J&J Innovative Medicine

Statistical Analysis Plan

Multiple Phase 3 Placebo-controlled and Deucravacitinib Active Comparator-controlled Studies Evaluating the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants with Moderate to Severe Psoriasis

ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2

Protocol 77242113PSO3002 and 77242113PSO3004 ; Phase 3

Amendment 2

JNJ-77242113

This Statistical Analysis Plan Covers the Following 2 Studies:

1. **A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled and Deucravacitinib Active Comparator-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Moderate to Severe Plaque Psoriasis (77242113PSO3002)**

2. **A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled and Deucravacitinib Active Comparator-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Moderate to Severe Plaque Psoriasis (77242113PSO3004)**

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Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

TABLE OF CONTENTS

VERSION HISTORY

SAP Version History Summary

SAP Version	Approval Date	Change	Rationale
1	3 June 2024	Not Applicable	Initial release
2	19 August 2024	Summarized in Page 8.	Based on Health Authority review on JNJ-77242113 psoriasis Phase 3 studies (77242113PSO3001 and 77242113PSO3003)
3	04 December 2024	Summarized in Page 9.	Based on Health Authority review and results from the Week 24 database lock of another ongoing Phase 3 psoriasis study 77242113PSO3001

LIST OF ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
ALT	alanine aminotransferase
AMER	North and South America
ANCOVA	analysis of covariance
APAC	Asia and Pacific
AST	aspartate aminotransferase
ATC	anatomic and therapeutic class
BMI	body mass index
BSA	body surface area
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CRF	case report form
CSR	Clinical Study Report
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DBL	database lock
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
ECG	electrocardiogram
eCRF	electronic case report form
EQ-VAS	EuroQol visual analogue scale
EQ-5D	EuroQol-5 Dimension
EQ-5D-5L	EuroQol-5 Dimension 5-level
EU	European Union
FAS	full analysis set
FCS	fully conditional specification
f-PGA	Fingernail Physician's Global Assessment
hf-PGA	Physician's Global Assessment of Hands and Feet
GenPs-SFQ	Genital Psoriasis Sexual Frequency Questionnaire
IGA	Investigator Global Assessment
IQ	Interquartile
IWRS	interactive web response system
LLOQ	lower limit of quantification
LS	least square
MAR	missing at random
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-effect Model for Repeated Measure
mNAPSI	modified Nail Psoriasis Severity Index
NAb	neutralizing antibodies
PASI	Psoriasis Area Severity Index
PD	pharmacodynamic(s)
PGA	Physician Global Assessment
PHQ-9	Patient Health Questionnaire-9
PK	pharmacokinetic(s)
PP	per protocol
PRO	patient reported outcome(s)
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
PsA	psoriatic arthritis
PSSD	Psoriasis Symptom and Sign Diary
PT	preferred term
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
sPGA-G	Static Physician's Global Assessment of Genitalia

ss-IGA	Scalp Specific IGA
TEAE	treatment-emergent adverse event
TSQM-E	Treatment Satisfaction Questionnaire for Medication-Effectiveness
VAS	visual analog scale
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

SUMMARY OF CHANGES IN AMANEDMENT 1

The statistical analysis plan (SAP) was amended to implement the following modifications to the original SAP:

The following modifications were made based on the regulatory review comments from 77242113PSO3001 and 77242113PSO3003 Statistical Analysis Plans. It is noted that 4 Phase 3 studies (77242113PSO3001, 77242113PSO3002, 77242113PSO3003 and 77242113PSO3004) are part of the JNJ-77242113 psoriasis clinical development program.

- Removed hypothetical estimand for the primary endpoint and key secondary endpoints.
- Added two sensitivity analyses (one using multiple imputation and one using tipping point analysis) to the co-primary estimand for the co-primary endpoints and main estimands for select key secondary endpoints.
- Added subgroup analysis based on ethnicity (Hispanic/Latino or Not Hispanic/Latino, Not Reported, and Unknown).

In addition, the following modifications were also made:

- Clarified the definition of "baseline".
- Clarified when an adverse event is considered treatment emergent by adding a 4-week window after last dose or treatment discontinuation.
- Clarified ECG analyses.
- Minor grammatical, formatting, or spelling changes were made.

SUMMARY OF CHANGES IN AMENDMENT 2

The statistical analysis plan (SAP) was amended to implement the modifications to the 77242113PSO3002-PSO3004 SAP Amendment 1.

The following modifications were made in Section 2.1.

- Clarified the question raised by Health Authority regarding multiple testing procedure for key secondary efficacy endpoints. That is, if any test within a tier is not significant, the assigned alpha for this tier will not be passed down to subsequent tier(s). The assigned alpha for each tier can be passed to other tiers ONLY if all hypotheses within the tier are rejected based on Bonferroni-Holm's procedure.
- Modified the multiple testing procedure for the key secondary endpoints based on the results from the Week 24 database lock of another ongoing Phase 3 psoriasis study 77242113PSO3001 in similar study population. The changes included slight modification of endpoint grouping in Week 4 and Week 8 endpoints (two tiers), re-ordering of testing tiers and slight change in weight assigned to endpoints of IGA 0/1 and PASI 75 at Week 16 comparing JNJ-77242113 and deucravacitinib.

1. INTRODUCTION

77242113PSO3002 and 77242113PSO3004 are Phase 3, randomized, double-blind, active comparator- and placebo-controlled, parallel group, multicenter, interventional studies- in adults with moderate to severe plaque psoriasis.

These 2 global psoriasis phase 3 studies have identical study design (except for the sample size and sample size allocation ratio to treatment groups) and study drug dosing schedule for placebo, JNJ-77242113, and deucravacitinib participants through the end of the study. In addition, these 2 studies have identical participant eligibility criteria, objectives, endpoints (including co-primary endpoints, key secondary endpoints).

Because of the similarity of these 2 studies, this Statistical Analysis Plan (SAP) will cover both studies and will provide the definitions of analyses sets, derived variables and address the statistical methods for all planned analyses of efficacy, safety, pharmacokinetics (PK), pharmacodynamics (PD), Immunogenicity and health related quality of life in both 77242113PSO3002 and 77242113PSO3004 Clinical Study Reports (CSR). Unless specified otherwise, all the content in each section specified in this SAP applies to both studies.

1.1. Objectives, Endpoints and/or Estimands

Objectives and Endpoints

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 compared with placebo in participants with moderate to severe plaque psoriasis.	• IGA score of 0 or 1 and a ≥2 grade improvement from baseline at Week 16. • PASI 90 at Week 16.
Secondary	
Key Secondary • To further evaluate the general and special area psoriasis efficacy of JNJ-77242113 compared with placebo in participants with moderate to severe plaque psoriasis.	• IGA score of 0 at Week 16. • PASI 75 at Week 4. • PASI 90 at Week 8. • PASI 75 at Week 16. • PASI 100 at Week 16. • ss-IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16.
• To evaluate the effect of JNJ-77242113 compared with placebo on PROs in participants with moderate to severe plaque psoriasis.	• PSSD symptom score of 0 at Week 8. • PSSD symptom score of 0 at Week 16. • ≥4-point improvement from baseline in PSSD Itch score at Week 4. • ≥4-point improvement from baseline in PSSD Itch score at Week 16.

Objectives	Endpoints
• To evaluate the efficacy and effect of JNJ-77242113 compared with deucravacitinib on ClinROs and a PRO in participants with moderate to severe plaque psoriasis.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16 and Week 24, evaluated separately. • IGA score of 0 at Week 16 and Week 24, evaluated separately. • PASI 75 at Week 16 and Week 24, evaluated separately. • PASI 90 at Week 16 and Week 24, evaluated separately. • PASI 100 at Week 16 and Week 24, evaluated separately. • PSSD symptom score of 0 at Week 16.
Other Secondary	
• To assess the safety and tolerability of JNJ-77242113 compared with placebo and deucravacitinib in participants with moderate to severe plaque psoriasis.	• Frequency and type of AEs and SAEs.
• To further evaluate the efficacy of JNJ-77242113 compared with placebo and deucravacitinib in participants with moderate to severe plaque psoriasis.	• Change from baseline in BSA at Week 16. • Change from baseline in PASI at Week 16. • Percent change in PASI at Week 16.
• To further evaluate the special area psoriasis efficacy of JNJ-77242113 compared with placebo in participants with moderate to severe plaque psoriasis.	• sPGA-G score of 0 or 1 and a ≥2 grade improvement from baseline at Week 16. • hf-PGA score of 0 or 1 and a ≥2 grade improvement from baseline at Week 16. • Percent change from baseline in mNAPSI score at Week 16. • f-PGA score of 0 or 1 at Week 16.
• To further evaluate the effect of JNJ-77242113 compared with placebo on PROs in participants with moderate to severe plaque psoriasis.	• Change from baseline in PSSD symptom score at Week 16. • Change from baseline in PSSD sign score at Week 16. • PSSD sign score of 0 at Week 16. • GenPs-SFQ Item 2 score of 0 or 1 at Week 16. • DLQI score of 0 or 1 at Week 16. • Change from baseline in total DLQI score at Week 16. • Change from baseline in domain scores of the PROMIS-29 score at Week 16.

Objectives	Endpoints
• To further evaluate the effect of JNJ-77242113 compared with deucravacitinib on PROs in participants with moderate to severe plaque psoriasis.	• DLQI score of 0 or 1 at Week 16 and Week 24, evaluated separately. • PSSD symptom score of 0 at Week 24.
• To evaluate the efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis who switched from deucravacitinib to JNJ-77242113 treatment at Week 24.	• PASI 75 after Week 24, among PASI 75 non-responders to deucravacitinib at Week 24. • PASI 90 after Week 24, among PASI 90 non-responders to deucravacitinib at Week 24. • IGA score of 0 or 1 after Week 24, among participants in the deucravacitinib group with IGA score ≥2 at Week 24.
Exploratory	
• To further assess the safety and tolerability of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• Frequency and type of related AEs and AEs leading to discontinuation of study intervention. • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time.
• To further evaluate the psoriasis efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	Endpoints will be based on the following assessments: • IGA, PASI, BSA, ss-IGA, sPGA-G, hf-PGA, f-PGA, mNAPSI.
• To further evaluate the effect of JNJ-77242113 on PROs in participants with moderate to severe plaque psoriasis.	Endpoints will be based on the following assessments: • PSSD, DLQI, GenPs-SFQ, PROMIS-29, TSQM-E, EQ-5D-5L, PsA Pain assessment, PsA Disease Activity assessment.
• To evaluate the PK and immunogenicity of JNJ-77242113 and explore the exposure-response relationship of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• JNJ-77242113 PK parameters. • The relationship between PK parameters and efficacy. • The incidence of ADAs to JNJ-77242113.
• To explore biomarkers in participants with moderate to severe plaque psoriasis.	• Change from baseline in cellular and molecular biomarkers in skin and blood.

1.2. Study Design

Both studies are Phase 3, randomized, double-blind, active comparator- and placebo-controlled, parallel group, multicenter, interventional studies in adults with moderate to severe plaque psoriasis.

- For study 77242113PSO3002, a target of 750 participants will be randomized in a 2:1:2 ratio to JNJ-77242113 200 mg once daily, placebo, or deucravacitinib 6 mg once daily.

Randomization will be stratified by weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC).

- For study 77242113PSO3004, a target of 675 participants will be randomized in a 4:1:4 ratio to JNJ-77242113 200 mg once daily, placebo, or deucravacitinib 6 mg once daily. Randomization will be stratified by weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC).

Both studies include a 5-week screening period and a 16-week placebo-controlled period which will run concurrently with a 24-week active comparator-controlled period. At Week 16, participants randomized to placebo will switch to JNJ-77242113 200 mg once daily through Week 156. At Week 24, participants randomized to deucravacitinib will switch to JNJ-77242113 200 mg once daily through Week 156. All participants will have a 4-week safety follow-up period after discontinuation of study intervention or at the end of the treatment period. The total study duration for each participant is approximately 165 weeks.

Efficacy, safety, PK, immunogenicity, and biomarkers will be assessed according to the SoA (Section 1.3 of the protocol). Additionally, 3 optional substudies will be available for participants who consent (where local regulations permit). Sample collections for these substudies include a pharmacogenomic blood sample, skin biopsy, and photography collection.

The first DBL for both studies will occur when all participants complete Week 24 of the study. The final global DBL (Week 160 DBL) for both studies will occur when all participants complete the study. Additional DBLs may also occur at other times after Week 24 to support publications or regulatory submissions.

Participants will be randomized based on the allocation ratio of each study to 1 of the 3 treatment arms:

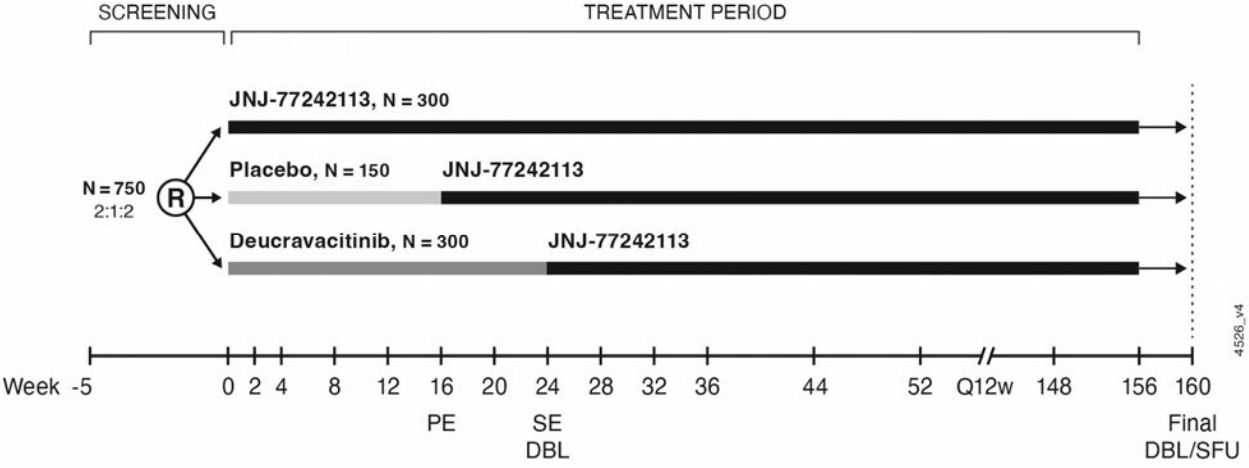
- **JNJ-77242113**: Participants in the JNJ-77242113 arm will receive JNJ-77242113 200 mg once daily from Week 0 through Week 156.
- **Placebo**: Participants in the placebo arm will receive matching placebo for JNJ-77242113 once daily from Week 0 through Week 16 and JNJ-77242113 200 mg once daily from Week 16 through Week 156.
- **Deucravacitinib**: Participants in the deucravacitinib arm will receive deucravacitinib 6 mg once daily from Week 0 to Week 24 and JNJ-77242113 200 mg once daily from Week 24 to Week 156.

Placebo will be administered in all treatment groups to maintain the blind until Week 24.

At the time of the Week 24 DBL, Sponsor will be unblinded to perform the analyses and plan for regulatory submission. Select Sponsor personnel will be unblinded to the individual treatment assignments, while others will only be unblinded to group level summaries. Details of the unblinding plan will be documented prior to Week 24 DBL and unblinding. The Sponsor, investigators, and participants will be unblinded after the last participant has completed the Week 52 visit.

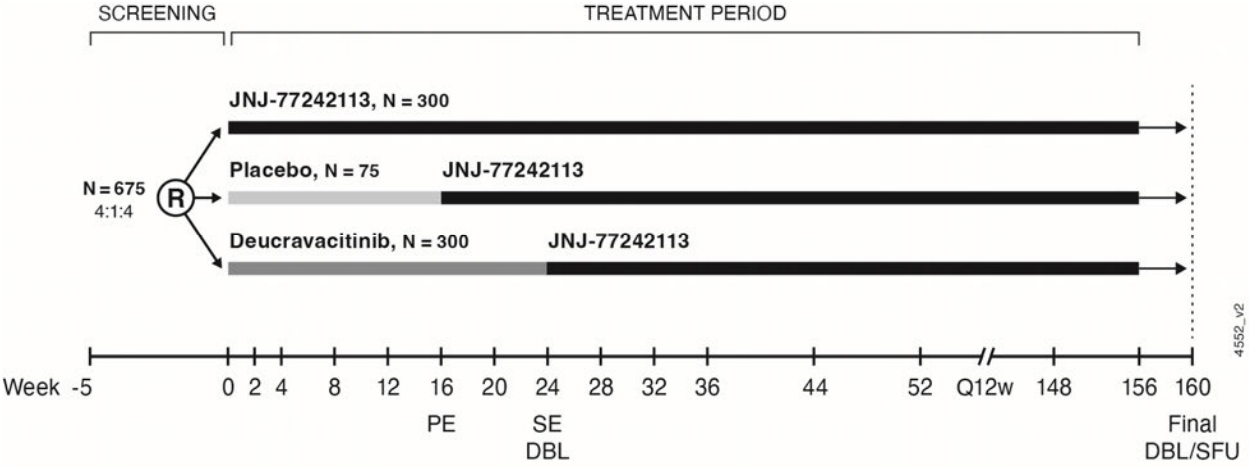
Diagrams of the study design for these two studies are provided in Figure 1 and Figure 2.

Figure 1 : Schematic Overview of the Study 77242113PSO3002



DBL=database lock; PE=primary endpoint; Q12w=every 12 weeks; R=randomization; SE=secondary endpoint; SFU=safety follow-up visit.

Figure 2: Schematic Overview of the Study 77242113PSO3004



DBL=database lock; PE=primary endpoint; Q12w=every 12 weeks; R=randomization; SE=secondary endpoint; SFU=safety follow-up visit.

2. STATISTICAL HYPOTHESES

The primary hypothesis is that JNJ-77242113 is superior to placebo in the treatment of participants with moderate to severe plaque psoriasis as assessed by the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16, and the proportion of participants who achieve a PASI 90 response at Week 16. If superiority for both endpoints is achieved, the study will be considered positive.

The null hypotheses are that there is no difference between JNJ-77242113 and placebo in either or both co-primary endpoints.

The select key secondary hypotheses related to JNJ-77242113 and deucravacitinib comparisons include the IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 and PASI 75 response at Week 16 (the co-primary endpoints from the deucravacitinib Phase 3 studies):

- JNJ-77242113 is superior to deucravacitinib in treatment of participants with moderate to severe plaque psoriasis as assessed by the proportion of participants who achieve an IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline at Week 16.
- JNJ-77242113 is superior to deucravacitinib in treatment of participants with moderate to severe plaque psoriasis as assessed by the proportion of participants who achieve an PASI 75 response at Week 16.
- JNJ-77242113 is superior to deucravacitinib in treatment of participants with moderate to severe plaque psoriasis as assessed by the proportion of participants who achieve an IGA score of cleared (0) at Week 24.
- JNJ-77242113 is superior to deucravacitinib in treatment of participants with moderate to severe plaque psoriasis as assessed by the proportion of participants who achieve a PASI 75 response at Week 24.

Overall, there are 2 co-primary endpoints:

- The proportion of subjects who achieve an IGA score of cleared (0) or minimal (1) at Week 16
- The proportion of subjects who achieve a PASI 90 response at Week 16

In addition, there are 21 key secondary endpoints including 25 key secondary analyses as summarized in Table 1.

Table 1: Key Secondary Endpoint Analyses

Analysis	Comparison	
	JNJ-77242113 vs Placebo	**JNJ-77242113 vs Deucravacitinib**
The proportion of participants with a PASI 75 response.	At Weeks 4 and 16	At Weeks 16 and 24[a]
The proportion of participants with a PASI 90 response.	At Week 8	At Weeks 16 and 24[b]
The proportion of participants with a PASI 100 response.	At Week 16	At Weeks 16 and 24[b]
The proportion of participants with an IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline.	NA (co-primary endpoint)	At Weeks 16 and 24[a]
The proportion of participants with an IGA score of cleared (0).	At Week 16	At Weeks 16 and 24[b]
The proportion of participants with an ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline among participants with a baseline ss-IGA score ≥2.	At Week 16	NA
The proportion of participants with a PSSD symptom score of 0 among participants with a baseline PSSD symptom score >0.	At Weeks 8 and 16	At Week 16[b]
The proportion of participants with a ≥4-point improvement in PSSD Itch score among participants with a baseline PSSD Itch score of ≥4 points.	At Weeks 4 and 16	NA

NA=not applicable.
[a] Non-inferiority tests with a non-inferiority margin of 12% will be performed before superiority tests.
[b] Only superiority tests will be performed.

2.1. Multiplicity Adjustment

Appropriate multiplicity adjustment procedure will be used to control the overall Type I error rate of α=0.05 (2-sided) for the primary and 21 key secondary endpoints. The testing procedure begins with the test of superiority of the JNJ-77242113 group compared with the placebo group in the co-primary endpoints. Key secondary endpoints will only be tested if both co-primary endpoints are significant. The testing strategy is devised based on the expected power and relative importance of the endpoints. If at least one of the coprimary endpoints is not significant (ie, p >0.05), all subsequent p-values in the testing hierarchy will be considered nominal. After testing of the co-primary endpoints, and if both p-values are ≤0.05, the testing procedure will continue with tests for the key secondary endpoints, which are grouped into different tiers as presented below by using the graphical approach with Type I error α-propagation.

In addition, for the key secondary analyses of the proportion of participants with a PASI 75 responses at Week 16 and Week 24, and the proportion of participants with an IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline at Week 16 and Week 24, non-inferiority test between JNJ-77242113 and deucravacitinib will be performed before the superiority test is performed respectively and will be part of the multiplicity adjustment procedure.

Tier 1 (comparisons between JNJ-77242113 and placebo at Week 16)

- IGA score of 0 at Week 16
- PASI 75 at Week 16

- PASI 100 at Week 16

Tier 2 (comparisons between JNJ-77242113 and deucravacitinib at Week 16, Non-inferiority)

- IGA score of 0 or 1 and ≥2-grade improvement from baseline at Week 16
- PASI 75 at Week 16

Tier 3 (comparisons between JNJ-77242113 and deucravacitinib at Week 16, Superiority)

- IGA score of 0 or 1 and ≥2-grade improvement from baseline at Week 16
- PASI 75 at Week 16

Tier 4 (comparisons between JNJ-77242113 and placebo at Week 16)

- ss-IGA score of 0 or 1 and ≥2-grade improvement from baseline at Week 16
- PSSD symptom score of 0 at Week 16
- ≥4 points improvement from baseline in PSSD itch score at Week 16

Tiers 5-9 (comparisons between JNJ-77242113 and deucravacitinib at Week 16 and Week 24)

Tier 5

- IGA score of 0 at Week 16
- PASI 90 at Week 16
- PASI 100 at Week 16

Tier 6

- IGA score of 0 at Week 24
- PASI 90 at Week 24
- PASI 100 at Week 24

Tier 7

- Non-inferiority: IGA score of 0 or 1 and ≥2-grade improvement from baseline at Week 24
- Non-inferiority: PASI 75 at Week 24

Tier 8

- Superiority: IGA score of 0 or 1 and ≥2-grade improvement from baseline at Week 24
- Superiority: PASI 75 at Week 24

Tier 9 (comparison between JNJ-77242113 and deucravacitinib at Week 16)

- PSSD symptom score of 0 at Week 16

Tiers 10-11 (comparisons between JNJ-77242113 and placebo early time points)

Tier 10

- PASI 75 at Week 4
- PASI 90 at Week 8

Tier 11

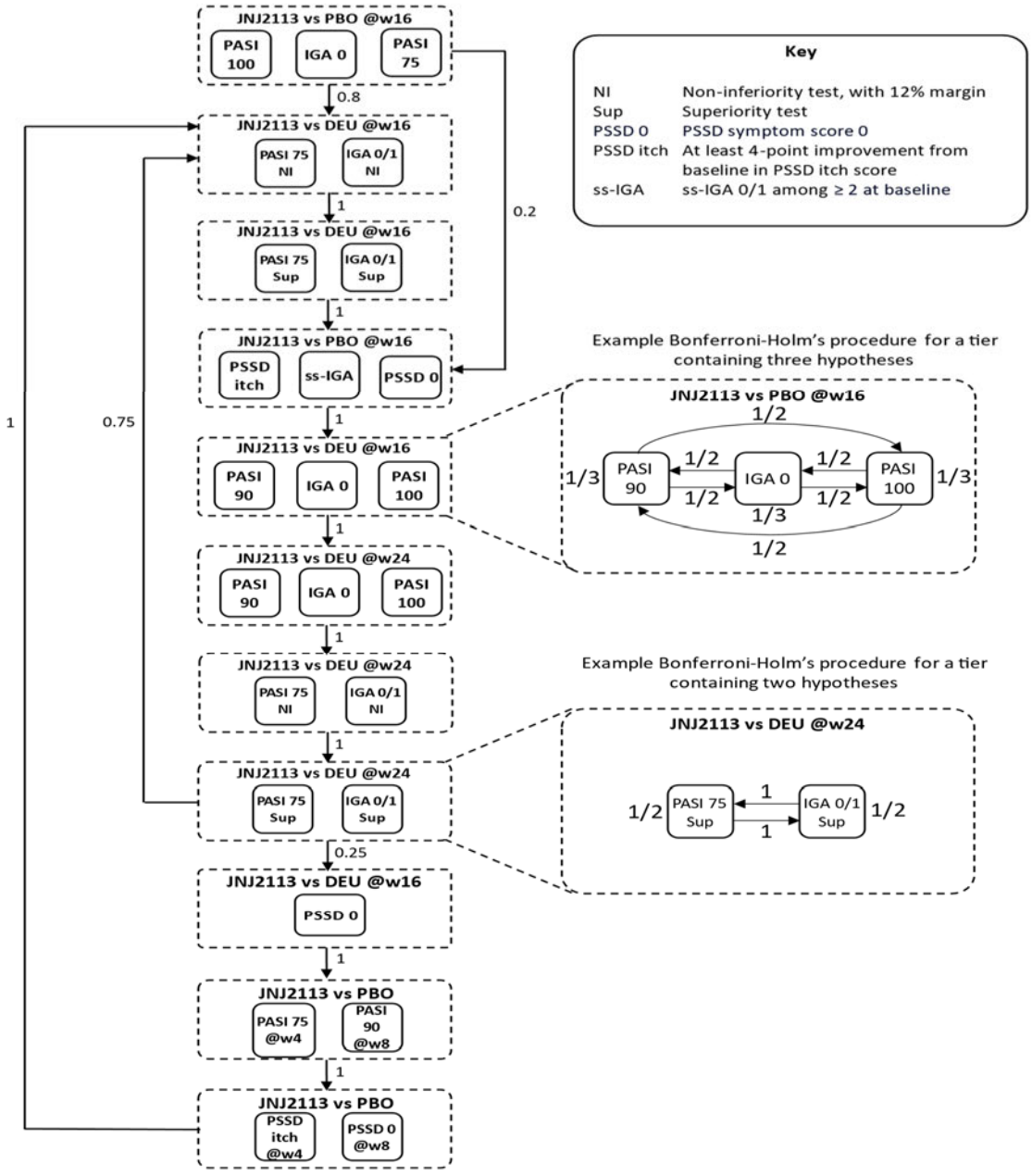
- PSSD symptom score of 0 at Week 8
- ≥4 points improvement from baseline in PSSD itch score at Week 4

When the co-primary endpoints are positive, a graphical approach as shown in Figure 3 will be applied to the key secondary endpoints.

The key secondary endpoint hypotheses are grouped into 11 tiers, and each tier will be tested in a pre-specified order as depicted in the below. Within each tier, the Bonferroni-Holm's (Holm, 1979) multiple comparison procedure will be used to test the endpoints in that tier with the assigned significance level. If any test within a tier is not significant, the other tests in the same tier could still be declared significant if they meet the Holm thresholds; however, the assigned alpha for this tier will not be passed down to subsequent tier(s). The assigned alpha for each tier can be passed to other tiers ONLY if all hypotheses within the tier are rejected based on Bonferroni-Holm's procedure. This testing procedure controls the overall Type I error rate at a 2-sided 0.05 significance level.

For all key secondary endpoint hypotheses specified in the graphical procedure of below, both adjusted and nominal p-values will be provided. Statistical significance will be claimed if the adjusted p-value is ≤0.05.

Figure 3: Testing procedure for the key secondary endpoints



No adjustments for multiple comparisons will be made for other secondary endpoints (Section 4.3.2) and exploratory endpoints (Section 4.4). Nominal p-values for other secondary and exploratory endpoints will be reported.

3. ANALYSIS SETS

For the efficacy analyses, the FAS will be used according to the participants' assigned treatment to which they were randomized, regardless of the treatment they actually received. The FAS will include all randomized participants.

Safety analyses will include all randomized participants who received at least 1 administration of study intervention, and participants will be analyzed based on the treatment they received, regardless of the treatment group to which they were assigned.

For purposes of analysis, the following analysis sets are defined Table 2:

Table 2: Definition of Analysis Sets

Population	Description
Enrolled	All participants who sign the ICF
Randomized	All participants who were randomized at Week 0 in the study.
Full Analysis Set (FAS)	All participants who were randomized at Week 0 in the study.
Per Protocol (PP)	The per protocol analysis set (PP) includes a subset of participants in the full analysis set (FAS) who were in general compliance with the protocol. Compliance is defined as participants in FAS and meet the following criteria: • Had a total BSA ≥10% at the screening and baseline visit. • Had a total PASI score ≥12 at the screening and baseline visit. • Had a total IGA score ≥3 at the screening and baseline visit. • Had an overall compliance of study treatment at least 80% and ≤120% prior to Week 16. Participants with intercurrent events 1 and 2 (Section 4.2.2.1.1) will be included in the per protocol analysis set.
Safety Analysis Set	All randomized participants who took at least 1 dose of study intervention.
PK Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113
Immunogenicity Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 and who had at least 1 sample obtained after the first dose of JNJ-77242113 for the detection of antibodies to JNJ-77242113.

4. STATISTICAL ANALYSES

4.1. General Considerations

Unless specified otherwise, efficacy data summaries will be provided by intervention group for the FAS. Data primarily will be summarized using descriptive statistics. Continuous variables will be summarized using the number of observations, mean, SD, median, interquartile range, minimum and maximum, as appropriate. Categorical values will be summarized using the number of observations and percentages as appropriate. In addition, graphical data displays (e.g., line plots) and participant listings may also be used to summarize/present the data.

For binary endpoints, treatment comparisons will be performed using a CMH test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC); in the situation of small sample size in a given stratum, pooling of the geographic region as appropriate may be applied. In case of rare events for binary endpoints, Fisher's exact test will be used. For

repeated measure continuous endpoints, treatment comparisons will be performed using a MMRM model. The MMRM will include treatment, baseline weight, geographic region, and baseline value, as explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. An unrestricted (UN) variance-covariance matrix for repeated measures within a participant will be used. If the model with unstructured covariance structure does not converge, alternative covariance structures will be tried in the following order, with the first structure that converges being used in the analysis: heterogeneous Toeplitz, standard Toeplitz, and autoregressive of order 1. The LS mean estimates and their corresponding 95% CI will be provided at each timepoint. The estimates of LS mean difference and 95% CIs between treatment groups will also be provided when appropriate.

Analysis of Covariance (ANCOVA) will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, baseline weight and geographic region. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference between treatment groups and 95% CIs will be provided.

In general, all statistical testing will be performed at a significance level of 0.05 (2-sided) unless otherwise specified. Multiplicity adjustment procedure will be used to control the overall Type I error rate of 0.05 (2-sided) for the primary and key secondary endpoints (Section 2.1). No adjustments for multiple comparisons will be made for other secondary endpoints and exploratory endpoints. Nominal p-values for other secondary and exploratory endpoints will be reported but should not be used to infer statistical significance.

The baseline measurement for efficacy endpoints is defined as the closest measurement taken prior to or on the first study agent administration date. The baseline measurement for other endpoints including safety, PK and immunogenicity is defined as the closest measurement taken prior to the time of the first study agent administration.

4.1.1. Visit Windows

Unless otherwise specified, nominal visits will be used for all by visit analyses. The study visits scheduled after randomization should occur at the time delineated in the Schedule of Activities of the protocol.

4.1.2. Reference Date, Study Day and Relative Day

The Reference Date is the date of the first study agent administration. If the date of the first study agent administration is missing or the first study agent administration is not done, then the Reference Date equals the corresponding visit date (eg, Week 0 visit date). If the corresponding visit date is also missing, then the Reference Date equals the randomization date. Study day is defined as the number of days from the study reference date to the event/visit date. It will be calculated as follows:

- If the event/assessment occurs on or after the reference date, then study day = event/assessment date – reference date + 1.

- If the event/assessment occurs before the reference date, then study day = event/assessment date – reference date.

Hence, the day of reference date is Study Day 1; the previous day is Study Day -1.

4.1.3. Change From Baseline

The change and percentage change from baseline are calculated using the formula:

$$Change = Post\ Baseline\ Value - Baseline\ Value$$

$$Percentage\ change = \frac{(Post\ Baseline\ Value - Baseline\ Value)}{Baseline\ Value}\ X\ 100$$

If a higher score indicates more severe disease in efficacy assessments, then a negative change indicates an improvement, and a positive change indicates worsening.

4.2. Co-Primary Endpoint(s)/Estimand(s) Analysis

4.2.1. Definition of Endpoints

The following co-primary efficacy endpoints are defined in the variable attribute of the co-primary estimands 1a and 1b.

- Achieving PASI 90 response at Week 16
- Achieving IGA 0 or 1 response at Week 16

4.2.1.1. Psoriasis Area and Severity Index

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy. In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities which account for 10%, 30%, 20%, and 40% of the total BSA, respectively. Each of these areas is assessed separately for erythema, induration, and scaling, which are each rated on a scale of 0 to 4; and the area of involvement for psoriatic lesion is rated on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The PASI produces a numeric score that can range from 0 (no psoriasis) to 72. A higher score indicates more severe disease.

Meeting the PASI 90 criteria: defined as having at least a 90% improvement from baseline in PASI total score.

4.2.1.2. Investigator's Global Assessment

The IGA documents the physician's assessment of the participant's psoriasis status according to the following categories: induration, scaling, and erythema. The participant's psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4).

Meeting the IGA 0 or 1 criteria: defined as achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline.

4.2.2. Estimands

Primary Study Objective: To evaluate the efficacy of JNJ-77242113 compared to placebo at Week 16 in participants with moderate to severe plaque psoriasis.

Clinical Questions of Interest:

For an adult patient with moderate to severe psoriasis, what would be the expected effect of being assigned JNJ-77242113 on the likelihood of experiencing a treatment response at Week 16?

4.2.2.1. Co-Primary Estimands (1a and 1b)

The co-primary estimands, aligned with the above primary objective and clinical question of interest, provide precise descriptions of the treatment effect of interest that are defined by the following 5 attributes. Both co-primary estimands have the same attributes, except for the variable that corresponds to each co-primary endpoint.

4.2.2.1.1. Co-Primary Estimand 1a

- Treatment condition of interest vs alternative treatment condition:
  - Experimental: JNJ-77242113 200 mg QD
  - Placebo
- **Population:** Adult patients with moderate to severe psoriasis
- **Variable:** Achieving a PASI 90 response at Week 16, where a PASI 90 responder is defined as a patient meeting the PASI 90 criteria at Week 16 and not experiencing either ICE 1 or 2
- Intercurrent Events (ICEs) and Corresponding Strategies (Refer to Table 3):

Table 3: ICEs and Their Corresponding Strategies

ICEs	Strategy for Addressing Intercurrent Events
1. Discontinuation of treatment due to lack of efficacy, or due to an AE of worsening of psoriasis. 2. Initiation of other medication or therapy that could improve psoriasis (see Appendix 7).	**Composite Strategy:** The occurrence of these ICEs is captured in the variable definition as patients with these ICEs are considered non-responders.
3. Discontinuation of treatment for other reasons than ICE 1	**Treatment Policy:** Strategy targeting the effect of treatment assignment, regardless of the occurrence of this ICE.

Note: For patients experiencing multiple ICEs, ICE 2 will override ICE 3 and the composite strategy will be applied.

- **Population Level Summary:** Difference in the proportions between JNJ-77242113 and placebo.

4.2.2.1.2. Co-Primary Estimand 1b

The estimand 1b has the same attributes as in estimand 1a, except for the variable definition:

Achieving IGA 0 or 1 response at Week 16, where an IGA 0 or 1 responder is defined as a patient meeting the IGA 0 or 1 criteria at Week 16 and not experiencing either ICE 1 or 2.

4.2.2.2. Supplementary Estimands Sup1a and Sup1b (Treatment Policy Estimands):

In these supplementary estimands, the components that change from the definition of the co-primary estimands are:

Variable: Achieving a response at Week 16 based on a scale will be the same as meeting the defined efficacy criteria, without accounting for ICEs 1 and 2 in the response definition of co-primary estimand's Variable attribute.

Treatment Policy Strategy: Strategy targeting the effect of treatment assignment, regardless of the occurrence of ICEs.

4.2.3. Analysis Methods

4.2.3.1. Main Analytical Approach

Analysis for the co-primary endpoints will be based on FAS, including data from all randomized participants. Participants will be analyzed based on their assigned intervention group, regardless of the actual intervention received.

According to the co-primary estimands 1a and 1b, participants with ICEs 1-2 before Week 16 will be considered as non-responders in co-primary endpoints at Week 16. For participants with ICE 3, observed data after this ICE will be utilized in the analysis. For participants experiencing multiple ICEs, an ICE2 will override an ICE 3. After accounting for the ICEs for the primary estimands, participants with missing value for the co-primary endpoints at Week 16 will be considered as non-responders.

In the primary analyses, the proportions of PASI 90 responders and IGA 0 or 1 responders at Week 16 will be summarized by treatment group. To address the primary objective, P-values based on the Cochran-Mantel-Haenszel chi-square statistic stratified by baseline weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC) at a 2-sided significance level of 0.05 will be reported. In addition, difference in response rates between JNJ-77242113 group and the placebo group at Week 16 and their corresponding 95% CIs (using Miettinen-Nurminen method [Miettinen and Nurminen 1985]) will be calculated adjusting for baseline weight category (≤90 kg, >90 kg) and geographic region using Mantel-Haenszel weight.

The study will be considered positive if the JNJ-77242113 group is significantly different from the placebo group for both co-primary endpoints. If at least one of the comparisons is not significant at the 2-sided α-level of 0.05, the co-primary endpoints will be considered not significant.

In addition, the proportions of PASI 90 responders and IGA 0 or 1 responders at Week 16 will be summarized by region, country, and investigator site. This analysis will be descriptive and statistical testing will not be applied. To evaluate the consistency of the efficacy, subgroup analyses of the co-primary endpoints based on demographics, baseline disease characteristics and previous psoriasis medications and therapies will be performed. Detailed subgroup analyses for the coprimary endpoints are specified in Section 4.6.6.

4.2.3.2. Sensitivity Analyses

To address the robustness of the primary endpoint analysis results, two sensitivity analyses will be performed to assess missing data assumptions.

4.2.3.2.1. Sensitivity Analysis 1: Multiple Imputation

Under co-primary estimands, a sensitivity analysis using multiple imputation will be performed for each co-primary endpoint. In this sensitivity analysis, after accounting for the ICEs, missing data will then be imputed using multiple imputations (MI) by fully conditional specification (FCS).

More specifically, the missing PASI 90 responses will be imputed with FCS logistic regression including treatment group, baseline PASI score, PASI 90 response status through Week 16, baseline weight category and geographic region in the model with seed = 456 and 500 imputations.

A CMH test stratified by baseline weight category and geographic region will be used to obtain the CMH statistic for each imputed dataset.

The values of the general association test statistics from the CMH test for each imputed dataset will be transformed using the Wilson-Hilferty transformation (Wilson and Hilferty, 1931) to create a more normal distributed statistic:

$$Z = \frac{(CMH)^{(1/3)} - 7/9}{(2/9)^{(1/2)}}.$$

The resulting transformed values will be combined using SAS PROC MIANALYZE to obtain an overall p-value for the CMH test.

The common risk differences and 95% CIs in co-primary endpoints will be calculated using Mantel-Haenszel stratum weights and Sato variance estimator (Sato, 1989) adjusting for baseline weight category, and geographic region for each imputed dataset. The resulting values will be combined to obtain an overall risk difference and 95% CI.

A similar approach will be applied to the endpoint of proportion of participants achieving an IGA 0 or 1 response at Week 16 with FCS logistic regression including treatment group, baseline IGA score, IGA 0 or 1 response status through Week 16, baseline weight category (≤90 kg, >90 kg) and geographic region in the model with seed = 456 and 500 imputations.

4.2.3.2.2. Sensitivity Analysis 2: Tipping Point Based on Multiple Imputation with Bernoulli Draws

Under the co-primary estimands, another sensitivity analysis will also be performed using a tipping point analysis with Bernoulli draws to impute missing PASI 90 and IGA 0 or 1 response status at Week 16 after intercurrent events are accounted for. This tipping point analysis involves the following distinct steps:

1. Some *p* will be assumed for each treatment group's response rate, which could vary by treatment group, to impute the response status (Yes/No) for participants with a missing response based on a Bernoulli distribution. This will be repeated 200 times with seed = 20240719 to generate 200 multiple imputations.
2. The common risk difference between JNJ-77242113 and placebo will be calculated using Mantel-Haenszel stratum weights adjusting for baseline weight category and geographic region for each imputed dataset. The resulting values will be combined to obtain an overall risk difference.
3. The results (with a Wilson-Hilferty transformation) from the imputed data sets will then be combined to produce p-values based on Rubin's rules.

The analysis will be repeated for a range of values for *p* (for example, 0% to 100% in increments of 10% independently, for both the placebo and the JNJ-77242113 groups independently). This tipping point sensitivity analysis will allow for assumptions about the response rates in the two arms to vary independently; furthermore, it will include scenarios where imputed missing values on JNJ-77242113 group have worse outcomes than missing values on the placebo group.

4.2.3.3. Supplementary Analysis Sup1a and Sup1b (Treatment Policy Estimand)

The co-primary endpoints will also be analyzed utilizing the treatment policy estimand. For participants who experience an ICE through Week 16, the analysis will be performed using observed data regardless of intercurrent events. Participants with missing data will be imputed as non-responders. The same CMH test as for the primary estimands will be used.

4.2.3.4. Per Protocol Analysis

The co-primary efficacy endpoints will be evaluated for comparisons between the JNJ-77242113 group and the placebo group in the PP population based on the primary estimand. The same data handling rules and analysis method specified in Section 4.2.3.1 will be applied.

4.3. Secondary Endpoints/Estimands Analysis

4.3.1. Key Secondary Endpoints

The key secondary endpoints of both the 77242113PSO3002 and 77242113PSO3004 studies are listed below:

Set 1: The key secondary endpoints in Set 1 will be based on comparisons between the JNJ-77242113 group and the placebo group:

- IGA score of cleared (0) at Week 16

- PASI 75 response at Week 4
- PASI 90 response at Week 8
- PASI 75 response at Week 16
- PASI 100 response at Week 16
- ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline at Week 16
- PSSD symptom score of 0 at Week 8
- PSSD symptom score of 0 at Week 16
- At least 4-point improvement in PSSD Itch score at Week 4
- At least 4-point improvement in PSSD Itch score at Week 16

Set 2: The key secondary endpoints in Set 2 will be based on comparisons between the JNJ-77242113 group and the deucravacitinib group:

- IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline at Week 16
- IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline at Week 24
- IGA score of cleared (0) at Week 16
- IGA score of cleared (0) at Week 24
- PASI 75 response at Week 16
- PASI 75 response at Week 24
- PASI 90 response at Week 16
- PASI 90 response at Week 24
- PASI 100 response at Week 16
- PASI 100 response at Week 24
- PSSD symptom score of 0 at Week 16

The comparisons of clinical endpoints in IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline and PASI 75 response between JNJ-77242113 versus deucravacitinib at Week 16 and Week 24 in set 2 above will be tested for non-inferiority first, and if non-inferiority is established, then superiority will be tested. Other key secondary efficacy endpoints for the comparisons between JNJ-77242113 and deucravacitinib (eg, PASI 90, PASI 100, PSSD symptom score of 0 at Week 16) will only be tested for superiority (Section 2.1).

4.3.1.1. Definition of Endpoint(s)

4.3.1.1.1. Investigator's Global Assessment

Refer to Section 4.2.1.2 for details.

Meeting the IGA 0 criteria: defined as having an IGA score of cleared (0).

4.3.1.1.2. Psoriasis Area and Severity Index

Refer to Section 4.2.1.1 for details.

Meeting the PASI 75 criteria: defined as having ≥75% improvement in PASI from baseline.

Meeting the PASI 100 criteria: defined as having 100% improvement in PASI from baseline.

4.3.1.1.3. Psoriasis Symptom and Sign Diary

The PSSD includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit. There are two versions of the PSSD: a 24-hour recall version that asks the participant to answer the questions thinking about the last 24 hours and a 7-day recall version asking the participant to answer the questions thinking about the last 7 days. The 24-hour recall version will be used through Week 24 while the 7-day recall version will be used after Week 24. Both versions of the PSSD are self-administered PRO instruments and include 11 items in total, with 5 items covering symptoms (itch, pain, stinging, burning and skin tightness) and 6 items covering participant-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness and bleeding). A 0 to 10 numerical rating scales for severity is used. For both the 24-hour and 7-day recall versions, two subscores will be derived each ranging from 0 to 100: the psoriasis symptom score and the psoriasis sign score. Additionally, for both versions, an item-level score will be derived for each PSSD item, ranging from 0 to 10. For all scores, a higher score indicates more severe disease.

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

PSSD Item Score (0-10)

a. PSSD 24hr recall, each individual item score over seven days is averaged into a weekly item score (i.e. 7 days [from day -7 to -1] prior to a visit).

b. PSSD 7-day recall, each individual item response is used as the score.

Symptom Score (0-100)

a. Symptom score includes the following items: itch (Q1), skin tightness (Q4), burning (Q9), stinging (Q10), and pain (Q11).

b. PSSD 24hr recall: Compute the average of the 5 weekly symptom item scores when at least 3 items are available (≥50% of 5 items). Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

c. PSSD 7-day recall: Average symptom items when at least 3 items (≥50% of 5 items) on this scale are answered. Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

Sign Score (0-100)

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

b. PSSD 24hr recall: Compute the average of the 6 weekly sign item scores when at least 3 items are available (≥50% of 6 items). Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

c. PSSD 7-day recall: Average sign items when at least 3 items (≥50% of 6 items) on this scale are answered. Multiply the average by 10 to convert into 0-100 scoring (0-least severe, 100-most severe).

For the PSSD 24-hr recall, at least four non-missing days of assessments out of 7 days (either consecutive or nonconsecutive) prior to a specific visit are necessary to derive a weekly score for that visit. For select time points (i.e., baseline, Week 4, Week 8, and Week 16), if there are less than 4 non-missing days of assessments in the 7-day window, the most recent 4 non-missing days of assessments in the 10-day window prior to that specific visit will be used. If there are less than 4 non-missing days of assessments in the 10-day window for baseline, Week 4, Week 8, and Week 16, or 7-day window for other visits (weeks 2, 12, 20, and 24), data are considered missing for that visit.

Meeting the PSSD symptom score of 0 criteria: defined as having a PSSD symptom score of 0 among participants with a baseline PSSD symptom score >0.

Meeting the PSSD itch ≥4 points improvement criteria: defined as having at least 4 points improvement from baseline in PSSD itch score and with a baseline PSSD Itch score ≥4.

4.3.1.1.4. Scalp Specific Investigator Global Assessment

The ss-IGA instrument is used to evaluate the disease severity of scalp psoriasis. The lesions are assessed in terms of the clinical signs of redness, thickness, and scaliness which are scored as: absence of disease (0), very mild disease (1), mild disease (2), moderate disease (3), and severe disease (4).

Meeting the ss-IGA score of 0 or 1 criteria: defined as having an ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline.

4.3.1.2. Estimands

4.3.1.2.1. Main Estimands for the Key Secondary Endpoints in Set 1 (Estimands Sec1-Sec10)

The main estimands for key secondary endpoints in **Set 1** have the same attributes as co-primary estimands, except for attributes of variable and population defined in Table 4.

Table 4: List of Variables and Population for the Main Estimands for the Key Secondary Endpoints in Set 1

Estimands	Variable Achieving a response based on:	Population
Sec 1	IGA score of 0 response at Week 16	Same population as the primary estimand specified in Section 4.2.2.1
Sec 2	PASI 75 response at Week 4	
Sec 3	PASI 90 response at Week 8	
Sec 4	PASI 75 response at Week 16	
Sec 5	PASI 100 response at Week 16	
Sec 6	ss-IGA score of 0 or 1 and a ≥2 grade improvement from baseline response at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline ss-IGA score ≥2
Sec 7	PSSD symptom score of 0 response at Week 8	Patients with moderate to severe plaque psoriasis and with a baseline PSSD symptom score > 0
Sec 8	PSSD symptom score of 0 response at Week 16	
Sec 9	≥4-point improvement from baseline in PSSD itch score at Week 4	Patients with moderate to severe plaque psoriasis and with a baseline PSSD itch score ≥4
Sec 10	≥4-point improvement from baseline in PSSD itch score at Week 16	

As in the co-primary estimands, achieving a response based on a scale is defined as meeting the efficacy criteria based on that scale and not experiencing ICEs 1 and 2.

4.3.1.2.2. Main Estimands for the Key Secondary Endpoints in Set 2 (Estimands Sec11-Sec21)

The main estimands for key secondary endpoints in **Set 2** have the same attributes as co-primary estimands, except for attributes of treatment, variable, and population defined below.

- **Treatment condition of interest vs alternative treatment condition:**
  - Experimental: JNJ-77242113 200 mg QD
  - Deucravacitinib 6 mg QD
- **Variable and population**: Refers to Table 5

Table 5: List of Variables and Population for the Main Estimands for the Key Secondary Endpoints in Set 2

Estimands	Variable	Population
Sec 11	IGA score of 0 or 1 and a ≥2 grade improvement from baseline response at Week 16[a,b]	Same population as the primary estimand specified in Section 4.2.2.1.
Sec 12	IGA score of 0 or 1 and a ≥2 grade improvement from baseline response at Week 24[a]	
Sec 13	IGA score of 0 response at Week 16[b]	
Sec 14	IGA score of 0 response at Week 24	
Sec 15	PASI 75 response at Week 16[a,b]	
Sec 16	PASI 75 response at Week 24[a]	
Sec 17	PASI 90 response at Week 16[b]	
Sec 18	PASI 90 response at Week 24	
Sec 19	PASI 100 response at Week 16[b]	
Sec 20	PASI 100 response at Week 24	
Sec 21	PSSD symptom score of 0 response at Week 16[a,b]	Patients with moderate to severe plaque psoriasis and with a baseline PSSD symptom score >0

[a] Non-inferiority tests with a non-inferiority margin of 12% will be performed before superiority tests.
[b] Comparisons between deucravacitinib and placebo will be performed to demonstrate assay sensitivity.

As in the co-primary estimands, achieving a response based on a scale is defined as meeting the efficacy criteria based on that scale and not experiencing ICEs 1 and 2.

4.3.1.2.3. Supplementary Estimands for Key Secondary Endpoints

The supplementary estimands have the same components as the main estimands corresponding to set 1 and set 2 respectively for key secondary endpoints, except for the strategies used for ICEs and not counting ICEs as non-responders in the Variable definition. The same Treatment Policy estimands (Section 4.2.2.2) for the co-primary estimands will be used for the following selected key secondary endpoints. Supplementary estimands are not planned for the key secondary endpoints at early timepoints (i.e., Week 4, Week 8) due to the anticipated limited number of ICEs.

JNJ-77242113 vs Placebo

- IGA score of 0 at Week 16
- PASI 75 response at Week 16
- PASI 100 response at Week 16
- ss-IGA score of 0 or 1 and a ≥2 grade improvement from baseline at Week 16 among participants with a baseline ss-IGA score ≥2
- PSSD symptom score of 0 at Week 16 with a baseline PSSD symptom score >0

- ≥4 points improvement from baseline in PSSD itch score at Week 16 among participants with a baseline PSSD itch score ≥4

JNJ-77242113 vs Deucravacitinib

- IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline at Week 16
- IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline at Week 24
- IGA score of cleared (0) at Week 16
- IGA score of cleared (0) at Week 24
- PASI 75 response at Week 16
- PASI 75 response at Week 24
- PASI 90 response at Week 16
- PASI 90 response at Week 24
- PASI 100 response at Week 16
- PASI 100 response at Week 24
- PSSD symptom score of 0 at Week 16

4.3.1.3. Analysis Method

4.3.1.3.1. Analytical Approach for Main Estimands

The efficacy analyses for key secondary endpoints will be based on the FAS by intervention group. In order to control the overall Type I error rate (α=0.05), multiplicity adjustment will be applied to the analyses of the co-primary endpoints and key secondary endpoints listed above. The detailed methods of analysis and approach to control the Type I error for multiplicity is specified in Section 2.1.

Since all key secondary endpoints are binary endpoints the analysis approach of these key secondary endpoints for superiority testing is the same as the analysis method specified in Section 4.2.3.1 for the co-primary endpoints. More specifically, p-values based on the Cochran-Mantel-Haenszel chi-square statistic stratified by baseline weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC) at a 2-sided significance level of 0.05 will be reported. In addition, difference in response rates between each of the active treatment groups (JNJ-77242113 or deucravacitinib) and the placebo group and between the JNJ-77242113 and deucravacitinib groups and their corresponding 95% CIs (using Miettinen-Nurminen method) will be calculated adjusting for baseline weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC) using Mantel-Haenszel weight.

For the key secondary endpoints with comparisons between JNJ-77242113 and deucravacitinib at Week 16, p-values will also be provided for the comparison between the deucravacitinib and placebo groups to demonstrate assay sensitivity.

Non-inferiority Comparison between JNJ-77242113 and Deucravacitinib

For the following 4 key secondary analyses, non-inferiority will be assessed before superiority; and superiority will only be assessed once non-inferiority is established.

- Proportion of participants achieving PASI 75 (≥ 75% improvement from baseline in PASI) at Week 16 and at Week 24
- Proportion of participants achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement at Week 16 and Week 24

The non-inferiority margin for these comparisons is predefined as 12%. This margin is determined based on the historical data from placebo-controlled deucravacitinib Phase 3 studies (Armstrong 2023). Based on the meta-analyses of these 2 Phase 3 studies, the lower bound of the 95% CI for the treatment effect on the IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and PASI 75 response at Week 16 between the deucravacitinib and placebo groups was approximately 38.8% and 40.0%, respectively. Therefore, a non-inferiority margin of 12% is chosen to preserve approximately 70% of deucravacitinib benefit. IGA score of 0 or 1 and PASI 75 at Week 16 were selected as these 2 endpoints were used as co-primary endpoints in the Phase 3 studies constituting the basis for global regulatory approval of deucravacitinib.

A one-sided (α=0.025) Z test using MH weights adjusting for baseline weight category (≤90 kg, >90 kg) and geographic region (AMER, EU, APAC) will be conducted (Miettinen and Nurminen 1985). The 95% confidence interval for treatment difference between the JNJ-77242113 and deucravacitinib treatment groups (using Miettinen-Nurminen method) adjusting for baseline weight category and geographic region using Mantel-Haenszel weight will be provided. The designated non-inferiority margin is 12%. That is the lower bound of the 2-sided 95% confidence interval of P1 – P2 excluding -12% would constitute demonstration of non-inferiority, where P1 and P2 are the proportions of participants achieving the corresponding endpoints at Week 16 and Week 24 in the JNJ-77242113 and deucravacitinib groups, respectively.

4.3.1.3.2. Sensitivity Analysis for Select key Secondary Analysis

Under the co-primary estimands, the two similar sensitivity analyses specified in Section 4.2.3.2 for the co-primary endpoints will also be performed for the following 3 key secondary endpoints:

JNJ-77242113 vs deucravacitinib:

- Proportion of participants achieving PASI 75 at Week 16
- Proportion of participants achieving PASI 90 at Week 16
- Proportion of participants achieving IGA score of 0 or 1 and at least 2-grade improvement at Week 16

4.3.1.3.3. Supplementary Analyses

Similar to the co-primary supplementary analyses, the methods specified in Section 4.2.3.3 (Treatment Policy Estimand) will be applied to the select key secondary binary endpoints.

4.3.1.3.4. Subgroup Analysis

To evaluate the consistency of the efficacy, subgroup analyses of the following selected key secondary endpoints based on demographics, baseline disease characteristics and previous psoriasis medications and therapies will be performed (Section 4.6.6).

JNJ-77242113 vs placebo:

- Proportion of participants achieving PASI 75 at Week 16
- Proportion of participants achieving PASI 100 at Week 16
- Proportion of participants achieving IGA score of 0 at Week 16

JNJ-77242113 vs deucravacitinib:

- Proportion of participants achieving PASI 75 at Week 16 and Week 24
- Proportion of participants achieving PASI 90 at Week 16 and Week 24
- Proportion of participants achieving PASI 100 at Week 16 and Week 24
- Proportion of participants achieving IGA score of cleared (0) or minimal (1) with at least 2-grade improvement at Week 16 and Week 24
- Proportion of participants achieving IGA score of 0 at Week 16 and Week 24

In addition, summary of the proportion of participants achieving PASI 75, PASI 90, and IGA 0 or 1 responses at Week 16 and Week 24 (JNJ-77242113 and deucravacitinib) will be performed for each region, country and investigator site by treatment group. This analysis will be descriptive and statistical testing will not be applied.

4.3.2. Other Secondary Endpoint Analysis

The other secondary endpoints are listed below:

Set 1: The other secondary endpoints in Set 1 will be based on comparisons between the JNJ-77242113 group and the placebo group:

- Change from baseline in BSA
- Change from baseline in PASI at Week 16
- Percent change from baseline in PASI at Week 16
- sPGA-G score of 0 or 1 and a ≥2grade improvement from baseline at Week 16
- hf-PGA score of 0 or 1 and a ≥2grade improvement from baseline at Week 16
- Percent change from baseline in mNAPSI score at Week 16
- f-PGA score of 0 or 1 at Week 16
- Change from baseline in PSSD symptom score at Week 16
- Change from baseline in PSSD sign score at Week 16
- PSSD sign score of 0 at Week 16
- GenPs-SFQ Item 2 score of 0 or 1 at Week 16

- DLQI score of 0 or 1 at Week 16
- Change from baseline in total DLQI score at Week 16
- Change from baseline in each of the 8 PROMIS-29 individual domain scores (depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, ability to participate in social roles and activities, and pain intensity), physical component score (PCS) and mental component score (MCS) score of the PROMIS-29 at Week 16

Set 2: The other secondary endpoints in Set 2 will be based on comparisons between the JNJ-77242113 group and the deucravacitinib group:

- Change from baseline in BSA at Week 16
- Change from baseline in PASI at Week 16
- Percent change from baseline in PASI at Week 16
- DLQI score of 0 or 1 at Week 16
- DLQI score of 0 or 1 at Week 24
- PSSD symptom score of 0 at Week 24

4.3.2.1. Definition of Endpoints

4.3.2.1.1. Psoriasis Area and Severity Index

Refer to Section 4.2.1.1 for details.

4.3.2.1.2. Body Surface Area (BSA)

Body surface area is a commonly used measure of involvement of skin disease. It is defined as the percentage of surface area of the body involved with the condition being assessed, (i.e., plaque psoriasis). The handprint method for assessing BSA will be used, where the surface area of the participant's hand including the palm and all 5 digits is used as a guide to estimate 1% BSA.

4.3.2.1.3. Dermatology Life Quality Index Score

The Dermatology Life Quality Index (DLQI) is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a participant's quality of life. It is a 10-item questionnaire that in addition to evaluating overall quality of life, can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment.

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. A higher score indicates more severe disease. A score of ≤1 indicates no effect at all of disease on participant's health related quality of life, and an improvement of 5 points or more in total DLQI score is considered clinically meaningful improvement.

For a partially answered questionnaire (e.g., not all ten questions in a questionnaire were available):

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

Meeting the DLQI 0 or 1 criteria: defined as having a DLQI score of 0 or 1.

4.3.2.1.4. Psoriasis Symptom and Sign Diary

Refer to Section 4.3.1.1.3 for details.

Meeting the PSSD sign score of 0 criteria: defined as having a PSSD sign score of 0 indicates absence of psoriasis symptoms.

4.3.2.1.5. Patient-Reported Outcomes Measurement Information System-29 v2.1 (PROMIS-29)

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

The total raw score will be converted into a T-score for each participant based on the table in Appendix 9. The T-score rescales the raw score into a standardized score with a mean of 50 and an SD of 10. The standardized T-score is reported as the final score for each participant. Pain Intensity is presented as raw responses (0-10). For PROMIS domains of Depression, Anxiety, Physical Function, Pain Interference, Fatigue, a score of 50 is the average for the United States general population with a standard deviation of 10, because testing was performed on a large sample of the general population. However, the other two domains (Ability to Participate in Social Roles and Activities and Sleep Disturbance) were not centered in a national sample. For these two domains, a score of 50 represents the average of the calibration sample which was generally more enriched for chronic illness, and a score of 50 likely represents somewhat sicker people than the general population. A higher PROMIS T-score represents more of the concept being measured. For negatively-worded concepts like Anxiety, a T-score of 60 is one SD worse than average. By comparison, an Anxiety T-score of 40 is one SD better than average. However, for positively-worded concepts like Physical Function, a T-score of 60 is better than average while a T-score of 40 is better. The physical component score (PCS) and mental component score (MCS) will be derived from the domain scores. Change from baseline in PROMIS-29 domain score is defined as the domain score minus the participant's baseline domain score, where a negative change indicates an improvement for the following domains:

- Anxiety
- Depression

- Fatigue
- Sleep disturbance
- Pain interference

and a positive change indicates an improvement for the following domains:

- Physical function
- Ability to participate in social roles and activities
- Physical health component score
- Mental health component score

4.3.2.1.6. Static Physician's Global Assessment of Genitalia

The sPGA-G is a 6-point scale to assess the severity of genital psoriasis at a given time point (Merola 2017). The sPGA-G evaluates erythema, plaque elevation, and scale of genital psoriatic lesions. The severity of genital psoriasis is assessed as clear (0), minimal (1), mild (2), moderate (3), severe (4), and very severe (5). sPGA-G data is collected only for participants with active genital psoriasis at Week 0.

Meeting the sPGA-G 0 or 1 criteria: defined as having an sPGA-G score of clear (0) or minimal (1) and a ≥2- grade improvement from baseline.

4.3.2.1.7. Modified Nail Psoriasis Severity Index

The mNAPSI is an index used for assessing and grading the severity of nail psoriasis. Each of the participant's ten fingernails are evaluated on 7 features. The first three features are each scored from 0 to 3 in severity and are (1) onycholysis and oil-drop dyschromia, (2) pitting, and (3) nail plate crumbling. The next four features are each scored 0 absent or 1 present, and are (1) leukonychia, (2) splinter hemorrhages, (3) nail bed hyperkeratosis, and (4) red spots in the lunula. The score ranges from 0-13 per nail, and 0-130 for all fingernails.

4.3.2.1.8. Fingernail Physician's Global Assessment

The f-PGA is used to evaluate the current status of a participant's fingernail psoriasis on a scale of 0 to 4: clear (0), minimal (1), mild (2), moderate (3), and severe (4).

Meeting the f-PGA 0 or 1 criteria: defined as having an f-PGA score of clear (0) or minimal (1).

4.3.2.1.9. Physician's Global Assessment of Hands and Feet

The severity of hand and foot psoriasis has been assessed in various clinical studies using an hf-PGA instrument. The plaques are scored on a 5-point scale as: clear (0), almost clear (1), mild (2), moderate (3), and severe (4).

Meeting the hf-PGA 0 or 1 criteria: defined as having an hf-PGA score of clear (0) or almost clear (1) and a ≥2- grade improvement from baseline.

4.3.2.1.10. Genital Psoriasis Sexual Frequency Questionnaire

The GenPs-SFQ will be utilized in the adult population and is a 2-item participant-reported instrument used to assess the impact of genital psoriasis on the frequency of sexual activity in the last 7 days. Item 1 assesses overall frequency of sexual activity in the last 7 days (none/zero, once, or 2 or more times), and item 2 assesses how frequently genital psoriasis symptoms have limited the frequency of sexual activity in the last 7 days (never [0], rarely [1], sometimes [2], often [3], or always [4]) (Gottlieb 2018).

GenPs-SFQ data is collected only for adult participants with active genital psoriasis at Week 0.

Meeting the GenPs-SFQ 0 or 1 criteria: defined as having an GenPs-SFQ item 2 score of 0 or 1.

4.3.2.2. Estimands

4.3.2.2.1. Estimands for the Other Secondary Endpoints in Set 1 and Set 2

The main estimands for other secondary endpoints in **Set 1** and **Set 2** have the same attributes as main estimands of the key secondary endpoints (Section 4.3.1.2.1 [vs Placebo] and Section 4.3.1.2.2 [vs Deucravacitinib]) in treatment and ICEs respectively. The attributes for variable, population, and population level summary for the other secondary endpoints are listed in the Table 6.

Table 6: List of Variables, Populations and Population Level Summary for Other Secondary Endpoints

Variable	Population	Population Level Summary
Set 1 (JNJ-77242113 vs Placebo)		
Change from baseline in BSA at Week 16	Same population as the primary estimand	Difference in treatment means between
Change from baseline in PASI at Week 16		
Percent change in PASI at Week 16		
Change from baseline in PSSD symptom score at Week 16		
Change from baseline in PSSD sign score at Week 16		
Change from baseline in DLQI total score at Week 16		
Percent change from baseline in mNAPSI score at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline mNAPSI score >0	
Change from baseline in each of the 8 individual domain score, PCS and MCS scores of PROMIS-29 at Week 16	Same population as the primary estimand	
sPGA-G score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline sPGA-G score ≥2	Difference in proportions

Table 6: List of Variables, Populations and Population Level Summary for Other Secondary Endpoints

Variable	Population	Population Level Summary
hf-PGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline hf-PGA score ≥2	
f-PGA score of 0 or 1 at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline f-PGA score ≥2	
PSSD sign score of 0 at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline PSSD sign score >0	
GenPs-SFQ Item 2 score of 0 or 1 at Week 16	Patients with moderate to severe plaque psoriasis and a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥3	
DLQI score of 0 or 1 at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline DLQI score >1	
Set 2 (JNJ-77242113 vs Deucravacitinib)		
Change from baseline in BSA at Week 16	Same population as the primary estimand	Difference in treatment means
Change from baseline in PASI at Week 16		
Percent change in PASI at Week 16		
DLQI score of 0 or 1 at Week 16	Patients with moderate to severe plaque psoriasis and with a baseline DLQI score >1	Difference in proportions
DLQI score of 0 or 1 at Week 24		
PSSD symptom score of 0 at Week 24	Patients with moderate to severe plaque psoriasis and with a baseline symptom score >1	

4.3.2.3. Analysis Methods

The other secondary endpoints will be analyzed using the estimands described in Section 4.3.2.2 for FAS. All statistical testing will be performed at the 2-sided 0.05 significance level. No adjustments for multiple comparisons will be made for other secondary endpoints. Nominal p-values for other secondary and exploratory endpoints will be reported but should not be used to infer statistical significance.

Binary Endpoints

The same strategies for addressing ICEs for key secondary analysis (binary endpoint) will be used for other secondary binary endpoints. The proportions of participants achieving a clinical response for the efficacy endpoints will be provided by intervention group. The p-values, difference in proportions and 95% CIs will be provided based on the same model for key secondary endpoints specified in Section 4.3.1.3.1. Non-inferiority testing will not be performed for the other secondary endpoints for the comparison between JNJ-77242113 and deucravacitinib.

Continuous Endpoints

The analysis strategies for ICEs:

- Participants experiencing ICEs 1 and 2 will be handled with composite strategy and data will be imputed with a zero change (or zero improvement) from baseline from that point onward.
- Participants experiencing ICE 3 will be handled by the treatment policy strategy and observed data will be used regardless of intercurrent events. For participants experiencing multiple ICEs, ICE 2 will override an ICE 3.
- Missing data will not be imputed after applying the rules for intercurrent events. Missing data will be accounted for through correlation of repeated measures in the MMRM model.

For repeated measure continuous endpoints, treatment comparisons will be performed using a MMRM model. The MMRM will include treatment, baseline weight, geographic region and baseline value, as explanatory factors. The MMRM model will also include visit, treatment group by visit, and baseline value by visit interaction as additional explanatory factors. An unrestricted (UN) variance-covariance matrix for repeated measures within a participant will be used. If the model with unstructured covariance structure does not converge, alternative covariance structures will be tried in the following order, with the first structure that converges being used in the analysis: heterogeneous Toeplitz, standard Toeplitz, and autoregressive of order 1. The LS mean estimates and their corresponding 95% CI will be provided at each timepoint. In addition, the estimates of LS mean difference and 95% CIs between treatment groups will be provided when appropriate.

Analysis of covariance will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, baseline weight, and geographic region. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference and 95% CIs between treatment groups will be provided.

4.4. Exploratory Endpoint Analysis

4.4.1. Definition of Endpoint(s)

4.4.1.1. Investigator's Global Assessment (IGA)

Refer to Section 4.2.1.2. for details.

4.4.1.2. Psoriasis Area and Severity Index (PASI)

Refer to Section 4.2.1.1. for details.

4.4.1.3. Body Surface Area (BSA)

Refer to Section 4.3.2.1.2. for details.

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

Refer to Section 4.3.1.1.4. for details.

Meeting the ss-IGA score of 0 criteria: defined as achieving an ss-IGA score of absence of disease (0).

4.4.1.5. Static Physician's Global Assessment of Genitalia (s-PGA-G)

Refer to Section 4.3.2.1.6. for details.

4.4.1.6. Nail Psoriasis Area and Severity Index (NAPSI)

Refer to Section 4.3.2.1.7 for details.

4.4.1.7. Fingernail Physician's Global Assessment (f-PGA)

Refer to Section 4.3.2.1.8 for details.

Meeting the f-PGA 0 response criteria: defined as having an f-PGA score of clear (0).

4.4.1.8. Physician's Global Assessment of Hands and/or Feet (hf-PGA)

Refer to Section 4.3.2.1.9 for details.

Meeting the hf-PGA 0 criteria: defined as having an hf-PGA score of clear (0).

4.4.1.9. Dermatological Life Quality Index (DLQI)

Refer to Section 4.3.2.1.3 for details.

4.4.1.10. Psoriasis Symptom and Sign Diary (PSSD)

Refer to Section 4.3.1.1.3 for details.

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

Refer to Section 4.3.2.1.5. for details.

4.4.1.12. Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)

Refer to Section 4.3.2.1.10. for details.

4.4.1.13. Participant assessment of psoriatic arthritis (PsA) pain

This self-administered item is designed to assess the participant's reported pain associated with PsA over the past week on a VAS ranging from 0 (no pain) to 100 (worst possible pain). This assessment will be administered only to participants who report having PsA at or before Week 0.

4.4.1.14. Participant Assessment of Psoriatic Arthritis Disease Activity

This self-administered item is designed to assess the participant's overall well-being over the past week on a VAS ranging from 0 (very poor) to 100 (very well). This assessment will be administered only to participants who report having PsA at or before Week 0.

4.4.2. Analysis Methods

The efficacy analyses for exploratory endpoints will be based on FAS (Section 4.1). Simple descriptive summary statistics, such as n, mean, SD, median, interquartile range, minimum, and

maximum for continuous variables, and counts and percentages for discrete variables will be summarized by study intervention group.

Unless otherwise specified, the treatment comparisons for binary endpoints will be performed using the same analysis methods described in Section 4.3.1.3.1 for the main estimand of key secondary endpoints. The analysis strategy for ICEs and missing data will be handled in the same manner as key secondary endpoints (Section 4.3.1.3.1). For continuous variables, the analysis strategy for ICEs and missing data will be handled in the same manner as other secondary analyses (Section 4.3.2.3). No adjustments for multiple comparisons will be made for exploratory endpoints.

In addition, all endpoints with over time analyses will be descriptively summarized by treatment groups using descriptive statistics, such as mean, median, standard deviation, interquartile range, minimum and maximum for continuous variables, and counts and percentages for categorical variables.

For the efficacy analyses from Week 64 through Week 156, all participants randomized to JNJ-77242113 at Week 0 or placebo/deucravacitinib participants who crossed over to JNJ-77242113 at or after Week 16/Week 24 respectively will be included in the analyses. For select binary endpoints (eg. IGA and PASI responses), both modified non-responder imputation (mNRI) and as-observed cases (OC) will be performed to handle the missing data; other binary endpoints will only apply mNRI. mNRI will be the primary method to handle the missing data.

- Modified non-responder imputation (mNRI) for binary endpoints: Participants who meet ICE 1 (discontinuation of treatment due to lack of efficacy, or due to an AE of worsening of psoriasis) will be considered as non-responders for binary endpoints or zero change for continuous endpoints from that point forward. After accounting for the ICE, missing data will then be imputed using multiple imputations (MI) for binary endpoints and the same MI analysis method specified in Section 4.2.3.2.1 for Sensitivity Analysis 1 will be applied.
- Observed Cases (OC) for binary endpoints: in the as-observed analyses, no ICE rules will be applied, and missing data will not be imputed. Thus, a subject who does not have an evaluation on a scheduled visit will be excluded from the as-observed analysis for that visit.

For continuous endpoints, participants with ICE 1 will be considered as zero change or zero percent change from baseline from that point forward. After accounting for ICE 1, MMRM will be used to account for missing data under the assumption of MAR.

Additionally, graphical data displays may also be used to summarize the overtime data if applicable.

4.4.2.1. Analysis Through Week 24

Efficacy analyses at Week 16, Week 24, and over time through Week 24 will be summarized by randomized treatment group at Week 0 as following:

- **JNJ-77242113 vs Placebo at Week 16**
  - **Placebo**: efficacy in participants randomized to placebo group at Week 0.
  - **JNJ-77242113**: efficacy in participants randomized to JNJ-77242113 at Week 0.
- **JNJ-77242113 vs deucravacitinib:**
- At Week 16
  - **Placebo**: efficacy in participants randomized to placebo group at Week 0.
  - **JNJ-77242113**: efficacy in participants randomized to JNJ-77242113 at Week 0.
  - **Deucravacitinib**: efficacy in participants randomized to deucravacitinib at Week 0.
- At Week 24
  - **Deucravacitinib**: efficacy in participants randomized to deucravacitinib at Week 0.
  - **JNJ-77242113**: efficacy in participants randomized to JNJ-77242113 at Week 0.
- **Efficacy data through Week 24:**
  - **Placebo → JNJ-77242113**: efficacy in participants randomized to placebo group at Week 0.
    - For over time summaries at Week 20 and Week 24 only participants who crossed over to receive JNJ-77242113 treatment will be included in the placebo group.
  - **JNJ-77242113**: efficacy in participants randomized to JNJ-77242113 at Week 0.
  - **Deucravacitinib**: efficacy in participants randomized to deucravacitinib at Week 0.

4.4.2.2. Analyses After Week 24

4.4.2.2.1. Analyses Through Week 52

- Unless specify otherwise, efficacy analyses over time through Week 52 will be summarized by the following treatment group:

- **Placebo-> JNJ-77242113**: Participants randomized to placebo group at Week 0.
  - Only participants who crossed over to receive JNJ-77242113 treatment on or after Week 16 will be included in the placebo →JNJ-77242113 group for visits after Week 16 visit.
- **JNJ-77242113**: Participants randomized to JNJ-77242113 treatment group at Week 0.
- **Deucravacitinib → JNJ-77242113**: Participants randomized to deucarvacitinib group at Week 0.
  - Only participants who crossed over to receive JNJ-77242113 on or after Week 24 will be included in the Deucravacitinib → JNJ-77242113 group for visits after Week 24 visit.

4.4.2.2.2. Analyses From Week 64 Through Week 156

Unless specified otherwise, efficacy over time analyses from Week 64 over time through Week 156 will be summarized by the following treatment group:

- **JNJ-77242113**: Participants randomized to JNJ-77242113 treatment group at Week 0, or participants randomized to placebo group at Week 0 and crossed over to received JNJ-77242113 at or after Week 16.
- **Deucravacitinib → JNJ-77242113:** Only include participants randomized to deucravacitinib at Week 0 and crossed over to JNJ-77242113 at or after Week 24**.**
- **Combined JNJ-77242113**

4.4.2.3. Analysis Related to PASI

Through Week 24 and/or Week 52

- The change from baseline and percent change from baseline in PASI total score will be summarized by visit and treatment group.
- The change from baseline and the percent change from baseline in PASI total score will be compared between the JNJ-77242113 and the deucravacitinib groups at Weeks 24.
- The proportions of PASI responses (PASI 75, PASI 90, and PASI 100) will be summarized over time by visit and treatment group.
- The proportions of participants achieving 100% improvement, ≥90%, 75% improvement from baseline in PASI disease component (Induration, Erythema, and Scaling) and region component (head, trunk, upper extremities, and lower extremities) will be summarized at Week 16 by treatment group.
- PASI responses will be summarized over time among PASI 75 responders at Week 16 in the JNJ-77242113 group.
- PASI responses will be summarized over time among PASI 90 responders at Week 16 in the JNJ-77242113 group.

In addition, to evaluate the efficacy of JNJ-77242113 in deucravacitinib participants who switched from deucravacitinib to JNJ-77242113 treatment at Week 24, PASI 75, PASI 90, and PASI 100 responses will be summarized over time among Week 24 PASI 75, PASI 90, and PASI 100 non-responders at Week 24 in the deucravacitinib group.

From Week 64 Through Week 156

- The change and the percent change from baseline in PASI total score will be summarized over time by visit and treatment group.
- The proportion of PASI responses (PASI 75, 90, and 100) will be summarized over time by visit and treatment group.

4.4.2.4. Analyses Related to IGA

Through Week 24 and/or Week 52

- The proportions of subjects achieving an IGA score of cleared (0) and IGA score of cleared (0) or minimal (1) will be summarized over time by visit and treatment group.
- IGA responses will be summarized over time among IGA 0/1 responders at Week 16 in the JNJ-77242113 group.

In addition, to evaluate the efficacy of JNJ-77242113 in deucravacitinib participants who switched from deucravacitinib to JNJ-77242113 treatment at Week 24, IGA 0/1 and IGA 0 responses will be summarized over time among Week 24 IGA 0/1 and IGA 0 non-responders at Week 24 in the deucravacitinib group.

From Week 64 Through Week 156

- The proportion of IGA responses (IGA 0 and IGA 0 or 1) will be summarized over time by visit and treatment group.

4.4.2.5. Analyses Related to BSA

Through Week 24 and/or Week 52

- The change from baseline in BSA (%) will be compared between the JNJ-77242113 and deucravacitinib groups at Weeks 24.

4.4.2.6. Analyses Related to Special Area Psoriasis

4.4.2.6.1. Analyses Related to ss-IGA

Through Week 24 and/or Week 52

- The proportion of participants who achieve an ss-IGA score of 0 or 1 at Week 16 will be compared between JNJ-77242113 and the placebo groups among participants with baseline ss-IGA score ≥3.
- The proportion of participants who achieve an ss-IGA score of 0 at Week 16 will be compared between JNJ-77242113 and the placebo groups among randomized participants with baseline ss-IGA score ≥2 and ≥3 respectively.
- The proportion of participants who achieve an ss-IGA score of 0 or 1 and at least a 2-grade improvement from baseline at Week 16 and Week 24 will be compared between the JNJ-77242113 and deucravacitinib groups among participants with a baseline ss-IGA score ≥2.
- The proportion of participants who achieve ss-IGA score of 0 and ss-IGA score 0 or 1 and at least a 2-grade improvement from baseline will be summarized over time by visit and treatment group among participants with a baseline ss-IGA score ≥2 and ≥3 respectively.

4.4.2.6.2. Analyses Related to Static Physician's Global Assessment of Genitalia

Through Week 24 and/or Week 52

- The proportion of participants achieving a sPGA-G score of clear (0) or minimal (1) will be compared between JNJ-77242113 and the placebo groups at Week 16 among participants with a baseline sPGA-G score ≥3.
- The proportion of participants achieving a sPGA-G score of clear (0) at Week 16 will be compared between JNJ-77242113 and the placebo groups among participants with baseline sPGA-G score ≥2 and ≥3 respectively.
- The proportion of participants achieving a sPGA-G score of clear (0) or minimal (1) and at least a 2-grade improvement will be compared between the JNJ-77242113 and deucravacitinib groups at Week 16 and Week 24 among participants with baseline sPGA-G score ≥2.
- The sPGA-G score of 0 and sPGA-G score 0 or 1 and at least a 2-grade improvement from baseline will also be summarized over time by visit and treatment group among participants with baseline sPGA-G score ≥2 and ≥3 respectively.

4.4.2.6.3. Analyses Related to Physician's Global Assessment of Hands and/or Feet

Through Week 24 and/or Week 52

- The proportions of participants achieving an hf-PGA score of clear (0) or almost clear (1) at Week 16 will be compared between the JNJ-77242113 and placebo groups among participants with a baseline hf-PGA score ≥3.
- The proportions of participants achieving an hf-PGA score of clear (0) at Week 16 will be compared between the JNJ-77242113 and placebo groups among participants with a baseline hf-PGA score ≥2 and ≥3 respectively.
- The proportions of participants achieving an hf-PGA score of clear (0) or almost clear (1) and at least a 2-grade improvement from baseline at Week 16 and Week 24 will be compared between the JNJ-77242113 and deucravacitinib groups among participants with a baseline hf-PGA score ≥2.
- The proportions of participants who achieve hf-PGA score 0 and hf-PGA score of 0 or 1 and at least a 2-grade improvement from baseline will be summarized over time by visit and treatment group among participants with a baseline hf-PGA score ≥2 and ≥3 respectively.

4.4.2.6.4. Analysis Related to Fingernail Physician's Global Assessment

Through Week 24 and/or Week 52

- The proportions of participants who achieve a f-PGA score of 0 at Week 16 will be compared between the JNJ-77242113 and placebo groups among participants with a baseline f-PGA score ≥2.

- The proportions of participants who achieve a f-PGA score of clear (0) or minimal (1) at Week 16 and Week 24 will be compared between the JNJ-77242113 and deucravacitinib groups among participants with a baseline f-PGA score ≥2.
- The proportions of participants who achieve an f-PGA score of 0 and f-PGA score of 0 or 1 will be summarized over time by visit and treatment group among participants with a baseline f-PGA score ≥2.

4.4.2.6.5. Analyses Related to Modified Nail Psoriasis Area and Severity Index

Through Week 24 and/or Week 52

- The percent change from baseline in mNAPSI score at Week 16 and Week 24 will be summarized and will be compared between the JNJ-77242113 and deucravacitinib groups among participants with a baseline mNAPSI score >0.
- The percent change from baseline in mNAPSI score will be summarized over time by visit and treatment group among participants with baseline mNAPSI score >0.

4.4.2.7. Analyses Related to Patient Reported Outcome

4.4.2.7.1. Analyses Related to DLQI

Through Week 24 and/or Week 52

- The change from baseline in DLQI score at Week 16 and Week 24 will be compared between the JNJ-77242113 and deucravacitinib groups.
- The proportion of participants with DLQI score of 0 and 1 will be summarized over time by visit and treatment group for the randomized participants with baseline DLQI score >1.
- The change from baseline in DLQI will be summarized over time by visit and treatment group.

From Week 64 Through Week 156

- The proportions of participants with DLQI score of 0 or 1 will be summarized over time by visit and treatment group among participants with baseline DLQI score >1.
- The change from baseline in DLQI score will be summarized over time by visit and treatment group.

4.4.2.7.2. Analyses Related to Psoriasis Symptom and Sign Diary

Through Week 24 and/or Week 52

- The change from baseline in PSSD individual scale score at Week 16 will be compared between the JNJ-77242113 and the placebo group.
- The proportions of participants who achieve a PSSD sign score =0 at Week 16 and Week 24 will be compared between the JNJ-77242113 and deucravacitinib groups among participants with baseline sign score >0.

- The proportion of participants who achieve a ≥4 points improvement from baseline in PSSD itch individual score at Week 16 and Week 24 will be compared between the JNJ-77242113 and the deucravacitinib groups among participants with a baseline PSSD itch score ≥4.
- The change from baseline in PSSD symptom score and PSSD sign score will be summarized over time by visit and treatment group.
- The proportions of participants who achieve a PSSD symptom score =0 and PSSD sign score =0 among participants with a baseline symptom score and sign score >0 will be summarized over time by visit and treatment group, respectively.
- The proportion of participants who achieve a ≥4-point improvement from baseline in PSSD itch score will be summarized over time by visit and treatment group among participants with a baseline PSSD itch score ≥4.

From Week 64 Through Week 156

- The change from baseline in PSSD symptoms score, and sign score will be summarized by visit and treatment group.
- The proportion of participants who achieve a PSSD symptoms score of 0, and sign score of 0 will be summarized over time by visit and treatment group among participants with a baseline PSSD symptom score>0, and a baseline sign score >0, respectively.
- The proportion of participants who achieve a ≥4-point improvement from baseline in PSSD itch score will be summarized over time by visit and treatment group among participants with a baseline PSSD itch score ≥4.

4.4.2.7.3. Analyses Related to PROMIS-29

Through Week 24 and/or Week 52

- The change from baseline in each PROMIS-29 domain score (T-scores), Physical Component Score (PCS), and Mental Component Score (MCS) will be summarized over time by visit and treatment group.

From Week 64 Through Week 156

- The change from baseline in PROMIS-29 PCS and MCS scores will be summarized over time by visit and treatment group.

4.4.2.7.4. Analysis Related to Genital Psoriasis Sexual Frequency Questionnaire

Through Week 24 and/or Week 52

- The proportion of participants with a GenPs-SFQ item 2 score of 0 at Week 16 will be compared between the JNJ-77242113 group and placebo among participants with a baseline GenPs-SFQ item 2 score ≥2 and sPGA-G score ≥3.
- The proportion of participants with a GenPs-SFQ item 2 score of 0, and score of 0 or 1 at Week 16 will be compared between the JNJ-77242113 group and placebo among participants with a baseline GenPs-SFQ item 2 score ≥2 and sPGA-G score ≥2.

- The GenPs-SFQ item 2 scores will be summarized over time by visit and treatment group among participants with a baseline GenPs-SFQ item 2 score ≥2 and sPGA-G score ≥3.
- The GenPs-SFQ item 2 score of 0 and score of 0 or 1 will be summarized over time by visit and treatment group among participants with a baseline GenPs-SFQ item 2 score ≥2 and sPGA-G score ≥2.

4.4.2.7.5. Analyses related to PsA Pain Assessment

Through Week 24 and/or Week 52

- The change from baseline in PsA pain (VAS) will be summarized over time by visit and treatment group among participants with a diagnosis of PsA at or before screening.

4.4.2.7.6. Analyses Related to PsA Disease Activity Assessment

Through Week 24 and/or Week 52

- The change from baseline in PsA disease activity (VAS) will be summarized over time by visit and treatment group among participants with a diagnosis of PsA at or before screening.

4.5. Safety Analyses

All safety analyses will be performed using safety analysis set based on actual intervention received unless otherwise specified. No formal statistical comparison is planned.

For all continuous safety variables, descriptive statistics by intervention group will include the N, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized by intervention group using frequency counts and percentages. The cumulative safety data will be analyzed through different study periods which include but not limited to through Week 16, Week 24, and through the whole study period as appropriate. Unless otherwise specified, tabular summaries of safety events for key study periods are in general presented as following:

Summaries through Week 16 (placebo-controlled period):

Safety data through Week 16 will be summarized by treatment group:

- Placebo
- JNJ-77242113
- Deucravacitinib

This allows between-group comparisons of safety between the JNJ-77242113 group and the placebo group or the deucravacitinib group based on similar follow-up period in each group.

Summaries through Week 24

Safety data through Week 24 will be summarized by treatment group:

- Placebo → JNJ-77242113

- JNJ-77242113
- Deucravacitinib

This allows safety comparisons between the JNJ-77242113 and deucravacitinib treatment groups through Week 24 based on the similar follow-up time in each group.

For participants who were randomized to placebo at Week 0 and discontinued treatment prior to Week 16, the safety events/measurements that occurred after Week 16 will be provided in a listing.

Summary through reporting period with a safety data cutoff date:

- Placebo → JNJ-77242113: all participants who were randomized to placebo at Week 0, and later crossed over to receive treatment with JNJ-77242113 at or after Week 16. Only the safety events/measurements from these participants that occurred on or after Week 16 will be included.
- JNJ-77242113: Participants who were randomized to JNJ-77242113 at Week 0 and were treated with JNJ-77242113, All the safety events/measurements from these participants that occurred at and after Week 0 will be included in this group.
- Combined JNJ-77242113: all participants as described above in the Placebo → JNJ-77242113 and the JNJ-77242113 groups.
- Deucravacitinib → JNJ-77242113: all participants who were randomized to deucravacitinib at Week 0, and later crossed over to receive treatment with JNJ-77242113 at or after Week 24. Only the safety events/measurements from these participants that occurred on or after Week 24 will be included.

Summaries through Week 160

Safety data through Week 160 will be summarized for participants exposed to JNJ-77242113 and will be summarized by treatment group defined as follows:

JNJ-77242113: all participants who were randomized to JNJ-77242113 at Week 0 and were treated with JNJ-77242113 and participants who were randomized to placebo at Week 0, and later crossed over to receive treatment with JNJ-77242113 at or after Week 16.

Deucravacitinib → JNJ-77242113: all participants who were randomized to deucravacitinib at Week 0, and later crossed over to receive treatment with JNJ-77242113 at or after Week 24.

Combined JNJ-77242113: all participants as described above in the JNJ-77242113 and Deucravacitinib → JNJ-77242113 groups.

4.5.1. Extent of Exposure

The extent of exposure will be summarized for randomized participants that received at least one study agent administration. Distribution of study agent lot will be summarized over time. In addition, the number and percentage of participants who receive study intervention will be summarized by visit. Descriptive statistics for the cumulative total dose of study intervention and duration of study intervention will be summarized.

The total duration of exposure to study medication (weeks) will be summarized, including days off medication as calculated below:

Total duration of exposure = last day of study medication - first day of study medication + 1.

Study intervention compliance will be summarized descriptively. See Appendix 6 for further details.

4.5.2. Adverse Events

The verbatim terms used in the CRF by investigators to identify adverse events will be coded using the MedDRA. Any AE occurring at or after the initial administration of study intervention up to 4 weeks after the last dose or treatment discontinuation is considered to be treatment emergent. If the event occurs on the day of the initial administration of study intervention, and either event time or time of administration are missing, then the event will be assumed to be treatment emergent. If the event date is recorded as partial or completely missing, then the event will be considered to be treatment emergent unless it is known to be prior to the first administration of study intervention based on partial onset date or resolution date. All reported treatment-emergent adverse events will be included in the analysis. For each adverse event, the number and percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

Summary tables will be provided for treatment-emergent adverse events:

- AEs
- Serious AEs (SAEs)
- AEs of Special Interest (AESIs)
- AEs leading to discontinuation of study intervention
- AEs of severe intensity
- AEs and SAEs related to study intervention.
- AE of psoriasis

In addition to the summary tables, listings will be provided for participants who:

- Had SAEs
- Had AESIs
- Had AEs leading to discontinuation of study intervention
- Had AEs of severe intensity
- Had AE of psoriasis
- Had suicidal ideation or suicidal behavior
- Had serious hypersensitivity including anaphylactic reactions

A listing of participants who died will be provided.

Since safety should be assessed relative to follow-up, most AE summary tables will include average weeks of follow-up for each intervention group.

An AESI, which may be serious or non-serious, is an AE of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and expedited communication (within 24 hours) by the investigator to the sponsor is warranted. The AESIs for JNJ-77242113 are active TB, malignancy, and possible Hy's law cases.

A **possible Hy's law case** is defined by the occurrence of ALT/AST ≥3×ULN, together with Tbili ≥2×ULN or INR >1.5 (if measured).

Adjudicated results for events such as Cardiovascular events, TB and Opportunistic Infections will be summarized.

4.5.3. Additional Safety Assessments

4.5.3.1. Clinical Laboratory Tests

Clinical laboratory tests will be displayed for the participants included in the safety analysis set.

Box plots of laboratory measurements and change from baseline will be provided for the select laboratory measurement.

Applicable laboratory results will be graded according to National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE) v5.0. The proportion of participants with post-baseline values by maximum toxicity grade for clinical laboratory tests will be summarized by study intervention group. Participants with toxicity grades ≥2 will be listed.

In addition, for selected laboratory parameters (i.e. ALT, AST), ULN will also be used to identify abnormal laboratory test results. Lipids and hs-CRP will be summarized. The 4-week window after the last dose or treatment discontinuation will be applied.

4.5.3.2. Vital Signs and Physical Examination Findings

Incidence of treatment-emergent markedly abnormal vital signs during intervention, as defined in Table 7, will be summarized for participants who had a baseline assessment and at least 1 postbaseline assessment for that vital sign. A listing of participants with treatment-emergent markedly abnormal vital signs will be presented. The 4-week window after the last dose or treatment discontinuation will be applied.

Table 7: Markedly Abnormal Vital Signs

Vital Sign	Criteria
Pulse	>120 bpm and with >30 bpm increase from baseline
	<50 bpm and with >20 bpm decrease from baseline
Systolic blood pressure	>180 mm Hg and with >40 mm Hg increase from baseline
	<90 mm Hg and with >30 mm Hg decrease from baseline
Diastolic blood pressure	>105 mm Hg and with >30 mm Hg increase from baseline
	<50 mm Hg and with >20 mm Hg decrease from baseline
Respiratory rate	>20 breaths per minute
Temperature	>38°C and with ≥1°C increase from baseline

4.5.3.3. Columbia-Suicide Severity Rating Scale

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

Two versions of the C-SSRS will be used, the *Baseline/Screening* version and the *Since Last Visit* version. The *Baseline/Screening* version will be conducted during the screening visit and the *Since Last Visit* version will be conducted at all other visits.

The investigator or trained study-site personnel will interview the participant in a private place and complete the C-SSRS on the eCOA device. At the conclusion of each assessment, the trained personnel administering the C-SSRS will determine the level of suicidal ideation or behavior, if any. They will then determine the next course of action if any level of suicidal ideation or behavior is reported. The participant should not be released from the site until the C-SSRS has been reviewed by the investigator and the participant's risk has been assessed and follow-up determined, as appropriate.

The following are C-SSRS categories and have binary responses (yes/no). A "yes" response to any C-SSRS category will be assigned a score as below:

Suicidal Ideation (1-5)

1 = Wish to be Dead

2 = Non-specific Active Suicidal Thoughts

3 = Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act

4 = Active Suicidal Ideation with Some Intent to Act, without Specific Plan

5 = Active Suicidal Ideation with Specific Plan and Intent

Suicidal Behavior (6-10)

6 = Preparatory Acts or Behavior

7 = Aborted Attempt

8 = Interrupted Attempt

9 = Actual Attempt (non-fatal)

10 = Completed Suicide

If no events qualify for a score of 1 to 10, a score of 0 will be assigned (0 = "Negative result [no suicidal ideation or behavior]"). Higher scores indicate greater severity.

Suicidal ideation and behavior will be summarized by C-SSRS categories and intervention group based on the most severe/maximum post baseline C-SSRS outcome or AE of suicidal ideation, suicidal behavior excluding completed suicide, or completed suicide through Week 16, through Week 24, through reporting period with a safety data cutoff date, and through Week 160. The baseline is defined as the most severe/maximum C-SSRS score at either screening or Week 0.

The maximum score assigned for each participant will also be summarized into one of three broad categories: No suicidal ideation or behavior, suicidal ideation, and suicidal behavior. A shift table for change in C-SSRS categories of no suicidal ideation or behavior, suicidal ideation, and suicidal behavior from baseline through Week 16, through Week 24, through reporting period with a safety data cutoff date, and through Week 160 will be presented, where the baseline category is based on C-SSRS score and the post baseline is based on C-SSRS or AE data.

4.5.3.4. PHQ-9

The PHQ-9 is self-administered, 9-item questionnaire measuring symptoms and severity of depression. The recall period for all items is the past 2 weeks. The items include: diminished interest or pleasure, depressed mood, insomnia/hypersomnia, fatigue or loss of energy, weight loss or weight gain/appetite loss or appetite gain, feelings of worthlessness, diminished concentration/indecisiveness, psychomotor agitation/retardation, and thoughts of death/suicide. Each item is rated on a 4-point Likert scale ranging from 0 "not at all" to 3 "nearly every day". Higher scores indicate more severe depressive symptoms. The PHQ-9 scores for depression range from 0 to 27 with higher scores indicating worse state (more severe depressive symptoms). A score of 5 to 9 is considered to be minimal symptoms of depression. A score of 5 to 9 is considered to be minimal symptoms of depression. A score of 10 to 14 is considered minor depression, dysthymia, or mild major depression. A score of 15 to 19 is considered to indicate moderately severe major depression, and a score ≥20 is considered to be severe major depression.

- The shift table will be provided summarizing the shift in values from baseline to postbaseline.
- A listing will be produced for all PHQ-9 scores including unscheduled visits for participants with PHQ-9 score ≥15.

4.5.3.5. Electrocardiogram

The Electrocardiogram data will be summarized by ECG parameter. Descriptive statistics will be calculated at baseline and for observed values and change from baseline at each scheduled time point.

In addition, summary of post-baseline ECG abnormalities different from Week 0 and a listing of subjects with any post-baseline ECG abnormalities different from Week 0 measurement will be provided. The 4-week window after the last dose or treatment discontinuation will be applied.

4.6. Other Analyses

4.6.1. Pharmacokinetics

4.6.1.1. JNJ-77242113 Concentrations

PK analyses will be performed on the PK analysis set, defined as participants who have received at least 1 dose of JNJ-77242113 and have at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113.

Plasma JNJ-77242113 concentrations will be summarized by visit and treatment group. Plasma concentration will be summarized using descriptive statistics (i.e., n, arithmetic mean, standard deviation [SD], coefficient of variation [%CV], median, range [minimum and maximum], and interquartile [IQ] range) at each visit. PK data may be displayed graphically.

The following analyses will be performed as appropriate.

- Summary of plasma JNJ-77242113 concentration over time
- Proportion of participants with plasma JNJ-77242113 concentration below the lowest quantifiable concentration in a sample at each visit
- Plots of median plasma JNJ-77242113 concentrations over time

JNJ-77242113 concentrations below the lowest quantifiable concentration will be imputed as zero in the summary statistics. All plasma concentrations below the lowest quantifiable concentration or missing data will be labeled as such in the concentration database. PK data may be displayed graphically, such as mean +/- SD PK concentrations over time by baseline weight group (≤90 kg, >90 kg).

All participants and samples excluded from the analysis will be clearly documented.

If sufficient data are available, then population PK analysis using plasma concentration-time- data of JNJ-77242113 will be performed using nonlinear mixed-effects modeling. Data may be combined with those of other selected studies to support a relevant structural model. Available baseline participant characteristics (eg, demographics, laboratory variables, race) will be evaluated as potential covariates affecting PK parameters. Details will be given in a population PK analysis plan and the results of the population PK analysis will be presented in a separate report.

The effect of plasma JNJ-77242113 concentrations on efficacy will be explored (Section 4.6.3).

4.6.1.2. Data Handling Rules

Unless otherwise specified, the following data handling rules will apply to PK sample analyses:

- Plasma concentration summaries will be based on the actual treatment received.
- All plasma concentration summaries for a particular timepoint will include data obtained from treated participants at the timepoint of interest without imputing any missing data.
- A concentration not quantifiable (below the lower limit of quantification) will be treated as 0 in the summary statistics and shown as the lower limit of quantification (< LLOQ) in the data listings.
- The data from a participant who discontinued study agent will be excluded from the by-visit data analyses from that point onwards. In addition, the data from a participant who received an incomplete/ incorrect or skipped dose based on the dose prior to the PK sample collection will be excluded for that visit.

4.6.2. Immunogenicity

4.6.2.1. Antibodies to JNJ-77242113

The antibody to JNJ-77242113 status (positive at any time, negative) and titers will be summarized by treatment group for participants who receive a dose of JNJ-77242113 and have appropriate samples for detection of antibodies to JNJ-77242113 (ie, participants with at least 1 sample obtained after their first dose of JNJ-77242113).

"Sample ADA status" and sample titer as well as the cumulative "subject ADA status" and peak titer through the visit will be coded and provided by the bioanalytical group.

Participants with treatment-emergent antibodies to JNJ-77242113 include participants with treatment-induced antibodies to JNJ-77242113 and treatment-boosted antibodies to JNJ-77242113.

Participants with treatment-induced antibodies to JNJ-77242113 will have a sample that is negative for antibodies to JNJ-77242113 prior to JNJ-77242113 administration and at least one sample that is positive for antibodies to JNJ-77242113 after JNJ-77242113 administration.

Participants with treatment-boosted antibodies to JNJ-77242113 have a sample that is positive for antibodies to JNJ-77242113 prior to JNJ-77242113 administration and at least one sample that is positive for antibodies to JNJ-77242113 after JNJ-77242113 administration with a 4-fold increase in titer over baseline.

If titer remains the same or increases less than 4-fold after intervention or if ADA titer reduces or ADA disappears, the participant is classified as "treatment-emergent ADA negative". Participants with baseline negative and all post intervention samples negative are also classified as "treatment-emergent ADA negative". Participants that are unavailable for treatment-emergent ADA following intervention will be classified as "participants with baseline samples only", ie, no appropriate sample is available after intervention.

The antibodies to JNJ-77242113 summary and analysis will be based on the observed data; therefore, no imputation of missing data will be performed. Note: participant status is through each visit, thus, participant status and peak titers may change as the study progresses over time. Therefore, the 'subject ADA status' at a visit represents the cumulative ADA status through that visit. For example, if a study has a lock at Week 24, datasets through Week 24 will have participant level status (eg, negative) but at Week 52, they may have developed ADA and the participant status becomes "treatment-emergent ADA positive" from the interim to the final DBL. Peak titers can also change (increase) if a higher titer occurs after an initial DBL.

Incidence of antibody (evaluable, treatment-emergent ADA positive, treatment-emergent ADA negative) status will be summarized.

In addition, listings of participants with baseline positive ADA samples, participants who are classified as positive for treatment-emergent antibodies to JNJ-77242113 and participants who discontinue the study by antibodies to JNJ-77242113 status may be presented. The sample antibody status and the titer will be listed by visit. This listing will also provide information regarding JNJ-77242113 plasma concentration and select efficacy parameters.

4.6.2.2. Other Immunogenicity Analyses

The following analyses may be conducted if there is a sufficient number (eg, ≥20) of participants that are ADA positive.

Treatment-induced Onset (data summarized will be exclusive to baseline negative participants)

Descriptive statistics for days from first administration of study intervention to the date of first instance of treatment-induced ADA (positive for treatment-induced antibody) will be summarized.

Number of days until first instance of treatment-induced ADA = (First date for positive antibody-Date of first administration of study intervention+1);

Duration of Treatment-induced ADA (data summarized is exclusive to baseline negative participants).

The duration of treatment-induced ADA refers to the longevity of treatment-induced ADA.

Descriptive statistics for duration of treatment-induced ADA among those who developed antibody will be summarized.

4.6.2.3. Neutralizing Antibodies to JNJ-77242113

The incidence of neutralizing antibodies (NAbs) to JNJ-77242113 will be summarized for participants who are positive for antibodies to JNJ-77242113 and have samples evaluable for NAbs to JNJ-77242113.

4.6.2.4. Antibody vs Efficacy/PK/Safety

To explore the relationship between antibodies to JNJ-77242113 status and plasma JNJ-77242113 concentrations and efficacy, the following analysis may be performed as appropriate:

- Summary of select clinical responses (e.g., PASI 90 and IGA 0 or 1) by antibody to JNJ-77242113 status.
- Summary of plasma JNJ-77242113 concentrations over time by antibody to JNJ-77242113 status.
- Summary of plasma JNJ-77242113 concentrations over time by first positive antibody timepoint.
- Summary of safety by antibody to JNJ-77242113 status.
- Plots of median (IQ) plasma JNJ-77242113 concentrations over time by antibody to JNJ-77242113 status.
- Plots of median (IQ) plasma JNJ-77242113 concentrations over time by first positive antibody timepoint.

4.6.3. Pharmacokinetic/Pharmacodynamic Relationships

To explore the relationship between JNJ-77242113 plasma concentrations and efficacy endpoints, the following analyses may be explored:

- The relationship between JNJ-77242113 plasma trough concentrations (quartiles) and clinical responses (e.g., PASI 90 and IGA 0 or 1) at Week 16 and/or other timepoints may be explored. The relationship between JNJ-77242113 plasma concentrations and other endpoints may also be explored.

If data permit, the relationship between JNJ-77242113 plasma concentration and efficacy may be analyzed graphically. If any visual trend is observed, a suitable exposure-response (E-R) model may be developed to describe the E-R relationship. Details will be given in an E-R analysis plan and results will be presented in a separate technical report.

4.6.4. Biomarkers

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information.

Changes in biomarkers over time will be summarized by intervention group. Associations between baseline levels and changes from baseline in select markers and clinical response to treatment will be explored. Biomarker analyses will be summarized in separate technical reports.

4.6.5. Pharmacogenomic Analyses

Genetic (DNA) analyses will be conducted only in participants who sign the consent form to participate in the optional pharmacogenetics substudy.

These results are considered exploratory and will be presented in a separate report.

4.6.6. Subgroup Analyses

4.6.6.1. Definition

To evaluate the consistency of efficacy, subgroup analyses in the co-primary endpoints and selected key secondary endpoints over demographic, baseline disease characteristics, and psoriasis medication history, subgroup analyses will be performed when the number of participants in the subgroups permits.

For each of the subgroups defined below, the difference between the JNJ-77242113 treatment groups and placebo/deucravacitinib groups in the proportion of participants achieving co-primary endpoints and select key secondary endpoints (Section 4.3.1.3.4) and their confidence intervals will be calculated. No p-values will be provided. Subgroup analyses will not be stratified by weight category and geographic region.

Demographic subgroups

Subgroup	Definition
Baseline demographics:	
Region	Define based on UN guidance as per the M49 standard • AMER • EU • APAC
Sex	• male • female • other
Race	• American Indian or Alaska Native • Asian • Black or African American • Native Hawaiian or Other Pacific Islander • White • Multiple • Unknown • Not reported
Ethnicity	• Hispanic or Latino • Not Hispanic or Latino • Unknown • Not reported
Age Group (years)	• <45 • 45-64 • ≥65
BMI	• normal <25 kg/m^2 • overweight 25-<30 kg/m^2 • obese ≥30 kg/m^2
Body Weight Group (kg)	• ≤90 kg, >90 kg
Baseline disease characteristics:	
Age at diagnosis (years)	• < median • ≥ median
Psoriasis disease duration (years)	• < median • ≥ median
Baseline PASI	• <20

Subgroup	Definition
	• ≥20
Baseline IGA	• =4 • ≤3
Baseline BSA	• <20% • ≥20%
Baseline DLQI	• <10 • ≥10
Psoriatic arthritis	• Yes • No
Psoriasis medication history:	
Phototherapy (ultraviolet B light [UVB] or psoralen and ultraviolet A light therapy [PUVA])	• Never used • Ever used
Systemics (Conventional non-biologic systemics, Novel non-biologic systemics, systemic 1,25-dihydroxy vitamin D3 and analogues, phototherapy, biologics)	• Never used • Ever used
Conventional non-biologic systemics (PUVA, MTX, cyclosporine, acitretin, azathioprine, or fumarate)	• Never used • Ever used
Novel non-biologic systemics (apremilast or tofacitinib)	• Never used • Ever used
Biologics (etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol)	• Never used • Ever used
Anti-TNFα agent (etanercept, infliximab, certolizumab pegol, or adalimumab)	• Never used • Ever used
IL-12/23 inhibitors (ustekinumab, briakinumab)	• Never used • Ever used
IL-23 inhibitors (guselkumab, tildrakizumab, risankizumab)	• Never used • Ever used
IL-17 inhibitors (secukinumab, ixekizumab, or brodalumab)	• Never used • Ever used

4.6.7. Interim Analysis

No interim analysis is planned. However, a Data Monitoring Committee (DMC) will monitor the safety.

4.6.7.1. Data Monitoring Committee or Other Review Board

An Independent external DMC will be commissioned to ensure the continuing safety of participants enrolled. This committee will consist of at least one medical expert in the relevant therapeutic area and at least one statistician; committee membership responsibilities, authorities, and procedures will be documented in its charter. The committee will meet periodically to review interim data. After the review, the DMC will make recommendations regarding the continuation of the study.

The DMC will consist of 5 members with 4 clinicians (including 2 dermatologists, one cardiologist and 1 infectious disease specialist), and one statistician with all DMC members having voting rights.

The major function of the DMC is to monitor the safety of the study agent by reviewing the serious adverse events (SAEs) each month and by reviewing the study safety data approximately every 4 months. The content of the safety summaries are defined and documented in the DMC SAP developed by the sponsor. No hypothesis testing will be conducted.

The DMC roles and responsibilities and the general procedures (including communications) are defined and documented in the Data Monitoring Plan developed by the sponsor detailing the safety data monitoring to be conducted by the DMC.

In addition, during the study, the sponsor's study responsible physician (or designee) will regularly review blinded safety data from the sites and notify the DMC and appropriate sponsor personnel of any issues.

5. SAMPLE SIZE DETERMINATION

Two studies are designed to evaluate the efficacy of JNJ-77242113 vs placebo and to evaluate the efficacy of JNJ-77242113 vs deucravacitinib. The sample size was also chosen to ensure a reasonable safety database to assess the overall safety of JNJ-77242113. Study objectives were taken into consideration in determining the sample size.

The assumptions for the sample size and power calculations were based on placebo response rates from the historical psoriasis clinical studies, data from the JNJ-77242113 Phase 2b study (77242113PSO2001), and 2 deucravacitinib Phase 3 studies (POETYK PSO-1 and POETYK PSO-2) that evaluated the safety and efficacy of deucravacitinib in the treatment of adult participants with moderate to severe psoriasis.

- The proportion of participants in the placebo group who achieve an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and a PASI 90 response at Week 16 is 8% and 5%, respectively.
- The proportion of participants in the JNJ-77242113 who achieve an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and a PASI 90 response at Week 16 is 64% and 59%, respectively.
- The proportion of participants in the JNJ-77242113 who achieve PASI 75 response at Week 16 is 75%.
- The proportion of participants in the deucravacitinib group who achieve an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and a PASI 75 response and a PASI 90 response at Week 16 is 51%, 55%, and 30%, respectively.

Based on the above assumptions, with a total of approximately 750 participants to be randomized in a 2:1:2 ratio to JNJ-77242113 (n=300), placebo (n=150), and deucravacitinib (n=300) in 77242113PSO3002 and 675 participants to be randomized in a 4:1:4 ratio to JNJ-77242113 (n=300), placebo (n=75), and deucravacitinib (n=300) in 77242113PSO3004 at Week 0:

- There will be >99% power at a 2-sided significance level of 0.05 to detect significant differences for both coprimary endpoints in the proportion of participants achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and the proportion of participants who achieve a PASI 90 response between the placebo and JNJ-77242113 groups at Week 16.
- There will be >99% power to detect a 20-percentage difference respectively in the proportion of participants achieving a PASI 75 response between the deucravacitinib and JNJ-77242113 groups at Week 16 at a 2-sided significance level of 0.05.
- There will be approximately 90% power at a 2-sided significance level of 0.05 to detect a true 13% difference in the proportion of participants with an IGA score of cleared (0) or minimal (1) between the JNJ-77242113 and deucravacitinib groups at Week 16 or Week 24

Table 8 provides the power for detecting a treatment difference under varying assumptions for the primary and select key secondary endpoints specified in Section 4.2.1 and Section 4.3.1.

Table 8: Power to Detect a Treatment Effect Based on Different Proportions of Participants Who Achieve the Co-primary Endpoints and Select Key Secondary Endpoints

Co-primary Endpoints

IGA cleared (0) or minimal (1) response at Week 16

Placebo (n=150)	JNJ-77242113 (n=300)	Power
8%	60%	>99.9%
	64%	>99.9%
	70%	>99.9%
Placebo (n=75)	**JNJ-77242113 (n=300)**	
8%	60%	>99.9%
	64%	>99.9%
	70%	>99.9%

PASI 90 response at Week 16

Placebo (n=150)	JNJ-77242113 (n=300)	Power
5%	50%	>99.9%
	55%	>99.9%
	59%	>99.9%
Placebo (n=75)	**JNJ-77242113 (n=300)**	
5%	50%	>99.9%
	55%	>99.9%
	59%	>99.9%

Select Key Secondary Endpoints

PASI 75 response or IGA cleared (0) or minimal (1) response at Week 16 and Week 24

(difference of 13 percentage points)

deucravacitinib (n=300)	JNJ-77242113 (n=300)	Power
51%	64%	89.8%
52%	65%	90.0%
55%	68%	90.7%

(difference of 15 percentage points)

deucravacitinib (n=300)	JNJ-77242113 (n=300)	Power
45%	60%	95.8%
50%	65%	96.2%

Table 8: Power to Detect a Treatment Effect Based on Different Proportions of Participants Who Achieve the Co-primary Endpoints and Select Key Secondary Endpoints

55%	70%	96.8%
60%	75%	97.6%

PASI 90 response at Week 16 and Week 24 (difference of 15 percentage points)

deucravacitinib (n=300)	JNJ-77242113 (n=300)	Power
30%	45%	96.8%
35%	50%	96.2%

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 Participant Dispositions

Screened participants and reason for screen failures will be summarized overall.

The number of participants in the following disposition categories will be summarized throughout the study by intervention group and overall:

- Participants randomized
- Participants who received study intervention
- Participants who completed the study
- Participants who discontinued study intervention
- Reasons for discontinuation of study intervention
- Participants who terminated study prematurely
- Reasons for termination of study

The above categories will include summaries through Week 16, through Week 24, through a reporting period with a safety data cutoff date, and through Week 160.

Listings of participants will be provided for the following categories:

- Participants who discontinued study intervention
- Participants who terminated study prematurely
- Participants who were unblinded during the study period
- Participants who were randomized yet did not receive study intervention
- Participants who were randomized with incorrect stratum

6.2. Appendix 2 Baseline Characteristics and Demographics

The number of participants in each analysis set will be summarized and listed by intervention group and overall. In addition, the distribution of participants by region, country, and site ID will be presented unless otherwise noted.

Table 9 presents a list of the demographic variables that will be summarized by intervention group and overall for the full analysis set.

Table 9: Demographic Variables

Continuous Variables:	**Summary Type**
Age ([years])	Descriptive statistics (N, mean, standard deviation [SD], median and range [minimum and maximum], and IQ range).
Weight (kg)	
Height (cm)	
Body Mass Index (BMI) (kg/m2)	
Categorical Variables	
Age (<45 years, 45-64 years, and >=65 years)	Frequency distribution with the number and percentage of participants in each category.
Sex (male, female)	
Weight (≤90 kg, >90 kg)	
Race[a] (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Not reported, Unknown, Multiple)	
Ethnicity (Hispanic or Latino, not Hispanic or Latino, Not Reported, Unknown)	
BMI ([normal <25 kg/m2, overweight 25-<30 kg/m2, obese >=30 kg/m2])	

[a] If multiple race categories are indicated, the Race is recorded as 'Multiple'

Participants' Psoriasis Baseline Clinical Disease Characteristics (e.g., psoriasis disease duration [years], age at diagnosis [years], BSA [%], IGA score, PASI score, ss-IGA, f-PGA, mNAPSI, hf-PGA, sPGA-G, plaque psoriasis, facial psoriasis, and inverse psoriasis), and Patient Reported Outcomes at baseline (e.g., PSSD [total, sign score, symptom score, and individual score], DLQI, GenPs-SFQ, PROMIS-29 [domain scores, PCS, and MCS], GenPs-SFQ, PsA pain and PsA disease activity will be summarized. In addition, summaries of participants' medical history and current diagnoses, alcohol intake, and smoking status will be provided by treatment group.

6.3. Appendix 3 Protocol Deviations and Quality Tolerance Limits

In general, the following list of major protocol deviations may have the potential to impact participants' rights, safety or well-being, or the integrity and/or result of the clinical study. Participants with major protocol deviations will be identified prior to database lock and the participants with major protocol deviations will be summarized by category.

- Developed withdrawal criteria but not withdrawn
- Entered but did not satisfy criteria
- Received a disallowed concomitant treatment
- Received wrong treatment or incorrect dose
- Other

A listing of participants with major protocol deviations will also be provided by randomized treatment group.

QTL parameters and thresholds are defined and will be monitored in this study. QTL parameters will be summarized. More details are described in the Integrated Analytical Risk-Based Monitoring Plan.

6.4. Appendix 4 Prior/Concomitant Medications (including dictionary)

Prior medications are defined as any therapy used before the day of first dose (partial or complete) of study intervention. Previous psoriasis medications/therapy will be summarized by intervention group.

Concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD). Concomitant medications are defined as any therapy used on or after the same day as the first dose of study intervention, including those that started before and continue after the first dose of study intervention.

Summaries of concomitant medications will be presented by anatomic and therapeutic class (ATC) term and intervention group. The proportion of participants who receive each concomitant medication will be summarized as well as the proportion of participants who receive at least 1 concomitant medication.

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

Participants who received concomitant corticosteroids for indications other than psoriasis and/or psoriatic arthritis will be listed. Participants with concomitant prophylactic treatments for latent TB infection will also be listed.

6.5. Appendix 5 Medical History

Summaries of participants' medical history, general medical history, alcohol intake, and smoking status will be provided by treatment group. In addition, the distribution of participants by prior biologic use (yes/no) and type of biologic therapy will also be provided.

6.6. Appendix 6 Intervention Compliance

Treatment compliance will be assessed through Week 16, Week 24, and through Week 44 and or Week 52 reporting periods based on the full analysis set (FAS). Compliance will be summarized descriptively (sample size, mean, standard deviation, median, and range). Overall compliance will be categorized as > 120%, 80 to ≤ 120%, and < 80%.

Compliance will be calculated as follows:

Compliance (%) = (actual number of tablets/capsules taken/total number of tablets/capsules supposed to be taken) x100.

In addition, treatment compliance will be summarized by protocol deviation reporting for incorrect study agent administration or for treatment compliance that is less than 80% or greater than 120% of the number of expected tablets/capsules during participation in this study, unless study intervention is withheld for safety reasons.

6.7. Appendix 7 Medications of Special Interest

Other medication or therapy that could improve psoriasis (Intercurrent Event 2)

(1) any topical therapies used for psoriasis (with the exception of topical moisturizers and shampoos containing tar or salicylic acid only)

(2) any systemic corticosteroid used for psoriasis with the exception of intra-articular corticosteroids

(3) any other anti-psoriatic systemic therapy or biologic therapy

(4) Phototherapy of UVB or PUVA or any other phototherapy used for psoriasis.

Psoriasis Concomitant Medications

Topical Therapy

Week 0 to Week 52

Medicated shampoos containing salicylic acid and bland emollients are allowed on all body regions but should not be used within 24 hours before any study visit. Nonmedicated shampoos may be used on the day of the study visit.

Other topical therapies that could affect psoriasis evaluations including but not limited to topical corticosteroids, topical calcineurin inhibitors, vitamin D analogs, vitamin A analogs, retinoids, tar, anthralin, calcipotriene, tazarotene, methoxsalen, trimethylpsoralens, fumarate, PDE4 inhibitors, topical JAK inhibitors, aryl hydrocarbon receptor-modulating agents; shampoos that contain corticosteroids, coal tar, or vitamin D3 analogs; and herbal treatments and traditional Taiwanese, Korean, or Chinese medicines are not permitted.

Week 52 to Week 160

After the Week 52 visit, most topical therapies are permitted for treatment of psoriasis; ultra-high potency corticosteroids and topical JAK inhibitors are still prohibited during this period.

Phototherapy or Systemic Therapy

The use of phototherapy or systemic medications that could affect psoriasis evaluations is not permitted at any time during the study.

These medications include:

- those targeted for reducing TNFα (including but not limited to adalimumab, infliximab, or etanercept).

- drugs targeted for reducing IL-12/23, IL-17, or IL-23 (including but not limited to ustekinumab, briakinumab, guselkumab, tildrakizumab, secukinumab, risankizumab, ixekizumab, or brodalumab).
- alpha-4 integrin antagonists (including but not limited to natalizumab).
- JAK inhibitors (including but not limited to TYK2 inhibitors).
- PDE4 inhibitors (including but not limited to apremilast).
- oral and injectable (IV, intramuscular, or intralesional) corticosteroids.
- any other conventional systemic therapies that could affect psoriasis evaluations (including but not limited to methotrexate, cyclosporine A, acitretin, or other retinoids).
- antimalarial agents.
- herbal treatments.
- traditional Taiwanese, Korean, or Chinese medicines.

Concomitant Medications for Indications Other Than Psoriasis

The use of systemic corticosteroids for indications other than psoriasis should be limited to situations for which, in the opinion of the treating physician, there are no adequate alternatives. Systemic corticosteroids should be used on a short-term basis, preferably for ≤2 weeks. Longer term use of corticosteroids should be discussed with the medical monitor or designee and may require discontinuation of study intervention. Inhaled, otic, ocular, nasal, or other routes of mucosal delivery of corticosteroids are allowed throughout the study. After Week 24, intra-articular corticosteroids are allowed for indications other than psoriasis. Vitamin D3 and analogs for dietary supplementation are permitted.

6.8. Appendix 8 Laboratory Toxicity Grading

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

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

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

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

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
Blood and lymphatic system disorders					
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hemoglobin (Hgb) <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hemoglobin (Hgb) <8.0 g/dL; <4.9 mmol/L; <80 g/L; *transfusion indicated*	*Life-threatening consequences; urgent intervention indicated*	Clinical signs and symptoms are not taken into consideration for grading.
Leukocytosis	-	-	>100,000/mm3; >100 x 10e9 /L	*Clinical manifestations of leucostasis; urgent intervention indicated*	Clinical signs and symptoms are not taken into consideration for grading; Added ranges in SI unit (x 10e9 /L)
Investigations					
Activated partial thromboplastin time prolonged	>ULN - 1.5 x ULN	>1.5 - 2.5 x ULN	>2.5 x ULN; *bleeding*	-	Clinical signs and symptoms are not taken into consideration for grading.
Alanine aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Alkaline phosphatase increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Aspartate aminotransferase increased	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Blood bilirubin increased	>ULN - 1.5 x ULN if baseline was normal;	>1.5 - 3.0 x ULN if baseline was normal;	>3.0 - 10.0 x ULN if baseline was normal;	>10.0 x ULN if baseline was normal;	Ranges defined for "abnormal baseline" are

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
	> 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x baseline if baseline was abnormal	applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
CD4 lymphocytes decreased	<LLN - 500/mm3; <LLN - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200 - 50/mm3; <0.2 x 0.05 - 10e9 /L	<50/mm3; <0.05 x 10e9 /L	
Cholesterol high	>ULN - 300 mg/dL; >ULN - 7.75 mmol/L	>300 - 400 mg/dL; >7.75 - 10.34 mmol/L	>400 - 500 mg/dL; >10.34 - 12.92 mmol/L	>500 mg/dL; >12.92 mmol/L	
CPK increased	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN	CPK (Creatine Phosphokinase) and CK (Creatine Kinase) are synonyms
Creatinine increased	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN	
Fibrinogen decreased	<1.0 - 0.75 x LLN; if abnormal, <25% decrease from baseline	<0.75 - 0.5 x LLN; if abnormal, 25 - <50% decrease from baseline	<0.5 - 0.25 x LLN; if abnormal, 50 - <75% decrease from baseline	<0.25 x LLN; if abnormal, 75% decrease from baseline; absolute value <50 mg/dL	Ranges defined for "abnormal" are applied only on values < LLN. Grade 0 will be assigned to values > ULN.
GGT increased	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Ranges defined for "abnormal baseline" are applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
Haptoglobin decreased	<LLN	-	-	-	
Hemoglobin increased	Increase in >0 - 2 g/dL; Increase in >0 - 20 g/L	Increase in >2 - 4 g/dL; Increase in >20 - 40 g/L	Increase in >4 g/dL; Increase in >40 g/L	-	The increase indicates the level of increase above normal (above ULN). Applied as, e.g. grade 1 (g/dL): >ULN – ULN+2 g/dL; Added ranges in SI unit (g/L).
INR increased	>1.2 - 1.5; *>1 - 1.5 x baseline if on anticoagulation;*	>1.5 - 2.5; *>1.5 - 2.5 x baseline if on anticoagulation;*	>2.5; *>2.5 x baseline if on anticoagulation;* *bleeding*	-	Concomitant therapy or clinical signs and symptoms are not taken

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
	monitoring only indicated	*dose adjustment indicated*			into consideration for grading.
Lipase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN; *>2.0 - 5.0 x ULN and asymptomatic*	>2.0 - 5.0 x ULN with signs or symptoms; *>5.0 x ULN and asymptomatic*	>5.0 x ULN and with signs or symptoms	"Asymptomatic" ranges are not taken into consideration for grading, i.e. worst case grading is applied.
Lymphocyte count decreased	<LLN - 800/mm3; <LLN - 0.8 x 10e9/L	<800 - 500/mm3; <0.8 - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200/mm3; <0.2 x 10e9 /L	
Lymphocyte count increased	-	>4000/mm3 - 20,000/mm3; >4 - 20 x 10e9 /L	>20,000/mm3; >20 x 10e9 /L	-	Added ranges in SI unit (x 10e9 /L).
Neutrophil count decreased	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L	Both Neutrophils and segmented neutrophils are graded using these criteria.
Platelet count decreased	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L	
Serum amylase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN; *>2.0 - 5.0 x ULN and asymptomatic*	>2.0 - 5.0 x ULN *with signs or symptoms; >5.0 x ULN and asymptomatic*	>5.0 x ULN *and with signs or symptoms*	"Asymptomatic" ranges are not taken into consideration for grading, i.e. worst case grading is applied.
White blood cell decreased	<LLN - 3000/mm3; <LLN - 3.0 x 10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x 10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x 10e9 /L	<1000/mm3; <1.0 x 10e9 /L	
Metabolism and nutrition disorders					
Acidosis	pH <normal, but >=7.3	-	pH <7.3	*Life-threatening consequences*	pH <normal is implemented as pH <LLN. Clinical signs and symptoms are not taken into consideration for grading.
Alkalosis	pH >normal, but <=7.5	-	pH >7.5	*Life-threatening consequences*	pH >normal is implemented as pH >ULN. Clinical signs and symptoms are not taken

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

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
Hypocalcemia	Corrected serum calcium of <LLN - 8.0 mg/dL; <LLN - 2.0 mmol/L; Ionized calcium <LLN - 1.0 mmol/L	Corrected serum calcium of <8.0 - 7.0 mg/dL; <2.0 - 1.75 mmol/L; Ionized calcium <1.0 - 0.9 mmol/L; *symptomatic*	Corrected serum calcium of <7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L; Ionized calcium <0.9 - 0.8 mmol/L; *hospitalization indicated*	Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L; Ionized calcium <0.8 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading. Note: For Hypercalcemia or Hypocalcemia in the CTCAE Lab Toxicity grading scale, the reference ranges from serum calcium (ULN /LLN) from the local or central lab are being utilized.
Hypoglycemia	Glucose <LLN - 55 mg/dL; <LLN - 3.0 mmol/L	Glucose <55 - 40 mg/dL; <3.0 - 2.2 mmol/L	Glucose <40 - 30 mg/dL; <2.2 - 1.7 mmol/L	Glucose <30 mg/dL; <1.7 mmol/L; *life-threatening consequences; seizures*	Clinical signs and symptoms are not taken into consideration for grading. Urine glucose is not graded.
Hypokalemia	*Potassium <LLN - 3.0 mmol/L*	*Symptomatic with* Potassium <LLN - 3.0 mmol/L; intervention indicated	Potassium <3.0 - 2.5 mmol/L; *hospitalization indicated*	Potassium <2.5 mmol/L; *life-threatening consequences*	"Symptomatic" ranges are applied for grade 2, grade 1 not assigned, i.e. worst case applied. Clinical signs and symptoms are not taken into consideration for grading of grade 3 and 4.
Hypomagnesemia	Magnesium <LLN - 1.2 mg/dL; <LLN - 0.5 mmol/L	Magnesium <1.2 - 0.9 mg/dL; <0.5 - 0.4 mmol/L	Magnesium <0.9 - 0.7 mg/dL; <0.4 - 0.3 mmol/L	Magnesium <0.7 mg/dL; <0.3 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.
Hyponatremia	Sodium <LLN - 130 mmol/L	*Sodium 125-129 mmol/L and asymptomatic*	*Sodium 125-129 mmol/L symptomatic; 120-124 mmol/L regardless of symptoms*	Sodium <120 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	J&J Implementation Notes
			Sodium <130-120 mmol/L		Worst case ("<130-120 mmol/L" for grade 3 added by Janssen) is applied across grade 2/3 ranges: 120-129 mol/L assigned to grade 3, grade 2 not used.
Renal and urinary disorders					

Proteinuria	1+ proteinuria;
	urinary protein ≥ULN - <1.0 g/24 hrs;
	urinary protein ≥ULN - <1000 mg/day
		Adult:
		2+ and 3+ proteinuria;
		urinary protein 1.0 - <3.5 g/24 hrs;
		urinary protein 1000 - <3500 mg/day
			Adult:
			4+ proteinuria;
			urinary protein >=3.5 g/24 hrs;
			urinary protein >=3500 mg/day;
				-	In case both 24-h urine collection and dipstick are collected, then worst case is taken, as opposed to having 24-h urine collection take precedence over dipstick.
					Added ranges in SI unit for urinary protein (mg/day) and for urine P/C (g/mol).
					Adult grading is applied for ages [>18].

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

6.9. Appendix 9 PROIMIS-29 T-score

PROMIS 29 – PROFILE v2.1
PROMIS 29 + 2 PROFILE v2.1 (PROPr)

Adult v2.0 - Physical Function 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	22.5	4.0
5	26.6	2.8
6	28.9	2.5
7	30.5	2.4
8	31.9	2.3
9	33.2	2.3
10	34.4	2.3
11	35.6	2.3
12	36.7	2.3
13	37.9	2.3
14	39.2	2.4
15	40.5	2.4
16	41.9	2.5
17	43.5	2.6
18	45.5	2.8
19	48.3	3.3
20	57.0	6.6
*SE = Standard Error on T-score metric		

Adult v1.0 - Anxiety 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	40.3	6.1
5	48.0	3.6
6	51.2	3.1
7	53.7	2.8
8	55.8	2.7
9	57.7	2.6
10	59.5	2.6
11	61.4	2.6
12	63.4	2.6
13	65.3	2.7
14	67.3	2.7
15	69.3	2.7
16	71.2	2.7
17	73.3	2.7
18	75.4	2.7
19	77.9	2.9
20	81.6	3.7
*SE = Standard Error on T-score metric		

Adult v1.0 - Depression 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	41.0	6.2
5	49.0	3.2
6	51.8	2.7
7	53.9	2.4
8	55.7	2.3
9	57.3	2.3
10	58.9	2.3
11	60.5	2.3
12	62.2	2.3
13	63.9	2.3
14	65.7	2.3
15	67.5	2.3
16	69.4	2.3
17	71.2	2.4
18	73.3	2.4
19	75.7	2.6
20	79.4	3.6
*SE = Standard Error on T-score metric		

Adult v1.0 - Fatigue 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	33.7	4.9
5	39.7	3.1
6	43.1	2.7
7	46.0	2.6
8	48.6	2.5
9	51.0	2.5
10	53.1	2.4
11	55.1	2.4
12	57.0	2.3
13	58.8	2.3
14	60.7	2.3
15	62.7	2.4
16	64.6	2.4
17	66.7	2.4
18	69.0	2.5
19	71.6	2.7
20	75.8	3.9
*SE = Standard Error on T-score metric		

Adult v1.0 - Sleep Disturbance 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	32.0	5.2
5	37.5	4.0
6	41.1	3.7
7	43.8	3.5
8	46.2	3.5
9	48.4	3.4
10	50.5	3.4
11	52.4	3.4
12	54.3	3.4
13	56.1	3.4
14	57.9	3.3
15	59.8	3.3
16	61.7	3.3
17	63.8	3.4
18	66.0	3.4
19	68.8	3.7
20	73.3	4.6
*SE = Standard Error on T-score metric		

Adult v1.0 – Ability to Participate in Social Roles and Activities 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	27.5	4.1
5	31.8	2.5
6	34.0	2.3
7	35.7	2.2
8	37.3	2.1
9	38.8	2.2
10	40.5	2.3
11	42.3	2.3
12	44.2	2.3
13	46.2	2.3
14	48.1	2.2
15	50.0	2.2
16	51.9	2.2
17	53.7	2.3
18	55.8	2.3
19	58.3	2.7
20	64.2	5.1
*SE = Standard Error on T-score metric		

Adult v1.0 - Pain Interference 4a		
Short Form Conversion Table		
Raw Summed Score	T-score	SE*
4	41.6	6.1
5	49.6	2.5
6	52.0	2.0
7	53.9	1.9
8	55.6	1.9
9	57.1	1.9
10	58.5	1.8
11	59.9	1.8
12	61.2	1.8
13	62.5	1.8
14	63.8	1.8
15	65.2	1.8
16	66.6	1.8
17	68.0	1.8
18	69.7	1.9
19	71.6	2.1
20	75.6	3.7
*SE = Standard Error on T-score metric		

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