Janssen Research & Development

Statistical Analysis Plan

Multiple Phase 2b Studies Evaluating the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants with Moderate to Severe Psoriasis

Protocol JNJ77242113PSO2001 and 77242113PSO2002; Phase 2b

JNJ-77242113

This Statistical Analysis Plan Covers the Following 2 Studies:

1. **A Phase 2b Multicenter, Randomized, Placebo-controlled, Dose-ranging Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis (77242113PSO2001)**

2. **A Phase 2b Multicenter, Long-Term Extension, Dose-ranging Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis (J77242113PSO2002)**

Status: Approved
Date: 15 December 2022

Prepared by: Janssen Research & Development, LLC
Document No.: EDMS-RIM-790323, 1.0

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

TABLE OF CONTENTS

VERSION HISTORY

Table [xx] – SAP Version History Summary

SAP Version	Approval Date	Change	Rationale
1	15-December 2022	Not Applicable	Initial release

1. INTRODUCTION

77242113PSO2001 is a randomized, double-blind, placebo-controlled, dose-ranging, parallel group, multicenter, interventional study in participants with moderate-to-severe plaque psoriasis.

At Week 16 of 77242113PSO2001 study, eligible participants will have the option to enroll in a 36-week treatment long term extension (LTE) study (77242113PSO2002); all participants will be treated with active study intervention in the LTE.

This Statistical Analysis Plan (SAP) contains definitions of analyses sets, derived variables and address the statistical methods for all planned analyses for both 77242113PSO2001 (through the Week 16 Database lock (DBL)) and 77242113PSO2002 (through Week 40 database lock) studies as 77242113PSO2002 study is the long term extension (LTE) study of the original study (77242113PSO2001)

1.1. Objectives and Endpoints

1.1.1. JNJ-77242113PSO2001

Objectives	Endpoints
Primary	
To evaluate the dose response of JNJ-77242113 at Week 16 in participants with moderate-to-severe plaque psoriasis	Proportion of participants achieving PASI 75 (≥75% improvement from baseline in PASI) at Week 16
Secondary	
To characterize additional efficacy of JNJ-77242113 versus placebo in participants with moderate-to-severe plaque psoriasis	• Change from baseline in PASI total score at Week 16 • Proportion of participants achieving PASI 90 (≥90% improvement from baseline in PASI) at Week 16 • Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16 • Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16 • Proportion of participants achieving an IGA score of cleared (0) at Week 16 • Change from baseline in BSA at Week 16
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity versus placebo in participants with moderate-to-severe plaque psoriasis	• Change from baseline in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 16 • Change from baseline in PSSD signs score at Week 16 • Proportion of participants achieving PSSD symptoms score=0 at Week 16 among participants with a baseline symptoms score~~s~~ ≥1. • Proportion of participants achieving PSSD signs score=0 at Week 16 among participants with a baseline signs score ≥1.

Objectives	Endpoints
To evaluate the effect of JNJ-77242113 treatment on dermatology-specific health-related quality of life versus placebo in participants with moderate-to-severe plaque psoriasis	• Proportion of participants achieving a DLQI of 0 or 1 at Week 16 among participants with baseline DLQI score >1
To evaluate the effect of JNJ-77242113 treatment on general health-related quality of life versus placebo in participants with moderate-to-severe plaque psoriasis	• Change from baseline in domain scores of the Patient-Reported Outcomes Measurement Information System (PROMIS-29) at Week 16 • Proportion of participants who achieve at least a 5-point improvement from baseline in each PROMIS-29 domain at Week 16
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	• Frequency and type of AEs and SAEs
Exploratory	
To evaluate the PK and immunogenicity of JNJ-77242113, and explore the PK/PD relationship of JNJ-77242113 for biomarkers, efficacy, and safety in participants with moderate-to-severe plaque psoriasis	• JNJ-77242113 PK parameters (ie, plasma concentration just prior to the beginning or at the end of the dosing interval [Ctrough], C_{max}, tmax, and AUC) • The relationship between PK parameters and PD (ie, skin, blood cellular and molecular biomarker activity as well as clinical endpoints and safety parameters) • The incidence of anti-drug antibodies to JNJ-77242113
To characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis	• Proportion of participants achieving an ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline at Week 16 among those participants randomized with scalp psoriasis and an ss-IGA score ≥2 at baseline • Percent change from baseline in NAPSI at Week 16 among participants randomized with a NAPSI score >0 at baseline • Proportion of participants achieving an f-PGA score of clear (0) or minimal (1) at Week 16 among those participants randomized with nail psoriasis and an f-PGA ≥2 score at baseline • Proportion of participants who achieve an hf-PGA score of clear (0) or almost clear (1) and a reduction of at least 2 grades on the hf-PGA scale from baseline at Week 16 among those participants with hand and/or foot psoriasis and an hf-PGA score ≥2 at baseline • Proportion of participants achieving a sPGA of genitalia score of clear (0) or minimal (1) at Week 16 among participants randomized with

Objectives	Endpoints
	genital psoriasis and an sPGA of genitalia score ≥3 at baseline • Proportion of participants achieving a GenPs-SFQ item 2 score of never (0) or rarely (1) at Week 16 among those participants with a GenPs-SFQ item 2 score ≥2 at baseline
To further assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	• Frequency and type of related AEs, and AEs leading to discontinuation of study intervention • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time • Systolic and diastolic blood pressures over time
To explore biomarkers in participants with moderate-to-severe plaque psoriasis	• Change from baseline in levels of skin and blood biomarkers
To explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	• Assessment of treatment satisfaction domains at Week 16 using the Treatment Satisfaction Questionnaire for Medications-9 items (TSQM-9)

1.1.2. JNJ-77242113PSO2002

Objectives	Endpoints
Primary	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	Proportion of participants achieving Psoriasis Area and Severity Index (PASI) 75 (≥75% improvement in PASI from baseline of the originating* study) at Week 36
Secondary	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	• Proportion of participants achieving PASI 90 (≥90% improvement in PASI from baseline of the originating study) at Week 36 • Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) at Week 36 • Change from baseline of the originating study in PASI total score at Week 36 • Proportion of participants achieving an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) at Week 36
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis	• Change from baseline of the originating study in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 36 • Change from baseline of originating study in PSSD signs score at Week 36 • Proportion of participants achieving PSSD symptoms score=0 at Week 36 among participants with a baseline (in the originating study) symptoms score ≥1 • Proportion of participants achieving PSSD signs score=0 at Week 36 among participants with a baseline (in the originating study) signs score ≥1
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	• Frequency and type of adverse events (AEs) and serious adverse events (SAEs)

Objectives	Endpoints
Exploratory	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	• Proportion of participants achieving PASI 75 (≥75% improvement in PASI from baseline of the originating study) over time through Week 36 • Change from baseline of the originating study in PASI total score over time through Week 36 • Proportion of participants achieving PASI 90 (≥90% improvement in PASI from baseline of the originating study) over time through Week 36 • Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) over time through Week 36 • Proportion of participants achieving an IGA score of cleared (0) or minimal (1) over time through Week 36 • Proportion of participants achieving an IGA score of cleared (0) over time through Week 36 • Change from baseline of the originating study in body surface area (BSA) over time through Week 36
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis	• Change from baseline of the originating study in PSSD symptoms score over time through Week 36 • Change from baseline of the originating study in PSSD signs score over time through Week 36 • Proportion of participants achieving PSSD symptoms score=0 over time through Week 36 among participants with a baseline (in the originating study) symptoms score ≥1 • Proportion of participants achieving PSSD signs score=0 over time through Week 36 among participants with a baseline (in the originating study) signs score ≥1
To evaluate the effect of JNJ-77242113 treatment on dermatology-specific health-related quality of life (HRQoL) in participants with moderate-to-severe plaque psoriasis	• Proportion of participants achieving a Dermatological Life Quality Index (DLQI) of 0 or 1 over time through Week 36 among participants with a baseline (in the originating study) DLQI score >1
To evaluate the effect of JNJ-77242113 treatment on general HRQoL in participants with moderate-to-severe plaque psoriasis	• Change from baseline of the originating study in domain scores of the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) over time through Week 36

Objectives	Endpoints
	• Proportion of participants who achieve at least a 5-point improvement from baseline of the originating study in each PROMIS-29 domain over time through Week 36
To evaluate the pharmacokinetics (PK) and immunogenicity of JNJ-77242113, and explore the PK/pharmacodynamic (PD) relationship of JNJ-77242113 for biomarkers, efficacy, and safety in participants with moderate-to-severe plaque psoriasis	• JNJ-77242113 PK parameters (ie, plasma concentration just prior to the beginning or at the end of the dosing interval [C_{trough}], maximum observed plasma concentration [C_{max}], time to maximum plasma concentration [t_{max}], and area under the plasma concentration versus time curve [AUC]) • The relationship between PK parameters and PD, ie, blood cellular and molecular biomarker activity as well as clinical endpoints and safety parameters • The incidence of anti-drug antibodies (ADAs) to JNJ-77242113
To characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis	• Proportion of participants achieving a Scalp Specific Investigator Global Assessment (ss-IGA) score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline of the originating study over time through Week 36 among those participants with scalp psoriasis and an ss-IGA score ≥2 at baseline of the originating study • Percent change from baseline of the originating study in Nail Psoriasis Area and Severity Index (NAPSI) over time through Week 36 among participants with a NAPSI score >0 at baseline of the originating study • Proportion of participants achieving a Fingernail Physician's Global Assessment (f-PGA) score of clear (0) or minimal (1) over time through Week 36 among those participants with nail psoriasis and an f-PGA score ≥2 at baseline of the originating study • Proportion of participants who achieve a Physician's Global Assessment of Hands and/or Feet (hf-PGA) score of clear (0) or almost clear (1) and a reduction of at least 2 grades on the hf-PGA scale from baseline of the originating study over time through Week 36 among those participants with hand and/or foot psoriasis and an hf-PGA score ≥2 at baseline of the originating study • Proportion of participants achieving a Static Physician's Global Assessment (sPGA-G) of genitalia score of clear (0) or minimal (1) over time through Week 36 among participants with genital psoriasis and an sPGA-G of

Objectives	Endpoints
	genitalia score ≥ 3 at baseline of the originating study • Proportion of participants achieving a score of never (0) or rarely (1) in Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) item 2 over time through Week 36 among participants with a GenPs-SFQ item 2 score ≥2 at baseline of the originating study
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	• Frequency and type of related AEs, and AEs leading to discontinuation of study intervention • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time • Systolic and diastolic blood pressures over time
To explore biomarkers in participants with moderate-to-severe plaque psoriasis	• Change from baseline of the originating study in levels of blood biomarkers
To explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	• Assessment of treatment satisfaction domains over time through Week 36 using the Treatment Satisfaction Questionnaire for Medications-9 items (TSQM-9)

1.2. Study Design

1.2.1. JNJ-77242113PSO2001

This is a randomized, double-blind, placebo-controlled, dose-ranging, parallel group, multicenter, interventional study in participants with moderate-to-severe plaque psoriasis.

A target of 240 participants will be enrolled in this study with 40 participants planned per intervention group.

Participants will be instructed to take the study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water at approximately the same time every day. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking the study intervention and abstaining from food and liquid intake for at least 30 min after taking the study intervention. Dietary intake should be recorded per study manual.

The study intervention may be delivered directly to the participants from a courier as permitted by local requirements and/or regulations if approved by the Independent Ethics Committee (IEC)/ Institutional Review Board (IRB); Section 6.2 of the protocol. Details regarding delivery are provided in the study manual. The participant has the ability to opt-in or opt-out of using this service throughout the duration of the study.

Group 1: JNJ-77242113 (25 mg QD): Participants will receive JNJ-77242113 25 mg QD from Week 0 through Week 16

Group 2: JNJ-77242113 (50 mg QD): Participants will receive JNJ-77242113 50 mg QD from Week 0 through Week 16

Group 3: JNJ-77242113 (100 mg QD): Participants will receive JNJ-77242113 100 mg QD from Week 0 through Week 16

Group 4: JNJ-77242113 (25 mg BID): Participants will receive JNJ-77242113 25 mg BID from Week 0 through Week 16

Group 5: JNJ-77242113 (100 mg BID): Participants will receive JNJ-77242113 100 mg BID from Week 0 through Week 16

Group 6: Placebo: Participants will receive placebo BID from Week 0 through Week 16

At Week 16, eligible participants will have the option to enroll in a 36-week treatment long term extension (LTE) study; all participants will be treated with active study intervention in the LTE (77242113PSO2002).

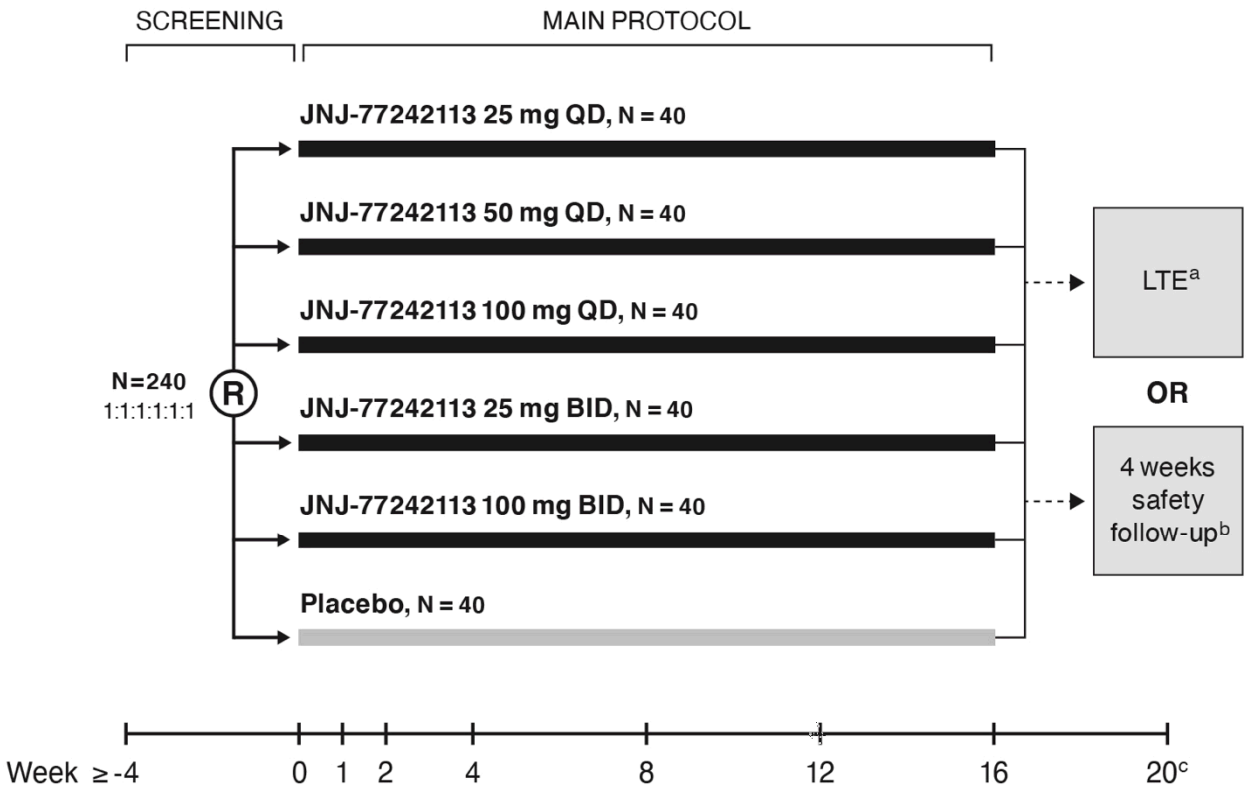
For JNJ-77242113PSO2001 study, one planned database lock (DBL) will occur at Week 16. Two interim analyses will occur in this study at Week 4 and Week 16, respectively.

At the time of the 77242113PSO2001 Week 16 DBL, Sponsor will be unblinded to perform the analyses and Phase 3 planning. Select Sponsor personnel will be unblinded to the individual treatment assignments, while others will only be unblinded to group level summaries. Details of the unblinding plan will be documented prior to DBL and unblinding. Investigators and sites will remain blinded until the end of 77242113PSO2002 (LTE study) study and the final database lock of the 77242113PSO2002 study.

For the interim analyses, group level summaries will be unblinded to Interim Analysis Committee (IAC) and the individual treatment assignment information will be unblinded to the Statistical Supporting Group (SSG) for analyses. The study team will not be unblinded to either the group level summaries or the individual treatment assignments at this time. The SSG and IAC must keep the treatment assignment information confidential until the study unblinding at the 77242113PSO2002 study Week 16 DBL or termination of the study. The investigator sites and participants will continue to be blinded to treatment assignment until the final database lock from 77242113PSO2002.

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

Figure 1: Schematic Overview of 77242113PSO2001



1.2.2. JNJ-77242113PSO2002

JNJ-77242113PSO2002 study is a multicenter, LTE, double-blind, dose-ranging, parallel group, interventional study in participants with moderate-to-severe plaque psoriasis.

All eligible participants from Protocol 77242113PSO2001 will be given the option to enroll in this LTE study, JNJ-77242113PSO2002.

All participants randomized to an active JNJ-77242113 dose regimen (25 mg QD, 50 mg QD, 100 mg QD, 25 mg BID, or 100 mg BID) in Protocol 77242113PSO2001 will continue to receive the same dosing regimen of JNJ-77242113 in this study in a blinded manner. Participants randomized to placebo in Protocol 77242113PSO2001 will receive JNJ-77242113 100 mg QD starting at Week 0 through the end of the treatment period in this study.

If the Week 0 visit for this study takes place on a different day as the Week 16 visit of study 77242113PSO2001, the sponsor and medical monitor must be notified. Approval from the medical

monitor or designee is required to enroll participants into study 77242113PSO2002 with a gap in study intervention administration between study 77242113PSO2001 and 77242113PSO2002.

The following JNJ-77242113 dosing regimens will be studied in this protocol:

Group 1: JNJ-77242113 (25 mg QD): Participants will receive JNJ-77242113 25 mg QD from Week 0 through Week 36

Group 2: JNJ-77242113 (50 mg QD): Participants will receive JNJ-77242113 50 mg QD from Week 0 through Week 36

Group 3: JNJ-77242113 (100 mg QD): Participants will receive JNJ-77242113 100 mg QD from Week 0 through Week 36

Group 4: JNJ-77242113 (25 mg BID): Participants will receive JNJ-77242113 25 mg BID from Week 0 through Week 36

Group 5: JNJ-77242113 (100 mg BID): Participants will receive JNJ-77242113 100 mg BID from Week 0 through Week 36

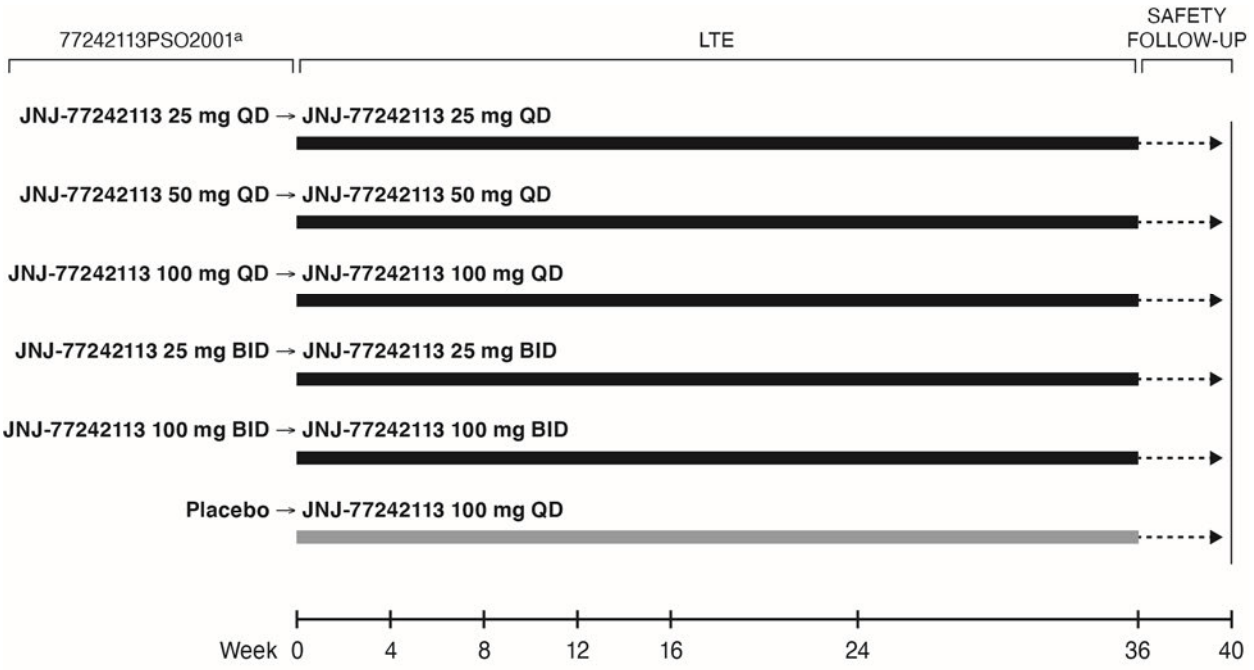
Group 6: Placebo → JNJ-77242113 (100 mg QD): Participants originally randomized to placebo in Protocol 77242113PSO2001 will receive JNJ-77242113 100 mg QD from Week 0 through Week 36

One planned database lock (DBL) will occur at Week 40. The study protocol may be amended at the sponsor's decision to extend the treatment period to provide participants access to one or more of the JNJ-77242113 doses. No formal interim analyses are planned for this study. However, selected efficacy, safety, and other data through Week 36 of this LTE study may be included in the interim analyses of the originating study (77242113PSO2001) for those participants who have entered the LTE study when the interim analyses occur. In addition, selected efficacy, safety, and other data through Week 36 of this LTE study may be included in the Week 16 DBL of the originating study (77242113PSO2001) for those participants who have entered the LTE study when the Week 16 DBL occur.

An external Independent Data Monitoring Committee (iDMC) has been commissioned for study 77242113PSO2001 and this study (77242113PSO2002) to review the safety data at an ongoing basis.

A diagram of the study design is provided in Figure 2.

Figure 2: Schematic Overview of 77242113PSO2002



[a] Participants who have completed study 77242113PSO2001 through Week 16 may be eligible to participate in this LTE study. All participants who were originally randomized to a JNJ-77242113 active dosing arm in study 77242113PSO2001 and enroll in this LTE study will continue to be treated with their assigned dosing regimens from study 77242PSO2001 in a blinded manner. All participants who were originally randomized to placebo in study 77242113PSO2001 will receive JNJ-77242113 100 mg QD starting at Week 0 through the end of this LTE study in a blinded manner.

BID = twice daily; LTE = long-term extension; QD = once daily

3695_v5

2. STATISTICAL HYPOTHESES

2.1. 77242113PSO2001

The hypothesis of this study is that there is a dose response relationship for JNJ-77242113 in the proportion of participants achieving a PASI 75 response at Week 16 in participants with moderate to severe psoriasis disease.

The null hypothesis to be tested is that there is no dose-response for the JNJ-77242113 doses and placebo in proportion of participants achieving a PASI75 response at Week 16 in participants with moderate to severe psoriasis disease.

2.2. 77242113PSO2002

The objective of this LTE study is to evaluate the long-term clinical response and safety of JNJ-77242113 treatment in participants with moderate-to-severe psoriasis. All of the analyses will be descriptive in order to evaluate the longer-term effects of efficacy and safety and no statistical hypothesis is specified.

3. SAMPLE SIZE DETERMINATION

3.1. 77242113PSO2001

This study is designed to enroll approximately 240 participants, in order to provide sufficient data to have adequate power to detect a JNJ-77242113 dose-response signal for the proportion of participants achieving PASI 75 at Week 16 using the Multiple Comparison Procedures with modeling techniques (MCP-Mod) method.

The sample size of 240 participants was also chosen in order to have sufficient power to detect a difference between the JNJ-77242113 groups and the placebo group for the primary endpoint of the proportion of participants achieving PASI 75 at Week 16.

The assumptions for the sample size and power calculations specified below were mainly based on the clinical data from the guselkumab Phase 2 and Phase 3 clinical studies that evaluated the safety and efficacy of guselkumab in the treatment of adult participants with moderate-to-severe plaque psoriasis.

The null hypothesis of no dose-response relationship is to be tested at an overall Type 1 error rate of 0.05 (2-sided). Assuming a PASI 75 response rate of 6% and 80% in the placebo and JNJ-77242113 highest dose groups, respectively, a sample size of approximately 40 participants in the placebo group and each of the JNJ-77242113 treatment groups will provide an average power of at least 95% to detect a dose-response signal across different candidate dose-response models. Table 1 and Table 2 below show the candidate dose response models and the power to detect a dose-response signal based on the primary endpoint of the proportion of participants achieving PASI 75 at Week 16 for various candidate models.

Table 1: Candidate Dose-response[a] Models

Model Type	Model specification[b]
E_{max} 1	dose/(35+dose) (ED_{50}=35)
E_{max} 2	dose/(50+dose) (ED_{50}=50)
Logistic	1/{1+exp[(35 –dose)/15]} (ED_{50}=35, δ=15)
SigEMax	$Dose^3/((35)^3+dose^3)$ (ED_{50}=35, h=3)
Linear	dose
Quadratic	dose-0.002*(dose**2) (δ=-0.002)

[a] Response is PASI 75 response at Week 16.
[b] A standardized version of the dose response model

Table 2: Summary of powers for each candidate models

Sample size Per Group	Emax 1	Emax 2	Logistic	SigEMax	Linear	Quadratic	Mean Power
40	>95%	>95%	>95%	>95%	>95%	>95%	>95%

Furthermore, assuming PASI 75 response rates at Week 16 are 5% to 10% for placebo, 30% to 80% for the JNJ-77242113 dose groups, respectively, with 40 participants in each of the treatment groups, approximately 240 participants are planned to be randomized in equal ratio to the placebo and each of JNJ-77242113 dose groups (n=40/arm), this study provides:

At least 90% power to detect a 35% treatment difference between the JNJ-77242113 treatment groups (n=40) and the placebo group (n=40) in the proportion of participants who achieve a PASI 75 response at Week 16 at a significant level of 0.05 (2-sided) based on a 2-sample Z-test.

3.2. 77242113PSO2002

Protocol 77242113PSO2002 is the LTE study of Protocol 77242113PSO2001, therefore there is no formal calculation of the sample size for study 77242113PSO2002. The sample size of this LTE study will be determined by the number of participants who enroll in study 77242113PSO2001 and are eligible to enter and choose to participate in this LTE study.

4. POPULATIONS (ANALYSIS SETS) FOR ANALYSIS

Unless specified otherwise, data included in the analyses for both studies are briefly summarized below:

4.1. 77242113PSO2001

All data available through Week 16 database lock of the 77242113PSO2001 study will be included. The populations for analysis are defined in Table 3 below.

Table 3: Populations for Analyses for 77242113PSO2001

Population	Description
Enrolled	All participants who signed the ICF
Randomized	All participants who were randomized in the study
FAS	All randomized participants who took at least 1 dose of study intervention
Per Protocol (PP)	The per protocol analysis set (PP) includes a subset of participants in the full analysis set (FAS) who were in compliance with the protocol. Compliance is defined as participants in FAS and meet the following criteria: • Has a total BSA ≥10% at the screening and baseline visit. • Has a total PASI score ≥12 at the screening and baseline visit • Gas a total IGA score ≥3 at the screening and baseline visit • Received all scheduled treatment and with overall compliance of study treatment at least 80% prior to Week 16, Or participants who did not completed all scheduled study intervention administration due to intercurrent events (i.e., discontinued the study intervention due to lack of efficacy, an AE of worsening of psoriasis, or started a protocol-prohibited medication or therapy during the study that could improve psoriasis)
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 complete 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
PD Analysis Set	All randomized participants who received at least 1 complete dose of JNJ-77242113

4.2. 77242113PSO2002

For selected subject's information and all safety analyses, combined data from 77242113PSO2001 and 77242113PSO2002 studies for participants initially randomized to JNJ-77242113, and who crossed over and received JNJ-77242113 for participants initially randomized to placebo will be included. In addition, safety data form 77242113PSO2002 data will also be summarized for randomized participants in 77242113PSO2001 who entered the long-term extension study 77242113PSO2002 and received at least one dose of study intervention (including a partial dose) during the 77242113PSO2002 study period. For efficacy and PK/PD analyses, efficacy and PK/PD data from 77242113PSO2001 and 77242113PSO2002 studies will be included and summarized.

The populations for analysis are defined in Table 4 below.

Table 4: Population for analysis for 77242113PSO2002

Population	Description
FAS	Randomized participants who received at least one dose of study intervention in the originating study (77242113PSO2001) for participants initially randomized to JNJ-77242113, and participants who crossed over and received JNJ-77242113 for participants initially randomized to placebo
Safety Analysis Set	Randomized participants who received at least one dose of study intervention in the originating study (77242113PSO2001) for participants initially randomized to JNJ-77242113, and participants who crossed over and received JNJ-77242113 for participants initially randomized to placebo
LTE Safety Analysis Set	The LTE safety analysis set consists of randomized participants in 77242113PSO2001 who entered the long-term extension study 77242113PSO2002 and received at least one dose of study intervention (including a partial dose) during the 77242113PSO2002 study period
PK Analysis Set	All participants in 77242113PSO2001 or 77242113PSO2002 who received at least 1 complete 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 participants in 77242113PSO2001 or 77242113PSO2002 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

Unless otherwise specified, all over-time (e.g., Week 0-52) efficacy analyses will be based on the Full Analysis Set (FAS), and safety analyses with cumulative safety data by combining studies JNJ-77242113PSO2001 and JNJ-77242113PSO2002 will be based on the Safety Analysis Set. All LTE-specific safety analyses (include data only from JNJ-77242113PSO2002 study) will be based on the LTE Safety Analysis Set.

5. STATISTICAL ANALYSES

5.1. General Considerations

Unless specified otherwise, efficacy data summaries will be provided by intervention group for the FAS for 77242113PSO2001 and 77242113PSO2002 respectively defined in Section 4.1 and Section 4.2. 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 (eg, line plots) and participant listings may also be used to summarize/present the data.

Study 77242113PSO2001

In addition, for binary response efficacy endpoints, comparisons between each of the JNJ-77242113 groups versus placebo will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by the baseline weight (≤90 kg, >90 kg). For continuous efficacy endpoints, treatment comparisons will be performed using a Mixed-Effect Model Repeated Measure (MMRM) model. The MMRM model will have treatment group, baseline weight (≤90 kg, >90 kg), and baseline value for the corresponding efficacy endpoint as explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, baseline weight (≤90 kg, >90 kg) by visit interaction, and baseline value by visit interaction as additional explanatory factors. The Least Square mean (LSmean) estimates and their corresponding 95% confidence interval (CI) will be provided at each time point. In addition, the estimates of LSmean difference and 95% CIs between the JNJ-77242113 groups and placebo will be provided.

In general, all statistical tests will be performed at a 2-sided significance level of α=0.05. No multiplicity adjustment will be made for the secondary endpoints being tested and nominal p-values will be reported.

The baseline measurement is defined as the closest measurement taken prior to or at the time of the first study agent administration date unless otherwise specified.

Study 77242113PSO2002

Study 77242113PSO2002 is the LTE study of the originating study 77242113PSO2001 and no formal hypothesis testing will be performed for the primary and secondary endpoints. The baseline data from the originating study (77242113PSO2001) will be used to calculate the change-from-baseline-related endpoints.

5.1.1. Visit Windows

The schedules for visits of the study will follow per protocol 'Schedule of Activities' table. Nominal visits will be used for all by-visit analyses in the study.

- 77242113PSO2001: Visits at Week 1 and Week 2 should occur within ± 2 days of the scheduled visit; and the visits after Week 2 though Week 16 should occur within ± 4 days of the scheduled visit.

- 77242113PSO2002: the visits through Week 36 should occur within ± 4 days of the scheduled visit.

5.1.2. Reference Date, Study Day and Relative Day

Study 77242113PSO2001

The Reference Date is the date of the first study agent administration in study 77242113PSO2001. If the date of the first study agent administration is missing or the first study agent administration is not done, then the Reference Date equals the corresponding visit date (eg, Week 0 visit date). If the corresponding visit date is also missing, then the Reference Date equals the randomization date. Study day is defined as the number of days from the study reference date to the event/visit date. It will be calculated as follows:

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

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

Study 77242113PSO2002

For summaries based on the combined data from studies 77242113PSO2001 and 77242113PSO2002 (eg, safety through Week 56 [Week 40 of the 77242113PSO2002 study]), the reference date of the study 77242113PSO2001 defined above will be used. Same calculation algorithm to calculate the study day specified above for study 77242113PSO2001 will be applied.

For summaries based on data from 77242113PSO2002 only (eg, safety from Week 0 through Week 40 of the 77242113PSO2002 study) the reference date is the date of the enrollment in study 77242113PSO2002. If the enrollment date is missing then the Reference Date equals the corresponding visit date (eg, Week 0 visit date of 77242113PSO2002). If the corresponding visit date is also missing, then the Reference Date equals the estimated Week 16 visit date of the participant in study 77242113PSO2001. Same calculation algorithm to calculate the study day specified above for study 77242113PSO2001 will be applied.

5.1.3. Treatment Groups

5.1.3.1. Study 77242113PSO2001

In the efficacy analyses, FAS (Section 4.1) will be used and the participants will be analyzed according to the randomized treatment groups they were assigned to, regardless of the treatments they actually received. Unless otherwise specified, efficacy analyses for placebo comparisons at Week 16 or through Week 16 will be summarized and displayed as follows:

- **Placebo**: Participants randomized to placebo group at Week 0.
- **JNJ-77242113 25 mg QD**: Participants randomized to 25 mg QD group at Week 0.
- **JNJ-77242113 50 mg QD**: Participants randomized to 50 mg QD group at Week 0.
- **JNJ-77242113 25 mg BID**: Participants randomized to 25 mg BID at Week 0.
- **JNJ-77242113 100 mg QD**: Participants randomized to 100 mg QD at Week 0.
- **JNJ-77242113 100 mg BID**: Participants randomized to 100 mg BID at Week 0.

5.1.3.2. Study 77242113PSO2002

Efficacy summaries for 77242113PSO2002 study will be based on the pooled data from both 77242113PSO2001 and 77242113PSO2002 studies, FAS (Section 4.2) will be used and participants will be summarized and presented by randomized treatment group at Week 0 of 77242113PSO2001 study:

- **Placebo→**: **JNJ-77242113 100 mg QD:** Participants randomized to placebo group at Week 0.
  - Only participants crossed over to receive JNJ-77242113 100 mg QD at Week 16 will be included in the summary for the visits after Week 16.
- **JNJ-77242113 25 mg QD**: Participants randomized to 25 mg QD group at Week 0.
- **JNJ-77242113 50 mg QD**: Participants randomized to 50 mg QD group at Week 0.
- **JNJ-77242113 25 mg BID**: Participants randomized to 25 mg BID at Week 0.
- **JNJ-77242113 100 mg QD**: Participants randomized to 100 mg QD at Week 0.
- **JNJ-77242113 100 mg BID**: Participants randomized to 100 mg BID at Week 0.

For the efficacy overtime analyses that combines the 77242113PSO2001 and 77242113PSO2002 studies, Week 4 visit of the study 77242113PSO2002 will be aligned as Week 20 for the combined study and will be denoted as "Week 20 (LTE Week 4)" in the summary table; similar notation will be applied for the subsequent visits of the study 77242113PSO2002.

5.2. Participant Dispositions

The number of screened participants 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

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

The above categories will include summaries over the placebo-controlled period (through Week 16) for study 77242113PSO2001 and through Week 52 for the combined study 77242113PSO2001 and study 77242113PSO2002.

In addition, a listing of participants who were randomized with incorrect stratum and a listing of participants who did not enter to 77242113PSO2002 study will be provided for 77242113PSO2001 study.

5.3. Primary Endpoint Analysis

5.3.1. Study 77242113PSO2001

5.3.1.1. Definition of Primary Endpoints

The primary efficacy endpoint is the proportion of participants achieving PASI 75 response at Week 16, defined as at least a 75% reduction from baseline in PASI total score.

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.

Efficacy endpoints related to the PASI score are defined below:

PASI 50 Responders

Participants with ≥50% improvement in PASI from baseline will be considered PASI 50 responders.

PASI 75 Responders

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

PASI 90 Responders

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

PASI 100 Responders

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

5.3.1.2. Estimands

Primary Trial Objective: To evaluate the dose response of JNJ-77242113 at Week 16 in participants with moderate-to-severe plaque psoriasis.

Estimand Scientific Question of Interest: What is the proportion of participants considered to have benefited from JNJ-77242113 versus placebo assessed by the PASI75 response at Week 16?

5.3.1.2.1. Primary Estimand (Estimand 1)

The primary estimand, based on the above primary objective, is defined by the following 5 attributes which assess the treatment effects not only based on the variable measurements, but also based on intercurrent events:

Study intervention:

- JNJ77242113 25 mg QD, 50 mg QD, 25 mg BID, 100 mg QD, and 100 mg BID.
- Placebo

Population: adult participants with moderate to severe psoriasis

Variable/endpoint: Binary response variable, where a responder is defined as a participant achieving a PASI75 response at Week 16. A participant with an intercurrent event in categories 1-2 defined below will be considered as a non-responder.

Intercurrent Events (ICEs) and their corresponding strategies.

ICEs	Analysis Strategy for Addressing Intercurrent Events
1. Discontinuation of study intervention due to lack of efficacy, or an AE of worsening of psoriasis prior to Week 16	**Composite Strategy:** Participants with these intercurrent event are considered as non-responders. The occurrence of these intercurrent events is captured in the variable definition.

2. Initiation of a protocol-prohibited medication or therapy during the study that could improve psoriasis prior to Week 16	
3. Discontinuation of study intervention for reasons other than ICE 1	**Treatment Policy:** observed data will be used regardless of whether or not this intercurrent event had occurred.

- ICEs 1 and 2 will be handled by the composite strategy, where the occurrence of the ICE will be incorporated into the variable definition. Participants experiencing ICE 1 or 2 will be considered not to have achieved the primary endpoint.
- ICE 3 will be handled using the treatment policy strategy regardless of the intercurrent event.

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

A list of Participants who experienced ICEs 1-3 will be provided.

Population level summary: Difference in the proportions of participants achieving a PASI 75 responses at Week 16 between the treatment groups.

5.3.1.2.2. Supplementary Estimands

The supplementary estimands defined below will be used for the pairwise comparisons of the analyses specified in Section 5.3.1.2.3.1.

5.3.1.2.2.1. Supplementary Estimand 1 (Hypothetical Estimand):

In this supplementary estimand, the only component that changes from the definition of the primary estimand is the hypothetical strategy will be used for addressing ICEs 1-3.

Hypothetical strategy: assess the treatment effect as if the intercurrent event would not have occurred. Under the hypothetical strategy, data collected after ICEs 1-3 will not be used in analysis and will be imputed using a MAR multiple imputation method.

5.3.1.2.2.2. Supplementary Estimand 2 (Treatment Policy Estimand):

This supplementary estimand has the same components as the primary estimand, except for the strategies used for ICEs 1-3.

Treatment policy strategy: assess the treatment effect regardless of whether or not intercurrent events had occurred. Under the treatment policy strategy, observed data collected after ICEs will be used in analysis.

5.3.1.2.3. Analysis Methods for the Primary Estimand

The primary endpoint will be analyzed based on the primary estimand (Section 5.3.1.2.1) and the data from all participants in FAS (Section 4.1) will include data from all randomized participants who received at least one administration of study intervention based on their assigned intervention group, regardless of the actual intervention received.

Participants with ICEs 1-2 before Week 16 will be considered as PASI75 non-responders at Week 16. Participants with ICE 3, observed PASI data after this ICE will be utilized in the analysis. After accounting for the ICEs for the primary estimand, participants with the missing data of the primary endpoint at Week 16 will be considered as non-responders.

The MCP-Mod will be used to test if there is a positive overall treatment effect based on candidate dose-response models. For each candidate model a contrast test statistic, based on a linear combination of the treatment estimates per dose will be derived. The contrast coefficients will be chosen to maximize the power to detect the pre-specified candidate models. The global test decision is based on the maximum of the contrast test statistics. The overall positive dose-response will be tested at a 2-sided 5% significance level. This procedure takes into account the multiplicity arising from testing several models and thus preserving the family wise Type I error rate.

CCI [redacted]

Generalized Multiple Comparison Modelling (gMCP-Mod)

To demonstrate the dose-response relationship across JNJ-77242113 treatment groups and placebo for the primary endpoint, the primary analysis will be based on a generalized Multiple Comparisons and Modeling (gMCP-Mod) analysis[1,2]. This analysis tests for a dose-response relationship, allowing for uncertainty in the dose-response relationship through inclusion of contrasts from multiple pre-specified candidate models to assess dose-response. If a dose-response relationship exists, then fitted estimates for the incidence of the primary endpoint will be calculated in each of the treatment groups using the selected dose-response models.

The gMCP-Mod procedure extends the MCP-Mod methodology to non-continuous endpoints. This is accomplished by decoupling the dose-response model from the expected response through the use of an ANOVA style parameterization of the dose-response parameter. For the binary endpoint used in this study, a logistic regression of the event proportion at each dose level will be used. After this first step, the mean parameter estimates from the logistic model and the corresponding covariance matrix, both of which are on the logit scale, will then be used during the rest of the gMCP-Mod procedure. Point estimates from the selected models will be displayed on the proportion scale in all statistical outputs.

Candidate Models and Multiple Testing Procedure

There are six candidate models (Section 3.1) that will be considered for the primary analysis. These are 2 Emax models (ED_{50} = 35 mg and 50 mg respectively), logistic model (ED_{50} = 35 mg, δ=15), SigEMax model (ED_{50} = 35 mg, h=3), linear model, and quadratic model (δ=-0.002) where dose-response will be tested using dose levels of 0 (placebo), and JNJ-77242113 treatment groups[4].

The gMCP-Mod procedure requires certain parameter estimates be pre-specified for the candidate models based on available information in order to derive optimum contrast coefficients for testing the null hypothesis: that a dose-response does not exist in any of the candidate models. It is through testing this hypothesis that the model which best describes the dose-response relationship will be identified. The parameters used to determine the contrast for testing will assume a placebo PASI 75 rate of 6% and maximum treatment effect be 74% (placeb-adjusted).

The gMCP-Mod procedure for non-continuous endpoints diverges from the original MCP-Mod procedure in the calculation of the optimum contrast coefficients. The gMCP-Mod methods that will be used to calculate the optimum contrast coefficients require the pre-specified model parameters from above along with the covariance matrix from the logistic regression in the first step. In practice, since the covariance matrix in the first step is based on actual data, the optimum contrast coefficients are recalculated when the actual data become available. The parameter estimates for the candidate models, however, will remain fixed.

For each candidate model, the contrast test statistic (z_m) is calculated as standardized linear combinations of the estimated event rate on the logit scale from the logistic regression using the optimal contrast coefficients associated with that candidate model. The optimal contrast coefficients are list in Table 5

A multiplicity-adjusted critical value will be determined from the joint multivariate normal distribution of the contrast test statistics at the overall one-sided alpha level of 0.025. If at least one of the test statistics exceeds this critical value, a dose-response relationship is demonstrated.

CCI

Table 5: Optimal contrast coefficients for each candidate response curve

Candidate models/Doses	0 mg	25 mg	50 mg	75 mg*	100 mg	300 mg**
EMax1 (ED_{50}=35)	-0.6154	-0.294	-0.0982	0.0773	0.2572	0.6731
Emax 2 (ED_{50}=50)	-0.5451	-0.3132	-0.1366	0.0382	0.2263	0.7304
Logistic (ED_{50}=35, δ=15)	-0.5557	-0.4825	-0.0921	0.2487	0.4277	0.453
SigEMax (ED_{50}=35, h=3)	-0.5656	-0.497	-0.0344	0.2295	0.3942	0.4732
Linear	-0.2081	-0.2206	-0.2132	-0.1741	-0.0917	0.9077
Quadratic (δ=-0.002)	-0.3778	-0.3314	-0.2289	-0.0578	0.1849	0.8109
* 25 mg BID ** 100 mg BID.						

Modelling and Estimation

The model for estimation will be selected from among the six candidate models with a contrast test statistic that is greater than or equal to the multiplicity-adjusted critical value. If 2 or more candidate models have such contrast test statistics, then these models will be employed using a weighted averaging technique based on their relative Akaike Information Criterion (AIC) , for the purposes of estimation. If no candidate model has a contrast test statistic that is greater than or equal to the multiplicity-adjusted critical value, then the analysis will end, indicating that a dose-response relationship cannot be established.

5.3.1.2.3.1. Pairwise Comparisons

In addition to the dose-response analysis, pairwise comparisons of each JNJ-77242113 treatment group versus the placebo group will be performed for the primary endpoint of PASI 75 at Week 16. Pairwise comparisons will not be adjusted for multiplicity. The Cochran-Mantel-Haenszel chi-square statistic stratified by baseline weight category (≤ 90 kg, > 90 kg) at a 2-sided significance level of 0.05 will be used. Difference in response rates between each of the active groups and the placebo group adjusted for baseline weight category (≤ 90 kg, > 90 kg) using Mantel-Haenszel weight and the corresponding 95% CI will be presented.

In addition, the proportion of participants achieving a PASI75 response at Week 16 by investigator site will be summarized.

5.3.1.2.4. Sensitivity Analysis

A simple semi-parametric Bayesian normal dynamic linear model (NDLM) will also be explored for does response to complement the frequentist gMCP-Mod analysis as a sensitivity analysis. This analysis will be performed through FACTS engine which will only be for internal use and will not be presented in Clinical Study Report (CSR).

A Bayesian approach will be used for this analysis. The longitudinal beta-binomial model will be used to analyze the primary endpoint PASI 75 at Week 16 in conjunction with participant's primary endpoint values.

$$Y_{di} \sim \text{Bernoulli}(P_d)$$

where Y_{di} is the PASI 75 outcome measures at 16 weeks for the i^{th} participant in arm d respectively. P_d is the underlying response rate for arm d. The response rates were transformed onto the log-odds scale to allow modeling on a continuous scale:

$$\theta_d = \log\left(\frac{P_d}{1 - P_d}\right).$$

The logit response rate is modeled through simple normal dynamic linear model (NDLM) for active dose groups while placebo group is modeled separately with the following non-informative priors derived from previous psoriasis studies:

$$\theta_d \sim N(-2.75,10)$$

Similar to the primary analysis, the sensitivity analysis will include data from all randomized participants who received at least one administration of study intervention (FAS, Section 4.1) based on their assigned intervention group, regardless of the actual intervention received.

Participants with ICEs 1-2 before Week 16 will be considered as PASI75 non-responders at Week 16. Participants with ICE 3, observed PASI data after this ICE will be utilized in the analysis. For participants experiencing multiple ICEs, an ICE 2 will override an ICE 3.

After accounting for the ICEs for the primary estimand, the remaining missing data of the primary endpoint at Week 16 will remain missing, and no imputation will be performed outside of the FACTS Engine. However, missing data will be imputed inside FACTS Engine by multiple imputation when performing the model-based analysis using Bayesian longitudinal model.

5.3.1.2.5. Analysis for Supplementary Estimands

The analyses specified below for supplementary estimands will be applied to the pairwise comparisons for the primary endpoint.

5.3.1.2.5.1. Supplementary Analysis 1 (Hypothetical Estimand)

Under this estimand, PASI 75 response will be considered missing after intercurrent events; and after accounting for the ICEs, all other missing data will be remaiining missing. All missing data will then be imputed using multiple imputations (MI) by fully conditional specification (FCS).

More specifically, the missing PASI75 responses will be imputed with FCS logistic regression including treatment group, baseline PASI score, and PASI75 response status through Week 16 in the model with seed = 789 and 500 imputations. The proportion difference of PASI75 response between each JNJ-77242113 group and placebo group at Week 16 adjusted for baseline weight category (≤ 90 kg, > 90 kg) using Mantel-Haenszel weight and its 95% CI combining multiple datasets will also be provided. A CMH test stratified by baseline weight category (≤ 90 kg, > 90 kg) will be used to obtain the CMH statistic for each imputed dataset.

The values of the general association test statistics from the CMH test for each imputed dataset will be transformed using the Wilson-Hilferty transformation 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 and obtain the overall p-value for the CMH test. Difference in PASI75 response rates at Week 16 between each of the active intervention groups and the placebo group at Week 16 adjusted for baseline weight category using Mantel-Haenszel weight and its 95% CI combining multiple datasets will also be provided.

5.3.1.2.5.2. Supplementary Analysis 2 (Treatment Policy Estimand)

The primary endpoint will also be analyzed utilizing the treatment policy estimand. For participants who experience an intercurrent event through Week 16, the analysis will be performed using observed data regardless of intercurrent events. Missing data will be imputed using multiple imputation method specified in Section 5.3.1.2.5.1.

5.3.1.2.6. Per Protocol Analysis

The primary efficacy endpoint will be evaluated for pairwise comparison in the PP population based on the primary estimand except that ICE 3 will not be applied. Participants with ICE 3 who do not complete all scheduled study administration prior to Week 16 will be excluded from the per protocol analysis. The same data handling rule and analysis method specified in Section 5.3.1.2.3 will be applied.

5.3.2. Study 77242113PSO2002

5.3.2.1. Definition of Primary Endpoint

The primary efficacy endpoint of 77242113PSO2002 study is the proportion of participants achieving PASI 75 at Week 36, defined as at least a 75% improvement in PASI from baseline of the originating study (77242113PSO2001). The definition of PASI responses is described in Section 5.3.1.1

5.3.2.2. Estimands

5.3.2.2.1. Primary Estimand

In this primary estimand, the components that are different from the definition of the primary estimand of study 77242113PSO2001 are the intervention attribute, Variable/endpoint, and Population level summary; and all other components are the same as the primary estimand as specified in Section 5.3.1.2.1.

Study intervention: JNJ-77242113 25 mg QD, 50 mg QD, 25 mg BID, 100 mg QD, 100 mg BID, and placebo → 100 mg QD

Variable/endpoint: Binary response variable, where a responder is defined as a participant achieving a PASI75 response at Week 36. A participant with an intercurrent event in categories 1-2 defined in Section 5.3.1.2.1 will be considered as a non-responder.

Population level summary: Descriptive summary statistics for the proportions of participants achieving a PASI 75 responses at Week 36 for each of the treatment groups.

Note: If the Week 0 visit for study 77242113PSO2002 takes place on a different day as the Week 16 visit of study 77242113PSO2001with a gap greater than 4 weeks, the participants are allowed to take medications specified in 77242113PSO2002 that could improve psoriasis after 4 weeks from the Week 16 visit of study 77242113PSO2001 and before entering the study of 77242113PSO2002; ICE 2 specified in Section 5.3.1.2.1 will not be applied in this situation.

5.3.2.3. Analysis Methods for Primary Estimand

The primary efficacy analysis for study 77242113PSO2002 will be based on the FAS defined in Section 4.2. Since there is no control arm (placebo), in this primary analysis, only the proportion of participants who achieve a PASI75 response and its 95% confidence interval at Week 36 will be summarized for each intervention group.

The data handling method specified in Section 5.3.1.2.3 will be applied. More specifically, participants with ICEs 1-2 before Week 36 will be considered as PASI75 non-responders at Week 36. Participants with ICE 3, observed PASI data after this ICE will be utilized in the analysis. After accounting for the ICEs for the primary estimand, participants with the missing data of the primary endpoint at Week 36 will be considered as non-responders.

5.4. Secondary Endpoints Analysis

5.4.1. Study 77242113PSO2001

5.4.1.1. Multiplicity Adjustment for Testing Procedures

No multiplicity adjustment will be made for the secondary endpoints for study 77242113PSO2001. All statistical testing will be performed at the 2-sided 0.05 significance level. Nominal p-values will be presented.

5.4.1.2. Secondary Endpoint(s)

The secondary objectives are: (a) To characterize additional efficacy of JNJ-77242113 versus placebo, (b) To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity versus placebo and (c) To evaluate the effect of JNJ-77242113 treatment on dermatology-specific and general health-related quality of life versus placebo in participants with moderate-to-severe plaque psoriasis.

The secondary endpoints to address these objectives are the following:

To characterize additional efficacy of JNJ-77242113 versus placebo

1. Proportion of participants achieving PASI 90 (≥ 90% improvement from baseline in PASI) at Week 16
2. Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16
3. Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16
4. Proportion of participants achieving an IGA score of cleared (0) at Week 16
5. Change from baseline in PASI total score at Week 16
6. Change from baseline in BSA at Week 16

To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity versus placebo

7. Change from baseline in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 16

8. Change from baseline in PSSD signs score at Week 16

9. Proportion of participants achieving PSSD symptoms score=0 at Week 16 among participants with a baseline symptoms score ≥1.

10. Proportion of participants achieving PSSD signs score=0 at Week 16 among participants with a baseline signs score ≥1.

To evaluate the effect of JNJ-77242113 treatment on dermatology-specific and general health-related quality of life versus placebo

11. Proportion of participants achieving a DLQI of 0 or 1 at Week 16 among participants with baseline DLQI score >1

12. Change from baseline in domain scores of the Patient-Reported Outcomes Measurement Information System (PROMIS-29) at Week 16

13. Proportion of participants who achieve at least a 5-point improvement from baseline in each PROMIS-29 domain at Week 16

5.4.1.2.1. Definition of Endpoint(s)

5.4.1.2.1.1. Psoriasis Area and Severity Index (PASI)

Details refer to section 5.3.1.1.

5.4.1.2.1.2. Investigator's Global Assessment (IGA)

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

5.4.1.2.1.3. Body Surface Area (BSA)

Body Surface Area is a commonly used measure of severity of skin disease. It is defined as the percentage of surface area of the body involved with the condition being assessed, (ie, plaque psoriasis). The handprint method for assessing BSA will be used in this study, where the surface area of the patient's hand including the palm and all five digits is used as a guide to estimate 1% BSA.

5.4.1.2.1.4. Psoriasis Symptom and Sign Diary (PSSD)

The PSSD includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit. This study uses a 7-day recall version of the PSSD that asks the participant to answer the questions thinking about the last 7 days. The PSSD is a self-administered PRO instrument and includes 11 items covering symptoms (itch, pain, stinging, burning, and skin tightness) and patient-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, and bleeding) using 0 to 10 numerical rating scales for severity. Two

sub-scores are derived each ranging from 0 to 100: the psoriasis symptom score and the psoriasis sign score. A higher score indicates more severe disease.

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

Symptom Score (0-100)

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

b. Averaging items on 7 days recall symptom scores when at least 3 items (≥50% of 5 items) on this scale are answered. Then, the average value is converted into 0-100 scoring such that Symptom score = average value x 10 with 0 representing the least severe and 100 the most severe.

Sign Score (0-100)

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

b. Averaging items on 7 days recall sign scores when at least 3 items (≥50% of 6 items) on this scale are answered. Then, the average value is converted into 0-100 scoring such that Sign score = average value x 10 with 0 representing the least severe and 100 the most severe.

5.4.1.2.1.5. Dermatological Life Quality Index (DLQI)

The DLQI is a dermatology-specific health-related quality of life (HRQoL) instrument designed to assess the impact of the disease on a participant's HRQoL. It is a 10-item questionnaire that assesses HRQoL over the past week and in addition to evaluating overall HRQoL, 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 total score ranges from 0 to 30 with a higher score indicating greater impact on QoL

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

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

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

The PROMIS-29 is a 29-item generic HRQoL survey, assessing each of the 7 PROMIS domains (depression; anxiety; physical function; pain interference; fatigue; sleep disturbance; and ability to

participate in social roles and activities) with 4 questions. The questions are ranked on a 5-point Likert Scale. There is also one 11-point rating scale for pain intensity.

The raw score of each domain is converted into a standardized score with a mean of 50 and a standard deviation (SD) of 10 (T-Score). The standardized T-score is reported as the final score for each participant. Pain Intensity is presented as raw responses (0-10). For PROMIS domains of Depression, Anxiety, Physical Function, Pain Interference, Fatigue, a score of 50 is the average for the United States general population with a standard deviation of 10, because testing was performed on a large sample of the general population. However, the other two domains (Ability to Participate in Social Roles and Activities and Sleep Disturbance) were not centered in a national sample. For these two domains, a score of 50 represents the average of the calibration sample which was generally more enriched for chronic illness, and a score of 50 likely represents somewhat sicker people than the general population. A higher PROMIS T-score represents more of the concept being measured. For negatively-worded concepts like Anxiety, a T-score of 60 is one SD worse than average. By comparison, an Anxiety T-score of 40 is one SD better than average. However, for positively-worded concepts like Physical Function, a T-score of 60 is better than average while a T-score of 40 is better. Participants will undergo this assessment at time points according to the SoA.

5.4.1.2.2. Main Estimands for Secondary Endpoints

The secondary endpoints will be analyzed similarly as the primary estimand described in section 5.3.1.2.1 as the main estimand. The main estimand will be considered for both binary and continuous secondary endpoints. The analysis strategy for ICEs and missing data will be handled in the same manner as the primary estimand for the primary endpoint

- ICEs 1-2: Composite strategy
- ICE 3: Treatment policy strategy

The study intervention and population are the same as the primary estimand.

BINARY ENDPOINTS

Variables and Population-level Summary: Difference in the proportions of participants achieving a clinical response (eg, PASI 90 responses at Week 16) between the treatment groups. The variables and population level summaries for the other secondary binary endpoints are similarly described.

CONTINUOUS ENDPOINTS

Variable (Endpoint): change from baseline to Week 16 (change = Week 16 - baseline).

- Participants who have intercurrent events in categories 1, 2 through Week 16 will have a zero change from baseline assigned from the point of the ICE, regardless of the observed data.

Population-level summary: LSMean difference in change from baseline in eg, change from baseline in total PASI score at Week 16 between JNJ-77242113 treatment groups and the placebo group. The variables and population -level summaries for the other secondary continuous endpoints are similarly described.

5.4.1.2.3. Supplementary Estimands

The supplementary estimands defined in Section 5.3.1.2.2.1 (Hypothetical Strategy) and Section 5.3.1.2.2.2 (Treatment Policy Strategy) for the primary endpoint will also be used for selected binary secondary endpoints:

- Proportion of participants achieving PASI 90 (≥ 90% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) at Week 16

The following table provides the list of variables, summary measure (population-level summary) and intercurrent event strategy for secondary endpoints.

Secondary Endpoint	Variable	Summary Measure (Population-level summary)	Intercurrent Event Strategy
1	Binary response variable, where a responder is defined as a participant achieving a PASI 90 response at Week 16	Difference in the proportions of participants achieving a PASI 90 response at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.1.2.1 and two supplementary estimands specified in section 5.3.1.2.2.
2	Binary response variable, where a responder is defined as a participant achieving a PASI 100 response at Week 16	Difference in the proportions of participants achieving a PASI 100 response at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.1.2.1 and two supplementary estimands specified in section 5.3.1.2.2.
3	Binary response variable, where a responder is defined as a participant achieving an IGA scores of cleared (0) or minimal (1) at Week 16	Difference in the proportions of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.1.2.1 and two supplementary estimands specified in section 5.3.1.2.2.

4	Binary response variable, where a responder is defined as a participant achieving an IGA scores of cleared (0) at Week 16	Difference in the proportions of participants achieving an IGA score of cleared (0) at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand as specified in section 5.3.1.2.1 and two supplementary estimands specified in section 5.3.1.2.2.
5	Continuous variable, change from baseline in PASI score at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline in PASI at Week 16 between JNJ-77242113 treatment groups and the placebo group.	Same analysis strategies as the primary estimand specified in section 5.4.1.2.2
6	Continuous variable, change from baseline in BSA at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline atWeek 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.4.1.2.2
7	Continuous variable, change from baseline in PSSD symptoms score at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.4.1.2.2
8	Continuous variable, change from baseline in PSSD sign at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.4.1.2.2
9	Binary response variable, where a responder is defined as a participant with baseline symptom score ≥ 1 and achieving PSSD symptom score =0 at Week 16	Difference in the proportions of participants achieving efficacy responses at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.3.1.2.1.
10	Binary response variable, where a responder is defined as a participant with baseline sign score ≥ 1 and achieving a PSSD signs score of 0 at Week 16	Difference in the proportions of participants achieving a PSSD signs score of 0 at Week 16 between JNJ-77242113	Same analysis strategies as the primary estimand specified in section 5.3.1.2.1.

		treatment groups and placebo group.	
11	Binary response variable, where a responder is defined as a participant with baseline DLQI score > 1 and achieving a DLQI score of 0 or 1 at Week 16	Difference in the proportions of participants achieving a DLQI score of 0 or 1 at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.3.1.2.1.
12	Continuous variable, change from baseline in domain scores of the Patient-Reported Outcomes Measurement Information System (PROMIS-29) symptom at Week 16 (change = Week 16 - baseline)	LSMean difference in change from baseline at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.4.1.2.2
13	Binary response variable, where a responder is defined as a participant achieving at least a 5-point improvement from baseline in each PROMIS-29 domain at Week 16	Difference in the proportions of participants achieving at least a 5-point improvement from baseline in each PROMIS-29 domain at Week 16 between JNJ-77242113 treatment groups and placebo group.	Same analysis strategies as the primary estimand specified in section 5.3.1.2.1.

5.4.1.3. Analysis Methods

The secondary efficacy analysis of data for study 77242113PSO2001 will be based on the FAS defined in Section 4.1. The endpoints will be summarized by intervention group. Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for continuous variables and counts and percentages for discrete variables will be used to summarize most data. All statistical testing will be performed at a 2-sided 0.05 significance level. Nominal p-values will be presented. No adjustments for multiple comparisons will be made for the secondary endpoints.

5.4.1.3.1. Binary Endpoints

The binary secondary endpoints at Week 16 will be analyzed using the estimands described in section 5.4.1.2.2. The analysis strategy for ICEs and missing data will be handled in the same manner as the primary estimand for the primary analysis (Section 5.3.1.2.3). The proportions of participants for the above secondary efficacy endpoints will be summarized for each intervention group.

The Cochran-Mantel-Haenszel chi-square statistic stratified by baseline weight category (≤ 90 kg, > 90 kg) at a 2-sided significance level of 0.05 will be used. Difference in response rates between

each of the active and placebo groups at Week 16 adjusted for baseline weight category (≤ 90 kg, > 90 kg) using Mantel-Haenszel weight and the corresponding 95% CI will be presented.

In case of rare events, the Fisher's Exact test will be used for treatment comparisons in binary response endpoints. The proportion differences between JNJ-77242113 groups and placebo and the exact confidence intervals will be provided.

5.4.1.3.1.1. Analysis for Supplementary Estimands

Similar to the primary analysis of pair comparison, the analyses specified in Section 5.3.1.2.5.1 (Hypothetical Estimand) and Section 5.3.1.2.5.2 (Treatment Policy Estimand) for supplementary estimands will be applied to the following secondary endpoints:

- Proportion of participants achieving PASI 90 (≥ 90% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving PASI 100 (100% improvement from baseline in PASI) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 16
- Proportion of participants achieving an IGA score of cleared (0) at Week 16

5.4.1.3.2. Continuous Endpoints

Unless otherwise specified, the analyses for continuous secondary endpoints at Week 16 will be based on the following strategies to handle ICEs and missing data.

- ICEs in categories 1 - 2 in the primary estimand (definitions in Section 5.3.1.2.1) will be handled with the Composite Strategy. Participants experiencing ICEs 1-2 will have a zero change (or zero improvement) from baseline assigned from that point onward.
- ICEs in categories 3 in the primary estimand (definitions in Section 5.3.1.2.1) will be handled by the Treatment Policy strategy. The analysis will be performed using observed data regardless of intercurrent events. For participants experiencing multiple ICEs, an ICE in categories 2 of the primary estimand will override an ICE in category 3.
- Missing data will not be imputed after applying the rules for intercurrent events.

To account for the missing data for continuous endpoints of change (or percent change) from baseline measured at more than one post-baseline visit, a MMRM will be used. In MMRM, missing data will not be imputed, but rather missing data will be accounted for through correlation of repeated measures in the model.

Treatment comparisons for the secondary continuous endpoints at Week 16 will also be performed using a Mixed-Effect Model Repeated Measure (MMRM) model under the assumption of missing at random (MAR) with intervention group, visit, baseline weight category (≤ 90 kg, > 90 kg), baseline value for the efficacy endpoint, treatment by visit, baseline weight category by visit and baseline value by visit interaction as explanatory factors, if appropriate. 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.

5.4.2. Study 77242113PSO2002

5.4.2.1. Multiplicity Adjustment for Testing Procedures

Similar to the primary endpoint analysis of study 77242113PSO2002, since there is no reference arm (placebo), no statistical comparisons will be performed for the secondary endpoints.

5.4.2.2. Secondary Endpoints

The secondary objectives of this study are: (a) To evaluate long-term clinical response of JNJ-77242113 treatment and (b) To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis.

The secondary endpoints to address these objectives are the following:

To evaluate long-term clinical response of JNJ 77242113 treatment

1. Proportion of participants achieving PASI 90 (≥90% improvement in PASI from baseline of the originating study) at Week 36
2. Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) at Week 36
3. Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 36
4. Change from baseline of the originating study in PASI total score at Week 36

To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity

5. Change from baseline of the originating study in PSSD symptoms score at Week 36
6. Change from baseline of originating study in PSSD signs score at Week 36
7. Proportion of participants achieving a PSSD symptoms score of 0 at Week 36 among participants with a baseline (in the originating study) symptoms score ≥1
8. Proportion of participants achieving a PSSD signs score of 0 at Week 36 among participants with a baseline (in the originating study) signs score ≥1

5.4.2.2.1. Definition of Endpoints

5.4.2.2.1.1. Psoriasis Area and Severity Index (PASI)

Details refer to section 5.3.1.1.

5.4.2.2.1.2. Investigator's Global Assessment (IGA)

Details refer to section 5.4.1.2.1.2.

5.4.2.2.1.3. Psoriasis Symptom and Sign Diary (PSSD)

Details refer to section 5.4.1.2.1.4.

5.4.2.2.2. Estimand for Secondary Endpoints

Same analysis strategies as the main estimand of the study 77242113PSO2001 specified in section 5.4.1.2.2. will be used

- ICEs 1 - 2 in the primary estimand (definitions in Section 5.3.1.2.1)will be handled with the Composite Strategy.
- ICE 3 in the primary estimand will be handled with Treatment Policy strategy

5.4.2.2.3. Analysis Methods

Unless otherwise specified, the analysis population will be based on FAS defined in Section 4.2, more specifically, randomized participants who received at least one dose of study intervention in the originating study (77242113PSO2001) for participants initially randomized to JNJ-77242113, and participants who crossed over and received JNJ-77242113 for participants initially randomized to placebo.

Similar to the secondary endpoint efficacy analyses for study 77242113PSO2001, the endpoints will be summarized by intervention group. Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for continuous variables and counts and percentages for discrete variables will be used to summarize most data. No formal statistical testing will be performed. The baseline data from the originating study (77242113PSO2001) will be used to calculate the change-from-baseline-related endpoints.

Binary Endpoints

The analysis strategy for ICEs and missing data will be handled in the same manner as the primary estimand for the primary endpoint of 77242113PSO2002 (Section 5.3.2.3). The proportions of participants who achieved a clinical response and its 95% confidence interval for the above binary secondary efficacy endpoints will be provided for each intervention group.

Continous Endpoints

Unless otherwise specified, the analyses for continuous secondary endpoints at Week 36 and other time points will be based on the strategies specified in Section 5.4.1.3.2 to handle ICEs and missing data.

- ICEs 1 - 2 in the primary estimand (definitions in Section 5.3.1.2.1) will be handled with the composite strategy. Participants experiencing ICEs 1-2 will have a zero change (or zero improvement) from baseline assigned from that point onward.

- ICE 3 in the primary estimand (definitions in Section 5.3.1.2.1) will be handled by the treatment policy strategy. The analysis will be performed using observed data regardless of intercurrent events. For participants experiencing multiple ICEs, ICE 2 will override an ICE 3.

- Missing data will not be imputed after applying the rules for intercurrent events.

For continuous endpoints, the change from baseline at each week will be analyzed using a restricted maximum likelihood-based mixed model for repeated measures with fixed effects for treatment, visit, stratification factor of baseline weight category (≤ 90 kg, >90 kg), baseline value, baseline value by week interaction, baseline weight category by week interaction, and the treatment-by-week interaction. 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. Least Square means (LSmeans) and their corresponding 95% confidence interval will be provided, and no statistical testing will be performed.

5.5. Exploratory Endpoint(s) Analysis

5.5.1. Study 77242113PSO2001

Objective: To characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis and to explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis

In addition to the primary and secondary efficacy endpoints, the analyses for exploratory efficacy endpoints (including the over time summaries through Week 16) will be performed. These efficacy endpoints include the endpoints related to

- PASI
- IGA
- BSA
- Patient-reported Outcomes

  PSSD

  DLQI

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

  Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)

  Patient Global Impression- Severity (PGI-S) and Change (PGI-C)

In addition, to characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis and to explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis, the following exploratory endpoints will be evaluated at Week 16 and over time.

- To characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis:

  Nail Psoriasis Area and Severity Index (NAPSI)

  Fingernail Physician's Global Assessment (f-PGA)

  Static Physician's Global Assessment of Genitalia (sPGA-G)

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

  Scalp Specific Investigator Global Assessment (ss-IGA)

- To explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis

  Treatment Satisfaction Questionnaire for Medications (TSQM-9 domains)

5.5.1.1. Endpoint Definitions

5.5.1.1.1. Psoriasis Area and Severity Index (PASI)

Details refer to section 5.3.1.1

5.5.1.1.2. Investigator's Global Assessment (IGA)

Details refer to section 5.4.1.2.1.2

5.5.1.1.3. Body Surface Area (BSA)

Details refer to section 5.4.1.2.1.3

5.5.1.1.4. Psoriasis Symptom and Sign Diary (PSSD)

Details refer to section 5.4.1.2.1.4

5.5.1.1.5. Dermatological Life Quality Index (DLQI)

Details refer to section 5.4.1.2.1.5

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

Details refer to section 5.4.1.2.1.6

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

The GenPs-SFQ is a 2-item patient reported survey 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 two 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]).

The analyses for GenPs-SFQ item 2 will be based on participants randomized at Week 0 with a GenPs-SFQ item 2 score ≥2 at baseline.

5.5.1.1.8. Patient Global Impression- Severity (PGI-S) and Change (PGI-C)

Interpreting meaningful change in scores on PRO instruments is an important step in evaluating results and is included in FDA guidelines. The methods for interpreting meaningful change have evolved over time and various approaches exist. Anchor-based methods are often preferred. Anchor-based methods link scores on the PRO to an external criterion that identifies participants who have experienced an important change in their condition. The PGI-S and PGI-C will be used as anchors, external criteria, to determine meaningful change in scores for other PROs in this population. The PGI-S contains 1 question on how the participant would currently rate severity of disease in the past 7 days, with responses ranging from 1=”None” to 5=”Very severe.” The PGI-C contains 1 question on how the participant would rate the change from their first treatment in this study. The response options are presented on a 7-point scale from 1="A lot better now” to 7="A lot worse now.”

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

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

The analyses for ss-IGA will be based on Participants randomized at week 0 with scalp psoriasis and an ss-IGA score ≥2 at baseline.

5.5.1.1.10. Nail Psoriasis Area and Severity Index (NAPSI)

The NAPSI is an index used for assessing and grading the severity of nail psoriasis. Each of the participant’s 20 nails (fingernails and toenails) is divided into quadrants and is assessed for any presence of nail psoriasis in the nail matrix (pitting, leukonychia, red spots in the lunula, and nail plate crumbling) and any presence of nail psoriasis in the nail bed (onycholysis, splinter hemorrhages, oil drop discoloration, and nail bed hyperkeratosis). Both the nail matrix (score 0-4) and nail bed (score 0-4) scores equal the number of quadrants affected by nail/nailbed psoriasis. The total individual nail score is the sum of the nail matrix and nail bed score and ranges from 0 to 8. The sum of all 20 individual nail scores is the total NAPSI score (0 to 160).

The analyses related to NAPSI will be based on Participants randomized at Week 0 with nail psoriasis present at Week 0.

5.5.1.1.11. Fingernail Physician’s Global Assessment (f-PGA)

The f-PGA is used to evaluate the current status of a participant’s fingernail psoriasis on a scale of 0 to 4 similar to the IGA (clear [0], minimal [1], mild [2], moderate [3], or severe [4]).

The analyses for f-PGA will be based on participants randomized at Week 0 with nail psoriasis and an f-PGA score greater than or equal to 2 at baseline.

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

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

The analyses for hf-PGA will be based on participants randomized at Week 0 with hand and/or foot psoriasis and an hf-PGA score greater than or equal to 2 at baseline.

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

The sPGA-G is a 6-point numerical rating scale to assess the severity of genital psoriasis at a given time point. 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].

The analyses for sPGA-G will be based on participants randomized at Week 0 with genital psoriasis and an sPGA of genitalia score ≥3 at baseline.

5.5.1.1.14. Treatment Satisfaction Questionnaire for Medications (TSQM-9 domains)

The abbreviated 9-item TSQM-9 includes 3 treatment satisfaction domains: effectiveness, convenience, and global satisfaction. Positive changes in domain scores (0 to 100) indicate improvement. The questions are ranked on a 5-point or 7-point Likert Scale (Bharmal 2009).

The calculations specific to each domain are presented in detail below:

- Effectiveness: (Item 1 + Item 2 + Item3) – 3] divide by 18) * 100; if one item is missing, use [(sum of the two completed items)) – 2] divide by 12) * 100.
- Convenience: (Item 4 + Item 5 + Item 6) – 3] divide by 18) * 100; if one item is missing, use [(sum of the 2 completed items)) – 2] divide by 12) * 100.
- Global satisfaction: (Item 7 + Item 8 + Item 9) – 3] divide by 14) * 100; if item 9 is missing, use [(sum (item 7 and Item 8)) – 2] divide by 8) * 100.

5.5.1.2. Analysis Methods

The efficacy data from all participants in FAS (Section 4.1) will be included and analyzed by study intervention group from Week 0 through Week 16.

Similar to the secondary efficacy analyses for 77242113PSO2001 study, the endpoints will be summarized by intervention group. Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for continuous variables and counts and percentages for discrete variables will be used to summarize most data. All statistical testing will be performed at the 2-sided 0.05 significance level. Nominal p-values will be presented. No adjustments for multiple comparisons will be made for the secondary endpoints.

5.5.1.2.1. At Week 16

The exploratory endpoints at Week 16 will be analyzed using the same main estimands and the same analysis methods described in section 5.4.1.2.2, section 5.4.1.3.1 and section 5.4.1.3.2 respectively for secondary endpoints respectively. The analysis strategy for ICEs and missing data will be handled in the same manner as the main estimand for the secondary analyses (section 5.4.1.2.2).

5.5.1.2.2. Over Time Summaries Through Week 16

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

Similar to the Week 16 analyses for the secondary continuous endpoints, MMRM model approach specified in Section 5.4.1.3.2 will be used for the over time summaries through Week 16. Least Square means (LSmeans), LS means differences and their corresponding 95% confidence interval will be provided over time through Week 16 by visit and treatment group in addition to the descriptive summary statistics.

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

5.5.1.2.3. Analyses Related to PASI

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

5.5.1.2.4. Analysis Related to IGA

- The proportions of participants achieving an IGA score of cleared (0); IGA score of cleared (0) or minimal (1) and the proportion of participants achieving a IGA score of mild or better (≤2) overall and by weight (≤90 kg, >90 kg) will be summarized by treatment group over time through Week 16.

5.5.1.2.5. Analyses Related to BSA

- The change from baseline in BSA will be summarized by treatment group over time through Week 16.

5.5.1.2.6. Psoriasis Symptom and Sign Diary

The analyses for PSSD data are specified below and in general can be summarized in 3 categories as follows:

(a) Proportion of subjects who achieved clinically meaningful improvement in PSSD symptom score, sign score, and each individual scale score.

- The threshold for a clinically meaningful change from baseline in PSSD scores is defined as a change of ≥40 points in PSSD symptom and sign scores, change of ≥3 points in bleeding and stinging scores, change of ≥4 points in itch, dryness, cracking, skin tightness, burning and pain scores, and change of ≥5 points in scaling, shedding or flaking and redness scores.

- These analyses include only subjects who had at least minimal severity by each corresponding measure at baseline, i.e., a score of ≥40 in PSSD symptom and sign scores, ≥3 in bleeding and stinging scores; ≥4 in itch, dryness, cracking, skin tightness, burning, and pain scores, and ≥5 in scaling, shedding or flaking and redness scores.

(b) The proportions of subjects who achieve a score of 0 in PSSD symptom score, sign score, and each individual scale score among those who have a baseline PSSD symptom score, baseline sign score, and each individual baseline scale score that is >0.

(c) Change from baseline in PSSD symptom score, sign score, and each individual scale score

5.5.1.2.6.1. Analyses Related to Psoriasis Symptom and Sign Diary

- The proportion of subjects with clinically meaningful improvement from baseline in PSSD symptom score, sign score, and each individual scale score at Week 16 will be compared between each of the JNJ-77242113 group and the placebo group among participants with at least minimal severity in PSSD individual scale scores at baseline, respectively.
- The proportion of subjects with clinically meaningful improvement from baseline in PSSD symptom score, sign score, and each individual scale score will be summarized through Week 16 among participants with at least minimal severity in PSSD individual scale scores at baseline, respectively by treatment group.
- The change from baseline in each PSSD individual scale score at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group.
- The proportions of participants who achieve a score of 0 in each individual PSSD scale score at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group among participants with a baseline PSSD individual scale score >0 respectively.
- The change from baseline in PSSD symptoms score, signs score, and each PSSD individual scale score will also be summarized over time through Week 16 by treatment group.
- The proportions of participants who achieve a PSSD symptoms score of 0, signs score of 0 and each individual scale score of 0 will be summarized over time through Week 16 among participants with a baseline PSSD symptoms score>0, baseline signs score >0, and baseline individual scale score >0 respectively by treatment group.

5.5.1.2.7. Analyses Related to DLQI

- The change from baseline in DLQI score will be summarized at Week 8 and Week 16; and the change from baseline in DLQI score at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group.
- The proportions of participants with DLQI score of 0 and 1 for the participants with baseline DLQI score >1 will be summarized at Week 8.
- The proportion of participants with a reduction of 5 or more points in DLQI score for the participants with baseline DLQI score ≥ 5 at Week 16 will be compared between each JNJ-77242113 treatment group and the placebo group and will also be summarized by treatment group at Week 8.
- The change from baseline in DLQI component scores at Week 16 will be compared between each JNJ-77242113 treatment group and the placebo group.

5.5.1.2.8. Analyses Related to PROMIS-29

- The improvement from baseline in each PROMIS-29 domain score (T-scores) will be summarized at Week 8 by treatment group.
- The proportions of participants who achieve ≥ 5-point improvement from baseline in each PROMIS-29 domain score will be summarized at Week 8 by treatment group.
- The proportions of participants who achieve ≥ 5-point improvement from baseline in PROMIS-29 PCS score and MCS score will be summarized at Week 8 and Week 16 by treatment group; and will be compared between each of the JNJ-77242113 treatment groups and the placebo group at Week 16.

5.5.1.2.9. Analysis Related to Genital Psoriasis Sexual Frequency Questionnaire

- The proportion of participants achieving a GenPs-SFQ item 2 score of never (0) or rarely (1) at Week 16 among those participants with a GenPs-SFQ item 2 score ≥2 at baseline will be compared between each of the JNJ-77242113 groups and placebo.
- The GenPs-SFQ item 2 scores will also be summarized at Week 8 and Week 16 by treatment group among those participants with a GenPs-SFQ item 2 score ≥2 at baseline.
- The GenPs-SFQ item 1 scores will be summarized overtime by treatment group.

5.5.1.2.10. Analysis Related to PGI-c

- The distribution of the PGI-c scale will be compared between each of the JNJ-77242113 groups and the placebo group at Week 16.
- The distribution of the PGI-c scale will be summarized at Week 8 by treatment group.

5.5.1.2.11. Analysis Related to PGI-s

- The distribution of the PGI-s scale at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group.

- The proportion of participants who achieved PGI-s of none (1), none (1) or mild (2) at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group respectively among participants with a baseline PGI-s score ≥3.
- The proportion of participants who achieved PGI-s of none (1), none (1) or mild (2) and at least a 2-grade improvement at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group respectively among participants with a baseline PGI-s score ≥3.
- Summary of PGI-s symptom status will be summarized at Week 8 by treatment group.

5.5.1.2.12. Analysis Related to Regional Psoriasis Disease

ss-IGA

- The proportion of participants who achieve ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline at Week 16 will be compared between each of the JNJ-77242113 groups and placebo group among participants with a baseline ss-IGA score ≥2.
- The ss-IGA scores will also be summarized at Week 8 and Week 16 by treatment group among participants with a baseline ss-IGA score ≥2 and participants with a baseline ss-IGA score ≥3 respectively.

Nail Psoriasis Area and Severity Index

- The percent improvement from baseline in NAPSI at Week 16 will be compared between each of the JNJ-77242113 groups and placebo group for participants with a baseline NAPSI score >0.
- The percent improvement from baseline in NAPSI will also be summarized at Week 8 by treatment group for participants with a baseline NAPSI score >0.

Fingernail Physician's Global Assessment

- The proportions of participants who achieve an f-PGA score of clear (0) or minimal (1) at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group among participants with a baseline f-PGA score ≥2.
- The proportions of participants who achieve an f-PGA score of clear (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group among participants with a baseline f-PGA score ≥2.
- The f-PGA scores will also be summarized at Week 8 and Week 16 by treatment group among participants with a baseline f-PGA score ≥2 and participants with a baseline f-PGA score ≥3 respectively.

Physician's Global Assessment of Hands and/or Feet

- The proportions of participants who achieve hf-PGA score of clear (0) or almost clear (1) and a reduction of at least 2 grades on the hf-PGA scale from baseline at Week 16 among participants with a baseline hf-PGA score ≥2 will be compared between each of the JNJ-77242113 groups and placebo.

- The hf-PGA scores will also be summarized at Week 8 and Week 16 by treatment group among participants with a baseline hf-PGA score ≥2 and participants with a baseline hf-PGA score ≥3 respectively.

Static Physician's Global Assessment of Genitalia

- The proportion of participants achieving a sPGAof genitalia score of clear (0) or minimal (1) at Week 16 among participants randomized with genital psoriasis and an s-PGAof genitalia score ≥3 at baseline will be compared between each of the JNJ-77242113 groups and placebo.
- The proportion of participants achieving a sPGA of genitalia score of clear (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 among participants randomized with genital psoriasis and an sPGA of genitalia score ≥2 at baseline will be compared between each of the JNJ-77242113 groups and placebo.
- The sPGA-G scores will also be summarized at Week 8 and Week 16 by treatment group among participants with a baseline sPGA-G score ≥2 and participants with a baseline sPGA-G score ≥3 respectively.

5.5.1.2.13. Analysis Related to Treatment Satisfaction Questionnaire for Medications

- The TSQM-9 domains will be summarized at Week 8 and Week 16; and the TSQM-9 domains at Week 16 will be compared between each of the JNJ-77242113 groups and the placebo group.

5.5.2. Study 77242113PSO2002

The objectives of the study are to evaluate long-term clinical response, patient-reported psoriasis severity, dermatology-specific health-related quality of life (HRQoL), regional psoriasis, and to explore treatment satisfaction after using JNJ 77242113 in participants with moderate to severe plaque psoriasis, the exploratory endpoints analyses will be performed.

5.5.2.1. Endpoint Definitions

The definitions of the exploratory endpoints for study 77242113OSO2002 are described in Section 5.5.1.1.

5.5.2.2. Analysis Methods

For exploratory efficacy analyses of the study 77242113PSO2002, efficacy data from the combined 77242113PSO2001 and 77242113PSO2002 studies will be included (FAS (Section 4.2)). More specifically, efficacy data will be summarized over time from Week 1 of study 77242113PSO2001 through Week 52 (Week 36 of the 77242113PSO2002 study) by treatment groups.

For overtime efficacy analyses that combines the 77242113PSO2001 and 77242113PSO2002 studies, Week 4 visit of the study 77242113PSO2002 will be aligned as Week 20 for the combined study and will be denoted as "Week 20 (LTE Week 4)" in the summary table; similar notation will be applied for the subsequent visits of the study 77242113PSO2002.

Similar to the exploratory endpoints in 77242113PSO2001, the analysis strategy for ICEs and missing data for the exploratory analyses for 77242113PSO2002 will be handled in the same manner as the main estimand for the secondary analyses of the study 77242113PSO2001 (5.4.1.2.2, section 5.4.1.3.1 and section 5.4.1.3.2) .

Since 77242113PSO2002 is a LTE study following the originating study 77242113PSO2001 and no formal hypothesis testing. Simple descriptive summary statistics, such as n, mean, standard deviation (SD), median, interquartile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data. The baseline data from the originating study (77242113PSO2001) will be used to calculate the change-from-baseline-related endpoints.

For exploratory continuous endpoints, same MMRM model approach specified in Section 5.4.1.3.2 will be used for the change from baseline at each week. Least Square means (LSmeans) and their corresponding 95% confidence interval will be provided, and no statistical testing will be performed.

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

5.5.2.2.1. Analyses Related to PASI

- The proportions of PASI 75 responders, PASI 90 responders, and PASI 100 responders will be summarized by treatment group over time through Week 52.
- The change from baseline in PASI total score will be summarized by treatment group over time through Week 52.

5.5.2.2.2. Analysis Related to IGA

- The proportions of participants achieving an IGA score of cleared (0); IGA score of cleared (0) or minimal (1) and the proportion of participants achieving a IGA score of mild or better (≤2) will be summarized by treatment group over time through Week 52.

5.5.2.2.3. Analyses Related to BSA

- The change from baseline in BSA will be summarized by treatment group over time through Week 52.

5.5.2.2.4. Analyses Related to PSSD

- The change from baseline in PSSD symptom score, sign score, and each PSSD individual scale score will also be summarized over time through Week 52 by treatment group.

- The proportion of subjects with clinically meaningful improvement from baseline in PSSD symptom score, sign score, and each individual scale score will be summarized through Week 52 among participants with at least minimal severity in PSSD individual scale scores at baseline by treatment group.

- The proportions of participants who achieve a PSSD symptoms score of 0, signs score of 0 and each individual scale score of 0 will be summarized through Week 52 among participants with a baseline PSSD symptoms score >0, baseline signs score >0, and baseline each individual scale score >0 respectively by treatment group.

5.5.2.2.5. Analyses Related to DLQI

- The change from baseline in DLQI score will be summarized over time through Week 52 by treatment groups.
- The proportions of participants with DLQI score of 0 and 1 for the participants with a baseline DLQI score >1 will be summarized over time through Week 52 by treatment groups.

5.5.2.2.6. Analyses Related to PROMIS-29

- The improvement from baseline in each PROMIS-29 domain score (T-scores) and pain intensity raw score will be summarized over time through Week 52 by treatment groups.
- The proportions of participants who achieve ≥ 5-point improvement from baseline in PROMIS-29 PCS score and MCS score will be summarized overtime through Week 52 by treatment group.

5.5.2.2.7. Analysis Related to Genital Psoriasis Sexual Frequency Questionnaire

- The GenPs-SFQ item 2 scores will be summarized over time through Week 52 by treatment group.
- The GenPs-SFQ item 1 scores will be summarized over time through Week 52 by treatment group.
- Frequency in sexual activity shift from baseline to Week 52 will be summarized over time through Week 52 by treatment groups.

5.5.2.2.8. Analysis Related to PGI-c

- The distribution of the PGI-c scale will be summarized over time through Week 52 by treatment group

5.5.2.2.9. Analysis Related to PGI-s

- Summary of PGI-s symptom status will be summarized over time through Week 52 by treatment groups.
- The distribution of the PGI-s scale will be summarized over time through Week 52 by treatment group.

5.5.2.2.10. Analysis Related to Regional Psoriasis Disease

ss-IGA

- The ss-IGA scores will also be summarized over time through Week 52 by treatment group among participants with a baseline ss-IGA score ≥2 and participants with a baseline ss-IGA score ≥3 respectively.

Nail Psoriasis Area and Severity Index

- The percent improvement from baseline in NAPSI will be summarized over time through Week 52 by treatment group for participants with a baseline NAPSI score >0.

Fingernail Physician's Global Assessment

- The f-PGA scores will be summarized over time through Week 52 by treatment group among participants with a baseline f-PGA score ≥2 and participants with a baseline f-PGA score ≥3 respectively.

Physician's Global Assessment of Hands and/or Feet

- The hf-PGA scores will also be summarized over time through Week 52 by treatment group among participants with a baseline hf-PGA score ≥2 and participants with a baseline f-PGA score ≥3 respectively.

Static Physician's Global Assessment of Genitalia

- The sPGA of genitalia scores will be summarized over time through Week 52 by treatment group among participants randomized with genital psoriasis and an sPGA of genitalia score ≥ 2 and ≥3 at baseline respectively.

5.5.2.2.11. Analysis Related to Treatment Satisfaction Questionnaire for Medications

- The TSQM-9 domains will be summarized over time by treatment groups.

5.6. 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.

Depending on the study, the cumulative safety data will be analyzed through different study and study periods as shown below. Unless otherwise specified, tabular summaries of safety events are also presented as following:

Study 77242113PSO2001

The safety data through the end of the main study 77242113PSO2001 will be included and safety analysis set (Section 4.1) will be used. For participants who entered 7242113PSO2002 study at the time of Week 16 visit (without a gap period), safety data through Week 16 are included. For participants who completed the participation of the 77242112PSO2001 study but either had a delay in joining or didn't participate 77242113PSO2002 study, safety data through end of the study are included. Safety data through the end of the 77242113PSO2001 study will be summarized by following intervention group:

- Placebo
- JNJ-77242113 25 mg QD
- JNJ-77242113 50 mg AD
- JNJ-77242113 25 mg BID
- JNJ-77242113 100 mg QD
- JNJ-77242113 100 mg BID
- Combined JNJ-77242113 groups

Study 77242113PSO2002

(a) Safety data from Week 16 (Week 0 of 77242113PSO2002 study) through Week 56 (Week 40 of 77242113PSO2002 study) for participants enter the 77242113PSO2002 will be included and LTE safety analysis set (Section 4.2) will be used. Safety data from Week 16 through Week 56 will be summarized by following intervention group:

- Placebo → JNJ-77242113 100 mg QD
- JNJ-77242113 25 mg QD
- JNJ-77242113 50 mg QD
- JNJ-77242113 25 mg BID
- JNJ-77242113 100 mg QD
- JNJ-77242113 100 mg BID
- Combined JNJ-77242113 groups

(b) Safety data through Week 56 (Week 40 of 77242113PSO2002 study) with the combined data of 77242113PSO2001 and 77242113PSO2002 studies will be included and safety analysis set (Section 4.2) will be used. Safety data through Week 56 will be summarized by following intervention groups.

- Placebo
- Placebo → JNJ-77242113 100 mg QD
- JNJ-77242113 25 mg QD
- JNJ-77242113 50 mg QD
- JNJ-77242113 25 mg BID
- JNJ-77242113 100 mg QD
- JNJ-77242113 100 mg BID
- Combined JNJ-77242113 groups

5.6.1. Extent of Exposure

The extent of exposure will be summarized for randomized participants that received at least one study agent administration. Distribution of participants through Week 16 and through Week 52 by study agent lot will be analyzed for 77242113PSO2001 and 77242113PSO2002 respectively. In addition, the number (%) of participants receiving the study drug during double blind treatment phase will be summarized by treatment group.

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

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

5.6.2. Adverse Events

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

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

- AEs
- Serious AEs (SAEs)
- AEs leading to discontinuation of study intervention
- AEs of severe intensity
- AEs related to study intervention

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

- Had SAEs
- Had AEs leading to discontinuation of study intervention
- Had AEs of severe intensity
- Had AE for psoriasis

- Had suicidal ideation or suicidal behavior
- Had anaphylactic or serum sickness 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.

5.6.3. Additional Safety Assessments (if applicable)

5.6.3.1. Clinical Laboratory Tests

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

Descriptive statistics and graphical displays will be presented for selected chemistry and hematology laboratory tests at scheduled time points.

Change from baseline through different study periods in both studies as specified in Section 5.6 will be summarized for chemistry, and hematology tests and displayed by intervention group. Box plots of laboratory measurements and change from baseline will be provided for the selected laboratory measurement.

- **Hematology** will include but are not limited to the following: Basophils, Eosinophils, Hemoglobin, Lymphocytes, Monocytes, Neutrophils, Platelets, WBC, CRP and ESR.
- **Chemistry** will include but are not limited to the following: ALT, AST, Albumin, Alkaline Phosphatase, Bicarbonate (CO2), Corrected Calcium, Chloride, Creatinine, GGT, Glucose, Potassium, SGOT, SGPT, Sodium, Total Bilirubin, Total Protein, Urea Nitrogen.

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 by study intervention group. Participants with toxicity grades ≥2 will be listed.

In addition, for selected laboratory parameters, ULN will also be used to identify abnormal laboratory test results, and the incidence and severity of abnormal laboratory parameters (hematology and chemistry) will be summarized by treatment group. Participants with maximum post-baseline elevated liver function tests through Week 16 (77242113PSO2001) and through Week 56 relative to ULN will be summarized in categories as shown below will be provided.:

- > 1 x ULN
- ≥ 3 x ULN
- ≥ 5 x ULN
- ≥ 10 x ULN

- ≥ 20 x ULN

In addition, Summary of potential Hy's Law case (ALT or AST ≥3 x ULN and total bilirubin ≥2 x ULN) through Week 16 and Week 56 respectively will also be provided.

5.6.3.2. Vital Signs

Continuous vital sign parameters including pulse, blood pressure (systolic and diastolic) will be summarized at each assessment time point. Change from baseline by study and study periods as specified in Section 5.6 will be summarized. Descriptive statistics (mean, standard deviation, median, minimum and maximum) will be presented.

Incidence of treatment-emergent abnormal vital signs during intervention, as defined in Table 6, will be summarized for participants who had a baseline assessment and at least 1 postbaseline assessment for that vital sign.

Table 6: Clinically Important/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

5.6.3.3. 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 measures 5 possible levels of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior. The assessment is a fully-structured, participant self-report C-SSRS questionnaire, including standardized questions, follow-up prompts, error handling routines, and scoring conventions. Two versions of the C-SSRS will be used in this study, the *Lifetime* version and the *Since Last Contact* version. The *Lifetime* version will be conducted during the screening visit and the *Since Last Contact* version will be conducted at all other visits.

At the screening visit, the C-SSRS should be completed as the first assessment after signing informed consent and before any other tests, procedures, or other consultations. For subsequent visits, the C-SSRS should be completed after all PROs and before any other tests, procedures, or

other consultations. Participants will be interviewed by the investigator or trained study site personnel in a private, quiet place.

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 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 for 77242113PSO2001 study or through Week 56 (Week 40 of the 77242113PSO2002 study), and from Week 16 (Week 0 of the 77242113PSO2002) through Week 56 (Week 40 of the 77242113PSO2002 study) for participants in the 77242113PSO2002 study period. In addition, frequency distribution of the most severe/maximum post baseline C-SSRS outcome will be tabulated by C-SSRS categories and intervention group through Week 16 and through Week 56. 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, 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 for study 77242113PSO2001 and through 56 for the

combined 77242113PSO2001 and 77242113PSO2002 studies, and from Week 16 through Week 56 for participants in the 77242113PSO2002 study period will be presented, where the baseline category is based on C-SSRS score form study 77242113PSO2001and the post baseline is based on C-SSRS or AE data.

5.7. Other Analyses

5.7.1. Pharmacokinetics

5.7.1.1. JNJ-77242113 Concentrations

The PK evaluable population is defined as all the participants who received at least 1 complete dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113.

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

The following analyses will be performed as appropriate.

- Summary of plasma JNJ-77242113 concentration over time
- Proportion of participants with plasma JNJ-77242113 concentration below the lowest quantifiable concentration in a sample at each visit
- Summary of plasma JNJ-77242113 concentrations over time by baseline body weight (≤90 kg, >90 kg). Other covariates may also be applied
- Plots of median plasma JNJ-77242113 concentrations over time
- Plots of median plasma JNJ-77242113 concentrations over time by baseline body weight (≤median, >median)

Concentrations below the lowest quantifiable concentration will be treated as zero in the summary statistics. All plasma concentrations below the lowest quantifiable concentration or missing data will be labeled as such in the concentration database. PK data may also be displayed graphically.

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

77242113PSO2001

For study 77242113PSO2001, PK analysis set (Section 4.1) will be used and the analyses will be summarized through Week 16.

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

- JNJ-77242113 25 mg QD
- JNJ-77242113 50 mg QD
- JNJ-77242113 25 mg BID
- JNJ-77242113 100 mg QD
- JNJ-77242113 100 mg BID

77242113PSO2002

For study 77242113PSO2002, PK analysis set (Section 4.2) will be used and the analyses will be summarized through Week 52 (Week 36 of the study 77242113PSO2002).

- Placebo → JNJ-77242113 100 mg QD
- JNJ-77242113 25 mg QD
- JNJ-77242113 50 mg QD
- JNJ-77242113 25 mg BID
- JNJ-77242113 100 mg QD
- JNJ-77242113 100 mg BID

5.7.1.2. 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(s) based on 2 previous doses prior to the PK sample collection or data from a participant who skip dose prior to PK sample collection will be excluded for that visit.

5.7.1.3. PK vs Efficacy

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 PASI /IGA responses at Week 16 may be explored for study 77242113PSO2001.
- The relationship between JNJ-77242113 plasma trough concentrations (quartiles) and PASI /IGA responses at Week 52 (Week 36 of study 77242113PSO2002) may be explored for study 77242113PSO2002.

CCI

[redacted]

CCI

[redacted]

5.7.3. Pharmacokinetic/Pharmacodynamic Relationships

If data permit, the relationship between plasma concentration of JNJ-77242113 and PD (IL-23 mediated interferon-gamma production) may be analyzed graphically. If deemed necessary, a previously developed PK/PD model may be updated to describe the exposure-response relationship. If this is performed, details will be given in a population PK/PD analysis plan and results of the population PK/PD analysis will be presented in a separate technical report.

5.7.4. 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.

5.7.5. Definition of Subgroups

To evaluate the consistency of the primary efficacy endpoint PASI75 response at Week 16, subgroup analyses may be performed in study 77242113PSO2001 when the number of participants in the subset permits

For each of the subgroups defined below, the difference between the JNJ-77242113 treatment groups and placebo group in the proportion of the PASI 75 responders at Week 16, the proportion of subjects achieving IGA score of cleared (0) or minimal (1), and its exact confidence intervals

will be calculated. No p-values will be provided. Subgroup analyses will not be stratified by weight category (≤90 kg, >90kg).

Demographic subgroups

Subgroup	Variant	Definition
Region	1	Define based on UN guidance as per the M49 standard • Asian Pacific • North America • Europe
Sex	1	• male • female
Race	1	• American Indian or Alaska Native • Asian • Black or African American • White • Other
Age Group	1	• <45 • 45-64 • >=65
BMI	1	• <25 kg/m^2 • 25-<30 kg/m^2 • >=30 kg/m^2
Body Weight Group	1	• ≤90 kg • >90 kg

Baseline disease characteristics and psoriasis medication subgroups

Subgroup	Variant	Definition
Age at diagnosis (years)	1	• < median • ≥ median
Psoriasis disease duration (years)	1	• < median • ≥ median
Baseline PASI	1	• <20 • ≥20
Baseline IGA	1	• < 4 • = 4
Baseline BSA	1	• < 20% • ≥ 20%
Baseline DLQI		• <10 • ≥ 10
Psoriatic arthritis		• Yes • No
Topical agents (Topical non-corticosteroids, Topical corticosteroids)		• Never used • Ever used
Phototherapy (ultraviolet B light [UVB] or psoralen and ultraviolet A light therapy [PUVA])	1	• Never used • Ever used
Systemics (Conventional non-biologic systemics, Novel non-biologic systemics, 1,25-vitamin D3 and analog, phototherapy, biologics)		• Never used • Ever used

Subgroup	Variant	Definition
Conventional non-biologic systemics (PUVA, MTX, cyclosporine, acitiretin, or Azathioprine)		• 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-17 inhibitors (secukinumab, ixekizumab, or brodalumab)		• Never used • Ever used

5.8. Interim Analyses

An internal independent interim analysis committee (IAC) will be established to review the interim data including data from the LTE available at the time of the IA to formulate recommended decisions and/or actions in accordance with the objectives of the interim analyses. The IAC will consist of at least a clinician and a statistician (neither of whom are involved in study conduct), one of whom will chair the committee, and other members as required. The details will be provided in a separate IAC charter.

The IAC will review the unblinded efficacy data and provide recommendations about the next step of study conduct and the future development of the compound based upon the results of the first (when approximately 50% (n=120) of the participants reach Week 4) and/or second (when approximately 2/3 (n=160) of the participants reach Week 16) interim efficacy analyses. The first IA will be for nonbinding futility and to inform the planning for the clinical development for JNJ-77242113 for other indications based on the proportion of participants achieving PASI 50 response at Week 4. The second IA will be used for planning of future psoriasis studies and will be based on the primary endpoint which is the proportion of participants achieving PASI 75 response at Week 16. Other selected supportive efficacy endpoints could also be reviewed. The unblinded results will be limited to specific sponsor personnel not involved in the study conduct. Interim analysis results will not be disseminated to investigators or individuals associated with the conduct of the study.

Details of the plan for the interim analyses will be specified in the Interim Analysis SAP.

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

An external independent data monitoring committee (iDMC) whose members are not directly involved in the conduct of the 77242113PSO2001 and 77242113PSO2002 studies, will review unblinded safety data to ensure the safety of the participants enrolled in this study. The committee will meet regularly to review unblinded safety data. After the review, the iDMC will make recommendations to the sponsor regarding the conduct of the study. The iDMC will consist of at least one clinical physician and one statistician, not involved in the conduct of the study. The iDMC responsibilities, authorities, and procedures will be documented in the iDMC charter

An independent, external DMC has been established to monitor data on an ongoing basis to ensure the continuing safety of the participants enrolled in this study. The DMC consists of 3 members (including 1 dermatologist, one cardiologist and one statistician) who are independent of the sponsor. None of the members is participating as an investigator in the current study.

The major function of the DMC is to monitor the safety of the study agent by reviewing the serious adverse events (SAEs) each month and by reviewing the study safety data approximately every 4 months. The content of the safety summaries for this study are defined and documented in the DMC SAP developed by the sponsor. No hypothesis testing will be conducted. An independent statistical supporting group, provided by SGS, supports the DMC and is the liaison between sponsor and the DMC.

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

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 List of Abbreviations

ADA	anti-drug antibody
AE	adverse event
ALT/SGPT	alanine aminotransferase
AST/SGOT	aspartate aminotransferase
ATC	anatomic and therapeutic class
AUC	area under the curve
BID	twice daily
BMI	body mass index
BSA	body surface area
CI	confidence interval
Cmax	maximum concentration
CRF	case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
DPS	Data Presentation Specifications
eCRF	electronic case report form
F (%)	absolute SC bioavailability
FAS	full analysis set
FDA	Food and Drug Administration
f-PGA	Fingernail Physician's Global Assessment
GenPs-SFQ	Genital Psoriasis Sexual Frequency Questionnaire
GMS	Global Medical Safety
hf-PGA	Physician's Global Assessment of Hands and/or Feet
IA	Interim analysis
IAC	Interim analysis Committee
IAS	Interim analysis set
ICH	International Conference on Harmonisation
IGA	Investigator Global Assessment
IQ	interquartile
IWRS	interactive web response system
LLOQ	lower limit of quantification
LTE	long-term extension
PK	pharmacokinetic(s)
QD	once daily
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-Effect Model Repeated Measure
MRD	minimum required dilution
NAb	neutralizing antibodies
NAPSI	Nail Psoriasis Area and Severity Index
PASI	Psoriasis Area and Severity Index
PD	pharmacodynamic(s)
PI	principal investigator
PK	pharmacokinetic(s)
PP	per protocol
PRO	patient-reported outcome(s) (paper or electronic as appropriate for this study)
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
PSSD	Psoriasis Symptom and Sign Diary
QD	once daily
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation

SMQs	standardised MedDRA queries
TEAE	treatment-emergent adverse event
Tmax	time to maximum concentration
US NCI	United States National Cancer Institute
V	volume distribution
Vz	volume of distribution based on terminal phase
Vz/F	apparent volume of distribution based on terminal phase after extravascular administration
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary
PGI-C	Patient Global Impression-Change
PGI-S	Patient Global Impression-Severity
s-PGA	Static Physician's Global Assessment
ss-IGA	Scalp Specific Investigator Global Assessment
TSQM-9	Treatment Satisfaction Questionnaire for Medications-9 items
TYK	tyrosine kinase
ULN	upper limit of normal
US	United States
WBC	white blood cell

6.2. Appendix 2 Changes to Protocol-Planned Analyses

N/A

6.3. Appendix 3 Demographics and Baseline Characteristics

For study 77242113PSO2001, the number of participants in each analysis set will be summarized and listed by intervention group, combined active intervention group, and overall. In addition, the distribution of participants by region, country, and site ID will be presented unless otherwise noted.

Table 7 presents a list of the demographic variables that will be summarized by intervention group, combined active intervention group, and overall for the FAS analysis set.

Table 7: Demographic Variables

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

Baseline disease characteristics (e.g., duration of psoriasis disease, , baseline PASI score, baseline IGA score, baseline BSA, baseline PRO related measurements, and baseline reginal psoriasis related measurements) will be summarized by treatment group. In addition, summaries of participants' medical history and current diagnoses, alcohol intake, and smoking status will be provided by treatment group will also be provided.

Since study 77242113PSO2002 is the LTE of study 77242113PSO2002, the summaries specified above will only be done for study 77242113PSO2001.

6.4. Appendix 4 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 through Week 16 and through the end of study.

- 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. In addition, analyses of COVID-19 related protocol deviations will be provided.

6.5. Appendix 5 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 [ie, AEs], or other) will be summarized by randomized treatment group.

The number of participants who received concomitant treatment of moisturizer for psoriasis will be summarized by randomized treatment group.

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

6.6. Appendix 6 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.

6.7. Appendix 7 Intervention Compliance

Treatment compliance will be assessed based through Week 16 on the full analysis set (FAS) for study 77242113PSO2001 and through Week 52 (Week 36 of the 77242113PSO2002 study) on full analysis set for study 77242113PSO2002, Descriptive summaries (sample size, mean, standard deviation, median, and range) will be presented for the percent of compliance defined as the number of tablets taken divided by the number of tablets that should have been taken. Overall compliance will be categorized as > 120%, 80 to ≤ 120%, and < 80%. In addition, treatment compliance will be assessed by summarizing the protocol deviation of the study agent administration related to incorrect study agent or dose received and missed administrations.

6.8. Appendix 8 Extent of Exposure

The extent of exposure will be summarized for randomized participants that received at least one study agent administration. Descriptive statistics (N, mean, SD, median, IQ range, and range) for treatment duration (weeks), cumulative dose (mg), and average daily dose (mg/day) will be presented by treatment groups. The average daily dose (mg/day) for each dose regimen (25 mg QD, 50 mg QD, 25 mg BID, 100 mg QD, 100 mg BID) is calculated as:

Number of the total active tablets taken x tablet's strength (25 mg or 100 mg) / (the last dose date – the first dose date +1)

In addition, distribution of participants through Week 16 and through Week 52 (Week 36 of the 77242113PSO2002) by study agent lot will be analyzed for 77242113PSO2001 and 77242113PSO2002 respectively.

6.9. Appendix 9 Adverse Events of Special Interest

Not Applicable.

6.10. Appendix 10 Medications of Special Interest

Not Applicable.

6.11. Appendix 11 Laboratory Toxicity Grading

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

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

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

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

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
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	Janssen implementation notes
	> 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x baseline if baseline was abnormal	applied only if baseline > ULN. If baseline < LLN, then ranges for "normal baseline" are applied.
CD4 lymphocytes decreased	<LLN - 500/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	
Creatinine increased	Creatine Kinase >ULN - 1.5 x ULN	Creatine Kinase >1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	Creatine Kinase >3.0 x baseline; >3.0 - 6.0 x ULN	Creatine Kinase >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; monitoring only indicated*	>1.5 - 2.5; *>1.5 - 2.5 x baseline if on anticoagulation; dose adjustment indicated*	>2.5; *>2.5 x baseline if on anticoagulation; bleeding*	-	Concomitant therapy or clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
Lipase increased	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN; *>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 into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
Hypercalcemia	Corrected serum calcium of >ULN - 11.5 mg/dL; >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.
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.
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;	Corrected serum calcium of <7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L; Ionized calcium <0.9 - 0.8 mmol/L;	Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L; Ionized calcium <0.8 mmol/L;	Clinical signs and symptoms are not taken into consideration for grading.

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
		symptomatic	*hospitalization indicated*	*life-threatening consequences*	
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 <130-120 mmol/L	Sodium <120 mmol/L; *life-threatening consequences*	Clinical signs and symptoms are not taken into consideration for grading. Worst case ("<130-120 mmol/L" for grade 3 added by Janssen) is applied across grade 2/3 ranges: 120-129 mol/L assigned to grade 3, grade 2 not used.
Renal and urinary disorders					
Proteinuria	1+ proteinuria; urinary protein ≥ULN - <1.0 g/24 hrs; urinary protein ≥ULN - <1000 mg/day	**Adult:** 2+ and 3+ proteinuria; urinary protein 1.0 - <3.5 g/24 hrs;	**Adult:** 4+ proteinuria; urinary protein >=3.5 g/24 hrs;	-	In case both 24-h urine collection and dipstick are collected, then worst case is taken, as opposed to having 24-h urine

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Janssen implementation notes
		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	urinary protein >=3500 mg/day; **Pediatric:** Urine P/C (Protein/Creatinine) ratio >1.9; Urine P/C (Protein/Creatinine) >214.7 g/mol		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.

7. REFERENCES

1 Bretz F, Pinheiro JC, Branson M. Combining multiple comparisons and modeling techniques in dose-response studies. Biometrics 2005; 61:738–748.

2 Pinheiro J, Bornkamp B, Glimm E, Bretz F. Model-based dose finding under model uncertainty using general parametric models. Stat Med. 2014 May 10;33(10):1646-61

3 Bharmal M (2009), Payne K, Atkinson MJ, Desrosiers M-P, Morisky DE, Gemmen E. Validation of an abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9) among patients on antihypertensive medications. Health Qual Life Outcomes. 2009;7:36.