Janssen Research & Development *

Clinical Protocol

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

ICONIC-LEAD

Protocol 77242113PSO3001; Phase 3

Version: Amendment 2

JNJ-77242113

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United States (US) sites of this study will be conducted under US Food & Drug Administration Investigational New Drug (IND) regulations (21 CFR Part 312). Studies conducted at sites in the European Economic Area (EEA) will be conducted under Regulation [EU] No. 536/2014.

Regulatory Agency Identifier Number(s)

Registry	**ID**
IND:	156446
EU TRIAL NUMBER	2023-505120-59

Status:	Approved
Document Date:	24 November 2023
Prepared by:	Janssen Research & Development, LLC
EDMS Number:	EDMS-RIM-926290, 3.0

GCP Compliance: This study will be conducted in compliance with Good Clinical Practice, and applicable regulatory requirements.

PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

DOCUMENT HISTORY		
Document	**Country/Territory Affected**	**Date**
Amendment 2	All	24-November-2023
Amendment 1	All	03-August-2023
Original Protocol	All	22-May-2023

Amendment 2 (24 November 2023)

Overall Rationale for the Amendment: Upon health authority feedback, language was added to state that studies conducted at sites in the EEA will be conducted under Regulation (EU) No. 536/2014. Additionally, several clarifications were made.

The changes made to the clinical protocol 77242113PSO3001 as part of Protocol Amendment 2 are listed below, including the rationale of each change and a list of all applicable sections. Changes made in Protocol Amendment 1 are listed in Section 10.10 Appendix 10: Protocol Amendment History.

Section Number and Name	Description of Change	Brief Rationale
Cover Page	Addition of text to state that studies conducted at sites in the EEA will be conducted under Regulation (EU) No. 536/2014.	Updated per regulatory feedback.
1.3.1 Schedule of Activities – Screening Through Week 52	Updated peak/trough sample collection details.	To support participant/site flexibility and decrease burden of sample collection.
2.1 Study Rationale	Updated the study rationale to include a justification for inclusion of adolescents in the study.	Updated per regulatory feedback.
2.3.3 Benefit-risk Assessment for Study Participation	Added a paragraph on benefit-risk assessment for adolescent participation.	Updated per regulatory feedback.
4.2 Scientific Rationale for Study Design 8.10 Medical Resource Utilization and Health Economics	Removed reference to the EQ-5D-5L questionnaire as treatment cost and other health economic information will not be collected in this trial. The sponsor plans to collect EQ-5D-5L to measure the patient's health status.	Updated per regulatory feedback.
4.2.2 Study-specific Ethical Design Considerations	Clarified that blood draws do not exceed 3% of the total blood volume over a period of four weeks and do not exceed 1% at any single time.	Updated per regulatory feedback.
5.1 Inclusion Criteria	Removed "or their legally acceptable representative must sign" from the adult section, as this trial will not enroll adult patients who are unable to comprehend the information provided. The language is kept in the adolescent section.	Updated per regulatory feedback.
5.4 Screen Failures	Clarified that participants retain their original identification numbers at rescreening.	Updated per regulatory feedback.
6.3 Assignment to Study Intervention	Clarified that the study uses a 2:1 randomization ratio.	Updated per regulatory feedback.

Section Number and Name	Description of Change	Brief Rationale
6.2 Preparation/Handling/ Storage/Accountability 8.4 Adverse Events, Serious Adverse Events, and Other Safety Reporting 10.2.3 Informed Consent Process and Assent Form 10.2.5 Data Protection	Clarified that the legally acceptable representative pertains to adolescent participants, where applicable.	Updated per regulatory feedback
8.1.1 Physical Examinations	Updated physical examinations to add local regulation requirements.	Updated per regulatory feedback.
8.4.4 Regulatory Reporting Requirements for Serious Adverse Events 10.3.1 Adverse Event Definitions and Classifications	Clarified that serious unexpected AEs considered at least possibly related to study intervention will be reported to the relevant health authorities, IRBs and ethics committees per local requirements.	Updated per regulatory feedback
9.2 Analysis Sets	Added the per protocol analysis set definition.	Updated per regulatory feedback.
9.3.1 General Considerations 9.3.3 Key Secondary Endpoints	Added the general description of the multiplicity control approach. Added analysis methods and data handling rules for key secondary endpoints.	Updated per regulatory feedback.
10.8 Appendix 8: Investigator's Global Assessment	Revised text to state the use of the National Psoriasis Foundation Reference card *may* be used.	To clarify that the National Psoriasis Foundation cards are an optional resource for sites.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted

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ABBREVIATIONS [AND DEFINITIONS OF TERMS]

β-hCG	β-human chorionic gonadotropin
ADA	anti-drug antibody
AE	adverse event
AESI	adverse event of special interest
ALT	alanine transaminase
ANCOVA	analysis of covariance
anti-HBc	hepatitis B core antibody
anti-HBs	hepatitis B surface antibody
AST	aspartate transferase
AUC	area under the plasma concentration versus time curve
AxMP	Auxiliary Medicinal Product (also known as NIMP)
BCG	Bacille Calmette-Guérin
BID	twice daily
BSA	body surface area
CDLQI	Children's Dermatology Life Quality Index
CI	confidence interval
ClinRO	clinician-reported outcome
C_{max}	maximum plasma concentration
CMH	Cochran-Mantel-Haenszel
COA	clinical outcome assessment (paper or electronic as appropriate for this study)
COVID-19	Coronavirus disease 2019
CRF	case report form(s) (paper or electronic as appropriate for this study)
C-SSRS	Columbia-Suicide Severity Rating Scale
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
C_{trough}	plasma concentration just prior to the beginning or at the end of a dosing interval
DBili	direct bilirubin
DBL	database lock
DLQI	Dermatological Life Quality Index
DMC	Data Monitoring Committee
DNA	Deoxyribonucleic acid
DR	delayed-release
EC	exclusion criterion/criteria
ECG	electrocardiogram
eDC	electronic data capture
EEA	European Economic Area
eGFR	estimated glomerular filtration rate
ePRO	electronic patient reported outcome
EQ-VAS	EuroQol visual analogue scale
EQ-5D	EuroQol-5 Dimension
EQ-5D-5L	EuroQol-5 Dimension 5-level
E-R	exposure-response
EU	European Union
FAS	full analysis set
FIH	first-in-human
FOIA	Freedom of Information Act
f-PGA	Fingernail Physician's Global Assessment
FSH	follicle stimulating hormone
GCP	Good Clinical Practice
GenPs-SFQ	Genital Psoriasis Sexual Frequency Questionnaire
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
hf-PGA	Physician's Global Assessment of hands and feet
HIV	human immunodeficiency virus
HRQoL	Health-related Quality of life

hs-CRP	high sensitivity C-reactive protein
IB	Investigator's Brochure
IC_{50}	half maximal inhibitory concentration
ICE	intercurrent event
ICF	informed consent form
ICH	International Council on Harmonisation
IEC	Independent Ethics Committee
IGA	Investigator Global Assessment
IGRA	interferon gamma release assay
IL	interleukin
IL-12Rβ1	IL-12 receptor beta 1
IL-23R	IL-23 receptor
IMP	Investigational Medicinal Product
INR	International Normalized Ratio
IR	immediate-release
IRB	Institutional Review Board
IV	intravenous(ly)
IWRS	interactive web response system
JAK	Janus kinase
LC-MS/MS	liquid chromatography-mass spectrometry/mass spectrometry
LS	least squares
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-effect Model Repeated Measure
mNAPSI	modified Nail Psoriasis Severity Index
NAb	neutralizing antibody
NIMP	Non-Investigational Medicinal Product (also known as AxMP)
NOAEL	no-observed-adverse-effect-level
PASI	Psoriasis Area and Severity Index
PCR	polymerase chain reaction
PD	pharmacodynamic(s)
PDE4	phosphodiesterase 4
PGA	Physician Global Assessment
PHQ-9	Patient Health Questionnaire-9
PK	pharmacokinetic(s)
PQC	Product Quality Complaint
PRO	patient reported outcome(s) (paper or electronic as appropriate for this study)
PROMIS-25	Patient-Reported Outcomes Measurement Information System-25
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
PsA	psoriatic arthritis
PSSD	Psoriasis Symptom and Sign Diary
PT	preferred term
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SoA	Schedule of Activities
SOC	system organ class
sPGA-G	Static Physician's Global Assessment of Genitalia
ss-IGA	scalp specific Investigator Global Assessment
STAT	signal transducers and activators of transcription
TB	tuberculosis
TBili	total bilirubin
t_{max}	time to reach the maximum observed plasma analyte concentration
TNF	tumor necrosis factor
TSQM-E	Treatment Satisfaction Questionnaire for Medication-Effectiveness
TYK2	tyrosine kinase 2
ULN	upper limit of normal
US	United States
VAS	visual analog scale

1. PROTOCOL SUMMARY

1.1. Synopsis

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

Registry	**ID**
IND:	156446
EU TRIAL NUMBER	2023-505120-59

DESCRIPTION OF COMPOUND

JNJ-77242113 is a peptide that binds directly to the interleukin-23 receptor (IL-23R) subunit and prevents IL-23 binding, thereby inhibiting proximal IL-23R signaling and downstream effector functions (eg, cytokine secretion). JNJ-77242113 has high potency with an IC_{50} of ~20 to 30 pM in peripheral human cell based functional assays. Despite its low oral bioavailability (<1%), JNJ-77242113 has demonstrated systemic effects and has provided substantial efficacy in plaque psoriasis clearance in doses 25 mg once daily and greater in the Phase 2b, 77242113PSO2001 study. Therefore, JNJ-77242113 is a promising candidate for further development in systemic, IL-23-driven diseases such as plaque psoriasis.

BENEFIT-RISK ASSESSMENT

JNJ-77242113 has provided substantial efficacy in plaque psoriasis clearance in Study 77242113PSO2001. No risks associated with JNJ-77242113 have been identified; however, risks associated with study procedures (ie, skin biopsy) could occur.

OBJECTIVES, ENDPOINTS, AND ESTIMANDS

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

Objectives	Endpoints
	• ≥4-point improvement from baseline in PSSD Itch score at Week 4. • ≥4-point improvement from baseline in PSSD Itch score at Week 16.
• To evaluate the maintenance of efficacy of JNJ-77242113 compared with treatment withdrawal during the randomized withdrawal period.	• PASI 75 at Week 52. • PASI 90 at Week 52. • Time to loss of PASI 75. • Time to loss of PASI 90.

HYPOTHESIS

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

OVERALL DESIGN

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

An Independent Data Monitoring Committee will be commissioned for this study.

NUMBER OF PARTICIPANTS

A target of 600 participants will be enrolled in this study.

STUDY ARMS AND DURATION

The total duration of this study for each participant is approximately 165 weeks, which includes a 5-week screening period, a placebo-controlled period through Week 16 and a randomized withdrawal and retreatment period from Week 24 through Week 52. At Week 52, participants will be transitioned to open-label JNJ-77242113 through Week 156 and a 4-week safety follow-up period will be observed for participants who discontinue study intervention during the study or at the end of the treatment period.

Participants will be randomized with a 2:1 randomization ratio to JNJ-77242113 200 mg or placebo in the following groups:

- Adult participants
    - JNJ-77242113 200 mg once daily
        - Week 0 to Week 24: Participants will be treated with JNJ-77242113 200 mg once daily
        - Week 24 to Week 52:
            - Participants who are PASI 75 responders or IGA 0 or 1 responders (ie, those who achieve an IGA score of 0 or 1 and have ≥2-grade improvement from baseline) at Week 24 will be re-randomized 1:1 to either continue JNJ-77242113 or to be transitioned to placebo. Participants transitioned to placebo will be retreated with JNJ-77242113 200 mg once daily upon loss of ≥50% of Week 24 PASI improvement or starting at Week 52 if loss of response

is not observed. All participants will be treated with JNJ-77242113 at Week 52.

- Participants who are both PASI 75 non-responders and IGA 0 or 1 non-responders at Week 24 will continue to receive JNJ-77242113 200 mg once daily through Week 52.

- Week 52 to Week 156: Participants will receive JNJ-77242113 200 mg once daily through Week 156.

- Placebo to JNJ-77242113 200 mg once daily
  - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
  - Week 16 to Week 156: Participants will cross-over to receive JNJ-77242113 200 mg once daily through Week 156.

- Adolescent participants
  - JNJ-77242113 200 mg once daily
    - Week 0 to Week 156: Participants will be treated with JNJ-77242113 200 mg once daily
    - Adolescents will not participate in re-randomization regardless of their PASI score or IGA score at Week 24.
  - Placebo to JNJ-77242113 200 mg once daily
    - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
    - Week 16 to Week 156: Participants will cross-over to receive JNJ-77242113 200 mg once daily through Week 156.

EFFICACY EVALUATIONS

Investigator assessments:

- Investigator Global Assessment (IGA)
- Psoriasis Area and Severity Index (PASI)
- Body surface area (BSA)
- scalp specific Investigator Global Assessment (ss-IGA)
- Static Physician's Global Assessment of Genitalia (sPGA-G)
- Physician's Global Assessment of hands and feet (hf-PGA)
- Fingernail Physician's Global Assessment (f-PGA)
- modified Nail Psoriasis Severity Index (mNAPSI)
- Physician Global Assessment (PGA) of Disease Activity for PsA

Patient-reported outcomes (PROs):

- Psoriasis Symptom and Sign Diary (PSSD)
- Dermatology Life Quality Index (DLQI)
- Children's Dermatology Life Quality Index (CDLQI)

- Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)
- Patient -Reported Outcomes Measurement Information System-29 (PROMIS-29)
- Patient-Reported Outcomes Measurement Information System Pediatric-25 v2.0 (PROMIS-25)
- Treatment Satisfaction Questionnaire for Medication - Effectiveness (TSQM-E)
- EuroQol-5 Dimension 5-level (EQ-5D-5L)
- Participant assessments of psoriatic arthritis (PsA) pain
- Participant assessments of PsA disease activity
- Participant assessment of acceptability and palatability

Photography assessments (optional)

PHARMACOKINETIC EVALUATIONS

Plasma samples will be used to evaluate the pharmacokinetics of JNJ-77242113.

IMMUNOGENICITY EVALUATIONS

Serum samples will be evaluated for antibodies to JNJ-77242113.

PHARMACODYNAMIC AND BIOMARKER EVALUATIONS

Biomarker assessments will be made to examine the biological response to treatment and to identify biomarkers that are relevant to JNJ-77242113 treatment response and/or psoriasis, where local regulations permit. Assessments will include the evaluation of relevant biomarkers in serum and skin biopsy samples (optional) collected.

PHARMACOGENOMIC (DNA) EVALUATIONS

A pharmacogenomic blood sample will be collected to allow for pharmacogenomic research, as necessary where local regulations permit. Participation in the pharmacogenomic research is optional.

SAFETY EVALUATIONS

Safety assessments for all participants will include adverse events (AEs), serious adverse events (SAEs), adverse events of special interest (AESIs), clinical laboratory assessments (hematology, chemistry including lipid panel, high sensitivity C-reactive proteins, pregnancy testing, and urinalysis), vital signs including blood pressure, electrocardiograms, depression screening and symptoms monitoring (Patient Health Questionnaire-9 [PHQ-9]), suicidal ideation and behavioral risk monitoring (Columbia-Suicide Severity Rating Scale), and tuberculosis (TB) evaluations.

STATISTICAL METHODS

Simple descriptive summary statistics, such as n, mean, SD, median, interquartile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data.

For binary endpoints, treatment comparisons will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by age group (adolescents <18 years and adults ≥18 years), baseline weight category for adults (≤90kg, >90kg) and geographic region. In case of rare events for binary endpoints, Fisher's exact test will be used. For repeated measure continuous endpoints, treatment comparisons will be performed using a Mixed-effect Model Repeated Measure (MMRM) model. The MMRM will include treatment, age group (adolescents <18 years and adults ≥18 years), baseline weight, geographic region and baseline value, as

explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. The LS mean estimates and their corresponding 95% CI will be provided at each timepoint. In addition, the estimates of LS mean difference and 95% CIs between treatment groups will be provided. Analysis of covariance (ANCOVA) will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, weight, geographic region and age group. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference and 95% CIs between treatment groups will be provided. For time to event endpoints, treatment comparisons will be performed using a log-rank test stratified by baseline weight category for adults (≤90kg, >90kg), geographic region and age group. Kaplan-Meier or life-table estimates of cumulative rate by treatment group will be provided to evaluate the timing of event occurrence in different treatment groups.

In general, all statistical tests will be performed at a significance level of 0.05 (2-sided) unless otherwise specified. Appropriate multiplicity adjustment procedure will be used to control the overall Type I error rate of α=0.05 (2-sided) for the primary and key secondary endpoints.

Primary Endpoints/Estimand

There are 2 co-primary endpoints in this study: an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 and a PASI 90 response at Week 16.

The primary estimand (ie, a precise definition of the primary targeted treatment effect) is defined by the following 5 attributes:

- **Study intervention:**
  - Experimental: JNJ-77242113
  - Placebo
- **Population:** participants ≥12 years of age with moderate to severe plaque psoriasis
- **Variable:** Binary response variables for the co-primary endpoints
  - IGA 0/1 response: a responder is defined as a participant achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 who does not have intercurrent events in categories 1 or 2.
  - PASI 90 response: a responder is defined as a participant achieving a PASI 90 response at Week 16 who does not have intercurrent events in categories 1 or 2.
- **Intercurrent event:**

Intercurrent Events and Corresponding Strategies

1.	Discontinuation of study intervention due to lack of efficacy or due to an AE of worsening psoriasis prior to Week 16.	**Composite Strategy:** Participants with these ICEs are considered as IGA score of 0 or 1, and PASI 90, non-responders at Week 16. The occurrence of these ICEs 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 prior to Week 16.	**Treatment Policy:** observed data will be used regardless of whether or not this ICE had occurred.

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

- **Population level summary:** Difference in the proportion of participants achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and the proportion of participants achieving a PASI 90 response at Week 16 between the JNJ-77242113 and placebo intervention groups.

Primary Endpoint Analysis

The co-primary endpoints will be analyzed using the primary estimand. After accounting for the ICEs for the primary estimand, participants with missing data for the co-primary endpoints at Week 16 will be considered as non-responders.

The co-primary endpoints will be compared between the JNJ-77242113 group and the placebo group by CMH chi-square test stratified by age group, baseline weight category for adult, and geographic region at a 2-sided α level of 0.05. The study will be considered positive if the JNJ-77242113 group is significantly different from the placebo group for both co-primary endpoints. If at least one of the comparisons is not significant at the 2-sided α level of 0.05, the co-primary endpoints will be considered not significant.

Key Secondary Endpoints

The proportion of participants who achieve following key secondary endpoints will be compared between the JNJ-77242113 group and the placebo group:

- IGA score of cleared (0) at Week 16
- PASI 75 response at Week 4
- PASI 90 response at Week 8
- PASI 75 response at Week 16
- PASI 100 response at Week 16
- ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline at Week 16 among participants with a baseline ss-IGA score ≥2.
- PSSD symptom score of 0 at Week 8 among participants with a baseline PSSD symptom score >0.
- At least a 4-point improvement from baseline in PSSD Itch score at Week 4 among participants with baseline PSSD Itch score of ≥4-points.
- At least a 4-point improvement from baseline in PSSD Itch score at Week 16 among participants with a baseline PSSD Itch score ≥4-points.
- PSSD symptom score of 0 at Week 16 among participants with a baseline PSSD symptom score >0.
- PASI 75 response at Week 52 among participants who are PASI 75 responders randomized at Week 24.
- PASI 90 response at Week 52 among participants who are PASI 90 responders randomized at Week 24.
- Time to loss of PASI 75 response among participants who are PASI 75 responders randomized at Week 24.
- Time to loss of PASI 90 response among participants who are PASI 90 responders randomized at Week 24.

Safety Analyses

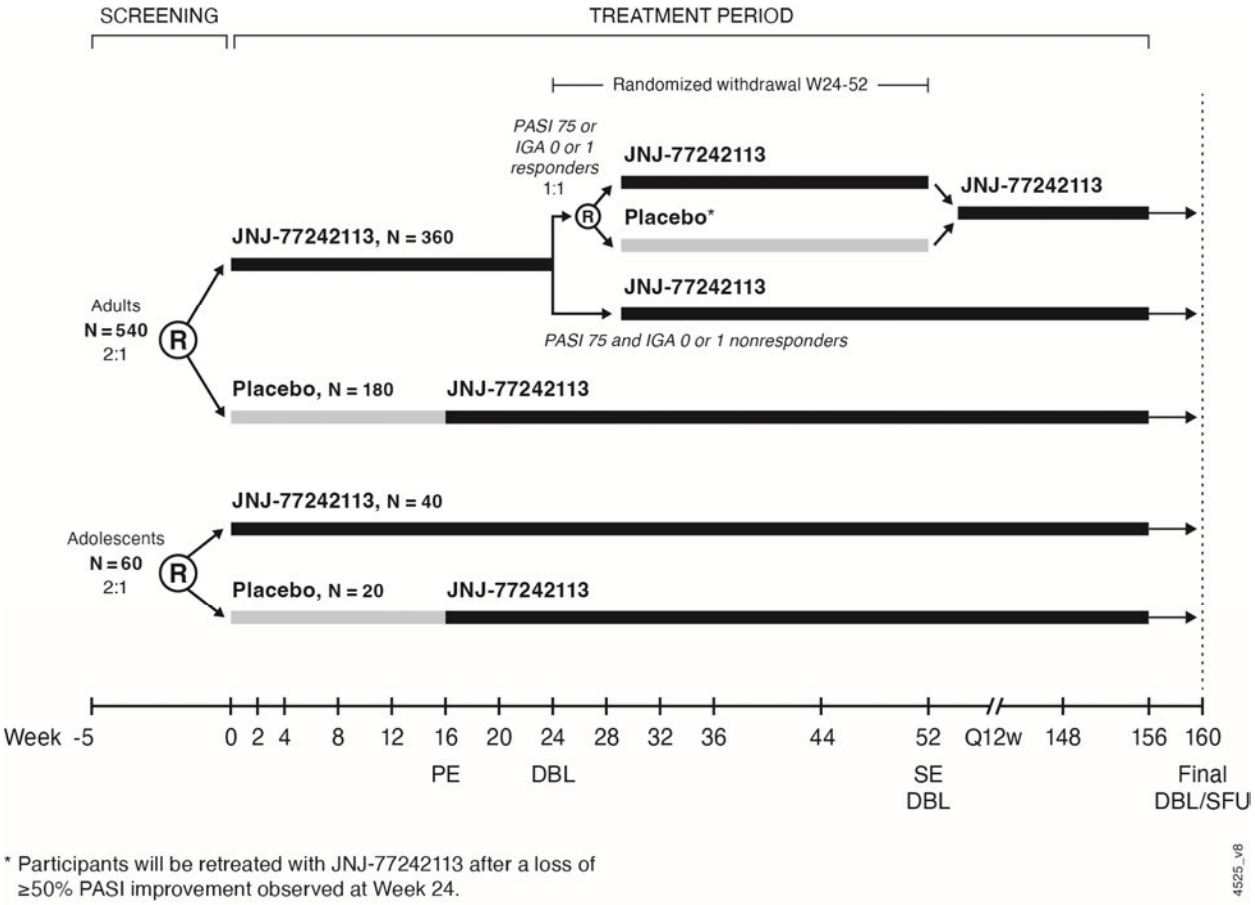
Safety data, including but not limited to, AEs, SAEs, AESIs (active TB, malignancy, possible Hy's Law cases), discontinuation of study intervention due to AEs, changes in laboratory assessments, changes in vital signs, changes in weight, changes in PHQ-9 scores, and changes in C-SSRS will be summarized. Treatment- emergent AEs will be summarized by treatment group and Medical Dictionary for Regulatory Activities system organ class and preferred terms. Details will be specified in the SAP.

Other Analyses

Pharmacokinetic analyses of plasma JNJ-77242113 concentrations will be summarized by visit and treatment group. Immunogenicity analyses of the incidence and titer of antibodies to JNJ-77242113 will be summarized for all participants who receive at least 1 dose of JNJ-77242113 and have appropriate samples for detection of antibodies to JNJ-77242113 (ie, participants with at least 1 sample obtained after their first dose of JNJ-77242113).

1.2. Schema

Figure 1 Schematic Overview of the Study



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

1.3. Schedule of Activities (SoA)

1.3.1. Schedule of Activities – Screening Through Week 52

Period	Screening	Placebo-controlled					JNJ-77242113 Treatment		Randomized withdrawal and retreatment						Unscheduled[a,b]	Notes: See Section 1.3.2 for Early Termination Visit procedures.
Week (W)	-5-0	0	2	4	8	12	16	20	24	28	32	36	44	52		
Visit Window (days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4		
Study Procedure																
Screening/Administrative																
ICF/assent	X															Must be signed before first study-related activity.
ICF/assent for optional skin biomarker substudy	X															ICF/assent for optional substudies can be signed at the Week 0 visit before any related substudy assessment are performed.
ICF/assent for optional photography substudy	X															
ICF/assent for optional DNA/ genomics substudy	X															
Demographics	X															
Medical history	X															Including psoriasis diagnosis.
Prestudy therapy	X															Review of medications, including previous psoriasis medications.
Inclusion/exclusion criteria (Section 5)	X	X														Minimum criteria for the availability of documentation supporting the eligibility criteria are described in Source Documents section of Appendix 2. Check clinical status again before first dose of study intervention.
Chest imaging	X															Chest radiographs or CT ≤12 weeks before first administration of study

Period	Screen-ing	Placebo-controlled					JNJ-77242113 Treatment		Randomized withdrawal and retreatment						Unsch-eduled[a,b]	Notes: See Section 1.3.2 for Early Termination Visit procedures.
Week (W)	-5-0	0	2	4	8	12	16	20	24	28	32	36	44	52		
Visit Window (days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4		
Study Procedure																
																intervention. This is optional for adolescent participants.
IGRA	X															Includes either QuantiFERON®-TB Gold Plus or T-SPOT® TB. In addition to IGRA, tuberculin skin test may be used to screen for latent TB if preferred by local health authorities or the investigator.
Hepatitis B and C serology	X															
HIV antibody test	X															
FSH	X															If needed to confirm postmenopausal status.
eDiary Compliance	X	X	X	X	X	X	X									Check eDiary completion and retraining of participants as necessary. Additional checks maybe performed as needed.
Study Intervention Administration																
Randomization		X							X							Randomization at W24 is rerandomization for adult participants receiving JNJ-77242113 from W0 to W24.
Dispense study intervention		X	X	X	X	X	X	X	X	X	X	X	X	X		Dispense study intervention after all other procedures. Study intervention may also be dispensed between visits.
Administer study intervention		Oral study intervention will be self-administered daily (Section 6.1).														Study intervention will be taken at the site during the baseline (W0), W4, and W16 visits, where both a pre- and post-dose PK sample will be drawn. At W16 study intervention will be

Period	Screen-ing	Placebo-controlled					JNJ-77242113 Treatment		Randomized withdrawal and retreatment						Unsch-eduled[a,b]	Notes: See Section 1.3.2 for Early Termination Visit procedures.
Week (W)	-5-0	0	2	4	8	12	16	20	24	28	32	36	44	52		
Visit Window (days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4		
Study Procedure																
																taken from a newly dispensed drug blister pack at the visit.
Study intervention accountability			X	X	X	X	X	X	X	X	X	X	X	X	X	
Efficacy Assessments																
PROs: Complete in the order shown before any tests, procedures, or consultations for all visits unless otherwise noted.																
PSSD (24-hour recall)	Daily Diary beginning at Screening through W16.															
PSSD (7-day recall)								X	X	X	X	X	X	X	X	
DLQI or CDLQI		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
GenPs-SFQ		X			X		X		X			X		X		W8-W52: Collect only for participants with active genital psoriasis at W0. Only for participants ≥18 years of age.
PROMIS-29 or PROMIS-25		X			X		X		X			X		X		PROMIS-25 is only for participants <18 years of age.
TSQM-E							X							X		Effectiveness domain only (Section 8.2.10.7).
EQ-5D-5L		X			X		X		X			X		X		
PsA Pain Assessment		X			X		X							X		W8-W52: Collect only for participants with a diagnosis of PsA at or before screening.
PsA Disease Activity Assessment		X			X		X							X		
Acceptability and palatability assessment		X					X									Only for participants <18 years of age.
ClinROs																
IGA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PASI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
BSA	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

Period	Screen-ing	Placebo-controlled					JNJ-77242113 Treatment		Randomized withdrawal and retreatment						Unsch-eduled[a,b]	Notes: See Section 1.3.2 for Early Termination Visit procedures.
Week (W)	-5-0	0	2	4	8	12	16	20	24	28	32	36	44	52		
Visit Window (days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4		
Study Procedure																
ss-IGA		X			X		X		X			X		X		W8-W52: collect only for participants with active scalp psoriasis at W0.
sPGA-G		X			X		X		X			X		X		W8-W52: collect only for participants with active genital psoriasis at W0.
hf-PGA		X			X		X		X			X		X		W8-W52: collect only for participants with active palmoplantar psoriasis at W0.
f-PGA		X			X		X		X			X		X		W8-W52: collect only for participants with active nail psoriasis at W0.
mNAPSI		X			X		X		X			X		X		
PGA of Disease Activity		X			X		X							X		Only for participants <18 years of age with a previous diagnosis of PsA at or before screening.
Photography (optional substudy)		X		X			X									
Safety Assessments																
Full physical examination	X	X												X		
Targeted physical examination			X	X	X	X	X	X	X	X	X	X	X			Recommended to include skin and general exam with additional organ systems based on investigator's judgement.
Tanner Staging		X												X		W52: Only for participants <18 years old at screening with previous Tanner stage <5.
Height	X	X					X							X		At screening, W16 and W52: Only for participants <18 years at Screening.
Weight	X	X					X							X		At screening: Only for participants <18 years of age.

Period	Screen-ing	Placebo-controlled					JNJ-77242113 Treatment		Randomized withdrawal and retreatment						Unsch-eduled[a,b]	Notes: See Section 1.3.2 for Early Termination Visit procedures.
Week (W)	-5-0	0	2	4	8	12	16	20	24	28	32	36	44	52		
Visit Window (days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4		
Study Procedure																
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Including temperature, heart rate, respiratory rate, and blood pressure.
12-lead triplicate ECG	X						X							X		
PHQ-9	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
TB evaluation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy test for female participants of childing bearing potential	X (serum)	X	X	X	X	X	X	X	X	X	X	X	X	X		A negative urine test result is required at each visit prior to dispensing study intervention. A urine pregnancy test may be performed at any time during the visit including before PROs.
Clinical Laboratory Tests																
Hematology	X	X		X	X	X	X	X	X	X	X	X	X	X		
Chemistry	X	X		X	X	X	X	X	X	X	X	X	X	X		
Lipid panel		X					X							X		Fasting requirement: ≥6 h unless medically contraindicated.
hs-CRP		X					X							X		
Urinalysis		X		X	X	X	X	X	X	X	X	X	X	X		May be performed any time during the study visit including before PRO collection.
Clinical Pharmacology Assessments																
JNJ-77242113 concentration (plasma)[c]		X		X		X	X			X		X		X		Collect 1 trough and 1 peak sample at W4 and W16. Details to be specified during training. If peak/trough collection at the W4 and W16 visits is not feasible, collection at an alternative visit is allowed.

Period	Screen-ing	Placebo-controlled					JNJ-77242113 Treatment		Randomized withdrawal and retreatment						Unsch-eduled[a,b]	Notes: See Section 1.3.2 for Early Termination Visit procedures.
Week (W)	-5-0	0	2	4	8	12	16	20	24	28	32	36	44	52		
Visit Window (days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4		
Study Procedure																
Antibodies to JNJ-77242113 (serum)		X		X		X	X			X		X		X		
Pharmacodynamics and Biomarkers																
Serum Biomarkers	X	X		X			X		X	X		X		X		Sample collection and testing will comply with local regulations.
Skin biopsy (optional skin biomarker substudy)		X							X					X		W0: Collect 1 lesional and 1 nonlesional biopsy. W24 and W52: Collect 1 lesional biopsy. Sample collection and testing will comply with local regulations.
Pharmacogenomics (DNA)																
Whole blood sample collection (optional substudy)		X														May be collected after W0 without constituting a protocol deviation. Sample collection and testing will comply with local regulations.
Ongoing Participant Review																
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Record all medications taken and new or worsening AEs reported after signing the ICF.
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

a. Additional assessments may be performed at the Unscheduled Visit at the investigator's discretion.

b. During the randomized withdrawal and retreatment period (Week 24 to Week 52) if a participant's psoriasis worsens and the participant and investigator would like to have the participant return to the site for reevaluation of PASI score an Unscheduled Visit can be conducted. At this visit if the participant is part of the blinded treatment group withdrawn from JNJ-77242113 treatment and has lost 50% or greater of their PASI score from Week 24, the participant will be retreated with JNJ-77242113 in a blinded manner. If a participant is not part of the withdrawn treatment group, they will continue on their treatment per study design.

c. At Week 0, all blood samples should be collected prior to study intervention administration and the date and time of collection should be recorded as instructed in the laboratory manual. At all other study visits where applicable, the date and time of the dose prior to the PK sample should be recorded as instructed in the CRF completion guidelines.

1.3.2. Schedule of Activities – Open Label Treatment

Period	Open-label Treatment									Safety Follow-up	Early Termination[a]	
Week (W)	64	76	88	100	112	124	136	148	156	160		
Visit Window (days)	±6	±6	±6	±6	±6	±6	±6	±6	±6	±6		
Study Procedure												**Notes:**
Study Intervention Administration												
Dispense study intervention	X	X	X	X	X	X	X	X				
Administer study intervention	Oral study intervention will be self-administered daily (Section 6.1).											
Study intervention accountability	X	X	X	X	X	X	X	X	X		X	
Efficacy Assessments												
PROs: Complete in the order shown before any tests, procedures, or consultations for all visits unless otherwise noted.												
PSSD (7-day recall)	X	X	X	X	X	X	X	X	X		X	
DLQI or CDLQI	X	X	X	X	X	X	X	X	X		X	
GenPs-SFQ	X		X		X		X		X		X	Collect only for participants with active genital psoriasis at W0. Only for participants ≥18 years of age.
PROMIS-29 or PROMIS-25	X		X		X		X		X		X	PROMIS-25 is only for participants <18 years of age.
PsA Pain Assessment	X		X		X		X		X		X	Collect only for participants with a diagnosis of PsA at or before screening.
PsA Disease Activity Assessment	X		X		X		X		X		X	
ClinROs												
IGA	X	X	X	X	X	X	X	X	X		X	
PASI	X	X	X	X	X	X	X	X	X		X	
BSA	X	X	X	X	X	X	X	X	X		X	
ss-IGA	X		X		X		X		X		X	Collect only for participants with active scalp psoriasis at W0.
sPGA-G	X		X		X		X		X		X	Collect only for participants with active genital psoriasis at W0.

Period	Open-label Treatment									Safety Follow-up	Early Termination[a]	
Week (W)	64	76	88	100	112	124	136	148	156	160		
Visit Window (days)	±6	±6	±6	±6	±6	±6	±6	±6	±6	±6		
Study Procedure												**Notes:**
hf-PGA	X		X		X		X		X		X	Collect only for participants with active palmoplantar psoriasis at W0.
f-PGA	X		X		X		X		X		X	Collect only for participants with active nail psoriasis at W0.
mNAPSI	X		X		X		X		X		X	
Safety Assessments												
Full physical examination					X				X		X	
Targeted physical examination	X	X	X	X		X	X	X		X		Recommended to include skin and general exam with additional organ systems based on investigator's judgement.
Tanner Staging					X				X			Only for participants <18 years old at Screening with previous Tanner stage <5.
Height					X				X			Only for participants <18 years old at screening.
Weight					X				X		X	
Vital signs	X	X	X	X	X	X	X	X	X	X	X	Including temperature, heart rate, respiratory rate, and blood pressure.
12-lead triplicate ECG					X				X		X	
PHQ-9	X	X	X	X	X	X	X	X	X	X	X	
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	
TB evaluation	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy test for female participants of childbearing potential	X	X	X	X	X	X	X	X	X	X	X	A negative urine test result is required at each visit prior to dispensing study intervention. A urine pregnancy test may be performed at any time during the visit, including before PROs.

Period	Open-label Treatment									Safety Follow-up	Early Termination[a]	
Week (W)	64	76	88	100	112	124	136	148	156	160		
Visit Window (days)	±6	±6	±6	±6	±6	±6	±6	±6	±6	±6		
Study Procedure												**Notes:**
Clinical Laboratory Tests												
Hematology	X		X		X		X		X	(X)	X	Safety follow-up sample only required if clinically significant at W156.
Chemistry	X		X		X		X		X	(X)	X	
Urinalysis	X		X		X		X		X		X	May be performed any time during the study visit including before PRO collection.
Clinical Pharmacology Assessments												
JNJ-77242113 concentration (plasma)[b]	X				X				X		X	
Antibodies to JNJ-77242113 (serum)	X				X				X		X	
Pharmacodynamics and Biomarkers												
Serum Biomarkers					X				X		X	Sample collection and testing will comply with local regulations.
Ongoing Participant Review												
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	Record all medications taken and new or worsening AEs reported after signing the ICF. See CRF completion guidelines.
Adverse events	X	X	X	X	X	X	X	X	X	X	X	

a. Participants who terminate study intervention early should have an Early Termination Visit approximately 4 weeks after their last administration of study intervention. If a scheduled visit occurs ≥ 4 weeks after the last dose, an additional ET visit is not required.

b. The date and time of the dose prior to the PK sample should be recorded as instructed in the CRF completion guideline.

2. INTRODUCTION

IL-23 is a disulfide-linked heterodimer of the IL-23p19 and IL-12/23p40 subunits. The receptor for IL-23 comprises the IL-23R and IL-12R subunits (Bloch 2018). IL-23p19 binding to the N-terminal immunoglobulin-like domain of IL-23R is followed by IL-12/23p40 binding to IL-12Rβ1. Ligand binding leads to phosphorylation and nuclear translocation of STAT proteins.

JNJ-77242113 is a peptide that binds directly to the IL-23R subunit and prevents IL-23 binding, thereby inhibiting proximal IL-23R signaling and downstream effector functions (eg, cytokine secretion). JNJ-77242113 has high potency with an IC50 of ~20-30 pM in peripheral human cell based functional assays. Despite its low oral bioavailability (<1%), JNJ-77242113 has demonstrated systemic effects and has provided substantial efficacy in plaque psoriasis clearance in doses 25 mg once daily and greater in the Phase 2b Study, 77242113PSO2001. Therefore, JNJ-77242113 is a promising candidate for further development in systemic, IL-23-driven diseases, such as plaque psoriasis.

To date, JNJ-77242113 has been studied in several Phase 1 and Phase 2 studies. For the most comprehensive nonclinical and additional clinical information regarding JNJ-77242113, refer to the latest version of the IB and Addenda for JNJ-77242113.

The term "study intervention" throughout the protocol, refers to study agent as defined in Section 6.1. Study Intervention(s) Administered.

The term "sponsor" used throughout this document refers to the entities listed in the Contact Information page(s), which will be provided as a separate document.

2.1. Study Rationale

In the United States, European Union, and Japan, there are approximately 3.5 million patients living with moderate to severe plaque psoriasis (BSA >10%). These patients are traditionally managed with topical and conventional therapies prior to advancing to subcutaneously administered biologics targeting TNF, IL-23, IL-12/23, or IL-17. Oral therapies, such as apremilast (PDE4 inhibitor) and deucravacitinib (TYK2 inhibitor), are also available as advanced therapeutic options for adults but are less efficacious relative to subcutaneously administered biologics (Armstrong 2020, 2023; Strober 2023). For adolescent plaque psoriasis participants (12-<18 years old), for which prevalence ranges from 0.25%/0.33% (male/female) to 2.15% (Parisi 2013; Wu 2011), treatment options for advanced disease are limited to subcutaneously administered biologics targeting TNF, IL-12/23 and IL-17, as IL-23 biologics and oral therapies are not yet approved for use. For those adult and adolescent patients who prefer oral medication, oral therapies with high efficacy, long-term clinical remission, and good safety profile remain a substantial unmet need (Nasa 2019).

Targeting IL-23 is a highly validated approach for treating moderate to severe plaque psoriasis. Interleukin-23 is composed of a unique p19 subunit coupled with the common p40 subunit shared with IL-12, and signals through the heterodimeric IL-23R/ IL-12Rβ1 complex (Teng 2015). Binding of IL-23 to the IL-23R complex leads to phosphorylation of STAT3 and IL-23 induced expression of proinflammatory cytokines, such as IL-17A/F and IL-22. Existing highly successful biologic therapies targeting IL-23, including those which target the p40 subunit of IL-23 (namely,

ustekinumab which is approved in adults and adolescents [REFERENCE]) and those targeting the p19 subunit of IL-23 (such as guselkumab [Blauvelt 2017; Reich 2017a] and risankizumab [Gordon 2018], which are approved in adults and being studied in pediatrics), act by preventing engagement of this ligand with the IL-23R ultimately causing reduced signaling. Available data from previous adult studies and pediatric studies highlight the critical role the IL-23/IL-23R axis has in the pathogenesis of psoriasis in both pediatric and adult patients and indicate that the clinical response, clinical manifestations, and histological features of psoriasis are generally similar between the pediatric and adult psoriasis populations.

JNJ-77242113 has shown good efficacy and was well tolerated in the Phase 2b Study 77242113PSO2001. Results from this study show that JNJ-77242113 met the primary endpoint of PASI 75 at Week 16 demonstrating a statistically significant dose response across the treatment groups (placebo, 25 mg once daily, 25 mg twice daily, 50 mg once daily, 100 mg once daily and 100 mg twice daily). JNJ-77242113 was well tolerated by participants in all treatment groups, and the proportion of participants who experienced 1 or more AE was comparable between the JNJ-77242113 groups and the placebo group (Section 2.2).

Based on the positive results observed in the Phase 2 study, JNJ-77242113 is being further assessed in this Phase 3 program. The enrollment of adolescents concurrently with adults in this Phase 3 program is supported by the safety profile established with JNJ-77242113, the scientific rationale that adults and adolescents with psoriasis have the same clinical manifestations, histological features, and anticipated response to JNJ-77242113, and indirectly through the safety and efficacy profile of other IL-23 inhibitors which are used to treat adult psoriasis and studied in ongoing trials for pediatric psoriasis. The Phase 3 Study 77242113PSO3001 is a randomized, double-blind, parallel-group, placebo-controlled study with randomized withdrawal and retreatment of JNJ-77242113 designed to evaluate the efficacy and safety of JNJ-77242113 in participants ≥12 years of age with moderate to severe plaque psoriasis.

2.2. Background

A Phase 1 PK study in healthy participants has been completed. One Phase 2b study of JNJ-77242113 for the treatment of moderate to severe plaque psoriasis (77242113PSO2001) has been also completed and demonstrated a favorable efficacy and safety profile for JNJ-77242113.

Clinical Studies

Efficacy/Safety Studies

Phase 1

Overall, the safety data from 3 Phase 1 studies in healthy participants demonstrate that single and multiple oral doses of JNJ-77242113 administered as an oral solution (PN-235-01, final data) and single oral doses administered as IR tablets or DR tablets with CCI (77242113PSO1002 and 77242113PSO1003, preliminary data) were generally well tolerated and with no safety signals. Refer to the JNJ-77242113 IB for more information.

Phase 2

77242113PSO2001, was a Phase 2b multicenter, randomized, double-blind, placebo-controlled, dose-ranging, parallel-group, multicenter study to evaluate the efficacy and safety of JNJ-77242113 treatment in 255 adults with moderate to severe plaque psoriasis over 16 weeks. In Study 77242113PSO2001, a dose response was observed for the primary endpoint (PASI 75 response at Week 16). A statistically significant higher proportion of participants in each JNJ-77242113 dose group achieved a PASI 75 response at Week 16 (37.2% for 25 mg once daily, 58.1% for 50 mg once daily, 51.2% for 25 mg BID, 65.1% for 100 mg once daily, 78.6% for 100 mg BID; nominal p=0.002 for 25 mg once daily; nominal p<0.001 for all other dose groups) than the placebo group (9.3%). All statistical testing was performed at the 2-sided 0.05 significance level.

Secondary endpoints (IGA score of cleared [0] or minimal [1], IGA score of cleared [0], PASI 90 score, PASI 100 score and DLQI score of 0 or 1) achieved statistical significance at a nominal significance level of 0.05 (2-sided) at Week 16 for all doses compared with placebo. At Week 16, participants in each of the JNJ-77242113 dose groups had a statistically significant greater improvement (reduction) as measured by PASI total score, BSA, PSSD symptom score, and PSSD sign score from baseline than participants treated with placebo.

Safety data are summarized for participants who completed 77242113PSO2001 at the Week 16 visit:

- Overall, there was no clear evidence of a dose-dependent increase in the occurrence of specific AEs across the JNJ-77242113 groups.
- The proportions of participants who experienced 1 or more AEs were similar in the combined JNJ-77242113 (52.4%) and placebo (51.2%) groups.
- The most frequently reported AEs were in the Infections and infestations SOC and were similar between the combined JNJ-77242113 (30.2%) and placebo (27.9%) groups. The most common AEs by PT in this SOC were COVID-19 (10.8% and 11.6%), nasopharyngitis (7.1% and 4.7%), and upper respiratory tract infection (2.4% and 2.3%) in the combined JNJ-77242113 and placebo groups, respectively. In the Gastrointestinal disorders SOC, AEs were reported in 11.3% of participants in the combined JNJ-77242113 group and 11.6% in the placebo group. Other AEs by PT reported by at least 5% of participants included headache and cough.
- The percentage of participants with one or more SAEs through the end of study was small, with 3 participants (1.4%) experiencing one SAE each. All events were singular in nature and deemed not related to study intervention per the investigator.
- The proportion of participants who discontinued study intervention due to 1 or more AEs was small (n=6). Three out of the six events were in the Gastrointestinal SOC (n=1 each: abdominal pain, abdominal discomfort, and nausea). The other three events included suicide attempt, weight increase, and transaminases increase (n=1 each).
- Rates of abnormal labs were generally low and comparable between the treatment groups.
- There were no deaths or malignancies reported.

Human Pharmacokinetics and Immunogenicity

The clinical data available to date supporting the safety, PK and PD of JNJ-77242113 are from completed Phase 1 studies in healthy subjects and Phase 2 studies in adults with moderate to severe plaque psoriasis.

PK data from FIH study PN-235-01 indicate that systemic exposure (Cmax and AUC) to JNJ-77242113 is dose proportional across the dose range evaluated to date. After multiple once daily dosing, steady state was achieved by Day 7 (earliest timepoint evaluated), with minimal drug accumulation consistent with the observed mean terminal phase half-life of approximately 9 to 12 hours.

The PK results from 77242113PSO1003 indicate that concomitant food (high calorie, high-fat or low calorie, low-fat breakfast) increased the median time to reach tmax and significantly reduced the rate (Cmax) and extent (AUC) of JNJ-77242113 absorption. Based on the food effect data from protocol 77242113PSO1003, study intervention should be administered under fasted conditions.

Using the population PK model, a number of baseline participant characteristics were evaluated as potential covariates affecting JNJ-77242113 PK parameters. Of the covariates evaluated, only CCI were found to be significant. Of note, laboratory markers of renal and hepatic function were not found to be significant covariates affecting the PK of JNJ-77242113, consistent with the nonclinical and clinical metabolic clearance and excretion of the drug.

No CCI have been detected in the completed Phase 1 clinical studies. The overall incidence of CCI in the Phase 2b study (77242113PSO2001) was CCI Given that the peptide is administered by the oral route and does not have an endogenous counterpart, the risk of adverse effects caused by CCI is expected to be minimal.

2.3. Benefit-risk Assessment

More detailed information about the known and expected benefits and risks of JNJ-77242113 may be found in the IB.

2.3.1. Risks for Study Participation

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
Potential Risks Due to Study Intervention JNJ-77242113		
Hypersensitivity Reactions	Exogenous peptides administered orally or systemically have the potential to cause hypersensitivity reactions.	• This potential risk will be explained in the ICF, and participants will be trained to recognize early signs of impending anaphylaxis (Sampson 2006) and seek medical attention. • Participants with known allergy, hypersensitivity, or intolerance to JNJ-77242113 or its excipients will be excluded from the study. • Any participant who develops a serious hypersensitivity reaction such as anaphylaxis must discontinue study intervention (Section 7).

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
ADA production	Exogenous peptides administered orally or systemically can have the potential to induce ADA production, which may mediate untoward reactions such as reduced efficacy or hypersensitivity.	• This potential risk will be explained in the ICF and evaluated by measuring ADAs and PK for analysis. • Participants are encouraged to consistently take their study intervention 24 hours apart, as directed.
Infection	Clinical experience with marketed IL-23 pathway blockers include precautions for infections and TB.	• This potential risk is included in the ICF. • Participants with evidence of active TB will be excluded from the study (Section 5.2). • Participants must agree not to receive a live viral or live bacterial vaccination 4 weeks prior to enrollment in the study or during the study and for 4 weeks after receiving the last dose of study intervention (Section 5). Additional guidance is provided for the BCG vaccine in Section 5.2. • Participants will be educated and instructed to seek medical attention if they develop signs or symptoms suggestive of an infection, and investigators are instructed to monitor for signs or symptoms of infections, including TB (Section 8.3.7). • Discontinuation of a participant's study intervention must be strongly considered if the participant develops a serious infection, including but not limited to sepsis or pneumonia. In addition, any serious infection should be discussed with the medical monitor or designee, and study intervention should be withheld until the clinical assessment is complete (Section 7).
Risks Due to Study Procedures		
Skin biopsy (optional substudy)	Mild bleeding, pain, discomfort, scarring, discoloration, and infection may occur as part of biopsy procedure.	This risk will be included in the sub-study ICF. Trained and experienced physicians will be performing the procedure during this study.

2.3.2. Benefits for Study Participation

JNJ-77242113 has demonstrated significant efficacy compared with placebo for both ClinROs and PROs including disease severity and extent, quality of life measures and patient reported signs and symptoms of psoriasis based on a Phase 2b Study 77242113PSO2001 (Section 2.2). Participants treated with JNJ-77242113 may benefit from receiving this medication and may benefit from receiving routine clinical care during this study.

2.3.3. Benefit-risk Assessment for Study Participation

The measures taken to minimize risk to participants of this study, the potential risks identified in association with JNJ-77242113 are justified by the anticipated benefits that may be afforded to participants with moderate to severe plaque psoriasis.

Direct benefits and risks for adolescent participants have not been established in previous clinical trials of JNJ-77242113, but because adult and adolescent moderate to severe plaque psoriasis patients share similar clinical manifestations, histological features, and anticipated response to JNJ-77242113 the benefit and risks to study participation for adults and adolescents are anticipated to be the same (Section 2.1 Study Rationale).

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16. • PASI 90 at Week 16.
Secondary	
Key Secondary • To further evaluate the general and special area psoriasis efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• IGA score of 0 at Week 16. • PASI 75 at Week 4. • PASI 90 at Week 8. • PASI 75 at Week 16. • PASI 100 at Week 16. • ss-IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16.
• To evaluate the effect of JNJ-77242113 on PROs in participants with moderate to severe plaque psoriasis.	• PSSD symptom score of 0 at Week 8. • PSSD symptom score of 0 at Week 16. • ≥4-point improvement from baseline in PSSD Itch score at Week 4. • ≥4-point improvement from baseline in PSSD Itch score at Week 16.
• To evaluate the maintenance of efficacy of JNJ-77242113 compared with treatment withdrawal during the randomized withdrawal period.	• PASI 75 at Week 52. • PASI 90 at Week 52. • Time to loss of PASI 75. • Time to loss of PASI 90.
Other Secondary • To assess the safety and tolerability of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• Frequency and type of AEs and SAEs.
• To further evaluate the general and special area psoriasis efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• Change from baseline in BSA at Week 16. • Change from baseline in PASI at Week 16. • Percent improvement in PASI at Week 16.

Objectives	Endpoints
	• sPGA-G score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16. • hf-PGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16. • Percent change from baseline in mNAPSI score at Week 16. • f-PGA score of 0 or 1 at Week 16.
• To further evaluate the effect of JNJ-77242113 on PROs in participants with moderate to severe plaque psoriasis.	• Change from baseline in PSSD symptom score at Week 16. • Change from baseline in PSSD sign score at Week 16. • PSSD sign score of 0 at Week 16. • GenPs-SFQ Item 2 score of 0 or 1 at Week 16. • DLQI score of 0 or 1 at Week 16. • Change from baseline in DLQI total score at Week 16. • Change from baseline in the domain scores of the PROMIS-29 score at Week 16. • CDLQI score of 0 or 1 at Week 16. • Change from baseline in CDLQI at Week 16. • Change from baseline in the domain scores of the PROMIS-25 pediatric score at Week 16.
• To further evaluate the maintenance of efficacy of JNJ-77242113 compared with treatment withdrawal during the randomized withdrawal period.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 52. • IGA score of 0 at Week 52. • PASI 100 at Week 52. • Time to loss of IGA 0 or 1 response.
• To evaluate long-term psoriasis efficacy of JNJ-77242113 in adolescent participants with moderate to severe plaque psoriasis.	• IGA 0 or 1 and a ≥2-grade improvement from baseline at Week 52. • PASI 75 at Week 52. • PASI 90 at Week 52.
Exploratory	
• To further assess the safety and tolerability of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• Frequency and type of related AEs and AEs leading to discontinuation of study intervention. • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time.

Objectives	Endpoints
• To further evaluate efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	Endpoints will be based on the following assessments: • IGA, PASI, BSA, ss-IGA, sPGA-G, hf-PGA, f-PGA, mNAPSI, PGA of Disease activity.
• To further evaluate the effect of JNJ-77242113 on PROs in participants with moderate to severe plaque psoriasis.	Endpoints will be based on the following assessments: • PSSD, GenPs-SFQ, TSQM-E efficacy domain, DLQI/CDLQI, EQ-5D-5L, PROMIS-29/ PROMIS-25, PsA Pain assessment, PsA Disease Activity assessment.
• To evaluate the PK and immunogenicity of JNJ-77242113 and explore the E-R relationship of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• JNJ-77242113 PK parameters. • The relationship between PK parameters and efficacy. • The incidence of anti-drug antibodies to JNJ-77242113.
• To explore biomarkers in participants with moderate to severe plaque psoriasis.	• Change from baseline in cellular and molecular biomarkers in skin and blood.
• To evaluate the efficacy of JNJ-77242113 retreatment after relapse for adult participants who were withdrawn from JNJ-77242113 at Week 24.	• Endpoints will be based on the following assessments: PASI, IGA, PSSD.

ESTIMANDS

The primary estimand (ie, a precise definition of the primary targeted treatment effect) is defined by the following 5 attributes:

- **Study intervention:**
  - Experimental: JNJ-77242113
  - Placebo
- **Population:** participants ≥12 years of age with moderate to severe plaque psoriasis.
- **Variable:** Binary response variables for the co-primary endpoints:
  - IGA 0/1 response: a responder is defined as a participant achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 who does not have intercurrent events in categories 1 or 2 (Table 1).
  - PASI 90 response: a responder is defined as a participant achieving a PASI 90 response at Week 16 who does not have intercurrent events in categories 1 or 2 (Table 1).
- **Intercurrent event:** (Table 1)
- **Population level summary:** Difference in the proportion of participants achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and the

proportion of participants achieving a PASI 90 response at Week 16 between the JNJ-77242113 and placebo intervention groups.

Refer to Section 8. Study Assessments and Procedures for evaluations related to endpoints.

HYPOTHESIS

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

4. STUDY DESIGN

4.1. Overall Design

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

A target of 600 participants will be enrolled in this study. Approximately 540 adults and 60 adolescent participants will be randomized with a 2:1 randomization ratio to JNJ-77242113 200 mg or placebo. Randomization will be separately performed for adult and adolescent groups. Within the adult group, randomization will be further stratified by baseline weight category (≤90kg, >90kg) and geographic region. Within the adolescent group, randomization will be further stratified by geographic region.

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

    - Week 52 to Week 156: Participants will receive JNJ-77242113 200 mg once daily through Week 156.
  - Placebo to JNJ-77242113 200 mg once daily
    - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
    - Week 16 to Week 156: Participants will cross-over to receive JNJ-77242113 200 mg once daily through Week 156.
- Adolescent participants
  - JNJ-77242113 200 mg once daily
    - Week 0 to Week 156: Participants will be treated with JNJ-77242113 200 mg once daily
    - Adolescents will not participate in re-randomization regardless of their PASI score or IGA score at Week 24.
  - Placebo to JNJ-77242113 200 mg once daily
    - Week 0 to Week 16: Participants will receive placebo once daily through Week 16.
    - Week 16 to Week 156: Participants will cross-over to receive JNJ-77242113 200 mg once daily through Week 156.

This study includes a 5-week screening period, a placebo-controlled period through Week 16 and a randomized withdrawal and retreatment period from Week 24 through Week 52. At Week 52, participants will be transitioned to open-label JNJ-77242113 through Week 156. All participants will have a 4-week safety follow-up period after the last administration of study intervention or at the end of the treatment period. The total duration of this study for each participant is approximately 165 weeks.

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

The first DBL will occur when all participants (adults and adolescents) complete Week 24 of the study. An additional DBL will occur after all adult participants complete Week 52 of the study. Additional DBLs may occur between Week 52 to 160 to support publication or regulatory submissions including when additional time may be needed to reach country-specific data requirements. Details of the DBL(s) will be included in the SAP.

An independent DMC will be commissioned for this study. Refer to Committees Structure in Appendix 2, Regulatory, Ethical, and Study Oversight Considerations for details. A diagram of the study design is provided in Section 1.2., Schema.

4.2. Scientific Rationale for Study Design

Blinding, Control, Study Phase/Periods, Intervention Groups

A placebo control will be used to establish the frequency and magnitude of changes in clinical endpoints that may occur in the absence of active intervention. Randomization will be used to minimize bias in the assignment of participants to intervention groups, to increase the likelihood that known and unknown participant attributes (eg, demographic and baseline characteristics) are evenly balanced across intervention groups, and to enhance the validity of statistical comparisons across intervention groups. Blinded intervention will be used to reduce potential bias during data collection and evaluation of clinical endpoints.

DNA and Biomarker Collection

It is recognized that genetic variation can be an important contributory factor to interindividual differences in intervention distribution and response and can also serve as a marker for disease susceptibility and prognosis. Pharmacogenomic research may help to explain interindividual variability in clinical outcomes and may help to identify population subgroups that respond differently to an intervention. The goal of the pharmacogenomic component is to collect DNA to allow the identification of genetic factors that may influence the PK, PD, efficacy, safety or tolerability of JNJ-77242113 and to identify genetic factors associated with moderate to severe plaque psoriasis.

Biomarker samples will be collected to evaluate mechanism of action of JNJ-77242113 help to explain interindividual variability in clinical outcomes or may help to identify population subgroups that respond differently to an intervention. The goal of the biomarker analyses is to evaluate the PD of JNJ-77242113 and aid in evaluating the intervention-clinical response relationship.

DNA and biomarker samples may be used to help address emerging issues and to enable the development of safer, more effective, and ultimately individualized therapies. Sample collection and testing will comply with local regulations.

4.2.1. Participant Input into Design

In setting the strategy for the treatment of moderate to severe plaque psoriasis, participants were engaged early, systematically, and directly across important aspects of the drug development process.

Patient input was used to design the following elements of this study:

- The once daily dose regimen was chosen to increase convenience compared with twice daily regimen.
- Lifestyle considerations were modified based on patient feedback related to sun exposure.
- The SoA was developed to ensure the number of visits, frequency of visits, and tests within each visit were manageable for participants with moderate to severe plaque psoriasis.

The results of the study may be made available to all participants through a plain language summary; a technical summary of results on clinicaltrials.gov and/or clinicaltrialsregister.eu

and/or other national registries at the conclusion of the study according to local standards/restrictions.

4.2.2. Study-specific Ethical Design Considerations

Potential participants and legal guardians of adolescent participants, if appropriate, will be fully informed of the risks and requirements of the study, and during the study, participants will be given any new information that may affect their decision to continue participation. They will be told that their consent (and assent, if applicable) to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only participants who are fully able to understand the risks, benefits, and potential AEs that may be associated with study participation, and provide their consent voluntarily will be enrolled. Only adolescent participants whose legal guardian(s) are fully able to understand the risks, benefits, and potential AEs of the study, and provide their consent voluntarily will be enrolled. Written consent/assent may be obtained through various sources (eg, paper or electronic such as eConsent, eSignature, or digital signature) as determined by regulations as well as study and/or participant preferences.

The primary ethical concern for participants is for participants in the placebo control arm who will not receive active treatment. This concern will be mitigated by the cross-over design which allows participants in the placebo group to receive active treatment with JNJ-77242113 after Week 16, which has been shown to be efficacious in the treatment of moderate to severe plaque psoriasis in Study 77242113PSO2001. An additional concern is for adult participants who are transitioned from JNJ-77242113 to placebo from Week 24 to Week 52. This concern will be mitigated as all participants will be retreated with JNJ-77242113 upon loss of ≥50% of Week 24 PASI improvement or starting at Week 52 if loss of response is not observed.

Participants will be discontinued from study intervention if the investigator considers it is in the best interest of the participant (Section 7.1).

The total blood volume to be collected is considered to be an acceptable amount of blood to be collected over this time period from the population in this study based upon the standard of the American Red Cross (approximately 450 mL every 8 weeks). Blood draws do not exceed 3% of the total blood volume over a period of four weeks and do not exceed 1% at any single time. For more details regarding blood collection, see Blood Sample Collection in Section 8.

4.3. Justification for Dose

The observed human PK and PD data from the FIH study were used to develop preliminary population PK and PK/PD models along with the in vitro pathway inhibition data. The JNJ-77242113 dose selection for the Phase 3 studies in psoriasis is based on CCI [redacted] Phase 2b Study, 77242113PSO2001. A population PK-based E-R analysis of Study 77242113PSO2001 data shows that C_{avg} JNJ-77242113 concentrations describe the E-R relationship better than C_{trough}. In the 77242113PSO2001 study, both a dose-response and an E-R analysis show a dose/exposure-dependent increase in clinical efficacy with a JNJ-77242113 dose of 100 mg twice daily providing biologic-like efficacy without evidence of dose related safety or

tolerability signals. Based on several modeling approaches, it is predicted that a JNJ-77242113 200 mg once daily dose will provide comparable inhibition of IL-23R and clinical efficacy (ie, PASI and IGA) as the 100 mg twice daily dose. Therefore, considering the simpler once daily vs twice daily dose regimen from a patient acceptability and compliance perspective, a dose of JNJ-77242113 200 mg once daily has been selected for the Phase 3 efficacy and safety studies. The AUC exposure estimate at the regimen of 200 mg once daily is at least [redacted]-fold lower than exposures at the NOAEL in the rat and monkey chronic studies.

The dose and regimen of JNJ-77242113 selected for this Phase 3 study, based on the Phase 2b clinical dose-response and E-R modeling, will maximize the likelihood of a positive study outcome and is supported by human safety and tolerability data from the Phase 1 and Phase 2 studies and the toxicology margins.

4.4. End of Study Definition

End of Study Definition

The end of study is considered as the last scheduled study assessment shown in the SoA for the last participant in the study. The final data from the study site will be sent to the sponsor (or designee) after completion of the final participant assessment at that study site, in the time frame specified in the Clinical Trial Agreement.

Participant Study Completion Definition

A participant will be considered to have completed the study if the participant has completed assessments at Week 160. Disposition of study participation will be collected at each DBL.

5. STUDY POPULATION

Screening for eligible participants will be performed within 5 weeks before administration of the study intervention.

The inclusion and exclusion criteria for enrolling participants in this study are described below. Efforts will be made to ensure broad representation in terms of race, ethnicity, and sex. If there is a question about these criteria, the investigator must consult with the appropriate sponsor representative and resolve any issues before enrolling a participant in the study. Waivers are not allowed. For a discussion of the statistical considerations of participant selection, refer to Section 9.5, Sample Size Determination.

5.1. Inclusion Criteria

Each potential participant must satisfy all of the following criteria to be enrolled in the study:

Age

1. ≥12 years of age at the screening visit.

Type of Participant and Disease Characteristic(s)

2. Diagnosis of plaque psoriasis, with or without psoriatic arthritis, for at least 26 weeks prior to the first administration of study intervention.
3. Total BSA ≥10% at screening and baseline.
4. Total PASI ≥12 at screening and baseline.
5. Total IGA ≥3 at screening and baseline.
6. Candidate for phototherapy or systemic treatment for plaque psoriasis.

Weight

7. For participants ≥12 to <18 years of age, body weight must be ≥40 kg at baseline.

Sex and Contraceptive/Barrier Requirements

8. A female participant of childbearing potential must have a negative highly sensitive serum pregnancy test (β-hCG) at screening and a negative urine pregnancy test at Week 0 prior to administration of study intervention.
9. A female participant must agree to not be pregnant, breastfeeding, or planning to become pregnant while enrolled in this study or within 4 weeks after the last dose of study intervention.
10. A female participant must be (as defined in Appendix 4, Contraceptive and Barrier Guidance).
    a. Not of childbearing potential

    OR

b. of childbearing potential and

- Practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) and agrees to remain on a highly effective method while receiving study intervention and until 4 weeks after last dose. The investigator must evaluate the potential for contraceptive method failure (eg, noncompliance, recently initiated) in relationship to the first dose of study intervention. The method selected must meet local/regional regulation/guidelines. Examples of highly effective methods of contraception are located in Appendix 4, Contraceptive and Barrier Guidance.

  Note: If a participant's childbearing potential changes after start of the study (eg, a premenarchal female participant experiences menarche) or the risk of pregnancy changes (eg, a female participant who is not heterosexually active becomes active), a female participant must begin using a highly effective method of contraception (Appendix 4, Contraceptive and Barrier Guidance).

11. A female participant must agree not to donate eggs (ova, oocytes) or freeze for future use for the purposes of assisted reproduction during the study and for at least 4 weeks after the last dose of study intervention.

12. A male participant must agree not to plan to father a child while enrolled in this study or within 90 days after the last dose of study intervention.

13. A male participant who has not had a vasectomy must agree to use a barrier method of birth control (eg, either wear a condom [with spermicidal foam/gel/film/cream/suppository if available in their locale] or a partner with an occlusive cap [diaphragm or cervical/vault caps] plus spermicidal foam/gel/film/cream/suppository if available in their locale) when engaging in any activity that allows for passage of ejaculate to a female of childbearing potential during the study and for 90 days after the last dose of study intervention. Male participants must also be advised of the benefit for a female partner to use a highly effective method of contraception as condom may break or leak.

14. A male participant must agree not to donate sperm for the purpose of reproduction during the study and for a minimum of 90 days after receiving the last dose of study intervention.

Informed Consent

15. Criterion modified per Global Amendment 2

    15.1 Must sign an ICF indicating that participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.

    For participants under the legal age of consent, parent(s) (preferably both if available or as per local requirements) (or their legally acceptable representative) must sign an ICF indicating that they understand the purpose of, and procedures required for, the study and is/are willing to allow the child to participate in the study. Per local requirements, assent is also required of children capable of understanding the nature of the study, and once children or minors have reached the legal age of consent, they will be required to sign the ICF.

16. Criterion modified per Global Amendment 2

    16.1 Must sign a separate ICF for the respective substudy(ies) if the participant agrees to provide the optional DNA sample, skin biopsies, or photographs for research (where local regulations permit). Refusal to give consent for the optional DNA research sample, skin biopsies, or photographs does not exclude a participant from participation in the study.

    For participants under the legal age of consent, parent(s) (preferably both if available or as per local requirements) (or their legally acceptable representative) must sign a separate ICF for the respective substudy(ies) if they agree to the child providing an optional DNA sample, skin biopsies, or photographs for research. Per local requirements, assent is also required of children capable of understanding the nature of the study, and once children or minors have reached the legal age of consent, they will be required to sign the ICF.

17. Is willing and able to adhere to the lifestyle restrictions specified in this protocol (Section 5.3).

5.2. Exclusion Criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the study:

Medical Conditions

1. Nonplaque form of psoriasis (eg, erythrodermic, guttate, or pustular).
2. Current drug-induced psoriasis (eg, a new onset of psoriasis or an exacerbation of psoriasis from beta blockers, calcium channel blockers, or lithium).
3. A current diagnosis or signs or symptoms of severe, progressive, or uncontrolled renal, liver, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances.
4. Known allergies, hypersensitivity, or intolerance to JNJ-77242113 or its excipients (refer to the JNJ-77242113 IB).
5. Major surgical procedures, (eg, requiring general anesthesia) within 8 weeks before screening, or will not have fully recovered from a surgical procedure or has a surgical procedure planned during the time the participant is expected to participate in the study. Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate.
6. Transplanted organ (with exception of a corneal transplant >12 weeks before the first administration of study intervention).
7. All Participants with:
   - Suicidal ideation in the 26 weeks prior to screening that may be defined as a C-SSRS rating of: Wish to be Dead, Non-Specific Active Suicidal Thoughts, or Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act and is considered to be at risk by the investigator.

   Participants ≥18 years if age with:

- Suicidal ideation or suicidal behavior in the 26 weeks prior to screening that may be defined as a C-SSRS rating of: Suicidal Ideation with Intention to Act, Suicidal Ideation with Specific Plan and Intent, Actual suicide attempt, Interrupted suicide attempt, Aborted suicide attempt, or Preparatory behaviors for making a suicide attempt, and is considered to be at risk by the investigator based on an evaluation by a mental health professional.

Participants ≥12 to <18 years of age with:

- Suicidal ideation or non-suicidal self-injurious behavior in the 26 weeks prior to screening that may be defined as a C-SSRS rating of: Suicidal Ideation with Intention to Act, Suicidal Ideation with Specific Plan and Intent, or non-suicidal self-injurious behavior.
- Any suicidal behavior in their lifetime that maybe defined as a C-SSRS rating at screening of: Actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt.

8. History of drug or alcohol abuse within 1 year before screening.

Prior/Concomitant Therapy

9. Previously received JNJ-77242113.
10. Experienced primary efficacy failure (no response within 16 weeks) to 1 or more agents directly targeting IL-23 or has had a clinically significant AE to 1 or more agents directly targeted to IL-23.

    Note: This criterion does not apply to previous IL-12/23 use.

	Prohibited Medication or Class of Medications	Restriction Duration (through End of Study)
11.	Agents that deplete B cells: • alemtuzumab or rituximab	26 weeks prior to the first administration of study intervention
12.	Any biologic therapy including but not limited to: • IL-23-inhibitors: guselkumab, tildrakizumab, risankizumab (Additional exclusions apply; see EC 9 and 10). • IL-17 inhibitors: secukinumab, brodalumab, ixekizumab. • IL-12/23 inhibitors: ustekinumab, briakinumab. • TNFα antagonists: adalimumab, infliximab, etanercept, certolizumab, golimumab. • natalizumab • belimumab • abatacept • visilizumab	12 weeks or 5 half-lives, whichever is longer, prior to the first administration of study intervention

	• experimental or investigational therapy	
	Prohibited Medication or Class of Medications	**Restriction Duration (through End of Study)**
13.	Systemic immunomodulating treatments including but not limited to: • methotrexate, azathioprine, cyclosporine A, corticosteroids, cyclophosphamide, tofacitinib, apremilast, deucravacitinib Other therapeutic procedures: • phototherapy Systemic medications that could affect psoriasis evaluations including, but not limited to: • acitretin, retinoids, herbal treatments, or traditional Taiwanese, Korean, or Chinese medicines Nonbiologic experimental therapies or investigational agents	4 weeks prior to the first administration of study intervention
14.	Topical medications/treatments that could affect psoriasis evaluations including, but not limited to: • Corticosteroids, calcineurin inhibitors, vitamin D analogs, vitamin A analogs, retinoids, tar, anthralin, calcipotriene, tazarotene, methoxsalen, trimethylpsoralens, fumarate, PDE4 inhibitors, aryl hydrocarbon receptor-modulating agents • Shampoos that contain corticosteroids, coal tar, or vitamin D3 analogs • Herbal treatments or traditional Taiwanese, Korean, or Chinese medicines	2 weeks prior to the first administration of study intervention
15.	Live virus or bacterial vaccination	4 weeks (or longer if required per vaccine package insert) prior to the first administration of study intervention
16.	BCG vaccination	1 year prior to the first administration of study intervention

Diagnostic Assessments

17. Screening laboratory test results within the following parameters:
    - Hemoglobin: <10 g/dL (SI: <100 g/L)
    - White blood cells: <3.5 x 10^3/µL (SI: <3.5 GI/L)

- Neutrophils: <1.5 x 10^3/µL (SI: <1.5 GI/L)
- Platelets: <100 x 10^3/µL (SI: <100 GI/L)
- eGFR: <60 mL/min/1.73 m^2
- Aspartate aminotransferase: >2 × ULN
- Alanine aminotransferase: >2 × ULN

If one or more of the laboratory parameters is out of range, a single retest of laboratory values is permitted during the screening period.

18. Test positive for the following infections at screening:
    a. HBV (Appendix 7)
    b. Hepatitis C (seropositive for antibodies and positive confirmatory test for HCV, ie, HCV PCR [Appendix 7])
    c. HIV
19. Has a chest radiograph (or CT scan) within 12 weeks that shows evidence of ongoing infection or malignancy.
    a. Chest radiograph is optional for participants under 18 years of age at time of screening.

Infections or Predisposition to Infections

20. History of chronic or recurrent infectious disease, including but not limited to chronic renal infection, chronic chest infection (eg, bronchiectasis), recurrent urinary tract infection (recurrent pyelonephritis or chronic nonremitting cystitis), severe fungal infection (mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.
21. History of an infected joint prosthesis or has received antibiotics for a suspected infection of a joint prosthesis, if that prosthesis has not been removed or replaced.
22. Known or suspected immunodeficiency, including history of invasive opportunistic infections (eg, active TB, nontuberculous mycobacterial infection, histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis, aspergillosis, HIV) or otherwise recurrent infections of abnormal frequency or prolonged duration, despite infection resolution, suggesting an immune-compromised status, as judged by the investigator.
23. Serious infection (eg, disseminated herpes zoster, sepsis, pneumonia, or pyelonephritis), or has been hospitalized or received IV antibiotics for an infection during the 8 weeks before screening.
24. Tested positive for or been exposed to COVID-19 within 4 weeks prior to the first dose of study intervention.

    Exceptions: Participants who have tested positive for or been exposed to COVID-19 may participate if they have both an absence of symptoms and a negative validated COVID-19 test obtained at least 2 weeks after symptom onset (or the first positive test for asymptomatic infection) or exposure.

Follow local regulations for validated COVID-19 testing procedures and standard definition of COVID-19 exposure.

Malignancy or Increased Potential for Malignancy

25. Current malignancy or history of malignancy within 5 years before screening (except nonmelanoma skin cancer or cervical carcinoma in situ that has been adequately treated with no evidence of recurrence for at least 12 weeks before the first study intervention administration).

26. History of lymphoproliferative disease, including lymphoma; a history of monoclonal gammopathy of undetermined significance; or signs and symptoms suggestive of possible lymphoproliferative disease, such as splenomegaly or significant lymphadenopathy.

Tuberculosis

27. Criterion modified per Global Amendment 1

    27.1 Known active TB infection. IGRA TB test will be performed during screening. IGRA testing includes either QuantiFERON®-TB Gold Plus or T-SPOT®TB.

    a. Participants with history of active TB based on medical history will be excluded.

    b. Participants with a positive (or indeterminate) test result may participate in the study if further work up (according to local practice/guidelines) establishes conclusively that the participant has no evidence of active tuberculosis. If presence of latent tuberculosis is established, participants who are at low risk of reactivation, defined by local health authorities and investigator judgment, do not require prophylactic anti-tuberculosis treatment prior to or during the study. The decision to treat or not should be made by the treating physician/investigator. If the decision is made to treat the participant for latent TB, latent TB treatment must be initiated prior to the first administration of study intervention per local guidelines.

Other Exclusions

28. An employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.

29. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

Additional Medical Conditions

30. PHQ-9 score ≥15 at screening or baseline.

Note: Investigators must ensure that all study enrollment criteria have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of

additional medical records) after screening but before the first dose of study intervention is given such that the participant no longer meets all eligibility criteria, then the participant must be excluded from participation in the study. Section 5.4., Screen Failures, describes options for retesting. The required source documentation to support meeting the enrollment criteria are noted in Appendix 2, Regulatory, Ethical, and Study Oversight Considerations.

5.3. Lifestyle Considerations

Participants must be willing and able to adhere to the following lifestyle restrictions to be eligible for participation:

1. Recommended to be up to date on all age-appropriate vaccinations prior to screening as per routine local medical guidelines. It is strongly recommended that participants will have completed a locally approved (or emergency use-authorized) COVID-19 vaccination regimen at least 2 weeks prior to study-related visits or procedures. Study participants should follow applicable local vaccine labelling, guidelines, and standards-of-care for participants receiving immune targeted therapy when determining an appropriate interval between vaccination and study enrollment (Section 6.9.1).
2. Refer to Section 6.9, Concomitant Therapy for details regarding prohibited and restricted therapy during the study.
3. Agree to take study interventions as instructed and comply with fasting requirements (Section 6.1).
4. Agree to fast for at least 6 hours prior to lipid panel blood sample collection unless medically contraindicated (Section 1.3).
5. Strenuous exercise (eg, body building, long distance training [running/cycling]) may affect study specified assessments and safety laboratory results; for this reason, strenuous exercise should be avoided within 2 to 3 days before all planned study visits where laboratory tests are collected.
6. Agree to limit prolonged, direct sunlight exposure such as tanning in direct sunlight without sunscreen and avoid artificial sunlight (tanning beds or phototherapy). Participants are encouraged to use sun protective measures (such as a hat, sunglasses, protective clothing, sunscreen) during study participation, as ultraviolet exposure may affect psoriasis efficacy assessments.
7. Agree to remove nail coverings prior to or at all visits where nail psoriasis is assessed.
8. Must intend to comply with completion of the PROs and be willing to work with smartphones/tablets/computers.
9. For adolescent participants, who are not of legal age of consent, a legal guardian or primary caregiver is recommended to:
    - Accompany the participant to the study site on each assessment day according to the SoA.
    - Accurately and reliably assist participant with study intervention compliance as directed.

5.4. Screen Failures

Participant Identification, Enrollment, and Screening Logs

The investigator agrees to complete a participant identification and enrollment log to permit easy identification of each participant during and after the study. This document will be reviewed by the sponsor study site contact for completeness. This study will use IWRS. The investigator will not generate screening and enrollment logs directly from IWRS.

The participant identification and enrollment log will be treated as confidential and will be filed by the investigator in the study file. To ensure participant confidentiality, no copy will be made. All reports and communications relating to the study will identify participants by participant identification and age at initial informed consent. In cases where the participant is not randomized into the study, the date seen and age at initial informed consent will be used.

Rescreening

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened once. Medical Monitor approval is required prior to rescreening. Rescreened participants must be assigned new participant numbers and retain their original identification numbers, undergo the informed consent process, and meet all criteria as defined in Section 5. Waivers to eligibility criteria are not permitted.

Retesting

Retesting of abnormal screening values that lead to exclusion will be allowed once. Retesting can occur at an unscheduled visit during the screening period (to reassess eligibility) within the specified screening window of up to 5 weeks. In such cases, the first abnormal test result will not constitute a screen failure. If a laboratory abnormality occurs, the site is encouraged to wait for all laboratory tests to be completed to ensure other laboratory tests do not need to be repeated, as only 1 retest of laboratory tests is allowed. Screening laboratory test(s) analyzed by the central laboratory may be repeated more than once in the event of suspected error in sample collection or analysis as long as the result is obtained within the screening period.

5.5. Criteria for Temporarily Delaying Administration of Study Intervention

Not applicable.

6. STUDY INTERVENTION AND CONCOMITANT THERAPY

6.1. Study Intervention(s) Administered

The study intervention will be provided as tablets for oral administration.

For adult participants:
For adult participants, the study intervention must be swallowed whole. Participants will be instructed to take the study intervention at approximately the same time every day upon waking with 240 mL (8 oz) water on an empty stomach (no food intake for at least 2 hours before and for at least 30 minutes after taking the study intervention).

For adolescent participants:

For adolescent participants, the participant's legal guardian or caregiver may assist with administration of the study intervention.

For adolescent participants, the study intervention should be swallowed whole. Adolescent participants will be instructed to take the study intervention at approximately the same time every day upon waking with 240 mL (8 oz) water on an empty stomach (no food intake for at least 2 hours before and for at least 30 minutes after taking the study intervention).

If adolescent participants have difficulty swallowing tablets, the study intervention may be suspended in a glass of water and taken within 15 minutes. It may take a few minutes for the tablet to fully disperse. The tablet may not disperse completely (milky to cloudy appearance), and small pieces may be seen in the water and are safe to swallow. After drinking the study intervention, rinse and swirl the glass with more water and swallow to ensure all the study intervention is taken. The total amount of water to be used for the dispersion of the tablet and rinsing should be at least 240 mL (about 8 oz or 1 cup).

Study personnel should review dose administration requirements with the participant, as appropriate, and with the delegated caregiver(s) before administration and throughout the study as necessary.

<table>
<tr><th>Designation</th><th>Product</th></tr>
<tr><td>Investigational Medicinal Product(s)</td><td>JNJ-77242113, placebo for JNJ-77242113

Authorization status in the EU/EEA
<table><tr><td>Authorized</td><td>Not applicable</td></tr><tr><td>Unauthorized</td><td>JNJ-77242113, placebo for JNJ-77242113</td></tr></table></td></tr>
<tr><td>NIMP/AxMP</td><td>Not applicable</td></tr>
</table>

Study intervention administration must be captured in the source documents and the CRF per study manual and CRF completion guidelines. Study site personnel will instruct participants on how to store study intervention for at-home use as indicated for this protocol.

JNJ-77242113 will be manufactured and provided under the responsibility of the sponsor. Refer to the IB for a list of excipients.

For a definition of study intervention overdose, refer to Section 6.8, Treatment of Overdose.

Description of Interventions

Intervention Label		
Intervention Name	JNJ-77242113	Matching Placebo for JNJ-77242113
Intervention Description	film-coated tablet containing 200 mg JNJ-77242113	film-coated tablet without JNJ-77242113
Type	Drug	Drug
Dose Formulation	Tablet	Tablet
Unit Dose Strength(s)	200 mg per tablet	Not applicable
Dosage Level(s)	1 x 200 mg tablet once daily	Not applicable
Route of Administration	Oral	Oral
Use	Experimental	Placebo comparator
Investigational Medicinal Product (IMP)	Yes	Yes
Non-Investigational Medicinal Product/Auxiliary Medicinal Product (NIMP/AxMP)	No	No
Sourcing	Provided centrally by the sponsor	Provided centrally by the sponsor
Packaging and Labeling (Labels will contain information to meet the applicable regulatory requirements)	Study intervention will be provided in blister packs. Each pack will be labeled as required per country requirements.	Study intervention will be provided in blister packs. Each pack will be labeled as required per country requirements.
	The blisters are packaged in child resistant Dosepaks.	The blisters are packaged in child resistant Dosepaks.
Delivery Instructions	Swallow tablet whole. Given with 240 mL water. The tablet should not be broken or crushed.	Swallow tablet whole. Given with 240 mL water. The tablet should not be broken or crushed.
Fasting Requirement	At least 2 hours before taking the study intervention and for at least 30 minutes after taking the study intervention.	At least 2 hours before taking the study intervention and for at least 30 minutes after taking the study intervention.
Current/Former Name(s) or Alias(es)	JNJ-77242113 and previously referred to as APi2915, PN21235, PN-21235, and PN-235.	Not applicable.

Description of Study Arms

Arm Title	JNJ-77242113	Placebo
Arm Type	experimental	placebo
Arm Description	Adult participants will receive: - JNJ-77242113 200 mg QD through Week 24 - At Week 24: o Participants who are both PASI 75 non-responders and IGA 0 or 1 non-responders at Week 24 will continue to receive JNJ-77242113 200 mg once daily through Week 52. o Participants who are PASI 75 responders or IGA 0 or 1 responders (ie, those who achieve an IGA score of 0 or 1 and have ≥2-grade improvement from baseline) at Week 24 will be re-randomized to receive either: ▪ JNJ-77242113 200 mg once daily OR ▪ placebo (and will be retreated with JNJ-77242113 200 mg once daily upon loss of ≥50% of their Week 24 PASI improvement) - At Week 52: o All participants will receive JNJ-77242113 200 mg once daily through Week 156 Adolescent participants will receive: - JNJ-77242113 200 mg once daily through Week 156	Adult and adolescent participants will receive: - Matching placebo for JNJ-77242113 on Week 0 through Week 16 - JNJ-77242113 200 mg once daily from Week 16 through Week 156
Associated Intervention Labels	Labels will be identical to maintain the blind.	Labels will be identical to maintain the blind.

6.2. Preparation/Handling/Storage/Accountability

Preparation/Handling/Storage

All study intervention must be stored at controlled temperatures ranging from 15°C to 25°C or per local label where applicable.

Refer to the study site investigational product and procedures manual for additional guidance on study intervention preparation, handling, and storage.

Accountability

The investigator is responsible for ensuring that all study intervention received at the site is inventoried and accounted for throughout the study.

The dispensing of study intervention to the participant, and the return of study intervention from the participant (if applicable), must be documented in the source and in the intervention accountability form. Participants, or their legally acceptable representatives in case of adolescents, where applicable, must be instructed to return all original containers, whether empty or containing study intervention. The study intervention administered to the participant must be documented on the intervention accountability form. All study intervention will be stored and disposed of according to the sponsor's instructions. Study -site personnel must not combine contents of the study intervention containers.

Study intervention must be handled in strict accordance with the protocol and the container label and must be stored at the study site in a limited-access area or in a locked cabinet under appropriate environmental conditions. Unused study intervention and study intervention returned by the participant, must be available for verification by the sponsor’s study site monitor during on-site monitoring visits. The return to the sponsor of unused study intervention or used returned study intervention for destruction, will be documented on the intervention return form. When the study site is an authorized destruction unit and study intervention supplies are destroyed on-site, this must also be documented on the intervention return form.

Potentially hazardous materials must be disposed of immediately in a safe manner and therefore will not be retained for intervention accountability purposes.

Study intervention must be dispensed under the supervision of the investigator or a qualified member of the study site personnel, or by a hospital/clinic pharmacist. Study intervention will be supplied only to participants or legal caregivers participating in the study. Returned study intervention must not be dispensed again, even to the same participant. Study intervention may not be relabeled or reassigned for use by other participants. The investigator agrees neither to dispense the study intervention from, nor store it at, any site other than the study sites agreed upon with the sponsor. Further guidance and information for the final disposition of unused study interventions are provided in the Study Reference Manual.

6.3. Assignment to Study Intervention

Central randomization will be implemented in conducting this study. Participants will be assigned to 1 of 2 intervention groups with a 2:1 randomization ratio to JNJ-77242113 or placebo, based on a computer-generated randomization schedule prepared before the study or under the supervision

of the sponsor. Permuted block randomization with stratification by age group (adolescents <18 years and adults ≥18 years), baseline weight category for adults only (≤90kg, >90kg) and geographic region will be used. The IWRS will assign a unique intervention code, which will dictate the intervention assignment and matching study intervention kit for the participant. The requestor must use his or her own user identification and personal identification number when contacting the IWRS and will then give the relevant participant details to uniquely identify the participant.

At Week 24, adult participants randomized to JNJ-77242113 200 mg once daily and who are PASI 75 responders or IGA 0 or 1 responders (ie, those who achieve an IGA score of 0 or 1 and have ≥2-grade improvement from baseline) will be re-randomized using the IWRS either to placebo or JNJ-77242113 200 mg once daily in a 1:1 ratio. Participants will be assigned to treatment groups using permuted block randomization and the randomization will be stratified by geographic region and PASI 90 response status at Week 24.

6.4. Blinding, Masking

Data that may potentially unblind the intervention assignment (ie, study intervention plasma concentrations, anti-JNJ-77242113 antibodies, study intervention preparation/accountability data, intervention allocation, biomarker data) will be handled with special care to ensure that the integrity of the blind is maintained and the potential for bias is minimized. This can include making special provisions, such as segregating the data in question from view by the investigators, clinical team, or others as appropriate until the time of database lock and unblinding.

Under normal circumstances, the blind should not be broken until the database is finalized. Otherwise, the blind should be broken only if specific emergency intervention/course of action would be dictated by knowing the intervention status of the participant. In such cases, the investigator may in an emergency determine the identity of the intervention by contacting the IWRS. While the responsibility to break the intervention code in emergency situations resides solely with the investigator, it is recommended that the investigator contact the sponsor or its designee if possible, to discuss the particular situation, before breaking the blind. Telephone contact with the sponsor or its designee will be available 24 hours per day, 7 days per week. In the event the blind is broken, the sponsor must be informed as soon as possible. The date, time, and reason for the unblinding must be documented by the IWRS, and in the source document. The documentation received from the IWRS indicating the code break must be retained with the participant's source documents in a secure manner.

Participants who have had their intervention assignment unblinded should continue to return for scheduled evaluations.

Randomization codes will be disclosed to select sponsor individuals only after the clinical database is closed after the Week 24 DBL. The randomization codes will not be disclosed to the investigator and participants until after the Week 52 DBL. Details of the unblinding will be descripted in a separate unblinding plan prior to the Week 24 DBL.

6.5. Study Intervention Compliance

Participant compliance with study intervention will be assessed at each visit during the treatment period by counting returned tablets.

Each participant's overall compliance with study intervention since the first dose of study intervention will be assessed by the site at each visit. A participant will be considered noncompliant with the study intervention if they take less than 80% or greater than 120% of the expected tablets during participation in this study, unless study intervention is withheld for safety reasons. Protocol deviations for compliance will be assessed at Week 16, Week 24 and Week 52 or if the early termination visit is performed before Week 52.

If a participant's study intervention intake is not according to the protocol, the investigator will take the necessary measures to ensure future adherence to the protocol. If necessary, the participant may be discontinued from study intervention by the investigator or medical monitor (Section 7). Study intervention compliance will be further detailed in the SAP.

6.6. Dose Modification

Not applicable.

6.7. Continued Access to Study Intervention After the End of the Study

Participants will be instructed that study intervention will not be made available to them after they have completed/discontinued study intervention and that they should return to their primary physician to determine standard of care.

6.8. Treatment of Overdose

For this study, any dose of JNJ-77242113 greater than 200 mg in a single day will be considered an overdose. The sponsor does not recommend specific treatment for an overdose.

Decisions regarding dose interruptions will be made by the investigator in consultation with the medical monitor based on the clinical evaluation of the participant.

In the event of an overdose, the investigator or treating physician should:

- Contact the Medical Monitor immediately.
- Closely monitor the participant for AE/SAE and laboratory abnormalities.
- Document the quantity of the excess dose as well as the duration of the overdosing in the source documents.
- Evaluate the participant to determine, in consultation with the Medical Monitor, whether study intervention should be interrupted.
- Obtain a plasma sample for PK analysis if requested by the Medical Monitor (determined on a case-by-case basis).

6.9. Prior and Concomitant Therapy

All prestudy psoriasis therapies and COVID-19 vaccinations administered before signing the ICF must be recorded at screening per CRF completion guidelines.

Concomitant therapy must be recorded throughout the study beginning with signing of the ICF through the last study visit (safety follow-up or early termination visit). Concomitant therapies must also be recorded beyond the last study visit in conjunction with SAEs that meet the criteria outlined in Serious Adverse Events in Section 8.4.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information.

All therapies (prescription or over-the-counter medications) different from the study intervention must be recorded in the CRF. Modification of an effective pre-existing therapy should not be made for the explicit purpose of entering a participant into the study.

Prohibited Therapy

All experimental therapies or new investigational interventions (except for study intervention administered as part of this study), including therapies for psoriasis or other conditions, must be discontinued prior to the first administration of study intervention per Exclusion criteria 12 and 13 (Section 5.2) and remain prohibited during the study. For guidance regarding the COVID-19 vaccine see Section 6.9.1.

The sponsor's medical monitor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered. The participant may be required to discontinue study intervention (Section 7.1). If a prohibited therapy is initiated during the safety follow-up period, the participant should complete his or her final study visit, and the medication should be recorded as a concomitant medication.

No rescue therapies for psoriasis are permitted in the study.

Psoriasis Concomitant Medications

Topical Therapy

Week 0 to Week 52

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

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

Week 52 to Week 160

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

Phototherapy or Systemic Therapy

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

These medications include:

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

Concomitant Medications for Indications other than Psoriasis

The use of systemic corticosteroids for indications other than psoriasis should be limited to situations for which, in the opinion of the treating physician, there are no adequate alternatives. Systemic corticosteroids should be used on a short-term basis, preferably for ≤2 weeks. Longer term use of corticosteroids should be discussed with the medical monitor or designee and may require discontinuation of study intervention. Inhaled, otic, ocular, nasal, or other routes of mucosal delivery of corticosteroids are allowed throughout the study. After Week 52, intra-articular corticosteroids are allowed for indications other than psoriasis.

Vitamin D3 and analogs for dietary supplementation are permitted.

6.9.1. Non-live Vaccinations (including COVID-19)

When considering use of locally approved non-live vaccines (including emergency use-authorized COVID-19 vaccines) in study participants, follow applicable local vaccine labelling, guidelines, and standards-of-care for participants receiving immune-targeted therapy. It is recommended to avoid use of vaccines 2 weeks prior to Week 16 and 2 weeks prior to Week 52.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION

7.1. Discontinuation of Study Intervention

If a participant discontinues study intervention for any reason before the end of the study, then the Early Termination Visit assessments must be obtained (Section 1.3.2). Study intervention assigned to the participant who discontinued study intervention may not be assigned to another participant (Section 6.2). Additional participants will not be entered in this study. Participants who discontinue

study intervention but do not terminate study participation will continue to return for protocol-specified procedures and evaluations. Discontinuation from study intervention does not mean that the participant is required to withdraw informed consent and leave the study.

7.1.1. Liver Chemistry Stopping Criteria

Refer to Appendix 5, Liver Safety: Suggested Actions and Follow-up Assessments.

7.1.2. Temporary Interruption (Withholding) of Study Intervention

Some possible reasons for temporarily withholding study intervention include, but are not limited to, the following:

- The participant develops a serious infection.
- The participant is suspected of having tuberculosis infection or has had close contact exposure to TB (Section 8.3.7).
- The participant has a hepatic event or liver test abnormality per Appendix 5, Liver Safety: Suggested Actions and Follow-up Assessments.
- The participant has a PHQ-9 score of ≥20 (Section 8.3.5).

Cases that may merit temporary withholding of the study intervention should be discussed with the medical monitor. The medical monitor, in consultation with the investigator, will determine when it is appropriate to recommence study treatment.

7.1.3. Permanent Discontinuation of Study Intervention

A participant's study intervention must permanently be discontinued for any of the following:

- Participant withdraws consent or assent to receive study intervention.
- The investigator believes that for safety reasons or tolerability reasons (eg, AE) it is in the best interest of the participant to discontinue study intervention.
- Participant meets the Sampson criteria for anaphylaxis (Sampson 2006) following study intervention administration.
- Participant becomes pregnant or plans a pregnancy during the study. Refer to Appendix 4, Contraceptive and Barrier Guidance.
- Participant initiates of protocol-prohibited medications, treatments, or interventions (outlined in Section 6.9) that have an impact on psoriasis efficacy evaluations at the discretion of the medical monitor.
- Participant develops a malignancy including squamous cell skin cancer. Consideration may be given to allow participants, who develop ≤2 basal cell skin cancers and who are adequately treated with no evidence of residual disease, to continue to receive study intervention.
- The participant develops a systemic opportunistic infection during the study period.
- Participant develops a recurrent or chronic serious infection during the study period.
- A diagnosis of active TB (Section 8.3.7).

- Substantial noncompliance with study visit schedule (Section 1.3) or study intervention administration (Section 6.5). Consideration for discontinuation must be discussed with the medical monitor.
- Hepatic or liver test abnormality outlined in Appendix 5, Liver Safety.
- Unblinding of the participant's treatment assignment for any reason (emergency or nonemergency).
- Participant reports suicidal ideation by answering "Yes" to Question 4 or 5 on the C-SSRS, or documents suicidal behavior on the C-SSRS at any time during the study and is considered at risk by the investigator after evaluation by a mental health professional. The investigator should contact the medical monitor for discussion.
- Sponsor decision.

Discontinuation of a participant's study intervention should be considered for the following:

- After completion of the placebo-controlled period (Week 16), all participants will be allocated to JNJ-77242113 until at least Week 24, when the randomized withdrawal period will begin. If after receiving JNJ-77242113 for a reasonable amount of time (eg, 12 to 16 weeks after Week 16) a participant is still not experiencing clinically meaningful benefit, the investigator should consider discontinuing the participant from the study intervention. However, if disease worsening occurs after Week 24, it is important to remember that the participant may be enrolled in the randomized withdrawal period before discontinuing a participant from the study intervention for disease worsening.

7.2. Participant Discontinuation/Withdrawal from the Study

A participant will be withdrawn from the study for any of the following reasons:

- Lost to follow-up
- Withdrawal of consent or assent
- Death

When a participant withdraws before study completion, the reason for withdrawal is to be documented in the CRF and in the source document. If the reason for withdrawal from the study is withdrawal of consent or assent, then no additional assessments are allowed.

Withdrawal of Consent

A participant declining to return for scheduled visits does not necessarily constitute withdrawal of consent. Alternate follow-up mechanisms that the participant agreed to when signing the consent form apply (eg, consult with family members, contacting the participant's other physicians, medical records, database searches, use of locator agencies at study completion) as local regulations permit.

Withdrawal of consent must be an infrequent occurrence in clinical studies (Rodriguez 2015) therefore, prior to the start of the study the sponsor and the investigator must discuss and reach a clear understanding of what constitutes withdrawal of consent in the context of the available reduced follow-up mechanisms listed.

7.2.1. Withdrawal From the Use of Research Samples

A participant who withdraws from the study will have the following options regarding the optional research samples:

- The collected samples will be retained and used in accordance with the participant's original separate informed consent for optional research samples.
- The participant may withdraw consent for optional research samples, in which case the samples will be destroyed and no further testing will take place. To initiate the sample destruction process, the investigator must notify the sponsor study site contact of withdrawal of consent for the optional research samples and to request sample destruction. The sponsor study site contact will, in turn, contact the biomarker representative to execute sample destruction. If requested, the investigator will receive written confirmation from the sponsor that the samples have been destroyed.

Withdrawal from the Optional Research Samples While Remaining in the Study

The participant may withdraw consent for optional research samples while remaining in the study. In such a case, the optional research samples will be destroyed. The sample destruction process will proceed as described above.

Withdrawal from the Use of Samples in Future Research

The participant may withdraw consent for use of samples for research (refer to Long-Term Retention of Samples for Additional Future Research in Appendix 2, Regulatory, Ethical and Study Oversight Considerations). In such a case, samples will be destroyed after they are no longer needed for the clinical study. Details of the sample retention for research are presented in the main ICF and in the separate ICF for optional research samples.

7.3. Lost to Follow up

To reduce the chances of a participant being deemed lost to follow up, prior to randomization attempts should be made to obtain contact information from each participant, eg, home, work, and mobile telephone numbers and email addresses for both the participant as well as appropriate family members.

A participant will be considered lost to follow up if the participant repeatedly fails to return for scheduled visits and is unable to be contacted by the study site. A participant cannot be deemed lost to follow-up until all reasonable efforts made by the study site personnel to contact the participant are deemed futile. The following actions must be taken if a participant fails to return to the study site for a required study visit:

- The study site personnel must attempt to contact the participant to reschedule the missed visit as soon as possible, to counsel the participant on the importance of maintaining the assigned visit schedule, to ascertain whether the participant wishes to or should continue in the study.
- Before a participant is deemed lost to follow up, the investigator or designee must make every reasonable effort to regain contact with the participant (where possible, 3 telephone calls, e-mails, fax, and, if necessary, a certified letter to the participant's last known mailing address,

or local equivalent methods. Locator agencies may also be used as local regulations permit. These contact attempts should be documented in the participant's medical records.

- Should the participant continue to be unreachable, they will be considered to have withdrawn from the study.
- Site personnel, or an independent third party, will attempt to collect the vital status of the participant within legal and ethical boundaries for all participants randomized, including those who did not get study intervention. Public sources may be searched for vital status information.

Should a study site close, eg, for operational, financial, or other reasons, and the investigator cannot reach the participant to inform them, their contact information will be transferred to another study site.

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

The SoA summarizes the frequency and timing of efficacy, PK, immunogenicity, biomarker, pharmacogenomic, photography and safety measurements applicable to this study (Section 1.3).

All visit-specific PRO assessments must be conducted/completed before any tests, procedures, or other consultations to prevent influencing participant responses unless otherwise specified in the SoA. Refer to the PRO completion guidelines for instructions on the administration of PROs.

Prior to the first assessment, each participant will be provided with an electronic device to enter study-related data. Study-site personnel will train the participants on how to use the electronic device, including instructions to capture the data according to the study design and not to wait until the study-site visit to record information. Participants will be provided with written instructions on how to get 24-hour technical support, if needed, for operation of the electronic device.

ECGs should precede vital signs and both procedures should be completed prior to any invasive procedures. Vital signs should be recorded from the opposite arm from which blood samples are being taken.

Blood collections for PK and biomarker assessments should be kept as close to the specified time as possible. Other measurements may be done earlier than specified timepoints if needed. Actual dates and times of assessments will be recorded in the source documentation and according to the CRF guidelines and laboratory manual.

Blood Sample Collection

The total blood volume to be collected from each participant through the duration of the study will be approximately 300 mL (this total includes the optional blood sampling). Repeat or unscheduled samples may be collected for safety reasons or for technical issues with the samples.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded in the CRF or laboratory requisition form. Refer to the SoA for the timing and frequency of all sample collections (Section 1.3).

Instructions for the collection, handling, storage, and shipment of samples are found in the laboratory manual that will be provided.

8.1. Administrative and General/Baseline Procedures

eDiary Compliance

Study-site personnel will review each participant's eDiary for completion as indicated in the SoA (Section 1.3). Additional compliance checks may be performed as necessary. The compliance checks include verifying ePRO completion and retraining of participants on ePRO completion responsibility, if necessary. At least 4 days of PSSD 24-hour assessments are required within 7 days before randomization and prior to Week 16 to support analyses. However, if <4 days of PSSD scores are recorded prior to baseline, the participant may still be randomized and the baseline values for PSSD will be considered missing.

Guidelines for handling of assessments affected by a major disruption are found in Appendix 6.

8.1.1. Physical Examinations

Full or Targeted Physical Examination

Physical examinations, including Tanner staging for sexual maturity (only for participants <18 years old at screening) will be performed by the investigator or designated physician, nurse practitioner or physician assistant, as applicable per local regulations and as specified in the SoA (Section 1.3). Targeted physical exams will include a skin exam, general exam, and any other organ system exam based on clinical judgement of the participant's presenting complaints or symptoms. Any new, clinically significant finding (in the opinion of the investigator) must be captured as an AE. In addition, resolution of any abnormal findings during the study will be noted in the source document.

Height and Weight

Height and weight will be measured as specified in the SoA (Section 1.3). Participants will be instructed to remove shoes and outdoor apparel and gear prior to these measurements.

8.2. Efficacy Assessments

Investigator assessments and PROs will be used to assess efficacy in this study.

- The PRO instruments will be provided in the local language in accordance with local guidelines.
- The PRO instruments will be available for regulators and for IRB/IEC submissions and will be provided separately in a companion manual with the instruments that will be submitted with the protocol.
- The PRO and AE data will not be reconciled with each other.
- Assessments will be performed for all participants at the baseline (Week 0) visit according to the SoA. After Week 0 the following assessments will only be performed in participants with active disease in the identified special area at Week 0. This is defined as any score >0 at Week 0. These assessments include ss-IGA, sPGA-G, hf-PGA, f-PGA, mNAPSI and GenPs-SFQ.

- The participant assessment of PsA disease activity, participant assessment of PsA pain PROs and PGA of Disease activity will only be administered at post-Week 0 in participants with a diagnosis of PsA.

8.2.1. Investigator's Global Assessment

The IGA documents the investigator's assessment of the participant's plaque psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling. The participant's plaque psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4) (Appendix 8).

8.2.2. Psoriasis Area and Severity Index

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy (Appendix 9) (Fredriksson 1978). In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities. Each of these areas is assessed and scored separately for erythema, induration, and scaling, which are each rated on a scale of 0 to 4 and extent of involvement on a scale of 0 to 6. The PASI produces a numeric score that can range from 0 to 72. A higher score indicates more severe disease.

8.2.3. Body Surface Area

Body surface area is a commonly used measure of involvement of skin disease. It is defined as the percentage of surface area of the body involved with the condition being assessed, (ie, plaque psoriasis). The handprint method for assessing BSA will be used in this study, where the surface area of the participant's hand including the palm and all 5 digits is used as a guide to estimate 1% BSA (Long 1992; Rossiter 1996; Thomas 2007).

8.2.4. Scalp-specific Investigator Global Assessment

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

8.2.5. Static Physician's Global Assessment of Genitalia

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

8.2.6. Physician's Global Assessment of Hands and Feet

The hf-PGA assesses the severity of hand and foot psoriasis using a 5-point scale to score the plaques on the hands and feet as: clear (0), almost clear (1), mild (2), moderate (3), and severe (4) (Goldblum 2013; Leonardi 2011).

8.2.7. Fingernail Physician's Global Assessment

The f-PGA is used to evaluate the current status of a participant's fingernail psoriasis on a scale of 0 to 4 (clear [0], minimal [1], mild [2], moderate [3], or severe [4]) (Blauvelt 2017).

8.2.8. Modified Nail Psoriasis Severity Index

The mNAPSI is an index used for assessing and grading the severity of nail psoriasis (Cassell 2007). Each of the participant's ten fingernails are evaluated on 7 features. The first three features are each scored from 0 to 3 in severity and are (1) onycholysis and oil-drop dyschromia, (2) pitting, and (3) nail plate crumbling. The next four features are each scored 0 - absent or 1 - present, and are (1) leukonychia, (2) splinter hemorrhages, (3) nail bed hyperkeratosis, and (4) red spots in the lunula. The score ranges from 0-13 per nail, and 0-130 for all fingernails.

8.2.9. Physician Global Assessment of Disease Activity

The PGA of Disease Activity is a 100 mm VAS and will be utilized in the adolescent population**.** Physicians are to complete the VAS to assess the participant's current arthritis activity. The anchors of the scale are "no arthritis activity" to "extremely active arthritis." Lower scores indicate less disease activity. The process for including this measure (PGA of disease activity) in the core set of variables for the assessment of JIA improvement has been captured in the literature (Giannini 1997).

8.2.10. Patient-reported Outcomes

8.2.10.1. Psoriasis Symptom and Sign Diary

The PSSD will be utilized in the adult and adolescent population and includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit (Feldman 2016). There are 2 versions of the PSSD: a 24-hour recall version that asks the participant to answer the questions thinking about the last 24 hours and a 7-day recall version asking the participant to answer the questions thinking about the last 7 days. Both versions of the PSSD are self-administered PRO instruments and include 11 items in total, with 5 items covering symptoms (itch, pain, stinging, burning, and skin tightness) and 6 covering participant-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, and bleeding). A 0 to 10 numerical rating scale for severity is used. For both versions, 2 subscores will be derived each ranging from 0 to 100: the psoriasis symptom score and the psoriasis sign score. Additionally, for both versions, an item-level score will be derived for the PSSD itch item. The PSSD itch score will range from 0 to 10. For all scores, a higher score indicates more severe disease.

8.2.10.2. Dermatology Life Quality Index

The DLQI will be utilized in the adult population and is a dermatology specific HRQoL instrument designed to assess the impact of the disease on a participant's HRQoL (Finlay 1994). 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 HRQoL.

8.2.10.3. Children's Dermatology Life Quality Index

The CDLQI is an adapted version of the DLQI for the pediatric population and will be utilized in the adolescent population in this study. The adaption and validation of the CDLQI was undertaken

by the original developer of the DLQI to ensure it addressed the specific needs of the pediatric population (Lewis-Jones 1995). The CDLQI is a 10-item instrument that has 4 item response options and a recall period of 1 week. Higher scores indicate greater impact on HRQoL. The instrument is designed for use in children is self-explanatory and can be simply handed to the participant who is asked to fill it in with the help of the child's parent or caregiver.

8.2.10.4. Genital Psoriasis Sexual Frequency Questionnaire

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

8.2.10.5. Patient-Reported Outcomes Measurement Information System-29

The PROMIS-29 will be utilized in the adult population and is a 29-item generic HRQoL survey, assessing each of the 7 PROMIS domains (depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and ability to participate in social roles and activities) with 4 questions for each domain. The questions are ranked on a 5-point Likert Scale. There is also one 11-point rating scale for pain intensity (Cella 2010).

8.2.10.6. PROMIS Pediatric-25 Profile v2.0

The PROMIS-25 will be utilized in the adolescent population and is a 25-item generic HRQoL survey. Six PROMIS domains (physical function mobility, anxiety, depressive symptoms, fatigue, peer relationships, pain interference) are each assessed with 4 questions. There is also one 11-point rating scale for pain intensity. The instrument is designed for use in ages 8-17 years of age and can be self-administered (Irwin 2010).

8.2.10.7. Treatment Satisfaction Questionnaire for Medication Effectiveness

The TSQM-E questionnaire will be utilized in adult and adolescent participants and measures participant satisfaction with treatment (Bharmal 2009). The recall period for all items is 2 to 3 weeks, or since the last medication use. The original instrument includes 3 domains: Effectiveness (3-items), Convenience (3-items) and Global Satisfaction Scale (3-items). This study will collect only the Effectiveness domain. Response to all Effectiveness domain items is rated on a 7-point Likert scale. The score ranges from 0 to 100, with higher scores indicating greater satisfaction.

8.2.10.8. EuroQol 5-Dimension 5 Level Questionnaire

The EQ-5D-5L will be used in the adult and adolescent population and is a self-administered, standardized measure of health status in a wide range of health conditions and treatments. The recall period for all items is ‘Today’. The EQ-5D-5L consists of the EQ-5D descriptive system and the EQ-VAS. The EQ-5D descriptive system is comprised of 5 items across the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ-5D-5L uses a 5-point Likert response scale ranging from “No problems” to “Extreme problems”. The EQ-5D also includes a visual analog scale (EQ-VAS) that has endpoints labeled "best imaginable health state" and "worst imaginable health state" anchored at 100 and

0, respectively. Participants are asked to indicate how they rate their own health by indicating the point on the EQ-VAS which best represents their own health on that day (EuroQol 1990; Herdman 2011; Janssen 2013).

8.2.10.9. Participant Assessment of Psoriatic Arthritis Pain

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

8.2.10.10. Participant Assessment of Psoriatic Arthritis Disease Activity

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

8.2.10.11. Participant Assessment of Acceptability and Palatability

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

8.2.11. Photographs

Efforts to standardize efficacy assessments in inflammatory dermatologic conditions have been challenging, but the visual nature of many manifestations of dermatologic disease provides opportunity for photographic assessment of efficacy endpoints. In this optional substudy, participants will have 2 options for image collection:

1. Lesional photographs: two areas of lesional skin will be photographed per patient. The same two areas will be photographed over time.
2. Full body photographs and lesional photographs: In addition to the two lesional photographs, full body photographs (front and back) will be collected.

These photographs will be used to virtually assess psoriasis disease severity by comparing investigator reported PASI scores to PASI scores assessed by a central reader. Details of these analyses will be provided in a separate substudy SAP. Participants will also be consented in order to use these photographs for future scientific communications and commercial purposes. Patients may agree to the photography substudy and may opt out of allowing photographs for scientific communications or commercial purposes. See site manual for photography instructions.

8.3. Safety Assessments

Details regarding the Independent DMC are provided in Committees Structure in Appendix 2, Regulatory, Ethical, and Study Oversight Considerations.

Adverse events will be reported and followed by the investigator as specified in Section 8.4, Adverse Events, Serious Adverse Events, and Other Safety Report and Appendix 3, Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

Any clinically relevant changes occurring during the study must be recorded on the Adverse Event section of the CRF.

The study will include the following evaluations of safety and tolerability according to the time points provided in the SoA.

8.3.1. Vital Signs

Temperature, pulse/heart rate, respiratory rate, blood pressure will be assessed.

Blood pressure and pulse/heart rate measurements will be assessed in a seated position preceded by at least 5 minutes of rest in a quiet setting without distractions (eg, television, cell phones) with a completely automated upper arm cuff device. Manual techniques will be used only if an automated device is not available.

8.3.2. Electrocardiograms

During the collection of ECGs, participants should be in a quiet setting without distractions (eg, television, cell phones). Participants should rest in a supine position for at least 5 minutes before ECG collection and should refrain from talking or moving arms or legs. If blood sampling or vital sign measurement is scheduled for the same time point as ECG recording, the procedures should be performed in the following order: ECG(s), vital signs, blood draw.

At each time point at which triplicate ECGs are required, 3 individual ECG tracings should be obtained as closely as possible in succession. Details regarding collection of ECGs are available in the site manual.

8.3.3. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology and urine sample for urinalysis will be collected as noted in Appendix 1, Clinical Laboratory Tests. The investigator must review the laboratory results, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF. The laboratory reports must be filed with the source documents.

The tests that will be performed by the central laboratory unless otherwise specified in the laboratory manual or approved by the medical monitor are specified in Appendix 1, Clinical Laboratory Tests.

8.3.4. Pregnancy Testing

Both serum and urine pregnancy testing will be performed for all females of childbearing potential according to the SoA. Additional serum or urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulation, to establish the absence of pregnancy at any time during the participation in the study.

8.3.5. Depression Screening and Symptoms Monitoring

The PHQ-9 is a self-administered, 9-item questionnaire measuring symptoms and severity of depression. The recall period for all items is the past 2 weeks. The items include: diminished interest or pleasure, depressed mood, insomnia/hypersomnia, fatigue or loss of energy, weight loss

or weight gain/appetite loss or appetite gain, feelings of worthlessness, diminished concentration/indecisiveness, psychomotor agitation/retardation, and thoughts of death/suicide. Each item is rated on a 4-point Likert scale ranging from 0 “not at all” to 3 “nearly every day.” The PHQ-9 can generally be completed in 2 to 3 minutes (Kroenke 2001).

The PHQ-9 scores for depression range from 0 to 27 with higher scores indicating worse state (more severe depressive symptoms). A score of 5 to 9 is considered to be minimal symptoms of depression. A score of 10 to 14 is considered minor depression, dysthymia, or mild major depression. A score of 15 to 19 is considered to indicate moderately severe major depression, and a score ≥20 is considered to be severe major depression.

The PHQ-9 will be completed per the SoA. The PHQ-9 result should be reviewed by the site staff prior to the participant leaving the visit to assess the level of depression.

A participant who scores ≥15 on the PHQ-9 during the study suggestive of moderately severe major depression should immediately be referred to a mental health professional for further evaluation. The investigator should contact the medical monitor for discussion.

In addition, a participant who scores ≥20 on the PHQ-9 should be temporarily discontinued from study intervention (refer to section 7.1.2.).

8.3.6. Suicidal Ideation and Behavior Risk Monitoring

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

Two versions of it will be used in this study: the ‘Baseline/Screening’ version of the C-SSRS will be conducted during the screening visit and the ‘Since Last Visit’ version of the C-SSRS will be completed at Week 0 and all other visits through the end of the study.

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

For each assessment after Week 0, the following actions should be taken, if applicable:

- No suicidal ideation or behaviors (including self-injurious behavior without suicidal intent): No further action is needed.
- Suicidal ideation levels 1-3 or non-suicidal self-injurious behavior: Participant risk is assessed by the investigator.
- Suicidal ideation levels 4 or 5 or any suicidal behavior: Participant risk assessed and referral to a mental health professional.

Any C-SSRS finding, which in the opinion of the investigator is new or considered to be a worsening and clinically significant, should be reported on the AE eCRF.

In addition, caregivers of the participants will be instructed to immediately report any suicidal ideation, suicidal behavior, or suicide attempt to the investigator.

8.3.7. Tuberculosis Evaluation

Participants will be evaluated for symptoms of active TB and/or possible risk of exposure to TB, such as close contact with a person with active TB, based on follow-up assessment questions (below) and/or physical examination.

- Participants with evidence of active TB must be referred to a specialist for appropriate treatment. Treatment with study intervention will be discontinued in cases of active TB.
- Participants with positive IGRA test result, in which active TB has been excluded, may remain on study intervention after discussion with a specialist and agreement with the sponsor's medical representative. If presence of latent tuberculosis is established, participants who are at low risk of reactivation, defined by local health authorities and investigator judgement, do not require prophylactic anti-tuberculosis treatment during the study. The decision to treat or not should be made by the treating physician/Investigator.

Ongoing Tuberculosis Evaluation

To aid in the early detection of TB infection or exposure during study participation, participants must be evaluated for TB signs, symptoms, and close contacts at scheduled visits or by telephone approximately every 2 to 12 weeks. The following series of questions is suggested for use during the evaluation:

For participants and/or caregivers, the following series of questions is suggested for use during the evaluation:

- "Have you had a new cough of >14 days duration or a change in a chronic cough?"
- "Have you had any of the following symptoms:
  - Persistent fever?
  - Unintentional weight loss?
  - Night sweats?"
- "Have you had close contact with an individual with active TB?" (If there is uncertainty as to whether a contact should be considered "close," a physician specializing in TB should be consulted.)

If the evaluation raises suspicion for TB infection or the participant has had a close contact exposure to TB, study intervention must be withheld and an immediate and thorough investigation must be undertaken, including consultation with a physician specializing in TB to determine if treatment is warranted prior to any further study intervention. Participants should be encouraged to return for all subsequent scheduled study visits according to the protocol.

8.4. Adverse Events, Serious Adverse Events, and Other Safety Reporting

Timely, accurate, and complete reporting and analysis of safety information, including AEs, serious AEs, and PQCs, from clinical studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established Standard Operating Procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of safety information; all clinical studies conducted by the sponsor, or its affiliates will be conducted in accordance with those procedures.

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally acceptable representative in case of adolescents, where applicable) for the duration of the study.

Further details on AEs, SAEs, and PQCs can be found in Appendix 3. Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

8.4.1. Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information

All Adverse Events

All AEs and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the participant's last study-related procedure, which may include contact for follow-up of safety.

All AEs with an onset date after the signing of the ICF and up to 4 weeks after study treatment discontinuation must be recorded on specific AE pages of the eCRF.

Serious Adverse Events

All SAEs occurring during the study must be reported to the appropriate sponsor contact person by study site personnel immediately but no later than 24 hours of their knowledge of the event.

Serious adverse events, including those spontaneously reported to the investigator within 4 weeks after the last dose of study intervention, must be reported. The sponsor will evaluate any safety information that is spontaneously reported by an investigator beyond the time frame specified in the protocol.

All SAEs occurring after signature of the ICF up to 4 weeks after study treatment discontinuation must be recorded on AE pages in the eCRF and on an SAE form, regardless of the investigator-attributed causal relationship with study treatment or study mandated procedures.

Information regarding SAEs will be transmitted to the sponsor using the Serious Adverse Event Form and Safety Report Form of the CRF, which must be completed and reviewed by a physician from the study site and transmitted to the sponsor immediately but no later than within 24 hours of their knowledge of the event. The initial and follow-up reports of an SAE should be transmitted electronically or by facsimile (fax). Telephone reporting should be the exception and the reporter should be asked to complete the appropriate form(s) first.

8.4.2. Method of Detecting Adverse Events and Serious Adverse Events

Care will be taken not to introduce bias when detecting adverse events or serious adverse events. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrence.

Solicited Adverse Events

Solicited AEs are predefined for which the participant is specifically questioned (Section 8, Study Assessments and Procedures).

Unsolicited Adverse Events

Unsolicited AEs are all AEs for which the participant is not specifically questioned.

8.4.3. Follow-up of Adverse Events and Serious Adverse Events

The investigator is obligated to perform or arrange for the conduct of supplemental measurements and evaluations as medically indicated to elucidate the nature and causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

AEs and the special reporting situation of pregnancy will be followed by the investigator as specified in Appendix 3, Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

8.4.4. Regulatory Reporting Requirements for Serious Adverse Events

The sponsor assumes responsibility for appropriate reporting of the safety information to the Health Authorities, IRBs and ethics committees, as per local requirements. Serious, unexpected AEs that are considered at least possibly related to study medication will be reported in an expedited manner.

8.4.5. Pregnancy

All initial reports of the Special Reporting Situation of pregnancy in female participants or partners of male participants must be reported to the sponsor by the study site personnel within 24 hours of their knowledge of the event using the appropriate Pregnancy Notification Form. Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs and must be reported using the SAE report form.

Any participant who becomes pregnant during the study must discontinue further study intervention.

Follow-up information regarding the outcome of the pregnancy for female participants who become pregnant, or where the pregnancy was the result of male participant and his partner, and any postnatal sequelae in the infant will be required. The participant may be asked to return to the study site for the collection of safety assessments.

8.4.6. Adverse Events of Special Interest

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

A **possible Hy's law case** is defined by the occurrence of ALT/AST ≥3×ULN, together with Tbili ≥2×ULN or INR >1.5 (if measured). Any possible Hy's Law case is considered a medically important event and must be reported to the sponsor in an expedited manner using the AESI form, even before all other possible causes of liver injury have been excluded (FDA 2009).

Any newly identified malignancy or case of active TB occurring after the first administration of study intervention must be reported by the investigator according to the procedures in Appendix 3. Investigators are also advised that active TB is considered a reportable disease in most countries/territories. An AESI is considered serious only if it meets the definition of an SAE.

8.5. Pharmacokinetics

Plasma samples will be used to evaluate the PK of JNJ-77242113. Plasma collected for PK may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period.

8.5.1. Evaluations

Venous blood samples of approximately 4 mL will be collected for measurement of plasma concentrations of JNJ-77242113 as indicated in the SoA (Section 1.3). Samples collected for analyses of JNJ-77242113 plasma concentration may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period or for the evaluation of relevant biomarkers. Genetic analyses will not be performed on these plasma samples. Participant confidentiality will be maintained. Additional information about the collection, handling, and shipment of biological samples can be found in the Laboratory Manual.

8.5.2. Analytical Procedures

PK plasma samples will be analyzed to determine concentrations of JNJ-77242113 using a validated, specific, and sensitive LC-MS/MS method by or under the supervision of the sponsor.

8.6. Pharmacodynamics

Pharmacodynamic assessments are described in Section 8.8, Biomarkers.

8.7. Genetics and Pharmacogenomics

A pharmacogenomic blood sample will be collected from participants who consent separately to this component of the study to allow for pharmacogenomic research, as necessary (where local regulations permit). Participation in pharmacogenomic research is optional. Sample collection and testing will comply with local regulations. The sponsor will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.

Genetic (DNA) variation may be an important contributory factor to interindividual variability in drug response and associated clinical outcomes. Genetic and epigenetic factors may also serve as markers for disease susceptibility and prognosis and may identify population subgroups that respond differently to an intervention. The optional pharmacogenomic samples may be analyzed for identification of genetic and epigenetic factors that may be associated with psoriasis or the response to JNJ-77242113. They may also be used to develop tests or assays related to psoriasis or JNJ-77242113. This research may consist of the analysis of 1 or more candidate genes, or the analysis of genetic and epigenetic markers throughout the genome, or analysis of the entire genome (as appropriate) in relation to the disease and treatments. These analyses will be performed at the sponsor's discretion and may be reported separately.

8.8. Biomarkers

Biomarker assessments will be used to define and identify PD markers of therapeutic response to better understand the mechanism of action of JNJ-77242113 in participants with psoriasis, and aid in evaluating the drug exposure versus clinical response relationship, and the pathophysiology of psoriasis. This will include evaluation of relevant disease and pathway engagement biomarkers in skin and serum. Serum will be collected from all participants; skin biopsies will also be collected in participants that consent to this optional part of the study. These assessments could also help explain interindividual variability including differences between responders and nonresponders to support participant stratification. Biomarker samples may also be used to help address emerging issues and to enable the development of safer, more effective, and ultimately individualized therapies as well as development of tests/ assays related to JNJ-77242113 and psoriasis. Biomarker samples collection will be conducted at the timepoints indicated in the SoA and instruction for the collection and shipment of these samples can be found in the Laboratory manual. Sample collection and testing will comply with local regulations.

Serum biomarkers

Level of mediators relevant to the pathophysiology of psoriasis or inflammation including but not limited to IL-23, IL-17A, IL-17F, IL-22 and beta-defensin-2 will be evaluated to assess the impact of JNJ-77242113 on inflammatory proteins in the serum.

Skin biomarkers

Skin biopsies will be collected from participants that consent to this optional part of the study. At baseline, skin biopsies will be collected from both lesional and adjacent non-lesional areas; at subsequent weeks, only lesional areas will be sampled. Skin biopsy samples will be used to investigate changes in skin cellular composition and differential gene expression during treatment to explore PD, mechanism of action, and differences in treatment response between individuals. In addition, skin biopsies may be analyzed to explore the effects of study intervention on cellular composition in skin using immunohistochemistry and histological readouts.

Stopping Analysis

Biomarker analyses are dependent upon the availability of appropriate biomarker assays and clinical response rates. Biomarker analysis may be deferred or not performed, if during or at the end of the study, it becomes clear that the analysis will not have sufficient scientific value for

biomarker evaluation, or if there are not enough samples or responders to allow for adequate biomarker evaluation. In the event the study is terminated early or shows poor clinical efficacy, completion of biomarker assessments is based on justification and intended utility of the data.

8.9. Immunogenicity Assessments

Antibodies to JNJ-77242113 will be evaluated in serum samples collected from all participants according to the SoA. Additionally, samples should also be collected at the final visit from participants who discontinued study intervention or were withdrawn from the study. These samples will be tested by the sponsor or sponsor's designee.

Samples will be screened for antibodies binding to JNJ-77242113 and the titer of confirmed positive samples will be reported. Other analyses may be performed to further characterize the immunogenicity of JNJ-77242113.

Samples collected for immunogenicity analyses may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period. Genetic analyses will not be performed on these serum samples. Participant confidentiality will be maintained.

Analytical Procedures

Antibodies to JNJ-77242113 will be further characterized and evaluated for their ability to neutralize the activity of the study intervention(s) using validated assays.

8.10. Medical Resource Utilization and Health Economics

Health Economics/Medical Resource Utilization parameters will not be evaluated in this study.

9. STATISTICAL CONSIDERATIONS

Statistical analysis will be done by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be used to analyze the efficacy and safety data is outlined below. Specific details will be provided in the Statistical Analysis Plan.

9.1. Statistical Hypotheses

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

The select key secondary hypothesis during the randomized withdrawal period is:

Continuous JNJ-77242113 treatment in participants with moderate to severe plaque psoriasis is superior to withdrawal of JNJ-77242113 treatment as assessed by the proportion of participants who achieve a PASI 75 response at Week 52.

9.2. Analysis Sets

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

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

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

Population	Description
Enrolled	All participants who sign the ICF
Randomized	All participants who were randomized in the study.
FAS	All participants who were randomized in the study.
Per-protocol Analysis Set	A subset of participants in the full FAS who were in general compliance with the protocol elements that could affect the efficacy assessments.
Safety Analysis Set	All randomized participants who take at least 1 dose of study intervention.
PK Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113
Immunogenicity Analysis Set	All randomized participants who received at least 1 dose of JNJ-77242113 and who had at least 1 sample obtained after the first dose of JNJ-77242113 for the detection of antibodies to JNJ-77242113.

In addition, select secondary efficacy analyses will also be performed on subpopulations of FAS (eg, participants randomized at Week 24).

9.3. Statistical Analyses

The statistical analysis plan will be finalized prior to DBL at Week 24, and it will include a more technical and detailed description of the statistical analyses described in this section. This section is a summary of the planned statistical analyses of the most important endpoints including primary and key secondary endpoints.

9.3.1. General Considerations

Simple descriptive summary statistics, such as n, mean, SD, median, interquartile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data.

For binary endpoints, treatment comparisons will be performed using a CMH test stratified by age group at screening (adolescents <18 years and adults ≥18 years), baseline weight category for adults (≤90kg, >90kg) and geographic region. In case of rare events for binary endpoints, Fisher's exact test will be used. For repeated measure continuous endpoints, treatment comparisons will be performed using a MMRM model. The MMRM will include treatment, age group (adolescents <18 years and adults ≥18 years), baseline weight, geographic region and baseline value, as explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. The LS mean estimates and their corresponding 95% CI will be provided at each timepoint. In addition, the estimates of LS mean difference and 95% CIs between treatment groups will be provided. Analysis of

covariance will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, weight, geographic region and age group. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference and 95% CIs between treatment groups will be provided. For time to event endpoints, treatment comparisons will be performed using a log-rank test stratified by baseline weight category for adults (≤90kg, >90kg), geographic region and age group. Kaplan-Meier or life-table estimates of cumulative rate by treatment group will be provided to evaluate the timing of event occurrence in different treatment groups.

In general, all statistical tests will be performed at a significance level of 0.05 (2-sided) unless otherwise specified. Appropriate multiplicity adjustment procedure will be used to control the overall Type I error rate of α=0.05 (2-sided) for the primary and key secondary endpoints (see Section 9.3.3). Since there are 2 randomizations utilized in the study (ie, 2 different experiments), the Week 16 endpoints and the endpoints related to the randomized withdrawal will each be assigned with a 2-sided significance level of 0.05. Details will be described in the SAP. No adjustments for multiple comparisons will be made for other secondary endpoints and exploratory endpoints. Nominal p-values for other secondary and exploratory endpoints will be reported but should not be used to infer statistical significance.

9.3.2. Primary Endpoints/Estimand

There are 2 co-primary endpoints in this study: an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 and a PASI 90 response at Week 16.

The primary estimand (ie, a precise definition of the primary targeted treatment effect) is defined by the following 5 attributes:

- **Study intervention:**
  - Experimental: JNJ-77242113
  - Placebo
- **Population:** participants ≥12 years of age with moderate to severe plaque psoriasis.
- **Variable:** Binary response variables for co-primary endpoints

IGA 0/1 response: a responder is defined as a participant achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline at Week 16 who does not have intercurrent events in categories 1 or 2 (Table 1).

PASI 90 response: a responder is defined as a participant achieving a PASI 90 response at Week 16 who does not have intercurrent events in categories 1 or 2 (defined below).

- **Intercurrent event:**

Table 1: Intercurrent Events and Corresponding Strategies

1. Discontinuation of study intervention due to lack of efficacy or due to an AE of worsening psoriasis prior to Week 16. 2. Initiation of a protocol-prohibited medication or therapy during the study that could improve psoriasis prior to Week 16.	**Composite Strategy:** Participants with these ICEs are considered as IGA score of 0 or 1, and PASI 90, non-responders at Week 16. The occurrence of these ICEs is captured in the variable definition.
3. Discontinuation of study intervention for reasons other than ICE 1 prior to Week 16.	**Treatment Policy:** observed data will be used regardless of whether or not this ICE had occurred.

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

- **Population level summary:** Difference in the proportion of participants achieving an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and the proportion of participants achieving a PASI 90 response at Week 16 between the JNJ-77242113 and placebo intervention groups.

Primary Endpoint Analysis

These 2 co-primary endpoints will be compared between the JNJ-77242113 group and the placebo group. In these primary efficacy analyses, data from all randomized participants will be analyzed according to their assigned treatment group. The number and proportion of participants with an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and PASI 90 response at Week 16 will be summarized for each treatment group.

The co-primary endpoints will be analyzed using the primary estimand. Participants with ICEs 1 or 2 before Week 16 will be considered as non-responders at Week 16. For participants with ICE 3, observed data after this ICE will be utilized in the analysis. For participants experiencing multiple ICEs, an ICE 2 will override an ICE 3.

After accounting for the ICEs for the primary estimand, participants with missing data for the co-primary endpoints at Week 16 will be considered as non-responders.

To address the primary objective, a 2-sided (α=0.05) CMH chi-square test stratified by age group, baseline weight category for adults, and geographic region will be used for the co-primary endpoints.

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

To examine the robustness of the primary endpoint analyses, additional analyses will be conducted using supplemental estimands; these analyses will be described in the SAP. In addition, per-protocol analyses will be performed for the co-primary endpoints using the per-protocol population, which includes participants who are generally compliant with the protocol. To evaluate the consistency of the efficacy, subgroup analyses of the co-primary endpoints based on

demographics (eg, adolescents versus adults), baseline disease characteristics and previous psoriasis medications and therapies will be performed.

9.3.3. Key Secondary Endpoints

The key secondary analyses are:

- The proportion of participants who achieve an IGA score of cleared (0) at Week 16 will be compared between the JNJ-77242113 group and the placebo group.
- The proportion of participants who achieve a PASI 75 response at Week 4 will be compared between the JNJ-77242113 group and the placebo group.
- The proportion of participants who achieve a PASI 90 response at Week 8 will be compared between the JNJ-77242113 group and the placebo group.
- The proportion of participants who achieve a PASI 75 response at Week 16 will be compared between the JNJ-77242113 group and the placebo group.
- The proportion of participants who achieve a PASI 100 response at Week 16 will be compared between the JNJ-77242113 group and the placebo group.
- The proportion of participants who achieve 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 will be compared between the JNJ-77242113 group and the placebo group among participants with a baseline ss-IGA score ≥2.
- The proportion of participants who achieve PSSD symptom score of 0 at Week 8 will be compared between the JNJ-77242113 group and the placebo group among participants with a baseline PSSD symptom score > 0.
- The proportion of participants who achieve at least a 4-point improvement from baseline in PSSD Itch score at Week 4 will be compared between JNJ-77242113 group and the placebo group among participants with baseline PSSD Itch score of ≥4-points.
- The proportion of participants who achieve at least a 4-point improvement from baseline in PSSD Itch score at Week 16 will be compared between the JNJ-77242113 group and the placebo group among participants with a baseline PSSD Itch score ≥4-points.
- The proportion of participants who achieve PSSD symptom score of 0 at Week 16 will be compared between the JNJ-77242113 group and the placebo group among participants with a baseline PSSD symptom score > 0.
- The proportion of participants who achieve a PASI 75 response at Week 52 will be compared between the JNJ-77242113 group and the withdrawal group among PASI 75 responders randomized at Week 24.
- The proportion of participants who achieve a PASI 90 response at Week 52 will be compared between the JNJ-77242113 group and the withdrawal group among PASI 90 responders randomized at Week 24.
- The time to loss of PASI 75 response through Week 52 will be compared between the JNJ-77242113 group and the withdrawal group among PASI 75 responders randomized at Week 24.

- The time to loss of PASI 90 response through Week 52 will be compared between the JNJ-77242113 group and the withdrawal group among PASI 90 responders randomized at Week 24.

To evaluate the consistency of the efficacy, subgroup analyses of select key secondary endpoints based on demographics (eg, adolescents versus adults), baseline disease characteristics and previous psoriasis medications and therapies will be performed.

In order to control the overall Type I error rate (α=0.05), multiplicity adjustment will be applied to the analyses of the co-primary endpoints and key secondary endpoints listed above. The multiplicity testing strategy will be devised based on the expected power and relative importance of the endpoints and will be performed via a graphical approach. A single SAP with a unified approach is targeted for this study. However, different regulatory authorities may require prioritization of different endpoints; detailed multiplicity-control procedures will only be defined in the SAP and not in the protocol.

The proportions of participants achieving a key secondary efficacy response will be summarized and compared between treatment groups in the same manner as the co-primary endpoints using the appropriate stratification factors. Similar data handling rules as the primary endpoints will be used for the key secondary binary endpoints. Specifically, composite strategy will be used for ICE 1-2 (as defined in Section 9.3.2) and/or ICE 4 (meeting retreatment criterion during the randomized withdrawal period; only applicable to Week 52 endpoints) where participants with those ICEs are considered as non-responders; treatment policy strategy will be used for ICE 3 (Section 9.3.2) where observed data will be used. After application of ICEs, participants with missing data will be imputed as non-responders. The same statistical method as that for the co-primary endpoints using the appropriate stratification factors will be used for analyzing the binary endpoints using the appropriate stratification factors (ie, age group, baseline weight category for adults, and geographic region for endpoints during the placebo-controlled period and geographic regions and PASI 90 response status at Week 24 for Week 52 endpoints) (Section 9.3.2). The analyses related to the time to event endpoints during the randomized withdrawal period will be performed using log-rank test stratified by geographic region and PASI 90 response status at Week 24.

9.3.4. Other Secondary Endpoints and Exploratory Endpoints

Other secondary and exploratory endpoints are listed in Section 3. The analyses for other secondary and exploratory efficacy endpoints at Week 16 (comparisons between JNJ-77242113 and placebo) and at Week 52 (comparisons between the JNJ-77242113 group and the withdrawal group among participants randomized at Week 24) will be performed. No adjustments for multiple comparisons will be made and nominal p-values will be provided. Selected efficacy endpoints will also be summarized over time. A complete list of the planned analyses of other secondary and exploratory endpoints will be described in the SAP.

9.3.5. Safety Analyses

Safety data, including but not limited to, AEs, SAEs, AESIs (active TB, malignancy, possible Hy's Law cases), discontinuation of study intervention due to AEs, changes in laboratory assessments, changes in vital signs, and changes in weight, changes in PHQ-9 scores, and changes in C-SSRS

will be summarized. Treatment-emergent AEs will be summarized by treatment group and MedDRA system organ class and preferred terms. Details will be specified in the SAP.

All safety analyses will be performed using the Safety Analysis Set; participants will be summarized by the intervention they received.

Adverse Events

The verbatim terms used in the CRF by investigators to identify AEs will be coded using the MedDRA. Any AE occurring at or after the initial administration of study intervention or that is a consequence of a pre-existing condition that has worsened since baseline is considered to be treatment emergent. All reported treatment-emergent AEs will be included in the analysis. For each AE, the percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

The following analyses will also be used to assess the safety of participants in the study:

- The incidence and type of AEs.
- The incidence and type of SAEs.
- The incidence and type of AESIs.
- The incidence and type of severe AEs.
- The incidence and type of treatment-related AEs and SAEs as assessed by the investigator.
- The incidence and type of AEs leading to discontinuation of study intervention.

Listings of participants with SAEs, severe AEs, AEs of psoriasis, AESIs and AEs leading to discontinuation of study intervention will also be provided. Summaries, listings, datasets, or participant narratives may be provided, as appropriate, for those participants who die, who discontinue intervention due to an AE, or who experience a severe or a SAE.

Clinical Laboratory Tests

Laboratory data will be summarized by type of laboratory tests. Selected laboratory parameters will be summarized by treatment group. Common Terminology Criteria for Adverse Events (CTCAE) and ULN will 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.

In addition, a listing of participants with Grade 2 or higher laboratory test results (based on the CTCAE criteria) will also be provided.

Reference ranges and markedly abnormal results (specified in the SAP) will be used in the summary of laboratory data. Descriptive statistics will be calculated for all selected laboratory analyte at baseline and for observed values and changes from baseline at each scheduled time point.

Vital Signs

Vital signs including temperature, pulse/heart rate, and blood pressure (systolic and diastolic) will be summarized at selected scheduled timepoints using descriptive statics.

Weight

Weight and height will be summarized over time using descriptive statistics for adolescent participants. Weight will be summarized over time using descriptive statistics for adult participants.

Tanner Staging

Count and percentage of Tanner scale (range from Stage 1 to Stage 5) will be summarized by gender and age group for adolescent participants.

PHQ-9

Depression severity based on the PHQ-9 will be summarized descriptively by treatment group.

C-SSRS

Suicide-related thoughts and behaviors based on the C-SSRS will be summarized descriptively by treatment group.

9.3.6. Other Analyses

9.3.6.1. Pharmacokinetic Analyses

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

Plasma JNJ-77242113 concentrations will be summarized by visit and treatment group. Descriptive statistics will be calculated at each sampling timepoint.

Population PK analysis of plasma concentration-time data of JNJ-77242113 will be performed to characterize the disposition characteristics of JNJ-77242113 in this study. Data may be combined with those of other selected studies to support a relevant structural model. The influence of important covariates (such as, body weight, renal and hepatic function variables) on the population PK parameters may be evaluated. 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.

9.3.6.2. Immunogenicity Analyses

The incidence and titers of anti-JNJ-77242113 antibodies will be summarized for all participants who receive at least 1 dose of JNJ-77242113 and have appropriate samples for detection of antibodies to JNJ-77242113 (ie, participants with at least 1 sample obtained after their first dose of JNJ-77242113).

A listing of participants who are positive for antibodies to JNJ-77242113 will be provided.

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

Other immunogenicity analyses may be performed to further characterize the immune responses that are generated.

9.3.6.3. Biomarker Analyses

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

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

9.3.6.4. Pharmacokinetic/Pharmacodynamic Analyses

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

9.3.6.5. Pharmacogenomic Analyses

Genetic (DNA) analyses will be conducted only in participants who sign the consent form to participate in the optional pharmacogenetics substudy. These results are considered exploratory and will be presented in a separate report.

9.4. Interim Analysis/Analyses

No interim analysis is planned.

9.5. Sample Size Determination

This study is designed to evaluate the efficacy of JNJ-77242113 versus placebo and to evaluate the maintenance of response for JNJ-77242113. The sample size was also chosen to ensure a reasonable safety database to assess the overall safety of JNJ-77242113. These study objectives were taken into consideration in determining the sample size.

The assumptions for the sample size and power calculations were based on placebo response rates from the historical psoriasis clinical studies and data from the JNJ-77242113 Phase 2b Study 77242113PSO2001.

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

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

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

Table 2 provides the power for detecting a treatment difference under varying assumptions for the primary and selected key secondary endpoints specified in Section 9.3.3.

Country-Specific Data

Additional country specific enrollment, incremental to the global cohort enrollment of 600 participants, may be allowed if required by local Health Authority for the purpose of local regulatory approval consideration. Any such country specific enrollment will be used to fulfill the local regulatory requirement for registration purpose, and the data from the additional enrollment may not be included in the initial global submission package.

Table 2: Power to Detect a Treatment Effect Based on Different Proportions of Participants Achieving the Co-primary Endpoints at Week 16 and PASI 75 at Week 52

Co-primary Endpoints		
IGA cleared (0) or minimal (1) response at Week 16		
Placebo (n=200)	JNJ-77242113 (n=400)	Power
8%	60%	>99.9%
	64%	>99.9%
	70%	>99.9%
PASI 90 response at Week 16		
Placebo (n=200)	JNJ-77242113 (n=400)	Power
5%	50%	>99.9%
	55%	>99.9%
	59%	>99.9%
Select Key Secondary Endpoint		
PASI 75 response at Week 52 (difference of 20 percentage points)		
Withdrawal Group (n=135)	JNJ-77242113 (n=135)	Power
60%	80%	95.2%
65%	85%	97.0%
70%	90%	98.6%

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Clinical Laboratory Tests

The following tests will be performed according to the Schedule of Activities (SoA).

The actual date of assessment and, if required, the actual time of the assessment of laboratory samples will be recorded in the source documentation and in the eCRF or laboratory requisition form.

Protocol-Required Laboratory Assessments

<table>
<tr><th>Laboratory Assessments</th><th colspan="3">Parameters</th></tr>
<tr><td rowspan="2">Hematology</td><td>Platelet count
Red blood cell count
Hemoglobin
Hematocrit</td><td><u>RBC Indices:</u>
Mean corpuscular volume (MCV)
Mean corpuscular hemoglobin (MCH)
% Reticulocytes</td><td><u>White Blood Cell (WBC) count with Differential:</u>
Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils</td></tr>
<tr><td colspan="3">Note: A WBC evaluation may include any abnormal cells, which will then be reported by the laboratory. An RBC evaluation may include abnormalities in the RBC count, RBC parameters, or RBC morphology, which will then be reported by the laboratory. In addition, any other abnormal cells in a blood smear will also be reported.</td></tr>
<tr><td>Clinical Chemistry</td><td colspan="2">Sodium
Potassium
Chloride
Bicarbonate
Blood urea nitrogen (BUN)
Creatinine
Glucose (nonfasting)
Aspartate aminotransferase (AST)/Serum glutamic-oxaloacetic
Alanine aminotransferase (ALT)/Serum glutamic-oxaloacetic
Gamma-glutamyltransferase (GGT)
estimated glomerular filtration rate (eGFR)*</td><td>Total and direct bilirubin (Tbili and Dbil)
Alkaline phosphatase
Creatine phosphokinase (CPK)
Lactic acid dehydrogenase (LDH)
Uric acid
Calcium
Phosphate
Albumin
Total protein
Cholesterol
Triglycerides
Magnesium</td></tr>
<tr><td rowspan="2">Lipid Panel</td><td colspan="3">Total cholesterol
High-density lipoprotein (HDL)
Low-density lipoprotein (LDL; calculated)
Triglycerides</td></tr>
<tr><td colspan="3">Note: Fasting requirements are described in the SoA (Section 1.3).</td></tr>
</table>

Laboratory Assessments	Parameters	
Routine Urinalysis	Dipstick Specific gravity pH Glucose Protein Blood Ketones Bilirubin Urobilinogen Nitrite Leukocyte esterase	Sediment (if dipstick result is abnormal) Red blood cells White blood cells Epithelial cells Crystals Casts Bacteria
	If dipstick result is abnormal, microscopy will be used to measure sediment. In the microscopic examination, observations other than the presence of WBC, RBC and casts may also be reported by the laboratory.	
Other Tests	• Serum and urine pregnancy testing (β-hCG) for female participants of childbearing potential only • Serology (HIV antibody, hepatitis B surface antigen [HBsAg], hepatitis C virus antibody), and HCV RNA polymerase chain reaction (PCR) test (only required if hepatitis C virus antibody positive) • high sensitivity C-reactive protein (hs-CRP) • QuantiFERON®-TB Gold Plus (or equivalent QuantiFERON® TB test made available during the study) or T-SPOT® TB • Follicle stimulating hormone (FSH) as needed to confirm postmenopausal status	

* eGFR will be calculated at screening only. Serum creatinine will be measured per SoA.
Additional details will be provided in the laboratory manual.

10.2. Appendix 2: Regulatory, Ethical, and Study Oversight Considerations

10.2.1. Regulatory and Ethical Considerations

Investigator Responsibilities

The investigator is responsible for ensuring that the study is performed in accordance with the protocol, current ICH guidelines on Good Clinical Practice (GCP), and applicable regulatory and country-or territory-specific requirements.

Good Clinical Practice is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and well-being of study participants are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the study data are credible.

Protocol Clarification Communications

If text within a final approved protocol requires clarification (eg, current wording is unclear or ambiguous) that does not change any aspect of the current study conduct, a protocol clarification communication (PCC) may be prepared. The PCC Document will be communicated to the Investigational Site, Site Monitors, Local Trial Managers (LTMs), Clinical Trial Managers (CTMs), and/or Contract Research Organizations (CROs) who will ensure that the PCC explanations are followed by the investigators.

The PCC Document may be shared by the sites with Independent Ethics Committees/Institutional Review Boards (IECs/IRBs) per local regulations.

The PCC Documents must NOT be used in place of protocol amendments, but the content of the PCC Document must be included in any future protocol amendments.

Protocol Amendments

Neither the investigator nor the sponsor will modify this protocol without a formal amendment by the sponsor. All protocol amendments must be issued by the sponsor and signed and dated by the investigator. Protocol amendments must not be implemented without prior IEC/IRB approval, or when the relevant competent authority has raised any grounds for non-acceptance, except when necessary to eliminate immediate hazards to the participants, in which case the amendment must be promptly submitted to the IEC/IRB and relevant competent authority. Documentation of amendment approval by the investigator and IEC/IRB must be provided to the sponsor. When the change(s) involves only logistic or administrative aspects of the study, the IEC/IRB (where required) only needs to be notified.

In situations where a departure from the protocol is unavoidable during the study, the investigator or other physician in attendance will contact the appropriate sponsor representative listed in the Contact Information page(s), which will be provided as a separate document. Except in emergency situations, this contact must be made before implementing any departure from the protocol. In all cases, contact with the sponsor must be made as soon as possible to discuss the situation and agree on an appropriate course of action. The data recorded in the CRF and source documents will reflect

any departure from the protocol, and the source documents will describe this departure and the circumstances requiring it.

Regulatory Approval/Notification

This protocol and any amendment(s) must be submitted to the appropriate regulatory authorities in each respective country/territory, if applicable. A study may not be initiated until all local regulatory requirements are met.

Required Prestudy Documentation

The following documents must be provided to the sponsor before shipment of study intervention to the study site:

- Protocol and amendment(s), if any, signed and dated by the principal investigator
- A copy of the dated and signed (or sealed, where appropriate per local regulations), written IEC/IRB approval of the protocol, amendments, ICF, any recruiting materials, and if applicable, participant compensation programs. This approval must clearly identify the specific protocol by title and number and must be signed (or sealed, where appropriate per local regulations) by the chairman or authorized designee.
- Name and address of the IEC/IRB, including a current list of the IEC/IRB members and their function, with a statement that it is organized and operates according to GCP and the applicable laws and regulations. If accompanied by a letter of explanation, or equivalent, from the IEC/IRB, a general statement may be substituted for this list. If an investigator or a member of the study site personnel is a member of the IEC/IRB, documentation must be obtained to state that this person did not participate in the deliberations or in the vote/opinion of the study.
- Regulatory authority approval or notification, if applicable
- Signed and dated statement of investigator (eg, Form FDA 1572), if applicable
- Documentation of investigator qualifications (eg, curriculum vitae)
- Completed investigator financial disclosure form from the principal investigator, where required
- Signed and dated clinical trial agreement, which includes the financial agreement
- Any other documentation required by local regulations

The following documents must be provided to the sponsor before enrollment of the first participant:

- Completed investigator financial disclosure forms from all subinvestigators
- Documentation of subinvestigator qualifications (eg, curriculum vitae)
- Name and address of any local laboratory conducting tests for the study, and a dated copy of current laboratory normal ranges for these tests, if applicable
- Local laboratory documentation demonstrating competence and test reliability (eg, accreditation/license), if applicable

Independent Ethics Committee or Institutional Review Board

Before the start of the study, the investigator (or sponsor where required) will provide the IEC/IRB with current and complete copies of the following documents (as required by local regulations):

- Final protocol and, if applicable, amendments
- Sponsor-approved ICF (and any other written materials to be provided to the participants)
- IB (or equivalent information) and amendments/addenda
- Sponsor-approved participant recruiting materials
- Information on compensation for study-related injuries or payment to participants for participation in the study, if applicable
- Investigator's curriculum vitae or equivalent information (unless not required, as documented by the IEC/IRB)
- Information regarding funding, name of the sponsor, institutional affiliations, other potential conflicts of interest, and incentives for participants
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after the IEC/IRB has given full approval of the final protocol, amendments (if any, excluding the ones that are purely administrative, with no consequences for participants, data or study conduct, unless required locally), the ICF, applicable recruiting materials, and participant compensation programs, and the sponsor has received a copy of this approval. This approval letter must be dated and must clearly identify the IEC/IRB and the documents being approved.

Approval for the collection of optional samples for research and for the corresponding ICF must be obtained from the IEC/IRB. Approval for the protocol can be obtained independent of this optional research component.

During the study the investigator (or sponsor where required) will send the following documents and updates to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct)
- Revision(s) to ICF and any other written materials to be provided to participants
- If applicable, new or revised participant recruiting materials approved by the sponsor
- Revisions to compensation for study-related injuries or payment to participants for participation in the study, if applicable
- New edition(s) of the IB and amendments/addenda
- Summaries of the status of the study at intervals stipulated in guidelines of the IEC/IRB (at least annually)
- Reports of AEs that are serious, unlisted/unexpected, and associated with the study intervention

- New information that may adversely affect the safety of the participants or the conduct of the study
- Deviations from or changes to the protocol to eliminate immediate hazards to the participants
- Report of deaths of participants under the investigator's care
- Notification if a new investigator is responsible for the study at the site
- Development Safety Update Report and Line Listings, where applicable
- Any other requirements of the IEC/IRB

For all protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data or study conduct), the amendment and applicable ICF revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).

At least once a year, the IEC/IRB will be asked to review and reapprove this study, where required.

At the end of the study, the investigator (or sponsor where required) will notify the IEC/IRB about the study completion (if applicable, the notification will be submitted through the head of investigational institution).

Other Ethical Considerations

For study-specific ethical design considerations, refer to Section 4.2.2.

10.2.2. Financial Disclosure

Investigators and subinvestigators will provide the sponsor with sufficient, accurate financial information in accordance with local regulations to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the study and for 1 year after completion of the study.

Refer to Required Prestudy Documentation (above) for details on financial disclosure.

10.2.3. Informed Consent Process and Assent Form

Each participant (or a legally acceptable representative in case of adolescents, where applicable) must give consent according to local requirements after the nature of the study has been fully explained. The ICF(s) must be signed before performance of any study-related activity. The ICF(s) and assent form that is/are used must be approved by both the sponsor and by the reviewing IEC/IRB and be in a language that the participant can read and understand. The informed consent must be in accordance with principles that originated in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy.

Before enrollment in the study, the investigator or an authorized member of the study site personnel must explain to potential participants or their legally acceptable representatives (in case of adolescents, where applicable), the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at

any time. They will be informed that choosing not to participate will not affect the care the participant will receive for the treatment of his or her disease. Participants will be told that alternative treatments are available if they refuse to take part and that such refusal will not prejudice future treatment. Finally, they will be told that the investigator will maintain a participant identification register for the purposes of long-term follow-up if needed and that their records may be accessed by health authorities and authorized sponsor personnel without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations. By signing the ICF the participant or a legally acceptable representative (in case of adolescents, where applicable) is authorizing such access, which includes permission to obtain information about his or her survival status. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed. The physician may also recontact the participant for the purpose of obtaining consent to collect information about his or her survival status.

The participant or legally acceptable representative (in case of adolescents, where applicable) will be given sufficient time to read the ICF and the opportunity to ask questions. After this explanation and before entry into the study, consent must be appropriately recorded by means of either the participant's or his or her legally acceptable representative's (in case of adolescents, where applicable) personally dated signature. After having obtained the consent, a copy of the ICF must be given to the participant.

Participants who are rescreened and required to sign a new ICF.

Participants will be asked for consent to provide optional samples for research (where local regulations permit). After informed consent for the study is appropriately obtained, the participant or his or her legally acceptable representative (in case of adolescents, where applicable) will be asked to sign and personally date a separate ICF indicating agreement to participate in the optional research component. Refusal to participate in the optional research will not result in ineligibility for the study. A copy of this signed ICF will be given to the participant.

Where local regulations require, a separate ICF may be used for the required DNA component of the study.

Participants under the legal age of consent can be enrolled only after obtaining consent of a legally acceptable representative. Assent must be obtained from children (minors) capable of understanding the nature of the study, typically participants 7 years of age and older, depending on the institutional policies. Assent must be obtained from participants who are able to write. A separate assent form in the language the participant can understand must be developed for adolescents. After having obtained the assent, a copy of the assent form must be given to the participant, and to the participant's parent(s) or if applicable legally acceptable representative.

10.2.4. Recruitment Strategy

Various resources will be developed to support study awareness and provide information and education to potential participants about the study and clinical studies in general. Materials may include posters, informational brochures, advertisements, study guides, and thank you cards.

10.2.5. Data Protection

Privacy of Personal Data

The collection and processing of personal data from participants enrolled in this study will be limited to those data that are necessary to fulfill the objectives of the study.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of participants confidential.

The informed consent obtained from the participant (or his or her legally acceptable representative in case of adolescents, where applicable) includes information about, and where required per applicable regulations, explicit consent for the processing of personal data and for the investigator/institution to allow direct access to his or her original medical records (source data/documents) for study-related monitoring, audit, IEC/IRB review, and regulatory inspection. The informed consent also provides information to address the lawful transfer of the data to other entities and to other countries/territories.

The participant has the right to request through the investigator access to his or her personal data and the right to request rectification of any data that are not correct or complete or make requests concerning his or her personal data in accordance with applicable data protection law. Reasonable steps will be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

In the event of a data security breach, the sponsor will apply measures to adequately manage and mitigate possible adverse effects taking into consideration the nature of the data security breach as necessary to address other obligations such as notifying appropriate authorities in accordance with applicable data protection law.

Exploratory research is not conducted under standards appropriate for the return of data to participants. In addition, the sponsor cannot make decisions as to the significance of any findings resulting from exploratory research. Therefore, exploratory research data will not be returned to participants or investigators, unless required by law or local regulations. Privacy and confidentiality of data generated in the future on stored samples will be protected by the same standards applicable to all other clinical data.

10.2.6. Long-term Retention of Samples for Additional Future Research

No additional research on study participants, study samples or data derived from the study other than that stipulated in this section will be conducted by the institution(s) or by a third party, without the prior written consent of the sponsor.

Samples collected in this study may be stored for up to 15 years (or according to local regulations) for additional research. Samples will only be used to understand JNJ-77242113, to understand moderate to severe plaque psoriasis, to understand differential intervention responders, and to

develop tests/assays related to JNJ-77242113 and moderate to severe plaque psoriasis. The research may begin at any time during the study or during the post-study storage period.

Stored samples will be coded throughout the sample storage and analysis process and will not be labeled with personal identifiers. Participants may withdraw their consent for their samples to be stored for research (refer to Section 7.2.1, Withdrawal from the Use of Research Samples).

10.2.7. Committees Structure

Data Monitoring Committee

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

Adjudication Committee

The sponsor will perform adjudication on certain AEs, including but not limited to major adverse cardiovascular, cerebrovascular and thrombotic events, during this study. If adjudication is required, the site will be required to provide medical records and other anonymized source documentation to the sponsor for this purpose. A separate adjudication charter will be available.

10.2.8. Publication Policy/Dissemination of Clinical Study Data

All information, including but not limited to information regarding JNJ-77242113 or the sponsor's operations (eg, patent application, formulas, manufacturing processes, basic scientific data, prior clinical data, formulation information) supplied by the sponsor to the investigator and not previously published, and any data, including exploratory research data, generated as a result of this study, are considered confidential and remain the sole property of the sponsor. The investigator agrees to maintain this information in confidence and use this information only to accomplish the goals of this study and will not use it for other purposes without the sponsor's prior written consent.

The investigator understands that the information developed in the study will be used by the sponsor in connection with the continued development of JNJ-77242113, and thus may be disclosed as required to other clinical investigators or regulatory agencies. To permit the information derived from the clinical studies to be used, the investigator is obligated to provide the sponsor with all data obtained in the study.

The results of the study will be reported in a Clinical Study Report generated by the sponsor and will contain data from all study sites that participated in the study as per protocol. Recruitment performance or specific expertise related to the nature and the key assessment parameters of the study will be used to determine a coordinating investigator for the study. Results of ad hoc analyses performed after the Clinical Study Report has been issued and will not require a revision of the Clinical Study Report.

Study participant identifiers will not be used in the publication of results. Any work created in connection with performance of the study and contained in the data that can benefit from copyright

protection (except any publication by the investigator as provided for below) shall be the property of the sponsor as author and owner of copyright in such work.

Consistent with Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines, the sponsor shall have the right to publish such primary (multicenter) data and information without approval from the investigator. The investigator has the right to publish study site-specific data after the primary data are published. If an investigator wishes to publish information from the study, a copy of the manuscript must be provided to the sponsor for review at least 60 days before submission for publication or presentation. Expedited reviews will be arranged for abstracts, poster presentations, or other materials. If requested by the sponsor in writing, the investigator will withhold such publication for up to an additional 60 days to allow for filing of a patent application. In the event that issues arise regarding scientific integrity or regulatory compliance, the sponsor will review these issues with the investigator. The sponsor will not mandate modifications to scientific content and does not have the right to suppress information. For multicenter study designs and sub-study approaches, secondary results generally should not be published before the primary endpoints of a study have been published. Similarly, investigators will recognize the integrity of a multicenter study by not submitting for publication data derived from the individual study site until the combined results from the completed study have been submitted for publication, within 18 months after the study end date, or the sponsor confirms there will be no multicenter study publication. Authorship of publications resulting from this study will be based on the guidelines on authorship, such as those described in the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals, which state that the named authors must have made a significant contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of the data, for the work; and drafted the work or revised it critically for important intellectual content; and given final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Registration of Clinical Studies and Disclosure of Results

The sponsor will register and disclose the interim results of clinical studies as required by law. The disclosure of the study results will be performed after the closure of the clinical database in order to ensure the statistical analyses are relevant.

10.2.9. Data Quality Assurance

Data Quality Assurance/Quality Control

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study sites, review of protocol procedures with the investigator and study site personnel before the study, periodic monitoring visits by the sponsor, and direct transmission of clinical laboratory data from a central laboratory into the sponsor's data base. Written instructions will be provided for collection, handling, storage, and shipment of samples.

Guidelines for CRF completion will be provided and reviewed with study site personnel before the start of the study.

The sponsor may review the CRF for accuracy and completeness during the on-site monitoring visits and after transmission to the sponsor; any discrepancies will be resolved with the investigator or designee, as appropriate. After upload of the data into the study database they will be verified for accuracy and consistency with the other sources.

10.2.10. Case Report Form Completion

Case report forms are prepared and provided by the sponsor for each participant in electronic format. All data relating to the study must be recorded in the CRF as described in the CRF guidelines. All CRF entries, corrections, and alterations must be made by the investigator or authorized study site personnel. The investigator must verify that all data entries in the CRF are accurate and correct.

The study data will be transcribed by study-site personnel from the source documents onto an electronic CRF, if applicable. Study-specific data will be transmitted in a secure manner to the sponsor.

Worksheets may be used for the capture of some data to facilitate completion of the CRF. Any such worksheets will become part of the participant's source documents. Data must be entered into CRF in English. The CRF must be completed as soon as possible after a participant visit and the forms must be available for review at the next scheduled monitoring visit. All participative measurements (eg, pain scale information or other questionnaires) will be completed by the same individual who made the initial baseline determinations whenever possible.

If necessary, queries will be generated in the eDC tool. If corrections to a CRF are needed after the initial entry into the CRF, this can be done in either of the following ways:

- Investigator and study-site personnel can make corrections in the eDC tool at their own initiative or as a response to an auto query (generated by the eDC tool).
- Sponsor or sponsor delegate can generate a query for resolution by the investigator and study-site personnel.

10.2.11. Source Documents

At a minimum, source documents consistent in the type and level of detail with that commonly recorded at the study site as a basis for standard medical care must be available for the following: participant identification, eligibility, and study identification; study discussion and date of signed informed consent; dates of visits; results of safety and efficacy parameters as required by the protocol; record of all AEs and follow-up of AEs; concomitant medication; intervention receipt/dispensing/return records; study intervention administration information; and date of study completion and reason for early discontinuation of study intervention or withdrawal from the study, if applicable.

The author of an entry in the source documents must be identifiable.

Given that patient reported outcomes (PROs) are reports of a patient's health condition that come directly from the patient, without interpretation by a clinician or anyone else, the responses to PRO measures entered by study participants into source records cannot be overridden by site staff or investigators In order to minimize inclusion bias, investigators participating in this study must

agree not to change such PRO data items once entered and saved permanently into the source records for the following instruments (and visits) as set forth in the Data Management Plan for this study:

- Psoriasis Symptoms and Signs Diary (PSSD)
- Dermatology Life Quality Index (DLQI)
- Children's Dermatology Life Quality Index (CDLQI)
- Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)
- Patient-reported Outcomes Measurement Information System-29 (PROMIS-29)
- Patient-Reported Outcomes Measurement Information System Pediatric-25 v2.0 (PROMIS-25)
- Treatment Satisfaction Questionnaire for Medication - Effectiveness (TSQM-E)
- EuroQol 5-Dimension 5-Level Questionnaire (EQ-5D-5L)
- PsA Pain Assessment
- PsA Disease Activity Assessment
- Participant Assessment of Acceptability and Palatability
- Patient Health Questionnaire-9 (PHQ-9)

Specific details required as source data for the study and source data collection methods will be reviewed with the investigator before the study and will be described in the monitoring guidelines (or other equivalent document).

The following data will be recorded directly into the CRF and will be considered source data.

- Race
- History of all nicotine use, eg, cigarettes (including e-cigarettes or equivalent), cigars, chewing tobacco, patch, gum
- Blood pressure and pulse/heart rate
- Height and weight

The minimum source documentation requirements for Section 5.1, Inclusion Criteria and Section 5.2, Exclusion Criteria that specify a need for documented medical history are as follows:

- Referral letter from treating physician or
- Complete history of medical notes at the site or
- Discharge summaries

Inclusion and exclusion criteria not requiring documented medical history must be verified at a minimum by participant interview or other protocol required assessment (eg, physical examination, laboratory assessment) and documented in the source documents.

An eSource system may be utilized, which contains data traditionally maintained in a hospital or clinic record to document medical care (eg, electronic source documents) as well as the clinical

study-specific data fields as determined by the protocol. This data is electronically extracted for use by the sponsor. If eSource is utilized, references made to the CRF in the protocol include the eSource system, but information collected through eSource may not be limited to that found in the CRF.

10.2.12. Monitoring

The sponsor will use a combination of monitoring techniques: central, remote, or on-site monitoring to monitor this study.

The sponsor will perform on-site monitoring visits as frequently as necessary, as outlined in the Monitoring Guidelines. The monitor will record dates of the visits in a study site visit log that will be kept at the study site. The first post-initiation visit will be made as soon as possible after screening has begun. At these visits, the monitor will compare data entered into the CRF with the source documents (eg, hospital/clinic/physician's office medical records); a sample may be reviewed. The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the CRF are known to the sponsor and study site personnel and are accessible for verification by the sponsor study site contact. If electronic records are maintained at the study site, the method of verification must be discussed with the study site personnel.

Direct access to source documents (medical records) must be allowed for the purpose of verifying that the recorded data are consistent with the original source data. Findings from this review will be discussed with the study site personnel. The sponsor expects that, during monitoring visits, the relevant study site personnel will be available, the source documents will be accessible, and a suitable environment will be provided for review of study-related documents. The monitor will meet with the investigator on a regular basis during the study to provide feedback on the study conduct.

In addition to on-site monitoring visits, remote contacts may occur as needed. It is expected that during these remote contacts, study site personnel will be available to provide an update on the progress of the study at the site.

Central monitoring will take place for data identified by the sponsor as requiring central review.

10.2.13. On-site Audits

Representatives of the sponsor's clinical quality assurance department may visit the study site at any time during or after completion of the study to conduct an audit of the study in compliance with regulatory guidelines and company policy. These audits will require access to all study records, including source documents, for inspection. Participant privacy must, however, be respected. The investigator and study site personnel are responsible for being present and available for consultation during routinely scheduled study site audit visits conducted by the sponsor or its designees.

Similar auditing procedures may also be conducted by agents of any regulatory body, either as part of a national GCP compliance program or to review the results of this study in support of a

regulatory submission. The investigator must immediately notify the sponsor if he or she has been contacted by a regulatory agency concerning an upcoming inspection.

10.2.14. Record Retention

In compliance with the ICH/GCP guidelines, the investigator/institution will maintain all CRF and all source documents that support the data collected from each participant, as well as all study documents as specified in ICH/GCP Section 8, Essential Documents for the Conduct of a Clinical Trial, and all study documents as specified by the applicable regulatory requirement(s). The investigator/institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

If the responsible investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the investigator relocate or dispose of any study documents before having obtained written approval from the sponsor.

If it becomes necessary for the sponsor or the appropriate regulatory authority to review any documentation relating to this study, the investigator/institution must permit access to such reports.

10.2.15. Study and Site Start and Closure

First Act of Recruitment

The first subject screened is considered the first act of recruitment and it becomes the study start date.

Study/Site Termination

The sponsor reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the sponsor or investigator may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IEC/IRB or local health authorities, the sponsor's procedures, or GCP guidelines.
- Inadequate recruitment of participants by the investigator.
- Discontinuation of further study intervention development.

10.3. Appendix 3: Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

10.3.1. Adverse Event Definitions and Classifications

Adverse Event

An AE is any untoward medical occurrence in a clinical study participant administered a pharmaceutical (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. (Definition per International Council on Harmonisation [ICH])

This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

Note: The sponsor collects AEs starting with the signing of the ICF (refer to All Adverse Events under Section 8.4.1, Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information, for time of last AE recording).

Serious Adverse Event

An SAE based on ICH and EU Guidelines on Pharmacovigilance for Medicinal Products for Human Use is any untoward medical occurrence that at any dose:

- Results in death
- Is life-threatening
  (The participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it was more severe.)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is a suspected transmission of any infectious agent via a medicinal product
- Is Medically Important*

*Medical and scientific judgment must be exercised in deciding whether expedited reporting is also appropriate in other situations, such as important medical events that may not be immediately life threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above. These should usually be considered serious.

If a serious and unexpected AE occurs for which there is evidence suggesting a causal relationship between the study intervention and the event (eg, death from anaphylaxis), the event must be reported as a serious and unexpected suspected adverse reaction even if it is a component of the study endpoint (eg, all-cause mortality). Serious, unexpected AEs that are considered at least possibly related to study medication will be reported in an expedited manner to the relevant health authorities, IRBs and ECs per local requirements.

Unlisted (Unexpected) Adverse Event/Reference Safety Information

An AE is considered unlisted if the nature or severity is not consistent with the applicable product reference safety information. For JNJ-77242113, the expectedness of an AE will be determined by whether or not it is listed in the IB.

10.3.2. Attribution Definitions

Assessment of Causality

The causal relationship to study intervention is assessed by the Investigator. The following selection must be used to assess all AEs.

Related

There is a reasonable causal relationship between study intervention administration and the AE.

Not Related

There is not a reasonable causal relationship between study intervention administration and the AE.

The term "reasonable causal relationship" means there is evidence to support a causal relationship.

10.3.3. Severity Criteria

An assessment of severity grade will be made using the following general categorical descriptors:

Mild: Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with everyday activities.

Moderate: Sufficient discomfort is present to cause interference with normal activity.

Severe: Extreme distress, causing significant impairment of functioning or incapacitation. Prevents normal everyday activities.

The investigator must use clinical judgment in assessing the severity of events not directly experienced by the participant (eg, laboratory abnormalities).

10.3.4. Special Reporting Situations

Safety events of interest on a sponsor study intervention in an interventional study that may require expedited reporting or safety evaluation include, but are not limited to:

- Overdose of a sponsor study intervention
- Suspected abuse/misuse of a sponsor study intervention

- Accidental or occupational exposure to a sponsor study intervention
- Unexpected therapeutic or clinical benefit from use of a sponsor study intervention
- Medication error, intercepted medication error or potential medication error involving a Johnson & Johnson medicinal product (with or without patient exposure to the Johnson & Johnson medicinal product, eg, product name confusion, product label confusion, intercepted prescribing or dispensing errors)
- Exposure to a sponsor study intervention from breastfeeding
- Reporting of participant pregnancy or participant partner(s) pregnancy

Participant-specific special reporting situations mush be recorded in the CRF. Any special reporting situation that meets the criteria of an SAE must be recorded on the SAE page of the CRF.

10.3.5. Procedures

All Adverse Events

All AEs, regardless of seriousness, severity, or presumed relationship to study intervention, must be recorded using medical terminology in the source document and the CRF. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (eg, cough, runny nose, sneezing, sore throat, and head congestion should be reported as "upper respiratory infection"). Investigators must record in the CRF their opinion concerning the relationship of the AE to study therapy. All measures required for AE management must be recorded in the source document and reported according to sponsor instructions.

For all studies with an outpatient phase, including open-label studies, the participant must be provided with a "wallet (study) card" and instructed to carry this card with them for the duration of the study indicating the following:

- Study number
- Statement, in the local language(s), that the participant is participating in a clinical study
- Investigator’s name and 24-hour contact telephone number
- Local sponsor’s name and 24-hour contact telephone number (for medical personnel only)
- Site number
- Participant number
- Any other information that is required to do an emergency breaking of the blind

Serious Adverse Events

All SAEs that have not resolved by the end of the study, or that have not resolved upon the participant’s discontinuation from the study, must be followed until any of the following occurs:

- The event resolves
- The event stabilizes
- The event returns to baseline, if a baseline value/status is available

- The event can be attributed to agents other than the study intervention or to factors unrelated to study conduct
- It becomes unlikely that any additional information can be obtained (participant or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts).

Any event requiring hospitalization (or prolongation of hospitalization) that occurs during participation in the study must be reported as an SAE, except hospitalizations for the following:

- Surgery or procedure planned before entry into the study (must be documented). Note: Hospitalizations that were planned before the signing of the ICF, and where the underlying condition for which the hospitalization was planned has not worsened, will not be considered SAEs. Any AE that results in a prolongation of the originally planned hospitalization is to be reported as a new SAE.

The cause of death of a participant in a study within 4 weeks of the last dose of study intervention, whether or not the event is expected or associated with the study intervention, is considered an SAE.

Information regarding SAEs will be transmitted to the sponsor using an SAE reporting form and safety report form of the CRF, which must be completed and reviewed by a physician from the study site and transmitted in a secure manner to the sponsor immediately, but no later than within 24 hours of their knowledge of the event. The initial and follow-up reports of an SAE should be transmitted in a secure manner electronically or by facsimile (fax). Telephone reporting should be the exception and the reporter should be asked to complete the appropriate form(s) first.

10.3.6. Product Quality Complaint Handling

Definition

A product quality complaint (PQC) is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, ie, any dissatisfaction relative to the identity, quality, durability, reliability or performance of a distributed product, including its labeling, drug delivery system, or package integrity. A PQC may have an impact on the safety and efficacy of the product. In addition, it includes any technical complaints, defined as any complaint that indicates a potential quality issue during manufacturing, packaging, release testing, stability monitoring, dose preparation, storage or distribution of the product or the drug delivery system.

Procedures

All initial PQCs must be reported to the sponsor by the study site personnel within 24 hours after being made aware of the event.

A sample of the suspected product should be maintained under the correct storage conditions until a shipment request is received from the sponsor.

10.3.7. Contacting Sponsor Regarding Safety, Including Product Quality

The names (and corresponding telephone numbers) of the individuals who must be contacted regarding safety issues, PQC, or questions regarding the study are listed in the Contact Information page(s), which will be provided as a separate document.

10.4. Appendix 4: Contraceptive and Barrier Guidance

Participants must follow contraceptive measures as outlined in Section 5.1, Inclusion Criteria. Pregnancy information will be collected and reported as noted in Section 8.4.5, Pregnancy and: Appendix 3, Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

Definitions

Female Participants of Childbearing Potential

A female participant is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

Female Participants Not of Childbearing Potential

- **premenarchal**
  A premenarchal state is one in which menarche has not yet occurred.
- **postmenopausal**
  A postmenopausal state is defined as no menses for 52 weeks without an alternative medical cause. A high follicle stimulating hormone (FSH) level (>40 IU/L or mIU/mL) in the postmenopausal range may be used to confirm a postmenopausal state in female participants not using hormonal contraception or hormonal replacement therapy (HRT), however in the absence of 52 weeks of amenorrhea, a single FSH measurement is insufficient. If there is a question about menopausal status in female participants on HRT, the female participant will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if they wish to continue HRT during the study.
- **permanently sterile (for the purpose of this study)**

Permanent sterilization methods include hysterectomy, or bilateral salpingectomy, or bilateral oophorectomy.

Has congenital abnormalities resulting in sterility.

Note: If the childbearing potential changes after start of the study (eg, a premenarchal female participant experiences menarche) or the risk of pregnancy changes (eg, a female participant who is not heterosexually active becomes active), a female participant must begin a highly effective method of contraception, as described throughout the inclusion criteria.

If reproductive status is questionable, additional evaluation should be considered.

Contraceptive (birth control) use by male participants or female participants must be consistent with local regulations regarding the acceptable methods of contraception for those participating in clinical studies.

Typical use failure rates may differ from those when used consistently and correctly. Use must be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.

Examples of Contraceptives

EXAMPLES OF CONTRACEPTIVES[a] ALLOWED FOR FEMALE PARTICIPANTS DURING THE STUDY INCLUDE:
USER INDEPENDENT **Highly Effective Methods That Are User Independent** *Failure rate of <1% per year when used consistently and correctly.*
• Implantable progestogen-only hormone contraception associated with inhibition of ovulation
• Intrauterine device (IUD)
• Intrauterine hormone-releasing system (IUS)
• Tubal closure (eg, bilateral tubal occlusion, bilateral tubal ligation)
• Azoospermic partner (vasectomized or due to medical cause) *(Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the female participant of childbearing potential and the absence of sperm has been confirmed. If not, additional highly effective method of contraception must be used.)*
USER DEPENDENT **Highly Effective Methods That Are User Dependent** *Failure rate of <1% per year when used consistently and correctly.*
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation – oral – intravaginal – transdermal – injectable
• Progestogen-only hormone contraception associated with inhibition of ovulation – oral – injectable
• Sexual abstinence *(Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.)*
NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION FOR FEMALE PARTICIPANTS DURING THE STUDY (not considered to be highly effective - failure rate of ≥1% per year)
• Progestogen-only oral hormonal contraception where inhibition of ovulation is not the primary mode of action.
• Male or female condom with or without spermicide
• Cap, diaphragm, or sponge with spermicide
• A combination of male condom with either cap, diaphragm, or sponge with spermicide (double-barrier methods)
• Periodic abstinence (calendar, symptothermal, post-ovulation methods)
• Withdrawal (coitus-interruptus)
• Spermicides alone
• Lactational amenorrhea method (LAM)

a) Typical use failure rates may differ from those when used consistently and correctly. Use must be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.

10.5. Appendix 5: Liver Safety: Suggested Actions and Follow-up Assessments

10.5.1. Liver Chemistry Criteria with Continued Study Intervention and Increased Monitoring

Liver Chemistry Criteria with Continued Study Intervention and Increased Monitoring	
Liver Chemistry Criteria	**Actions Required**
• ALT **or** AST ≥5×ULN but <8×ULN **and** total bilirubin <2×ULN with no symptoms.	• Repeat liver chemistry tests within **24 to 72 hours**: – ALT – AST – Total bilirubin – Alkaline phosphatase – INR[a] (if INR measured) • Monitor participants **weekly for ≥2 weeks** until liver chemistry abnormalities resolve, stabilize, or return to baseline. • If unable to monitor for **≥2 weeks** or if ALT or AST elevation persists for **≥2 weeks**, **immediately** discontinue study intervention and refer to Section 10.5.2, *Liver Chemistry Criteria with Stopping of Study Intervention Criteria and Follow-up Assessments* table. **Note:** Refer to the liver criterion below if retest shows ALT **or** AST ≥3×ULN but <5×ULN **and** total bilirubin <2×ULN with no symptoms to continue weekly monitoring.
• ALT **or** AST ≥3×ULN but <5×ULN **and** total bilirubin <2×ULN with no symptoms.	• Repeat liver chemistry tests within **24 to 72 hours**: – ALT – AST – Total bilirubin – Alkaline phosphatase – INR[a] (if INR measured) • Monitor participants **weekly for ≥4 weeks** until liver chemistry abnormalities resolve, stabilize, or return to baseline. • If unable to monitor for **≥4 weeks** or if ALT or AST elevation persists for **≥4 weeks**, **immediately** discontinue study intervention and refer to Section 10.5.2, *Liver Chemistry Criteria with Stopping of Study Intervention Criteria and Follow-up Assessments* table.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; INR=international normalized ration; ULN=upper limit of normal.
a. The INR stated threshold value will not apply to participants receiving anticoagulants.

10.5.2. Liver Chemistry Criteria with Stopping of Study Intervention and Follow-up Assessments

Determination of temporary interruption (withheld) versus permanent discontinuation of study intervention is described in the table below and should be discussed with the medical monitor.

Liver Chemistry Criteria with Stopping of Study Intervention Criteria and Follow-up Assessments		
Liver Chemistry Criteria	**Actions Required**	**Suggested Follow-up Assessments**
• ALT **or** AST ≥8×ULN. • ALT **or** AST ≥5×ULN but <8×ULN that persists for **≥2 weeks**, **or** that cannot be monitored for **≥2 weeks**. • ALT **or** AST ≥3×ULN but <5×ULN that persists for **≥4 weeks**, **or** that cannot be monitored for **≥4 weeks**. • ALT **or** AST ≥3×ULN associated with symptoms[a] (new or worsening) believed to be related to liver injury or hypersensitivity.	• **Immediately** discontinue study intervention. • Report the event to the sponsor within **24 hours**. • Complete an SAE data collection tool if the event also met the criteria for an SAE[b]. • Repeat liver chemistry tests within **24 to 72 hours**: – ALT – AST – Total bilirubin – Alkaline phosphatase – INR[b] (if INR measured) • Monitor participants **weekly** until liver chemistry abnormalities resolve, stabilize, or return to baseline. • Restart study intervention if liver event causality is determined to be "not related", restart may be permitted upon written approval of the sponsor.	• Viral hepatitis serology[c]. • Obtain a serum CPK and LDH. • Fractionated bilirubin. • Obtain complete blood count with differential to assess eosinophilia. • Obtain blood sample for PK analysis within 3 days after the most recent dose[d]. • Record the appearance or worsening of clinical symptoms of liver injury, or hypersensitivity CRF as per CRF completion guidelines. • Record use of concomitant medications (including acetaminophen, herbal remedies, recreational drugs and other over-the-counter medications). • Record alcohol use.

Liver Chemistry Criteria with Stopping of Study Intervention Criteria and Follow-up Assessments		
Possible Hy's Law		
Liver Chemistry Criteria	**Actions Required**	**Suggested Follow-up Assessments**
• ALT **or** AST ≥3×ULN **and** total bilirubin[b,e] ≥2×ULN (or at least a doubling of direct bilirubin in known Gilbert's syndrome). • ALT **or** AST ≥3×ULN **and** INR[b]>1.5 (if INR measured).	• **Immediately** discontinue study intervention. • Report the event to the sponsor within **24 hours**. • Complete an SAE data collection tool if the event also met the criteria for an SAE[b]. • Repeat liver chemistry tests within **24 hours**: – ALT – AST – Total bilirubin – Direct bilirubin – Alkaline phosphatase – INR[b] (if INR measured) • Monitor participants **twice weekly** until liver chemistry abnormalities resolve, stabilize, or return to baseline. • A specialist or hepatology consultation is recommended. • Restart study intervention if liver event causality is determined to be "not related", restart may be permitted upon written approval of the sponsor.	**In addition, to the suggested follow-up assessments for Liver Chemistry Criteria with Stopping of Study Intervention listed above, <u>obtain the following</u>:** • Anti-nuclear antibody, anti-smooth muscle antibody, Type 1 anti-liver kidney microsomal antibodies, and quantitative total IgG or gamma globulins. • Serum acetaminophen adduct assay (when available) to assess potential acetaminophen contribution to liver injury in participants with definite or likely acetaminophen use in the preceding week. • Liver imaging (ultrasound, magnetic resonance, or computerized tomography) to evaluate liver disease; CRF as per CRF completion guidelines. • Liver biopsy may be discussed with local specialist if available, for instance: – In patients when serology raises the possibility of AIH. – In patients when suspected DILI progresses or fails to resolve on withdrawal of study intervention. – In patients with acute or chronic atypical presentation: hepatic vascular disorder, chronic hepatitis fibrosis, microvesicular steatosis.

AIH=autoimmune hepatitis; ALT=alanine aminotransferase; AST=aspartate aminotransferase; CPK=creatine phosphokinase; CRF=case report form; DILI=drug-induced liver injury; IgG=immunoglobulin G; IgM=immunoglobulin M; INR=international normalized ration; LDH=lactic dehydrogenase; PK=pharmacokinetic; SAE=serious adverse event; ULN=upper limit of normal.

a. New or worsening symptoms believed to be related to liver injury (such as fatigue, nausea, vomiting, right upper quadrant pain or tenderness, or jaundice) or hypersensitivity (such as fever, rash, or eosinophilia).
b. All events of ALT or AST ≥3×ULN and total bilirubin ≥2×ULN (or at least a doubling of direct bilirubin for known Gilbert's syndrome) or ALT or AST ≥3×ULN and INR >1.5 may indicate severe liver injury (possible 'Hy's Law') and must be reported to sponsor in an expedited manner and as an SAE if SAE criteria met (excluding studies of hepatic impairment or cirrhosis). The INR stated threshold value will not apply to participants receiving anticoagulants.
c. Includes: hepatitis A immunoglobulin M antibody; hepatitis B surface antigen and hepatitis B core antibody; hepatitis C RNA; cytomegalovirus IgM antibody; Epstein-Barr viral capsid antigen IgM antibody (or if unavailable, heterophile antibody or monospot testing); and hepatitis E IgM antibody. In participants with underlying chronic hepatitis B at study

entry (identified by positive hepatitis B surface antigen) check quantitative hepatitis B DNA and hepatitis delta antibody. If hepatitis delta antibody assay cannot be performed, it can be replaced with a PCR of hepatitis D RNA virus (where needed) (Le Gal 2005).

d. PK sample may not be required for participants known to be receiving placebo or non-comparator interventions. Record the date/time of the PK blood sample draw and the date/time of the last dose of study intervention prior to the PK blood sample draw on the CRF. If the date or time of the last dose is unclear, provide the participant's best approximation. If the date/time of the last dose cannot be approximated OR a PK sample cannot be collected in the time period indicated above, do not obtain a PK sample. Instructions for sample handling and shipping are in the Study Reference Manual.

e. Serum bilirubin fractionation should be performed if testing is available. If serum bilirubin fractionation is not immediately available, stop study intervention if ALT or AST ≥3×ULN and total bilirubin ≥2×ULN. Additionally, if serum bilirubin fractionation testing is unavailable, record the absence/presence of detectable urinary bilirubin on dipstick which is indicative of direct bilirubin elevations suggesting liver injury.

References

Le Gal F (2005), Gordien E, Affolabi D, et al. Quantification of Hepatitis Delta Virus RNA in Serum by Consensus Real-Time PCR Indicates Different Patterns of Virological Response to Interferon Therapy in Chronically Infected Patients. J Clin Microbiol. 2005;43(5):2363-2369

10.6. Appendix 6: Study Conduct During a Natural Disaster/Major Disruption/Pandemic

It is recognized that the events causing major disruption such as COVID-19 pandemic, war, or natural disaster may have an impact on the conduct of this clinical study due to, for example, isolation or quarantine of participants and study site personnel; travel restrictions/limited access to public places, including hospitals; study site personnel being unavailable, isolated, relocated, or reassigned to critical tasks.

The sponsor is providing options for study related participant management in the event of disruption to the conduct of the study. This guidance does not supersede any local or government guidelines or requirements or the clinical judgment of the investigator to protect the health and well-being of participants and site staff. If, at any time, a participant's travel to the study site is considered to be at unacceptable safety risk, study participation may be interrupted, and study follow-up conducted. If it becomes necessary to discontinue participation in the study, the procedures outlined in the protocol for discontinuing study intervention will be followed.

If, as a result of the major disruption on scheduled visits cannot be conducted in person at the study site, the study visit will be performed to the extent possible remotely/virtually or delayed until such time that on-site visits can be resumed. At each contact, participants will be interviewed to collect safety data. Key efficacy endpoint assessments should be performed if required and as feasible. Participants will also be questioned regarding general health status to fulfill any physical examination requirement.

Every effort should be made to adhere to protocol-specified assessments for participants on study intervention, including follow-up. Modifications to protocol-required assessments may be permitted after consultation with the participant, investigator, and the sponsor.

Related to the COVID-19 pandemic, if a participant has tested positive for COVID-19, the investigator should contact the sponsor's medical officer or designee to discuss plans for administration of study intervention, performing study assessments, and follow-up.

The sponsor will continue to monitor the conduct and progress of the clinical study, and any changes will be communicated to the sites and to the health authorities according to local guidance. Modifications made to the study conduct as a result of the major disruption, should be summarized in the Clinical Study Report.

- Certain protocol-mandated visits to the study site may not be possible during the major disruption events. Therefore, temporary measures may be implemented if considered appropriate by the sponsor and investigator to maintain continuity of participant care and study integrity. Certain measures, such as those listed below, may be necessary and should be instituted in accordance with applicable (including local) laws, regulations, guidelines, and procedures:
    - remote (eg, by phone / telehealth) or in-person, off-site (eg, in-home) interactions between site staff (or designees) and participants for study procedures, eg, those related to safety monitoring / efficacy evaluation / study intervention storage and administration (including training where pertinent)

  - procurement of study intervention by participants (or designee) or shipment of study intervention from the study site directly to participants for at-home administration (including the potential for self-administration of study intervention)
  - laboratory assessments using a suitably accredited local laboratory; for selected measures (eg, urine pregnancy), home testing may be employed
  - other procedures, eg, imaging, may be conducted at an appropriate facility

- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented in the case report form (CRF).
  - other relevant study data elements impacted by the major disruption, should also be documented in CRFs and / or other study systems, as directed by detailed sponsor guidance. These may include missed / delayed / modified study visits / assessments / dosing, and instances where temporary measures such as those above are implemented.
- The sponsor will evaluate the totality of impact of major disruption events on collection of key study data and additional data analyses will be outlined in study SAP(s).

10.7. Appendix 7: Hepatitis B and Hepatitis C Virus Screening

Participants must undergo screening for hepatitis B virus (HBV) and hepatitis C virus (HCV). At a minimum, this includes testing for anti-HCV, hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and hepatitis B core antibody (anti-HBc) total. The eligibility criteria based on HBV test results are represented below. HBV DNA quantitation should be conducted according to local guidelines and local health authority requirements. Consultation with a specialist is recommended for participants excluded from the study due to HBV or HCV.

Eligibility Based on Hepatitis B Virus Test Results

HEPATITIS B TEST RESULT			STATUS
Hepatitis B Surface Antigen (HBsAg)	**Hepatitis B Surface Antibody (anti-HBs)**	**Hepatitis B Core Antibody (anti-HBc) total**	
negative	negative	negative	**Eligible**
negative	positive	negative	
negative	positive	positive	
positive	negative *or* positive	negative *or* positive	**Not eligible**
negative	negative	positive	**Require testing for presence of HBV DNA[a]**

a. If the HBV DNA is not detectable, the participant is eligible for this study. If HBV DNA is detectable, the participant is not eligible for this study. If HBV DNA testing cannot be performed, or there is evidence of chronic liver disease, the participant is not eligible for this study.

Eligibility Based on Hepatitis C Virus Test Results

- Participants with negative anti-HCV are eligible for this study.
- Participants with positive anti-HCV require a negative HCV RNA polymerase chain reaction (PCR) test result before being eligible for this study.

10.8. Appendix 8: Investigator's Global Assessment

Induration (I) (averaged over all lesions; may use the National Psoriasis Foundation Reference card for measurement)
0 = no evidence of plaque elevation
1 = minimal plaque elevation, = 0.25 mm
2 = mild plaque elevation, = 0.5 mm
3 = moderate plaque elevation, = 0.75 mm
4 = severe plaque elevation, > 1 mm

Erythema (E) (averaged over all lesions)
0 = no evidence of erythema, hyperpigmentation may be present
1 = faint erythema
2 = light red coloration
3 = moderate red coloration
4 = bright red coloration

Scaling (S) (averaged over all lesions)
0 = no evidence of scaling
1 = minimal; occasional fine scale over less than 5% of the lesion
2 = mild; fine scale dominates
3 = moderate; coarse scale predominates
4 = severe; thick, scale predominates

Total Average = (I + E + S) / 3 (average will be calculated in the device but not displayed. Numeric result will be included in data transfer)
Physician's Static Global Assessment based upon above Total Average
0 = Cleared, except for residual discoloration
1 = Minimal - majority of lesions have individual scores for I + E + S / 3 that averages 1
2 = Mild - majority of lesions have individual scores for I + E + S / 3 that averages 2
3 = Moderate - majority of lesions have individual scores for I + E + S / 3 that averages 3
4 = Severe - majority of lesions have individual scores for I + E + S / 3 that averages 4
Note: Scores should be rounded to the nearest whole number. If total ≤ 1.49, score = 1; if total ≥ 1.50, score = 2.

References

Langley RG, Feldman SR, Nyirady J, van de Kerkhof P, Papavassilis C. The 5-point Investigator's Global Assessment (IGA) Scale: a modified tool for evaluating plaque psoriasis severity in clinical trials. J Dermatol Treat. 2015;26(1):23-31.

10.9. Appendix 9: Psoriasis Area and Severity Index

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy. The PASI produces a numeric score that can range from 0 to 72. The severity of the disease is calculated as follows.

In the PASI system, the body is divided into 4 regions: the head (h), trunk (t), upper extremities (u), and lower extremities (l), 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 (0 = none, 1 = slight, 2 = moderate, 3 = severe, and 4 = very severe).

The scale for estimating the area of involvement for psoriatic lesions is outlined below.

0=no involvement

1=1% to 9% involvement

2=10% to 29% involvement

3=30% to 49% involvement

4=50% to 69% involvement

5=70% to 89% involvement

6=90% to 100% involvement

To help with the area assessments, the following conventions should be noted:

- The neck is considered part of the head.
- The axillae and groin are part of the trunk.
- The buttocks are part of the lower extremities.

The PASI formula is:

$PASI=0.1\ (E_h+I_h+S_h)\ A_h+0.3\ (E_t+I_t+S_t)\ A_t+0.2\ (E_u+I_u+S_u)\ A_u+0.4\ (E_l+I_l+S_l)\ A_l$

Where E=erythema, I=induration, S=scaling, and A=area.

10.10. Appendix 10: Protocol Amendment History

The Protocol Amendment Summary of Changes Table for the current amendment is located directly before the Table of Contents (TOC).

Amendment 1 (03 August 2023)

Overall Rationale for the Amendment: Upon health authority feedback, the population to be re-randomized at Week 24 was expanded to include adult participants who are either PASI 75 responders or IGA 0 or 1 responders at Week 24 and consequently some modifications and addition of endpoints associated with this change were made, PGA assessment for participants <18 years of age with a previous diagnosis of PsA at or before screening was added, PHQ-9 evaluations were added to provide assessments for depression at screening and during the study, discontinuation language was added for participants who do not experience a clinically meaningful benefit, and the safety follow-up and early termination visit periods were increased from 2 to 4 weeks.

The changes made to the clinical protocol 77242113PSO3001 as part of Protocol Amendment 1 are listed below, including the rationale of each change and a list of all applicable sections.

Section Number and Name	Description of Change	Brief Rationale
Synopsis, Study Arms and Duration; 1.2. Schema; 4.1. Overall Design; 6.1. Study Intervention(s) Administered; 6.3. Assignment to Study Intervention	The population to be re-randomized at Week 24 was expanded to include adult participants who are either PASI 75 responders or IGA 0 or 1 responders (ie, those who achieve an IGA score of 0 or 1 and have ≥2-grade improvement from baseline) at Week 24. Criteria for non-responders who continue to receive JNJ-77242113 at Week 24 was updated accordingly.	Updated per regulatory feedback.
3. Objectives, Endpoints and Estimands	Added time to loss of IGA 0 or 1 to other secondary endpoints.	Updated per regulatory feedback.
Synopsis, Efficacy Evaluations; 1.3.1. Schedule of Activities-Screening Through Week 52; 3. Objectives, Endpoints and Estimands; 8.2. Efficacy Assessments; 8.2.9. Physician Global Assessment of Disease Activity	Addition of PGA of Disease Activity only for adolescent participants <18 years of age with a previous diagnosis of PsA at or before screening.	Assessment included per regulatory feedback.
Synopsis, Key Secondary Endpoints 9.3.3. Key Secondary Endpoints 9.5. Sample Size Determination	Added text to detail key secondary endpoints for PASI 75 and PASI 90 responders at Week 24.	To clarify analysis population for the Week 52 key secondary endpoints.
Abbreviations; Synopsis, Safety Evaluations, Safety Analyses; 1.3.1. Schedule of Activities-Screening Through Week 52; 1.3.2. Schedule of Activities-Open Label Treatment; 5.2. Exclusion Criteria;	Addition of PHQ-9 assessments.	Assessment included per regulatory feedback.

Section Number and Name	Description of Change	Brief Rationale
7.1.2. Temporary Interruption (Withholding) of Study Intervention; 8.3.5. Depression Screening and Symptoms Monitoring; 9.3.5. Safety Analyses; 10.2.11. Source Documents		
Synopsis, Study Arms and Duration; 1.2. Schema; 1.3.2. Schedule of Activities-Open Label Treatment; 2.3.1. Risks for Study Participation; 4.1. Overall Design; 4.4. End of Study Definition; 6.9. Prior and Concomitant Therapy; 8.4.1. Time Period and Frequency for Collecting Adverse Event and Serious Adverse Event Information; 10.3.5. Procedures	Extended safety follow-up period and early termination period to 4 weeks.	Updated time intervals per regulatory feedback.
1.3.1. Schedule of Activities-Screening Through Week 52; 1.3.2. Schedule of Activities-Open Label Treatment; 8.2.10.9. Participant Assessment of Psoriatic Arthritis Pain; 8.2.10.10. Participant Assessment of Psoriatic Arthritis Disease Activity	PsA Pain and Disease activity assessments will be collected for participants with a PsA diagnosis before or at screening.	Clarified timepoint is at screening, and not at Week 0.
1.3.1. Schedule of Activities-Screening Through Week 52;	Addition of serum biomarker sampling at the screening visit of the SoA.	Included per regulatory feedback.
1.3.1. Schedule of Activities-Screening Through Week 52	Added height measurement for adolescents at screening.	Required for adolescent eGFR lab calculation.
1.3.1. Schedule of Activities-Screening Through Week 52	Modified the collection period of the JNJ-77242113 concentration (plasma) trough samples from predose to postdose.	Ensured consistency across program protocols.
5.2. Exclusion Criteria	If latent TB is to be treated, treatment must be initiated prior to first administration of study intervention according to local guidelines.	Updated text to adhere to local guidelines.
5.4. Screen Failures	Addition of text to specify that investigators will not use IWRS to directly generate screening and enrollment logs.	The text was modified to reduce protocol deviations.
6.1. Study Intervention(s) Administered	Updated instructions for swallowing the study intervention for adolescent participants.	To provide guidance for adolescents on dispersion of the tablet in water if necessary.

Section Number and Name	Description of Change	Brief Rationale
6.9. Prior and Concomitant Therapy	Addition of text clarifying that rescue therapies for psoriasis are not permitted in the study.	Updated text per regulatory feedback.
6.9. Prior and Concomitant Therapy	Addition of text stating that topical JAK inhibitors are not permitted from Week 0 to Week 160.	Topical JAK inhibitors are prohibited due to the potential for systemic absorption.
7.1. Discontinuation of Study Intervention	Clarified text regarding participants who discontinue study intervention.	Participants who discontinue study intervention but do not terminate study participation will continue to return in protocol-specified procedures and evaluations.
7.1.3. Permanent Discontinuation of Study Intervention	Addition of discontinuation text for participants who do not experience a clinically meaningful benefit after receiving JNJ-77242113 for a reasonable amount of time.	Updated text per regulatory feedback.
8.2.10.7. Treatment Satisfaction Questionnaire for Medication Effectiveness	Clarified that TSQM-E will be utilized in adolescents.	TSQM-E assessment is for both adolescent and adult populations.
8.3.7. Tuberculosis Evaluation	Updated TB evaluation text.	Ensured consistency across program protocols.
8.9. Immunogenicity Assessments	Updated analytical procedures text.	Updated text per regulatory feedback.
9.3.3. Key Secondary Endpoints	Clarified that multiplicity-control procedures will only be defined in the SAP.	Updated text per regulatory feedback.
9.3.6.2. Immunogenicity Analyses	Clarified that Immunogenicity analyses will be conducted during the study.	Updated text per regulatory feedback.
Appendix 1 Clinical Laboratory Tests	Clarified that eGFR will be calculated at screening only and that serum creatinine will be measured per SoA.	Height is required for adolescent eGFR.
10.2.7. Committees Structure	Updated the adjudication text.	To clarify that the sponsor will perform adjudication on certain AEs, including, but not limited to, major adverse cardiovascular, cerebrovascular and thrombotic events.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted.

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INVESTIGATOR AGREEMENT

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the study intervention, the conduct of the study, and the obligations of confidentiality.

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Signature: _____ Date: _____
(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____
(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): PPD MD

Institution: Janssen Research & Development

Signature: electronic signature appended at the end of the protocol Date: 24 November 2023
(Day Month Year)

Note: If the address or telephone number of the investigator changes during the study, written notification will be provided by the investigator to the sponsor, and a protocol amendment will not be required.