Statistical Analysis Plan

NCT Number: NCT04999839

Title: A Phase 2b, Randomized, Multicenter, Double-blind, Placebo-controlled, Multiple-dose Study to Evaluate the Efficacy, Safety, and Tolerability of NDI-034858 in Subjects With Moderate to Severe Plaque Psoriasis

Study Number: 4858-201 (TAK-279)

Document Version and Date: Version 1.0 (18-October-2022)

Certain information within this document has been redacted (i.e., specific content is masked irreversibly from view) to protect either personally identifiable information or company confidential information.

Statistical Analysis Plan

Study Title:	**A Phase 2b, Randomized, Multicenter, Double-Blind, Placebo-Controlled, Multiple Dose Study to Evaluate the Efficacy, Safety, and Tolerability of NDI-034858 in Subjects with Moderate to Severe Plaque Psoriasis**
Protocol Number:	**4858-201**
Protocol Version and Date:	**Version 3.0 (Amendment 2), 04-Feb-2022**
Product:	**NDI-034858**
Sponsor:	**Nimbus Lakshmi, Inc.** **130 Prospect Street, Suite 301** **Cambridge, Massachusetts, United States, 02139** **Telephone: 857-999-2009**
Date:	**18-Oct-2022**
Analysis Plan Version:	**Final v1.0**
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STATISTICAL ANALYSIS PLAN REVISION SUMMARY			
Version	**Version Date**	**Author**	**Summary of Changes**
Final v1.0	18-Oct-2022	[redacted]	Initial version

This statistical analysis plan will be reviewed and revised as needed. The most recent approved version will replace the previous version in place.

SIGNATURE PAGE

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Innovaderm Research	**STATISTICAL ANALYSIS PLAN, Version Final v1.0**
Protocol Number: 4858-201	Sponsor: Nimbus Lakshmi, Inc.

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TABLE OF CONTENT

ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	anatomical therapeutic chemical
BMI	body mass index
Bpm	beats per minute
[redacted]	[redacted]
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
COVID-19	Coronavirus Disease 2019
CRF	case report form
CRO	contract research organization
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DLQI	Dermatology Life Quality Index
ECG	Electrocardiogram
eCRF	electronic case report form
EOS	end of study
EOT	end of treatment
ET	early termination
HR	heart rate
ICH	International Council for Harmonisation
ITT	intent-to-treat (analysis set)
MedDRA	Medical Dictionary for Regulatory Activities
MH	Mantel-Haenszel
mITT	modified intent-to-treat (population)
IWRS	Interactive Web Response System
MMRM	mixed model repeated measures
[redacted]	[redacted]
PASI	Psoriasis Area and Severity Index
PASI-100	100% improvement from baseline in Psoriasis Area and Severity Index
[redacted]	[redacted]
PASI-75	75% improvement from baseline in Psoriasis Area and Severity Index
PASI-90	90% improvement from baseline in Psoriasis Area and Severity Index
PD	Pharmacodynamic
PGA	Physician's Global Assessment
PK	pharmacokinetic
PP	per protocol (analysis set)
PT	preferred term
QD	once daily
QT	QT interval
QTcF	Fridericia's correction formula for QT interval

SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System®
SE	Standard Error of the Mean
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TLF	Tables, Listings, and Figures
ULN	Upper Limit of Normal
WHO-DD	World Health Organization Drug Dictionary

1 INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned analyses and reporting for Nimbus Lakshmi, Inc Clinical Protocol 4858-201. Unless otherwise specified, the protocol indicated in this SAP is protocol Version 3.0 (Amendment 2), dated 04-Feb-2022. In case of discrepancies between the protocol and the SAP, the SAP will be used to guide the statistical analysis. Any deviations from the SAP will be described and justified in the final Clinical Study Report (CSR), as appropriate. This SAP complies with the International Conference for Harmonization (ICH) E9 'Statistical Principles for Clinical Trials'.

The SAP is designed to outline the methods to be used in the analysis of study data in order to answer the study objectives. Populations for analysis, data handling rules, statistical methods, and formats for data presentation are provided. The statistical analyses and summary tabulations described in this SAP will provide the basis for the results sections of the clinical study report (CSR) for this study. This SAP will be finalized prior to database lock, final unblinding, and final analyses. All final analyses will be performed after the clinical trial data are entered into the database, any discrepancies in the data are resolved, the database is locked, and following the signature of the SAP.

[redacted].

2 STUDY DESCRIPTION

2.1 Study Design

Study 4858-201 is a Phase 2b, randomized, multicenter, double-blind, placebo-controlled, multiple-dose study designed to evaluate the efficacy, safety, and tolerability of NDI-034858 in subjects with moderate to severe plaque psoriasis. This study will also evaluate the plasma concentrations of NDI-034858 and explore the immune response (in blood and skin) to NDI-034858 in subjects with moderate to severe plaque psoriasis.

Approximately 250 male and female subjects, aged 18 to 70 years (inclusive), with moderate to severe plaque psoriasis will be randomized in this study. To be eligible for the study, the subjects will need to have a history of plaque psoriasis for at least 6 months prior to the screening visit. In addition, the subjects will need to have the following characteristics at screening and on Day 1: PASI score ≥ 12, PGA score ≥ 3, and BSA involved with plaque psoriasis ≥ 10%.

All subjects will read and sign an informed consent form (ICF) prior to any screening procedures being performed. Subjects who fulfill all the inclusion criteria and none of the exclusion criteria will be included into the study. During a screening period of no longer than Day -30 to Day -1, subjects will be randomized (on Day -7) to receive either one of the four doses of NDI-034858 (2 mg, 5 mg, 15 mg, or 30 mg), or placebo on Day 1. The goal is to have approximately 50 subjects randomized per treatment group (1:1:1:1:1 ratio) on Day 1. During the treatment period, NDI-034858 (2 mg, 5 mg, 15 mg, or 30 mg) or placebo will be orally administered QD for 12 weeks. The 12-week treatment period will be followed by a 4-week safety follow-up period.

For scheduled study visits, subjects will come to the study site on 8 occasions: screening, Day 1, and Weeks 1, 2, 4, 8, 12 (end of treatment [EOT]), and 16 (end of study [EOS] / early termination visit [ET]).

Efficacy will be assessed using PASI, PGA, [redacted] Quality of life will be evaluated using DLQI.

Safety will be assessed by collecting AEs, recording vital signs, performing physical examinations, and evaluating clinical laboratory and ECGs results.

Blood samples will be collected to measure plasma levels of NDI-034858 as follows:

- On Day 1 prior to dosing and 1 hour (± 5 min) postdosing;
- At Week 4 prior to dosing, 1 hour (± 5 min) postdosing, and 4 hours (± 10 min) postdosing;
- At Week 8 prior to dosing;
- At Week 12 anytime (no study treatment administration at this visit).
- At ET visit anytime (if ET visit is planned before Week 12 visit).

[redacted]

[redacted]

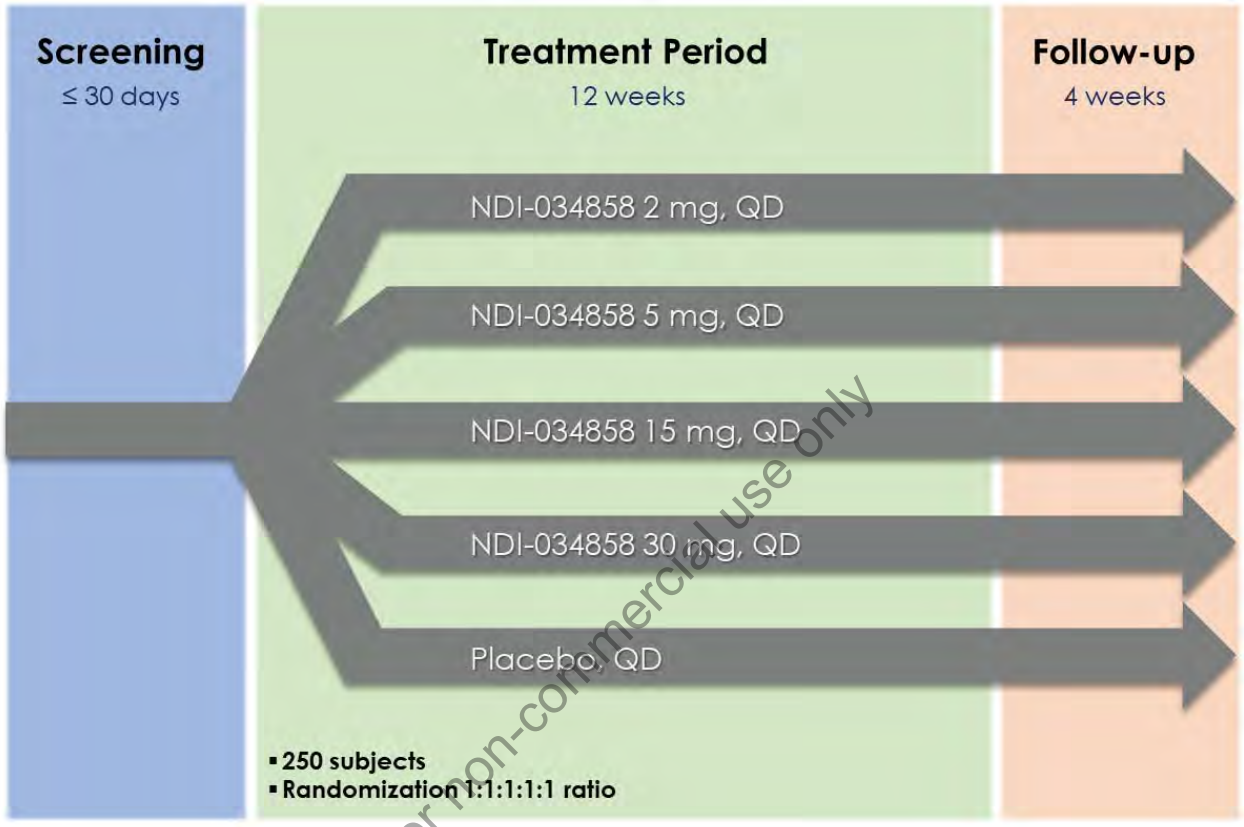
[redacted]

[redacted].

At certain study sites, in a subset of subjects who consent, optional medical photographs of full-body, front and back, will be taken to illustrate the outcome of the study.

No interim analysis is planned in this study.

Figure 1: Study Diagram



Abbreviation: QD, once daily.

2.2 Treatment Groups

Subjects will receive one of the following treatments for 12 weeks:

- NDI-034858 2 mg, QD
- NDI-034858 5 mg, QD
- NDI-034858 15 mg, QD
- NDI-034858 30 mg, QD
- Placebo, QD

2.3 Randomization

At the study site, each screened subject will be assigned a subject identifier number during screening that will be used on all subject documentation. The subject identifier number will contain the site number and the subject number and will be assigned in numerical order at the screening visit based on chronological order of screening dates (e.g., 02010 for the 10th subject screened at Site 02).

Approximately 250 subjects will be randomized 1:1:1:1:1 ratio to NDI-034858 at 2 mg, 5 mg, 15 mg, or 30 mg, or placebo (approximately 50 subjects per treatment group).

Randomization will occur at Day -7 visit. The randomization list will be generated using a validated software and will be stratified based on prior treatment with biologics (yes/no). The master randomization list will be kept secured until the study blind is broken at the end of study. This list will be uploaded into an Interactive Web Response System (IWRS). The investigator or designee will be able to acquire a randomization number for subjects by connecting to the IWRS. Of note, only eligible subjects (confirmed on Day 1) will receive the study treatment.

Subjects randomized but never dosed can be replaced when early terminated.

Further guidance and information can be obtained in the study manual.

2.4 Blinding and unblinding

This study is double-blinded. At all times, treatment and randomization information will be kept confidential and will not be released to the investigator, the study staff, the contract research organization (CRO), or the sponsor's study team until after the study completion.

Breaking the blind should be considered only when knowledge of the treatment assignment is deemed essential for the subject's care. In cases of accidental unblinding, the investigator should contact the medical monitor and ensure every attempt is made to preserve the blind.

The subject for whom the blind has been broken for a safety-related reason will be permanently discontinued from the study treatment. The primary reason for study treatment discontinuation (the event or condition which led to the unblinding) will be recorded.

3 STUDY OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS
Primary Objective	
To assess the efficacy of NDI-034858 orally administered QD at 2 mg, 5 mg, 15 mg, or 30 mg for 12 weeks in subjects with moderate to severe plaque psoriasis	**Primary Efficacy Endpoint** • Proportion of subjects achieving PASI-75 at Week 12 **Secondary Efficacy Endpoints** • Proportion of subjects achieving a PGA of clear (0) or almost clear (1) at Week 12 • Proportion of subjects achieving at least PASI-90 at Week 12 • Proportion of subjects achieving at least PASI-100 at Week 12 • Change from baseline in DLQI at Week 12
	Exploratory [redacted] Endpoints [redacted]
Secondary Objectives	
	Secondary Safety Endpoints

OBJECTIVES	ENDPOINTS
To assess the safety and tolerability of NDI-034858 orally administered QD at 2 mg, 5 mg, 15 mg, or 30 mg for 12 weeks in subjects with moderate to severe plaque psoriasis	• Incidence of AEs • Changes from baseline in vital signs, clinical laboratory parameters, and ECGs
To evaluate the plasma concentration of NDI-034858 orally administered QD at 2 mg, 5 mg, 15 mg, or 30 mg in subjects with moderate to severe plaque psoriasis	**Secondary Pharmacokinetic Endpoint** • Measurement of plasma concentrations of NDI-034858 in subjects receiving active treatment
Exploratory Objectives	
	Exploratory [redacted] Endpoints

OBJECTIVES	ENDPOINTS
[redacted]	[redacted]
[redacted]	**Exploratory [redacted] Endpoints** [redacted]
[redacted]	[redacted]

Abbreviations: AE, adverse event; [redacted]; DLQI, Dermatology Life Quality Index; ECG, electrocardiogram; [redacted]; PASI, Psoriasis Area and Severity Index; PASI-100, 100% improvement from baseline in PASI; [redacted]; PASI-75, 75% improvement from baseline in PASI; PASI-90, 90% improvement from baseline in PASI; PGA, Physician's Global Assessment; QD, once daily.

[redacted].

4 POPULATIONS FOR ANALYSIS

4.1 Intent-to-Treat Analysis Set

The intent-to-treat (ITT) analysis set will include all subjects who were randomized. All subjects will be analyzed according to the treatment group to which they were randomized.

4.2 Modified Intent-to-Treat Analysis Set

The modified intent-to-treat (mITT) analysis set will include all subjects who were randomized and received at least one dose of study treatment. All subjects will be analyzed according to the treatment group to which they were randomized. The mITT analysis set will be used as the primary analysis population for efficacy.

4.3 Per-Protocol Analysis Set

The per-protocol (PP) analysis set will include all subjects who were randomized, who received at least one dose of study product, and who provided evaluable data for the primary endpoint (PASI-75 at Week 12) with no major protocol deviations affecting the efficacy evaluations as defined in Appendix 3. All subjects will be analyzed according to the treatment group that they actually received. The primary efficacy analysis will be repeated based on the per protocol analysis set if it differs by more than 10% in number of subjects from the mITT analysis set. Details of major protocol deviations are provided in Appendix 3. The PP analysis set will be used as a supplementary analysis of the primary endpoint.

4.4 Safety Analysis Set

The safety analysis set will include all subjects who received at least one dose of the study product. All subjects will be analyzed according to the treatment group that they actually received.

4.5 Pharmacokinetic (PK) Analysis Set

The pharmacokinetic (PK) analysis set will include all subjects who received at least one dose of NDI-034858 and have evaluable plasma concentration data. All subjects will be analyzed according to the treatment group that they actually received.

[redacted].

5 GENERAL CONSIDERATIONS

Formats and layouts of tables, listings, and figures (TLF) will be provided in a separate document (output general layout is described in Appendix 1).

Unless otherwise noted, all statistical summaries will be done by treatment group and by visit, as applicable.

5.1 Sample Size

The sample size determination is based on testing equality of two independent response rates using a 2-sided test with significance level of alpha = 0.05 and power 85%. The formula used for the calculation is the same as used in the nQuery® (ie, normal approximation with Fleiss' formula and continuity correction).

Assuming the placebo response rate at end of Week 12 is 10% (proportion of subjects achieving PASI-75), at least one of the NDI-034858 dose treatment groups will have a response rate at least 40%, and after adjustment of 15% dropout rate between randomization and Day 1, approximately 250 subjects (50 per treatment group) will be randomized in the study.

5.2 Baseline

Unless otherwise specified, baseline value will be defined as the last non-missing assessment prior to or on the first study treatment dosing (including unscheduled assessments) or randomization if no study drug is given. If the last non-missing assessment is performed on the same date as the first study treatment administration (or randomization if no study drug is given) and time is not available, the assessment will be considered as baseline, except for adverse events (AEs) not related to a pre-dose assessment and medications starting on the first study treatment dose administration date which will be considered post-baseline.

5.3 Reference Start Date and Study Day

Study day will be calculated from the first study treatment administration date and will be used to show start/end day of assessments or events.

Study day = (Date of event – Date of first dose administration) + 1 if date of event is on or after the date of first dose administration of study treatment;

= (Date of event – Date of first dose administration) if date of event is before the date of first dose administration of study treatment.

There is no study day 0 defined for this study. In the situation where the assessment/event date is partial or missing, study day will be missing.

Study Day will be calculated from randomization date (instead of date of first dose administration) for randomized subjects who never received any study drug.

5.4 Analysis windows

All evaluation visits are expected to occur following the Schedule of Events per the protocol. For subject's visits done strictly as scheduled, the designation of visits will be based on the nominal visit recorded in the eCRF. When retests measurements are done for a nominal visit, the retest measurement will be used. For all other assessments (Unscheduled, Early Termination), the designation of visits will be based on analysis window (Table 1) rather than the nominal visit recorded in the eCRF, when no scheduled measurement was performed at that visit.

If subjects have multiple unscheduled or additional evaluations within an analysis visit window but no scheduled visit done at that visit, the evaluation closest to the target visit date will be used in the summary tabulations. In case of evaluations equidistant to the target visit date within an analysis visit window, results of the last evaluation will be used. This applies to all assessments without designated visits (Unscheduled, Early Termination).

Table 1 – Analysis Visit Windows

Analysis Visit	Target Study Day						
		Clinical lab, vital sign	ECG	Lipid panel	PASI/PGA	[redacted]	DLQI
Week 1	8	[1 post-dose, 11]	[1 post-dose, 11]				
Week 2	15	[12, 22]	[12, 22]				
Week 4	29	[23, 43]	[23, 43]				[1 post-dose, 43]
Week 8	57	[44, 71]	[44, 71]				[44, 71]
Week 12	85	[72, 99]	[72, EOS]	[1 post-dose, EOS]	[72, EOS]		[72, EOS]
Week 16	113	[100, EOS]					

5.5 Descriptive Statistics

All continuous variables will be summarized by presenting the number of subjects, mean, standard deviation (SD), median, minimum, maximum, Q1 and Q3. Categorical variables will be presented as frequencies and percentages. Summary tables will be presented by treatment and by visit, when applicable.

Change from baseline will be calculated as:

Assessment value at postbaseline visit X – baseline value.

Percent change from baseline (%) will be calculated as:

(Assessment value at postbaseline visit X – baseline value) / baseline value * 100.

Percent change from baseline will be missing in situation where baseline value equals to 0.

5.6 Statistical Tests

Unless otherwise specified, all statistical tests will be two-sided and will be performed with a significant level of 0.05. Confidence intervals (CIs) will be two-sided with 95% coverage.

5.7 Handling of Retests, Unscheduled Visits, and Early Termination Data

When retests measurements are done, the retest measurement will be considered for the summary analysis. All data from retest visits will be listed.

Unscheduled and early termination assessments will be remapped as defined in section 5.4.

5.8 Software Version

All analyses will be performed using SAS® software Version 9.4 or higher.

6 STATISTICAL CONSIDERATIONS

6.1 Adjustments for Covariates

Baseline value will be included as covariate in the statistical models for the analysis of the continuous efficacy endpoints on change and percent change from baseline using Mixed Model for Repeated Measures (MMRM) models (PASI, PGA, [redacted], DLQI [redacted]).

The odds ratio and difference in proportion of subjects achieving binomial endpoints between treatment group and placebo will be adjusted by prior treatment with biologics.

6.2 Handling of Dropouts or Missing data

See Appendix 2 for handling of completely or partially missing dates for prior and concomitant medications and AEs.

Unless otherwise specified, missing safety data will not be imputed.

For the categorical efficacy endpoints (e.g., proportion of subjects achieving at least a 75% improvement from baseline in PASI), subjects with a missing assessment at a specific visit will be considered as not having achieved the endpoint at that visit, and as not having achieved the endpoint for subsequent visits for discontinued subjects. For logistic regression models, missing values will not be imputed as non-responders and will be left as missing.

Missing observations for the efficacy continuous endpoints will be addressed by using the mixed model for repeated measures (MMRM) approach. The parameter estimations are based on the assumption of data being missing at random and using the method of restricted maximum likelihood (REML).

6.3 Interim Analysis and Data Monitoring

No interim analysis is planned for this study.

6.4 Multiple Comparisons/Multiplicity

All statistical tests will be two-sided and will be performed with a significant level of 0.05, unless otherwise specified. To account for the multiplicity testing in the primary endpoint analysis, each active treatment group will be compared to the placebo group using a hierarchical testing procedure, starting with the highest dose group, and ending with the lowest dose group (30-mg NDI-034858, 15-mg NDI-034858, 5-mg NDI-034858, and 2-mg NDI-034858, in order). If a comparison is not significant at level 0.05, all p-values in subsequent comparisons will be considered to be nominal and may be provided if applicable. No adjustment to alpha will be made to account for multiple testing between treatment groups for the secondary [redacted] efficacy endpoints.

7 STUDY SUBJECTS

7.1 Disposition of Subjects

All subjects who provide informed consent will be accounted for in this study. The number of subjects screened, rescreened, and who failed screening (screen failures) will be presented. The reason for screen failure will be presented for all screened subjects who failed screening and rescreening, if applicable. Moreover, the number of subjects randomized, the number of subject randomized but early terminated (ET) or lost-to-follow-up (LTFU) (i.e. discontinued) before first study treatment dose and associated reason, and the number of subjects included in each analysis set will be presented. Study completion status and the reason for study discontinuation, including related to COVID-19 or not, will also be presented. The percentage of subjects with screen failures will be calculated using the number of subjects screened as denominator. The percentage of screen failure by reasons will be calculated using the number of screen failures as denominator. The percentage of subjects with study discontinuation will be calculated by reasons using the number of subjects who did not complete study as denominator (and due to COVID-19 or not, as applicable). Otherwise, percentages will be calculated using the number of subjects randomized and dosed as denominator. Number of days in the study will be calculated as follows and summarized:

Number of days in study = Date of completion/discontinuation – 1st dose date +1

For subject who did not receive a dose of study treatment, the number of days in the study will be left as missing.

A listing of subject's disposition will be provided. Information on first screening for subjects who were rescreened, including the rescreened subject identifier and the reason for first screening failure, will be presented under the first screening subject identifier.

A listing of subject's randomization information, a listing subject randomized but deemed not eligible or lost-to-follow-up (i.e. discontinued) before receiving a first study treatment dose, and a listing of subjects included in each of the analysis sets will also be provided.

7.2 Protocol Deviations

A data review will be conducted prior to database lock and unblinding of treatment assignment by the Medical Monitor, Statistician and the Sponsor to classify protocol deviations as minor or major as defined in Appendix 3. Protocol deviations, including classification as Important/Non-

Important, will be classified as described in the Protocol Deviation Management Plan, based on Nimbus categorization.

The number of events and the number and percentage of subjects with at least one major protocol deviation (including major protocol deviations associated with COVID-19) will be summarized by deviation category, sub-category and treatment group using the safety analysis set. Important protocol deviations will be summarized separately in a similar way. A listing of all protocol deviations (including minor) will also be provided on the safety analysis set.

In addition, all the protocol deviations associated with COVID-19 will be summarized by deviation category and deviation sub-category and listed as described above. Protocol deviations will be sorted alphabetically by categories and within each category the sub-categories will be presented by decreasing order.

7.3 Demographic and Baseline Characteristics

Demographics and baseline characteristics will be summarized with descriptive statistics using the ITT, mITT and safety analysis set (if different from mITT) by treatment group and overall. The list of demographics and baseline characteristics to be summarized will include:

- Age at consent (years)
- Sex
- Race*
- Ethnicity
- Baseline Height (cm)
- Baseline Weight (kg)
- Baseline BMI (kg/m^2) **
- Prior Treatment with Biologics (Yes/No)
- Psoriasis Area and Severity Index
- Physician Global Assessment
- Body Surface Area (%)
- Pruritus Numeric Rating Scale
- Dermatology Life Quality Index
- Pain Numeric Rating Scale for subjects with concomitant psoriatic arthritis at baseline

*Subjects who reported more than one race will be summarized as 'Multiple' races in the table. All races selected will be displayed in the listing.

** Baseline BMI is calculated by using baseline height and baseline weight.

A listing of all demographics and baseline characteristics will be provided on the ITT analysis set.

7.4 Surgical and Medical History

Surgical and medical history will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA), Version 24.0.

Surgical and medical history (including disease-specific medical history) will be summarized by system organ class (SOC) and preferred term (PT) using the safety analysis set. A subject who experienced the same surgical and medical history event multiple times will be counted only once for the corresponding PT. Similarly, if a subject experienced multiple surgical and medical history events within the same SOC, the subject will be counted only once for that SOC. Surgical and medical history events will be sorted alphabetically by SOC and within each SOC the PT will be presented by decreasing order.

A listing of all surgical and medical history events will be provided.

Disease-specific medical history for the duration of plaque psoriasis and psoriatic arthritis will be summarized using the safety analysis set.

The disease duration for plaque psoriasis and psoriatic arthritis (in years) will be calculated as follows:

Disease duration of plaque psoriasis or psoriatic arthritis = (Date of first dose of study treatment – Start date of plaque psoriasis or psoriatic arthritis)/365.25.

Completely or partially missing dates for the start date of plaque psoriasis or psoriatic arthritis will be imputed as follows:

- Completely missing: Leave missing.
- Missing day and month: Impute to January 1st.
- Missing day: Impute to the 1st of the month.

Disease-specific medical history will be listed.

7.5 Prior and Concomitant Medications

Medications will be coded according to the World Health Organization Drug Dictionary (WHO-DD), March 2021 B3.

Prior medications are defined as any medication started and discontinued prior to the first study treatment dosing. Concomitant medications are defined as any medication taken after the first study treatment dosing, including those who started prior to the first study treatment date and continued past that date. See Appendix 2 for handling of completely or partially missing dates for prior and concomitant medications.

Incidence of prior and concomitant medications will be tabulated by anatomical therapeutic chemical (ATC) level 3 and PT using the safety analysis set. A subject with the same medication taken multiple times will be counted only once for the corresponding PT. Similarly, if a subject has taken more than one medication within the same ATC level, then the subject will be counted only once for that ATC. Prior and concomitant medications will be sorted alphabetically by ATC level and within each ATC level, the PT will be presented by decreasing order.

A listing of all prior and concomitant medications will be provided.

7.6 Study Treatment Exposure and Treatment Compliance

Duration of exposure to study treatment, in days, will be computed as follows:

$$\text{Duration of exposure} = [(\text{Date of last dose of study treatment} - \text{Date of first dose of study treatment}) + 1]$$

Compliance with study treatment (%) will be calculated as follows:

$$\frac{\text{Number of doses taken}}{\text{Total extent of exposure (in days)} * \text{Planned number of doses per day}} \times 100$$

For each subject, the planned number of doses per day corresponds to one dose per day.

Daily doses from the first dose of study treatment until the last dose of study treatment will be assumed as taken unless they are entered as missed doses in the diary. Missed doses with unknown dates will be considered as being missed between the first dose and last dose of study treatment.

Descriptive statistics for the duration of exposure and compliance to study treatment, and number of missed doses, will be presented by treatment group and overall based on the safety analysis set.

Frequency distribution will also be presented for the following compliance categories: <80%, 80% to 120%, >120%. The number and proportions of subjects in each study drug exposure category will be summarized using the following categories: ≤4 weeks (≤28 days), 4 weeks to ≤8 weeks (>28 to ≤56 days), 8 weeks to ≤12 weeks (>56 to ≤84 days), >12 weeks (>84 days), based on the number of subjects in the safety analysis set.

Listings of all study treatment administrations at the study site and missed doses as per diary, study drug accountability, and study treatment compliance and exposure will be provided on the safety analysis set. Additionally, a listing of study treatment overdose will be provided by subject on the safety analysis set.

8 EFFICACY ANALYSIS

8.1 Imputation of Values Due to Prohibited Medications

For all efficacy endpoints, any subject's assessment collected on the day of the start of a prohibited medication or after which was adjudicated as major protocol deviation (Appendix 3) will be set as missing (for continuous endpoints) and non-responder (for binary endpoints, including in logistic regression models) for the purpose of the efficacy analyses.

8.2 Analysis of Primary Efficacy Endpoint

8.2.1 Psoriasis Area and Severity Index (PASI)

The PASI quantifies the severity of a subject's psoriasis based on both lesion severity and the percentage of BSA affected. The PASI is a composite score ranging from 0 to 72 that that takes into account the degree of erythema, induration/infiltration, and desquamation (each scored from 0 to 4 separately) for each of four body regions, with adjustments for the percentage of BSA involved for each body region and for the proportion of the body region to the whole body. Scoring of the PASI is presented in protocol Appendix 2. The PASI score will be set as missing if at least one question value is missing.

8.2.2 PASI-75

The percentage change from baseline in PASI at Week 12 will be calculated using the following formula:

$$\frac{PASI\ score\ at\ Week\ 12 - PASI\ score\ at\ Baseline}{PASI\ score\ at\ Baseline} * 100$$

For a subject, achievement of PASI-75 is Yes if the percentage change from baseline is less than or equal to -75%, i.e., the subject has greater than or equal to 75% improvement in PASI score comparing to baseline. Otherwise, PASI-75 is No.

The primary endpoint is defined as follow:

- Proportion of subjects achieving at least a 75% improvement from baseline in Psoriasis Area and Severity Index (PASI-75) at Week 12.

8.2.3 Primary Analysis

The primary endpoint will be translated as a responder analysis, where a subject will be classified as responder if he or she achieves PASI-75 at Week 12. The primary efficacy analysis will be performed on the mITT analysis set.

Subjects with a missing postbaseline PASI results at Week 12 will be considered as not having achieved the PASI-75 at that Week 12 (i.e., as non-responder).

The following analyses will be provided for PASI-75:

- Descriptive statistics (frequencies and percentages) for PASI-75 will be presented by visit and treatment group.
- A longitudinal line plot of the response rate in PASI-75 by treatment group will be provided.
- The comparison between treatment groups (each active group vs placebo) will be done using a Cochran-Mantel-Haenszel (CMH) as the primary analysis, with prior treatment with biologics (Yes/No) included as a stratification factor. The odds ratio (odds in treatment group/odds in placebo) and the difference in the response rates calculated using the Mantel-Haenszel stratum-weighted method and their corresponding two-sided 95% confidence intervals (CIs) will be provided. If a subject is stratified incorrectly at randomization, the subject will be included into the analysis as stratified per the ITT principle.

  To account for the multiplicity testing in the primary endpoint analysis, each active treatment group will be compared to the placebo group using a hierarchical testing procedure, starting with the highest dose group and ending with the lowest dose group (30-mg NDI-034858, 15-mg NDI-034858, 5-mg NDI-034858, and 2-mg NDI-034858, in

order). If a comparison is not significant at level 0.05, all p-values in subsequent comparisons will be considered to be nominal and may be provided if applicable.

8.2.4 Supplementary Analysis

A logistic regression model analysis will be performed to evaluate the impact of treatments on PASI-75 at Week 12, with treatment group, age, gender, baseline weight, baseline BMI, baseline PASI score, and use of previous biologic treatment as covariates. Subjects with missing value will not be imputed to non-responders and will be left as missing for the purpose of this analysis.

To test the robustness of the analysis method, the primary analysis of the proportion of subjects achieving PASI-75 will be repeated using the ITT analysis set as a supplementary analysis. It will also be repeated using PP analysis set if it differs by more than 10% from the mITT analysis set.

Additionally, a repeat of the primary endpoint analysis will be performed based on Observed Cases (OC) only, i.e. excluding the imputed values as non-responders.

8.2.5 Subgroup analysis

To investigate the impact of the use of previous biologic treatment on the primary efficacy endpoint, subgroup analyses will be performed. The Chi-square test on the response rates in PASI-75 at Week 12 will be conducted and the odds ratio (odd in a treatment group/odd in placebo) in the response rates and its corresponding two-sided 95% CI will be provided.

8.3 Analyses of Secondary Efficacy Endpoints

All secondary endpoint analyses will be conducted using the mITT analysis set.

8.3.1 PASI-90 and PASI-100

The secondary efficacy endpoints involving proportion of subjects on PASI include PASI-90 and PASI-100. PASI-90, and PASI-100 are defined as at least 90%, and 100% improvement from baseline in PASI, respectively. PASI-90 and PASI-100 are defined similarly as PASI-75 in Section 8.1.2.

The PASI-90 and PASI-100 will be analyzed as follow using the mITT analysis set:

- Proportion of subjects achieving PASI-90 at Week 12,
- Proportion of subjects achieving PASI-100 at Week 12.

8.3.2 Physician's Global Assessment

The PGA of disease severity is a global assessment of the current state of the disease. It is a 5 -point morphological assessment of overall disease severity (0-Clear, 1-Almost clear, 2-Mild, 3-Moderate, 4-Severe).

The secondary endpoints on PGA will be analyzed as follow using the mITT analysis set:

- Proportion of subjects achieving a PGA of clear (0) or almost clear (1) at Weeks 12.

8.3.3 Dermatology Life Quality Index Questionnaire

The DLQI is a simple 10-question validated questionnaire that has been used in more than 40 different skin conditions. The DLQI is the most frequently used instrument in studies of randomized controlled trials in dermatology. Each question is scored on a four-point Likert scale: very much (3); a lot (2); a little (1); not at all (0); and not relevant (0). DLQI total score is defined as the sum of the 10 item scales, ranging from 0 to 30. If missing answers, the following rules will be followed:

- If one question is left unanswered, then the question is scored as 0 and the scores are summed and expressed as usual out of a maximum of 30.
- If two or more questions are left unanswered, then the questionnaire is not scored.
- If question 7 is answered 'yes', then this is scored as 3 (even if in the same question one of the other boxes is ticked).
- If question 7 is answered 'no' or 'not relevant' but then either 'a lot' or 'a little' is ticked, then this is scored as 2 or 1. If it is answered 'no', but the second half is left incomplete, the score will remain 0.

The secondary endpoint on the DLQI total score will be analyzed as follow on the mITT analysis set:

- Change from baseline in DLQI at Week 12.

Additionally, the number of subjects achieving a score of 0 or 1 will be descriptively summarized at each visit, with no imputation for missing values.

8.3.4 Analysis of Secondary Endpoints

For endpoints involving proportions of subjects, subjects with a missing postbaseline assessment at a specific visit will be considered as not having achieved the endpoint at that visit (and as not

having achieved the endpoint for subsequent visits for discontinued subjects), i.e., as non-responders.

The following analyses will be provided for the secondary endpoints of PASI-90, PASI-100, and proportion of subjects achieving a PGA of clear (0) or almost clear (1):

- PASI-90 and PASI-100, and the achievement of PGA score of 0/1 (0-Clear, 1-Almost Clear) will be presented using descriptive statistics (frequency and percentage) by visit for each group.
- A longitudinal line plot of the response rate in PASI-90, PASI-100 and achievement of PGA of 0/1 by treatment group will be provided.
- The comparison between treatment groups (each active group vs placebo) will be analyzed using the same approach (CMH test) as described for the primary efficacy analysis, at each visit.
- As a supplementary analysis, a logistic regression model analysis will be performed to evaluate the impact of treatments on achievement of PGA score of 0/1 at Week 12, with treatment group, age, gender, baseline weight, baseline BMI, baseline PASI score, and use of previous biologic treatment as covariates. Subjects with missing value will not be imputed to non-responders and will be left as missing for the purpose of this analysis.

No adjustments for multiple comparisons for secondary outcomes will be made.

The following analyses will be provided for the secondary endpoints of DLQI:

- Descriptive statistics on DLQI will be presented by visit and treatment group.
- Change from baseline will also be summarized descriptively by visit and treatment group.
- The change from baseline in DLQI will be analyzed using an MMRM. The model will include treatment group, visit (Weeks 4, 8, and 12), treatment-by-visit interaction, and prior treatment with biologics as fixed effects, and baseline score as a covariate. Unstructured covariance will be used to model the within-subject error. If convergence issues arise, the autoregressive (AR(1)) structure will be used. If the AR(1) structure also does not converge, other covariance structures (CS, Toeplitz) deemed appropriate to fit the data will be used. The Kenward Roger method will be used for computing the denominator degrees of freedom for the tests of fixed effects. The treatment effect will be the contrast between treatment groups at each scheduled post-baseline visit estimated through least squares (LS) means. The LS mean estimates, LS mean differences, associated two-sided 95%

confidence intervals, and p-values will be reported. The contrasts of interest will be of each active treatment group (2, 5, 15 and 30 mg NDI-034858) vs placebo group.

8.4 Analyses of Exploratory [redacted] Endpoints

8.4.1 [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

8.4.2 [redacted]

[redacted]

- [redacted]
- [redacted]

8.4.3 [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

8.4.4 [redacted]

[redacted]

8.4.5 [redacted]

[redacted]

8.4.6 [redacted]

[redacted]

8.4.7 [redacted]

[redacted]

8.4.8 [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

9 SAFETY ANALYSIS

All safety analyses will be conducted using the safety analysis set. No inferential statistics will be performed on safety variables.

9.1 Adverse Events

The primary focus of adverse event reporting will be on treatment-emergent adverse events (TEAEs). Pretreatment adverse events will be provided separately, in applicable listings.

Adverse events (AEs) will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA), Version 24.0.

Listings of all AEs, all AEs leading to death, all serious AEs, all TEAEs leading to study treatment discontinuation, all TEAEs leading to study discontinuation, AE of CPK elevation and AE of special interest will be provided. All information pertaining to AEs noted during the study will be listed by treatment group, subject, detailing verbatim, system organ class, preferred term, start date, stop date, intensity, outcome, action taken with respect to study product, and relationship to study product. The AE onset will also be shown relative (in number of days) to the day of study product administration.

Treatment emergent adverse events (TEAEs) will be derived as any AEs with onset date on or after the first study treatment dosing. AEs starting on the first study treatment dosing date and related to a pre-dose study assessment will not be considered as TEAE. See

Appendix 2 for handling of completely or partially missing dates for AEs. In the case where it is not possible to define an AE as treatment emergent or not, the AE will be classified as treatment emergent.

An overall summary table of adverse events will be provided. The number of events and the number and percentage of subjects who experienced TEAE, AE of special interest (AESI), TEAE by worst reported relationship, TEAE by worst reported severity, related TEAE by worst reported severity, serious AE (SAE), serious TEAE by worst reported severity, TEAE leading to study treatment discontinuation, TEAE leading to study discontinuation, and AE leading to death will be presented.

Unless otherwise specified, a subject experiencing the same TEAE multiple times will be counted only once for the corresponding preferred term (PT). Similarly, if a subject experiences multiple TEAEs within the same system organ class (SOC), the subject will be counted only once for that SOC. TEAEs will be sorted alphabetically by SOC and within each SOC the PT will be presented by decreasing order.

A treatment-related TEAE is defined as any TEAE that is assessed by the investigator as related to study treatment. TEAE that is assessed as not related will be defined as not treatment-related. If a subject experiences more than one TEAE within different relationship categories within the same SOC/PT, the subject will be counted only once for that SOC in the worst reported relationship category. A TEAE with an unknown relationship will be considered as treatment-related.

The severity of an AE or SAE is based on the National Cancer Institute (NCI) CTCAE, Version 5.0. A life-threatening or fatal adverse event is defined as any adverse events with a severity grade of 4 or higher (grade 4 (life-threatening) or grade 5 (fatal)). If a subject experiences more than one TEAE within different severity categories within the same SOC/PT, the subject will be counted only once for that SOC and the highest severity category. TEAE with an unknown severity will be considered as severe.

Adverse event incidence tables will present by primary SOC and PT for each treatment group, the number (n) and percentage (%) of participants experiencing the following:

- All TEAEs
- Treatment-related TEAEs
- TEAEs leading to discontinuation of study treatment
- TEAEs leading to study discontinuation
- TEAEs by severity (CTCAE grades 1, 2, 3, 4 or higher)
- TEAEs leading to death

- Treatment-emergent SAEs
- Treatment-related SAEs
- Treatment-emergent AESIs (as defined in Protocol section 8.4.7)
- Treatment-related AESIs

TEAEs will also be summarized by the following periods:

- The "On-treatment period" is defined as a TEAE with onset date from the date from first administration of study treatment to the last dose of treatment date (included).
- The "Post-treatment period" is defined as a TEAE with onset date from the last dose of treatment date + 1 to the end of study.

9.2 Clinical Laboratory

Descriptive statistics will be presented for data related to biochemistry ,hematology, coagulation, quantitative urinalysis, fasted lipids and lipids (including both fasted and non-fasted). Change from baseline values will be presented for each postbaseline assessment. Frequencies and percentages for each result will be provided for qualitative urinalysis data.

For fasted lipids, if the fasting status is unknown, it will be assumed that the subject did not fast.

Clinical laboratory results were graded with CTCAE grading report flag in laboratory service agreement LSA Medpace. CTCAE grading will not be derived for local laboratory results. Shift tables from baseline to each postbaseline assessments describing shifts in CTCAE grade will be provided as well for biochemistry, hematology, coagulation, fasted lipids and lipids (including both fasted and non-fasted). Only subjects with a baseline result and a result at the specified visit for the parameter will be considered. Additionally, shift tables from baseline to each postbaseline assessments describing shifts to out-of-normal range will be provided for qualitative urinalysis. The shift from baseline to maximum post-baseline CTCAE grade will also be reported.

In addition to the laboratory results reported by the laboratory service, other parameters will be derived.

The corrected calcium will be calculated and reported using the following formula:

Corrected Calcium (mmol/L)= Serum Calcium (mmol/L) + 0.02 * (40 – Patient Albumin in g/L)

Corrected calcium will be graded using CTCAE Grade v5.0 and reported as part of the biochemistry assessments.

For protein urine, a shift table from baseline to each post-baseline assessment describing the shift in value will be produced, based on the following categories: 0/Trace (Negative or ≤20 mg/dL), 1+ (>20 and ≤70 mg/dL) , 2+ (> 70 and ≤200 mg/dL) , 3+ (>200 and ≤600 mg/dL), 4+ (>600 mg/dL). The shift from baseline to maximum post-baseline value will also be reported. Protein urine will be graded using CTCAE Grade v5.0 and reported as part of the urinalysis assessments.

A shift table will also be produced for eGFR. eGFR will be derived at each visit using creatinine value:

eGFR (ml/min)= [(140 − Age) × Weight in kg/(72 × sCr)] × (0.85 if female).

Where weight is in kg, and Creatinine (sCr) is in mg/dL. If any value of this equation is missing for subject or visit, eGFR will be left as missing. The shift from baseline to worst post-baseline value will also be reported.

Separate listings of all data for biochemistry, hematology, coagulation, urinalysis, lipids and pregnancy test will be provided.

Frequency and percentage of subjects who experience treatment-emergent CTCAE Grade 1 or higher will be summarized for the following CTCAE terms: Anemia, Lymphocyte count decreased, Neutrophil count decreased, Platelet count decreased, White blood cell decreased, Hypoalbuminemia, Hypoglycemia, Activated partial thromboplastin time prolonged, INR increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, GGT increased, Alkaline phosphatase increased, Blood bilirubin increased, CPK increased, Cholesterol high, Hypertriglyceridemia, Creatinine increased, Hypocalcemia, Hypercalcemia, Hyponatremia, Hypernatremia, Hypokalemia, Hyperkalemia.. A similar table will be produced for treatment-emergent CTCAE Grade 2 or higher. Subjects experiencing multiple events within the same CTCAE term will be counted only once for that CTCAE term.

For the CTCAE terms mentioned above, a separate listing will be provided for each parameter where a subject had at least one clinically significant treatment-emergent (Grade 2 or higher) abnormal result.

Local laboratory results will be analyzed as other laboratory results.

9.3 Vital Signs

Descriptive statistics will be presented for data related to vital signs (systolic blood pressure diastolic blood pressure, pulse rate, and body temperature). Change from baseline values will be

presented for each post baseline assessment. Descriptive statistics will be presented for height, weight and BMI, including change from baseline for weight and BMI.

Tables describing abnormal results will be provided as well, based on the abnormality criteria in Table 2. Only subjects with a baseline result and a result at the specified visit for the parameter will be considered.

A listing of all vital sign assessments will be provided.

The following criteria will be used to determine vital sign results that are outside of a prespecified range of normality:

Table 2: Vital Sign Parameter Cut-Off Values

Parameter	Criteria
Pulse Rate (bpm)	Value > 100 and change from baseline > 30, or Value < 55 and change from baseline < -15
Systolic blood pressure (mmHg)	Value > 140 and change from baseline > 20, or Value < 90 and change from baseline < -20
Diastolic blood pressure (mmHg)	Value > 90 and change from baseline > 10, or Value < 55 and change from baseline < -10

In addition, participants with vital signs outside of this pre-specified range of normality (i.e., Table 2) will also be listed.

9.4 Physical Examination

A listing of all physical examinations will be provided.

9.5 Electrocardiogram

Descriptive statistics will be presented for data related to ECGs (heart rate, RR, PR, QRS, QT, QTcB and QTcF). Change from baseline values will be presented for each postbaseline assessment.

A listing of all ECG assessments will be provided.

The incidence of QTc prolongation (defined as QTcF or QTcB >= 480 or >=30 msec increase from baseline) at any time during the treatment-emergent adverse event period will be summarized by treatment group. A separate listing for the subjects with QTc prolongation will be provided.

9.6 Potential Drug Induced Liver Injury

Potential Drug Induced Liver Injury (DILI) are defined as alanine aminotransferase (ALT) or aspartate aminotransferase (AST) values ≥ 3 times the upper limit of normal (ULN) and total bilirubin > 2 times the ULN. A listing will be provided for potential drug induced liver injury by subject.

9.7 Consultation Notes

Consultation notes will be listed based on the safety analysis set.

10 PHARMACOKINETIC ANALYSES

Blood samples will be collected to measure plasma levels of NDI-034858 as follows:

- On Day 1 prior to dosing and 1 hour (± 5 min) postdosing;
- At Week 4 prior to dosing, 1 hour (± 5 min) postdosing, and 4 hours (± 10 min) postdosing;
- At Week 8 prior to dosing;
- At Week 12 anytime (no study treatment administration at this visit).
- At ET visit anytime (if ET visit is planned before Week 12 visit).

NDI-034858 plasma concentration reported as below the limit of quantification (BLQ) will be set to LLOQ/2 except in the listing. Samples with no reportable value will be set to “Missing”.

Descriptive statistics (including the coefficient of variation, geometric mean and geometric mean’s coefficient of variation) of the NDI-034858 plasma concentration data will be summarized based on nominal timepoints per dose level and will be presented in a table using the PK analysis set.

NDI-034858 plasma concentration data, including actual sampling time, will be listed per subject by visit and time points using the PK analysis set.

11 [redacted]

[redacted].

12 CHANGES FROM ANALYSIS SPECIFIED IN THE PROTOCOL

Changes made from the analysis specified in the protocol are the following:

Description of the Change	Rationale for the Change
Continuous variables summaries will also present Q1 and Q3 as part of the descriptive statistics.	To provide more information on descriptive statistics of continuous variables.
Addition of supplementary analysis on the primary endpoint: Based on observed cases, using a logistic regression model, and based on the ITT analysis set.	To study the robustness of the conclusion from the primary endpoint analysis.
Any subject's assessment collected on the day of the start of a prohibited medication or after which was adjudicated as major protocol deviation (Appendix 3) will be set as missing (for continuous endpoints) and non-responder (for binary endpoints, including in logistic regression models) for the purpose of the efficacy analyses.	Subjects with prohibited medication that could affect psoriasis condition should be treated as missing or non-responder (as applicable).
For the primary analysis, the odds ratio and proportion differences will be reported and calculated using the MH method.	To report and estimate the pooled odds ratios and proportions differences across strata.
Normal to abnormal shift tables for vital signs are replaced by abnormal vital signs tables based on cut-off values.	To use pre-defined criteria instead of PI assessment.

13 APPENDICES

Appendix 1

Output Conventions

TLF will be generated using SAS® and will be displayed on letter size paper with landscape orientation, 1 inch margins and 9 pt Courier New font.

The header section will comprise the sponsor's name, the protocol number, the delivery description, the data cut-off date (if applicable), the TLF number, the TLF title, the analysis set, and the page number (Page X of Y). The footer section will include the TLF footnotes, the CRO's name, the date and time of the execution of the program, related listings number (if applicable), and the name of the program.

P-values equal to or above 0.001 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001"; p-values greater than 0.999 will be reported as ">0.999".

The mean, median, Q1 and Q3 will be displayed to one more decimal place than the original value; minimum and maximum will keep the same number of decimal places as the original value; standard deviation, standard error and CI will be displayed to two more decimal places than the original value. If derived parameters are to be summarized, the number of decimals of the derived values is to be chosen on a case-by-case basis, but the rule above applies.

For categorical summary tables, percentages will be reported to one decimal place. Percentages between 0 and 0.1 (both exclusive) will be displayed as "<0.1". The denominator for each percentage will be the number of subjects within the analysis set per treatment group unless otherwise specified.

Listings will be ordered by treatment group, subject number, date and visit (where applicable). Nominal visit will be presented in the listings. Imputed dates will not be presented in the listings.

Dates & Times Format

Date and time (if available) will be presented in the format yyyy-mm-dd/hh:mm.

Appendix 2

Algorithm for Imputation of Start/End Date of Adverse Events and Prior/Concomitant Medications

Event Start Date Imputation

- Imputation of event end date should be done before imputation of event start date.
- Completely missing: Impute to the first study treatment date.
- Missing day and month: Impute to January 1st, unless year is the same as year of first study treatment dose date then impute to the first study treatment date.
- Missing day: Impute to the 1st of the month, unless month and year are the same as month and year of first study treatment dose date then impute to the first study treatment date.
- If imputed event start date is after event end date (imputed or not), set the event start date to the imputed event end date.

Event End Date Imputation

- Completely missing (and not flagged as "ongoing"): Impute to the last contact date.
- Missing day and month: Impute to December 31st, unless year is the same as last contact date then impute to the last contact date.
- Missing day: Impute to the last day of the month, unless year and month are the same as year and month of last contact date then impute to the last contact date.

Appendix 3

Major Protocol Deviation

Eligibility Deviations:

- Participants with a diagnosis of plaque psoriasis for < 6 months
- Body mass index (BMI) not within 18-42 kg/m^2 or total body weight ≤ 50 kg (110 lb.)
- Participant with psoriatic plaques cover < 10% of body surface area (BSA) at screening or Day 1
- Participant with PASI score < 12 or sPGA < 3 at screening or Day 1
- Diagnosis of non-plaque psoriasis

Incorrect dosing:

- Participants who receive treatment different than randomized group
- Participants taking less than 80% or more than 120% of the planned medication during the entire treatment period, based on calculated compliance
- Randomized participants who do not take any blinded study medication for ≥ two consecutive weeks
- Restricted and Prohibited medications (refer to Protocol Section 6.4.2):
- Participants receiving the following prohibited concomitant treatments while on study therapy:
    - Therapeutic agent targeting IL-12, IL-17, and/or IL-23 (eg, ustekinumab, secukinumab, ixekizumab, brodalumab, guselkumab, tildrakizumab, risankizumab)
    - Rituximab or other immune-cell depleting agents
    - Any marketed or investigational biological agent (except those listed above)
    - Systemic treatment that could affect psoriasis (including oral, intravenous, intramuscular, intraarticular, intrathecal, or intralesional corticosteroids; oral retinoids; immunosuppressive/immunomodulating medication; methotrexate; cyclosporine; oral JAK inhibitors; or apremilast)
    - PUVA treatment, UV-B phototherapy (including tanning beds), or excimer laser, or tanning booths
    - Topical medication used for psoriasis (including corticosteroids, retinoids, vitamin D analogues [such as calcipotriol], JAK inhibitors, or tar)