Janssen Research & Development *

Clinical Protocol

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

ICONIC-ADVANCE 1

Protocol 77242113PSO3002; 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)

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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	06 December 2023
Amendment 1	All	24 July 2023
Original Protocol	All	22 May 2023

Amendment 2 (06 December 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 77242113PSO3002 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 previous protocol amendments 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.
2.3.1 Risks for Study Participation	Revised text to clarify deucravacitinib warnings and precautions to AEs.	To clarify information presented in SOTYKTU label, ie, to better define events as AEs rather than warnings and precautions.
5.2 Exclusion Criteria	Exclusion Criterion 4 was updated to exclude participants with known allergies, hypersensitivity, or intolerance to deucravacitinib or to any of the excipients or components of the study intervention.	Updated per regulatory feedback.
5.4. Screen Failures	Revised text to state that the investigator will not generate screening and enrollment logs directly from IWRS.	Error in text. Reports in IWRS do not contain all of the information that the screening and enrollment logs require.
8.4.4 Regulatory Reporting Requirements for Serious Adverse Events 10.3.1 Adverse Event Definitions and Classifications 11 References	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.
9.3.1 General Considerations 9.3.3 Key Secondary Endpoints	Added the general description of the multiplicity control approach. Added data handling rules for key secondary and other secondary endpoints.	Updated per regulatory feedback.

Section Number and Name	Description of Change	Brief Rationale
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

β-hCG	β-human chorionic gonadotropin
ADA	anti-drug antibody
AE	adverse event
AESI	adverse event of special interest
ANCOVA	analysis of covariance
AUC	area under the plasma concentration versus time curve
AxMP	Auxiliary Medicinal Product (also known as NIMP)
BCG	Bacille Calmette-Guérin
BSA	body surface area
ClinRO	clinician-reported outcome
C_{max}	maximum observed plasma concentration or estimated from population PK modeling
CMH	Cochran-Mantel-Haenszel
COA	clinical outcome assessment (paper or electronic as appropriate for this study)
COVID-19	Coronavirus disease 2019
CPK	creatine phosphokinase
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
CTR	Clinical Trials Regulation
C_{trough}	plasma concentration just prior to the beginning or at the end of a dosing interval
DBL	database lock
DLQI	Dermatological Life Quality Index
DMC	Data Monitoring Committee
C [redacted]	
DVT	deep vein thrombosis
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
f-PGA	Fingernail Physician's Global Assessment
FSH	follicle stimulating hormone
GCP	Good Clinical Practice
GenPs-SFQ	Genital Psoriasis Sexual Frequency Questionnaire
GLP	Good Laboratory Practice
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
INR	international normalized ratio
C	[redacted]
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
MACE	major adverse cardiovascular events
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
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-29	Patient Reported Outcomes Measurement Information System-29
PsA	psoriatic arthritis
PSSD	Psoriasis Symptoms and Signs Diary
PT	preferred term
SAE	serious adverse event
SAP	Statistical Analysis Plan
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 and Deucravacitinib Active Comparator-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Moderate to Severe Plaque Psoriasis

Registry	**ID**
IND	156446
EU TRIAL NUMBER	2023-505121-14

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. Benefits and risks associated with deucravacitinib treatment are described in the local labeling information.

OBJECTIVES, ENDPOINTS, AND ESTIMANDS

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

Objectives	Endpoints
• To evaluate the effect of JNJ-77242113 compared with placebo on PROs in participants with moderate to severe plaque psoriasis.	• PSSD symptom score of 0 at Week 8. • PSSD symptom score of 0 at Week 16. • ≥4-point improvement from baseline in PSSD Itch score at Week 4. • ≥4-point improvement from baseline in PSSD Itch score at Week 16.
• To evaluate the efficacy and effect of JNJ-77242113 compared with deucravacitinib on ClinROs and a PRO in participants with moderate to severe plaque psoriasis.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16 and Week 24, evaluated separately. • IGA score of 0 at Week 16 and Week 24, evaluated separately. • PASI 75 at Week 16 and Week 24, evaluated separately. • PASI 90 at Week 16 and Week 24, evaluated separately. • PASI 100 at Week 16 and Week 24, evaluated separately. • PSSD symptom score of 0 at Week 16.

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, active comparator- and placebo-controlled, parallel-group, multicenter, interventional study in adults with moderate to severe plaque psoriasis.

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

NUMBER OF PARTICIPANTS

A target of 750 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 screening period of 5 weeks, followed by a 16-week placebo-controlled period which will run concurrently with a 24-week active comparator-controlled period, followed by treatment with JNJ-77242113 200 mg once daily through Week 156 and a 4-week safety follow-up period.

Participants will be randomized in a 2:1:2 ratio to 1 of the 3 treatment arms:

- **JNJ-77242113:** Participants in the JNJ-77242113 arm will receive JNJ-77242113 200 mg once daily from Week 0 through Week 156.

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

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

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)

Patient-reported outcomes (PROs):

- Psoriasis Symptom and Sign Diary (PSSD)
- Dermatology Life Quality Index (DLQI)
- Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)
- Patient Reported Outcomes Measurement Information System-29 (PROMIS-29)
- Treatment Satisfaction Questionnaire for Medication - Effectiveness (TSQM-E)
- EuroQol-5 Dimension 5-level (EQ-5D-5L)
- Participant assessment of psoriatic arthritis (PsA) pain
- Participant assessment of PsA disease activity

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 biologic 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, whole blood, and optional skin biopsy samples 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 protein, 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 baseline weight category (≤90 kg, >90 kg) 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, 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 least square (LS) mean estimates and their corresponding 95% CI will be provided at each timepoint. The estimates of LS mean difference and 95% CIs between treatment groups will be provided. Analysis of covariance (ANCOVA) will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, baseline weight, and geographic region. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference between treatment groups and 95% CIs will be provided.

In general, all statistical testing will be performed at a significance level of 0.05 (2-sided) unless otherwise specified. 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. Nominal p-values for other secondary and exploratory endpoints will be reported.

Efficacy Analyses

Primary Endpoints/Estimand

There are 2 co-primary endpoints in this study: an IGA score of cleared (0) or minimal (1) and at least 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:** adults 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 with 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 (ICEs) in categories 1 or 2.
  - PASI 90 response: a responder is defined as a participant with a PASI 90 response at Week 16 who does not have ICEs 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 nonresponders 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 with an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and the proportion of participants with 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 nonresponders.

The co-primary endpoints will be compared between the JNJ-77242113 group and the placebo group by CMH chi-square test stratified by baseline weight category (≤90 kg, >90 kg) 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 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.

Key Secondary Endpoint Analyses

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

NA=not applicable.
a. Noninferiority tests with a noninferiority margin of 12% will be performed before superiority tests.
b. Only superiority tests will be performed.

Safety Analyses

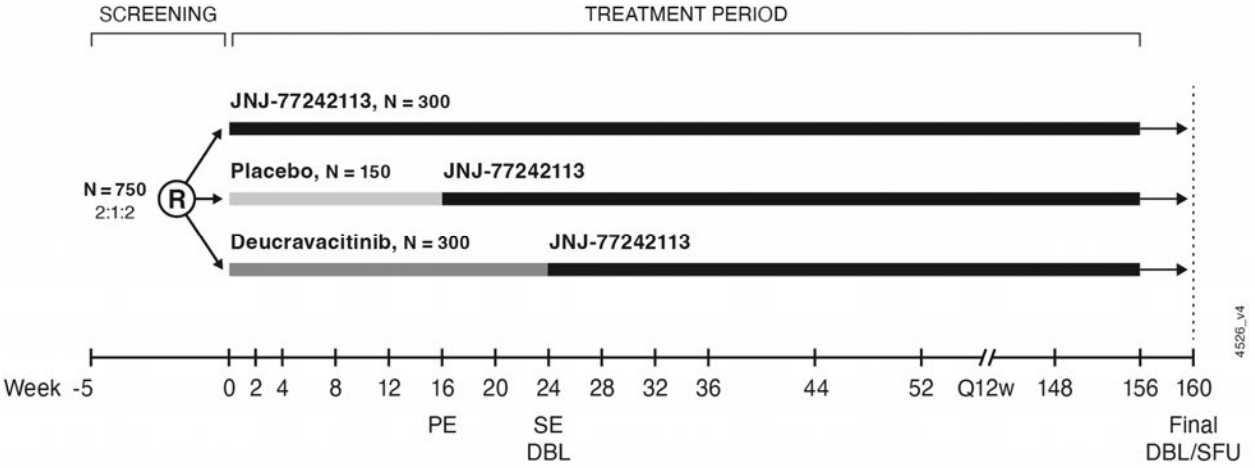
Safety data, including but not limited to, AEs, serious adverse events, adverse events of special interest (active TB, malignancy, potential Hy's Law cases), discontinuation of study intervention due to AEs, changes in laboratory assessments, changes in vital signs, changes in weight, changes in PHQ-9 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 titers of antibodies to JNJ-77242113 will be summarized for all participants who receive at least 1 dose of JNJ-77242113 and have appropriate samples for detection of antibodies to JNJ-77242113 (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	Screen-ing	Placebo- and Comparator-controlled								JNJ-77242113 Treatment					Unsch-eduled[a]	Notes:
Week (W)	-5 to 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		See Section 1.3.2 for Early Termination Visit procedures.
Study Procedure																
Screening/Administrative																
ICF	X															Must be signed before first study-related activity.
ICF for optional skin biomarker substudy	X															ICFs for optional substudies may also be signed at the W0 visit before any related substudy assessments are performed.
ICF for optional photography substudy	X															
ICF 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 radiograph or CT ≤12 weeks before first administration of study intervention.
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 requested by local health authorities or investigator.
Hepatitis B and C serology	X															

Period	Screening	Placebo- and Comparator-controlled								JNJ-77242113 Treatment					Unscheduled[a]	Notes:
Week (W)	-5 to 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		See Section 1.3.2 for Early Termination Visit procedures.
Study Procedure																
HIV antibody test	X															
FSH	X															If needed to confirm postmenopausal status.
eDiary Compliance	X	X	X	X	X	X	X	X	X							Check eDiary completion and retrain participants as needed. Additional checks may be performed as needed.
Study Intervention Administration																
Randomization		X														
Dispense study intervention		X	X	X	X	X	X	X	X	X	X	X	X	X		Dispense 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 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-h recall)	Daily diary beginning at screening through W24															
PSSD (7-day recall)										X	X	X	X	X		
DLQI		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.
PROMIS-29		X			X		X		X			X		X		
TSQM-E							X							X		Effectiveness domain only (Sec. 8.2.9.5)
EQ-5D-5L		X					X		X					X		

Period	Screening	Placebo- and Comparator-controlled								JNJ-77242113 Treatment					Unscheduled[a]	Notes:
Week (W)	-5 to 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		See Section 1.3.2 for Early Termination Visit procedures.
Study Procedure																
PsA Pain Assessment		X			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					X		
ClinROs																
IGA	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		
BSA	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
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		
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 examination with additional organ systems based on investigator's judgment.
Height		X														
Weight		X					X							X		
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		

Period	Screening	Placebo- and Comparator-controlled								JNJ-77242113 Treatment					Unscheduled[a]	Notes:
Week (W)	-5 to 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		See Section 1.3.2 for Early Termination Visit procedures.
Study Procedure																
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 childbearing potential	X (serum)	X	X	X	X	X	X	X	X	X	X	X	X	X		A negative urine test result is required prior to dispensing study intervention. A urine pregnancy test may be performed at any time during the visit including before PRO collection.
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 at any time during the visit including before PRO collection.
Clinical Pharmacology Assessments																
JNJ-77242113 concentration (plasma)[b]		X		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.
Antibodies to JNJ-77242113 (serum)		X		X		X	X		X	X		X		X		

Period	Screening	Placebo- and Comparator-controlled								JNJ-77242113 Treatment					Unscheduled[a]	Notes:
Week (W)	-5 to 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		See Section 1.3.2 for Early Termination Visit procedures.
Study Procedure																
Pharmacodynamics and Biomarkers																
Serum biomarkers	X	X		X			X		X			X		X		Sample collection and testing will comply with local regulations.
Whole blood (RNA) biomarkers		X					X		X					X		
Skin biopsy (optional biomarker substudy)		X					X							X		W0: Collect 1 lesional and 1 nonlesional biopsy. W16 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. 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	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.
PROMIS-29	X		X		X		X		X		X	
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.
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	

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:**
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 examination with additional organ systems based on investigator's judgment.
Weight					X				X		X	
Vital signs	X	X	X	X	X	X	X	X	X	X	X	
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 prior to dispensing study intervention. A urine pregnancy test may be performed at any time during the visit including before PRO collection.
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 at any time during the 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

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:**
Adverse events	X	X	X	X	X	X	X	X	X	X	X	signing the ICF. See CRF completion guidelines.

a. Participants who discontinue 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 Early Termination 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 guidelines.

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 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 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 Addendum for JNJ-77242113.

The term "study intervention" throughout the protocol, refers to study drugs 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 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 but are less efficacious relative to subcutaneously administered biologics (Armstrong 2020, 2023; Strober 2023). For those patients who prefer oral medication, oral therapies with high efficacy, long-term clinical remission, and a good safety profile, remain a substantial unmet need (Nasa 2019).

Targeting IL-23 is a highly validated approach for treating moderate to severe psoriasis. IL-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 the p19 subunit of IL-23, such as guselkumab (Blauvelt 2017; Reich 2017) and risankizumab (Gordon 2018), act by preventing engagement of this ligand with the IL-23R ultimately causing reduced signaling.

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 response 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 2b study, JNJ-77242113 is being further assessed in this Phase 3 program. The Phase 3 Study 77242113PSO3002 is a randomized, double-blind, parallel-group, active comparator- and placebo-controlled study of JNJ-77242113 designed to evaluate the efficacy and safety of JNJ-77242113 in adults 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 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 C[redacted] tablets or CCI tablets with CCI [redacted] (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 twice daily, 65.1% for 100 mg once daily, 78.6% for 100 mg twice daily; 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 6 events were in the Gastrointestinal SOC (n=1 each: abdominal pain, abdominal discomfort, and nausea). The other 3 events included suicide attempt, weight increase, and transaminases increase (n=1 each).
- Rates of abnormal laboratory test results 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 participants and Phase 2 studies in adults with moderate to severe plaque psoriasis.

PK data from FIH study PN-235-01 indicate that systemic exposure (C_{max} 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 t_{max} and significantly reduced the rate (C_{max}) and extent (AUC) of JNJ-77242113 absorption. Based on the food effect data from Study 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 body weight and food 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 low. 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.

2.2.1. Active Comparator

SOTYKTU™ (Deucravacitinib)

Deucravacitinib is a TYK2 inhibitor indicated for the treatment of adults with moderate-to-severe plaque psoriasis. Deucravacitinib was selected as the active comparator because it is a recently approved orally administered therapy with proven efficacy in patients with moderate-to-severe plaque psoriasis, and therefore provides a valuable benchmark for comparison with JNJ-77242113. Participants randomized to deucravacitinib will be treated according to the labeled dose regimen, 6 mg orally once daily.

For further information regarding deucravacitinib, refer to the local label (SOTYKTU USPI 2023, SmPC 2023).

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(s) 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).
ADA production	Exogenous peptides administered orally or systemically have the potential to induce ADA production, which may mediate untoward reactions such as	• This potential risk will be explained in the ICF and evaluated by measuring ADA and PK for analysis. • Participants are encouraged to consistently take their study intervention 24 hours apart, as directed.

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
	reduced efficacy or hypersensitivity.	
Infection	Clinical experience with marketed IL-23 pathway blockers includes precautions for infections and TB.	• This potential risk will be explained 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 5.2). 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 substudy ICF. Trained and experienced physicians will be performing the procedure during this study.

Considerations for the Active Comparator

The benefit:risk profile of deucravacitinib was established in the Phase 3 studies, which were the basis of the global approvals for deucravacitinib in the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. As of March 2023, warnings and precautions for deucravacitinib include hypersensitivity, infections including TB; malignancies; potential risks related to JAK inhibition (including MACE, DVT, and pulmonary embolism); rhabdomyolysis; laboratory abnormalities including elevations in CPK, triglycerides, and liver enzymes; the AE of decreased glomerular filtration rate; and advice to avoid use of live vaccines during deucravacitinib treatment. (SOTYKTU USPI 2023, SmPC 2023).

2.3.2. Benefits for Study Participation

JNJ-77242113 has demonstrated significant efficacy compared with placebo for ClinROs and PROs including disease severity and extent, quality of life measures, and patient-reported signs and symptoms of psoriasis based on 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.

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 compared with placebo in participants with moderate to severe plaque psoriasis.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16. • PASI 90 at Week 16.
Secondary	
Key Secondary • To further evaluate the general and special area psoriasis efficacy of JNJ-77242113 compared with placebo in participants with moderate to severe plaque psoriasis.	• IGA score of 0 at Week 16. • PASI 75 at Week 4. • PASI 90 at Week 8. • PASI 75 at Week 16. • PASI 100 at Week 16. • ss-IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16.
• To evaluate the effect of JNJ-77242113 compared with placebo on PROs in participants with moderate to severe plaque psoriasis.	• PSSD symptom score of 0 at Week 8. • PSSD symptom score of 0 at Week 16. • ≥4-point improvement from baseline in PSSD Itch score at Week 4. • ≥4-point improvement from baseline in PSSD Itch score at Week 16.
• To evaluate the efficacy and effect of JNJ-77242113 compared with deucravacitinib on ClinROs and a PRO in participants with moderate to severe plaque psoriasis.	• IGA score of 0 or 1 and a ≥2-grade improvement from baseline at Week 16 and Week 24, evaluated separately. • IGA score of 0 at Week 16 and Week 24, evaluated separately. • PASI 75 at Week 16 and Week 24, evaluated separately. • PASI 90 at Week 16 and Week 24, evaluated separately. • PASI 100 at Week 16 and Week 24, evaluated separately. • PSSD symptom score of 0 at Week 16.

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

Objectives	Endpoints
Exploratory	
• To further assess the safety and tolerability of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• Frequency and type of related AEs and AEs leading to discontinuation of study intervention. • Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time.
• To further evaluate the psoriasis efficacy of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	Endpoints will be based on the following assessments: • IGA, PASI, BSA, ss-IGA, sPGA-G, hf-PGA, f-PGA, mNAPSI.
• To further evaluate the effect of JNJ-77242113 on PROs in participants with moderate to severe plaque psoriasis.	Endpoints will be based on the following assessments: • PSSD, DLQI, GenPs-SFQ, PROMIS-29, TSQM-E, EQ-5D-5L, PsA Pain assessment, PsA Disease Activity assessment.
• To evaluate the PK and immunogenicity of JNJ-77242113 and explore the exposure-response relationship of JNJ-77242113 in participants with moderate to severe plaque psoriasis.	• JNJ-77242113 PK parameters. • The relationship between PK parameters and efficacy. • The incidence of ADAs to JNJ-77242113.
• To explore biomarkers in participants with moderate to severe plaque psoriasis.	• Change from baseline in cellular and molecular biomarkers in skin and blood.

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:** adults 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 with 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 ICEs in categories 1 or 2 (Table 1).
  - PASI 90 response: a responder is defined as a participant with a PASI 90 response at Week 16 who does not have ICEs in categories 1 or 2 (Table 1).
- **Intercurrent event:** Table 1.
- **Population level summary:** Difference in the proportions of participants with a PASI 90 response at Week 16 and the proportions of participants with an IGA score of cleared (0) or

minimal (1) and at least 2-grade improvement from baseline 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, active comparator- and placebo-controlled, parallel-group, multicenter, interventional study in adults with moderate to severe plaque psoriasis.

A target of 750 participants will be randomized in this study in a 2:1:2 ratio to JNJ-77242113 200 mg once daily, placebo, or deucravacitinib 6 mg once daily. Randomization will be stratified by weight category (≤90 kg, >90 kg) and geographic region.

This study includes a 5-week screening period and a 16-week placebo-controlled period which will run concurrently with a 24-week active comparator-controlled period. At Week 16, participants randomized to placebo will switch to JNJ-77242113 200 mg once daily through Week 156. At Week 24, participants randomized to deucravacitinib will switch to JNJ-77242113 200 mg once daily through Week 156. All participants will have a 4-week safety follow-up period after discontinuation of study intervention or at the end of the treatment period. The total 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 complete Week 24 of the study. The final global DBL will occur when all participants complete the study. Additional DBLs may also occur at other times after Week 24 to support publications or regulatory submissions including when additional time may be needed to reach country-specific data requirements. Details of the DBLs will be described 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. In addition to placebo control, an active control will be used to determine the sensitivity of the clinical endpoints in this study. 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 treatment response and the 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.

Health Economics Data Collection

The EQ-5D-5L will be used in this study to evaluate health economics for participants with moderate to severe plaque psoriasis.

4.2.1. Participant Input Into Design

In setting the strategy for the treatment of moderate to severe plaque psoriasis, patients 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 a participant 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 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 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 of the study, and provide their consent voluntarily will be enrolled. Written consent 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 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. Participants will be discontinued from study intervention if the investigator considers it is in the best interest of the participant (Section 7).

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). 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 the observed dose-response and modeled E-R analyses of efficacy data (ie, PASI and IGA) from the pivotal Phase 2b Study 77242113PSO2001. A population PK-based E-R analysis of Study 77242113PSO2001 data show that C_{avg} JNJ-77242113 concentrations describe the E-R relationship better than C_{trough}. In Study 77242113PSO2001, CCI [redacted] 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 16-fold lower than exposures at the NOAEL in the rat and monkey studies.

The dose and regimen of JNJ-77242113 selected for this Phase 3 study, CCI [redacted] 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. Refer to Section 5.4, Screen Failures for conditions under which the repeat of any screening procedures is allowed.

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. ≥18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place) at the screening visit.

Type of Participant and Disease Characteristic(s)

2. Diagnosis of plaque psoriasis, with or without PsA, 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.
7. Suitable candidate without contraindications for deucravacitinib treatment according to the respective country's approved deucravacitinib product labeling in the opinion of the investigator.

Weight

Not applicable.

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 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 regulations/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. 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.
16. 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.
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. Criterion modified per Global Amendment 2
   4.1 Known allergies, hypersensitivity, or intolerance to JNJ-77242113, deucravacitinib, or to any of the excipients or components of the study intervention (refer to the JNJ-77242113 IB, the deucravacitinib label, and Protocol Section 6.1).
5. Major surgical procedure, (eg, requiring general anesthesia) within 8 weeks before screening, or will not have fully recovered from 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. 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, Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act and is considered to be at risk by the investigator.
   - 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.

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

Prior/Concomitant Therapy

9. Previously received JNJ-77242113.

10. Previously received deucravacitinib.

11. Experienced primary efficacy failure (no response within 16 weeks) or a clinically significant AE related to agents directly targeting IL-23 or TYK2.

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

	Prohibited Medication or Class of Medications	Restriction Duration (through End of Study)
12.	Agents that deplete B cells: • alemtuzumab or rituximab	26 weeks prior to the first administration of study intervention
13.	Any biologic therapy including but not limited to: • IL-23-inhibitors: guselkumab, tildrakizumab, risankizumab (Additional exclusions apply. See EC 9 and 11.) • IL-17 inhibitors: secukinumab, brodalumab, ixekizumab • IL-12/23 inhibitors: ustekinumab, briakinumab • TNFα antagonists: adalimumab, infliximab, etanercept, certolizumab, golimumab • natalizumab • belimumab • abatacept • visilizumab • experimental or investigational therapy	12 weeks or 5 half-lives, whichever is longer, prior to the first administration of study intervention
14.	Systemic immunomodulating treatments including but not limited to: • methotrexate, azathioprine, cyclosporine A, corticosteroids, cyclophosphamide, tofacitinib, apremilast (Additional exclusions apply. See EC 10 and 11.) 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
	Prohibited Medication or Class of Medications	**Restriction Duration (through End of Study)**
15.	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,	2 weeks prior to the first administration of study intervention

	trimethylpsoralens, fumarate, PDE4 inhibitors, aryl hydrocarbon receptor-modulating agents • Shampoos that contain corticosteroids, coal tar, or vitamin D3 analogs • Herbal treatments and traditional Taiwanese, Korean, or Chinese medicines	
16.	Live virus or bacterial vaccination	4 weeks (or longer if required per vaccine package insert) prior to the first administration of study intervention
17.	BCG vaccination	1 year prior to the first administration of study intervention

Diagnostic Assessments

18. Screening laboratory test results within the following parameters:

- Hemoglobin: <10 g/dL (SI: <100 g/L)
- White blood cells: $<3.5\times10^3/\mu L$ (SI: <3.5 GI/L)
- Neutrophils: $<1.5\times10^3/\mu L$ (SI: <1.5 GI/L)
- Platelets: $<100\times10^3/\mu L$ (SI: <100 GI/L)
- eGFR: <60 mL/min/1.73 m^2
- Aspartate aminotransferase: >2×ULN
- Alanine aminotransferase: >2×ULN

If 1 or more of the laboratory parameters is out of range, a single retest of laboratory values is permitted.

19. Tests positive for the following infections at screening:

- HBV (See Appendix 7 for instructions)
- Hepatitis C (seropositive for antibodies and positive confirmatory test for HCV, ie, HCV PCR) (Appendix 7).
- HIV

20. Chest imaging (eg, chest radiograph or CT) within 12 weeks before the first administration of study intervention that shows an abnormality suggestive of a malignancy or active infection. For chest imaging suggestive of TB, see EC 28.

Infections or Predisposition to Infections

21. History of chronic or recurrent infectious disease, including but not limited to chronic renal infection, chronic chest infection (eg, bronchiectasis), recurrent urinary tract

infection (eg, recurrent pyelonephritis or chronic nonremitting cystitis), severe fungal infections (eg, mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.

22. 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.

23. 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.

24. Serious infection (eg, disseminated herpes zoster, sepsis, pneumonia, or pyelonephritis), or hospitalization or received IV antibiotics for an infection within 8 weeks before screening.

25. 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

26. 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).

27. 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

28. Meets **ANY** of the following TB screening criteria:

    Note: IGRA testing includes either QuantiFERON®-TB Gold Plus or T-SPOT® TB.

    a. History of active TB or show signs or symptoms suggestive of active TB upon medical history or physical examination at screening.

    b. History of untreated latent TB prior to screening. An exception is made for participants who are currently receiving treatment or will initiate treatment for latent TB prior to first administration of study intervention.

       Note: For participants with a history of treated latent TB there must be documentation of appropriate treatment prior to the first administration of study

intervention. It is the responsibility of the investigator to verify the adequacy of previous TB treatment and provide appropriate documentation. IGRA testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB.

c. Recent close contact with a person with active TB. An exception is made if such participants are referred to a physician specializing in TB to determine if treatment is warranted or not. This evaluation must be adequately documented and, if treatment is recommended, the participant must be receiving appropriate treatment prior to the first administration of study intervention.

d. Positive IGRA test result within 8 weeks prior to the first administration of study intervention. An exception is made for participants who have:

   - History of adequately treated latent TB described above.
   - Newly identified positive IGRA test result in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated prior to the first administration of study intervention.
   - False-positive IGRA test as determined by the following:
     - A suspected false-positive initial IGRA test must be repeated. If repeat testing is **NOT** positive, the participant must be referred to a physician specializing in TB to determine if the initial test can be considered a false positive. This evaluation must be adequately documented prior to the first administration of study intervention. If repeat testing is positive, however, it will be considered a true-positive and the participant is only eligible if active TB has been ruled out and appropriate treatment for latent TB has been initiated as described above.

   Note: Indeterminate/borderline results should be handled as outlined in Section 8.3.7.

e. Chest radiograph or chest CT within 12 weeks prior to the first administration of study intervention that shows abnormalities suggestive of active or inactive TB.

Other Exclusions

29. 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.

30. 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

31. A 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 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 labeling, guidelines, and standards-of-care for patients receiving immune-targeted therapy when determining an appropriate interval between vaccination and study enrollment (Section 6.9.1).
2. Refer to Section 6.9, Prior and 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 UV 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.

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, 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 tests 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 Interventions Administered

The study interventions will be provided as tablets and capsules for oral administration. The study interventions 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).

From Week 0 to Week 24, participants will take 1 tablet of JNJ-77242113 or matching placebo and 1 capsule of over-encapsulated deucravacitinib or matching placebo daily. After Week 24, participants will take 1 tablet of JNJ-77242113 daily.

Study personnel should review dose administration requirements with the participant, as appropriate, before administration, and throughout the study, as necessary.

Designation	Product
Investigational Medicinal Product(s)	JNJ-77242113, placebo for JNJ-77242113, deucravacitinib, and placebo for deucravacitinib

Designation	Product
	Authorization status in the EU/EEA Authorized: deucravacitinib Unauthorized: JNJ-77242113, placebo for JNJ-77242113, and placebo for deucravacitinib
NIMP/AxMP	Not applicable

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. Deucravacitinib will be manufactured under the responsibility of Bristol-Myers Squibb Company. Refer to the local deucravacitinib label for a list of excipients.

The deucravacitinib capsule used in this study will be encapsulated by the sponsor and will contain the deucravacitinib tablet and sugar spheres, gelatin, iron oxide red, and titanium dioxide as excipients. The qualitative composition of the placebo capsule formulation is identical to that of the deucravacitinib capsule except that there is no deucravacitinib tablet.

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

Description of Interventions

Intervention Name	JNJ-77242113	Matching placebo for JNJ-77242113	Deucravacitinib	Matching placebo for Deucravacitinib
Intervention Description	film-coated tablet containing 200 mg JNJ-77242113	film-coated tablet without JNJ-77242113	capsule containing 6 mg deucravacitinib	capsule without deucravacitinib
Type	Drug	Drug	Drug	Drug
Dose Formulation	Tablet	Tablet	Capsule	Capsule
Unit Dose Strength(s)	200 mg per tablet	Not applicable	6 mg per capsule	Not applicable
Dosage Level(s)	1×200 mg tablet once daily	Not applicable	1×6 mg capsule once daily	Not applicable
Route of Administration	Oral	Oral	Oral	Oral
Use	Experimental	Placebo comparator	Active comparator	Placebo comparator
Investigational Medicinal Product (IMP)	Yes	Yes	Yes	Yes
Non-Investigational Medicinal Product/Auxiliary Medicinal Product(NIMP/AxMP)	No	No	No	No
Sourcing	Provided centrally by the sponsor	Provided centrally by the sponsor	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.	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.	The blisters are packaged in child resistant Dosepaks.	The blisters are packaged in child resistant Dosepaks.

Intervention Name	JNJ-77242113	Matching placebo for JNJ-77242113	Deucravacitinib	Matching placebo for Deucravacitinib
Delivery Instructions	Swallow tablet whole. Given with 240 mL water. Do not crush, cut, or chew the tablets.	Swallow tablet whole. Given with 240 mL water. Do not crush, cut, or chew the tablets.	Swallow capsule whole. Given with 240 mL water. Do not crush, cut, or chew the capsules.	Swallow capsule whole. Given with 240 mL water. Do not crush, cut, or chew the capsules.
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	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	deucravacitinib, SOTYKTU	Not applicable

Description of Study Arms

Arm Title	JNJ-77242113	Placebo	Deucravacitinib
Arm Type	experimental	placebo	active comparator
Arm Description	Participants will receive: • JNJ-77242113 200 mg once daily on Week 0 through Week 156. • Matching placebo for deucravacitinib once daily on Week 0 through Week 24.	Participants will receive: • Matching placebo for JNJ-77242113 on Week 0 through Week 16. • Matching placebo for deucravacitinib on Week 0 through Week 24. • JNJ-77242113 200 mg once daily from Week 16 through Week 156.	Participants will receive: • Deucravacitinib 6 mg once daily on Week 0 through Week 24. • Matching placebo for JNJ-77242113 once daily on Week 0 through Week 24. • JNJ-77242113 200 mg once daily from Week 24 through Week 156.
Associated Intervention Labels	Labels will be identical to maintain the blind.	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 on the intervention accountability form. Participants must be instructed to return all original containers, whether empty or containing study intervention. 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 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 this study. Participants will be assigned to 1 of 3 intervention groups based on a computer-generated randomization schedule prepared before the study by or under the supervision of the sponsor. Permuted block randomization with stratification by weight category (≤90 kg, >90 kg) 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.

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, and 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 investigators and participants until all participants have completed the Week 52 Visit. Details of the unblinding will be described 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 and capsules.

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 number of expected tablets and capsules during this study, unless study intervention is withheld for safety reasons. Protocol deviations for compliance will be assessed at Week 16 and Week 24 or the Early Termination Visit if the early termination occurred before Week 24.

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 must 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 therapies must be recorded throughout the study beginning with signing 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 EC 13 and 14 (Section 5.2) and remain prohibited during the study. For guidance regarding vaccination including 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 (see 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 topical corticosteroids, topical calcineurin inhibitors, vitamin D analogs, vitamin A analogs, retinoids, tar, anthralin, calcipotriene, tazarotene, methoxsalen, trimethylpsoralens, fumarate, PDE4 inhibitors, topical JAK inhibitors, aryl hydrocarbon receptor-modulating agents; shampoos that contain corticosteroids, coal tar, or vitamin D3 analogs; and herbal treatments and traditional Taiwanese, Korean, or Chinese medicines are not permitted.

Week 52 to Week 160

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

Phototherapy or Systemic Therapy

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

These medications include:

- those targeted for reducing TNFα (including but not limited to adalimumab, infliximab, or etanercept).
- drugs targeted for reducing IL-12/23, IL-17, or IL-23 (including but not limited to ustekinumab, briakinumab, guselkumab, tildrakizumab, secukinumab, risankizumab, ixekizumab, or brodalumab).

- alpha-4 integrin antagonists (including but not limited to natalizumab).
- JAK inhibitors (including but not limited to TYK2 inhibitors).
- PDE4 inhibitors (including but not limited to apremilast).
- oral and injectable (IV, intramuscular, or intralesional) corticosteroids.
- any other conventional systemic therapies that could affect psoriasis evaluations (including but not limited to methotrexate, cyclosporine A, acitretin, or other retinoids).
- antimalarial agents.
- herbal treatments.
- traditional Taiwanese, Korean, or Chinese medicines.

Concomitant Medications for Indications Other Than Psoriasis

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

Vitamin D3 and analogs for dietary supplementation are permitted.

6.9.1. 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 labeling, 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 24.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

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

A participant's study intervention must be temporarily interrupted (withheld) if:

- Participant develops a serious infection.
- Participant is suspected of having a TB infection or has had a close contact exposure to TB (Section 8.3.7).
- Participant has a hepatic event or liver test abnormality per Appendix 5, Liver Safety: Suggested Actions and Follow-up Assessments.
- Participant has a CPK result >5×ULN or myopathy before Week 24.
- The participant has a PHQ-9 score of ≥20 (refer to 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 intervention.

7.1.3. Permanent Discontinuation of Study Intervention

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

- Participant withdraws consent 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 any protocol-prohibited medications, treatments, or interventions (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.
- Participant develops a systemic opportunistic infection during the study period.
- Participant develops a recurrent or chronic serious infection during the study period.
- Participant meets **ANY** of the following TB-related conditions:
  - A diagnosis of active TB is made.
  - A participant has symptoms suggestive of active TB based on follow-up assessment questions and/or physical examination or has had recent close contact with a person with active TB and cannot or will not continue to undergo additional evaluation.
  - A participant receiving treatment for latent TB discontinues latent TB treatment prematurely or is noncompliant with latent TB therapy.

- 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 event 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:

- After completion of the active comparator-controlled period (Week 24), all participants will be allocated to open-label JNJ-77242113. If, after receiving JNJ-77242113 for a reasonable amount of time (eg, 12 to 16 weeks after Week 24), a participant is still not experiencing clinically meaningful benefit, the investigator should consider discontinuing the participant from the study intervention.

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
- 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, 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 325 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 to establish a baseline measure and prior to primary and key secondary timepoints (Week 16 and Week 24) 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 will be performed by the investigator or designated physician, nurse practitioner or physician assistant. Targeted physical examinations will include a skin, general, and any other organ system examination based on clinical judgment 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 pain and participant assessment of PsA disease activity PROs will be administered at and 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

BSA 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 10 fingernails are evaluated for 7 features. The first 3 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 4 features are 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 to 13 per nail and 0 to 130 for all fingernails.

8.2.9. Patient-reported Outcomes

8.2.9.1. Psoriasis Symptoms and Signs Diary

The PSSD 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 items 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. 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.

8.2.9.2. Dermatology Life Quality Index

The DLQI 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.

8.2.9.3. Genital Psoriasis Sexual Frequency Questionnaire

The GenPs-SFQ 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)

8.2.9.4. Patient-reported Outcomes Measurement Information System-29

The PROMIS-29 is a 29-item generic HRQoL survey, assessing each of the 7 PROMIS domains (depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and ability to participate in social roles and activities) with 4 questions 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).

8.2.9.5. Treatment Satisfaction Questionnaire for Medication - Effectiveness

The TSQM-E questionnaire 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 a higher level of satisfaction.

8.2.9.6. EuroQol 5-Dimension 5-Level Questionnaire

The EQ-5D-5L 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 comprises 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 Website 2019; Herdman 2011; Janssen 2013)

8.2.9.7. 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 participants who report having PsA at or before Screening.

8.2.9.8. Participant Assessment of Psoriatic Arthritis Disease Activity

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

8.2.10. 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: 2 areas of lesional skin will be photographed per participant. The same 2 areas will be photographed over time.
2. Full body photographs and lesional photographs: In addition to the 2 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. Participants 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.

AEs 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 samples 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 to19 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 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 to 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.

8.3.7. Tuberculosis Evaluation

Initial Tuberculosis Evaluation

Participant medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB. The participant should be asked about past testing for TB, including chest imaging results and responses to tuberculin skin or other TB testing. Investigators have the option to use the tuberculin skin test in addition to IGRA testing to screen for latent TB if preferred by local health authorities, or if they believe based on their judgment that both tests are clinically indicated to evaluate a participant at high risk for latent TB.

Participants with a negative IGRA test (and tuberculin skin test as applicable) result are eligible to continue with prerandomization procedures. Participants with a newly identified positive IGRA test result must undergo an evaluation for active or latent TB, or suspected false-positive initial testing, and initiate appropriate treatment if needed (see Section 5.2, EC 28). Appropriate treatment for latent TB is defined according to local country guidelines for immunocompromised patients. If no local country guidelines for immunocompromised patients exist, US guidelines must be followed.

Participants with indeterminate/borderline IGRA test results should have the test repeated. Participants with persistently indeterminate/borderline IGRA test results must undergo an evaluation for active or latent TB, or suspected false-positive initial testing, and initiate appropriate treatment if needed (see Section 5.2, EC 28).

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 (refer to Section 1.3) or by telephone approximately every 2 to 12 weeks. 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 (Section 7.1), 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.

During the study, a participant with confirmed latent TB must initiate appropriate treatment for latent TB as defined by local country guidelines. If no local country guidelines exist, US guidelines must be followed.

Note: Investigators should be aware that TB reactivation in immunocompromised participants may also present as extrapulmonary or disseminated disease.

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.

AEs will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally acceptable representative) 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.

SAEs, 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 AEs or SAEs. 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 events for which the participant is specifically questioned.

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 (including SUSARs to Eudravigilance according to EU CTR 536/2014 [EU-CTR 2014]), IRBs, and Ethics Committees, as per local requirements. Suspected unexpected serious 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 to be 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 biologic 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 research related to psoriasis or response to treatment. They may also be used to develop tests or assays related to psoriasis or treatment. This research may consist of the analysis of 1 or more candidate genes, genetic and epigenetic markers throughout the genome, or 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 and compare the mechanism of action of JNJ-77242113 and deucravacitinib 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 serum, skin, and whole blood. Serum and whole blood 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 to 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 and 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 and deucravacitinib 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 nonlesional areas; at subsequent weeks, only lesional areas will be sampled. Skin biopsy samples will be used to investigate 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.

Whole Blood (RNA) Biomarkers

Whole blood will be collected from participants for RNA expression analysis. Total RNA will be isolated and used for differential gene expression analyses during treatment to explore PD and mechanisms of action that are relevant to treatment or psoriasis, or both.

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, serum 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.

Serum 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 will be evaluated in this study utilizing the EQ-5D-5L. 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 SAP.

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

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

- JNJ-77242113 is superior to deucravacitinib in treatment of participants with moderate to severe plaque psoriasis as assessed by the proportion of participants who achieve a PASI 75 response at Week 24.

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 were randomized, regardless of the treatment they actually received. The FAS will include all randomized participants.

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

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

Analysis Sets	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.
Safety Analysis Set	All randomized participants who received 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.

9.3. Statistical Analyses

The SAP 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 baseline weight category (≤90 kg, >90 kg) 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, 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. The estimates of LS mean difference and 95% CIs between treatment groups will also be provided. ANCOVA will be used to analyze some continuous endpoints when appropriate. The ANCOVA will include treatment group, baseline value, baseline weight and

geographic region. The LS mean estimates and their corresponding 95% CI will be provided. In addition, LS mean difference between treatment groups and 95% CIs will be provided.

In general, all statistical testing will be performed at a significance level of 0.05 (2-sided) unless otherwise specified. Appropriate multiplicity adjustment procedure will be used to control the overall Type I error rate of 0.05 (2-sided) for the primary and key secondary endpoints (see Section 9.3.3). 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 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:** adults 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 with 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 ICEs in categories 1 or 2 (Table 1).
  - PASI 90 response: a responder is defined as a participant with a PASI 90 response at Week 16 who does not have ICEs in categories 1 or 2 (Table 1).
- **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	**Composite Strategy:** Participants with these ICEs are considered as IGA score of 0 or 1, and PASI 90 nonresponders 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 with an IGA score of cleared (0) or minimal (1) and at least a 2-grade improvement from baseline and the proportion of participants with a PASI 90 response at Week 16 between the JNJ-77242113 and placebo intervention groups.

Primary Endpoint Analysis

The 2 co-primary endpoints will be compared between the JNJ-77242113 and placebo groups. 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 ICE 1 and ICE 2 before Week 16 will be considered as nonresponders at Week 16. For participants with ICE 3, observed data after this ICE will be utilized in the analysis. For participants who experience 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 nonresponders.

To address the primary objective, a 2-sided (α=0.05) CMH chi-squared test stratified by baseline weight category (≤90 kg, >90 kg) 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 1 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 supplementary 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, baseline disease characteristics, and previous psoriasis medications and therapies will be performed.

9.3.3. Key Secondary Endpoints

The key secondary endpoint analyses are provided in Table 2. The comparisons of clinical endpoints, IGA score of cleared (0) or minimal (1) and at least 2-grade improvement from baseline and PASI 75 response, specified below versus deucravacitinib will be tested for noninferiority at Week 16 and Week 24, and if noninferiority is established, then superiority will be tested at Week 16 and Week 24.

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

approval of deucravacitinib. Additional efficacy endpoints (eg, PASI 90, PASI 100, PSSD score of 0) will only be tested for superiority.

Table 2: Key Secondary Endpoint Analyses

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

NA=not applicable.
a. Noninferiority tests with a noninferiority margin of 12% will be performed before superiority tests.
b. Only superiority tests will be performed.

Additionally, the comparison between the deucravacitinib group and placebo group at Week 16 will also be performed for the related key secondary analyses mentioned above.

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

To control the overall Type I error rate (alpha=0.05), multiplicity adjustment will be applied to the analyses of the co-primary endpoints and key secondary endpoints listed in Table 2. 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.

Similar data handling rules as the co-primary endpoints will be used for the key secondary binary endpoints. Specifically, composite strategy will be used for ICEs 1 and 2 (as defined in Section 9.3.2 of the protocol) where participants with those ICEs are considered as non-responders; treatment policy strategy will be used for ICE 3 (Section 9.3.2 of the protocol) where observed data will be used. After application of ICEs, participants with missing data will be imputed as non-responders.

The same data handling rules will also be applied to the other secondary binary endpoints. For other secondary continuous endpoints, composite strategy will be used for ICEs 1 and 2 (as defined in Section 9.3.2 of the protocol) where participants with those ICEs are assumed to have zero change or zero percent change; treatment policy strategy will be used for ICE 3 (Section 9.3.2 of the protocol) where observed data will be used. To account for the missing data after application of ICEs for continuous endpoints of change (or percent change) from baseline, a MMRM will be used. In MMRM, missing data will not be imputed, but rather missing data will be accounted for through correlation of repeated measures in the model.

9.3.4. Other Secondary 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 or deucravacitinib) and Week 24 (comparisons between JNJ-77242113 and deucravacitinib) will be performed. No adjustments for multiple comparisons will be made, and nominal p-values will be provided. Select 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, potential 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 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 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 types 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 an SAE.

Clinical Laboratory Tests

Laboratory data will be summarized by type of laboratory test. Selected laboratory parameters will be summarized by treatment group. 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 laboratory analytes 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 will be summarized over time using descriptive statistics.

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 E-R model may be developed to describe the E-R relationship. Details will be given in an E-R analysis plan, and results will be presented in a separate technical report.

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 pharmacogenomics 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 vs placebo and to evaluate the efficacy of JNJ-77242113 vs deucravacitinib. The sample size was also chosen to ensure a reasonable safety database to assess the overall safety of JNJ-77242113. 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, data from the JNJ-77242113 Phase 2b study (77242113PSO2001), and 2 deucravacitinib Phase 3 studies (POETYK PSO-1 and POETYK PSO-2) that evaluated the safety and efficacy of deucravacitinib in the treatment of adult participants with moderate to severe psoriasis.

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

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

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

Table 3 provides the power for detecting a treatment difference under varying assumptions for the primary and select key secondary endpoints specified in Section 9.3.2 and Section 9.3.3.

Country-specific Data

Additional country-specific enrollment, incremental to the global cohort enrollment of 750 participants may be allowed if required by a 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 3: Power to Detect a Treatment Effect Based on Different Proportions of Participants Who Achieve the Co-primary Endpoints and Select Key Secondary Endpoints

Co-primary Endpoints

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

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

PASI 90 response at Week 16

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

Select Key Secondary Endpoints

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

(difference of 13 percentage points)

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

(difference of 15 percentage points)

deucravacitinib (n=300)	JNJ-77242113 (n=300)	Power
45%	60%	95.8%
50%	65%	96.2%
55%	70%	96.8%
60%	75%	97.6%

PASI 90 response at Week 16 and Week 24

(difference of 15 percentage points)

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

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	<u>Dipstick</u> Specific gravity pH Glucose Protein Blood Ketones Bilirubin Urobilinogen Nitrite Leukocyte esterase	<u>Sediment</u> (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	

Additional details will be provided in the laboratory manual.
*Assessment only from screening visit through the Week 24 visit.

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.

GCP 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

Each participant 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) 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 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 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 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 the participant's personally dated signature. After having obtained the consent, a copy of the ICF must be given to the participant.

Participants who are rescreened are 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 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.

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 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 and deucravacitinib, to understand moderate to severe plaque psoriasis, to understand differential intervention responders, and to develop tests/assays related to JNJ-77242113, deucravacitinib, 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 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 substudy 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 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 data 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)
- Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ)
- Patient-reported Outcomes Measurement Information System-29 (PROMIS-29)
- Treatment Satisfaction Questionnaire for Medication - Effectiveness (TSQM-E)
- EuroQol 5-Dimension 5-Level Questionnaire (EQ-5D-5L)
- Psoriatic Arthritis (PsA) Pain Assessment
- PsA Disease Activity Assessment

- 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. These data are 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 the 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). Suspected unexpected serious AEs that are considered at least possibly related to study medication will be reported in an expedited manner to Health Authorities (including SUSARs to Eudravigilance according to EU CTR 536/2014 [EU CTR 2014]), IRBs, and Ethics Committees, as 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. For study drugs with a marketing authorization, the expectedness of an AE will be determined by whether or not it is listed in the package insert/summary of product characteristics.

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 must 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 in the CRF). 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 / doses, 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 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 Psoriasis Area and Severity Index (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 (24 July 2023)

Overall Rationale for the Amendment: Upon health authority feedback, 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 77242113PSO3002 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
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; 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	Addition of PHQ-9 assessments.	Assessment included per regulatory feedback.
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	Revision of visit windows from Week 2 through Week 36 of the SoA.	Visit windows were increased for convenience to study participants.
1.3.1 Schedule of Activities-Screening Through Week 52	Modified the collection period of JNJ-77242113 concentration (plasma) trough samples from predose to postdose.	Ensured consistency across program protocols.
1.3.1 Schedule of Activities-Screening Through Week 52; 1.3.2 Schedule of Activities-Open Label Treatment;	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.

Section number and Name	Description of Change	Brief Rationale
8.2.9.7 Participant Assessment of Psoriatic Arthritis Pain; 8.2.9.8 Participant Assessment of Psoriatic Arthritis Disease Activity		
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.
2.3.1 Risks for Study Participation	Updated text to specify decreased glomerular filtration rate is a warning and precaution for deucravacitinib.	Updated per regulatory feedback.
2.3.1 Risks for Study Participation	Modified text in comparator section to state MACE, DVT, and pulmonary embolism are potential risks related to JAK inhibition (for deucravacitinib).	Additional text added for clarity.
5.4 Screen Failures	Addition of text to specify that investigators will use IWRS to directly generate screening and enrollment logs.	Process was modified to reduce protocol deviations.
6.1 Study Interventions Administered	Addition of encapsulation ingredients for deucravacitinib and deucravacitinib placebo.	Additional text added to describe deucravacitinib formulation.
6.9 Prior and Concomitant Therapy	Addition of text stating that rescue therapies for psoriasis are not permitted in the study.	Updated 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 per regulatory feedback.
8 Study Assessments and Procedures	Updated total blood volume.	Updated per regulatory feedback.
8.3.7 Tuberculosis Evaluation	Updated TB evaluation text.	Ensured consistency across program protocols.
8.9 Immunogenicity Assessments	Updated analytical procedures text.	Updated per regulatory feedback.
9.3.3 Key Secondary Endpoints	Clarified that multiplicity-controlled procedures will only be defined in the SAP.	Updated per regulatory feedback.
9.3.6.2 Immunogenicity Analyses	Deleted text stating if required.	Updated per regulatory feedback.
10.1 Appendix 1: Clinical Laboratory Tests	Specification of eGFR assessment from screening visit through Week 24 visit.	A footnote was added to specify eGFR calculations will only be performed at certain visits.
10.2.7 Committees Structure	Updated adjudication text.	To clarify that the sponsor will perform adjudication on certain AEs, including, but not limited to, major adverse cardiovascular,

Section number and Name	Description of Change	Brief Rationale
		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

Institution: Janssen Research & Development

Signature: electronic signature appended at the end of the protocol Date: 06 December 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.

Signature

User	Date	Reason
PPD	06-Dec-2023 21:32:47 (GMT)	Document Approval