of 0.05. If one of the comparisons is not significant at the 2-sided  $\alpha$ -level of 0.05, the co-primary endpoints will be considered not significant.

If the comparison is positive for the co-primary endpoints, the testing will continue to the major secondary endpoints for each of the cohort.

Participants with ICE categories of 1 or 2 before Week 16 will be considered as non-responders at Week 16. For participants with ICE categories of 3-4, observed value will be utilized in the analysis. After accounting for the ICEs for the primary estimand, participants with missing data of the primary endpoint at Week 16 will be considered as non-responders.

#### 5.3.4. Subgroup Analyses

For the consistency of treatment effect for each of the cohort, the co-primary endpoints will be evaluated for the subgroups defined in Section 5.7.8, using the primary estimand (**Estimand 1**). For each subgroup analysis, the analysis set is the individual subgroup (Section 5.7.8) of the primary efficacy analysis set.

- In cohort A, for each of the subgroups, the difference between the guselkumab treatment group and placebo group in the proportion of participants achieving IGA score of cleared (0) or minimal (1) and the proportion of the PASI 90 responders at Week 16 and its 95% confidence interval (when the numbers of participants permit) will be calculated.
- In cohort B, for each of the subgroups, the difference between the guselkumab treatment group and placebo group in the proportion of participants achieving ss-IGA score of absence of disease (0) or very mild disease (1) and the proportion of the PSSI 90 response at Week 16 and its 95% confidence interval (when the numbers of participants permit) will be calculated.

In addition, the co-primary endpoints at Week 16 by country and investigator site will be summarized.

CCI

#### 5.3.5. Summary of Analyses Related to the Primary Endpoint

Table 6 below provides an overview of the analyses related to the co-primary endpoints, the estimands, the analysis sets, the data handling rules to be used, and the analysis methods and summary statistics.

**Table 6: Summary of Analyses Related to the Co- Primary Endpoint at Week 16 for Each Cohort**

| Analysis (Analysis Set)                                                                                                                                                                                        | Missing data                                                                                                                                      | Analysis method/Summary statistics                                                                                                                                                                                                                                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Analyses based on <b>Primary Estimand (Estimand 1)</b> , where ICEs 1-2 are handled by the <b>composite strategy</b> , and ICE 3-4 is handled by the <b>treatment policy strategy</b>                          |                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                        |
| <b>Full Analysis Set (FAS) for cohort A</b><br>Or <b>CCI</b> for cohort B                                                                                                                                      | Missing data due to missed visits or missed data collection. Participants with missing data are considered to be non-responders' imputation (NRI) | <ul style="list-style-type: none"> <li>Summaries of the proportion of participants who achieved the endpoint.</li> <li>Treatment difference (guselkumab group-placebo group) and 95% CI.</li> <li>P-values based on CMH chi-squared test <b>CCI</b> and represents the comparison with placebo.</li> </ul>             |
| <b>Subgroup Analyses (Individual subgroup levels defined in Section 5.7.8, FAS for cohort A Or CCI for cohort B)</b>                                                                                           | Missing data due to missed visits or missed data collection. Participants with missing data are considered to be non-responders' imputation (NRI) | <ul style="list-style-type: none"> <li>Summaries of the proportion of participants who achieved the endpoint by subgroup.</li> <li>Treatment difference (guselkumab group-placebo group) and 95% CI.</li> <li>P-values based on CMH chi-squared test <b>CCI</b> and represents the comparison with placebo.</li> </ul> |
| Analyses based on <b>Supplementary Estimand (Estimand 2)</b> , where all the intercurrent events are addressed by the <b>composite strategy</b> in which non-responder is used after the occurrence of an ICE. |                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                        |
| <b>Supplementary Analysis 1 FAS for cohort A or CCI for cohort B</b>                                                                                                                                           | Missing data due to missed visits or missed data collection. Participants with missing data are considered to be non-responders' imputation (NRI) | <ul style="list-style-type: none"> <li>Summaries of the proportion of participants who achieved the endpoint.</li> <li>Treatment difference (guselkumab group-placebo group) and 95% CI.</li> <li>P-values based on CMH chi-squared test <b>CCI</b> and represents the comparison with placebo.</li> </ul>             |

## 5.4. Secondary Endpoint(s) Analysis

### 5.4.1. Major Secondary Endpoint(s)

There are 9 major secondary endpoints for each cohort and listed below:

#### To evaluate the additional efficacy of guselkumab vs placebo

##### Cohort A:

1. The proportion of participants who achieve an IGA score of cleared (0) at Week 16
2. The proportion of participants who achieve a PASI 100 response at Week 16
3. The change from baseline in PASI score at Week 16
4. The change from baseline in body surface area (BSA) at Week 16

5. The time to  $\geq 90\%$  reduction in PASI through Week 16
6. The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16
7. The proportion of participants who achieve  $\geq 4$ -point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch score  $\geq 4$  at baseline
8. The change from baseline in PSSD symptom score at Week 16
9. The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score  $\geq 1$

**Cohort B:**

1. The change from baseline in PSSI score at Week 16
2. The change from baseline in scalp surface area (SSA) at Week 16
3. The proportion of participants who achieve a ss-IGA score of absence of disease (0) at Week 16
4. The proportion of participants who achieve a PSSI 100 response at Week 16
5. The time to  $\geq 90\%$  reduction in PSSI through Week 16
6. The change from baseline in DLQI score at Week 16
7. The proportion of participants who achieve  $\geq 4$ -point reduction (improvement) from baseline in the scalp itch numeric rating scale (NRS) score at Week 16, among participants with baseline scalp itch score  $\geq 4$  at baseline
8. The change from baseline in PSSD symptom score at Week 16
9. The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score  $\geq 1$

**5.4.1.1. Definition of Endpoint(s)****5.4.1.1.1. Investigator's Global Assessment (IGA) Related Endpoints****IGA Cleared Responder**

Participants who achieve an IGA score of cleared (0) will be considered IGA cleared responders.

#### **5.4.1.1.2. Psoriasis Area and Severity Index (PASI) Related Endpoints**

##### **PASI 100 Responder**

Participants with a PASI score of 0 will be considered PASI 100 responders.

##### **Time to $\geq 90\%$ Reduction (Improvement)**

Defined as the time at which  $\geq 90\%$  improvement in PASI from baseline is observed.

#### **5.4.1.1.3. Scalp-Specific Investigator's Global Assessment (ss-IGA) Related Endpoints**

##### **ss-IGA Absence of Disease Responder**

Participants who achieve ss-IGA score of absence of disease (0) will be consider ss-IGA absence of disease responders.

#### **5.4.1.1.4. Psoriasis Scalp Severity Index (PSSI) Related Endpoints**

##### **PSSI 100 Responder**

Participants with a PSSI score of 0 will be considered PSSI 100 responders.

##### **Time to $\geq 90\%$ Reduction (Improvement) in PSSI**

Defined as the time at which  $\geq 90\%$  improvement in PSSI from baseline is observed.

#### **5.4.1.1.5. Body or Scalp Surface Area (BSA or SSA) Affected by Psoriasis**

The BSA is a measurement of involved skin over the whole body. The overall BSA affected by psoriasis is estimated based on the participant's handprint (defined as the entire palmar surface of the hand including fingers). 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 around 520-705 cm<sup>2</sup>, meaning that 1% SSA is about 5.2-7.1 cm<sup>2</sup>. The thumbprint has an average surface area of about 5.5 cm<sup>2</sup>  $\pm$  1.3 cm<sup>2</sup>. Hence, the thumb (in particular, the thumb projection) can be used as a tool for accurate measurement of 1% SSA. The overall SSA affected by psoriasis can thus be estimated based on the participant's thumb.

#### **5.4.1.1.6. Dermatology Life Quality Index (DLQI)**

The DLQI is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a participant's quality of life. It is a 10-item questionnaire that, in addition to evaluating overall quality of life, can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment. The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. A higher score indicates more severe disease.

A score of  $\leq 1$  indicates no effect at all of disease on participant's health related quality of life, and a reduction of 5 points or more in total DLQI score is considered clinically meaningful improvement.

For a partially answered questionnaire (eg, not all 10 answers in the DLQI questionnaire were available):

- If one question's answer is not available, this question will be scored 0. The total score will then be calculated.
- If two or more questions' answers are unavailable, the questionnaire is not scored. Hence, the total score and each of the 6 component scores will be set to missing.
- If one question from one of the 6 component scores is missing, the affected component score will be set to be missing.

#### **5.4.1.1.7. 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 48, participants will complete the 7-day recall version of the PSSD at study visits as indicated in the Schedule of Activities (See in the protocol).

The calculations of PSSD symptom, and sign scores are listed below:

##### **Symptom Score (0-100)**

- a. Symptom score includes itch (Q1), pain (Q11), stinging (Q10), burning (Q9) and skin tightness (Q4).
- b. Averaging items on the daily symptom scores when at least 3 items ( $\geq 50\%$  of 5 items) on this scale are answered. Then, the average value is converted into 0-100 scoring such that Symptom score = average value x 10 with 0 representing the least severe and 100 the most severe.

##### **Sign Score (0-100)**

- a. Sign score includes skin dryness (Q2), cracking (Q3), scaling (Q5), shedding or flaking (Q6), redness (Q7) and bleeding (Q8).

- b. Averaging items on the sign scores when at least 3 items ( $\geq 50\%$  of 6 items) on this scale are answered. Then, the average value is converted into 0-100 scoring such that Sign score = average value x 10 with 0 representing the least severe and 100 the most severe.

Seven daily symptom scores, and sign scores are averaged into a weekly score respectively (ie 7 days [from day -7 to -1] prior to a visit). Four days out of 7 days (either consecutive or nonconsecutive) are necessary to derive a weekly score; otherwise, data are considered missing for that week.

#### 5.4.1.1.8. 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. 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.

#### 5.4.1.2. Estimand(s)

The following describe the attributes of the estimands for the major secondary endpoints (corresponding to Estimands 3-11) for each cohort (see [Table 7](#) and [Table 8](#)):

- 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

**Table 7: Variables, Population-level Summary, and Intercurrent Event Strategy for each Major Secondary Endpoint for Cohort A (for Estimands 3a-11a)**

| Estimands | Variable (Endpoint)                                                                | Population-level summary                                                                                                                | Intercurrent Event Strategy                                                                                                                                                                                                                                                            |
|-----------|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3a        | The proportion of participants who achieve an IGA score of cleared (0) at Week 16. | Difference in proportion of participants who achieve an IGA score of cleared (0) at Week 16 between guselkumab group and placebo group. | A nonresponder status will be assigned to IGA (0) after the occurrence of ICE 1 or 2. Observed value will be used for IGA (0) after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. |

|    |                                                                                                                  |                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                  |
|----|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 4a | The proportion of participants who achieve a PASI 100 response at Week 16.                                       | Difference in proportion of participants who achieve a PASI 100 response at Week 16 between guselkumab group and placebo group.    | A nonresponder status will be assigned to PASI 100 response after the occurrence of ICE 1 or 2. Observed value will be used for PASI 100 after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.                                |
| 5a | The change from baseline in PASI score at Week 16.<br>(Change=Week 16-baseline)                                  | Difference in mean percentage change from baseline in PASI score at Week 16 between guselkumab group and placebo group.            | Percentage change from baseline in PASI score at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for PASI score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. |
| 6a | The change from baseline in body surface area (BSA) at Week 16<br>(Change=Week 16-baseline)                      | Difference in mean percentage change from baseline in BSA at Week 16 between guselkumab group and placebo group.                   | Percentage change from baseline in BSA at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for BSA score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.         |
| 7a | The time to $\geq 90\%$ reduction in PASI through Week 16                                                        | Difference in survival curves for time to $\geq 90\%$ reduction in PASI through Week 16 between guselkumab group and placebo group | For participants experiencing ICE's 1 or 2 will be censored.<br>Observed value will be used for the response after the occurrence of ICE 3 or 4.<br>For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.                                                         |
| 8a | The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16.<br>(Change=Week 16-baseline) | Difference in mean change from baseline in DLQI score at Week 16 between guselkumab group and placebo group.                       | Change from baseline in DLQI score at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for DLQI score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.            |

|     |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                       |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 9a  | The proportion of participants who achieve $\geq 4$ -point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch $\geq 4$ at baseline. | Difference in proportion of participants who achieve $\geq 4$ -point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch $\geq 4$ at baseline between guselkumab group and placebo group. | A nonresponder status will be assigned to PSSD itch score response after the occurrence of ICE 1 or 2. Observed value will be used for PSSD itch score response after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.              |
| 10a | The change from baseline in PSSD symptom score at Week 16 (Change=Week 16-baseline)                                                                                                                                                     | Difference in mean change from baseline in PSSD symptom score at Week 16 between guselkumab group and placebo group.                                                                                                                                                                         | Change from baseline in PSSD symptom score at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for PSSD symptom score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. |
| 11a | The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score $\geq 1$                                                                                | Difference in proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score $\geq 1$ between guselkumab group and placebo group.                                                                               | A nonresponder status will be assigned to PSSD symptom score of 0 response after the occurrence of ICE 1 or 2. Observed value will be used for PSSD symptom score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.            |

**Table 8: Variables, Population-level Summary, and Intercurrent Event Strategy for each Major Secondary Endpoint for Cohort B (for Estimands 3b-11b)**

| Estimands | Variable (Endpoint)                                                         | Population-level summary                                                                                                | Intercurrent Event Strategy                                                                                                                                                                                                                                                                                                      |
|-----------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3b        | The change from baseline in PSSI score at Week 16 (Change=Week 16-baseline) | Difference in mean percentage change from baseline in PSSI score at Week 16 between guselkumab group and placebo group. | Percentage change from baseline in PSSI score at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for PSSI score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. |
| 4b        | The change from baseline in scalp surface                                   | Difference in mean percentage change from baseline in SSA at Week 16                                                    | Percentage change from baseline in SSA at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for SSA after the occurrence of                                                                                                                                                |

|    |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                       |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | area (SSA) at Week 16 (Change=Week 16-baseline)                                                                                                                                                                                         | between guselkumab group and placebo group.                                                                                                                                                                                                                                                  | ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.                                                                                                                                                                                      |
| 5b | The proportion of participants who achieve a ss-IGA score of absence of disease (0) at Week 16                                                                                                                                          | Difference in proportion of participants who achieve a ss-IGA score of absence of disease (0) at Week 16 between guselkumab group and placebo group.                                                                                                                                         | A nonresponder status will be assigned to ss-IGA response after the occurrence of ICE 1 or 2. Observed value will be used for ss-IGA response after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.                |
| 6b | The proportion of participants who achieve a PSSI 100 response at Week 16.                                                                                                                                                              | Difference in proportion of participants who achieve a PSSI 100 response at Week 16 between guselkumab group and placebo group.                                                                                                                                                              | A nonresponder status will be assigned to PSSI 100 response after the occurrence of ICE 1 or 2. The observed value will be used for PSSI 100 after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.                 |
| 7b | The time to $\geq 90\%$ reduction in PSSI through Week 16                                                                                                                                                                               | Difference in survival curves for time to $\geq 90\%$ reduction in PSSI through Week 16 between guselkumab group and placebo group                                                                                                                                                           | For participants experiencing ICE's 1 or 2 will be censored. Observed value will be used for the response after the occurrence of ICE 3 to 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.                                                    |
| 8b | The change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16. (Change=Week 16-baseline)                                                                                                                           | Difference in mean change from baseline in DLQI score at Week 16 between guselkumab group and placebo group.                                                                                                                                                                                 | Change from baseline in DLQI score at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for DLQI score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. |
| 9b | The proportion of participants who achieve $\geq 4$ -point reduction (improvement) from baseline in the in the scalp itch numeric rating scale (NRS) score at Week 16, among participants with baseline scalp itch $\geq 4$ at baseline | Difference in proportion of participants who achieve $\geq 4$ -point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch $\geq 4$ at baseline between guselkumab group and placebo group. | A nonresponder status will be assigned to NRS score response after the occurrence of ICE 1 or 2. Observed value will be used for NRS score response after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.          |

|     |                                                                                                                                                          |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                       |
|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10b | The change from baseline in PSSD symptom score at Week 16 (Change=Week 16-baseline)                                                                      | Difference in mean change from baseline in PSSD symptom score at Week 16 between guselkumab group and placebo group.                                                                                           | Change from baseline in PSSD symptom score at Week 16 will be set to have zero change after the occurrence of ICE 1 or 2. Observed value will be used for PSSD symptom score after the occurrence of ICE 3 to 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. |
| 11b | The proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score $\geq 1$ | Difference in proportion of participants who achieve a PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score $\geq 1$ between guselkumab group and placebo group. | A nonresponder status will be assigned to PSSD symptom score of 0 response after the occurrence of ICE 1 or 2. Observed value will be used for PSSD symptom score after the occurrence of ICE 3 or 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4.            |

### 5.4.1.3. Analysis Methods

#### 5.4.1.3.1. Main Estimators (Analyses) for the Estimands

The major secondary endpoints, defined in Section 1.1, will be compared between guselkumab group and placebo group within each cohort. FAS for cohort A and CCI for cohort B and the estimands defined in Section 5.4.1.2. will be used.

The estimands (3a,4a,9a and 11a for cohort A, 5b,6b,9b and 11b for cohort B) will be estimated by differences between guselkumab group and placebo group in the proportion of participants who achieve each endpoint and their associated 95% CIs. Each endpoint will be compared between guselkumab group and the placebo group using the CMH Chi-square test (2-sided) CCI at a significance level of 0.05.

The estimands (5a,6a,10a for cohort A, 3b,4b,10b for cohort B) will be estimated by differences between guselkumab group and placebo group in the mean change from baseline. Each endpoint will be compared between guselkumab group and the placebo group using MMRM model with explanatory factors as treatment group, visit, baseline efficacy endpoint score, CCI, interaction term of visit with treatment group, and an interaction term of visit with baseline score. The difference in the least squares means (LSmeans) and 95% confidence interval (CI) for the differences in LSmeans and p-values will be calculated based on the MMRM model, at a significance level of 0.05.

The estimands (8a for cohort A, 8b for cohort B) will be estimated by differences between guselkumab group and placebo group in the mean change from baseline. Each endpoint will be compared between guselkumab group and the placebo group using ANCOVA model with explanatory factors as treatment group, baseline efficacy endpoint score CCI. The difference in the least squares means (LSmeans) and

95% confidence interval (CI) for the differences in LSmeans and p-values will be calculated based on the ANCOVA model, at a significance level of 0.05.

The estimands (7a for cohort A, 7b for cohort B) will be estimated by using life-table method, and the guselkumab group and the placebo group will be compared by using log-rank test CCI

#### **5.4.1.3.2. Data handling rules for major secondary endpoints**

##### **5.4.1.3.2.1. Binary Estimands (Cohort A :3a,4a,9a,11a) – Non-responder Imputation (NRI).**

Participants who are missing an IGA score at Week 16 (after accounting for the intercurrent events) will be considered non-responders for IGA score of cleared (0) at Week 16 (i.e., Non-responder Imputation (NRI)).

Participants who are missing a PASI score at Week 16 (after accounting for the intercurrent events) will be considered non-responders for PASI 100 at Week 16.

Participants who are missing PSSD itch score at Week 16, among participants with baseline PSSD itch  $\geq 4$  at baseline (after accounting for the intercurrent events) will be considered non-responders for the PSSD itch score  $\geq 4$ -point reduction (improvement) at Week 16.

Participants who are missing PSSD symptoms score at Week 16, among randomized participants with baseline PSSD symptom score  $\geq 1$  (after accounting for the intercurrent events) will be considered non-responders for PSSD symptom score of 0 at Week 16

##### **5.4.1.3.2.2. Binary Estimands (Cohort B: 5b,6b,9b,11b) – Non-responder Imputation (NRI).**

Participants who are missing an ss-IGA score at Week 16 (after accounting for the intercurrent events) will be considered non-responders for ss- IGA score of absence of disease (0) at Week 16 (i.e., Non-responder Imputation (NRI)).

Participants who are missing a PSSI score at Week 16 (after accounting for the intercurrent events) will be considered non-responders for PSSI 100 at Week 16.

Participants who are missing NRS score at Week 16, among participants with baseline scalp itch  $\geq 4$  at baseline (after accounting for the intercurrent events) will be considered non-responders for PSSD itch score  $\geq 4$ -point reduction (improvement) at Week 16.

Participants who are missing PSSD symptoms score at Week 16, among randomized participants with baseline PSSD symptom score  $\geq 1$  (after accounting for the intercurrent events) will be considered non-responders for PSSD symptom score of 0 at Week 16.

---

**5.4.1.3.2.3. Continuous Estimands (cohort A: 5a,6a,10a, cohort B: 3b,4b,10b)**

A missing score (after accounting for the intercurrent events) is not imputed and will be handled through the MMRM assuming missing at random (MAR).

**5.4.1.3.2.4. Continuous Estimands (cohort A: 8a, cohort B: 8b)**

A missing score (after accounting for the intercurrent events) will not be imputed.

**5.4.1.3.2.5. Time to an event Estimands (cohort A:7a, cohort B:7b)**

Participants who do not achieve the endpoint by Week 16 will be censored for the analysis.

**5.4.1.3.3. Supplementary Estimands for the major Secondary Endpoints**

Supplementary estimands may be performed for selected major secondary endpoints. In these supplementary estimands, all the intercurrent events are addressed by the **composite strategy**. The supplementary estimands for the major secondary endpoints acknowledge that having an intercurrent event is an unfavorable outcome. If a participant had any of the intercurrent events (ICE) prior to Week 16, the participant will be considered to be 'Non responder' in all binary endpoints and zero change from baseline at week 16 in all continuous variables from the visit when first ICE occurred.

**5.4.1.3.4. Summary of Analyses Related to Major Secondary Endpoints**

[Table 9](#) below provides an overview of all the analyses related to the major secondary endpoints, the estimands, the analysis sets, the data handling rules to be used, and the analysis methods and summary statistics.

**Table 9: Summary of Analyses Related to major Secondary Endpoints**

| Endpoints<br>(Analysis Set)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Missing data                                                                                                                                      | Analysis method/Summary statistics                                                                                                                                                                                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Main analyses based on Estimand (3a-11a and 3b-11b)</b> , where ICEs 1-2 are handled by the composite strategy, and ICE 3-4 is handled by the treatment policy strategy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                   |                                                                                                                                                                                                                                                                                                    |
| <b>Cohort A:</b> <ul style="list-style-type: none"> <li>IGA score of cleared (0) at Week 16</li> <li>PASI 100 response at Week 16</li> <li>A <math>\geq 4</math>-point reduction (improvement) from baseline in the Psoriasis Symptom and Sign Diary (PSSD) itch score at Week 16, among participants with baseline PSSD itch <math>\geq 4</math> at baseline</li> <li>A PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score <math>\geq 1</math></li> </ul> <b>Cohort B:</b> <ul style="list-style-type: none"> <li>ss-IGA score of absence of disease (0) at Week 16</li> <li>PSSI 100 response at Week 16</li> <li><math>\geq 90\%</math> reduction in PSSI through Week 16</li> <li>A <math>\geq 4</math>-point reduction (improvement) from baseline in the scalp itch numeric rating scale (NRS) score at Week 16, among participants with baseline scalp itch <math>\geq 4</math> at baseline</li> <li>A PSSD symptom score of 0 at Week 16, among randomized participants with baseline PSSD symptom score <math>\geq 1</math></li> </ul> (FAS for cohort A and CCI for cohort B) | Missing data due to missed visits or missed data collection. Participants with missing data are considered to be non-responders' imputation (NRI) | <ul style="list-style-type: none"> <li>Summaries of the proportion of participants who achieved the endpoint</li> <li>Treatment difference (guselkumab group-placebo group) and 95% CI</li> <li>P-value from the CMH test CCI</li> </ul>                                                           |
| <b>Cohort A:</b> <ul style="list-style-type: none"> <li>Change (percentage change) from baseline in PASI score at Week 16</li> <li>Change (percentage change) from baseline in body surface area (BSA) at Week 16</li> <li>Change from baseline in Dermatology Life Quality Index (DLQI) score at Week 16</li> <li>Change from baseline in PSSD symptom score at Week 16</li> </ul> <b>Cohort B:</b> <ul style="list-style-type: none"> <li>Change (percentage change) from baseline in PSSI score at Week 16</li> <li>Change (percentage change) from baseline in scalp surface area (SSA) at Week 16</li> <li>Change from baseline in DLQI score at Week 16</li> <li>Change from baseline in PSSD symptom score at Week 16</li> </ul> (FAS for cohort A and CCI for cohort B)                                                                                                                                                                                                                                                                                                                                                         | Missing data due to missed visits or missed data collection. Missing data is not imputed, but is handled through the MMRM assuming MAR.           | <ul style="list-style-type: none"> <li>Descriptive summary statistics</li> <li>MMRM model for <ul style="list-style-type: none"> <li>LS mean (95% CI) for each treatment group</li> <li>Treatment differences in LS means (95% CI)</li> </ul> </li> <li>P-values for comparing LS means</li> </ul> |

| Endpoints<br>(Analysis Set)                                                                                                                                                                                                                                        | Missing data                                                                                                     | Analysis method/Summary statistics                                                                                                                                                                                                                                                                               |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Cohort A/Cohort B</b> <ul style="list-style-type: none"> <li>Change from baseline in DLQI score at Week 16</li> </ul><br>(FAS for cohort A and CCI for cohort B)                                                                                                | Missing data due to missed visits or missed data collection. Missing data is not imputed.                        | <ul style="list-style-type: none"> <li>Descriptive summary statistics</li> <li>ANCOVA model for <ul style="list-style-type: none"> <li>LS mean (95% CI) for each treatment group</li> <li>Treatment differences in LS means (95% CI)</li> </ul> </li> <li>P-values for comparing LS means</li> </ul>             |
| <b>Cohort A /Cohort B:</b> <ul style="list-style-type: none"> <li>Time to <math>\geq 90\%</math> reduction in PASI through Week 16</li> <li>Time to <math>\geq 90\%</math> reduction in PSSI through Week 16</li> </ul><br>(FAS for cohort A and CCI for cohort B) | Participants who do not achieve the endpoint by Week 16, will be treated as censored for time to event analysis. | <ul style="list-style-type: none"> <li>Life tables estimates will be calculated for the response rate (95% CI) and the median time to <math>\geq 90\%</math> reduction in PASI or median time to <math>\geq 90\%</math> reduction in PSSI through Week 16</li> <li>P-value based on log-rank test CCI</li> </ul> |

#### 5.4.1.3.4.1. Multiplicity Adjustment for Testing Procedures

This study has 9 major secondary endpoints for each cohort (listed in section 2). The analyses of the major secondary endpoints in each cohort will be performed only if the primary analysis is significant and will be performed in the fixed sequence testing approach as specified in Table 2 for each cohort. If a given comparison is not significant at the 2-sided  $\alpha$ -level of 0.05, the remaining treatment group comparisons in this sequence for each cohort will not be considered significant.

#### 5.4.1.3.4.2. Level of Significance

The overall type I error will be controlled among the primary and major secondary endpoints at 5%.

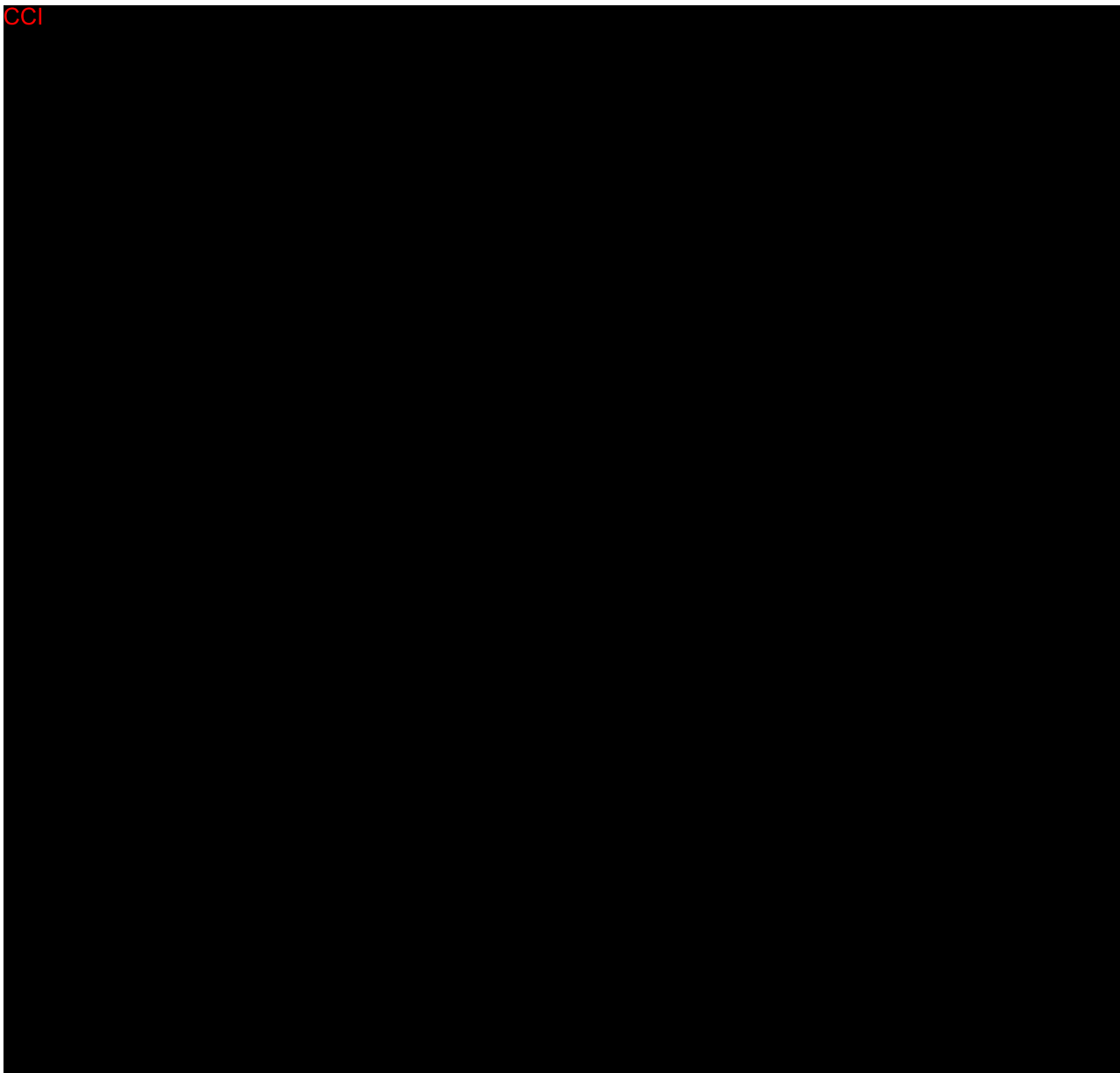
#### 5.4.2. Supportive Secondary Endpoint(s)

In addition to the primary and major secondary endpoints, other secondary endpoint and other prespecified endpoints will also be analyzed.

This section outlines the definition and analyses of the other secondary and other prespecified endpoints.

Other prespecified secondary efficacy endpoints through Week 16 will be analyzed at Week 16 DBL based on the Composite Estimand. Other prespecified secondary efficacy endpoints through Week 100 will be analyzed at Final DBL.

CCI



#### **5.4.2.2. Definition of other prespecified endpoint (s) through Week 16**

Details refer to section [5.4.1.1](#).

#### **5.4.2.3. Analysis method of other prespecified endpoint(s) through Week 16**

Other prespecified endpoints through Week 16 will be tested regardless of the significance of the primary and major secondary endpoints for each cohort; the testing of these endpoints will not be controlled for multiplicity. All statistical testing will be performed at the 2-sided 0.05 significance level. Nominal p-values will be presented.

The analyses of these other prespecified endpoints through Week 16 will be based on the FAS for cohort A and CCI for cohort B.

Descriptive statistics (i.e., N, mean, median, SD, 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 the data.

The comparisons of interest will be between guselkumab group and the placebo group.

**For continuous endpoints** the MMRM model will be used to test the difference between guselkumab group and the placebo group. This model relies on the Missing at Random (MAR) assumption for the missing responses. Under the assumption of MAR, the missing data will be accounted for through correlation of repeated measures in the model.

CCI

The estimates of the treatment difference between guselkumab group and the placebo group will be calculated by the difference in the least squares means (LS means). The 95% confidence interval (CI) for the differences in LS means and p-values will be calculated based on the MMRM. An unstructured covariance matrix for repeated measure within a participant will be used. The F-test will use Kenward-Roger's approximation for degrees of freedom. If the normality assumption is in question, an appropriate transformation will be used.

ANCOVA model will be used when there is only one post baseline efficacy endpoint collected from baseline through Week 16. The ANCOVA model will include treatment group, baseline efficacy endpoint score CCI as explanatory factors. In the ANCOVA model, participants with missing data will not be imputed.

Participants with an intercurrent event in category 1 or 2 prior to Week 16 will be considered to have zero change from baseline for that endpoint at Week 16. If a participant had any of the ICE categories 3 or 4 prior to Week 16, observed value will be used from the visit.

**For binary endpoints** chi-square test or Cochran-Mantel-Haenszel chi-square test (as appropriate) will be used to compare the proportion of participants achieving selected endpoints between the guselkumab treatment group and the placebo group. CCI In case of rare events, Fisher's exact test will be used for treatment comparisons.

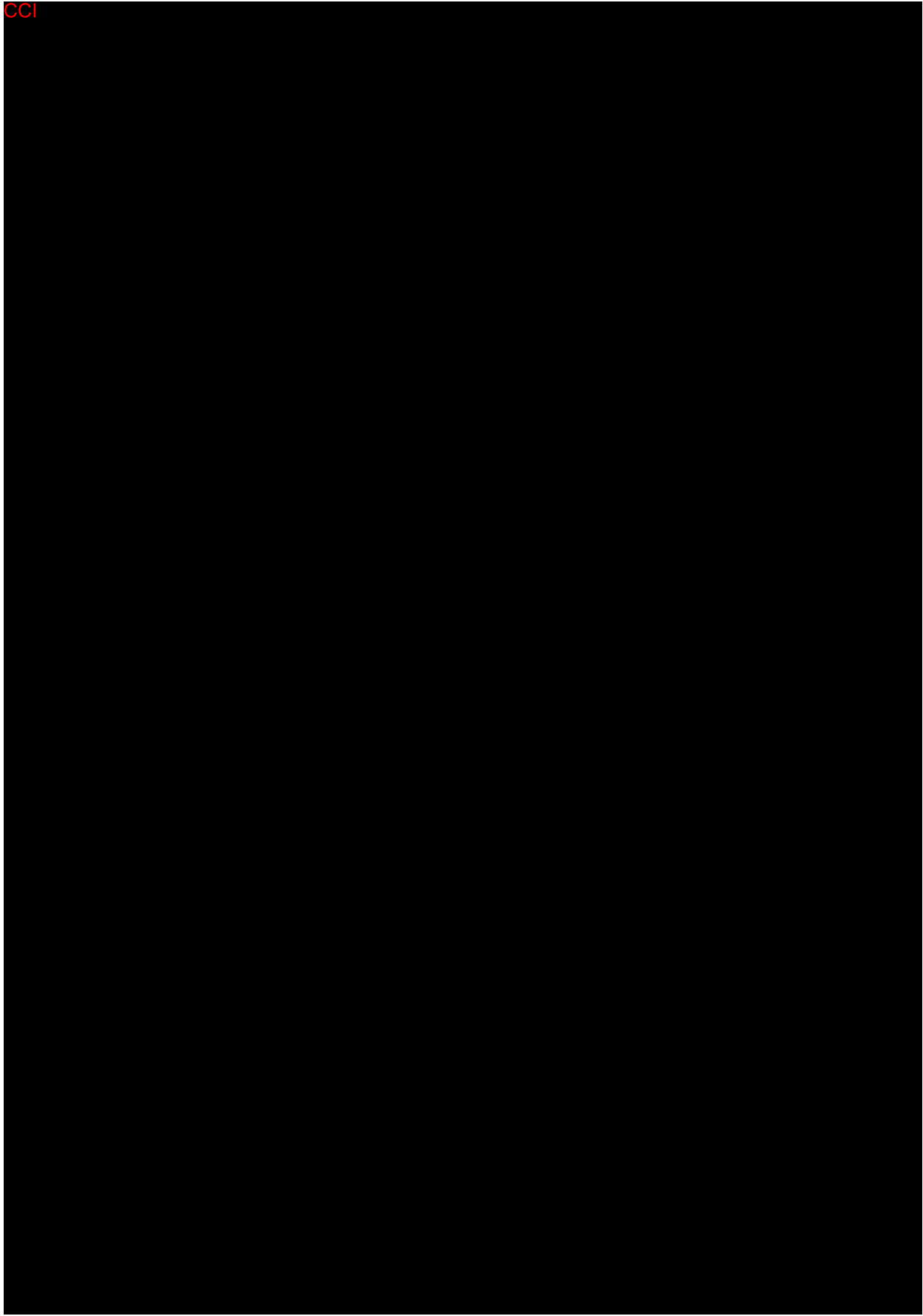
Participants with an intercurrent event in category 1 or 2 prior to Week 16 will be considered non-responder for the binary endpoint at Week 16. If a participant had any of the ICE categories 3 or 4, observed value will be used from the visit.

**For time to event endpoints**, life table estimates will be provided for the response rate (95% CI) and the median time to achieve the endpoint by Week 16. P-value will be calculated based on log-rank test **CCI**.

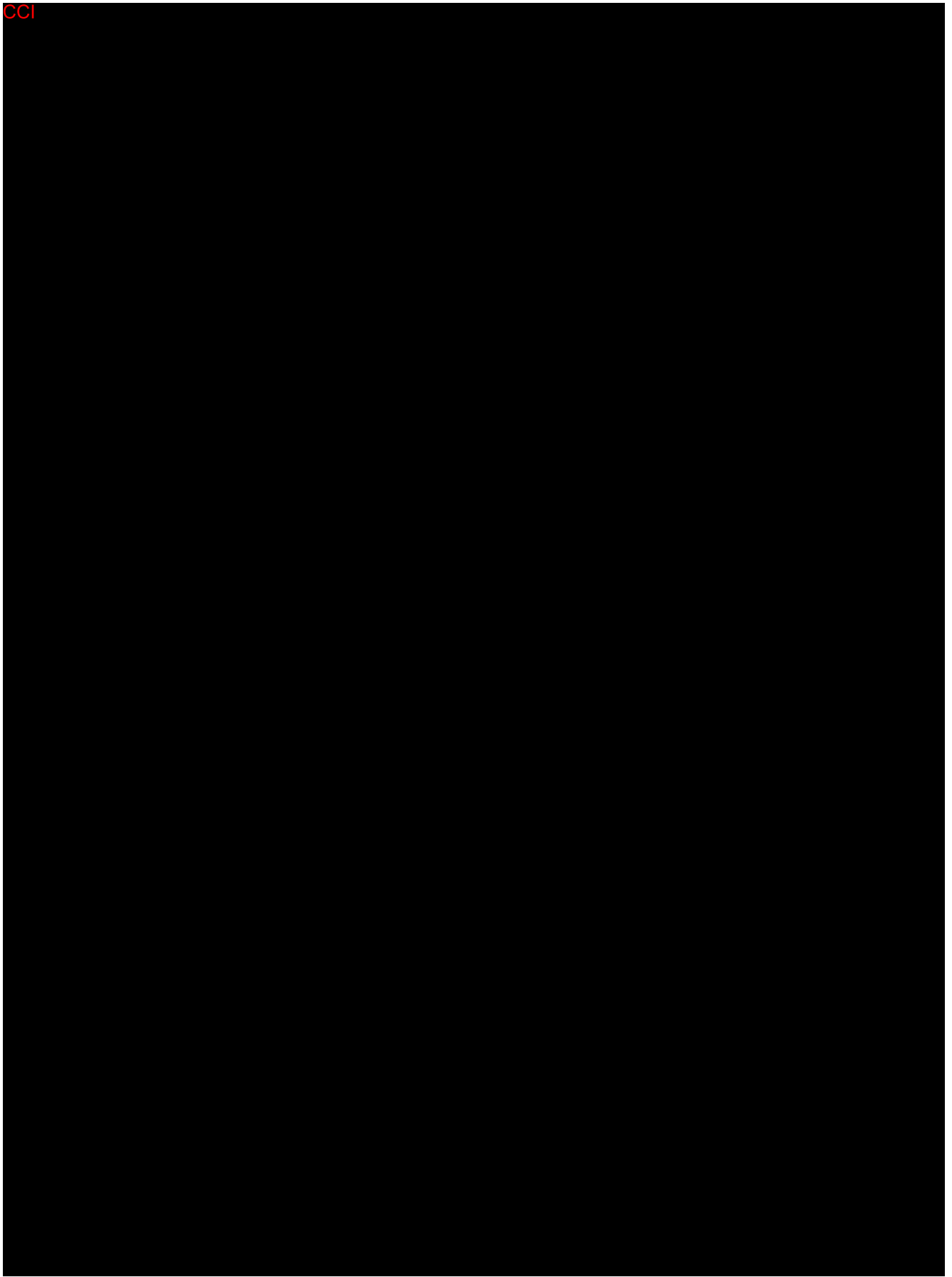
For participants experiencing ICE's 1 or 2 will be censored. Observed value will be used for the response after the occurrence of ICE 3 to 4. For participants experiencing multiple ICEs, an ICE in categories 1 or 2 will supersede an ICE in categories 3 or 4. Participants who do not achieve the endpoint by Week 16 will be censored for the analysis.

**CCI**

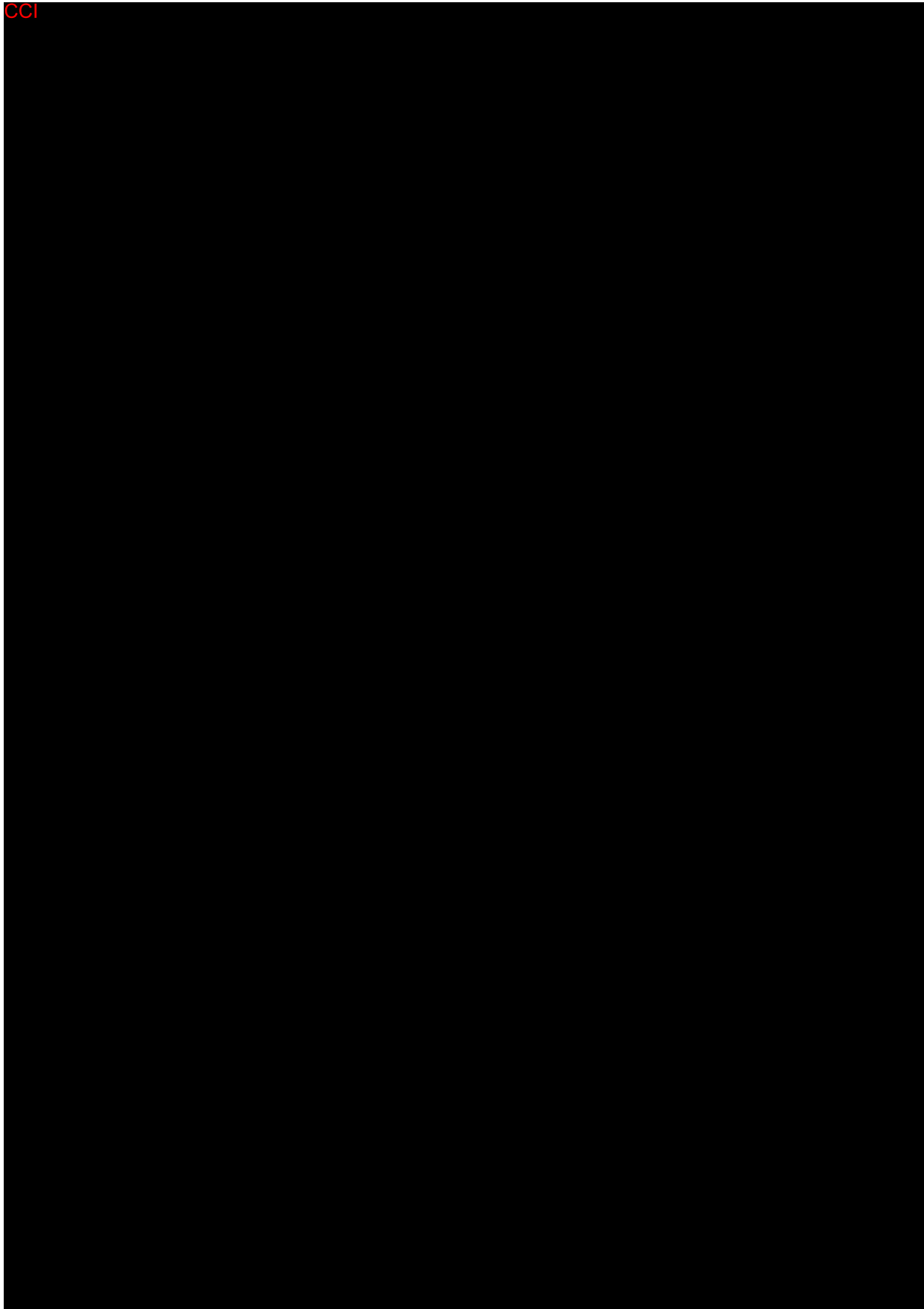
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#### 5.4.2.5. Definition of other prespecified endpoint (s) through Week 100

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

The PROMIS-29 is a 29-item generic HRQoL survey, assessing each of the 7 PROMIS domains (depression; anxiety; physical function; pain interference; fatigue; sleep disturbance; and ability to participate in social roles and activities) with 4 questions. The questions are ranked on a 5-point Likert Scale. There is also one 11-point rating scale for pain intensity.

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. Participants will undergo this assessment at time points according to the SoA in the protocol.

##### 5.4.2.5.1.2. Psoriasis Epidemiology Screening Tool (PEST)

The Psoriasis Epidemiology Screening Tool (PEST) is a validated screening tool for psoriatic arthritis. It is a 5-item questionnaire developed to help identify PsA at an early stage. In this study, the PEST will be administered at screening to those who do not report a prior history of confirmed PsA. CCI

##### 5.4.2.5.1.3. 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 in the protocol). Each domain has a different weight: pain, fatigue, and skin problems are those with a greater effect. CCI

CCI

#### **5.4.2.5.1.4. PIDASI**

The PIDASI includes 2 characteristics of dyspigmentation (intensity and heterogeneity), and the area involved. 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).

#### **5.4.2.5.1.5. Skin Discoloration Impact Evaluation Questionnaire (SDIEQ)**

This 5-question patient-reported outcome questionnaire was initially developed and used in the PIGMENT trial for facial melasma. Items from this questionnaire were validated and included as part of the MELASQOL. This PRO was also described in the paper that developed the PIDASI clinician reported outcome that will be utilized in this trial.

### **5.5. Tertiary/Exploratory Endpoint(s) Analysis**

No tertiary/exploratory endpoints in this study.

To assess the consistency between CNT01959PSO3018 and the guselkumab pivotal program in psoriasis (CNT01959PSO3001 and CNT01959PSO3002), the results from CNT01959PSO3018 may be evaluated and presented with existing results from the pivotal program.

### **5.6. Other Safety Analyses**

Safety will be assessed by summarizing the occurrences and type of AEs, vital signs (pulse, blood pressure, and weight), examining the changes in the laboratory parameters.

In all the safety analysis, participants who were randomized and received at least 1 (partial or complete) dose of study agent administration will be included and analyzed according to the treatment they actually received, regardless of the treatments they are randomized to.

For all continuous safety variables, descriptive statistics by intervention group will include the N, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized by intervention group using frequency counts and percentages.

There are 3 DBLs in this study, respectively, at Week 16, Week 48, and final DBL at Week 112. Depending on the safety data categories, the cumulative safety data will be analyzed through different study periods which may include but are not limited to safety data through Week 16, through Week 48, and through Week 112. Tabular summaries of safety events for key study periods are in general presented as follows:

#### **Summaries Through Week 16**

Safety data through Week 16 will be analyzed according to the following treatment groups:

1. **Placebo:** Participants who received placebo only and no guselkumab through Week 16.
2. **Guselkumab 100 mg at Weeks 0, 4, and then q8w:** Participants who received guselkumab 100 mg q8w through Week 16.

For participants who started treatment with placebo only but later received guselkumab prior to Week 16 inadvertently, the safety events/measurements on and after the first dose of guselkumab, will be excluded from the data summaries through Week 16. Only the safety events/measurements that occurred while the participants had been receiving placebo only will be included in the data summaries through Week 16.

### Summaries Through Week 48

Safety data through Week 48 will be analyzed according to the following treatment groups:

1. **Placebo → Guselkumab 100 mg q8w:** Participants who started treatment with placebo and later received treatment with guselkumab (due to crossed over or inadvertently) at Weeks 16 and 20 then q8w through Week 48. All the safety events/measurements that occurred on and after the first dose of guselkumab up to Week 48 will be included in this group.
2. **Guselkumab 100 mg:** Participants who received guselkumab 100 mg at Week 0, 4 and then every 8 weeks (q8w) through Week 48 for those randomized to guselkumab.

### Summaries Through Week 112

Safety data through Week 112 will be analyzed according to the following treatment groups:

3. **Placebo → Guselkumab 100 mg q8w:** Participants who started treatment with placebo and later received treatment with guselkumab (due to crossed over or inadvertently) at Weeks 16 and 20 then q8w through Week 112. All the safety events/measurements that occurred on and after the first dose of guselkumab up to Week 112 will be included in this group.
4. **Guselkumab 100 mg:** Participants who received guselkumab 100 mg at Week 0, 4 and then every 8 weeks (q8w) through Week 112 for those randomized to guselkumab.

#### 5.6.1. Extent of Exposure

The extent of exposure will be summarized for all treated participants. Descriptive statistics will be presented for number of study agent administrations and cumulative total dose by treatment received.

The exposure data will be summarized for the study periods of:

- Through Week 16
- Through Week 48
- Through Week 112

Study agent lots received by treatment, including matching placebo for active treatment will also be summarized.

### 5.6.2. Adverse Events

Adverse Events (AEs) that occurred any time over the study will be reported and coded using Medical Dictionary for Regulatory Activities (MedDRA). Analyses of AEs will be performed on those events that are considered treatment emergent. Treatment emergent AEs are those AEs that occurred after the start of initial study agent administration and those AEs that were present at baseline but worsened in severity after the start of initial study agent administration. Treatment emergent AEs will be summarized by MedDRA system organ class, preferred term, and actual treatment group. The numbers of participants reporting at least 1 event of the following treatment emergent AE categories will be summarized:

- Any AEs
- Serious adverse events (SAEs)
- AEs that are reasonably related to study agent
- AEs of severe intensity
- AEs that led to permanent discontinuation of study agent administration
- Injection-site reactions
- AEs of psoriasis

These summary tables will provide the count and percentage of participants with 1 or more of the specified AEs by treatment group. To adjust for the different duration of follow-up among treatment groups, the AE rates per hundred participant-years of follow-up will also be provided for the above AE categories, Malignancy, Tuberculosis, MACE, infections, and serious infections.

All AE summary tables will include average weeks of follow-up and average number of study agent administrations for each treatment group.

In addition to the summary tables, listings of participants with the following AEs will also be provided:

- SAEs
- AEs leading to permanent discontinuation of study agent
- Opportunistic infection
- Malignancies (non-melanoma skin cancer and other malignancies)

- Death
- Suicidal ideation and behavior
- Possible serum sickness-like reactions and anaphylactic reactions.

Any unfavorable or unintended sign that occurs at the injection site is an injection site reaction and will be recorded as an AE. An infection is defined as any AE that was recorded as an infection by the investigator on the eCRF.

Adverse events of psoriasis include any event of erythrodermic psoriasis, pustular psoriasis, guttate psoriasis, inverse psoriasis, palmo-plantar psoriasis and worsening or exacerbation of psoriasis.

In addition, impact of weight on safety will be evaluated for selected treatment emergent AE categories based on baseline weight ( $\leq 90$  kg,  $>90$  kg).

Since safety should be assessed relative to exposure and follow-up, most AE summary tables will include average weeks of follow-up and average number of study agent administrations for each treatment group.

### 5.6.3. Additional Safety Assessments (if applicable)

#### 5.6.3.1. Clinical Laboratory Tests

Blood samples for hematology and clinical chemistry will be collected based on the time and events schedule specified in the protocol. The clinical laboratory parameters to be evaluated by the central laboratory include but are not limited to:

| Laboratory Assessments | Parameters                                                                                                                                                                                                      |                                                                                                     |                                                                                                   |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Hematology             | Platelet count<br>Red blood cell count<br>Hemoglobin<br>Hematocrit                                                                                                                                              | <u>Red Blood Cell (RBC) Indices:</u><br>MCV<br>MCH<br>% Reticulocytes                               | <u>White Blood Cell (WBC) count with Differential:</u><br>Neutrophils<br>Lymphocytes<br>Monocytes |
| Clinical Chemistry     | Sodium<br>Potassium<br>Calcium<br>Chloride<br>Bicarbonate<br>Blood urea nitrogen (BUN)<br>Creatinine<br>Glucose (non-fasting, acceptable)<br>Aspartate aminotransferase (AST)<br>Alanine aminotransferase (ALT) | Total bilirubin<br>Alkaline phosphatase<br>Creatine phosphokinase (CPK)<br>Albumin<br>Total protein |                                                                                                   |

The following analyses will be performed as appropriate by actual treatment group:

- Plots of the observed values and changes from baseline over time for selected clinical laboratory parameters
- Number of participants with post-baseline values by maximum toxicity grade according to National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE) for parameters with NCI-CTCAE criteria defined. NCI-CTCAE criteria is listed in (Appendix 11)
- Listings of participants with 1 or more NCI-CTCAE toxicity Grade 2 or higher

#### **5.6.3.2. Vital Signs and Physical Examination Findings**

Vital signs will be measured at visits as per the schedule of events in the protocol. Descriptive statistics of the observed value and change from baseline of the vital signs will be summarized by treatment group.

#### **5.6.3.3. Electrocardiogram**

No analysis is planned.

#### **5.6.3.4. Other Safety Parameters**

No analysis is planned.

### **5.7. Other Analyses**

#### **5.7.1. Pharmacokinetics**

Blood samples for measuring serum guselkumab concentrations will be collected from all participants at scheduled visits as indicated in the Schedule of Events in the protocol.

The PK analysis will be based on participants who received at least 1 administration of guselkumab and had at least one evaluable serum sample. No imputation of missing concentration data will be performed, that is, data summaries will be based on the observed data.

For analysis on serum guselkumab concentrations, descriptive statistics, including arithmetic mean, SD, median, interquartile range, minimum, and maximum will be provided, where appropriate, by treatment group at each serum sampling time. The PK concentration data may also be displayed graphically. The following analyses will be performed by treatment group as appropriate:

- Summary of serum guselkumab concentrations at each visit by treatment group
- Participants with serum guselkumab concentration below the lowest quantifiable concentration in a sample will be summarized by treatment group overtime.
- Summary of serum guselkumab concentrations overall and by baseline weight ( $\leq 90$ kg,  $>90$  kg) will be summarized by treatment group overtime.
- Plot of median serum guselkumab concentrations over time by treatment group

In addition, the relationship between serum guselkumab concentrations and safety or efficacy may be explored.

For summary statistics of serum guselkumab concentrations, concentration values below the lower limit of quantification will be treated as zero. Once a Participant meets one of the following dosing deviation criteria, the participant's data will be excluded from the by-visit data analyses from that point onwards.

Dosing deviation criteria:

- Discontinue SC guselkumab administrations.
- Skipped an SC guselkumab administration.
- Received an incomplete/ incorrect SC dose.
- Received an incorrect SC study agent.
- Received an additional SC guselkumab dose.

In addition, if a participant has an administration outside of visit windows (Section 5.1.1), the concentration data collected at and after that visit will be excluded from the by-visit data analyses. Additional exclusions for incongruous PK data to be implemented based on Janssen SOP-07948.

If feasible, a population PK analyses will be performed to characterize the disposition characteristics of guselkumab based on the guselkumab concentration data from PSO studies. Data may be combined with other selected studies to support a relevant structural model. A detailed analysis plan for population PK analysis will be developed separately, and a stand-alone technical report will be written to summarize the results of the population PK analysis.

### PK analyses presentation

PK analyses will be summarized through the following time periods:

- Through Week 16
- Through Week 48
- Through End of Study (Week 112)

For the analyses, a Participant is included in one and only one treatment group on the basis of the treatment regimen followed. The description of treatment groups are as follows:

1. **Placebo → Guselkumab 100 mg q8w:** Participants randomized to placebo and were switched over to Guselkumab 100 mg q8w (due to crossed over) at Week 16.
2. **Guselkumab 100 mg at Week 0, Week 4, and then q8w:** Participants randomized to guselkumab 100 mg at Week 0, Week 4, and then q8w and received guselkumab 100 mg q8w throughout.

### 5.7.2. Immunogenicity (Antibodies to Guselkumab)

Blood samples will be collected to examine the formation of antibodies to guselkumab at the specified visits as shown in the schedule of events of the protocol. Serum samples will also be collected at the final visit from participants who terminate study participation early.

#### 5.7.2.1. Immunogenicity Analysis

The antibodies to guselkumab will be summarized based on Immunogenicity Analysis Set (Section 4). Participants will be analyzed according to the treatment groups that they actually received. No imputation for missing concentration data will be performed.

The following analysis of antibodies to guselkumab will be performed by treatment group:

- Summary of antibodies to guselkumab status
- Summary of neutralizing antibodies to guselkumab status
- List of participants positive for antibodies to guselkumab

In addition, to explore the relationship between antibodies to guselkumab status and serum guselkumab concentrations, efficacy and safety, the following analysis may be performed as appropriate:

- Summary of clinical response (e.g., IGA 0/1 response, PASI 90 response, ss\_IGA ,PSSI 90 response etc) by antibody to guselkumab status
- Summary of injection-site reactions by antibody to guselkumab status
- Summary of serum guselkumab concentrations by antibody to guselkumab status
- Plots of median trough serum guselkumab concentrations over time by antibody to guselkumab status

#### Immunogenicity analyses presentation

Immunogenicity analyses will be summarized through the following time periods:

- Through Week 16
- Through Week 48
- Through End of Study (Week 112)

For the immunogenicity analyses, the description of treatment groups is as follows:

1. **Placebo → Guselkumab 100 mg q8w:** Participants randomized to placebo and were switched over to Guselkumab 100 mg q8w (due to CO) at Week 16.
2. **Guselkumab 100 mg at Week 0, Week 4, and then q8w:** Participants randomized to guselkumab 100 mg at Week 0, Week 4, and then q8w and received guselkumab 100 mg q8w throughout with an additional dose at Week 4.

### **5.7.2.2. Other Immunogenicity Analyses**

No other immunogenicity analysis is planned.

### **5.7.3. Pharmacodynamics**

Samples for serum biomarkers will be collected for all participants as indicated in the Schedule of Activities in the protocol. The analyses on PD biomarkers are to better understand the biology of PSO, to provide a biological assessment of the participants' response to treatment with guselkumab, to analyze differences between responders and non-responders, and to determine if the markers can be used to classify participants as potential responders prior to treatment.

All PD analyses will be based on the PD Analysis Set (Section 4). Participants will be analyzed according to the treatment groups that they received. No imputation for missing concentration data will be performed. Detailed analysis plan and the PD analyses results will be provided in an independent technical report.

### **5.7.4. Pharmacokinetic/Pharmacodynamic Relationships**

If data permit, the relationships between serum guselkumab concentration and efficacy may be analyzed graphically. If any visual trend is observed, a suitable population PK/PD model may be developed to describe the exposure-response relationship. Details will be given in a population PK/PD analysis plan and results of the population PK/PD analysis will be presented in a separate technical report.

### **5.7.5. Biomarkers Analyses**

Biomarker analysis may be deferred or not performed, if during or at the end of the study, it becomes clear that the analysis will not have sufficient scientific value for biomarker evaluation, or if there are not enough samples or responders to allow for adequate biomarker evaluation. 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.

DNA samples may 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.

### **5.7.6. Health Economics**

No health economics measurement is collected in this study.

**5.7.7. Other Variables and/or Parameters****5.7.7.1. Definition****5.7.7.2. Analysis Method****5.7.8. Definition of Subgroups**

To evaluate the consistency of efficacy based on demographic characteristics, baseline disease characteristics, and psoriasis medication history, subgroup analyses will be performed for the coprimary endpoints and selected major secondary endpoints for both cohorts. The subgroups for subgroup analyses include, but are not limited to, the following:

**Baseline demographics – Cohort A & B**

- Sex (male, female)
- Race/ethnicity (Black, Asian, Hispanic or Latino, Multi-Racial, Middle Eastern, American Indian/Indigenous/Alaskan Native, Pacific Islander/Native Hawaiian, Other)
- Geographic location (US and Canada)
- Baseline Age ( $\leq 30$ ,  $>30$  to  $\leq 45$ ,  $>45$ )
- Baseline weight ( $\leq 90$  kg,  $>90$  kg)
- Baseline weight by quartiles
- BMI (Normal [ $<25$ ], Overweight [ $25$  to  $<30$ ], Obese [ $\geq 30$ ])
- Fitzpatrick Skin Type (I-III, IV-VI)

**Baseline disease characteristics:**

- Age at diagnosis (years) ( $<25$ ,  $\geq 25$ )
- Psoriasis disease duration (years) ( $\leq 2$ ,  $>2$  to  $\leq 5$ ,  $>5$ )
- Psoriatic arthritis CCI [REDACTED]
- Psoriasis Special Site Involvement (Scalp, Nail, Hand and/or Foot, Inverse, Genital)
- Baseline DLQI ( $<10$ ,  $\geq 10$ )

**Cohort A subgroups**

- Baseline PASI ( $<20$ ,  $\geq 20$ )
- Baseline IGA ( $<4$ ,  $= 4$ )
- Baseline BSA ( $<20\%$ ,  $\geq 20\%$ )

**Cohort B Subgroups**

- Baseline PSSI ( $<20$ ,  $\geq 20$ )
- Baseline ss-IGA ( $<4$ ,  $= 4$ )
- Baseline SSA ( $<50$ ,  $\geq 50\%$ )
- Baseline BSA ( $<5$ ,  $\geq 5$  to  $<10$ ,  $\geq 10$ )

**Psoriasis medication history:**

- Phototherapy (ultraviolet B light [UVB] or psoralen and ultraviolet A light therapy [PUVA])
  - ☐ Never used
  - ☐ Ever used
- Non-biologic systemics (PUVA, MTX, cyclosporine, acitretin)
  - ☐ Never used
  - ☐ Ever Used
- Biologics (etanercept, infliximab, adalimumab, certolizumab, ustekinumab, , secukinumab, ixekizumab, bimekizumab or brodalumab)
  - ☐ Never used
  - ☐ Ever Used
- Advanced Orals (apremilast, deucravacitinib)
  - ☐ Never used
  - ☐ Ever used
- Topicals
  - ☐ Never used
  - ☐ Ever used
- Anti-TNF $\alpha$  agent (etanercept, infliximab, adalimumab, certolizumab)
  - ☐ Never used
  - ☐ Ever used
- IL-12/23 inhibitors (ustekinumab)
  - ☐ Never used
  - ☐ Ever used
- IL-17 inhibitors (secukinumab, ixekizumab, bimekizumab or brodalumab)
  - ☐ Never used
  - ☐ Ever used
- Participants who had an inadequate response to or had a contraindication to any of the 4 non-biologic systemics therapies (PUVA, MTX, acitretin, or cyclosporine).

- Participants who had an inadequate response to or had a contraindication to any biologic therapies.
- Participants who had an inadequate response to or had a contraindication to any advanced oral therapies.

## **5.8. Interim Analyses**

No interim analysis is planned for this study.

### **5.8.1. Data Monitoring Committee (DMC) or Other Review Board**

No data monitoring committee or other review board is planned for this study.

## 6. SUPPORTING DOCUMENTATION

No data monitoring committee or other review board is planned for this study.

### 6.1. Appendix 1 List of Abbreviations

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| AE              | adverse event                                                             |
| ALT             | alanine aminotransferase                                                  |
| ANCOVA          | analysis of covariance                                                    |
| AST             | aspartate aminotransferase                                                |
| ATC             | anatomic and therapeutic class                                            |
| BMI             | body mass index                                                           |
| BSA             | body surface area                                                         |
| CI              | confidence interval                                                       |
| CMH             | Cochran-Mantel Haenszel                                                   |
| CRO             | contract research organization                                            |
| DBL             | Database lock                                                             |
| DLQI            | Dermatology Life Quality Index                                            |
| DMC             | Data Monitoring Committee                                                 |
| eCRF            | electronic case report form                                               |
| FAS             | full analysis set                                                         |
| FOIA            | Freedom of Information Act                                                |
| GCP             | Good Clinical Practice                                                    |
| HBsAg           | hepatitis B surface antigen                                               |
| HIV             | human immunodeficiency virus                                              |
| hsCRP           | high sensitivity C-Reactive Protein                                       |
| ICE             | Intercurrent Events                                                       |
| ICF             | informed consent form                                                     |
| ICH             | International Conference on Harmonisation                                 |
| IGA             | Investigator Global assessment                                            |
| IgG1λ           | immunoglobulin G1 lambda                                                  |
| IL              | interleukin                                                               |
| INR             | international normalized ratio                                            |
| IQ              | interquartile                                                             |
| LS              | Least Square                                                              |
| LTE             | Long-term extension                                                       |
| MedDRA          | Medical Dictionary for Regulatory Activities                              |
| CCI             | CCI                                                                       |
| MMRM            | MMRM mixed model for repeated measures                                    |
| MTX             | methotrexate                                                              |
| NCI-CTCAE       | National Cancer Institute –Common Terminology Criteria for Adverse Events |
| NRS             | numeric rating scale                                                      |
| PASI            | Psoriasis area and Severity Index                                         |
| PD              | pharmacodynamic(s)                                                        |
| PEST            | Psoriasis Epidemiology Screening Tool                                     |
| PIDASI          | Post-inflammatory Dyspigmentation Area and Severity Score                 |
| PIPA            | Post-inflammatory Pigment Alteration                                      |
| PK              | pharmacokinetic(s)                                                        |
| PP              | per protocol                                                              |
| 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                                            |
| PUVA            | Psoralen plus ultraviolet A                                               |
| q4w/q8w         | every 4 weeks/every 8 weeks                                               |
| QuantiFERON-TB® | QuantiFERON-TB® Gold In Tube test (for tuberculosis)                      |
| RBC             | Red blood cell                                                            |

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|        |                                                    |
|--------|----------------------------------------------------|
| SAE    | serious adverse event                              |
| SAP    | Statistical Analysis Plan                          |
| SC     | subcutaneous(ly)                                   |
| SD     | standard deviation                                 |
| SDIEQ  | Skin Discoloration Impact Evaluation Questionnaire |
| SSA    | scalp surface area                                 |
| ss-IGA | scalp surface –Investigator Global Assessment      |
| SoA    | Schedule of Activities                             |
| Tbili  | total bilirubin                                    |
| ULN    | upper limit of normal                              |
| USA    | United States of America                           |
| UVB    | Ultraviolet B light                                |
| WBC    | White blood cell                                   |

## 6.2. Appendix 2 Changes to Protocol-Planned Analyses

No change to protocol planned analyses.

## 6.3. Appendix 3 Demographics and Baseline Characteristics

Demographic and baseline characteristic variables will be descriptively summarized by randomized treatment group. No formal statistical comparison is planned. P-values will not be provided.

Demographic variables to be summarized will include sex, race, age, height, baseline weight, and baseline body mass index (BMI). Baseline characteristic variables to be summarized will include, but not be limited to, baseline disease characteristics (e.g., duration of disease, BSA [%], and baseline PASI score.

In addition, summaries of participants' medical history and current diagnoses, alcohol intake, and smoking status will be provided by treatment group. If imbalances are found at baseline, then additional analyses may be performed adjusting for baseline differences.

## 6.4. Appendix 4 Protocol Deviations

Participants with major protocol deviations, defined as having the potential to impact participants' rights, safety or well-being, or the integrity and/or result of the clinical study. Participants with major protocol deviations will be identified prior to database lock and the participants with major protocol deviations will be summarized by category through Week 16 and through the end of study. The major protocol deviations will be grouped into the following 5 categories:

- Entered the study without satisfying study selection criteria
- Developed study withdrawal criteria but not withdrawn
- Received a disallowed concomitant treatment
- Received wrong treatment or incorrect dose
- Other

A listing of participants with major protocol deviations will also be provided by randomized treatment group. In addition, analyses of COVID-19 related protocol deviations will be provided.

## 6.5. Appendix 5 Prior and Concomitant Medications

Participants' psoriasis medication history with topical agents, phototherapy, non-biologic systemic therapies, and biologic medications will be summarized by treatment group for all randomized Participants. If data are available, total cumulative duration of treatment with these medications will be summarized. In addition, reasons for which Participants discontinued previous systemic therapies (contraindication, inadequate response, or other) will be summarized by randomized treatment group.

The number of Participants who received concomitant treatment of moisturizer for psoriasis will be summarized by randomized treatment group. Participants who received concomitant corticosteroids for indications other than psoriasis will be listed. Participants with concomitant prophylactic treatments for latent tuberculosis infection will also be listed. Participants who receive concomitant medications for hyperpigmentation will be listed.

## 6.6. Appendix 6 Medical History

Medical history captured will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and summarized by number and percentage of patients in System Organ Class (SOC) and Preferred Term (PT) based on FAS for cohort A and CCI for cohort B. Through the end of the study, the MedDRA will be up versioned if a newer version is released, and the coding of medical history will be updated. The current version used in this study is MedDRA version 25.1.

## 6.7. Appendix 7 Intervention Compliance

Treatment compliance will be assessed by protocol deviations related to administration related to incorrect study agent or dose received and missed administrations.

## 6.8. Appendix 8 Adverse Events of Special Interest

Adverse events of special interest will be tabulated by actual treatment group based on safety analysis set.

## 6.9. Appendix 9 Medications of Special Interest

Prohibited medications for Post-inflammatory Pigment Alteration (PIPA) endpoints ([Appendix 10](#))

- ❖ Medications that may affect psoriasis or pigmentation and not allowed before Week 48:

- Topical corticosteroids of all classes

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That affect psoriasis:

- Topical steroids Class III-VII:
  - (a) Class III steroids: triamcinolone acetonide 0.5% cream, mometasone furoate 0.1% ointment, betamethasone dipropionate .05% cream, betamethasone valerate 0.1% ointment, fluocinonide .05% cream
  - (b) Class IV steroids: fluocinolone acetonide 0.2%, desoximetasone .05% cream, hydrocortisone valerate 0.2% ointment, flurandrenolide .05% ointment, triamcinolone acetonide 0.1% ointment, mometasone furoate 0.1% cream or lotion
  - (c) Class V steroids: desonide .05% ointment, fluocinolone acetonide .025% cream, fluticasone propionate .05% cream, betamethasone dipropionate lotion, betamethasone valerate 0.1% cream or lotion, flurandrenolide .05% cream or lotion, hydrocortisone butyrate 0.1% cream/ointment/solution
  - (d) Class VI steroids: alclometasone dipropionate .05% cream or ointment, desonide .05% cream/foam/gel/lotion, fluocinolone acetonide .01% shampoo or solution, flurandrenolide .025% cream, triamcinolone acetonide .025% cream or lotion
  - (e) Class VII steroids: hydrocortisone 0.5% cream or ointment, hydrocortisone 1.0% cream/lotion/ointment, hydrocortisone 2.5% cream/lotion/ointment

❖ Medications still NOT allowed after Week 48:

- Topical steroids Class I - II:
  - (a) Class I: clobetasol propionate .05% cream/gel/ointment/lotion/foam/shampoo/solution/spray, betamethasone dipropionate .05% gel/lotion/ointment, fluocinonide 0.1% cream, flurandrenolide tape (Cordran tape), halobetasol propionate .05% cream/ointment
  - (b) Class II: augmented betamethasone dipropionate .05% cream, betamethasone dipropionate .05% ointment, desoximetasone .025% cream or ointment, desoximetasone .05% gel, fluocinonide .05% cream/gel/ointment/solution, mometasone furoate 0.1% ointment, triamcinolone acetonide 0.5% ointment

CCI

### 6.11. Appendix 11 Laboratory Toxicity Grading

The grading scale use for lab assessments is based on ‘Common Terminology Criteria for Adverse Events (CTCAE) v5.0’.

If a laboratory value falls within the grading as specified below but also within the local laboratory normal limits, the value is considered to be normal and will be reset to grade 0.

Pre-baseline measurements will use the same grading ranges as applied to baseline measurements. In case a test has two sets of ranges – one for baseline normal and one for baseline abnormal, the one for baseline normal will be applied for all measurements taken pre-baseline and on baseline.

Text in gray italic in the table is present in the grading scale but is not applied by Janssen when grading lab data.

| CTCAE Term                                      | Grade 1                                                                                   | Grade 2                                                                                    | Grade 3                                                                                      | Grade 4                                                                          | Janssen implementation notes                                                                                                                 |
|-------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Blood and lymphatic system disorders</b>     |                                                                                           |                                                                                            |                                                                                              |                                                                                  |                                                                                                                                              |
| Anemia                                          | Hemoglobin (Hgb)<br><LLN - 10.0 g/dL;<br><LLN - 6.2 mmol/L;<br><LLN - 100 g/L             | Hemoglobin (Hgb)<br><10.0 - 8.0 g/dL;<br><6.2 - 4.9 mmol/L;<br><100 - 80g/L                | Hemoglobin (Hgb) <8.0 g/dL;<br><4.9 mmol/L;<br><80 g/L;<br><i>transfusion indicated</i>      | <i>Life-threatening consequences;<br/>urgent intervention indicated</i>          | Clinical signs and symptoms are not taken into consideration for grading.                                                                    |
| Leukocytosis                                    | -                                                                                         | -                                                                                          | >100,000/mm <sup>3</sup> ;<br>>100 x 10 <sup>9</sup> /L                                      | <i>Clinical manifestations of leucostasis;<br/>urgent intervention indicated</i> | Clinical signs and symptoms are not taken into consideration for grading;<br>Added ranges in SI unit (x 10 <sup>9</sup> /L)                  |
| <b>Investigations</b>                           |                                                                                           |                                                                                            |                                                                                              |                                                                                  |                                                                                                                                              |
| Activated partial thromboplastin time prolonged | >ULN - 1.5 x ULN                                                                          | >1.5 - 2.5 x ULN                                                                           | >2.5 x ULN;<br><i>bleeding</i>                                                               | -                                                                                | Clinical signs and symptoms are not taken into consideration for grading.                                                                    |
| Alanine aminotransferase increased              | >ULN - 3.0 x ULN if baseline was normal;<br>1.5 - 3.0 x baseline if baseline was abnormal | >3.0 - 5.0 x ULN if baseline was normal;<br>>3.0 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal;<br>>5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal;<br>>20.0 x baseline if baseline was abnormal | Ranges defined for “abnormal baseline” are applied only if baseline > ULN. If baseline < LLN, then ranges for “normal baseline” are applied. |
| Alkaline phosphatase increased                  | >ULN - 2.5 x ULN if baseline was normal;<br>2.0 - 2.5 x baseline if baseline was abnormal | >2.5 - 5.0 x ULN if baseline was normal;<br>>2.5 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal;<br>>5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal;<br>>20.0 x baseline if baseline was abnormal | Ranges defined for “abnormal baseline” are applied only if baseline > ULN. If baseline < LLN, then ranges for “normal baseline” are applied. |
| Aspartate aminotransferase increased            | >ULN - 3.0 x ULN if baseline was normal;<br>1.5 - 3.0 x baseline if baseline was abnormal | >3.0 - 5.0 x ULN if baseline was normal;<br>>3.0 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal;<br>>5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal;<br>>20.0 x baseline if baseline was abnormal | Ranges defined for “abnormal baseline” are applied only if baseline > ULN. If baseline < LLN, then ranges for “normal baseline” are applied. |
| Blood bilirubin increased                       | >ULN - 1.5 x ULN if baseline was normal;                                                  | >1.5 - 3.0 x ULN if baseline was normal;                                                   | >3.0 - 10.0 x ULN if baseline was normal;                                                    | >10.0 x ULN if baseline was normal;                                              | Ranges defined for “abnormal baseline” are                                                                                                   |

| CTCAE Term                | Grade 1                                                                                   | Grade 2                                                                                    | Grade 3                                                                                      | Grade 4                                                                              | Janssen implementation notes                                                                                                                              |
|---------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
|                           | > 1.0 - 1.5 x baseline if baseline was abnormal                                           | >1.5 - 3.0 x baseline if baseline was abnormal                                             | >3.0 - 10.0 x baseline if baseline was abnormal                                              | >10.0 x baseline if baseline was abnormal                                            | applied only if baseline > ULN. If baseline < LLN, then ranges for “normal baseline” are applied.                                                         |
| CD4 lymphocytes decreased | <LLN - 500/mm <sup>3</sup> ;<br><LLN - 0.5 x 10 <sup>9</sup> /L                           | <500 - 200/mm <sup>3</sup> ;<br><0.5 - 0.2 x 10 <sup>9</sup> /L                            | <200 - 50/mm <sup>3</sup> ;<br><0.2 x 0.05 - 10e <sup>9</sup> /L                             | <50/mm <sup>3</sup> ;<br><0.05 x 10e <sup>9</sup> /L                                 |                                                                                                                                                           |
| Cholesterol high          | >ULN - 300 mg/dL;<br>>ULN - 7.75 mmol/L                                                   | >300 - 400 mg/dL;<br>>7.75 - 10.34 mmol/L                                                  | >400 - 500 mg/dL;<br>>10.34 - 12.92 mmol/L                                                   | >500 mg/dL;<br>>12.92 mmol/L                                                         |                                                                                                                                                           |
| CPK increased             | >ULN - 2.5 x ULN                                                                          | >2.5 x ULN - 5 x ULN                                                                       | >5 x ULN - 10 x ULN                                                                          | >10 x ULN                                                                            |                                                                                                                                                           |
| Creatinine increased      | Creatine Kinase<br>>ULN - 1.5 x ULN                                                       | Creatine Kinase<br>>1.5 - 3.0 x baseline;<br>>1.5 - 3.0 x ULN                              | Creatine Kinase<br>>3.0 x baseline;<br>>3.0 - 6.0 x ULN                                      | Creatine Kinase<br>>6.0 x ULN                                                        |                                                                                                                                                           |
| Fibrinogen decreased      | <1.0 - 0.75 x LLN;<br>if abnormal, <25% decrease from baseline                            | <0.75 - 0.5 x LLN;<br>if abnormal, 25 - <50% decrease from baseline                        | <0.5 - 0.25 x LLN;<br>if abnormal, 50 - <75% decrease from baseline                          | <0.25 x LLN;<br>if abnormal, 75% decrease from baseline;<br>absolute value <50 mg/dL | Ranges defined for “abnormal” are applied only on values < LLN. Grade 0 will be assigned to values > ULN.                                                 |
| GGT increased             | >ULN - 2.5 x ULN if baseline was normal;<br>2.0 - 2.5 x baseline if baseline was abnormal | >2.5 - 5.0 x ULN if baseline was normal;<br>>2.5 - 5.0 x baseline if baseline was abnormal | >5.0 - 20.0 x ULN if baseline was normal;<br>>5.0 - 20.0 x baseline if baseline was abnormal | >20.0 x ULN if baseline was normal;<br>>20.0 x baseline if baseline was abnormal     | Ranges defined for “abnormal baseline” are applied only if baseline > ULN. If baseline < LLN, then ranges for “normal baseline” are applied.              |
| Haptoglobin decreased     | <LLN                                                                                      | -                                                                                          | -                                                                                            | -                                                                                    |                                                                                                                                                           |
| Hemoglobin increased      | Increase in >0 - 2 g/dL;<br>Increase in >0 - 20 g/L                                       | Increase in >2 - 4 g/dL;<br>Increase in >20 - 40 g/L                                       | Increase in >4 g/dL;<br>Increase in >40 g/L                                                  | -                                                                                    | The increase indicates the level of increase above normal (above ULN). Applied as, e.g. grade 1 (g/dL): >ULN – ULN+2 g/dL; Added ranges in SI unit (g/L). |
| INR increased             | >1.2 - 1.5;<br>>1 - 1.5 x baseline if on anticoagulation;<br>monitoring only indicated    | >1.5 - 2.5;<br>>1.5 - 2.5 x baseline if on anticoagulation;<br>dose adjustment indicated   | >2.5;<br>>2.5 x baseline if on anticoagulation;<br>bleeding                                  | -                                                                                    | Concomitant therapy or clinical signs and symptoms are not taken into consideration for grading.                                                          |

| CTCAE Term                                | Grade 1                                                             | Grade 2                                                                          | Grade 3                                                                 | Grade 4                                                 | Janssen implementation notes                                                                                    |
|-------------------------------------------|---------------------------------------------------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| Lipase increased                          | >ULN - 1.5 x ULN                                                    | >1.5 - 2.0 x ULN;<br>>2.0 - 5.0 x ULN and asymptomatic                           | >2.0 - 5.0 x ULN with signs or symptoms;<br>>5.0 x ULN and asymptomatic | >5.0 x ULN and with signs or symptoms                   | "Asymptomatic" ranges are not taken into consideration for grading, i.e. worst case grading is applied.         |
| Lymphocyte count decreased                | <LLN - 800/mm <sup>3</sup> ;<br><LLN - 0.8 x 10 <sup>9</sup> /L     | <800 - 500/mm <sup>3</sup> ;<br><0.8 - 0.5 x 10 <sup>9</sup> /L                  | <500 - 200/mm <sup>3</sup> ;<br><0.5 - 0.2 x 10 <sup>9</sup> /L         | <200/mm <sup>3</sup> ;<br><0.2 x 10 <sup>9</sup> /L     |                                                                                                                 |
| Lymphocyte count increased                | -                                                                   | >4000/mm <sup>3</sup> - 20,000/mm <sup>3</sup> ;<br>>4 - 20 x 10 <sup>9</sup> /L | >20,000/mm <sup>3</sup> ;<br>>20 x 10 <sup>9</sup> /L                   | -                                                       | Added ranges in SI unit (x 10 <sup>9</sup> /L).                                                                 |
| Neutrophil count decreased                | <LLN - 1500/mm <sup>3</sup> ;<br><LLN - 1.5 x 10 <sup>9</sup> /L    | <1500 - 1000/mm <sup>3</sup> ;<br><1.5 - 1.0 x 10 <sup>9</sup> /L                | <1000 - 500/mm <sup>3</sup> ;<br><1.0 - 0.5 x 10 <sup>9</sup> /L        | <500/mm <sup>3</sup> ;<br><0.5 x 10 <sup>9</sup> /L     | Both Neutrophils and segmented neutrophils are graded using these criteria.                                     |
| Platelet count decreased                  | <LLN - 75,000/mm <sup>3</sup> ;<br><LLN - 75.0 x 10 <sup>9</sup> /L | <75,000 - 50,000/mm <sup>3</sup> ;<br><75.0 - 50.0 x 10 <sup>9</sup> /L          | <50,000 - 25,000/mm <sup>3</sup> ;<br><50.0 - 25.0 x 10 <sup>9</sup> /L | <25,000/mm <sup>3</sup> ;<br><25.0 x 10 <sup>9</sup> /L |                                                                                                                 |
| Serum amylase increased                   | >ULN - 1.5 x ULN                                                    | >1.5 - 2.0 x ULN;<br>>2.0 - 5.0 x ULN and asymptomatic                           | >2.0 - 5.0 x ULN with signs or symptoms;<br>>5.0 x ULN and asymptomatic | >5.0 x ULN and with signs or symptoms                   | "Asymptomatic" ranges are not taken into consideration for grading, i.e. worst case grading is applied.         |
| White blood cell decreased                | <LLN - 3000/mm <sup>3</sup> ;<br><LLN - 3.0 x 10 <sup>9</sup> /L    | <3000 - 2000/mm <sup>3</sup> ; <3.0 - 2.0 x 10 <sup>9</sup> /L                   | <2000 - 1000/mm <sup>3</sup> ; <2.0 - 1.0 x 10 <sup>9</sup> /L          | <1000/mm <sup>3</sup> ;<br><1.0 x 10 <sup>9</sup> /L    |                                                                                                                 |
| <b>Metabolism and nutrition disorders</b> |                                                                     |                                                                                  |                                                                         |                                                         |                                                                                                                 |
| Acidosis                                  | pH <normal, but ≥7.3                                                | -                                                                                | pH <7.3                                                                 | Life-threatening consequences                           | pH <normal is implemented as pH <LLN. Clinical signs and symptoms are not taken into consideration for grading. |
| Alkalosis                                 | pH >normal, but ≤7.5                                                | -                                                                                | pH >7.5                                                                 | Life-threatening consequences                           | pH >normal is implemented as pH >ULN. Clinical signs and symptoms are not taken into consideration for grading. |

| CTCAE Term           | Grade 1                                                                                                      | Grade 2                                                                                                                                  | Grade 3                                                                                                                                                | Grade 4                                                                                                                              | Janssen implementation notes                                                                                                                                                                                                                                       |
|----------------------|--------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Hypercalcemia        | Corrected serum calcium of >ULN - 11.5 mg/dL;<br>>ULN - 2.9 mmol/L;<br><br>Ionized calcium >ULN - 1.5 mmol/L | Corrected serum calcium of >11.5 - 12.5 mg/dL;<br>>2.9 - 3.1 mmol/L;<br><br>Ionized calcium >1.5 - 1.6 mmol/L;<br><br><i>symptomatic</i> | Corrected serum calcium of >12.5 - 13.5 mg/dL;<br>>3.1 - 3.4 mmol/L;<br><br>Ionized calcium >1.6 - 1.8 mmol/L;<br><br><i>hospitalization indicated</i> | Corrected serum calcium of >13.5 mg/dL; >3.4 mmol/L;<br><br>Ionized calcium >1.8 mmol/L;<br><br><i>life-threatening consequences</i> | Clinical signs and symptoms are not taken into consideration for grading.<br>Note: For Hypercalcemia or Hypocalcemia in the CTCAE Lab Toxicity grading scale, the reference ranges from serum calcium (ULN /LLN) from the local or central lab are being utilized. |
| Hyperkalemia         | Potassium >ULN - 5.5 mmol/L                                                                                  | Potassium >5.5 - 6.0 mmol/L;<br><br><i>intervention initiated</i>                                                                        | Potassium >6.0 - 7.0 mmol/L;<br><br><i>hospitalization indicated</i>                                                                                   | Potassium >7.0 mmol/L;<br><br><i>life-threatening consequences</i>                                                                   | Clinical signs and symptoms are not taken into consideration for grading.                                                                                                                                                                                          |
| Hypermagnesemia      | Magnesium >ULN - 3.0 mg/dL;<br>>ULN - 1.23 mmol/L                                                            | -                                                                                                                                        | Magnesium >3.0 - 8.0 mg/dL;<br>>1.23 - 3.30 mmol/L                                                                                                     | Magnesium >8.0 mg/dL;<br>>3.30 mmol/L;<br><br><i>life-threatening consequences</i>                                                   | Clinical signs and symptoms are not taken into consideration for grading.                                                                                                                                                                                          |
| Hypernatremia        | Sodium >ULN - 150 mmol/L                                                                                     | Sodium >150 - 155 mmol/L;<br><br><i>intervention initiated</i>                                                                           | Sodium >155 - 160 mmol/L;<br><br><i>hospitalization indicated</i>                                                                                      | Sodium >160 mmol/L;<br><br><i>life-threatening consequences</i>                                                                      | Clinical signs and symptoms are not taken into consideration for grading.                                                                                                                                                                                          |
| Hypertriglyceridemia | Triglycerides 150 mg/dL - 300 mg/dL;<br>1.71 mmol/L - 3.42 mmol/L                                            | Triglycerides >300 mg/dL - 500 mg/dL;<br>>3.42 mmol/L - 5.7 mmol/L                                                                       | Triglycerides >500 mg/dL - 1000 mg/dL;<br>>5.7 mmol/L - 11.4 mmol/L                                                                                    | Triglycerides >1000 mg/dL;<br>>11.4 mmol/L;<br><br><i>life-threatening consequences</i>                                              | Clinical signs and symptoms are not taken into consideration for grading.                                                                                                                                                                                          |
| Hypoalbuminemia      | Albumin <LLN - 3 g/dL;<br><LLN - 30 g/L                                                                      | Albumin <3 - 2 g/dL;<br><30 - 20 g/L                                                                                                     | Albumin <2 g/dL;<br><20 g/L                                                                                                                            | <i>Life-threatening consequences;</i><br><i>urgent intervention indicated</i>                                                        | Clinical signs and symptoms are not taken into consideration for grading.                                                                                                                                                                                          |
| Hypocalcemia         | Corrected serum calcium of <LLN - 8.0 mg/dL;<br><LLN - 2.0 mmol/L;                                           | Corrected serum calcium of <8.0 - 7.0 mg/dL; <2.0 - 1.75 mmol/L;                                                                         | Corrected serum calcium of <7.0 - 6.0 mg/dL;<br><1.75 - 1.5 mmol/L;                                                                                    | Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L;                                                                                  | Clinical signs and symptoms are not taken                                                                                                                                                                                                                          |

| CTCAE Term     | Grade 1                                          | Grade 2                                                                                  | Grade 3                                                                                                                 | Grade 4                                                                                        | Janssen implementation notes                                                                                                                                                                                             |
|----------------|--------------------------------------------------|------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                | Ionized calcium <LLN - 1.0 mmol/L                | Ionized calcium <1.0 - 0.9 mmol/L;<br><i>symptomatic</i>                                 | Ionized calcium <0.9 - 0.8 mmol/L;<br><i>hospitalization indicated</i>                                                  | Ionized calcium <0.8 mmol/L;<br><i>life-threatening consequences</i>                           | into consideration for grading.<br>Note: For Hypercalcemia or Hypocalcemia in the CTCAE Lab Toxicity grading scale, the reference ranges from serum calcium (ULN /LLN) from the local or central lab are being utilized. |
| Hypoglycemia   | Glucose <LLN - 55 mg/dL;<br><LLN - 3.0 mmol/L    | Glucose <55 - 40 mg/dL;<br><3.0 - 2.2 mmol/L                                             | Glucose <40 - 30 mg/dL;<br><2.2 - 1.7 mmol/L                                                                            | Glucose <30 mg/dL;<br><1.7 mmol/L;<br><i>life-threatening consequences;</i><br><i>seizures</i> | Clinical signs and symptoms are not taken into consideration for grading. Urine glucose is not graded.                                                                                                                   |
| Hypokalemia    | <i>Potassium &lt;LLN - 3.0 mmol/L</i>            | <i>Symptomatic with</i><br>Potassium <LLN - 3.0 mmol/L;<br><i>intervention indicated</i> | Potassium <3.0 - 2.5 mmol/L;<br><i>hospitalization indicated</i>                                                        | Potassium <2.5 mmol/L;<br><i>life-threatening consequences</i>                                 | “Symptomatic” ranges are applied for grade 2, grade 1 not assigned, i.e., worst case applied. Clinical signs and symptoms are not taken into consideration for grading of grade 3 and 4.                                 |
| Hypomagnesemia | Magnesium <LLN - 1.2 mg/dL;<br><LLN - 0.5 mmol/L | Magnesium <1.2 - 0.9 mg/dL;<br><0.5 - 0.4 mmol/L                                         | Magnesium <0.9 - 0.7 mg/dL;<br><0.4 - 0.3 mmol/L                                                                        | Magnesium <0.7 mg/dL;<br><0.3 mmol/L;<br><i>life-threatening consequences</i>                  | Clinical signs and symptoms are not taken into consideration for grading.                                                                                                                                                |
| Hyponatremia   | Sodium <LLN - 130 mmol/L                         | <i>Sodium 125-129 mmol/L and asymptomatic</i>                                            | <i>Sodium 125-129 mmol/L symptomatic;</i><br><i>120-124 mmol/L regardless of symptoms</i><br><br>Sodium <130-120 mmol/L | Sodium <120 mmol/L;<br><i>life-threatening consequences</i>                                    | Clinical signs and symptoms are not taken into consideration for grading.<br>Worst case (“<130-120 mmol/L” for grade 3 added by Janssen) is applied across grade 2/3                                                     |

| CTCAE Term                         | Grade 1                                                                                                           | Grade 2                                                                                                                                                                                                                                                                   | Grade 3                                                                                                                                                                                                                                                 | Grade 4 | Janssen implementation notes                                                                                                                                                                                                                                                                                                                         |
|------------------------------------|-------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                    |                                                                                                                   |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                         |         | ranges: 120-129 mol/L assigned to grade 3, grade 2 not used.                                                                                                                                                                                                                                                                                         |
| <b>Renal and urinary disorders</b> |                                                                                                                   |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                         |         |                                                                                                                                                                                                                                                                                                                                                      |
| Proteinuria                        | 1+ proteinuria;<br>urinary protein $\geq$ ULN -<br><1.0 g/24 hrs;<br>urinary protein $\geq$ ULN -<br><1000 mg/day | <b>Adult:</b><br>2+ and 3+ proteinuria;<br>urinary protein 1.0 - <3.5<br>g/24 hrs;<br>urinary protein 1000 -<br><3500 mg/day<br><br><b>Pediatric:</b><br>Urine P/C<br>(Protein/Creatinine) ratio<br>0.5 - 1.9;<br>Urine P/C<br>(Protein/Creatinine) 56.5<br>– 214.7 g/mol | <b>Adult:</b><br>4+ proteinuria;<br>urinary protein $\geq$ 3.5<br>g/24 hrs;<br>urinary protein $\geq$ 3500<br>mg/day;<br><br><b>Pediatric:</b><br>Urine P/C<br>(Protein/Creatinine) ratio<br>>1.9;<br>Urine P/C<br>(Protein/Creatinine)<br>>214.7 g/mol | -       | In case both 24-h urine collection and dipstick are collected, then worst case is taken, as opposed to having 24-h urine collection take precedence over dipstick. Added ranges in SI unit for urinary protein (mg/day) and for urine P/C (g/mol). Pediatric grading is applied to age range [0-18]. Adult grading is applied for ages [ $\geq$ 18]. |

\* Grade 0 is assigned to a lab assessment when the lab test is described in the table, but the lab value is not assigned a grade 1 or higher.

## 7. REFERENCES

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.

Maurer, W., Hothorn, L. A., Lehmacher, W. Multiple comparisons in drug clinical trials and preclinical assays: a prior ordered hypotheses. *Biometrie in der Chemisch-in-Pharmazeutischen Industrie*. 1995, 3-18