### Statistical Analysis Plan

**Multicenter, randomized, open-label, efficacy assessor-blinded, active comparator-controlled phase 3b study to compare the efficacy of guselkumab to fumaric acid esters (Fumaderm® initial/ Fumaderm®) for adult patients with moderate to severe plaque psoriasis who are candidates for and naive to systemic treatment**

**POLARIS**

- **Week 24 Analysis -**

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<tr>
<th>Study Code</th>
<th>CNTO1959PSO3008</th>
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<td>EudraCT Number</td>
<td>2016-002135-15</td>
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<td>Study Design</td>
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<tr>
<td>Sponsor</td>
<td>Janssen-Cilag GmbH, Neuss Johnson &amp; Johnson Platz 1, 41470 Neuss, Germany</td>
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<tr>
<td>Contract Research Organization</td>
<td>acromion GmbH Europaallee 27 – 29 50226 Frechen, Germany</td>
</tr>
<tr>
<td>Version No., Date</td>
<td>Final 1.0, 10-July-2017</td>
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## 1.0 Signatures

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**Date:** 17/Jul/17

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**Senior Project Statistician, acromion GmbH**

**Date:** 17/Oct/17

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**Date:** 10/Jul/17

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HEMAR Strategy Lead, Janssen-Cilag GmbH, Neuss

**Date:** 10/Jul/17

**Signature**
2.0 List of Abbreviations

AE  Adverse Event
ANCOVA  Analysis of Covariance
BSA  Body Surface Area
CRF  Case Report Form(s)
CSP  Clinical Study Protocol
DLQI  Dermatology Life Quality Index
eCRF  electronic Case Report Form
EDC  Electronic Data Capture
e.g.  example given
FAE  Fumaric Acid Esters
HBV/ HCV  Hepatitis B virus/ Hepatitis C Virus
HIV  Human Immunodeficiency Virus
HTA  Health Technology Assessment
ICH  International Council on Harmonization
i.e.  that is
IGA  Investigator’s Global Assessment
IL  Interleukin
LOCF  Last Observation Carried Forward
MCS  Mental Component Summary
MedDRA  Medical Dictionary for Regulatory Activities
MTX  Methotrexate
NTEAE  Not Treatment Emergent Adverse Event
NTESAE  Not Treatment Emergent Serious Adverse Event
PASI  Psoriasis Area and Severity Index
PCS  Physical Component Summary
PRO  Patient-Reported Outcome(s)
PSSD  Psoriasis Symptom and Sign Diary
SAE  Serious Adverse Event
SAP  Statistical Analysis Plan
SC  subcutaneous
SF-36  Short Form (36-item) health survey
SOC  System Organ Class
SOP  Standard Operating Procedure
ss  scalp-specific
TB  tuberculosis
TEAE  Treatment Emergent Adverse Event
TES  Time and Events Schedule
TESAE  Treatment Emergent Serious Adverse Event
3.0 Introduction

The statistical analysis plan (SAP) is a detailed technical extension to the Clinical Study Protocol (CSP) and follows the principles of the guideline ICH E9 and the relevant acromion SOPs and/or guidelines. This plan describes the statistical analyses planned to be performed for the Week 24 analysis of Janssen-Cilag GmbH Clinical Study Protocol CNTO1959PSO3008 and should be read in conjunction with the CSP and the electronic Case Report Form (eCRF). Statistical analyses of study data recorded after Week 24 will be specified in a separate SAP which will be based on protocol amendment 1 to the CSP.

The Week 24 analysis will include the confirmatory analysis of the primary endpoint and the major secondary endpoints and exploratory analyses for all other predefined efficacy and safety analyses until Week 24. Evaluations on health technology assessment (HTA) will also be specified in this SAP. No separate HTA SAP will be provided. The Week 24 analysis will be performed after all subjects have completed their visit at 24 weeks after randomization or discontinued earlier. Data base lock for the Week 24 analysis will be after the Week 24 visit data are ready for statistical analysis (i.e., clean data).

This SAP is the core document for all statistical programming planned to be performed for the Week 24 analysis and is based on the following study documents to protocol no. CNTO1959PSO3008:

<table>
<thead>
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<th>Document</th>
<th>Version, Date</th>
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<tr>
<td>Protocol / Amendments</td>
<td>Version 1.0, 03-AUG-2016</td>
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<tr>
<td>eCRF</td>
<td>Version 1.0, 12-DEC-2016</td>
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<tr>
<td>Data Management Plan</td>
<td>Version 1.0, 09-DEC-2016</td>
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<tr>
<td>Data Validation Plan</td>
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4.0 Responsibilities

The responsibilities for the biometrical tasks at acromion GmbH are assigned as follows:

<table>
<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Statistician</td>
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<tr>
<td>Statistical Programmer</td>
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<tr>
<td>Medical Data Analyst</td>
<td>Medical Data Review and Coding</td>
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5.0 Software Utilized
The statistical analysis and generation of tables, patient data listings and figures will be performed using the SAS® software package version 9.4 under the Microsoft Windows® 7 operating system at the computer facilities of acromion GmbH. Additional analyses regarding health technology assessment (HTA) may be performed by or under the responsibility of Janssen-Cilag GmbH.

6.0 Coding Systems Utilized
The MedDRA-dictionary version 19.1 is used for coding of prior and concomitant diseases and for coding of adverse events. The following items are coded.

<table>
<thead>
<tr>
<th>eCRF Module</th>
<th>Item</th>
<th>SDTM Domain/ Variable Name</th>
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<tr>
<td>Medical History of Interest</td>
<td>Medical History Term</td>
<td>MH/MHTERM</td>
</tr>
<tr>
<td>Previous Phototherapy</td>
<td>Type of Phototherapy</td>
<td>MH/MHTERM</td>
</tr>
<tr>
<td>Concomitant Medication</td>
<td>Indication</td>
<td>CM/CMIND</td>
</tr>
<tr>
<td>Concomitant Therapy</td>
<td>Indication</td>
<td>CM/CMIND</td>
</tr>
<tr>
<td>(S)AE</td>
<td>Term</td>
<td>AE/AETERM</td>
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</table>

Prior and concomitant medications are coded according to the WHO terminology using the 2016/1 version of the WHO-Drug Dictionary. The following items are coded.

<table>
<thead>
<tr>
<th>eCRF Module</th>
<th>Item</th>
<th>SDTM Domain/ Variable Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous Topical Therapy</td>
<td>Medication/Therapy</td>
<td>MH/MHTERM</td>
</tr>
<tr>
<td>Concomitant Medication</td>
<td>Compound</td>
<td>CM/CMTRT</td>
</tr>
</tbody>
</table>

Details are specified in the Data Management Plan.
7.0 Study Objectives and Hypotheses

7.1 Objectives

Primary Objectives
The primary objectives of the study are

- to compare the efficacy of guselkumab to fumaric acid esters (FAE) in systemic treatment-naïve subjects with moderate to severe plaque-type psoriasis.
- to assess the safety and tolerability of guselkumab in systemic treatment-naïve subjects with moderate to severe plaque-type psoriasis.

Secondary Objective
The secondary objective is to compare improvement of health-related quality of life (QOL) and other patient-reported outcomes (PRO) when systemic treatment-naïve subjects with moderate to severe plaque-type psoriasis are treated with guselkumab compared to FAE.

7.2 Hypotheses
The primary hypothesis of this study is that guselkumab treatment is superior to FAE (Fumaderm® initial/ Fumaderm®) treatment as assessed by the proportion of subjects achieving a PASI 90 response at Week 24.

The major secondary hypotheses are:

- Guselkumab treatment is superior to FAE as assessed by the proportion of subjects achieving a PASI 75 response at Week 24
- Guselkumab treatment is superior to FAE as assessed by the proportion of subjects achieving a DLQI score of 0 or 1 at Week 24.

If the primary hypothesis is accepted, the study will be considered positive.
8.0 Study Endpoints

Primary Endpoint
The primary endpoint is the proportion of subjects achieving at least a 90% improvement of their psoriasis according to the Psoriasis Area and Severity Index (PASI 90 response) at Week 24.

Secondary Endpoints
The major secondary endpoints are:
• The proportion of subjects achieving at least a 75% improvement of their psoriasis according to the PASI at Week 24 (PASI 75 response)
• The proportion of subjects achieving a DLQI score of 0 or 1 at Week 24.

Other secondary endpoints are:
• The proportion of subjects achieving a 100% improvement of their psoriasis according to the PASI at Week 24 (PASI 100 response)
• The change from baseline in the signs and symptoms aggregate scores of the PSSD at Week 24
• The change from baseline in the individual scale scores for itch, pain, and scaling of PSSD components at Week 24
• The proportion of subjects achieving an absolute PASI score ≤1 at Week 24
• The proportion of subjects achieving an IGA score of cleared (0) at Week 24
• The change from baseline of body surface area (BSA) psoriatic involvement at Week 24
• The change from baseline in DLQI score at Week 24
• The proportion of subjects achieving an ss-IGA score of absence of disease (0) at Week 24 in randomized subjects with scalp psoriasis and an ss-IGA score ≥2 at baseline
• The change from baseline in the physical and mental component summary scores of SF-36 at Week 24
• Safety and tolerability data will be summarized using descriptive statistics.
9.0 Study Design

9.1 Overview

This is a randomized, open-label, efficacy assessor-blinded, single country, multicenter, active-comparator-controlled phase 3b study of guselkumab in adult subjects with moderate to severe plaque-type psoriasis who have not yet received any systemic therapy. The study will be performed at about 30 to 45 sites in Germany.

A total of 114 subjects will be randomized in a 1:1 ratio to either the study drug (guselkumab) or to the active comparator (FAE). Subjects of the guselkumab group will receive 100 mg guselkumab SC at Weeks 0, 4, 12, and 20. Subjects of the FAE group will receive commercially available Fumaderm® tablets specifically labeled for the study. An individual dosing for each subject representing the optimal benefit-risk ratio is aspired. As shown in Figure 1, the study will be conducted with a 24-week treatment phase and a subsequent post-treatment safety follow-up phase until Week 32. Together with a 3-week screening phase, the maximum duration of a subject’s participation in this study will be 35 weeks.

Efficacy of treatment will be assessed before any tests, procedures or other evaluations, first by the subject him/herself (1st DLQI, 2nd PSSD 7 day version, and 3rd SF-36), and subsequently by a blinded efficacy assessor (BSA%, IGA, ss-IGA, and PASI). Safety evaluations will include the monitoring of adverse events (including injection site and allergic reactions), physical examinations, measurement of body weight, vital sign measurement, clinical laboratory testing (HBV, HCV, HIV, hematology, chemistry), concomitant medication review, tuberculosis test and evaluation, urinalysis and pregnancy testing. A confirmatory interim analysis will not be conducted. However, in addition to the main analysis after Week 24, a follow-up safety analysis will be performed.

The study is considered completed with the last visit for the last subject participating in the study. The final data from the study site will be sent to the sponsor (or designee) after completion of the final subject visit at that site, in the time frame specified in the Clinical Trial Agreement. The overall duration of the study is expected to be approximately 14 months (start in December 2016, stop in February 2018). The estimated frequency and timing of the study visits are summarized in the 'Time and Events Schedule' (TES).

Figure 1: Schematic Overview of the Study

![Figure 1: Schematic Overview of the Study](image-url)
9.2 Sample Size Determination

The primary hypothesis of this study is that guselkumab treatment is superior to FAE (Fumaderm® initial/ Fumaderm®) treatment as assessed by the proportion of subjects achieving a PASI 90 response at Week 24.

The major secondary hypotheses are:

- Guselkumab treatment is superior to FAE as assessed by the proportion of subjects achieving a PASI 75 response at Week 24.
- Guselkumab treatment is superior to FAE as assessed by the proportion of subjects achieving a DLQI score of 0 or 1 at Week 24.

In order to control the overall experiment wise type 1 error rate, the primary endpoint and the two major secondary endpoints will be tested in a fixed sequence as a-priori ordered hypotheses. That is, the first major secondary endpoint will be tested only if the primary endpoint is positive (i.e., $p < 0.05$), and the second major secondary endpoint will be tested only if the first major secondary endpoint is positive (i.e., $p < 0.05$). Due to the testing of ordered hypotheses, no adjustment of the significance level with respect to the threefold test procedure is required.

The assumptions for the sample size and power calculations using the threefold test procedure were based on guselkumab phase 2 data and unpublished data from the German PsoBest Registry and are as follows: PASI 90 responder rates for guselkumab and FAE in Week 24 are assumed to be 60% and 25%, respectively. PASI 75 responder rates are assumed to be 80% and 45%, respectively. DLQI responder rates are assumed to be 60% and 30%, respectively.

Based on these assumptions, with a total of 114 subjects planned to be randomized in a 1:1 ratio to guselkumab ($n = 57$) and to FAE ($n = 57$), superiority of guselkumab vs. FAE can be demonstrated at a 5% significance level (two-sided) with power of at least 90% for each test of the threefold test procedure as displayed in the table below.

Table 1: Power to detect a treatment effect on expected proportions of subjects achieving the primary and the major secondary endpoints

<table>
<thead>
<tr>
<th>Order of testing</th>
<th>Endpoint in Week 24</th>
<th>Guselkumab (% responder)</th>
<th>FAE (% responder)</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PASI 90</td>
<td>60</td>
<td>25</td>
<td>97%</td>
</tr>
<tr>
<td>2</td>
<td>PASI 75</td>
<td>80</td>
<td>45</td>
<td>98%</td>
</tr>
<tr>
<td>3</td>
<td>DLQI 0/1</td>
<td>60</td>
<td>30</td>
<td>90%</td>
</tr>
</tbody>
</table>

Type 1 error rate alpha 5% (two-sided)
Sequential testing with a-priori ordered hypotheses (only proceed with testing, if $p < 0.05$)
Sample size $n = 114$ with 1:1 ratio guselkumab ($n = 57$) and FAE ($n = 57$)
Two group chi-square test; nQuery Advisor® Release 7.0
9.3 Randomization and Blinding

Procedures for Randomization

Central randomization is implemented in this study. Subjects will be randomly assigned to 1 of 2 treatment groups (1:1 ratio) based on a computer-generated randomization schedule prepared before the study by or under the supervision of the sponsor. The randomization will be balanced by using randomly permuted blocks. The interactive web-based eCRF will assign a unique treatment code, which will dictate the treatment assignment at baseline visit of the subject. The investigator will not be provided with randomization codes. The randomization codes will be stored invisible for the investigator in a separate, blind part of the EDC system.

Blinding

As this is an open study, blinding procedures for the treatment are not applicable. However, a blinded efficacy evaluator will assess effectiveness of treatment as described in Section 9.2.3 of the CSP.
## 10.0 Study Schedule

An overview of the study procedures is displayed in the following time and events schedule of the CSP.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Screening*</th>
<th>Active Treatment</th>
<th>Safety FUP (Final Study visit)</th>
<th>ETV^h</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week</td>
<td>max. -3</td>
<td>0 2 4 8 12 16 20 24 32</td>
<td></td>
<td></td>
<td>All visits should occur within ±7 days of the scheduled visit, Section 7</td>
</tr>
</tbody>
</table>

### Study Procedures^b

#### Screening/Administrative

- Informed consent: X
- Medical history and demographics: X

Minimum criteria for the availability of documentation supporting the eligibility criteria are described in protocol, Section 4; check clinical status again before first dose of study medication

#### Study Drug Administration

- Randomization: X
- Study drug administration: X^e

All study procedures and evaluations are to be completed before study drug administration

---

a: To occur within 3 weeks prior to Week 0

b: All study procedures and evaluations are to be completed before administration of study drug. For assessments on subjects who discontinue administration of study treatments, see Section 10.2

c: Subjects randomized to guselkumab will get guselkumab 100 mg on site at Weeks 0, 4, 12 and 20. Subjects randomized to FAEs will start with Fumaderm® initial regimen (0-0-1) at the day of the baseline visit; thereafter, FAE doses will be increased to find the optimal Fumaderm® dose for each subject as described in Section 6

h: Early Termination Visit; for subjects who discontinue study treatment or withdraw from study participation before or at Week 24, every effort should be made to conduct the final assessments (Early Termination Visit) and to conduct the post-treatment assessments (Safety Follow-up), see Section 9.1.4
<table>
<thead>
<tr>
<th>Phase</th>
<th>Screening</th>
<th>Active Treatment</th>
<th>Safety FUP (Final Study visit)</th>
<th>ETV&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Week</td>
<td>max. -3</td>
<td>0 2 4 8 12 16 20 24 32</td>
<td></td>
<td></td>
<td>All visits should occur within ±7 days of the scheduled visit, Section 7</td>
</tr>
</tbody>
</table>

### Study Procedures<sup>b</sup>

#### Safety Assessments

<table>
<thead>
<tr>
<th>Procedure</th>
<th>X</th>
<th>X</th>
<th>X</th>
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<sup>a</sup> To occur within 3 weeks prior to Week 0

<sup>b</sup> All study procedures and evaluations are to be completed before the subject administers study drug. For assessments on subjects who discontinue administration of study treatments, see Section 10.2

<sup>h</sup> Early Termination Visit; for subjects who discontinue study treatment or withdraw from study participation before or at Week 24, every effort should be made to conduct the final assessments (Early Termination Visit) and to conduct the post-treatment assessments (Safety Follow-up), see Section 9.1.4
### Phase Screen-*ing* Active Treatment Safety FUP (Final Study visit) ETV* Notes

<table>
<thead>
<tr>
<th>Week</th>
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All visits should occur within ±7 days of the scheduled visit, Section 7

### Study Proceduresb

#### Efficacy Assessments

<table>
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<tr>
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</tbody>
</table>

Order of assessment: 1<sup>st</sup> DLQI, 2<sup>nd</sup> PSSD, 3<sup>rd</sup> SF-36; should be performed before any tests, procedures or other evaluations (PASI, IGA, ss-IGA, BSA) for that visit; completion of the baseline PROs has to be done before randomization

a: To occur within 3 weeks prior to Week 0
b: All study procedures and evaluations are to be completed before the subject administers study drug. For assessments on subjects who discontinue administration of study treatments, see Section 10.2
c: Dermatological evaluation of the subjects will be done by a blinded assessor starting with the Baseline visit; assessments will be done before any study related procedure will take place
d: To be performed only for those subjects with a corresponding diagnosis at baseline (Week 0)
e: Early Termination Visit; for subjects who discontinue study treatment or withdraw from study participation before or at Week 24, every effort should be made to conduct the final assessments (Early Termination Visit) and to conduct the post-treatment assessments (Safety Follow-up), see Section 9.1.4
### Study Procedures

#### Clinical Laboratory Assessment

<table>
<thead>
<tr>
<th>Phase</th>
<th>Screening*</th>
<th>Active Treatment</th>
<th>Safety FUP (Final Study visit)</th>
<th>ETV</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Week</td>
<td>max. -3</td>
<td>0 2 4 8 12 16 20 24 32</td>
<td>All visits should occur within ±7 days of the scheduled visit, Section 7</td>
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</tbody>
</table>

**a:** To occur within 3 weeks prior to Week 0

**b:** All study procedures and evaluations are to be completed before the subject administers study drug. For assessments on subjects who discontinue administration of study treatments, see Section 10.2

**f:** The QuantiFERON-TB Gold Plus test will generally be performed by the central laboratory; however, if available, test results from local laboratory can be accepted

**g:** All blood samples must be collected before study drug administration at visits when a study drug administration is scheduled; fasting is not necessary; details will be provided in the Laboratory Manual

**h:** Early Termination Visit; for subjects who discontinue study treatment or withdraw from study participation before or at Week 24, every effort should be made to conduct the final assessments (Early Termination Visit) and to conduct the post-treatment assessments (Safety Follow-up), see Section 9.1.4

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**Tuberculosis test**: X

**Hepatitis B and C Serologies**: X

**HIV antibody test**: X

**Hematology**: X X X X X X X X X

**Chemistry**: X X X X X X X X X X

**Urinalysis**: X X X X X X X X X X

Laboratory tests are listed in Section 9.3

Laboratory tests are listed in Section 9.3

Laboratory tests are listed in Section 9.3

Urinalysis by dipstick: glucose and protein; if there are signs of proteins and/or glucose on urine test strip, the urine sample must be analyzed centrally; here, protein and glucose levels must not exceed trace levels, eg, ≤ (+); one re-test (central urine analysis) is allowed.
11.0 Analysis Sets

In this study, subjects will be included in the efficacy analyses according to their assigned treatment. In contrast to the efficacy analysis set, safety analyses will be performed according to the actual treatment received during the study.

11.1 Definition of Analysis Sets

The following analysis data sets will be defined:

- **Efficacy Analysis Set**
  The efficacy analysis set is defined as the set of all subjects who were randomized to one of the two treatment groups (guselkumab or FAE) at Week 0 regardless of the treatment they actually received ("intent-to-treat" principle).

- **Per-Protocol Analysis Set**
  The per-protocol analysis set will consist of all subjects in the efficacy analysis set terminating the study without any major deviation of the protocol and its procedures. Subjects with major protocol deviations will be excluded from the per-protocol analysis.

- **Safety Analysis Set**
  The safety analysis set is defined as the set of all subjects who were randomized to one of the two treatment groups (guselkumab or FAE) at Week 0 and who received at least one dose of study drug according to the actual treatment received during the study irrespective of the treatment assigned at randomization.

Unless otherwise specified, data on study subjects (including subject disposition, reasons for discontinuation of study treatment, protocol deviations, analysis sets) will be analyzed based on data from all subjects randomized at Week 0 (‘efficacy analysis set’).

Demographic and other baseline characteristics as well as treatment compliance will be analyzed based on data from all subjects randomized at Week 0 (‘efficacy analysis set’) and on all treated subjects (‘safety analysis set’).

All efficacy analyses to compare guselkumab vs. FAE will be performed for all subjects randomized at Week 0 (‘efficacy analysis set’). Additionally, all efficacy analysis will be performed for all treated subjects (‘safety analysis set’). The primary and the major secondary endpoints will also be analyzed using the per-protocol analysis set.

All safety analyses to compare guselkumab vs. FAE will be performed for all treated subjects (‘safety analysis set’). The safety analysis will be performed after all subjects have completed their visit 24 weeks after randomization or discontinued earlier.

If the efficacy analysis set and the safety analysis set will not be different, analyses of efficacy and safety will be performed on data from all subjects randomized at Week 0 (‘efficacy analysis set’).

11.2 Protocol Deviations

The determination of evaluability of subjects, especially in cases of protocol deviations, withdrawals or drop-outs and the assignment of subjects to the planned analysis sets will be performed according to the requirements of the study protocol. Minor and major and potentially major protocol deviations that can be expected based on the prescriptions in the protocol were defined by Janssen-Cilag GmbH during the trial set up period. A detailed description of major and potentially major protocol deviation criteria is included in a separate document.
Data on subjects who had a major protocol deviation will be documented continuously by Janssen-Cilag GmbH in a Clinical Trial Management System during the trial period. Final data on major protocol deviations regarding the Week 24 analysis will be transferred to the data management department of acromion GmbH as Excel spreadsheets and will be further processed for statistical analysis.

### 11.3 Screening Failures

The data of subjects who were not randomized will not be included in the statistical analyses. However, a separate listing will be presented providing the site / subject no. and the reason for not being randomized.
12.0 Definition and Calculation of Efficacy Endpoints

The following sections provide a detailed description of the definition and the planned calculation of the efficacy endpoints as defined in the CSP. The same applies also for additional endpoints not defined in the CSP.

12.1 Involved Body Surface Area (BSA%)

One physical measure to define disease severity is to determine how much of the Body Surface Area (BSA) is affected by psoriasis. Involved BSA is calculated by using the palm of the subject’s hand as equivalent to 1% of the BSA (rule of palm).

12.2 Investigator's Global Assessment (IGA)

The Investigator’s Global Assessment (IGA) documents the investigator’s assessment of the subject’s psoriasis at a given time. Overall lesions are graded for induration, erythema, and scaling. The subject’s psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4).

The efficacy endpoint related to the IGA score is defined below:

IGA cleared responder

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

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

The scalp-specific (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), and severe disease (4).

The analyses for ss-IGA will be based on subjects randomized at Week 0 with baseline ss-IGA score ≥2.

ss-IGA absence of disease responder

Subjects with an ss-IGA score ≥2 at baseline who achieve ss-IGA score of absence of disease (0) will be considered ss-IGA absence of disease responders.
12.4 Psoriasis Area and Severity Index (PASI)

The Psoriasis Area and Severity Index (PASI) is an instrument 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.

Efficacy endpoints related to the PASI score are defined below:

**PASI 75 Responder**

Subjects with ≥75% improvement in PASI from baseline will be considered PASI 75 responders.

**PASI 90 Responder**

Subjects with ≥90% improvement in PASI from baseline will be considered PASI 90 responders.

**PASI 100 Responder**

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

In addition, the time to PASI 75/90/100 response defined as time from baseline to first onset of response will be calculated. In the absence of documented response the time to PASI 75/90/100 response will be censored at the date of Week 24 or the date of discontinuation in case of early treatment discontinuation.

12.5 Dermatology Life Quality Index (DLQI)

The Dermatology Life Quality Index (DLQI) is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a subject’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: 1) symptoms and feelings, 2) daily activities, 3) leisure, 4) work or school performance, 5) personal relationships, and 6) 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 ≤1 indicates no effect at all of disease on subject’s health related quality of life.

For a partially answered questionnaire (e.g., not all 10 answers in the DLQI questionnaire were available) the following rules will be applied:

1. If one question is left unanswered this will be scored 0 and the scores will be summed and expressed as usual out of a maximum of 30.
2. If two or more questions are left unanswered the questionnaire will not be scored.
3. If question 7 is answered ‘yes’ this will be scored 3. If question 7 is answered ‘no’ or ‘not relevant’ but then either ‘a lot’ or ‘a little’ is ticked this will be scored 2 or 1. If it is answered ‘no’, but the second half is left incomplete, the score will remain 0.

In addition, the time to DLQI 0/1 response defined as time from baseline to first onset of response will be calculated. In the absence of documented response the time to DLQI 0/1 response will be censored at the date of Week 24 or the date of discontinuation in case of early treatment discontinuation.
12.6 Psoriasis Symptom and Sign Diary (PSSD)

The Psoriasis Symptom and Sign Diary (PSSD) is a patient-reported outcome (PRO) questionnaire designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit. The PSSD includes 11 items covering symptoms (itch, pain, stinging, burning and skin tightness) and subject observable signs (skin dryness, cracking, scaling, shedding or flaking, redness and bleeding) using 0 (=absent) to 10 (=worst imaginable) 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. Additionally, the single items itch, pain and scaling and also the other single items will be evaluated. The subjects will complete the 7-day recall version of the PSSD as indicated in the TES.

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 symptom scores when at least 3 items (≥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. Otherwise the symptom score will be set to missing.

**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 (≥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. Otherwise the sign score will be set to missing.
12.7 Short Form Health Survey (SF-36)

The Short Form Health Survey (SF-36) is a 36-item questionnaire used for subjects’ self-assessment of health-related quality of life, consisting of the following 8 dimensions: 1) limitations in physical functioning due to health problems, 2) limitations in usual role activities due to physical health problems, 3) bodily pain, 4) general mental health (psychological distress and well-being), 5) limitations in usual role activities due to personal or emotional problems, 6) limitations in social functioning due to physical or mental health problems, 7) vitality (energy and fatigue), and 8) general health perception.

A physical component summary (PCS) score and a mental component summary (MCS) score can be derived. The concepts measured by the SF-36 are not specific to age, disease or treatment group, allowing comparison of relative burden of different diseases and the relative benefit of different treatments.

Each of these 8 scales (domains) is scored from 0 to 100 with higher scores indicating better health. Based on the scale scores, the summary scores, PCS and MCS, will be derived. These summary scores are also scaled with higher scores indicating better health.

The QualityMetric Health Outcomes™ Scoring Software 5.0 offered by QualityMetric Incorporated will be used to score the SF-36. The Software is designed to provide users with standard scoring methods in an easy-to-use way. By using this Software, users will have the confidence that the data they obtain on their SF form are scored in accordance with standards set by the developers of the SF tools. The Software also provides evaluation of data quality and applies methods for missing data recovery. The PCS score can be calculated when seven scale scores are available and the Physical Functioning scale is not missing. The MCS score can be calculated when at least seven scale scores are available and the Mental Health scale is not missing.

A more detailed description of the scoring procedure is provided in the User's Guide of QualityMetric Health Outcomes™ Scoring Software 5.0 (see especially Appendix F).
13.0 Statistical Methodology

The statistical analyses in this study will focus on the comparison of the two randomized treatment groups (i.e., guselkumab vs. FAE). The analyses will be confirmatory for the primary endpoint and the major secondary endpoints, and exploratory for all other secondary endpoints.

The biometrical evaluation will be carried out by acromion GmbH under the authority of the sponsor. Statistical programming and analyses will be performed using the statistical software system SAS®.

The following sections provide a more detailed description of the planned statistical methodology.

13.1 Data Handling Rules

13.1.1 Baseline and Post-baseline Points in Time of Interest

Baseline Definition

In general, the values of the Week 0 visit (= day of randomization = first day of week 1) or the values of the screening visit (= day within 3 weeks before their randomization visit) will be used as baseline values, as applicable. If data for the same variable are available from both (i.e., screening and Week 0) visits then the result of the Week 0 visit will be used as baseline value, i.e., for each variable the baseline measurement is defined as the closest measurement taken prior to or at the Week 0 visit.

Definition of Post-baseline Points in Time of Interest

The primary point in time for efficacy assessment will be the Week 24 visit (= end of treatment visit 24 weeks after randomization). Secondary points in time for efficacy assessment will be the study visits scheduled at Week 4 and Week 16 during the treatment phase. Handling of missing values is described in SAP section 13.1.6.

The safety analysis will cover the time period until Week 24.

13.1.2 Definition of Within- and Between-Group Treatment Differences

Within-group treatment differences will be computed as differences of the post-baseline visits as compared to the baseline visit, if applicable:

- post-baseline visit minus baseline visit

The following between-group treatment difference to assess the treatment effect will be computed, if applicable:

- guselkumab minus FAE

13.1.3 Visit Windows

Nominal visits (i.e., visits as recorded in the eCRF) will be used for all by-visit analyses in the study. The study visits scheduled post randomization should occur at the times delineated in the Time and Events Schedule. No visit windows will be defined and used for analysis.
13.1.4 Treatment Failure Criteria

Subjects who discontinue study treatment due to lack of efficacy or an AE of worsening of psoriasis, or who started a protocol-prohibited medication/therapy during the study that could improve psoriasis are considered treatment failures.

By time period the particular protocol-prohibited medications/therapies include:

Topical Therapy

Topical therapies that could affect psoriasis (e.g., corticosteroids, tar, anthralin, calcipotriene, topical vitamin D derivatives, retinoids, tazarotene, methoxsalen, pimecrolimus, tacrolimus, and traditional Taiwanese, Korean, or Chinese medicines) are not permitted until Week 24.

(The only allowable concomitant treatments for psoriasis throughout the study are shampoos (containing tar or salicylic acid only) and topical moisturizers. (Subjects should not use the topical agents on the day of a study visit; non-medicated shampoos may be used.))

Phototherapy

Phototherapy including, but not limited to PUVA, narrow-band UVB, balneophototherapy is not permitted until Week 24.

Systemic Therapy for Psoriasis

Systemic Therapy for Psoriasis is not permitted until the Week 24 visit.

These medications include those targeted for reducing TNF (including but not limited to infliximab, adalimumab or etanercept), drugs targeted for reducing IL-12, IL-17, or IL-23 (including but not limited to ustekinumab, tildrakizumab [MK3222], secukinumab [AIN457], ixekizumab [LY2439821], or brodalumab [AMG827]), alpha-4 integrin antagonists (including but not limited to natalizumab), steroids, any conventional systemic therapy that could affect psoriasis (including but not limited to MTX, cyclosporine, acitretin), herbal treatments, or traditional Taiwanese, Korean, or Chinese medicines, and any other biological agent or other systemic medication that could affect psoriasis.

13.1.5 Treatment Failure Rules

No treatment failure rules will be applied.


13.1.6 Handling of Missing Values

All available data will be included in the analyses and will be summarized descriptively as far as possible. If not otherwise specified, there will be no substitution of missing data, i.e., missing data will not be replaced, missing data will be handled as 'missing' in the statistical evaluation ('observed cases analysis').

Missing data for the efficacy endpoints at key visits Week 4, 16, and 24 will be handled as follows for all inferential statistical analyses (confirmatory or exploratory).

**Missing data imputation for the efficacy endpoints at Week 4, 16, and 24:**

- Nonresponder imputation will be applied for binary endpoints
  - i.e., subjects with missing data at Week 4/16/24 will be considered non-responders at Week 4/16/24.

- Last observation carried forward (LOCF) will be applied for continuous endpoints
  - i.e., in subjects with missing data at Week 4/16/24 the last available observation after baseline will be calculated and used for analysis for continuous response variables at Week 4/16/24. This approach implies that a separate "endpoint" visit will be calculated that gets the imputed value, thus leaving the observed value as it is, if data are summarized descriptively only.

Sensitivity analyses with respect to the handling of missing values at Week 24 are described in SAP section 13.9.

13.1.7 Data Transformations

No data transformations (e.g. square root, logarithmic) to confirm basic statistical assumptions will be performed. All variables will be used in the analysis as reported.

13.2 Descriptive Statistics

13.2.1 Dichotomous and Categorical Variables

Categorical data will be presented in frequency tables using counts and percentages. Percentages will be based on the total number of subjects in the respective analysis set (i.e., missing values will be included in percentage calculation). Besides presentation of absolute values cross tabulation vs. baseline by study visit will be provided, if appropriate.

13.2.2 Continuous and Quasi-Continuous Variables

Standard descriptive summary statistics will be calculated for continuous and quasi-continuous variables: arithmetic mean, standard deviation, minimum value, lower quartile, median, upper quartile, maximum value, number of non-missing values. Besides presentation of absolute values tabulation for differences to baseline by study visit will be provided, if appropriate.
13.2.3 Graphical Presentations
Graphical presentation of pertinent data will be given by means of box plots, bar charts, and survival graphs, as appropriate. Additional forms of graphical presentations may be specified. Descriptions of graphical presentations are included in the appendix of this document.

13.3 Confirmatory Statistics
The statistical analyses will be confirmatory for the primary endpoint and the major secondary endpoints.

13.3.1 Statistical Hypotheses
The primary hypothesis of this study is that guselkumab treatment is superior to FAE (Fumaderm® initial/ Fumaderm®) treatment as assessed by the proportion of subjects achieving a PASI 90 response at Week 24.

The major secondary hypotheses are:

- Guselkumab treatment is superior to FAE as assessed by the proportion of subjects achieving a PASI 75 response at Week 24.
- Guselkumab treatment is superior to FAE as assessed by the proportion of subjects achieving a DLQI score of 0 or 1 at Week 24.

13.3.2 Estimation, Confidence Intervals and Hypotheses Testing
In order to control the overall experiment wise type 1 error rate, the primary endpoint and the two major secondary endpoints will be tested in a fixed sequence as a-priori ordered hypotheses. That is, the first major secondary endpoint will be tested only if the primary endpoint is positive (i.e., \( p < 0.05 \)), and the second major secondary endpoint will be tested only if the first major secondary endpoint is positive (i.e., \( p < 0.05 \)).

A two-sided (\( \alpha = 0.05 \)) chi-square test will be used for the confirmatory comparisons. In addition, two-sided 95% confidence intervals will be calculated for the response rates at Week 24 per treatment arm and for the difference between the two arms.

13.3.3 Significance Level
All statistical testing will be performed two-sided. The confirmatory significance level is fixed to a type 1 error rate alpha of 5% (two-sided).

Due to the testing of ordered hypotheses, no adjustment of the significance level with respect to the threefold test procedure is required.
13.4 Exploratory Statistics

Exploratory statistical analyses will be performed for the primary endpoint, the major secondary endpoints and the other secondary endpoints at Week 24, and at Week 4 and Week 16. All statistical tests and confidence intervals will be calculated two-sided and are to be interpreted in the exploratory sense only.

13.4.1 Binary Endpoints

For binary endpoints counts and percentage of subjects per treatment group along with odds ratio (OR), relative risk (RR) and risk difference (RD), 95% confidence intervals (95% CIs) and p-values for treatment effect using the chi-square test will be provided. Time-to-event analyses will be performed for binary endpoints PASI 75/90/100 response, DLQI 0/1 response, onset of any TEAE, serious TEAE, and treatment discontinuation due to TEAE using Kaplan-Meier product limit method and Cox proportional hazards model. Summary tables will provide counts and percentage of subjects per treatment group, the median time-to-event with 95% confidence intervals (CI), and the hazard ratio (including 95% CI and the p-value calculated from Cox-regression with the factor treatment group). The survival curves will also be displayed graphically. Time-to-event analyses of binary endpoints will be performed on the observed cases only (i.e., missing data will not be replaced for time-to-event analyses).

A logistic regression model will be used for subgroup analyses of selected binary endpoints (i.e., PASI 75/90/100 response, DLQI 0/1 response, onset of any TEAE, serious TEAE, and treatment discontinuation due to TEAE) at Week 24 with factors for treatment group, the respective subgroup and the interaction term between treatment and subgroup. Only the p-value of the interaction term will be provided from these analyses.

13.4.2 Continuous Endpoints

The change from baseline of continuous endpoints will be analyzed by an analysis of covariance model (ANCOVA) with the fixed effect factor for treatment group and the baseline value as covariate. The Least-Squares means (LS means), the LS mean difference and the standardized mean difference (computed according to Hedges’ g) with the 95% CI and two-sided p-value will be provided from the ANCOVA model. For subgroup analyses of continuous endpoints the ANCOVA model will be extended by the respective subgroup and the interaction term between treatment and subgroup.

13.5 Adjustment for Covariates

The baseline value will be used as covariate in the analysis of variance model (ANCOVA) for the change from baseline of continuous response parameters.

13.6 Interim Analyses

No confirmatory interim analysis is planned to be performed.
13.7 Multi-center Data

Exploration of possible heterogeneity of treatment effects across centers for the primary efficacy endpoint (i.e., the proportion of subjects achieving a PASI 90 response at Week 24) using nonresponder imputation will be performed by descriptive frequency statistics including graphical display of the results of the individual centers, as appropriate. No pooling of centers will be performed.

13.8 Subgroup Analyses

The following subgroup analyses at Week 24 are planned to be performed to evaluate consistency over demographics and baseline disease characteristics of the primary endpoint, all secondary efficacy endpoints and as well of the following safety endpoints: onset of any TEAE, serious TEAE, treatment discontinuation due to TEAE.

- Gender
  - male
  - female
- Age at baseline in years
  - < 45
  - ≥ 45 - < 65
  - ≥ 65
- PASI
  - < 20
  - ≥ 20

The subgroup analyses will also include time-to-event analyses for the binary endpoints PASI 75/90/100 response, DLQI 0/1 response, onset of any TEAE, serious TEAE, and treatment discontinuation due to TEAE.

Subgroup analyses for the primary endpoint and all secondary efficacy endpoints will be performed using the following different imputation rules of missing values at Week 24 (see SAP sections 13.1.6 and 13.9):

- Binary endpoint:
  - Nonresponder imputation
  - LOCF (only PASI 75/90 response, and DLQI 0/1 response)
  - Multiple imputation
- Continuous endpoint:
  - Multiple Imputation

Subgroup analyses will NOT be performed for the per-protocol analysis set.
13.9 Sensitivity Analyses

The following sensitivity analyses at Week 24 with respect to the handling of missing values are planned to be performed:

- Multiple imputation will be used for all binary and continuous endpoints.
  - For the multiple imputation, the repeated nature of the analysis is restricted to the imputation step (procedure "MI" in SAS). Basic premise is the creation of several datasets in which missing data is imputed in a random fashion and then analyses are performed to check for changes for the conclusion. The analysis will be done with SAS Proc MIANALYZE.

- LOCF imputation will be used for all binary endpoints (see SAP section 13.1.6).

- An 'observed cases analysis' for all binary and continuous endpoints without substitution of missing data will be used (see SAP section 13.1.6).

Sensitivity analyses at Week 24 with respect to the handling of missing values will be performed for all binary and all continuous efficacy endpoints.

Sensitivity analyses at Week 24 with respect to the handling of missing values will NOT be performed for the per-protocol analysis set.
14.0 Statistical Analyses

A table of contents of planned data displays is provided in section 18.1 of this document. The following sections are intended to provide more details of the planned analyses. In addition, mock tables will be created and will be used as template for statistical programming.

Data will be appropriately summarized and analyzed using tabulation and graphs with respect to demographic/baseline characteristics and efficacy/safety observations and measurements. Standard descriptive summary statistics (i.e., n, arithmetic mean, standard deviation, median, minimum/maximum value, quartiles) will be calculated for continuous variables. Categorical data will be presented in frequency tables using counts and percentages. In general, summary tables will be displayed by treatment group as the main classification variable and for the total of the sample in the respective analysis set. Additional classification variables are explicitly mentioned in the following text. Individual subject data listings will be presented parameter wise and will be sorted by treatment group, center, subject number and study visit, if applicable.

14.1 Study Subjects

Unless otherwise specified, data on study subjects will be analyzed based on data from all subjects randomized at Week 0 (‘efficacy analysis set’).

14.1.1 Disposition of Subjects

The overview of subject disposition will provide the respective frequency counts and percentages regarding the following subjects:

- Treatment phase until Week 24
  - Subjects who were enrolled (i.e., signed informed consent)
  - Subjects who were randomized
  - Subjects who were treated
  - Subjects with premature discontinuation of study treatment
  - Subjects who completed the treatment phase

The table will also include the total number of study sites and the dates of the enrollment of the first subject and the last visit of the last subject. Moreover, the overview of subject disposition will be broken down by center. A flow diagram (according to the CONSORT statement) giving an overview of subject disposition will also be provided.

In addition, the number and percentage of randomized subjects continuing and attending by study visit will be displayed in a separate table. Subjects will be counted as continuing at the time of visit whether they attend the visit or not. Only those subjects that prematurely discontinued before the visit will not be counted as attending.
14.1.2 Discontinuation of Study Treatment
The number and percentage of randomized subjects who discontinued study treatment prematurely within the 24 Weeks treatment period of the study will be tabulated for each reason of premature discontinuation (including tabulation of specifications for category 'other'). Moreover, the number of subjects enrolled but not randomized (i.e., screening failures) and the reasons for not being randomized will be given.

14.1.3 Protocol Deviations
In general, the following list of major protocol deviations may have the potential to impact subjects’ rights, safety or well-being, or the integrity and/or result of the clinical trial. Subjects with major protocol deviations will be summarized by category for all randomized subjects.
- Developed withdrawal criteria but not withdrawn
- Entered but did not satisfy criteria
- Received a disallowed concomitant treatment
- Received wrong treatment or incorrect dose
- Other

The summary table will provide the number of subjects per major protocol deviation and will also provide the number of major protocol deviations.

The study selection criteria will also be grouped into the following 5 categories: psoriasis disease criteria, medication criteria, laboratory criteria, medical history criteria, and other and will be summarized.

14.1.4 Analysis Sets
The number and percentage of randomized subjects included in each analysis set, together with a breakdown of the reasons for exclusion for non-evaluable subjects, will be provided.
14.2 Demographic and Other Baseline Characteristics

Generally, assessments made at the screening visit and the baseline visit will be summarized by treatment group and overall. These assessments will include demographic characteristics and other parameters (such as medical history, previous psoriasis therapy by type (phototherapy and topical therapy)) substance use (alcohol/tobacco), previous and concomitant diseases, prior and concomitant medication, physical examination). By-treatment summaries will serve to identify any imbalances between the treatment groups at baseline. Summary tables will be provided by means of descriptive statistics and frequency tables, where appropriate. Demographic and other baseline characteristics will be analyzed based on data from all subjects randomized at Week 0 ('efficacy analysis set') and on all treated subjects ('safety analysis set'). No analyses for baseline balance using statistical hypothesis tests or confidence intervals will be done.

14.2.1 Demographics

Age (categorized), gender, and race will be presented in a frequency table. Age group categories will be chosen as < 45; ≥ 45 - < 65; ≥ 65 years. Descriptive summary statistics will be calculated for age, body height, body weight and body mass index (BMI).

Tables for demographic data will also be stratified by gender. Age and gender distribution will be presented in a bar chart.

Note: Age is documented as 'age at date of informed consent signature' at the screening visit. Body height and body weight data will be taken from the vital signs eCRF form at the Week 0 visit. BMI will be calculated as body weight in kg / body height in m².

14.2.2 Medical History

Categorical family history data will be summarized by means of a frequency table. The number and percentage of subjects with findings regarding the medical history terms of interest will be displayed in MedDRA terminology as described in SAP section 14.6. Summary tabulation will also consider whether the disease is ongoing or not at screening visit.

14.2.3 Diagnosis of Psoriasis

The time from date of initial diagnosis of psoriasis to date of screening visit will be calculated and will be displayed by descriptive statistics. If the day is unknown the day will be set to day = 1. If the month is unknown the month will be set to month = July.

In addition, the disease characteristics will be summarized by providing the following relevant results: descriptive summary statistics of the PASI and the DLQI index at baseline, frequency distribution of the IGA categories and the PASI < 20 and PASI ≥ 20 subgroups at baseline.

14.2.4 Previous Psoriasis Therapy

Categorical data on previous psoriasis therapy (including data on previous phototherapy and previous topical therapy) will be displayed in frequency tables providing the number and percentage of subjects per category. Summary tabulation of data on previous phototherapy will consider the type of phototherapy. The number and percentage of subjects with use of other previous topical psoriasis therapy will be displayed in WHO-DD terminology as described in SAP section 14.7.
14.2.5  **Substance Use**
Categorical data on substance use (alcohol or tobacco) will be displayed in a frequency table providing the number and percentage of subjects per category. Summary tabulation will also consider whether the substance usage is current or former.

14.2.6  **Physical Examination**
Abnormal findings in physical examination (additional to psoriasis findings) at screening and baseline visit will be tabulated by the body systems given in the eCRF. Details on abnormal findings in verbatim terms will be displayed in individual data listings.

14.2.7  **Tuberculosis Evaluation**
Categorical data on tuberculosis evaluation at screening and baseline visit will be displayed in a frequency table providing the number and percentage of subjects per category.

14.2.8  **Chest Radiograph Result**
Categorical data on chest radiograph result at screening visit will be displayed in a frequency table providing the number and percentage of subjects per category. Details on findings in verbatim terms will be displayed in individual data listings.

14.2.9  **Concomitant Medication and Therapy**
Analyses of concomitant medication and therapy will only consider the data recorded within the 24 Weeks treatment period of the study. In case of early treatment discontinuation before Week 24 concomitant medication and therapy with a start date at or after the discontinuation date will not be considered.

**Concomitant Medication**
The number and percentage of subjects with use of concomitant medication will be displayed in WHO-DD terminology as described in SAP section 14.7. Concomitant medication will be identified from the *Concomitant Medication* form of the eCRF.
The number and percentage of subjects with indication for concomitant medication will be displayed in MedDRA terminology as described in SAP section 14.6.

**Concomitant Therapy**
The number and percentage of subjects with use of concomitant therapy will be displayed in MedDRA terminology as described in SAP section 14.6. Concomitant therapy will be identified from the *Concomitant Therapy* form of the eCRF.
The number and percentage of subjects with indication for concomitant therapy will be displayed in MedDRA terminology as described in SAP section 14.6.

14.2.10  **Shampoo and Moisturizer**
The number and percentage of subjects with use of shampoo or moisturizer will be displayed in a frequency table.
14.3 Treatment Compliance

Treatment compliance will be analyzed based on data from all subjects randomized at Week 0 (‘efficacy analysis set’) and on all treated subjects (‘safety analysis set’).

14.3.1 Visit Windows

The number of days between the scheduled study visits and the baseline visit will be calculated using the reported visit dates per scheduled study visit and will be displayed by summary descriptive statistics.

14.3.2 Study Medication

Categorical data on guselkumab administration recorded at Week 0, 4, 12, 20 will be summarized by frequency tabulation providing the number and percentage of subjects per category. Frequency tabulation and descriptive statistics will be presented for the overall number of guselkumab administrations.

Compliance to guselkumab administration will be calculated as follows based on the eCRF data:

- Compliance guselkumab in % = (number of actual administrations x 100 / number of planned administrations)

Categorical data on Fumaderm® initial/ Fumaderm® administration during initial up titration and/or maintenance period (including data on reasons for end of up titration and reasons for dose selection) recorded at each week until Week 24 will be summarized by frequency tabulation providing the number and percentage of subjects per category. The number of planned tablets to be taken in the morning, at noon, and in the evening will also be summed up and analyzed descriptively.

The number of dispensed and returned tablets of Fumaderm® initial/ Fumaderm® (including the difference of dispensed - returned tablets = actual tablets) will be displayed by descriptive summary statistics.

Compliance to Fumaderm® initial and Fumaderm® administration will be calculated as follows based on the eCRF data:

- Compliance FAE in % = (number of actual tablets x 100 / total number of tablets supposed to be taken)

Treatment compliance will also be assessed by protocol deviations related to study drug administration (i.e., incorrect study drug received and missed administrations).

For subjects who completed the Week 24 visit the dose of Fumaderm® in mg at Week 24 will be summarized by descriptive statistics and frequency tabulation. In addition, the maximum dose of Fumaderm® initial and Fumaderm® in mg will be calculated for all subjects and will be summarized by descriptive statistics and frequency tabulation.
14.4 Analysis of Efficacy

All efficacy analyses to compare guselkumab vs. FAE will be performed for all subjects randomized at Week 0 ('efficacy analysis set'). Additionally, all efficacy analysis will be performed for all treated subjects ('safety analysis set'). The primary and the major secondary endpoints will also be analyzed using the per-protocol analysis set. However, subgroup and sensitivity analyses at Week 24 will NOT be performed for the per-protocol analysis set.

All statistical tests will be performed two-sided. In order to control the overall experiment wise type 1 error rate, the primary endpoint and the two major secondary endpoints will be tested in a fixed sequence as a-priori ordered hypotheses. That is, the first major secondary endpoint will be tested only if the primary endpoint is positive (i.e., \( p < 0.05 \)), and the second major secondary endpoint will be tested only if the first major secondary endpoint is positive (i.e., \( p < 0.05 \)).

Handling of missing values, exploratory statistics, subgroup analyses, and sensitivity analyses will be performed as described in detail in the following sections of this SAP:

<table>
<thead>
<tr>
<th>SAP Section No.</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.1.6</td>
<td>Handling of missing values</td>
</tr>
<tr>
<td>13.4.1</td>
<td>Exploratory statistics - binary endpoints</td>
</tr>
<tr>
<td>13.4.2</td>
<td>Exploratory statistics - continuous endpoints</td>
</tr>
<tr>
<td>13.8</td>
<td>Subgroup analyses</td>
</tr>
<tr>
<td>13.9</td>
<td>Sensitivity analyses</td>
</tr>
</tbody>
</table>

Data at the scheduled points Week 4 and Week 16 during the active treatment period will be analyzed analogously to the Week 24 data. However, no subgroup or sensitivity analyses will be performed for these points in time.
14.4.1 Primary Endpoint

The proportion of subjects achieving at least a 90% improvement of their psoriasis according to the Psoriasis Area and Severity Index (PASI 90 response) at Week 24 will be displayed in a frequency table providing the number and percentage of subjects. Graphical presentation will be presented by means of a bar chart.

To address the primary objective, a two-sided (\( \alpha = 0.05 \)) chi-square test will be used for the primary confirmatory comparison. In addition, two-sided 95% confidence intervals will be calculated for the PASI 90 response rate at Week 24 per treatment arm and for the difference between the two arms.

Exploratory statistical analyses (also including analyses of time to PASI 90 response) will be performed as described in SAP section 13.4.1.

14.4.2 Major Secondary Endpoints

14.4.2.1 Endpoint related to PASI

The proportion of subjects achieving at least a 75% improvement of their psoriasis according to the PASI at Week 24 (PASI 75 response) will be displayed in a frequency table providing the number and percentage of subjects. Graphical presentation will be presented by means of a bar chart.

The chi-square test will be used to compare the proportion of subjects responding to treatment. Two-sided 95% confidence intervals will be calculated for the response rate at Week 24 per treatment arm and for the difference between the two arms.

Exploratory statistical analyses (also including analyses of time to PASI 75 response) will be performed as described in SAP section 13.4.1.

14.4.2.2 Endpoint related to DLQI

The proportion of subjects achieving a DLQI score of 0 or 1 at Week 24 will be displayed in a frequency table providing the number and percentage of subjects. Graphical presentation will be presented by means of a bar chart.

The chi-square test will be used to compare the proportion of subjects responding to treatment. Two-sided 95% confidence intervals will be calculated for the response rate at Week 24 per treatment arm and for the difference between the two arms.

Exploratory statistical analyses (also including analyses of time to DLQI 0/1 response) will be performed as described in SAP section 13.4.1.
14.4.3 Other Secondary Endpoints

14.4.3.1 Endpoints related to PASI

Other secondary endpoints related to PASI are:

- The proportion of subjects achieving a 100% improvement of their psoriasis according to the PASI at Week 24 (PASI 100 response)
- The proportion of subjects achieving an absolute PASI score ≤ 1 at Week 24

The proportion of responding subjects will be displayed in a frequency table providing the number and percentage of subjects. Graphical presentation will be presented by means of a bar chart.

The chi-square test will be used to compare the proportion of subjects responding to treatment. Two-sided 95% confidence intervals will be calculated for the response rate at Week 24 per treatment arm and for the difference between the two arms.

Additional exploratory statistical analyses (also including analyses of time to PASI 100 response) will be performed as described in SAP section 13.4.1.

14.4.3.2 Endpoints related to PSSD

Other secondary endpoints related to PSSD are:

- The change from baseline in the signs and symptoms aggregate scores of the PSSD at Week 24
- The change from baseline in the individual scale scores for itch, pain, and scaling of PSSD components at Week 24

The change from baseline will be summarized by descriptive statistics using appropriate tabulation and box plots. The baseline value, the Week 24 value and the change from the baseline value will be displayed.

Exploratory statistical evaluation of the change from baseline will be based on an analysis of covariance model (ANCOVA) with the fixed effect factor for treatment group and the baseline value as covariate (see SAP section 13.4.2).

In addition, the other individual scale scores will be analyzed analogously.
14.4.3.3 Endpoints related to IGA

Other secondary endpoints related to IGA are:

- The proportion of subjects achieving an IGA score of cleared (0) at Week 24

The proportion of responding subjects will be displayed in a frequency table providing the number and percentage of subjects. Graphical presentation will be presented by means of a bar chart.

The chi-square test will be used to compare the proportion of subjects responding to treatment. Two-sided 95% confidence intervals will be calculated for the response rate at Week 24 per treatment arm and for the difference between the two arms.

Additional exploratory statistical analyses will be performed as described in SAP section 13.4.1.

14.4.3.4 Endpoints related to BSA

Other secondary endpoints related to BSA are:

- The change from baseline of body surface area (BSA) psoriatic involvement at Week 24

The change from baseline will be summarized by descriptive statistics using appropriate tabulation and box plots. The baseline value, the Week 24 value and the change from the baseline value will be displayed.

Exploratory statistical evaluation of the change from baseline will be based on an analysis of covariance model (ANCOVA) with the fixed effect factor for treatment group and the baseline value as covariate (see SAP section 13.4.2).

14.4.3.5 Endpoints related to DLQI

Other secondary endpoints related to DLQI are:

- The change from baseline in DLQI score at Week 24

The change from baseline will be summarized by descriptive statistics using appropriate tabulation and box plots. The baseline value, the Week 24 value and the change from the baseline value will be displayed.

Exploratory statistical evaluation of the change from baseline will be based on an analysis of covariance model (ANCOVA) with the fixed effect factor for treatment group and the baseline value as covariate (see SAP section 13.4.2).
14.4.3.6 Endpoints related to ss-IGA

Other secondary endpoints related to ss-IGA are:

- The proportion of subjects achieving an ss-IGA score of absence of disease (0) at Week 24 in randomized subjects with scalp psoriasis and an ss-IGA score ≥2 at baseline

The proportion of responding subjects will be displayed in a frequency table providing the number and percentage of subjects. Graphical presentation will be presented by means of a bar chart.

The chi-square test will be used to compare the proportion of subjects responding to treatment. Two-sided 95% confidence intervals will be calculated for response rate at Week 24 per treatment arm and for the difference between the two arms.

Additional exploratory statistical analyses will be performed as described in SAP section 13.4.1.

14.4.3.7 Endpoints related to SF-36

Other secondary endpoints related to SF-36 are:

- The change from baseline in the physical and mental component summary scores of SF-36 at Week 24

The change from baseline will be summarized by descriptive statistics using appropriate tabulation and box plots. The baseline value, the Week 24 value and the change from the baseline value will displayed.

Exploratory statistical evaluation of the change from baseline will be based on an analysis of covariance model (ANCOVA) with the fixed effect factor for treatment group and the baseline value as covariate (see SAP section 13.4.2).

14.4.4 Other Efficacy Assessments

In addition to the efficacy analyses described above all efficacy data related to PASI, DLQI, PSSD, IGA, ss-IGA, and SF-36 at all scheduled study visits during the active treatment period until Week 24 will be summarized descriptively without any imputation of missing data (‘observed cases analysis’; see SAP section 13.1.6).
14.5 Analysis of Safety

Safety data, including but not limited to, adverse events (AEs), serious adverse events (SAEs), infections, serious infections, mortality, changes in laboratory assessments, and changes in vital signs will be summarized using descriptive statistics. All safety analyses to compare guselkumab vs. FAE will be performed for all treated subjects ('safety analysis set').

14.5.1 Extent of Exposure

Extent of exposure will be defined as the total number of days from baseline to Week 24 (for all patients still under treatment) or to study discontinuation.

Descriptive summary statistics and frequency tables (using appropriate categories) will be provided for the extent of exposure.

14.5.2 Adverse Events

Adverse events data will be processed in the statistical analysis after coding according to the MedDRA dictionary version 19.1. All reported AEs with onset date during the active treatment period until Week 24 (i.e., treatment emergent AEs) will be included in the analysis. In case of early treatment discontinuation before Week 24 all reported AEs with onset date during the safety follow-up period until Week 24 (i.e., treatment emergent AEs) will be included in the analysis. AEs reported after Week 24 will NOT be considered in the analysis.

14.5.2.1 Definitions

The following definitions will be applied in the present study

Crude Incidence Rate

Where percentages of subjects are reported in summary tables, incidences provide information on the proportion of subjects experiencing adverse events in relation to the total number of subjects exposed, i.e., if not otherwise specified, the crude incidence rate will be used.

The crude incidence rate is defined as the number of subjects experiencing a certain event, divided by the number of subjects exposed to study treatment, regardless of duration of use:

\[
\text{Crude incidence rate} = 100 \times \frac{\text{number of patients with adverse events}}{\text{number of patients exposed}}
\]

Treatment Emergent Adverse Events

Treatment emergent adverse events (TEAEs) are those AEs that occurred during the active treatment period until Week 24 after the start of initial study drug administration and those AEs that were present at baseline but worsened in severity after the start of initial study drug administration. AEs reported after Week 24 will NOT be considered in the analysis.

In case of early treatment discontinuation before Week 24 all reported AEs with onset date during the safety follow-up period until Week 24 will be included in the analyses. Thus, identification of TEAEs (distinguished by subjects who completed or discontinued the treatment period until Week 24) will be performed as follows:
TEAE for Completer: Date of Week 0 < Start Date of AE < Date of Week 24
TEAE for Non-Completer: Date of Week 0 < Start Date of AE < Date of Week 0 + 168 Days

AEs which are not classified as TEAEs will be considered as not treatment emergent adverse events (NTEAEs).

14.5.2.2 Analyses

Overview of adverse events

For summary presentation of the overall adverse event experience overview tables will be provided for AEs and SAEs including the following information:

Adverse events:
- n (%) of subjects with AEs *)
- n (%) of subjects with NTEAEs *)
- n (%) of subjects with TEAEs *)
- n (%) of subjects with TEAEs by highest causality to study medication
- n (%) of subjects with TEAEs by worst severity
- n (%) of subjects with TEAEs leading to dose modification *)
- n (%) of subjects with TEAEs leading to permanent stop of study medication *)

Serious Adverse events:
- n (%) of subjects with SAEs *)
- n (%) of subjects with NTESAEs *)
- n (%) of subjects with TESAEs *)
- n (%) of subjects with TESAEs leading to death *)
- n (%) of subjects with TESAEs by highest causality to study medication
- n (%) of subjects with TESAEs by worst severity
- n (%) of subjects with TESAEs leading to permanent stop of study medication *)

*) the number of events (i.e., number of coded preferred terms) will also be given.

TEAEs/TESAEs leading to dose modification will be defined as all events with ‘Action taken with study treatment’ is not equal to ‘DOSE NOT CHANGED’.

In addition, the number of TEAEs will be displayed for the following investigator’s ratings:
- severity
- seriousness
- causality
- action taken
- outcome
Detailed display of adverse events

For a more detailed display, adverse events will be presented in summary tables, listing these events in code form according to the preferred term. These tables will show the number of subjects per group presenting an adverse event and the incidence of its occurrence. Adverse events will be grouped by primary SOC (System Organ Class) and will be stratified additionally by highest causality to study treatment (not related, doubtful, possible, probable, or very likely) and by worst severity (mild, moderate, or severe). The incidence of adverse events will be presented by decreasing order of frequency at preferred term level within the primary SOC.

The following tables will be provided for the detailed display of adverse events:

**Adverse events:**
- TEAEs by primary SOC and preferred term *)
- TEAEs by primary SOC and preferred term stratified by highest causality
- TEAEs by primary SOC and preferred term stratified by worst severity
  - thereof
    - Drug related TEAEs
    - Not drug related TEAEs
- TEAEs leading to permanent stop of study medication by primary SOC and preferred term *)

**Serious Adverse events:**
- TESAEs by primary SOC and preferred term *)
- TESAEs by primary SOC and preferred term stratified by highest causality
- TESAEs by primary SOC and preferred term stratified by worst severity
- TESAEs leading to permanent stop of study medication by primary SOC and preferred term *)
- TESAEs leading to death by primary SOC and preferred term *)

**Not treatment emergent adverse events:**
- NTEAEs by primary SOC and preferred term *)

*) These tables will show additionally the number of events (i.e., number of coded preferred terms).

Summary tabulation of TEAEs and TESAEs by primary SOC and preferred term will also be provided for the following types of adverse events:
- injection site reactions (according to the tick box in the e-CRF)
- infections (according to the tick box in the e-CRF)
  - thereof, infections treated with oral or parenteral antibiotics
- adverse events of psoriasis (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; final allocation will be performed after blinded data review).

Note that the summary tables will provide the number of subjects per event (i.e., coded as preferred term) and will also provide the number of events for certain tables.
For calculation of the number of subjects per event each preferred term will be counted only once per subject and will be linked to the primary SOC. A subject may contribute with more than one different adverse event (at preferred term level); however, a subject with more than one occurrence of the same adverse event (at preferred term level) is displayed and counted only once for this event in the tables.

Tables that are stratified by the severity of adverse events will summarize the worst severity per subject and preferred term.

Tables that are stratified by the relationship of adverse events will summarize the highest relationship per subject and preferred term.

For presentation of drug related/ not drug related adverse events the following categories will be used:

- **drug related** = very likely, probable, possible
- **not drug related** = doubtful, not related

For summarization of severity of drug related TEAEs, events with a causality assessment of 'doubtful/not related' will be excluded and the worst severity will be tabulated as described above. Summarization of severity of not drug related TEAEs will be performed likewise.

The following safety endpoints will be defined and used for the statistical analyses for HTA purposes:

- The proportion of subjects with any TEAE within the 24 Weeks treatment period
- The proportion of subjects with serious TEAE within the 24 Weeks treatment period
- The proportion of subjects with treatment discontinuation due to TEAE within the 24 Weeks treatment period
- The proportion of subjects with any TEAE by preferred term and SOC within the 24 Weeks treatment period

Counts and percentage of subjects per treatment group along with odds ratio (OR), relative risk (RR) and risk difference (RD), 95% confidence intervals (95% CIs) and p-values for treatment effect using the chi-square test will be provided. In addition, time-to-event analyses and logistic regression analyses as described in SAP section 13.4.1 will be conducted for the onset of any TEAE, serious TEAE, and treatment discontinuation due to TEAE.

Subgroup analyses will be performed for the subgroups defined in SAP section 13.8 for the proportion of subjects with any TEAE, serious TEAE, and treatment discontinuation due to TEAE.

The cut-off ≥ 5% (i.e., percentage of subjects ≥ X% in at least one treatment group) will be used for analyses of TEAEs by preferred term for any TEAE.
Listings
All adverse events (AEs) and serious adverse events (SAEs) will be listed in the individual subject data listings by treatment group, study center and subject number including all information documented on the respective form of the eCRF. Separate listings of subjects with the following AEs will be provided: SAEs, SAEs leading to death, AEs of severe intensity, AEs leading to permanent discontinuation of study medication.

Verbatim description of the adverse event reported by the investigator, MedDRA preferred terms and primary SOCs (system organ class) for all adverse events will be contained in the data listings. Non treatment emergent adverse events will be flagged in the respective listings.

14.5.3 Clinical Laboratory Tests
Laboratory data will be summarized by type of laboratory test. Reference ranges will be used in the summary of laboratory data. Descriptive statistics will be calculated for each laboratory item at each scheduled time. Changes from baseline results will be presented in pre- versus post-treatment cross-tabulations (with classes for below, within, and above normal ranges).

Results of tuberculosis testing, serology, urine pregnancy testing and local urinalysis (glucose, protein) will be displayed in frequency tables providing the number and percentage of subjects per category (i.e., negative or positive) at each scheduled time.

The results of all laboratory tests will be provided in individual subject data listings including the reference ranges. Abnormal values will be identified by flagging all values below and above the reference range.

A listing of subjects with any laboratory results outside the reference ranges will be provided.

For the lymphocyte count the following subjects will be listed and summarized in a frequency table:

- lowest lymphocyte count < 500/µl
- 500/µl ≤ lowest lymphocyte count <700/µl
- 700/µl ≤ lowest lymphocyte count < lower limit of normal range

Graphical presentation of quantitative laboratory data will be given by means of box plots.
14.5.4 Vital Signs

Descriptive statistics of pulse and blood pressure (systolic and diastolic) values and changes from baseline will be summarized at each scheduled time. Subjects reporting vital signs findings beyond clinically important limits will be identified using the following criteria.

Criteria for Identifying Potentially Clinically Significant Vital Signs Findings

<table>
<thead>
<tr>
<th>Variable (units)</th>
<th>Criterion Value*</th>
<th>Change from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>&gt;200 &lt;80</td>
<td>Increase of &gt;40 Decrease of &gt;40</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>&gt;120 &lt;40</td>
<td>Increase of &gt;30 Decrease of &gt;30</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>&gt;110 &lt;40</td>
<td></td>
</tr>
</tbody>
</table>

* In order to be identified as an abnormality of potential clinical importance, a value would need to meet the criterion value or also represent a change of at least the magnitude noted in the change column.

Vital signs values of potentially clinically significant importance will be analyzed by providing the number and percentages of subjects with values of potential clinical importance per scheduled study visit, overall during the study and with first occurrence after baseline.

14.5.5 Physical Examination

Physical examination findings will be tabulated by the body systems given in the eCRF at each scheduled time. Moreover, abnormal findings with first occurrence after baseline reported during the treatment phase and follow-up phase will be presented. Details on abnormal findings in verbatim terms will be displayed in individual subject data listings.

14.5.6 Body Weight

For body weight absolute values and changes from baseline values will be presented by descriptive statistics at each scheduled time.

14.5.7 Early Detection of Active Tuberculosis

Categorical data on early detection of active tuberculosis will be presented in a frequency table providing the number and percentage of subjects per category at each scheduled time.
14.6 Analysis of MedDRA Codes

Previous / concomitant diseases (including indications for use of concomitant and other medications) and adverse events will be coded with version 19.1 of the MedDRA-dictionary.

In general, tabulation will be displayed by preferred term and primary SOC.

14.7 Analysis of WHO Drug Dictionary Codes

The use of concomitant and other medications will be coded using the WHO Drug Dictionary (version 2016/1). Medications will be tabulated by preferred name (i.e., the decode of the code which results when SEQ1 and SEQ2 are set to 01 and 001, respectively (usually resulting in a decode close to the generic drug name)) and they will be grouped by level 2 of the Anatomical Therapeutic Chemical (ATC) code. Codes being linked to more than one ATC code at this level will be assigned to one primary ATC code by medical data analysts.

15.0 Changes to Planned Analyses

This statistical analysis plan includes the following relevant changes to the planned analyses which are described in the clinical study protocol.

- Evaluations on health technology assessment (HTA) will also be specified in this SAP. No separate SAP for evaluations on health technology assessment will be provided (see SAP section 3.0 and CSP section 11).
- A per-protocol analysis will be performed for the primary and the major secondary endpoints (see SAP section 11.0).
- No treatment failure imputation rules will be applied (see to SAP section 13.1.5 and CSP section 11.4).
- The following safety endpoints will be defined and used for the statistical analyses for HTA purposes:
  - The proportion of subjects with any TEAE within the 24 Weeks treatment period
  - The proportion of subjects with serious TEAE within the 24 Weeks treatment period
  - The proportion of subjects with treatment discontinuation due to TEAE within the 24 Weeks treatment period
  - The proportion of subjects with any TEAE, serious TEAE, treatment discontinuation due to TEAE by preferred term and SOC within the 24 Weeks treatment period
- Time-to-event analyses for binary endpoints PASI 75/90/100 response, DLQI 0/1 response, onset of TEAE, serious TEAE, and treatment discontinuation due to TEAE will be performed using Kaplan-Meier product limit method and Cox proportional hazards model.

Any major changes to this plan after sign-off of the latest final version will be specified in the clinical study report.
16.0 Tabulation

16.1 General
The statistical output will be prepared in American English. No separate statistical report will be written.

16.2 Format of Data Displays
The layout of all tables, listings and figures will be drafted by acromion GmbH when providing the first draft tables, listings and figures on final data. No sponsor or other requirements for layout specifications have to be followed.

The SAS outputs will be post-processed within Microsoft Word®. SAS tables and listings will be integrated into Microsoft Word® using the SAS Monospace 8 points font.

Separate appendices will be provided for tables, listings, and figures. For each appendix a corresponding table of contents will be generated. All pages within one appendix will be numbered consecutively. Tables, listings and figures generally should be self-explaining. Abbreviations will be described in the footnote if necessary.

16.2.1 Tables
SAS summary tables will be produced using a landscape page. The maximum number of lines per page will be pagesize = 40 and the number of characters in one line will be linesize = 140.

16.2.2 Listings
SAS subject data listings will be produced using a landscape page. The maximum number of lines per page will be pagesize = 40 and the number of characters in one line will be linesize = 140.

Data listings will be created for groups of variables which logically belong together (e.g. demographic variables) and will be sorted by treatment group, center, subject and visit (if applicable).
16.2.3 Figures

Figures will be created using the following graphical SAS options, if not otherwise specified:

GOPTIONS
RESET = ALL
NOBORDER
KEYMAP = WINANSI
DEVMAP = WINANSI
DEV = EMF
TARGET = WINPRTC
GUNIT = CM
CTEXT = BLACK
FTEXT = 'Arial/bold'
HTEXT = 0.5 CM
LFACTOR = 1
HSIZE = 6 IN
VSIZE = 5 IN;

Variables may be presented in the following graphical formats, if applicable:

Box plot

Box plots summarize the data by a box reaching from the 1st to the 3rd quartile. The median is displayed inside this box by a horizontal line. Above the box a vertical line indicates the region from the 3rd quartile to the max. value below the upper fence; below the box a vertical line indicates the region from the 1st quartile to the min. value above the lower fence. The upper fence lies 1.5 interquartile-ranges above the 3rd quartile, the lower fence lies 1.5 interquartile ranges below the 1st quartile. Values outside the fences are displayed by a distinct marker.

A graphical presentation is given below:
16.2.3 Figures

Figures will be created using the following graphical SAS options, if not otherwise specified:

GOPTIONS
RESET   = ALL
NOBORDER
KEYMAP = WINANSI
DEVMAP = WINANSI
DEV     = EMF
TARGET  = WINPRTC
GUNIT   = CM
CTEXT   = BLACK
FTEXT   = 'Arial/ bold'
HTEXT   = 0.5 CM
LFACTOR=  1
HSIZE   = 6 IN
VSIZE   = 5 IN;

Variables may be presented in the following graphical formats, if applicable:

Box plot

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A graphical presentation is given below:
Bar chart
A bar chart displays a categorical variable. A sample display is provided below.

Survival Graph
A survival graph displays the survival distribution functions according to Kaplan-Meier. A sample display is provided below.

16.3 Data Format
Unless otherwise specified, percentage values will be printed with one digit to the right of the decimal point.
In general, minima and maxima will be quoted to the number of decimal places as recorded in the eCRF; means, standard deviations and medians will be quoted to one further decimal place.
All p-values will be given by four digits to the right of the decimal point. Verbatim terms documented in the eCRFs will be presented as entered in the clinical data base.
17.0 References

Study Documents:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version, Date</th>
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<tr>
<td>Protocol / Amendments</td>
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<td>eCRF</td>
<td>Version 1.0, 12-DEC-2016</td>
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<tr>
<td>Data Management Plan</td>
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SOPs and Guidelines acromion:

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<td>acromion SOP BM05</td>
<td>Determination of Availability of Data for Analysis, Oct-2016</td>
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<td>acromion SOP BM06</td>
<td>Generation and Release of Blinded Randomization Code, Oct-2016</td>
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<tr>
<td>acromion SOP BM07</td>
<td>Programming of Derived Data Sets, Oct-2016</td>
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<td>acromion SOP BM08</td>
<td>Programming of SAS Data Displays, Oct-2016</td>
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<td>acromion SOP BM11</td>
<td>Documentation and Project Close-Out, Oct-2016</td>
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<td>acromion Guideline BM01</td>
<td>SAS Programming Guideline, Oct-2016</td>
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<tr>
<td>acromion Guideline BM02</td>
<td>Biometrics Naming Conventions for SAS Datasets and SAS Programs, Oct-2016</td>
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Other Documents:

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<th>Document</th>
<th>Title, Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH Guideline E 9</td>
<td>Statistical Principles for Clinical Trials, final approval 1998</td>
</tr>
</tbody>
</table>
18.0 Appendices

18.1 Table of Contents for Data Displays

The tables, subject data listings and figures will be provided using the following numbering system, which will be updated after start of programming the data displays. However, this section does not include the HTA analyses for the topline results described in SAP section 14.6. The numbering system for the HTA analyses will be provided with the HTA mock tables.

All summary tables will start with the one-character identifier for the displayed analysis set followed by the one-digit identifier for the displayed analysis chapter as listed below.

Identifier for displayed analysis set:
- **A**: Efficacy analysis set
- **B**: Safety analysis set
- **C**: Per-protocol analysis set

Identifier for displayed analysis chapter:
- **1**: Study subjects
- **2**: Demographics and other baseline characteristics
- **3**: Treatment compliance
- **4**: Analysis of efficacy
- **5**: Analysis of safety

Data displays will be provided for the following analysis sets:

<table>
<thead>
<tr>
<th>Chapter No.</th>
<th>Chapter Title</th>
<th>Analysis set</th>
</tr>
</thead>
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<tr>
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<td>Study subjects</td>
<td>• A: efficacy analysis set</td>
</tr>
<tr>
<td>2</td>
<td>Demographic and other baseline characteristics</td>
<td>• A: efficacy analysis set</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• B: safety analysis set</td>
</tr>
<tr>
<td>3</td>
<td>Treatment compliance</td>
<td>• A: efficacy analysis set</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• B: safety analysis set</td>
</tr>
<tr>
<td>4</td>
<td>Analysis of efficacy</td>
<td>• A: efficacy analysis set</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• B: safety analysis set</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• C: per-protocol analysis set</td>
</tr>
<tr>
<td>5</td>
<td>Analysis of safety</td>
<td>• B: safety analysis set</td>
</tr>
</tbody>
</table>

All individual subject data listings will start with the one-digit identifier for the displayed chapter analogously as for the summary tables. Data displays and subject data listings will be provided in separate appendices and pages will be numbered for each appendix separately starting with page no. 1.
### 18.1.1 Tables

#### Study Subjects, Prefix A

<table>
<thead>
<tr>
<th>No.</th>
<th>Analysis Chapter</th>
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<tbody>
<tr>
<td>1.1</td>
<td>Disposition of subjects</td>
</tr>
<tr>
<td>1.2</td>
<td>Discontinuation of study treatment</td>
</tr>
<tr>
<td>1.3</td>
<td>Protocol deviations</td>
</tr>
<tr>
<td>1.4</td>
<td>Analysis sets</td>
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</table>

#### Demographic and Other Baseline Characteristics, Prefix A, B

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<th>Analysis Chapter</th>
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<tr>
<td>2.1</td>
<td>Demographics</td>
</tr>
<tr>
<td>2.2</td>
<td>Medical history</td>
</tr>
<tr>
<td>2.3</td>
<td>Diagnosis of Psoriasis</td>
</tr>
<tr>
<td>2.4</td>
<td>Previous Psoriasis Therapy</td>
</tr>
<tr>
<td>2.5</td>
<td>Substance Use</td>
</tr>
<tr>
<td>2.6</td>
<td>Physical Examination</td>
</tr>
<tr>
<td>2.7</td>
<td>Tuberculosis Evaluation</td>
</tr>
<tr>
<td>2.8</td>
<td>Chest Radiograph Result</td>
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<tr>
<td>2.9</td>
<td>Concomitant Medication and Therapy</td>
</tr>
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<td>2.10</td>
<td>Shampoo and Moisturizer</td>
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#### Treatment Compliance, Prefix A, B

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<td>3.1</td>
<td>Visit windows</td>
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<td>3.2</td>
<td>Study medication</td>
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#### Analysis of Efficacy, Prefix A, B, C

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<th>No.</th>
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<td>4.1</td>
<td>- Primary Endpoint -</td>
</tr>
<tr>
<td>4.1.1</td>
<td>PASI 90% Response</td>
</tr>
<tr>
<td>4.2.1</td>
<td>Endpoint Related to PASI</td>
</tr>
<tr>
<td>4.2.2</td>
<td>Endpoint Related to DLQI</td>
</tr>
<tr>
<td>4.3.1</td>
<td>Endpoints related to PASI</td>
</tr>
<tr>
<td>4.3.2</td>
<td>Endpoints related to PSSD</td>
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<td>4.3.3</td>
<td>Endpoints related to IGA</td>
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<td>Endpoints related to SF-36</td>
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<td>- Other Efficacy Assessments -</td>
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#### Analysis of Safety, Prefix B

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<td>Body Weight</td>
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<td>Early Detection of Active Tuberculosis</td>
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### 18.1.2 Listings

#### Study Subjects

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<tr>
<td>1.1</td>
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<td>Discontinuation of study treatment</td>
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<td>Protocol deviations</td>
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#### Demographic and Other Baseline Characteristics

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#### Treatment Compliance

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#### Analysis of Efficacy

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#### Analysis of Safety

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18.1.3 Figures

### Analysis of Efficacy, Prefix A, B, C

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<td>4</td>
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<td>Vital Signs</td>
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