J&J Innovative Medicine

Statistical Analysis Plan

A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants with Moderate to Severe Plaque Psoriasis with Randomized Withdrawal and Retreatment

Protocol **77242113PSO3001; Phase 3**

Amendment 1

JNJ-77242113

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

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SUMMARY OF CHANGES IN AMENDMENT 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 comments:

- Removed hypothetical estimand for the co-primary endpoints and key secondary endpoints.
- Added two sensitivity analyses (one using multiple imputation and one using tipping point analysis) to the primary estimands for the co-primary 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 when evaluating safety for the 200 mg QD regimen. The same 4-week window rule applies to lab, vital sign and ECG data analyses.
- Clarified the calculations for PSSD symptom score and sign score.
- Clarified ECG analyses.
- Removed GenPs-SFQ analysis from Week 64 through Week 156.
- Noted that multiplicity adjusted p-values will be provided.
- Added safety summary through Week 52.
- Minor grammatical, formatting, or spelling changes were made.

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
CDLQI	Children's Dermatology Life Quality Index
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
EU	European Union
eCRF	electronic case report form
EQ-VAS	EuroQol visual analogue scale
EQ-5D	EuroQol-5 Dimension
EQ-5D-5L	EuroQol-5 Dimension 5-level
FAS	full analysis set
FCS	fully conditional specification
f-PGA	Fingernail PGA
hf-PGA	Hand and/or feet PGA
GenPs-SFQ	Genital Psoriasis Sexual Frequency Questionnaire
IGA	Investigator's 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 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-25	Patient-Reported Outcomes Measurement Information System-25
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

1. INTRODUCTION

77242113PSO3001 is a randomized, double-blind, placebo-controlled, parallel-group, multicenter interventional study with randomized withdrawal and retreatment in participants with moderate to severe plaque psoriasis.

This Statistical Analysis Plan (SAP) contains definitions of analysis sets, derived variables and statistical methods of planned analyses for 77242113PSO3001 Clinical Study Report (CSR).

1.1. Objectives, Endpoints and/or Estimands

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 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 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 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.
• To evaluate the maintenance of efficacy of JNJ-77242113 compared with treatment withdrawal during the randomized withdrawal period.	• PASI 75 at Week 52. • PASI 90 at Week 52. • Time to loss of PASI 75. • Time to loss of PASI 90.
Other Secondary • To assess the safety and tolerability of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• Frequency and type of AEs and SAEs
• To further evaluate the general and special area psoriasis efficacy of JNJ-77242113 in	• Change from baseline in BSA at Week 16. • Change from baseline in PASI at Week 16.

Objectives	Endpoints
participants with moderate to severe plaque psoriasis.	• Percent improvement in PASI at Week 16. • 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 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 DLQI total score at Week 16. • Change from baseline in the domain scores of the PROMIS-29 score at Week 16. • CDLQI score of 0 or 1 at Week 16. • Change from baseline in CDLQI at Week 16. • Change from baseline in the domain scores of the PROMIS-25 pediatric score at Week 16.
• To further evaluate the maintenance of efficacy of JNJ-77242113 compared with treatment withdrawal during the randomized withdrawal period.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 52. • IGA score of 0 at Week 52. • PASI 100 at Week 52. • Time to loss of IGA 0 or 1 response.
• To evaluate long-term psoriasis efficacy of JNJ-77242113 in adolescent participants with moderate to severe plaque psoriasis.	• IGA 0 or 1 and a ≥2-grade improvement from baseline at Week 52. • PASI 75 at Week 52. • PASI 90 at Week 52.
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.

Objectives	Endpoints
	• Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time.
• To further evaluate 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, PGA of Disease activity
• 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, GenPs-SFQ, TSQM-E efficacy domain, DLQI/CDLQI, EQ-5D-5L, PROMIS-29/ PROMIS-25, PsA Pain assessment, PsA Disease Activity assessment.
• To evaluate the PK and immunogenicity of JNJ-77242113 and explore the E-R 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 anti-drug antibodies 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.
• To evaluate the efficacy of JNJ-77242113 retreatment after relapse for adult participants who were withdrawn from JNJ-77242113 at Week 24.	• Endpoints will be based on the following assessments: PASI, IGA, PSSD.

1.2. Study Design

This is a Phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter interventional study with randomized withdrawal and retreatment in participants with moderate to severe plaque psoriasis.

A target of 600 participants will be enrolled in this study. Approximately 540 adults and 60 adolescent participants will be randomized with a 2:1 randomization ratio to JNJ-77242113 200 mg or placebo. Randomization will be separately performed for adult and adolescent groups. Within the adult group, randomization will be further stratified by baseline weight category (≤90kg, >90kg) and geographic region (AMER, EU, and APAC). Within the adolescent group, randomization will be further stratified by geographic region. This study includes a 5-week screening period, a placebo-controlled period through Week 16 and a randomized withdrawal and retreatment period from Week 24 through Week 52. At Week 52, participants will be transitioned to open-label JNJ-77242113 through Week 156. A 4-week safety follow-up period will be observed for participants who discontinue study intervention

during the study or at the end of the treatment period. The total duration of this study for each participant is approximately 165 weeks.

- Adult participants
  - JNJ-77242113 200 mg once daily
    - Week 0 to Week 24: Participants will be treated with JNJ-77242113 200 mg once daily
    - Week 24 to Week 52:
      - Participants who are PASI 75 responders or IGA 0 or 1 responders (i.e., those who achieve an IGA score of 0 or 1 and have ≥ 2-grade improvement from baseline) at Week 24 will be re-randomized 1:1 to either continue JNJ-77242113 or to be transitioned to placebo. Participants transitioned to placebo will be retreated with JNJ-77242113 200 mg once daily upon loss of ≥50% of Week 24 PASI improvement or starting at Week 52 if loss of response is not observed. All participants will be treated with JNJ-77242113 at Week 52.
      - Participants who are PASI 75 non-responders and IGA 0 or 1 non-responders at Week 24 will continue to receive JNJ-77242113 200 mg once daily through Week 52.
    - Week 52 to Week 156: Participants will receive JNJ-77242113 200 mg once daily through Week 156.
  - Placebo to JNJ-77242113 200 mg once daily
    - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
    - Week 16 to Week 156: Participants will cross-over to receive JNJ-77242113 200 mg once daily through Week 156.
- Adolescent participants
  - JNJ-77242113 200 mg once daily
    - Week 0 to Week 156: Participants will be treated with JNJ-77242113 200 mg once daily
    - Adolescents will not participate in re-randomization regardless of their PASI score at Week 24.
  - Placebo to JNJ-77242113 200 mg once daily
    - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
    - Week 16 to Week 156: Participants will cross-over to receive JNJ-77242113 200 mg once daily through Week 156.

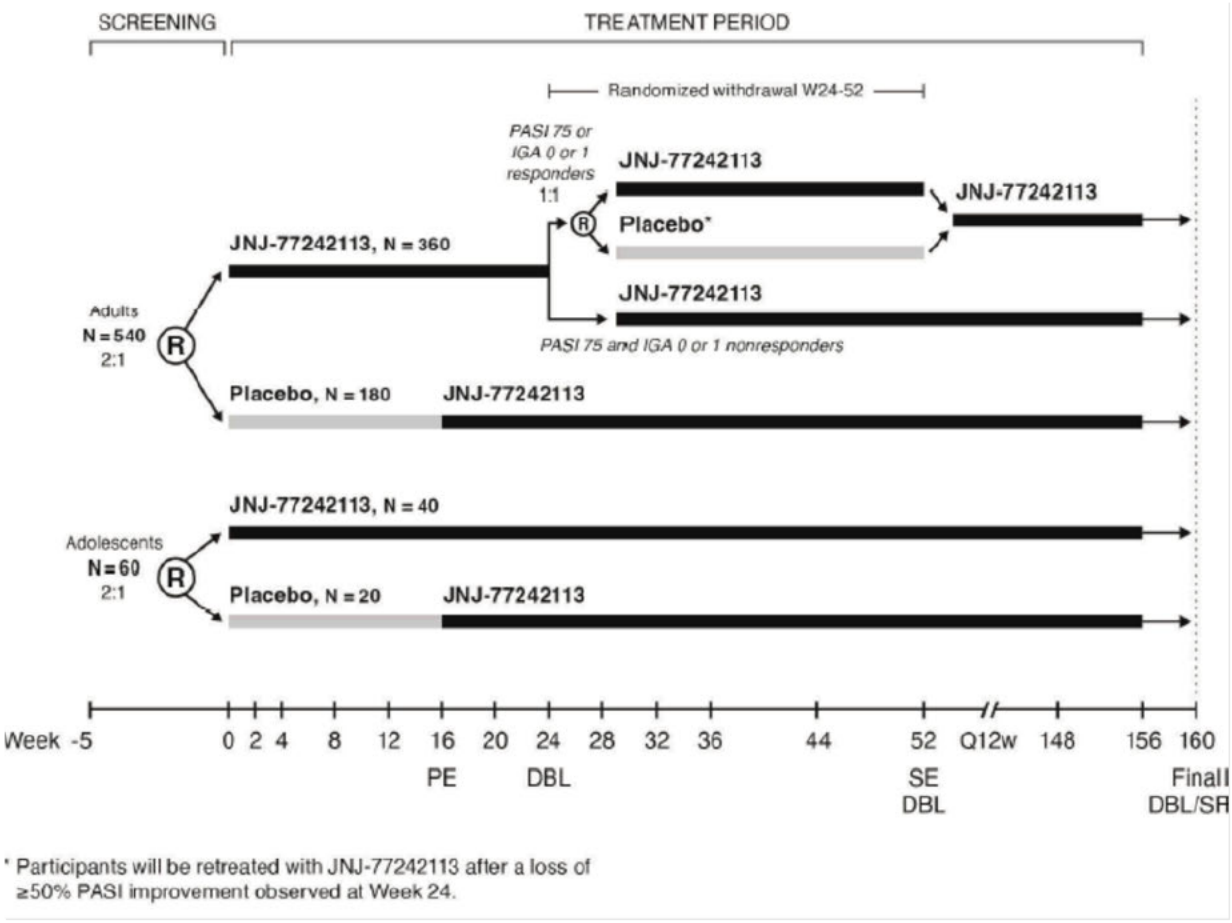
This study includes a 5-week screening period, a placebo-controlled period through Week 16 and a randomized withdrawal and retreatment period from Week 24 through Week 52. At Week 52, participants will be transitioned to open-label JNJ-77242113 through Week 156. All

participants will have a 4-week safety follow-up period after the last administration of study intervention or at the end of the treatment period. The total duration of this study for each participant is approximately 165 weeks.

The first database locks (DBL) will occur when all participants (adults and adolescents) complete Week 24 of the study. An additional DBL will occur after all adult participants complete Week 52 of the study. Additional DBLs may occur between Week 52 and Week 160 to support publication or regulatory submissions. The final DBL will occur when all participants complete the study.

An independent DMC will be commissioned for this study to review the safety data on an ongoing basis. A diagram of the study design is provided Figure 1.

Figure 1: Schematic Overview of the Study



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 hypotheses of this study are 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.

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 hypothesis during the randomized withdrawal period is:

Continuous JNJ-77242113 treatment in participants with moderate to severe plaque psoriasis is superior to withdrawal of JNJ-77242113 treatment as assessed by the proportion of participants who achieve a PASI 75 response at Week 52. The corresponding null hypothesis is that there is no difference between continuous JNJ-77242113 treatment and withdrawal of JNJ-77242113 treatment in this endpoint.

2.1. Multiplicity Adjustment

Multiplicity adjustment procedure will be used to control the overall Type I error rate for the 2 co-primary and 14 key secondary endpoints. Since there are 2 randomizations utilized in the study (i.e., 2 different experiments), the endpoints prior to or at Week 16, and the endpoints related to the randomized withdrawal will each be assigned with a 2-sided significance level of 0.05. The testing procedure begins with the test of superiority of JNJ-77242113 group compared with placebo group in the co-primary endpoints. Key secondary endpoints will only be tested if the co-primary endpoints are significant. The testing strategy is devised based on the expected power and relative importance of the endpoints. If either test of the co-primary endpoints is not significant (i.e., $p>0.05$), all subsequent p-values for all the key secondary endpoints 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 superiority tests for the key secondary endpoints.

The endpoints during the first 16 weeks of placebo-controlled period are grouped in 4 tiers. Within each tier, the Bonferroni–Holm's (Holm S 1979) procedure (see Figure 2 below for an illustration of the full testing procedure) will be used to test all endpoints in that tier with an overall type I error rate of 0.05 (2-sided). 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, but the formal testing will stop and all p-values in subsequent tiers will be considered nominal. If all tests within a tier are significant based on Bonferroni–Holm's procedure, then testing will continue to the next tier.

Tier 1 (comparison between JNJ-77242113 and placebo group randomized at Week 0)

- PASI 75 at Week 16
- PASI 100 at Week 16
- IGA score of 0 at Week 16

Tier 2 (comparison between JNJ-77242113 and placebo group randomized at Week 0)

- PSSD symptom score of 0 at Week 16
- ≥4-point improvement from baseline in PSSD itch score at Week 16

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

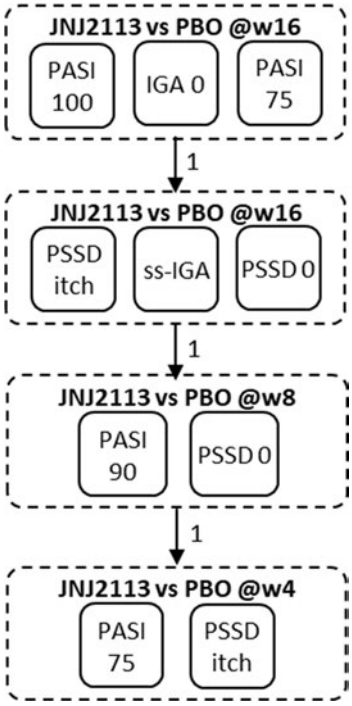
Tier 3 (comparison between JNJ-77242113 and placebo group randomized at Week 0)

- PASI 90 at Week 8
- PSSD symptom score of 0 at Week 8

Tier 4 (comparison between JNJ-77242113 and placebo group randomized at Week 0)

- PASI 75 response at Week 4.
- ≥4-point improvement from baseline in PSSD itch score at Week 4

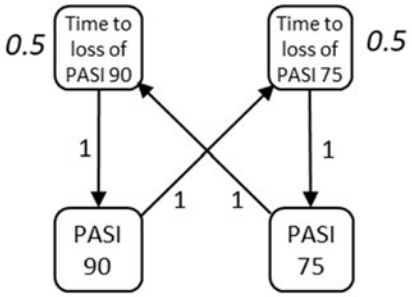
Figure 2: Testing procedure for the key secondary endpoints during the placebo-controlled period



Additionally, if the co-primary endpoints are significant, the following endpoints during the randomized withdrawal portion will also be tested using the graphical approach at a 2-sided overall alpha of 0.05 (Figure 3).

- Time to loss of PASI 75, Time to loss of PASI 90
- PASI 75 response at Week 52, PASI 90 response at Week 52

Figure 3: Testing procedure for the endpoints during the randomized withdrawal period



The study will be considered successful if the tests for both co-primary endpoints are positive. For all key secondary endpoints specified above, both multiplicity-adjusted and nominal p-values will be provided. Statistical significance will be claimed if the adjusted p-value is ≤0.05. No multiplicity adjustments will be made for the other secondary and exploratory endpoints and these statistical testing will be performed at the 2-sided 0.05 significance level. Nominal p-values will be presented.

3. ANALYSIS SETS

For purposes of analysis, the following analysis sets are defined in Table 1:

Table 1: Definition of Analysis Sets

Population	Description
Enrolled	All participants who signed the ICF
Randomized	All participants who were randomized at Week 0 in the study.
Randomized at Week 24	All participants who were rerandomized at Week 24 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 age group at screening (adolescents <18 years and adults ≥18 years), baseline weight category for adults (i.e., ≤90kg in adults, >90kg in adults, adolescents) and geographic region (AMER, EU, and APAC) if applicable. A stratification factor may not be used if the sample size is small within that stratum among adolescents. 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, age group, 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% CIs will be provided at each timepoint. In addition, the estimates of LS mean difference and 95% CIs between treatment groups will be provided. Analysis of covariance (ANCOVA) will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, baseline weight, geographic region and age group. 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. For time to event endpoints during the randomized withdrawal period, treatment comparisons will be performed using a log-rank test. Life table estimates of cumulative rate by treatment group will be provided to evaluate the timing of event occurrence in different treatment groups.

In general, all statistical tests 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 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. Analysis 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 (e.g., 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 and Percent Change From Baseline

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

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

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

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 Endpoints/Estimands 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 (PASI)

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy. In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities 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 (IGA)

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 or adolescent 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 definition 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: Patients ≥12 years of age with moderate to severe plaque 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 2**):**

Table 2: 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 6.7).	**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 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 an 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.

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 proportion of PASI 90 responders and IGA 0 or 1 responders at Week 16 will be summarized by treatment group. To address the primary objective, a 2-sided (α=0.05) CMH chi-square test stratified by age group (adults, adolescents), baseline weight category for adults (≤90kg in adults, >90kg in adults, adolescents), and geographic region (AMER, EU, APAC) will be used.

Difference in response rates between the JNJ-77242113 group and the placebo group at Week 16 and their corresponding 95% CIs (using Miettinen-Nurminen method [REFERENCES]) will be calculated adjusting for age group, baseline weight category for adults, and geographic region using Mantel-Haenszel (MH) weights.

The study will be considered positive if the JNJ-77242113 group is significantly different from the placebo group for both co-primary endpoints. Both co-primary endpoints will be tested at a 2-sided α level of 0.05. 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 proportion of PASI 90 responders and IGA 0 or 1 responders at Week 16 will be summarized by region, country, and investigator site. The coprimary endpoints will also by summarized and compared between treatment group among adolescent participants. 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. The 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

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

More specifically, the missing PASI 90 response and IGA 0 or 1 response will be imputed with FCS logistic regression including treatment group, baseline PASI score or IGA score, PASI 90 response or IGA 0 or 1 response status through Week 16, age group, baseline weight category for adults, and geographic region in the model with seed = 789 and 500 imputations.

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

The general association test statistic 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 age group, baseline weight category for adults, and geographic region for each imputed dataset. The resulting values will be combined to obtain an overall risk difference and 95% CI.

4.2.3.2.2. Sensitivity Analysis 2

Under the co-primary estimands, another sensitivity analysis will 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 ICEs are accounted for. The 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 age group, baseline weight category for adults, 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-value based on Rubin's rule.

The analysis will be repeated for a range of values for p (for example, 0% to 100% in increments of 10%, for the placebo group and the JNJ-77242113 group independently). For this tipping point analysis, the 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 Analyses

4.2.3.3.1. 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 estimand will be used.

4.2.3.4. Per Protocol Analysis

The co-primary efficacy endpoints will be evaluated for comparisons between JNJ-77242113 group and placebo group in the per protocol 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 Analysis

4.3.1. Key Secondary Endpoints/Estimands

4.3.1.1. Definition of Endpoints

4.3.1.1.1. Investigator's Global Assessment (IGA)

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 (PASI)

Refer to section 4.2.1.1 for details.

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

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

The time to loss of PASI 75 response through Week 52: PASI 75 response will be assessed at each visit between Week 24 and Week 52. Participants who experience a loss of PASI 75 response (<75% improvement from baseline) at any visit between Week 24 and Week 52 will be considered as having an 'event'. The time to loss of PASI 75 response is defined as the time from rerandomization at Week 24 to the visit of loss of PASI 75 response. Participants who do not experience any event between Week 24 and Week 52 will be censored at the last disease assessment visit or Week 52.

The time to loss of PASI 90 response through Week 52: similar to the definition of time to loss of PASI 75 response except using loss of PASI 90 response, which is when < 90% improvement from baseline is observed.

4.3.1.1.3. Psoriasis Symptom and Sign Diary (PSSD)

The PSSD will be utilized in the adult and adolescent population and 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 through Week 16 visit and a 7-day recall version asking the participant to answer the questions thinking about the last 7 days after Week 16. 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 each item. For both the 24-

hour and 7-day recall versions, two subscores will be derived each ranging from 0 to 100: the PSSD symptom score and the PSSD sign score. 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 24-hr 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 24-hr 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 24-hr 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 timepoints (i.e., baseline, Week 4, 8 and 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 7-day (i.e., Week 2 and 12) or 10-day (i.e., baseline, Week 4, 8 and 16) window, data are considered missing for that visit.

Meeting PSSD symptom score of 0 criteria: defined as having a PSSD symptom score of 0.

Meeting PSSD itch score ≥4-point improvement criteria: defined as having at least 4-point improvement from baseline in PSSD itch score.

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 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 Key Secondary Endpoints (Sec 1-14)

Endpoints at or prior to Week 16 (Sec 1-10)

The main estimands for key secondary endpoints at or prior to Week 16 have same attributes as co-primary estimands, except for attributes of variable and population defined in Table 3.

Table 3: List of Variables and Populations for Key Secondary Endpoints at or Prior to Week 16

Estimands	**Variable** Achieving a response based on:	**Population**
Sec 1	IGA score of 0 at Week 16	Same population as the primary estimand specified in section 4.2.2.1
Sec 2	PASI 75 at Week 4	
Sec 3	PASI 90 at Week 8	
Sec 4	PASI 75 at Week 16	
Sec 5	PASI 100 at Week 16	
Sec 6	ss-IGA score of 0 or 1 and a ≥2 grade improvement from baseline at Week 16	Patients ≥12 years of age with moderate to severe plaque psoriasis and with a baseline ss-IGA score ≥2
Sec 7	PSSD symptom score of 0 at Week 8	Patients ≥12 years of age with moderate to severe plaque psoriasis and with a baseline PSSD symptom score > 0
Sec 8	PSSD symptom score of 0 at Week 16	
Sec 9	≥4-point improvement from baseline in PSSD itch score at Week 4	Patients ≥12 years of age 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.

Endpoints at Week 52 (Sec 11-14)

Main question of interest is:

For adult patients with moderate to severe plaque psoriasis who are PASI 75 or IGA 0 or 1 responders at Week 24, what is the effect up to Week 52 of continuing JNJ-77242113 versus treatment withdrawal?

The main estimands for key secondary endpoints at Week 52 are defined by the following 5 attributes.

Treatment condition of interest vs Alternative treatment condition:

Assignment to continuation of JNJ-77242113 200 mg QD vs withdrawal group (Placebo).

ICEs and their corresponding strategies:

Same ICEs 1-3 as those defined in the co-primary estimands. In addition, ICE 4 is defined as meeting criteria of loss of ≥50% Week 24 PASI improvement. Patients with this ICE will be handled using the composite strategy.

Variable, Population and Population Level Summary: Refer to Table 4

Table 4: Variables, Populations and Population Level Summaries for Key Secondary Endpoints at Week 52

Estimands	Variable	Population	Population Level Summary
Sec 11	Achieving a PASI 75 response at Week 52	Adult patients with moderate to severe plaque psoriasis who are PASI 75 responders randomized at Week 24	Difference in proportions
Sec 12	Achieving a PASI 90 response at Week 52	Adult patients with moderate to severe plaque psoriasis who are PASI 90 responders randomized at Week 24	
Sec 13	Time to loss of PASI 75 through Week 52 (defined in Section 4.3.1.1.2)	Adult patients with moderate to severe plaque psoriasis who are PASI 75 responders randomized at Week 24	Hazard ratio (HR) vs placebo
Sec 14	Time to loss of PASI 90 through Week 52 (defined in Section 4.3.1.1.2)	Adult patients with moderate to severe plaque psoriasis who are PASI 90 responders randomized at Week 24	

Note: For participants experiencing multiple ICEs, ICE 2 and 4 will override an ICE 3.

4.3.1.2.2. Supplementary Estimands for Key Secondary Endpoints

The supplementary estimands have the same components as the main estimands 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 endpoints will be used for the following selected key secondary endpoints. Supplementary estimands are not planned for the secondary endpoints at early timepoints (i.e., Week 4, Week 8) due to the anticipated limited ICEs.

- IGA scores of cleared (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
- ≥4-point improvement from baseline in PSSD itch score at Week 16 among participants with a baseline PSSD itch score ≥4
- PSSD symptom score of 0 at Week 16 among participants with a baseline PSSD symptom score >0
- PASI 75 response at Week 52 among PASI 75 responders randomized at Week 24
- PASI 90 response at Week 52 among PASI 90 responders randomized at Week 24

4.3.1.3. Analysis Methods

4.3.1.3.1. Analytical Approaches for Main Estimands

The efficacy analyses for key secondary endpoints will be based on the FAS or randomized at Week 24 analysis set by intervention group. The detailed methods of analysis and approach to control multiplicity is specified in Section 2.1.

Binary Endpoint Analyses

The binary key secondary endpoints will be analyzed using the main estimands described in section 4.3.1.2.1. Composite strategy will be used for ICEs 1, 2 and/or 4 (as applicable) where participants with those ICEs will be considered as non-responders and treatment policy strategy will be used for ICE 3 where observed data will be used. For the analysis at Week 52, participants experiencing an ICE 2 from Week 24 to Week 52 will be considered non-responders at Week 52, regardless of whether an ICE 2 occurred prior to Week 24. After the application of ICEs, participants with missing data will be imputed as non-responders. The proportions of participants achieving a key secondary efficacy response will be summarized and compared between treatment groups in the same manner as the co-primary endpoints using the appropriate stratification factors. For endpoints at or prior to Week 16, the stratification factors for randomization at baseline may be used in analyses. Geographic region may be removed as a stratification factor in CMH tests for endpoints with low response rates. For the analyses of PASI 75 at Week 52, stratification factors of PASI 90 response status at Week 24, and geographic region may be used in the analyses. A stratification factor of geographic region may be used for the analysis of PASI 90 at Week 52.

In addition, key endpoints at or prior to Week 16 (defined in 4.3.1.2.1) will be summarized and compared between treatment group among adolescent participants using a CMH test stratified by geographic region.

Time to Event Analyses

For the analyses related to the time to event endpoints (i.e., time to loss of PASI 75, time to loss of PASI 90) during the withdrawal period, composite strategy will be used for ICEs 1, 2 and 4 where participant with these ICEs will be considered as an 'Event' of loss of PASI response.

Treatment policy strategy will be used for ICE 3 where observed data after this ICE will be utilized in the analysis. The remaining missing PASI score after the Week 24 visit will not be imputed.

The life table method will be used to estimate the distribution of time to loss of PASI response for intervention group. The median time of loss of PASI response will be provided. The number and percent of participants who had a loss of response or were censored will be reported. In addition, the cumulative percent of participants who maintained a PASI response with 95% CI will be estimated by life table method after Week 24 (at 4 weeks, 8 weeks, and 12 weeks, etc.) and a survival curve (probability that participants maintain a PASI response) will also be plotted by intervention group.

The comparison of the distribution of loss of response between JNJ-77242113 and placebo group will be based on a stratified log-rank test. Hazard ratio and its 95% confidence interval will be estimated based on a stratified Cox's regression model with intervention as the explanatory variable. Stratification factors used in these analyses include PASI 90 response status at Week 24 (if applicable), and geographic region.

4.3.1.3.2. Supplementary Analyses

Similar to the co-primary supplementary analyses, the methods specified in Section 4.2.3.3.1 will be applied to the selected key secondary binary endpoints using Treatment Policy Estimands (Section 4.3.1.2.2).

4.3.1.3.3. Subgroup Analyses

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).

- IGA score of 0 at Week 16
- PASI 75 at Week 16
- PASI 100 at Week 16

4.3.2. Other Secondary Endpoints Analyses

4.3.2.1. Definition of Endpoints

4.3.2.1.1. Investigator's Global Assessment

Refer to section 4.2.1.2 for details.

4.3.2.1.2. Psoriasis Area and Severity Index

Refer to section 4.2.1.1 for details.

4.3.2.1.3. Dermatology Life Quality Index/Children's 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.

The Children's Dermatology Life Quality Index (CDLQI) is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a child's quality of life. It is an adapted version of DLQI. The CDLQI, a 10-item questionnaire has 4 items response options and a recall period of 1 week. In addition to evaluating overall quality of life, the CDLQI can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment.

The CDLQI 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. 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.
- If both questions in question 7 are completed, the higher of the two scores should be counted for question 7.

Meeting DLQI/CDLQI 0 or 1 criteria: defined as having a DLQI/CDLQI score of 0 or 1 with baseline DLQI/CDLQI score >1.

4.3.2.1.4. Psoriasis Symptom and Sign Diary

Refer to section 4.3.1.1.3 for details.

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

4.3.2.1.5. 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 in this study, 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.

4.3.2.1.6. 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 sPGA-G 0 or 1 criteria: 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. 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 6.9. 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

4.3.2.1.9. Patient-Reported Outcomes Measurement Information System-25 v2.0 (PROMIS-25)

The PROMIS-25 will be utilized in the adolescent population and is a 25-item generic HRQoL survey utilized in the adolescent population. Six PROMIS domains (physical function mobility, anxiety, depressive symptoms, fatigue, peer relationships, pain interference) are assessed with 4 items, ranked on a 5-point Likert Scale. There is also one 11-point rating scale for pain intensity. The instrument is designed for use in ages 8-17 years of age and can be self-administered.

The total raw score will be converted into a T-score for each participant based on the table in Appendix 6.10. The T-score rescales the raw score into a standardized score with a mean of 50 and an SD of 10. Change from baseline in PROMIS-25 domain score: defined as the domain score minus the participant's baseline domain score, where a negative change indicates an improvement for the following domains:

- Anxiety
- Depressive symptoms
- Fatigue
- Pain interference

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

- Physical function mobility
- Peer relationships

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

4.3.2.1.11. Physician's Global Assessment of Hands and/or 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 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.

4.3.2.1.12. 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]).

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

Meeting GenPs-SFQ item 2 score 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 Other Secondary Endpoints - at Week 16

The estimands for other secondary endpoints at Week 16 have the same attributes as the co-primary estimands in treatment and ICEs. The attributes for variable, population and population level summary for the other secondary endpoints are listed in Table 5.

Table 5: List of Variables, Populations and Population Level Summary for Other Secondary Endpoints

Variable	Population	Population Level Summary
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		
Change from baseline in PSSD symptom score at Week 16		
Change from baseline in PSSD sign score at Week 16		

Table 5: List of Variables, Populations and Population Level Summary for Other Secondary Endpoints

Change from baseline in DLQI total score at Week 16		
Percent change from baseline in mNAPSI score at Week 16	Patients ≥ 12 years of age 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 score of PROMIS-29 at Week 16	Adult patients with moderate to severe plaque psoriasis	
Change from baseline in CDLQI at Week 16	Adolescent patients with moderate to severe plaque psoriasis	
Change from baseline in each of the 7 individual domain score, and total score of the PROMIS-25 at Week 16	Adolescent patients with moderate to severe plaque psoriasis	
sPGA-G score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16	Patients ≥ 12 years of age with moderate to severe plaque psoriasis and with a baseline sPGA-G score ≥2	Difference in treatment proportions
hf-PGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16	Patients ≥ 12 years of age 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 ≥ 12 years of age with moderate to severe plaque psoriasis and with a baseline f-PGA score ≥2	
PSSD sign score of 0 at Week 16	Patients ≥ 12 years of age 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	Adult patients with moderate to severe plaque psoriasis, with a baseline GenPs-SFQ item 2 score ≥2, and a baseline sPGA-G score ≥3	
DLQI score of 0 or 1 at Week 16	Adult patients with moderate to severe plaque psoriasis and with a baseline DLQI Score >1	
CDLQI score of 0 or 1 at Week 16	Adolescent patients with moderate to severe plaque psoriasis and with a baseline CDLQI Score >1	

Note: composite strategy will be applied for patients with ICEs 1-2 and non-responders will be considered for binary endpoints and zero change / zero percent change will be considered for continuous endpoints.

4.3.2.2.2. Estimands for Other Secondary Endpoints at Week 52 for adults

Treatment and ICEs: Same as those specified for the main estimand for key secondary endpoints at Week 52 (Section 4.3.1.2.1)

Variable and Population: The variable, population and summary measure for the other secondary binary endpoints are listed in Table 6 below.

Table 6: List of Variable, Population, and Population Level Summary for Other Secondary Endpoints at Week 52 in Adults

Variable	Population	Population Level Summary
IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 52	Adult patients with moderate to severe plaque psoriasis, who are IGA 0 or 1 responders randomized at Week 24.	difference in proportions
IGA score of 0 at Week 52	Adult patients with moderate to severe plaque psoriasis, who are IGA 0 responders randomized at Week 24.	
PASI 100 at Week 52	Adult patients with moderate to severe plaque psoriasis, who are PASI 100 responders randomized at Week 24.	
Time to loss of IGA 0 or 1 response	Adult patients with moderate to severe plaque psoriasis, who are IGA 0 or 1 responders randomized at Week 24.	hazard ratio

4.3.2.2.3. Estimands for Other Secondary Endpoints at Week 52 in Adolescents

Treatment: JNJ-77242113

Population: Adolescent patients with moderate to severe plaque psoriasis

Intercurrent event: The ICEs and corresponding strategies are same as those defined in co-primary estimands.

Variable and Population Level Summary: The variable and summary for the other secondary binary endpoints at Week 52 are listed in the below Table 7.

Table 7: List of Variable and Population Level Summary for Other Secondary Endpoints at Week 52 in Adolescents

Variable	Population Level Summary
IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 52	proportions
PASI 75 at Week 52	
PASI 90 at Week 52	

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 or randomized at Week 24 analysis set. 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 analyses (binary endpoints) 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.

In addition, PSSD sign score of 0 at Week 16 will be compared between treatment group, among adolescent participants with a baseline PSSD sign score > 0, using a CMH test stratified by geographic region.

Continuous Endpoints

The analysis strategies for ICEs:

- Participants experiencing ICEs 1, 2 and 4 (only apply to Week 52 endpoints after retreatment among adult participants) 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, ICEs 2 and 4 will override an ICE 3.

- Missing data will not be imputed after applying the rules for ICEs. 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, age group, baseline weight, geographic region and baseline value, as explanatory factors, if applicable. 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.

Analysis of covariance will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, baseline weight, geographic region and age group. 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.

The analysis of time to loss of IGA 0 or 1 response will be performed in the same manner as the key secondary analyses of time to loss of PASI responses (refer to section 4.3.1.2.1) with the same data handling rule for ICEs and missing data.

4.4. Exploratory Endpoints Analysis

4.4.1. Definition of Endpoints

For the following endpoints, refer to previous sections for details.

PASI (section 4.2.1.1), IGA (section 4.2.1.2), DLQI/CDLQI (section 4.3.2.1.3), PSSD (section 4.3.1.1.3), mNAPSI (section 4.3.2.1.7), PROMIS-29 (section 4.3.2.1.8), and PROMIS-25 (section 4.3.2.1.9).

4.4.1.1. Scalp Specific Investigator Global Assessment

Refer to section 4.3.1.1.4 for details.

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

4.4.1.2. Fingernail Physician's Global Assessment

Refer to section 4.3.2.1.10 for details.

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

4.4.1.3. Physician's Global Assessment of Hands and/or Feet

Refer to section 4.3.2.1.11 for details.

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

4.4.1.4. Static Physician's Global Assessment of Genitalia

Refer to section 4.3.2.1.6 for details.

Meeting sPGA-G score of 0 criteria: having an sPGA-G score of clear (0).

4.4.1.5. Physician Global Assessment of Disease Activity

The PGA of Disease Activity is a 100 mm VAS and will be utilized for adolescent participants with a diagnosis of PsA at or before screening. Physicians are to complete the VAS to assess the participant's current arthritis activity. The anchors of the scale are "no arthritis activity" to "extremely active arthritis." Lower scores indicate less disease activity. The process for including this measure (PGA of disease activity) in the core set of variables for the assessment of JIA improvement has been captured in the literature.

4.4.1.6. Participant Assessment of Psoriatic Arthritis 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 adult and adolescent participants who report having PsA at or before Week 0.

4.4.1.7. 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 adult and adolescent participants who report having PsA at or before Week 0.

4.4.1.8. Participant Assessment of Acceptability and Palatability

Adolescent participants will be asked to provide responses to questions designed to assess the acceptability and palatability of the study drug.

4.4.1.9. Genital Psoriasis Sexual Frequency Questionnaire

Refer to section 4.3.2.1.12 for details.

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

4.4.2. Analysis Methods

In general, the efficacy analyses for exploratory endpoints will be based on FAS or randomized at Week 24 analysis set (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 will be performed using the same analysis methods described in Section 4.3.2.3 for other secondary endpoints. 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.

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

4.4.2.1. Analyses Through Week 24

Efficacy analyses at Week 16 and over time through Week 24 will be summarized by randomized treatment group at Week 0.

- **Placebo**: participants randomized to the 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 cross over group.

- **JNJ-77242113**: participants randomized to the JNJ-77242113 treatment group at Week 0

4.4.2.2. Analyses From Week 24 Through Week 52 – Randomized Withdrawal and Retreatment Period

Randomized Withdrawal Period

To evaluate the maintenance of efficacy of JNJ-77242113 compared with treatment withdrawal

during the randomized withdrawal period, efficacy analyses at Week 52 and from Week 24 through Week 52 (withdrawal and retreatment period) will be summarized among adult participants who were rerandomized at Week 24.

- **Placebo (withdrawal group):** participants rerandomized to the placebo group at Week 24
- **JNJ-77242113**: participants rerandomized to the JNJ-77242113 treatment group at Week 24

Participants experiencing ICEs 1, 2 and/or 4 between Week 24 and Week 52 will be handled in the same manner as the other secondary analyses (section 4.3.2.3).

Retreatment period

To evaluate the efficacy of retreatment after relapse with JNJ-77242113, efficacy data at and after retreatment relative to the time of retreatment (i.e., at the time of retreatment, 4 weeks after retreatment, 8 weeks after retreatment) will be summarized for adult participants who were randomized to placebo at Week 24, were withdrawn from study agent at Week 24, experienced a loss of at least 50% of the Week 24 PASI improvement, and were retreated with JNJ-77242113. Selected endpoints will be summarized at scheduled visits after retreatment.

Participants experiencing ICEs 1-3 after retreatment will be handled in the same manner as the other secondary analyses (section 4.3.2.3) regardless of ICEs occurred prior to retreatment.

4.4.2.3. Analyses Through Week 52 – Non-randomized JNJ-77242113 Treatment

For participants who were not randomized at Week 24, efficacy data will be summarized over time from Week 24 through Week 52 in following treatment groups.

- **Placebo-> JNJ-77242113 (adults and adolescents)**: participants randomized to placebo group at Week 0 and crossed over to receive JNJ-77242113 at or after Week 16
- **JNJ-77242113 (adult non-responders)**: adult participants randomized to JNJ-77242113 treatment group at Week 0 who were both PASI 75 and IGA 0 or 1 non-responders at Week 24, and did not undergo randomization at Week 24

To evaluate efficacy of JNJ-77242113 in adolescent participants, efficacy data will be summarized from Week 0 through Week 52.

- **JNJ-77242113 (adolescents)**: adolescent participants randomized to JNJ-77242113 treatment group at Week 0.

4.4.2.4. Analyses From Week 64 Through Week 156

The efficacy analyses from Week 64 through Week 156 will be performed for participants randomized to JNJ-77242113 at Week 0, or participants randomized to placebo at Week 0 and crossed over to receive JNJ-77242113 at or after Week 16 based on following data handling rules for ICE and missing data.

- Modified Non-Responder Imputation (mNRI) for binary endpoints: participants with ICE 1 will be considered as non-responders from that point forward. After accounting for ICE 1, missing data will be imputed using the same multiple imputations (MI) method specified in Section 4.2.3.2.1 for sensitivity analysis 1.
- Observed Cases (OC) for binary endpoints: selected endpoints (e.g., PASI responses, and IGA responses) will be summarized based on the observed data. No ICE rules will be applied, and missing data will not be imputed.
- MMRM model for continuous endpoints: participants with ICE 1 will be considered as zero change or zero percent change from baseline from that point forward. Missing data will be accounted for through correlation of repeated measures in the MMRM model.

4.4.2.5. Analyses Related to PASI

Through Week 24

- The change and percent change from baseline in PASI total score will be summarized over time through Week 24 by treatment group.
- The proportions of PASI responses (PASI 75, PASI 90, and PASI 100) will be summarized over time through Week 24 by treatment group.
- The proportions of participants achieving ≥75% improvement, ≥90% improvement, or achieving 100% improvement from baseline in PASI disease component (Induration, Erythema, and Scaling) and region component (head, trunk, upper extremities, and lower extremities) at Week 16 will be summarized by treatment group.

From Week 24 Through Week 52 – Randomized Withdrawal and Retreatment Period

Randomized Withdrawal period

- The Life table method will be used to estimate the distribution of time to loss of ≥50% of the Week 24 PASI improvement (i.e., time to retreatment) after withdrawal. The median time to loss of ≥50% of the Week 24 PASI improvement will be provided.
- The proportion of PASI responses (PASI 75, 90, and 100) will be summarized over time from Week 24 through Week 52 for participants randomized at Week 24.
- The change and percent change from baseline in PASI total score will be summarized over time from Week 24 through Week 52 for participants randomized at Week 24.

Retreatment period

- The change and percent change from baseline in PASI total score will be summarized at the time of retreatment and over time (e.g., 4 weeks after retreatment, 8 weeks after retreatment, 12 weeks after retreatment).
- The PASI responses (PASI 75, 90 and 100) with respect to baseline will be summarized over time (e.g., 4 weeks after retreatment, 8 weeks after retreatment, 12 weeks after retreatment) following retreatment with JNJ-77242113.

Through Week 52 – Non-randomized JNJ-77242113 Treatment

- The change and percent change from baseline in PASI will be summarized over time by treatment group.
- The proportion of PASI responses (PASI 75, 90, and 100) will be summarized over time by treatment group.
- The proportion of participants who achieve a PASI 75 response at Week 52 will be summarized among adolescent participants who were randomized to JNJ-77242113 at Week 0 and were PASI 75 responders at Week 24.
- The proportion of participants who achieve a PASI 90 response at Week 52 will be summarized among adolescent participants who were randomized to JNJ-77242113 at Week 0 and were PASI 90 responders at Week 24.

From Week 64 Through Week 156

- The change and percent change from baseline in PASI total score will be summarized over time.
- The proportion of PASI responses (PASI 75, 90, and 100) will be summarized over time based on mNRI and observed data after accounting for ICE 1.

4.4.2.6. Analyses Related to IGA

Through Week 24

- The proportions of IGA responses (IGA 0, IGA 0 or 1) will be summarized over time through Week 24 by treatment group.

From Week 24 Through Week 52 – Randomized Withdrawal and Retreatment Period

Randomized Withdrawal period

- The proportion of IGA responses (IGA 0, IGA 0 or 1) will be summarized over time through Week 52 for participants randomized at Week 24.

Retreatment period

- IGA scores at the time of retreatment of JNJ-77242113 and the proportion of retreated participants who achieve an IGA 0, and an IGA 0 or 1 responses over time (e.g., 4 weeks after retreatment, 8 weeks after retreatment, 12 weeks after retreatment) following the retreatment of JNJ-77242113 will be summarized for participants randomized at Week 24.

Through Week 52 – Non-randomized JNJ-77242113 Treatment

- The proportion of IGA responses (IGA 0, and IGA 0 or 1) will be summarized over time by treatment group.
- The proportion of participants who achieve an IGA 0 or 1 response at Week 52 will be summarized among adolescent participants who were randomized to JNJ-77242113 at Week 0 and were IGA 0 or 1 responders at Week 24.

From Week 64 Through Week 156

- The proportion of IGA responses (IGA 0, and IGA 0 or 1) will be summarized over time based on mNRI and observed data after accounting for ICE 1.

4.4.2.7. Analyses Related to ss-IGA

Through Week 24

- The proportion of ss-IGA responses (ss-IGA score of 0, ss-IGA score 0 or 1 and at least a 2-grade improvement from baseline) will be summarized through Week 24 by treatment group among participants with a baseline ss-IGA score ≥2 and ≥3 respectively. In addition, the proportion of ss-IGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline ss-IGA score ≥2 and ≥3 respectively. The proportion of ss-IGA score of 0 or 1 will be compared between treatment groups at Week 16 among participants with a baseline ss-IGA score ≥3.

4.4.2.8. Analysis Related to Static Physician's Global Assessment of Genitalia

Through Week 24

- The proportion of sPGA-G responses (sPGA-G score of 0, sPGA-G score 0 or 1 and at least a 2-grade improvement from baseline) will be summarized through Week 24 among participants with an sPGA-G score ≥2 and ≥3 at baseline respectively. In addition, the proportion of sPGA-G score of 0 will be compared between treatment groups at Week 16 among participants with a baseline sPGA-G score ≥2 and ≥3 respectively. The proportion of sPGA-G score of 0 or 1 will be compared between treatment groups at Week 16 among participants with a baseline sPGA-G score ≥3.

4.4.2.9. Analysis Related to Physician's Global Assessment of Hands and/or Feet

Through Week 24

- The proportion of hf-PGA responses (hf-PGA score of 0, hf-PGA score of 0 or 1 and at least a 2-grade improvement from baseline) will be summarized through Week 24 among participants with a baseline hf-PGA score ≥2 and ≥3 respectively. In addition, the proportion of hf-PGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline hf-PGA score ≥2 and ≥3 respectively. The proportion of hf-PGA score of 0 or 1 will be compared between treatment groups at Week 16 among participants with a baseline hf-PGA score ≥3.

4.4.2.10. Analysis Related to Fingernail Physician's Global Assessment

Through Week 24

- The proportion of f-PGA responses (f-PGA score of 0, and f-PGA score of 0 or 1) will be summarized through Week 24 by treatment group among participants with a baseline f-PGA score ≥2. In addition, the proportion of f-PGA score of 0 will be compared between treatment groups at Week 16 among participants with a baseline f-PGA score ≥2.

4.4.2.11. Analysis Related to Modified Nail Psoriasis Area and Severity Index

Through Week 24

- The percent change from baseline in mNAPSI will be summarized through Week 24 by treatment group for participants with a baseline mNAPSI score >0.

4.4.2.12. Analysis Related to PGA of Disease Activity (adolescent)

Through Week 52

- The change from baseline in PGA disease activity score will be summarized through Week 52 by treatment group among adolescent participants with a previous diagnosis of PsA at or before screening.

4.4.2.13. Analyses Related to Psoriasis Symptom and Sign Diary

Through Week 24

- The change from baseline in PSSD symptom score and sign score will be summarized over time through Week 24 by treatment group.
- The proportions of participants who achieve a PSSD symptom score of 0 and sign score of 0 will be summarized over time through Week 24 among participants with a baseline PSSD symptom score>0, and baseline sign score >0 respectively by treatment group. Additionally, these endpoints will be summarized over time by treatment group and age group.
- The proportion of participants who achieve a ≥4-point improvement from baseline in PSSD itch score will be summarized over time through Week 24 among participants with baseline PSSD itch score ≥4. Additionally, this endpoint will be summarized over time by treatment group and age group.
- The change from baseline in each PSSD individual scale score will be compared between treatment groups at Week 16.

Through Week 52 – adolescent

- The change from baseline in PSSD symptom score and sign score will be summarized over time through Week 52 by treatment group among adolescent participants.
- The proportion of participants who achieve a PSSD symptom score of 0, sign score of 0, and ≥4-point improvement from baseline in PSSD itch score will be summarized over time through Week 52 by treatment group among adolescent participants with a baseline PSSD symptom score>0, baseline sign score >0, and baseline PSSD itch score ≥4 respectively.

From Week 64 Through Week 156

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

4.4.2.14. Analyses Related to DLQI (adult) and CDLQI (adolescent)

Through Week 24

- The change from baseline in DLQI score will be summarized over time through Week 24 by treatment group among adult participants.
- The change from baseline in CDLQI will be summarized over time through Week 24 by treatment group among adolescent participants.
- The proportion of participants with DLQI score of 0 or 1 will be summarized over time through Week 24 by treatment group among adult participants with a baseline DLQI score >1.
- The proportion of participants with CDLQI score of 0 or 1 will be summarized over time through Week 24 by treatment group among adolescent participants with a baseline CDLQI score >1.

Through Week 52 – adolescent

- The change from baseline in CDLQI will be summarized over time by treatment group among adolescent participants.
- The proportion of participants with CDLQI score of 0 or 1 will be summarized over time among the adolescent participants with a baseline CDLQI score >1.

From Week 64 Through Week 156

- The change from baseline in DLQI score will be summarized over time among adult participants.
- The change from baseline in CDLQI will be summarized over time among adolescent participants.
- The proportion of participants with DLQI score of 0 or 1 will be summarized over time among the adult participants with a baseline DLQI score >1.
- The proportion of participants with CDLQI score of 0 or 1 will be summarized over time among the adolescent participants with a baseline CDLQI score >1.

4.4.2.15. Analysis Related to Adult Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) (adult)

Through Week 24

- 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 adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline 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 adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥2.
- The GenPs-SFQ item 2 score of 0 and score of 0 or 1 will be summarized over time through Week 24 by treatment group among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥3.

- The GenPs-SFQ item 2 score of 0 and score of 0 or 1 will be summarized over time through Week 24 by treatment group among adult participants with a baseline GenPs-SFQ item 2 score ≥2 and a baseline sPGA-G score ≥2.

4.4.2.16. Analyses Related to PROMIS-29 (adult) and PROMIS-25 (adolescent)

Through Week 24

- The change from baseline in PROMIS-29 domain scores, Physical Component Score (PCS), and Mental Component Score (MCS) will be summarized through Week 24 by treatment group among adult participants.
- The change from baseline in PROMIS-25 domain scores will be summarized through Week 24 by treatment group among adolescent participants.

Through Week 52 – adolescent

- The change from baseline in PROMIS-25 domain scores will be summarized over time by treatment group among adolescent participants.

From Week 64 Through Week 156

- The change from baseline in PROMIS-29 PCS and MCS will be summarized over time among adult participants.
- The change from baseline in PROMIS-25 domain scores will be summarized over time among adolescent participants.

4.4.2.17. Analysis Related to PsA Pain Assessment

Through Week 24

- The change from baseline in PsA pain will be summarized at Week 8 and Week 16 by treatment group among participants with a diagnosis of PsA at or before screening.

Through Week 52 – adolescent

- The change from baseline in PsA pain will be summarized through Week 52 by treatment group among adolescent participants with a diagnosis of PsA at or before screening.

4.4.2.18. Analysis Related to PsA Disease Activity

Through Week 24

- The change from baseline in PsA disease activity will be summarized at Week 8 and Week 16 by treatment group among participants with a diagnosis of PsA at or before screening.

Through Week 52 – adolescent

- The change from baseline in in PsA disease activity will be summarized through Week 52 by treatment group among adolescent participants with a diagnosis of PsA at or before screening.

4.4.2.19. Analysis Related to Acceptability and Palatability (Adolescent)

Through Week 16

- The acceptability and palatability (e.g. sweetness, bitterness, overall, and swallowability) will be summarized at Week 0 and Week 16 by treatment among adolescent participants.

4.5. Safety Analyses

All safety analyses will be performed using safety analysis set based on actual intervention received. 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 as shown below. Unless otherwise specified, tabular summaries of safety events are also presented as following:

Summary through Week 16:

- Placebo
- JNJ-77242113

Summary through Week 24:

- Placebo → JNJ-77242113
- JNJ-77242113

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

Summary through Week 52 and /or through the reporting period (approximately the date when last participant finishing Week 52 visit):

Safety data will be summarized by intervention group defined as follows:

- 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 at 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 or after Week 0 administration will be included in this group. However, safety events that occurred during the withdrawal period (on and after Week 28 and before retreatment) may be excluded for participants who were rerandomized to placebo at Week 24.
- Combined JNJ-77242113: all participant as described above in the Placebo → JNJ-77242113 and the JNJ-77242113 groups.

In addition, selected safety analysis from Week 24 through Week 52 may be performed among participants who were randomized to either receive placebo or continue to receive JNJ-77242113 at Week 24.

- Placebo (withdrawal): Participants who were randomized to JNJ-77242113 at Week 0, were PASI 75 or IGA 0 or 1 responders at Week 24, and rerandomized to placebo group at Week 24. Only the safety events/measurements from these participants that occurred at or after Week 24 randomization and before retreatment with JNJ-77242113 will be included in this group.
- Placebo → retreatment: Participants who were randomized to placebo at Week 24, started treatment with placebo, and retreated with JNJ-77242213 upon loss of 50% Week 24 PASI improvement. Only the safety events that occurred at or after their first retreatment of JNJ-77242113 will be included in this group.
- Placebo (combined 1 and 2 above): Participants who were randomized to placebo at Week 24. All safety events/measurements from these participants that occurred at or after Week 24 randomization will be included.
- JNJ-77242113 (Rerandomization): Participants who were randomized to JNJ-77242113 at Week 24 and continue to receive treatment with JNJ-77242113. All safety events occurred at or after Week 24 rerandomization will be included in this group.

Summary through Week 160:

- Safety data through Week 160 will be summarized for participant exposure to JNJ-77242113.

4.5.1. Extent of Exposure

The extent of exposure will be summarized for randomized participants who received at least one study agent administration. Distribution of study agent lot will be summarized over time. Descriptive statistics for the average daily dose of study intervention and duration of exposure to study medication (weeks) will be summarized.

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

Study intervention compliance will be summarized descriptively. See Appendix 6.6 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. In general, 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. The overall AEs will also be summarized by age group (adult, adolescent) and 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 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).

Psoriasis rebound will be assessed during the withdrawal period for adult participants who were randomized to placebo at Week 24 and withdrawn from JNJ-77242113. Psoriasis rebound is defined as an event of new erythrodermic or pustular psoriasis, or a PASI of ≥125% of the baseline PASI (ie, a worsening of PASI by 25% or greater from baseline) that occurred within 3 months

during the withdrawal period from the time participants were withdrawn from JNJ-77242113 at Week 24.

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 measurements. In addition, box plot for select laboratory measurements may be provided among adolescent participants.

Applicable laboratory results will be graded according to National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE). The proportion of participants with post-baseline values by maximum toxicity grade for clinical laboratory tests will be summarized overall and by age 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. Lipid 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

Vital signs and change from baseline will be summarized over time. Incidence of treatment-emergent markedly abnormal vital signs during intervention, as defined in Table 8, 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 8: 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. 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 in this study, 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 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 the reporting period at Week 52 DBL, 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 24, through reporting period of Week 52 DBL, 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. Tanner Staging

Count and percentage of Tanner scale (range from Stage 1 to Stage 5) will be summarized by gender for adolescent participants with previous Tanner stage <5.

4.5.3.5. 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 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 to summarize the shift in values from baseline to postbaseline.
- A listing will be produced for all PHQ-9 score including unscheduled visits for participants with PHQ-9 score ≥15.

4.5.3.6. 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 also 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.

Descriptive statistics (N, mean, SD, median, range, coefficient of variation [%CV], and interquartile [IQ] range) will be used to summarize JNJ-77242113 concentrations at post-dose sampling time intervals classified as peak, intermediate and trough. PK data may be displayed graphically, such as mean +/-SD PK concentrations over time by intervention group.

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.

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 (e.g., 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 analysis will be presented in a separate report.

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 incidence and titers of antibodies to JNJ-77242113 will be summarized for all participants who receive at least 1 dose of JNJ-77242113 and have appropriate samples for detection of

antibodies to JNJ-77242113 (i.e., 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 participant 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 will 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 with a 4-fold increase in titer over baseline.

If the 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”, i.e., 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 ‘participant ADA status’ at a visit represents the cumulative ADA status through that visit. For example, datasets through Week 24 will have participant level status (e.g., 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 agent 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, safety 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 concentration and other endpoints may also be explored.

If data permit, the relationships between JNJ-77242113 concentrations 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.

Change in biomarkers over time will be summarized by treatment group. Associations between baseline levels and changes from baseline in select markers and response to treatment will be explored. The analyses will aim to identify biomarker relevant to treatment. These analyses are considered exploratory and will be summarized in a separate technical report.

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 key selected secondary endpoints at Week 16 over demographic, baseline disease characteristics, and psoriasis medication history, subgroup analyses will be performed when the number of participants in the subgroups permits. In addition, other subgroup analyses not limited to efficacy and safety endpoints may be performed and reported in a separate report for regional regulatory filing purpose.

For each of the subgroups defined below, the difference between the JNJ-77242113 treatment group and placebo group on the proportion of participants with an IGA 0 or 1 and PASI 90 response rate and key selected secondary endpoints at Week 16, and their 95% confidence intervals will be calculated. No p-values will be provided.

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 • Not Reported • Unknown
Age Group (years)	• <18 • 18-<45 • 45-<65 • ≥ 65 years
BMI	• normal <25 kg/m^2 • overweight 25-<30 kg/m^2 • obese ≥30 kg/m^2
Body Weight Group (kg)	• ≤90kg, >90kg
Baseline disease characteristics:	
Age at diagnosis (years) (adults)	• <median (adults) • ≥median (adults)
Age at diagnosis (years) (adolescents)	• <median (adolescents) • ≥median (adolescents)
Psoriasis disease duration (years) (adults)	• <median (adults) • ≥median (adults)
Psoriasis disease duration (years) (adolescents)	• <median (adolescents) • ≥median (adolescents)
Baseline PASI	• <20 • ≥20
Baseline IGA	• =4 • ≤3
Baseline BSA	• <20% • ≥20%
Baseline DLQI, CDLQI	• <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

Subgroup	Definition
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, acitiretin, azathioprine, or fumarate)	• Never used • Ever used
Novel non-biologic systemics (apremilast, deucravacitinib, 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

4.7. Interim Analysis

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

4.7.1. Data Monitoring Committee or Other Review Board

An independent external DMC will monitor data on an ongoing basis to ensure the continuing safety of the participants enrolled in the psoriasis studies and to provide recommendations to the Sponsor Committee. The DMC will make recommendations concerning the conduct of the study including changes to the informed consent.

The DMC will consist of 5 members with 4 clinicians (including 2 dermatologists, one cardiologist and 1 infectious disease specialists), 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 and provide recommendations for placing the study on hold or stopping the study in the event of serious safety concerns. The content of the safety summaries, the DMC roles and responsibilities and the general procedures (including communication plan), and their possible recommendations on study conduct will be defined and documented in the DMC Charter prior to the first DMC review.

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

This study is designed to evaluate the efficacy of JNJ-77242113 versus placebo and to evaluate the maintenance of response for JNJ-77242113. The sample size was also chosen to ensure a reasonable safety database to assess the overall safety of JNJ-77242113. These 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 and data from the JNJ-77242113 Phase 2b Study 77242113PSO2001.

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

Based on the above assumptions, a total of approximately 600 participants to be randomized in a 2:1 ratio to JNJ-77242113 200 mg once daily (n=400) or placebo (n=200) at Week 0 will provide >99% power to detect significant differences at a 2-sided significance level of 0.05 for both co-primary endpoints in the proportion of participants achieving an IGA score of cleared (0) or minimal (1) and the proportion of participants who achieve a PASI 90 response between the placebo and JNJ-77242113 groups at Week 16.

In addition, assuming approximately 75% of the adult participants originally randomized to JNJ-77242113 group are PASI 75 responders and will be randomized in a 1:1 ratio to either continue receiving JNJ-77242113 or undergoing withdrawal of JNJ-77242113 at Week 24. This portion of the study will ensure at least 95% power to detect a 20 percentage points of difference in PASI 75 response rates at Week 52 between these 2 groups.

Table 9 provides the power for detecting a treatment difference under varying assumptions for the primary and selected key secondary endpoints.

Table 9: Power to Detect a Treatment Effect Based on Different Proportions of Participants Achieving the Co-primary Endpoints at Week 16 and PASI 75 at Week 52

Co-primary Endpoints		
IGA cleared (0) or minimal (1) response at Week 16		
Placebo (n=200)	JNJ-77242113 (n=400)	Power
8%	60%	>99.9%
	64%	>99.9%
	70%	>99.9%
PASI 90 response at Week 16		
Placebo (n=200)	JNJ-77242113 (n=400)	Power
5%	50%	>99.9%
	55%	>99.9%
	59%	>99.9%

Table 9: Power to Detect a Treatment Effect Based on Different Proportions of Participants Achieving the Co-primary Endpoints at Week 16 and PASI 75 at Week 52

Select Key Secondary Endpoint **PASI 75 response at Week 52** **(difference of 20 percentage points)**		
Withdrawal Group (n=135)	JNJ-77242113 (n=135)	Power
60%	80%	95.2%
65%	85%	97.0%
70%	90%	98.6%

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 may include summaries across various time intervals if appropriate (e.g., through Week 16, through Week 24, through withdrawal/retreatment period, through reporting period, 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 will be provided

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 10 presents a list of the demographic variables that will be summarized by intervention group and overall for the full analysis set. Demographics will also be summarized by age group using the FAS.

Table 10: 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)	
BMI (kg/m2)	
Categorical Variables	
Age (<18, ≥18-<45, ≥45-<65, ≥ 65 years)	Frequency distribution with the number and percentage of participants in each category.
Sex (male, female, unknown, undifferentiated)	
Weight (≤90kg, >90kg)	
Race (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, PGA of disease activity, plaque psoriasis, facial psoriasis, and inverse psoriasis), and Patient Reported Outcomes at baseline (e.g., PSSD [total, sign, symptom score, and individual sore], DLQI, CDLQI, GenPs-SFQ, PROMIS-29 [domain scores, PCS, and MCS], PROMIS-25 domain scores, GenPs-SFQ, PsA pain, PsA disease activity, acceptability and palatability) will be summarized. In addition, summaries of participants' medical history, alcohol intake, and smoking status will be provided by treatment group.

6.3. Appendix 3 Protocol Deviations

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 and Concomitant Medications

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 on 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 [i.e., 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 Week 52 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 taken/total number of tablets 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 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, IL17, 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 52, 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 use for lab assessments is based on 'CCTCAE'.

If a laboratory value falls within the grading as specified below but also within the 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 J&J) 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
		
		Pediatric:
		Urine P/C (Protein/Creatinine) ratio 0.5 - 1.9;
		Urine P/C (Protein/Creatinine) 56.5 – 214.7 g/mol
			Adult:
			4+ proteinuria;
			urinary protein >=3.5 g/24 hrs;
			urinary protein >=3500 mg/day;
			
			Pediatric:
			Urine P/C (Protein/Creatinine) ratio >1.9;
			Urine P/C (Protein/Creatinine) >214.7 g/mol
				-	In case both 24-h urine collection and dipstick are collected, then worst case is taken, as opposed to having 24-h urine collection take precedence over dipstick. Added ranges in SI unit for urinary protein (mg/day) and for urine P/C (g/mol). Pediatric grading is applied to age range [0-18]. Adult grading is applied for ages [>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 – PROFILE v2.1 T-score

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		

6.10. Appendix 10 PROIMIS-25 T-score

PROMIS Pediatric – 25 v2.0 scoring tables

Anxiety 4b
Short Form Conversion Table

Raw Score	T-score	SE*
4	35.6	6.4
5	40.9	5.6
6	44.1	5.4
7	47.2	5.2
8	49.9	5.1
9	52.4	5
10	54.8	5
11	57.2	5
12	59.5	5
13	61.8	5
14	64	5.1
15	66.3	5.1
16	68.7	5.1
17	71.1	5.1
18	73.7	5.2
19	76.3	5.1
20	79.5	5.1

*SE = Standard Error

Depressive Symptoms 4b
Short Form Conversion Table

Raw Score	T-score	SE*
4	37.7	6.4
5	43.5	5.2
6	46.8	5
7	49.8	4.6
8	52.3	4.5
9	54.6	4.4
10	56.7	4.4
11	58.8	4.3
12	60.7	4.3
13	62.6	4.3
14	64.6	4.3
15	66.6	4.3
16	68.6	4.3
17	70.7	4.4
18	73	4.5
19	75.4	4.5
20	78.7	4.8

*SE = Standard Error

Fatigue 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	35.4	6.5
5	40.6	5.6
6	44.1	5.4
7	47.2	5.2
8	49.8	5.1
9	52.2	5
10	54.4	5
11	56.5	4.9
12	58.6	4.9
13	60.6	4.9
14	62.6	4.9
15	64.7	4.9
16	66.9	4.9
17	69.1	4.9
18	71.5	5
19	74.1	5
20	77.6	5.2

*SE = Standard Error

Mobility 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	20.1	4.4
5	23.1	4
6	25.1	3.9
7	26.9	3.9
8	28.4	3.8
9	30	3.8
10	31.5	3.8
11	32.9	3.8
12	34.4	3.8
13	35.9	3.8
14	37.6	3.9
15	39.3	4.1
16	41.2	4.4
17	42.9	4.2
18	45.5	4.4
19	48.9	4.7
20	57.1	7

*SE = Standard Error

Pain Interference 4a
Short Form Conversion Table

Raw Score	T- Score	SE*
4	36.7	6.1
5	42	4.9
6	44.4	4.8
7	47.2	4.4
8	49.3	4.3
9	51.3	4.1
10	53.2	4.1
11	55	4
12	56.7	4
13	58.4	4
14	60.1	4
15	61.8	4
16	63.6	4.1
17	65.5	4.1
18	67.7	4.2
19	70	4.3
20	74	4.9

*SE = Standard Error on T-score

Peer Relationships 4a
Short Form Conversion Table

Raw Score	T- Score	SE*
4	23	5.1
5	25.7	4.7
6	27.7	4.7
7	29.8	4.5
8	31.7	4.5
9	33.6	4.4
10	35.4	4.4
11	37.2	4.4
12	38.9	4.4
13	40.7	4.4
14	42.6	4.5
15	44.5	4.6
16	46.7	4.8
17	48.9	4.7
18	51.9	5.1
19	55.3	5.4
20	61.1	6.6

*SE = Standard Error on T-score

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