

Janssen Research & Development ***Clinical Protocol**

Protocol Title

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

FRONTIER 2

Short Title

A Long-Term Extension Study of JNJ-77242113
in Participants with Moderate-to-Severe Plaque Psoriasis

**Protocol 77242113PSO2002; Phase 2b
Amendment 1**

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).

Regulatory Agency Identifier Number(s):

IND: 156446

EudraCT NUMBER: 2021-004320-16

Status: Approved

Date: 06 April 2022

Prepared by: Janssen Research & Development, LLC

EDMS number: EDMS-RIM-467890, 2.0

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

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PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

DOCUMENT HISTORY	
Document	Date
Amendment 1	06-April-2022
Original Protocol	23-September-2021

Amendment 1 (06 April 2022)

Overall Rationale for the Amendment: The protocol is primarily being amended to include toxicology data, update the study intervention dosing instructions to include a fasting requirement, and to update the analysis strategy regarding discontinuations due to COVID-19 (intercurrent event number 3) to a Treatment Policy strategy.

Section Number and Name	Description of Change	Brief Rationale
SOA	Update Footnote e text to remove examples of the samples that need to be recorded per study manual.	The study manual will outline which samples the date and time should be recorded for and where that information should be recorded.
Section 2.2, Background	Added the long-term toxicology data from the JNJ-77242113 study.	The long-term toxicology data was added to support the extended dosing of JNJ-77242113 in this long-term extension study
Section 2.2, Background	Add interim results from an ongoing bioavailability study (77242113PSO1003).	This information was added to justify the change from dosing with or without food to dosing on an empty stomach as defined in Section 4.1 and Section 6.1.
Section 4.1, Overall Design; Section 6.1, Study Interventions Administered	Update study intervention administration instructions to include taking study intervention on an empty stomach.	Interim results from an ongoing, multipart, randomized, open-label, single-dose, crossover study in healthy participants (77242113PSO1003) indicate that the oral bioavailability and PK profile of JNJ-77242113 administered under fasted conditions as an immediate-release (IR) tablet formulation is similar to the oral solution used in the FIH study PN-235-01. The PK results also indicate that concomitant food (high calorie, high-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 interim food effect data from protocol 77242113PSO1003, study intervention should be administered under fasted conditions.
Section 5.1, Inclusion Criteria	Modified Inclusion Criteria #4	Clarify that it only applies to topicals which would affect psoriasis or PASI/IGA

Section Number and Name	Description of Change	Brief Rationale
Section 5.1	Modified Inclusion Criteria #8	To provide clarification on contraception information for male participants
Section 5.2, Exclusion Criteria	Modified Exclusion Criteria #7	Clarify hepatitis B criteria
Section 8.2.8 Tuberculosis Evaluation(s)	Updated instructions for TB evaluations	Additional instructions added to clarify what to do with a positive or indeterminate TB test result as a result of ad hoc TB testing.
Section 8.2.4 Clinical Safety Laboratory Assessments; Section 10.2, Appendix 2: Clinical Laboratory Tests	The text was modified since some of the listed laboratory tests will be performed locally, instead of centrally. The location is defined in the study manual.	Error in text.
Section 9.4.2.1.1, Primary Estimand	Changed the analysis strategy for addressing Intercurrent Event 3 (Discontinuation of study intervention due to COVID-19 related reasons [excluding COVID-19 infection]) to Treatment Policy strategy and combined it with Intercurrent Event 4	Since COVID-19 can no longer be viewed as a temporary problem, all COVID-19 related reasons will be treated similarly to “Discontinuations of study intervention due to other reasons (excluding reasons indicative of lack of efficacy)” for which treatment policy strategy was used in the past.
Section 10.7, Contraceptive and Barrier Guidance	<p>The headers and sub-headers in the table for Examples of Contraceptives have been modified as follows: ‘EXAMPLES OF CONTRACEPTIVE* ALLOWED DURING THE STUDY FOR FEMALE PARTICIPANTS INCLUDE: NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION DURING THE STUDY FOR FEMALE PARTICIPANTS (not considered to be highly effective- failure rate of > or = 1% per year)’.</p> <p>Added a footnote to clarify that the contraceptives listed as "not allowed as the sole method of contraception" can only be used in combination with a highly effective form of birth control.</p>	Clarification that this table, which lists examples of contraceptives, is applicable to female participants only.
Throughout the protocol	Minor grammatical, formatting, or spelling changes were made.	Minor errors were noted.

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1. PROTOCOL SUMMARY:

1.1. Synopsis

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

Short title: A Long-Term Extension Study of JNJ-77242113 in Participants with Moderate-to-Severe Plaque Psoriasis

DESCRIPTION OF COMPOUND

JNJ-77242113 is a 13-amino acid peptide that binds directly to the interleukin 23 receptor (IL-23R) subunit and prevents IL-23p19 from engaging its receptor, thereby inhibiting proximal IL-23R signaling and downstream effector functions (eg, cytokine secretion). JNJ-77242113 has high potency with a half-maximal inhibitory concentration (IC₅₀) of ~20 to 30 pM in peripheral human cell based functional assays, so despite its very low oral bioavailability (<1%), it has the potential to provide systemic/skin efficacy.

OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	Proportion of participants achieving Psoriasis Area and Severity Index (PASI) 75 (≥75% improvement in PASI from baseline of the originating* study) at Week 36
Secondary	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Proportion of participants achieving PASI 90 (≥90% improvement in PASI from baseline of the originating study) at Week 36 Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) at Week 36 Change from baseline of the originating study in PASI total score at Week 36 Proportion of participants achieving an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) at Week 36
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 36 Change from baseline of originating study in PSSD signs score at Week 36 Proportion of participants achieving PSSD symptoms score=0 at Week 36 among participants with a baseline (in the originating study) symptoms score ≥1 Proportion of participants achieving PSSD signs score=0 at Week 36 among participants with a baseline (in the originating study) signs score ≥1

Objectives	Endpoints
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Frequency and type of adverse events (AEs) and serious adverse events (SAEs)
Exploratory	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Proportion of participants achieving PASI 75 ($\geq 75\%$ improvement in PASI from baseline of the originating study) over time through Week 36 Change from baseline of the originating study in PASI total score over time through Week 36 Proportion of participants achieving PASI 90 ($\geq 90\%$ improvement in PASI from baseline of the originating study) over time through Week 36 Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) over time through Week 36 Proportion of participants achieving an IGA score of cleared (0) or minimal (1) over time through Week 36 Proportion of participants achieving an IGA score of cleared (0) over time through Week 36 Change from baseline of the originating study in body surface area (BSA) over time through Week 36
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in PSSD symptoms score over time through Week 36 Change from baseline of the originating study in PSSD signs score over time through Week 36 Proportion of participants achieving PSSD symptoms score=0 over time through Week 36 among participants with a baseline (in the originating study) symptoms score ≥ 1 Proportion of participants achieving PSSD signs score=0 over time through Week 36 among participants with a baseline (in the originating study) signs score ≥ 1
To evaluate the effect of JNJ-77242113 treatment on dermatology-specific health-related quality of life (HRQoL) in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Proportion of participants achieving a Dermatological Life Quality Index (DLQI) of 0 or 1 over time through Week 36 among participants with a baseline (in the originating study) DLQI score > 1
To evaluate the effect of JNJ-77242113 treatment on general HRQoL in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in domain scores of the Patient-Reported Outcomes Measurement Information

Objectives	Endpoints
	<p>System-29 (PROMIS-29) over time through Week 36</p> <ul style="list-style-type: none"> Proportion of participants who achieve at least a 5-point improvement from baseline of the originating study in each PROMIS-29 domain over time through Week 36
<p>To evaluate the pharmacokinetics (PK) and immunogenicity of JNJ-77242113, and explore the PK/pharmacodynamic (PD) relationship of JNJ-77242113 for biomarkers, efficacy, and safety in participants with moderate-to-severe plaque psoriasis</p>	<ul style="list-style-type: none"> JNJ-77242113 PK parameters (ie, plasma concentration just prior to the beginning or at the end of the dosing interval [C_{trough}], maximum observed plasma concentration [C_{max}], time to maximum plasma concentration [t_{max}], and area under the plasma concentration versus time curve [AUC]) The relationship between PK parameters and PD, ie, blood cellular and molecular biomarker activity as well as clinical endpoints and safety parameters The incidence of anti-drug antibodies (ADA) to JNJ-77242113
<p>To characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis</p>	<ul style="list-style-type: none"> Proportion of participants achieving a Scalp Specific Investigator Global Assessment (ss-IGA) score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline of the originating study over time through Week 36 among those participants with scalp psoriasis and an ss-IGA score ≥ 2 at baseline of the originating study Percent change from baseline of the originating study in Nail Psoriasis Area and Severity Index (NAPSI) over time through Week 36 among participants with a NAPSI score >0 at baseline of the originating study Proportion of participants achieving a Fingernail Physician's Global Assessment (f-PGA) score of clear (0) or minimal (1) over time through Week 36 among those participants with nail psoriasis and an f-PGA score ≥ 2 at baseline of the originating study Proportion of participants who achieve a Physician's Global Assessment of Hands and/or Feet (hf-PGA) score of clear (0) or almost clear (1) and a reduction of at least 2 grades on the hf-PGA scale from baseline of the originating study over time through Week 36 among those participants with hand and/or foot psoriasis and an hf-PGA score ≥ 2 at baseline of the originating study Proportion of participants achieving a Static Physician's Global Assessment (s-PGA) of genitalia score of clear (0) or minimal (1) over

Objectives	Endpoints
	<p>time through Week 36 among participants with genital psoriasis and an s-PGA of genitalia score ≥ 3 at baseline of the originating study</p> <ul style="list-style-type: none"> Proportion of participants achieving a score of never (0) or rarely (1) in Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) item 2 over time through Week 36 among participants with a GenPs-SFQ item 2 score ≥ 2 at baseline of the originating study
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Frequency and type of related AEs, and AEs leading to discontinuation of study intervention Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time Systolic and diastolic blood pressures over time
To explore biomarkers in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in levels of blood biomarkers
To explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Assessment of treatment satisfaction domains over time through Week 36 using the Treatment Satisfaction Questionnaire for Medications-9 items (TSQM-9)

*Throughout table “originating study” refers to Protocol 77242113PSO2001

OVERALL DESIGN

This is a multicenter, long-term extension (LTE), double-blind, dose-ranging, parallel group, interventional study in participants with moderate-to-severe plaque psoriasis. All eligible participants from the originating study (Protocol 77242113PSO2001) will be given the option to enroll in this LTE study, 77242113PSO2002.

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

Efficacy, safety, PK, immunogenicity, and biomarkers will be assessed according to the Schedule of Activities (SoA).

One planned database lock (DBL) will occur at Week 40 of this LTE study.

The end of study is considered as the last visit for the last participant in the study. This study protocol may be amended at the sponsor’s decision to extend the treatment period to provide participants access to one or more of the JNJ-77242113 doses.

An external Independent Data Monitoring Committee (iDMC) has been commissioned for study 77242113PSO2001 and this study (77242113PSO2002). Refer to Committees Structure in Appendix 3 for details.

INTERVENTION GROUPS AND DURATION

The total duration of this study is up to 40 weeks: a 36-week treatment period and a 4-week safety follow-up period after the last study intervention administration.

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

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

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

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

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

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

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

EFFICACY EVALUATIONS

Investigator assessments and patient-reported outcomes (PROs) of efficacy include the following:

- PASI
- IGA
- BSA
- NAPSI
- f-PGA
- s-PGA of genitalia
- hf-PGA
- ss-IGA
- PRO measures to assess: PSSD, DLQI, PROMIS-29, GenPs-SFQ, Patient Global Impression-Severity (PGI-S) and Change (PGI-C), TSQM-9

PHARMACOKINETIC EVALUATIONS

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

IMMUNOGENICITY EVALUATIONS

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.

PHARMACODYNAMIC AND BIOMARKER EVALUATIONS

Pharmacodynamic markers will be evaluated using blood samples collected at visits as indicated in the SoA. Biomarker assessments will be made to examine the biological response to treatment and to identify biomarkers that are relevant to JNJ-77242113 treatment response and/or psoriasis, where local regulations permit. Assessments will include the evaluation of relevant biomarkers in serum collected as specified in the SoA where local regulations permit.

SAFETY EVALUATIONS

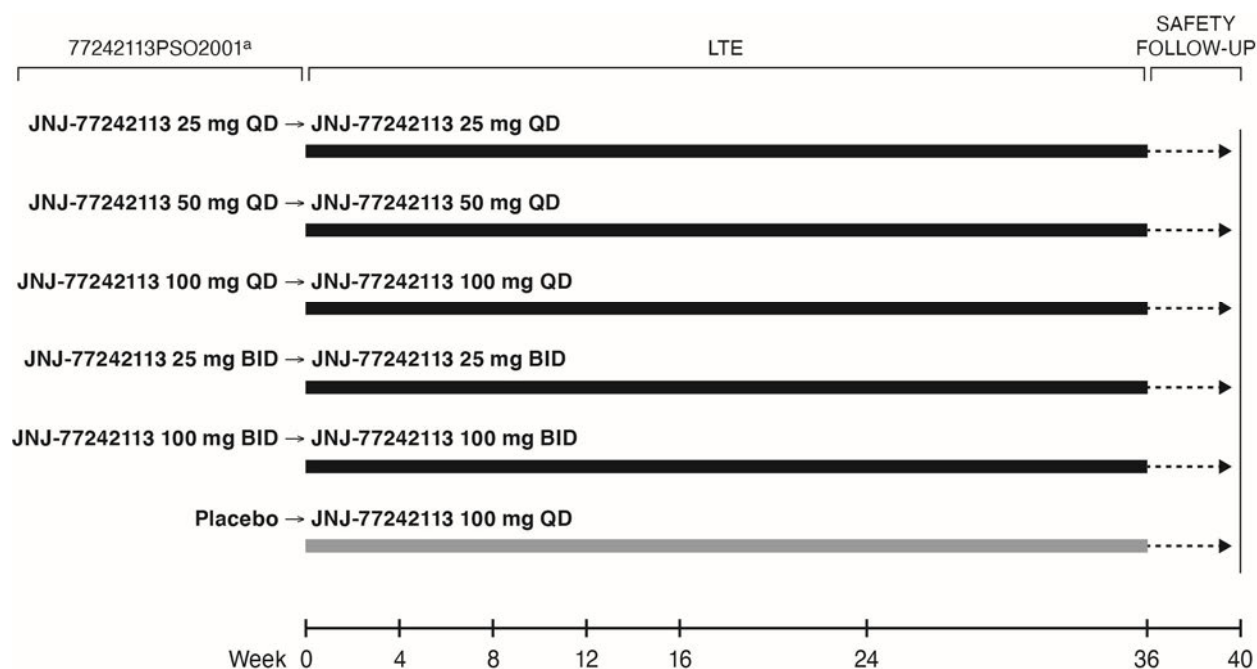
Key safety assessments include AEs, SAEs, adverse events of special interest (AESI), laboratory parameters (hematology and chemistry, including lipid panel, and urinalysis), vital signs, systolic and diastolic blood pressures over time, and the Columbia-Suicide Severity Rating Scale (C-SSRS).

STATISTICAL METHODS

This study is an LTE following the originating study 77242113PSO2001 and no formal hypothesis testing will be performed. Descriptive statistics will be provided for efficacy, safety, and PK parameters. The number of participants enrolled will depend on the number of participants in the originating study who are eligible for and choose to enroll in this study.

1.2. Schema

Figure 1: Schematic Overview of 77242113PSO2002



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

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

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1.3. Schedule of Activities (SoA)

Table 1: Long-Term Extension Study 77242113PSO2002									
Period	Active Treatment							Final Safety Follow-up Visit ^a	Early Termination ^b
Week	0 ^{f,g}	4	8	12	16	24	36	40	
Visit Window (Days)		(+/- 4 days)							
Study Procedure ^c									Notes:
Screening/Administrative									
Informed consent (ICF)	X								Must be signed before first study-related activity.
Inclusion/exclusion criteria	X								Minimum criteria for the availability of documentation supporting the eligibility criteria are described in Section 5.1 and Section 5.2. Check clinical status before dispensing study intervention at Week 0.
Study Intervention Administration									
Dispense study intervention	X	X	X	X	X	X			May also be dispensed between visits.
Administer study intervention	Daily Self-Administration								
Study intervention accountability		X	X	X	X	X	X		X
Safety Evaluations									
Full physical examination	X ^d							X	X
Targeted physical examination		X	X	X	X	X	X		
Weight	X ^d							X	X
Vital signs	X ^d	X	X	X	X	X	X	X	X
TB evaluation	X ^d	X	X	X	X	X	X	X	X
12-lead triplicate ECG	X ^d			X			X		X
C-SSRS	X ^d	X	X	X	X	X	X	X	X
Urine pregnancy test	X ^d	X	X	X	X	X	X	X	X
Concomitant therapy	X ^d	X	X	X	X	X	X	X	X

Table 1: Long-Term Extension Study 77242113PSO2002										
Period	Active Treatment							Final Safety Follow-up Visit ^a	Early Termination ^b	
Week	0 ^{f,g}	4	8	12	16	24	36	40		
Visit Window (Days)		(+/- 4 days)								
Adverse Events	X ^d	X	X	X	X	X	X	X	X	
Efficacy Evaluations										
PROs										
PSSD (7-Day recall)	X ^d		X		X	X	X	X	X	To be completed before any tests, procedures, or other consultations for all visits to prevent influencing participants' perceptions, unless otherwise noted.
DLQI	X ^d		X		X	X	X		X	
PROMIS-29 (v2.1)	X ^d		X		X	X	X		X	
GenPs-SFQ	X ^d		X		X	X	X		X	
PGI-S	X ^d		X		X	X	X		X	
PGI-C	X ^d		X		X	X	X		X	
TSQM-9	X ^d		X				X		X	
ClinROs										
PASI	X ^d	X	X	X	X	X	X	X	X	
IGA	X ^d	X	X	X	X	X	X	X	X	
BSA	X ^d	X	X	X	X	X	X		X	
NAPSI	X ^d		X			X	X		X	
f-PGA	X ^d		X			X	X		X	
s-PGA of genitalia	X ^d		X		X	X	X		X	
hf-PGA	X ^d		X			X	X		X	
ss-IGA	X ^d		X			X	X		X	
Clinical Laboratory Tests										
Hematology ^e	X ^d	X	X	X	X	X	X	X	X	
Chemistry ^e	X ^d	X	X	X	X	X	X	X	X	
Lipid Panel ^e	X ^d						X		X	Fasting lipid panel at Week 0 and Week 36. Nonfasting lipid panel at the Early Termination Visit. Fasting is recommended for at least 6 hours unless medically contraindicated.
Urinalysis	X ^d	X	X	X	X	X	X	X	X	

Table 1: Long-Term Extension Study 77242113PSO2002										
Period	Active Treatment							Final Safety Follow-up Visit^a	Early Termination^b	
Week	0^{f,g}	4	8	12	16	24	36	40		
Visit Window (Days)	(+/- 4 days)									
High sensitivity C-reactive protein ^e	X ^d						X		X	
Clinical Pharmacology Assessments^e										
Plasma JNJ-77242113 concentrations	X ^d		X		X	X	X	X	X	At least one trough sample and one peak sample will be collected during the study. Instructions for scheduling those collections will be provided during site training.
Serum ADA to JNJ-77242113	X ^d		X		X	X	X	X	X	
Biomarkers^e										
Serum Biomarkers	X ^d		X		X	X	X		X	

Abbreviations: ADA=anti-drug antibody; ClinRO=clinician-reported outcome; BSA=body surface area; C-SSRS=Columbia-Suicide Severity Rating Scale; DLQI=Dermatological Life Quality Index; ECG=electrocardiogram; f-PGA=Fingertail Physician's Global Assessment; GenPs-SFQ=Genital Psoriasis Sexual Frequency Questionnaire; hf-PGA=Physician's Global Assessment of Hands and/or Feet; ICF=informed consent form; IGA=Investigator Global Assessment; LTE=long-term extension; NAPSI=Nail Psoriasis Area and Severity Index; PASI=Psoriasis Area and Severity Index; PGI-C=Patient Global Impression-Change; PGI-S=Patient Global Impression-Severity; PK=pharmacokinetic(s); PRO=patient-reported outcome; PROMIS-29=Patient-Reported Outcomes Measurement Information System-29; PSSD=Psoriasis Symptom and Sign Diary; SoA=Schedule of Activities; s-PGA=Static Physician's Global Assessment; ss-IGA=Scalp Specific Investigator Global Assessment; TB=tuberculosis; TSQM-9=Treatment Satisfaction Questionnaire for Medications-9 items

Footnotes:

- The Final Safety Follow-up Visit (ie, Week 40) will be conducted approximately 4 weeks after the last administration of study intervention.
- Participants who terminate study intervention early should have an Early Termination Visit approximately 4 weeks after their last administration of study intervention.
- At all visits where study intervention will be dispensed, all study procedures and evaluations are to be completed before study intervention is dispensed.
- If the Week 0 visit takes place on the same day as the Week 16 visit of study 77242113PSO2001, this assessment does not need to be repeated.
- If study intervention will be taken by the participant in clinic, all blood samples should be collected prior to study intervention administration. The date and time of the 2 previously received doses and the date and time of the samples should be recorded, as instructed in the study manual.
- If the Week 0 visit for this study takes place on a different day as the Week 16 visit of study 77242113PSO2001, the sponsor and medical monitor must be notified. Approval from the medical monitor or designee is required to enroll participants into study 77242113PSO2002 with a gap in study intervention administration between study 77242113PSO2001 and 77242113PSO2002.
- At the time of enrollment, if a participant's study intervention was interrupted in Protocol 77242113PSO2001, the participant may still be enrolled in this LTE study but may not receive study intervention until the investigator confirms re-initiation of study intervention is appropriate.

2. INTRODUCTION

Interleukin (IL)-23 is a disulfide-linked heterodimer of the IL-23p19 and IL-12/23p40 subunits. The receptor for IL-23 comprises the IL-23 receptor (IL-23R) and IL-12R subunits (Bloch 2018). Interleukin-23p19 binding to the N-terminal immunoglobulin (Ig)-like domain of IL-23R is followed by IL-12/23p40 binding to IL-12R beta 1 (IL-12Rβ1). Ligand binding results in the phosphorylation of Janus kinase (JAK) 2 and tyrosine kinase (TYK) 2, leading to phosphorylation and nuclear translocation of signal transducers and activators of transcription (STAT) proteins.

JNJ-77242113 is a 13-amino acid peptide that binds directly to the IL-23R subunit and prevents IL-23p19 from engaging its receptor, thereby inhibiting proximal IL-23R signaling and downstream effector functions (eg, cytokine secretion). JNJ-77242113 has high potency with a half maximal inhibitory concentration (IC₅₀) of ~20 to 30 pM in peripheral human cell based functional assays, so despite its very low oral bioavailability (<1%), it has the potential to provide systemic/skin efficacy. This makes JNJ-77242113 a promising candidate for development in systemic, IL-23-driven diseases, such as psoriasis and psoriatic arthritis. Once present in the systemic circulation, JNJ-77242113 is expected to have good distribution to target organs such as the skin.

To date, JNJ-77242113 has been studied in one Phase 1a clinical study (PN-235-01) of healthy participants to assess the safety and tolerability of JNJ-77242113 over the dose range tested, and it is currently being studied in one Phase 2b study (77242113PSO2001) of participants with moderate-to-severe plaque psoriasis to assess the efficacy and safety of JNJ-77242113. All eligible participants in Protocol 77242113PSO2001 will be given the option to enroll in this study, 77242113PSO2002, which will serve as the long-term extension (LTE) to Protocol 77242113PSO2001.

For the most comprehensive nonclinical and clinical information regarding JNJ-77242113, refer to the latest version of the Investigator's Brochure (IB) for JNJ-77242113.

The term “study intervention” throughout the protocol, refers to study drug as defined in Section 6.1.

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 (US), European Union (EU), and Japan, there are approximately 3.5 million patients living with moderate-to-severe psoriasis (body surface area [BSA] >10%). These patients are traditionally managed with topical and conventional therapies prior to advancing to subcutaneously administered biologics targeting tumor necrosis factor (TNF), IL-23, IL-12/23, or IL-17. Oral therapies, such as apremilast (phosphodiesterase [PDE] 4 inhibitor), are also available as advanced therapeutic options, but only provide modest efficacy relative to subcutaneously administered biologics (Armstrong 2020) and have demonstrated gastrointestinal intolerability in

some patients (Otezla USPI 2020). For those patients who prefer oral medication, healthcare providers agree that oral therapies with high efficacy and long-term clinical remission, remain a substantial unmet need (Nasa 2019).

Targeting IL-23 is a highly validated approach for treating moderate-to-severe psoriasis. Interleukin-23 is composed of a unique p19 subunit coupled with the common p40 subunit shared with IL-12, and signals through the heterodimeric IL-23R/IL-12R β 1 complex (Teng 2015). The IL-23R is expressed by cells of both the innate and adaptive immune systems, including innate lymphoid cells, natural killer (NK) cells, NK T cells, gamma delta T cells, and subsets of memory CD4⁺ and CD8⁺ alpha beta T cells (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 and ultimately cause reduced signaling through IL-23R. Moreover, since polymorphisms in IL-23R are associated with susceptibility to psoriasis and the precise anatomical expression of IL-23R dictates where disease develops (Sherlock 2012), targeting this receptor directly is expected to treat psoriasis at a fundamental level and in a way comparable to inhibiting the ligand.

JNJ-77242113 is a 13-amino acid peptide that binds directly to the IL-23R subunit and prevents IL-23p19 from engaging its receptor, inhibiting proximal IL-23R signaling and downstream effector functions (eg, cytokine secretion). Because of this validated mechanism of action in the treatment of moderate-to-severe psoriasis patients, JNJ-77242113 has the potential to have similar efficacy and safety profiles to subcutaneously administered anti-IL-23 biologics, but with the convenience of oral administration. Validation of this treatment pathway in an orally administered form would significantly increase the therapeutic options for those patients in need of advanced therapies who prefer oral to subcutaneously administered medications.

This study, 77242113PSO2002, is the LTE to Protocol 77242113PSO2001, a Phase 2b dose-ranging study of JNJ-77242113. 77242113PSO2002 is designed to evaluate the long-term efficacy and safety of JNJ-77242113 in adults with severe plaque psoriasis.

2.2. Background

Nonclinical Pharmacology and Toxicology

JNJ-77242113 is a potent and selective IL-23R peptide antagonist as shown in various binding and cell-based assays. In vivo, JNJ-77242113 is efficacious in attenuating local inflammatory responses in the ear in an IL-23 induced skin inflammation model in rats, and in the gut in a 2,4,6-trinitrobenzene sulfonic acid (TNBS) induced rat model of colitis.

The toxicology profile of JNJ-77242113 has been evaluated in a comprehensive program of Good Laboratory Practice (GLP)-compliant studies that have also included toxicokinetic profiles. The Sprague-Dawley rat and cynomolgus monkey were selected for toxicology testing based on the

ability of JNJ-77242113 to bind to IL-23R from rat and cynomolgus monkey and inhibit its activity.

JNJ-77242113 was not genotoxic in the bacterial reverse mutation (Ames) assay, in the in vitro chromosome aberration assay, and in the in vivo rat comet and micronucleus assay. JNJ-77242113, given orally via gavage, did not elicit any treatment-related adverse effects in any in vivo GLP safety pharmacology studies assessing effects on cardiovascular function in telemeterized cynomolgus monkeys, (up to 300 mg/kg), and respiratory function and neurobehavioral endpoints in rats (up to 600 mg/kg).

In repeat-dose studies in rats, JNJ-77242113 was well tolerated with no adverse toxicological findings at oral doses up to 1000 mg/kg/day for 7 days (non-GLP), 600 mg/kg/day for 14 days (GLP), 70 mg/kg/day for 6 weeks (GLP), or 20 mg/kg/day for 6 months (GLP). The no-observed-adverse-effect-level (NOAEL) was the highest dose tested in each study. In cynomolgus monkeys, JNJ-77242113 was well tolerated with no adverse toxicological findings following a single oral dose up to 1000 mg/kg/day (non-GLP) and repeat-doses up to 300 mg/kg for 14 days (GLP), up to 600 mg/kg/day for 17 weeks (GLP) or up to 200 mg/kg/day for 9-months (GLP). The NOAEL was the highest dose tested in each study. JNJ-77242113 was shown to CCI in most rats and monkeys and this resulted, CCI

However, the animals remained exposed to active drug as demonstrated using ex-vivo pharmacodynamic activity assays. In rats, at the end of dosing at Week 26, associated total AUC exposure margins relative to estimated human exposure following 100 mg twice daily (34.6 ng·h/mL) were 16- to 65-fold and associated free AUC exposure margins were 3- to 6-fold. In the monkey 9-month study, at the NOAEL of 200 mg/kg/day, the associated Day 273 total (male and female) AUC exposure margin was 396-fold. Free CCI concentrations were generally similar to total concentrations, except on Day 273, when mean free concentrations were reduced to 35 to 61% of total concentrations.

JNJ-77242113 was evaluated for effects on embryo-fetal development in rats dosed up to 1000 mg/kg (for 12 days) and rabbits dosed up to 500 mg/kg (for 13 days). In rats, no maternal or fetal developmental toxicity was reported at any dose and the NOAEL was the highest dose tested (1000 mg/kg). In rabbits, JNJ-77242113 dosing was associated with maternal toxicity leading to abortions in 2 dams on gestation day 26. There was a slight increase, above historical control values, in the incidence of fused ribs in fetuses from dams dosed at 500 mg/kg. CCI detectable in rabbits. The NOAEL was the mid-dose of 200 mg/kg, and AUC exposure was 28-fold over the expected exposure level in humans following a dose of 100 mg BID (34.6 ng·h/mL). Although the relevance to humans of these adverse findings at the high dose (150-fold exposure margins) is unknown, based on the high margins at the NOAEL (28-fold), the risk to pregnant women is considered low ([International Council for Harmonisation \[ICH\] S5\[R3\] Guidance 2020](#)).

Overall, these data support a low potential for on- or off-target toxicity of JNJ-77242113 in humans. CCI

In summary, the available in vitro and in vivo pharmacology and nonclinical safety evaluation studies support the proposed Phase 2b clinical study in participants with moderate-to-severe plaque psoriasis.

Refer to the JNJ-77242113 IB for additional details.

Pharmacokinetic Profile

The absorption, distribution, metabolism, and excretion of JNJ-77242113 have been evaluated in multiple in vitro and in vivo studies in nonclinical species. JNJ-77242113 has low passive permeability and is primarily gut restricted. Oral bioavailability ranged from 0.1% to 0.3% in rat and monkey studies. Human plasma protein binding values ranged from 49.74% to 55.18% and was similar in nonclinical species based on in vitro experiments. After IV dosing in nonclinical species, volume of distribution was low and plasma half-life was short (1 to 3 hours). After oral dosing of [¹⁴C]-JNJ-77242113 in monkeys, the major route of excretion was feces, since the majority of dose is unabsorbed; 1% of the radioactive dose was recovered in urine. In both rat and monkey, unchanged drug was the major species found in feces and plasma after oral dosing, with small amounts of metabolites detected. JNJ-77242113 has a low risk of cytochrome P450-mediated drug-drug interactions and is not a P-glycoprotein substrate or inhibitor.

Clinical Studies

The PN-235-01 study was a first-in-human (FIH), randomized, placebo-controlled study of single and multiple ascending (SAD and MAD) doses of JNJ-77242113. The objectives were to assess the safety and tolerability of JNJ-77242113 after single (10, 25, 100, 300, or 1000 mg, Part 1, double-blinded) and multiple (10, 25, 100, 300, or 1000 mg, once daily [QD] dosing for 10 days, Part 2, double-blinded) ascending oral dose administration in healthy participants, to evaluate the PK and PD of JNJ-77242113, to assess the bioavailability of a tablet formulation of JNJ-77242113 relative to a solution, and to evaluate the effect of a high-fat meal on the tablet formulation PK (25 mg, Part 3).

Safety results from PN-235-01 show that JNJ-77242113 was well tolerated with no significant safety signals or concerns identified. There were no deaths or serious adverse events (SAEs) reported. The final cohort of the MAD (1000 mg QD) was interrupted after a preliminary echocardiogram for a single participant was misread and on final report was deemed to be normal. At the time the study was interrupted, in the 1000 mg QD cohort, 8 participants had completed 8 out of the planned 10 days of treatment, and 2 participants had completed 7 days of treatment.

Refer to the JNJ-77242113 IB for the most up to date safety information from this clinical study.

Pharmacokinetic Summary

Pharmacokinetic data from FIH study PN-235-01 indicate that systemic exposure (C_{\max} and AUC) to JNJ-77242113 is approximately dose proportional across the dose range evaluated to date. After multiple QD 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.

Interim results from an ongoing, multipart, randomized, open-label, single-dose, crossover study in healthy participants (77242113PSO1003) indicate that the oral bioavailability and PK profile of JNJ-77242113 administered under fasted conditions as an immediate-release (IR) tablet formulation is similar to the oral solution used in the FIH study PN-235-01. The PK results also indicate that concomitant food (high calorie, high-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 interim food effect data from protocol 77242113PSO1003, study intervention should be administered under fasted conditions (Section 4.1).

Refer to the JNJ-77242113 IB and IB Addendum 1 for more information on human PK.

2.3. Benefit-Risk Assessment

This study is the LTE for the first JNJ-77242113 study conducted in participants with psoriasis (77242113PSO2001). Therefore, the benefit-risk profile of JNJ-77242113 in patients with psoriasis has not been established. No risks have been observed for JNJ-77242113. The risks described in Table 2 are based on the drug platform (ie, a peptide therapeutic), risks that could occur from blocking the IL-23 pathway based on information from monoclonal antibodies, or study procedures.

2.3.1. Risks for Study Participation

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

Table 2: Potential Risks of JNJ-77242113 for the Treatment of Psoriasis		
Potential Risks of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Risks Due to Study Intervention		
Hypersensitivity Reactions	Exogenous peptides administered orally or systemically have the potential to cause hypersensitivity reactions.	<ul style="list-style-type: none"> This potential risk will be explained in the informed consent form (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

		<p>JNJ-77242113 or its excipients will be excluded from the study.</p> <ul style="list-style-type: none"> Any participant who develops a serious hypersensitivity reaction such as anaphylaxis must discontinue study intervention (Section 7.1).
Anti-drug antibody production	Exogenous peptides administered orally or systemically have the potential to induce ADA production, which may mediate untoward reactions such as reduced efficacy or hypersensitivity.	<ul style="list-style-type: none"> 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 12 hours apart, as directed. Drug accountability will be performed at each study visit to assess study intervention compliance.
Infection	Clinical experience with marketed IL-23 pathway blockers includes precautions for infections and tuberculosis (TB).	<ul style="list-style-type: none"> This risk is included in the ICF. Participants with evidence of active TB will be excluded from the study (Section 5.2). Participants must agree not to receive a live viral or live bacterial vaccination 12 weeks prior to enrollment in the study or during the study and for 4 weeks after receiving the last dose of study intervention (Section 5). Additional guidance is provided for the BCG vaccine in Section 5.2. Participants will be educated and instructed to seek medical attention if they develop signs or symptoms suggestive of an infection, and investigators are instructed to monitor for signs or symptoms of infections, including TB (Section 8.2.8). 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 7.1).

2.3.2. Benefits for Study Participation

Inhibiting IL-23 has been demonstrated to be efficacious in patients with psoriasis as shown in studies with monoclonal antibodies such as ustekinumab (IL-12/23), guselkumab, tildrakizumab, and risankizumab (IL-23). The clinical benefit of JNJ-77242113 in patients with psoriasis remains to be established.

2.3.3. Benefit-Risk Assessment for Study Participation

Protocol 77242113PSO2002 is the LTE study for 77242113PSO2001, the first study conducted in participants with psoriasis, and therefore the benefit-risk profile of JNJ-77242113 in patients with psoriasis has not been established. However, JNJ-77242113 blocks the IL-23R and thereby targets the IL-23 pathway, similar to the approved monoclonal antibodies ustekinumab (targeting IL-12/IL-23), guselkumab, tildrakizumab, and risankizumab (targeting IL-23). JNJ-77242113 has the potential for efficacy in psoriasis given the observed systemic exposures and high potency against the IL-23R. The potential benefits should justify the risks, which will be mitigated by measures taken during the conduct of the study.

3. OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	Proportion of participants achieving Psoriasis Area and Severity Index (PASI) 75 ($\geq 75\%$ improvement in PASI from baseline of the originating* study) at Week 36
Secondary	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Proportion of participants achieving PASI 90 ($\geq 90\%$ improvement in PASI from baseline of the originating study) at Week 36 Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) at Week 36 Change from baseline of the originating study in PASI total score at Week 36 Proportion of participants achieving an Investigator Global Assessment (IGA) score of cleared (0) or minimal (1) at Week 36
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in Psoriasis Symptoms and Signs Diary (PSSD) symptoms score at Week 36 Change from baseline of originating study in PSSD signs score at Week 36 Proportion of participants achieving PSSD symptoms score=0 at Week 36 among participants with a baseline (in the originating study) symptoms score ≥ 1 Proportion of participants achieving PSSD signs score=0 at Week 36 among participants with a baseline (in the originating study) signs score ≥ 1

Objectives	Endpoints
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Frequency and type of adverse events (AEs) and SAEs
Exploratory	
To evaluate long-term clinical response of JNJ-77242113 treatment in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Proportion of participants achieving PASI 75 ($\geq 75\%$ improvement in PASI from baseline of the originating study) over time through Week 36 Change from baseline of the originating study in PASI total score over time through Week 36 Proportion of participants achieving PASI 90 ($\geq 90\%$ improvement in PASI from baseline of the originating study) over time through Week 36 Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) over time through Week 36 Proportion of participants achieving an IGA score of cleared (0) or minimal (1) over time through Week 36 Proportion of participants achieving an IGA score of cleared (0) over time through Week 36 Change from baseline of the originating study in BSA over time through Week 36
To evaluate the effect of JNJ-77242113 treatment on patient-reported psoriasis severity in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in PSSD symptoms score over time through Week 36 Change from baseline of the originating study in PSSD signs score over time through Week 36 Proportion of participants achieving PSSD symptoms score=0 over time through Week 36 among participants with a baseline (in the originating study) symptoms score ≥ 1 Proportion of participants achieving PSSD signs score=0 over time through Week 36 among participants with a baseline (in the originating study) signs score ≥ 1
To evaluate the effect of JNJ-77242113 treatment on dermatology-specific health-related quality of life (HRQoL) in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Proportion of participants achieving a Dermatological Life Quality Index (DLQI) of 0 or 1 over time through Week 36 among participants with a baseline (in the originating study) DLQI score > 1
To evaluate the effect of JNJ-77242113 treatment on general HRQoL in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in domain scores of the Patient-Reported Outcomes Measurement Information

Objectives	Endpoints
	<p>System-29 (PROMIS-29) over time through Week 36</p> <ul style="list-style-type: none"> Proportion of participants who achieve at least a 5-point improvement from baseline of the originating study in each PROMIS-29 domain over time through Week 36
<p>To evaluate the PK and immunogenicity of JNJ-77242113, and explore the PK/PD relationship of JNJ-77242113 for biomarkers, efficacy, and safety in participants with moderate-to-severe plaque psoriasis</p>	<ul style="list-style-type: none"> JNJ-77242113 PK parameters (ie, plasma concentration just prior to the beginning or at the end of the dosing interval [C_{trough}], C_{max}, time to maximum plasma concentration [t_{max}], and AUC) The relationship between PK parameters and PD (ie, blood cellular and molecular biomarker activity as well as clinical endpoints and safety parameters) The incidence of ADA to JNJ-77242113
<p>To characterize additional efficacy of JNJ-77242113 versus placebo for the treatment of regional psoriasis</p>	<ul style="list-style-type: none"> Proportion of participants achieving a Scalp Specific Investigator Global Assessment (ss-IGA) score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline of the originating study over time through Week 36 among those participants with scalp psoriasis and an ss-IGA score ≥ 2 at baseline of the originating study Percent change from baseline of the originating study in Nail Psoriasis Area and Severity Index (NAPSI) over time through Week 36 among participants with a NAPSI score >0 at baseline of the originating study Proportion of participants achieving a Fingernail Physician's Global Assessment (f-PGA) score of clear (0) or minimal (1) over time through Week 36 among those participants with nail psoriasis and an f-PGA score ≥ 2 at baseline of the originating study Proportion of participants who achieve a Physician's Global Assessment of Hands and/or Feet (hf-PGA) score of clear (0) or almost clear (1) and a reduction of at least 2 grades on the hf-PGA scale from baseline of the originating study over time through Week 36 among those participants with hand and/or foot psoriasis and an hf-PGA score ≥ 2 at baseline of the originating study Proportion of participants achieving a Static Physician's Global Assessment (s-PGA) of genitalia score of clear (0) or minimal (1) over time through Week 36 among participants with genital psoriasis and an s-PGA of

Objectives	Endpoints
	genitalia score ≥ 3 at baseline of the originating study <ul style="list-style-type: none"> Proportion of participants achieving a score of never (0) or rarely (1) in Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) item 2 over time through Week 36 among participants with a GenPs-SFQ item 2 score ≥ 2 at baseline of the originating study
To assess the safety and tolerability of JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Frequency and type of related AEs, and AEs leading to discontinuation of study intervention Laboratory parameters and change from baseline in laboratory parameters (hematology and chemistry) over time Systolic and diastolic blood pressures over time
To explore biomarkers in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Change from baseline of the originating study in levels of blood biomarkers
To explore treatment satisfaction after using JNJ-77242113 in participants with moderate-to-severe plaque psoriasis	<ul style="list-style-type: none"> Assessment of treatment satisfaction domains over time through Week 36 using the Treatment Satisfaction Questionnaire for Medications-9 items (TSQM-9)

* Throughout table “originating study” refers to Protocol 77242113PSO2001

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

HYPOTHESIS:

There is no formal hypothesis for this study.

4. STUDY DESIGN

4.1. Overall Design

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

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

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

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

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

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

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

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

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

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

The total duration of this study is up to 40 weeks: a 36-week treatment period and a 4-week safety follow-up period after the last study intervention administration.

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

The study intervention may be delivered directly to the participants from a courier as permitted by local requirements and or regulations if approved by the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) (Section 6.2). Details regarding delivery are provided in the study manual. The participant has the ability to opt-in or opt-out of using this service throughout the duration of the study. Participants may also opt to return to the site for dispensing visits in between the scheduled visits indicated in the Schedule of Activities (SoA, Section 1.3).

Efficacy, safety, PK, immunogenicity, and biomarkers will be assessed according to the SoA (Section 1.3, Table 1).

One planned database lock (DBL) will occur at Week 40. The study protocol may be amended at the sponsor's decision to extend the treatment period to provide participants access to one or more of the JNJ-77242113 doses.

An external Independent Data Monitoring Committee (iDMC) has been commissioned for study 77242113PSO2001 and this study (77242113PSO2002). Refer to Committees Structure in Section 10.3 for details.

A diagram of the study design is provided in [Figure 1](#).

4.2. Scientific Rationale for Study Design

Blinding, Control, Study Phase/Periods, Intervention Groups

Blinded intervention will be used to reduce potential bias during data collection and evaluation of clinical endpoints.

Biomarker Collection

Biomarker samples will be collected to evaluate the mechanism of action of JNJ-77242113 or help to explain inter-individual 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.

Biomarker samples may be used to help address emerging issues and to enable the development of safer, more effective, and ultimately individualized therapies.

4.2.1. 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.

The primary ethical concern is that although the mechanism of action of blocking IL-23R is well established to be efficacious in psoriasis, as shown by clinical trials of subcutaneously administered biologic therapies (Section 2.1, Study Rationale), treatment with JNJ-77242113 has not been shown to be efficacious in psoriasis patients and the response to this medication is theoretical at this time.

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

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

Protocol 77242113PSO2002 is the LTE study of Protocol 77242113PSO2001, and therefore the doses studied are an extension of the doses studied in Protocol 77242113PSO2001. Protocol 77242113PSO2002 will evaluate these doses for long-term efficacy and safety.

A FIH study (PN-235-01) was conducted to evaluate SAD and MAD (QD for 10 days) doses of JNJ-77242113 (10, 25, 100, 300, and 1000 mg) in healthy participants. The study demonstrated that single and multiple oral doses up to 1000 mg/day are safe and generally well tolerated with no safety signal of concern. CCI

Refer to the IB for additional details regarding the FIH study results.

The observed data from the FIH study indicate that CCI are associated with systemic activity as evidenced CCI

The total daily doses selected for Protocol 77242113PSO2001 and 77242113PSO2002 range from 25 mg to 200 mg per day and include both QD (25 mg QD, 50 mg QD, and 100 mg QD) and BID (25 mg BID and 100 mg BID) dosing regimens. Participants initially randomized to placebo in 77242113PSO2001 will be transitioned to JNJ-77242113 100 mg QD in this LTE (77242113PSO2002), because this is the highest QD dose and is expected to be efficacious.

These doses and dosing regimens are based on preclinical and clinical exposure-response modeling and are supported by nonclinical safety margins and human safety/tolerability data from the FIH study. CCI

Based on emerging data from the originating study, 77242113PSO2001, modifications to the dosing regimen and/or length of this study may be implemented by the sponsor through a protocol amendment.

4.4. End of Study Definition

End of Study Definition

The end of study is considered as the last visit 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 visit at that study site, in the time frame specified in the Clinical Trial Agreement.

Study Completion Definition

A participant will be considered to have completed the study if he or she has completed scheduled study interventions through Week 36 and has completed assessments at the safety follow-up visit.

5. STUDY POPULATION

The inclusion and exclusion criteria for enrolling participants in this study are described below. 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.

5.1. Inclusion Criteria

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

Type of Participant and Disease Characteristic

1. Must have completed the Week 16 visit in Protocol 77242113PSO2001.
2. In the opinion of the investigator, may benefit from inclusion in this LTE study.
3. Must agree to avoid prolonged sun exposure and avoid use of tanning booths or other ultraviolet light sources during the study.
4. Modified in Amendment 1
 - 4.1 Must agree to discontinue all topical therapies that could affect psoriasis or the PASI or IGA evaluation, other than nonmedicated emollient and salicylic acid shampoos, prior to first administration of study intervention.

Sex and Contraceptive/Barrier Requirements

5. A woman of childbearing potential must have a negative urine pregnancy test at Week 0 prior to dispensing study intervention.
6. Before dispensing study intervention at Week 0, a woman must be (as defined in Section 10.7) either:
 - a. Not of childbearing potential
 - b. Of childbearing potential and
 - Practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) prior to receiving study intervention, during the study, and for at least 12 weeks after receiving the last administration of study intervention, consistent with local regulations regarding the use of birth control methods for participants participating in clinical studies.
 - The investigator should evaluate the potential for contraceptive method failure (eg, noncompliance, recently initiated) in relationship to the first dose of study intervention. Examples of highly effective methods of contraception are located in Section 10.7.

NOTE: If a female participant's childbearing potential changes after start of the study (eg, a woman who is not heterosexually active becomes active, a premenarchal woman experiences menarche), she must begin practicing a highly effective method of birth control, as described above.

7. A woman 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 12 weeks after receiving the last administration of study intervention.
8. Modified in Amendment 1
 - 8.1 A male participant who is sexually active with a woman of childbearing potential and who has not had a vasectomy must agree to use a barrier method of birth control (eg, either 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), during the study and for at least 12 weeks after receiving the last administration of study intervention. Male participants should also be advised of the benefit for female partner to use a highly effective method of contraceptive as condoms may break or leak.
9. A male participant must agree not to donate sperm for the purpose of reproduction during the study and for at least 12 weeks after receiving the last administration of study intervention.

Vaccination

10. Agree not to receive a live virus or live bacterial vaccination during the study, or within 4 weeks after the last administration of study intervention.

General

11. Must sign a ICF indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study.
12. Willing and able to adhere to the lifestyle restrictions specified in this protocol.

5.2. Exclusion Criteria

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

1. Was permanently discontinued from study intervention in Protocol 77242113PSO2001 for any reason.
2. Has received any biologic therapy or experimental therapy since completion of the originating study, 77242113PSO2001.
3. Has received any phototherapy or systemic treatment, with the exception of systemic corticosteroids taken <2 weeks in duration, that could impact the assessment of psoriasis

(PASI/IGA) since completion of the originating study, 77242113PSO2001, and within 4 weeks of the first administration of study intervention.

NOTE: Systemic treatments include, but are not limited to, JAK inhibitors, PDE4 inhibitors, immunosuppressants (eg, methotrexate, azathioprine, cyclosporine, 6-thioguanine, mercaptopurine, mycophenolate mofetil, tacrolimus), acitretin, retinoids, 1,25-dihydroxy vitamin D3 and analogues, herbal treatments or traditional Taiwanese, Korean or Chinese medicines.

4. Has received any live virus or bacterial vaccination within 12 weeks before the first administration of study intervention. For exclusions related to the bacille Calmette-Guerin (BCG) vaccine, see Exclusion 5.
5. Has received the BCG vaccine within 12 months of the first administration of study intervention.
6. Known allergies, hypersensitivity, or intolerance to JNJ-77242113 or its excipients (refer to the JNJ-77242113 IB)
7. Modified in Amendment 1

7.1 Currently has hepatitis B surface antigen (HBsAg) or hepatitis C antibody (anti-HCV) positive, or has other clinically active liver disease, or tests positive for HBsAg or anti-HCV.

NOTE: Hepatitis B/C testing will only occur in this LTE study if, after assessment of the participant, the investigator feels it is necessary to further assess the participant's risk of hepatitis B/C.

8. Currently has or has a history of being human immunodeficiency virus (HIV) antibody positive, or tests positive for HIV.

NOTE: HIV testing will only occur in this LTE study if, after assessment of the participant, the investigator feels it is necessary to further assess the participant's risk of HIV.

9. Currently has a malignancy or has a history of malignancy within 5 years before the first administration of study intervention (with the exception of a non-melanoma skin cancer or cervical carcinoma in situ that has been adequately treated with no evidence of recurrence).
10. Has suicidal ideation or suicidal behavior that may be defined as a Columbia-Suicide Severity Rating Scale (C-SSRS) rating at Week 0 of: Suicidal Ideation with Intention to Act ("Ideation level 4"), Suicidal Ideation with Specific Plan and Intent ("Ideation level 5"), or suicidal behavior (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 the since last visit version of the C-SSRS. For these participants, consultation with a mental health professional is required prior to study intervention administration. In addition, participants with C-SSRS ratings of Wish to be Dead (“Ideation level 1”), Non-Specific Active Suicidal Thoughts (“Ideation level 2”), Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act (“Ideation level 3”) or non-suicidal self-injurious behavior who are determined to be at risk by the investigator may not be enrolled.

11. **NOTE:** TB testing will only occur in this LTE study if, after evaluation (Section 8.2.8), the investigator feels it is necessary to further assess the participant’s risk of TB.

If applicable, a participant will be excluded if they meet **ANY** of the following TB criteria:

NOTE: Interferon gamma release assay (IGRA) testing includes either QuantiFERON-TB® or T-SPOT® TB.

- a. Have a history of active TB or show signs or symptoms suggestive of active TB upon medical history and/or physical examination.
- b. Have a history of untreated latent TB. 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.

- c. Have had 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. Have a positive IGRA test result within 2 months prior to the first administration of study intervention. An exception is made for participants who:
 - have a history of adequately treated latent TB described above.
 - have a 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.
 - have a false-positive IGRA test as determined by the following:
 - A suspected false-positive 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 8.2.8.

- e. Have a chest radiograph or chest computed tomography within 3 months prior to the first administration of study intervention that shows abnormalities suggestive of active or inactive TB.
- 12. Has a current diagnosis or signs or symptoms of severe, progressive, or uncontrolled medical condition that in the opinion of the investigator might interfere with participant's full participation in the study, or might jeopardize the safety of the participant or the validity of the study results.
- 13. Is 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.
- 14. Has a history of drug or alcohol abuse according to Diagnostic and Statistical Manual of Mental Disorders (5th edition) criteria within 12 months before study intervention administration.
- 15. Is pregnant, or breastfeeding, or planning a pregnancy (both men and women) while enrolled in the study or within 12 weeks following the last dose of study intervention.
- 16. Has 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

NOTE: Investigators should ensure that all study enrollment criteria have been met before enrollment. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after enrollment but before the first dose of study intervention is given such that the participant no longer meets all eligibility criteria, then the participant should be excluded from participation in the study. The required source documentation to support meeting the enrollment criteria are noted in Section 10.3.10.

5.3. Lifestyle Considerations

Potential participants must be willing and able to adhere to the following lifestyle restrictions during the study to be eligible for participation:

- 1. Refer to Section 6.8, Concomitant Therapy for details regarding prohibited and restricted therapy during the study.

It is recommended to be up to date on all age-appropriate vaccinations prior to entering the study per routine local medical guidelines. It is strongly recommended that

participants will have completed a locally-approved (or emergency use-authorized) Coronavirus Disease 2019 (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 (see also Section 6.8.1).

2. A woman of childbearing potential who is heterosexually active must remain on a highly effective method of birth control (see Inclusion Criterion 6) during the study and for at least 12 weeks after receiving the last administration of study intervention.
3. A woman must agree not to donate eggs (ova, oocytes) during the study and for a period of at least 12 weeks following the last administration of study intervention.
4. A man who is sexually active with a female of childbearing potential and has not had a vasectomy must agree to use a barrier method of birth control (see Inclusion Criterion 8) during the study and for at least 12 weeks after receiving the last administration of study intervention.
5. A man must agree to not donate sperm during the study and for at least 12 weeks after receiving the last administration of study intervention.
6. Agree to use sun protective measures (such as a hat, sunglasses, protective clothing, sunscreen), limit prolonged exposure to natural sunlight, and avoid artificial sunlight (tanning beds or phototherapy) during the study.
7. Agree to remove nail polish and/or artificial nails prior to or at the visits where nail psoriasis is assessed.
8. Agree to follow all requirements that must be met during the study as noted in the Inclusion and Exclusion Criteria (eg, contraceptive requirements).

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.

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 enrolled 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 (considered a screen failure for the purpose of the LTE) may repeat the eligibility procedures (be rescreened) 1 time. Rescreened participants will undergo the informed consent process. Waivers to eligibility criteria are not permitted. All rescreens must be agreed to by the medical monitor.

6. STUDY INTERVENTION AND CONCOMITANT THERAPY

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 JNJ-77242113 IB for a list of excipients.

For a definition of study intervention overdose, refer to Section 6.7, Treatment of Overdose.

6.1. Study Interventions Administered

Group/Arm Name	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Intervention Name	JNJ-77242113	JNJ-77242113	JNJ-77242113	JNJ-77242113	JNJ-77242113	Placebo → JNJ-77242113
Dose Formulation	Yellow colored, film-coated tablets	Yellow colored, film-coated tablets	Yellow colored, film-coated tablets	Yellow colored, film-coated tablets	Yellow colored, film-coated tablets	Yellow colored, film-coated tablets
Unit Dose Strength(s)	25 mg	25 mg	100 mg	25 mg	100 mg	100 mg
Dosage Level(s) and Frequency	25 mg QD (AM) and placebo (PM)	50 mg QD (AM) and placebo (PM)	100 mg QD (AM) and placebo (PM)	25 mg BID (AM and PM)	100 mg BID (AM and PM)	100 mg QD (AM) and placebo (PM)
Route of Administration	<input checked="" type="checkbox"/> Oral	<input checked="" type="checkbox"/> Oral	<input checked="" type="checkbox"/> Oral	<input checked="" type="checkbox"/> Oral	<input checked="" type="checkbox"/> Oral	<input checked="" type="checkbox"/> Oral
Dosing Instructions	Participants should take study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking study intervention and	Participants should take study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking study intervention and	Participants should take study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking study intervention and	Participants should take study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking study intervention and	Participants should take study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking study intervention and	Participants should take study intervention in the morning (AM) and in the evening (PM) on an empty stomach with approximately 240 mL of noncarbonated water. An empty stomach is defined as abstaining from food intake for at least 2 hours before taking study intervention and

Group/Arm Name	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
	abstaining from food and liquid intake for at least 30 minutes after taking the study intervention. Placebo will be administered to maintain the blind.	abstaining from food and liquid intake for at least 30 minutes after taking the study intervention. Placebo will be administered to maintain the blind.	abstaining from food and liquid intake for at least 30 minutes after taking the study intervention. Placebo will be administered to maintain the blind.	abstaining from food and liquid intake for at least 30 minutes after taking the study intervention. Placebo will be administered to maintain the blind.	abstaining from food and liquid intake for at least 30 minutes after taking the study intervention. Placebo will be administered to maintain the blind.	abstaining from food and liquid intake for at least 30 minutes after taking the study intervention. Placebo will be administered to maintain the blind.
Use	<input checked="" type="checkbox"/> Experimental	<input checked="" type="checkbox"/> Experimental	<input checked="" type="checkbox"/> Experimental	<input checked="" type="checkbox"/> Experimental	<input checked="" type="checkbox"/> Experimental	<input checked="" type="checkbox"/> Experimental
Investigational Medicinal Product (IMP)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Non-Investigational Medicinal Product (NIMP)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

6.2. Preparation/Handling/Storage/Accountability

Preparation/Handling/Storage

The study intervention may be delivered directly to the participants from the site by a courier. Each courier will adhere to privacy requirements approved by the IEC/IRB. The capability to utilize these direct-to-patient shipments will be assessed by the sponsor to ensure that it is allowable per local regulations.

All study intervention must be stored at site at controlled temperatures ranging from 2°C to 8°C. Study-site personnel will instruct participants on how to store and administer study intervention for at-home use as indicated in this protocol.

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 study intervention dispensed to the participant must be documented on the intervention accountability form. All study intervention will be stored and disposed of according to the sponsor's instructions. Study-site personnel must not combine contents of the study intervention containers.

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

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

Study intervention should 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. Measures to Minimize Bias: Randomization and Blinding

Intervention Allocation

Participants will be assigned to the same interventional groups as they were originally randomized to in Protocol 77242113PSO2001, with the exception that participants who were randomized to placebo in Protocol 77242113PSO2001 will receive 100 mg QD dosing starting at Week 0 through the end of the treatment period in this LTE study. Participants will not be re-randomized in this study.

Blinding

The investigator will not be provided with randomization codes. The codes will be maintained within the interactive web response system (IWRS), which has the functionality to allow the investigator to break the blind for an individual participant.

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 DBL and unblinding.

Under normal circumstances, the blind should not be broken until all participants have completed the study and the database is finalized. 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.

In general, treatment assignments will be disclosed fully only if this LTE study is completed, and the clinical database is closed.

6.4. Study Intervention Compliance

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

A participant will be considered noncompliant if he or she misses more than 20% of the prescribed doses of study intervention during the study, unless study intervention is withheld for safety

reasons. Similarly, a participant will be considered significantly noncompliant if he or she is judged by the investigator to have intentionally or repeatedly taken 20% or more than prescribed amount of study intervention during the study.

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 Statistical Analysis Plan (SAP).

6.5. Dose Modification

Dose modifications will not be applicable to this study.

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

Participants will be instructed that study intervention is not currently planned to 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.

6.7. Treatment of Overdose

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

Decision 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 electronic case report form (eCRF).
- Evaluate the participant to determine, in consultation with the medical monitor, whether study intervention should be interrupted.
- Obtain a plasma sample for PK analysis as soon as possible from the date of the last dose of study intervention if requested by the medical monitor (determined on a case-by-case basis).

6.8. Concomitant Therapy

Concomitant therapies must be recorded throughout the study once a participant signs the informed consent through the end of study participation.

All therapies (prescription or over-the-counter medications) different from the study intervention must be recorded in the eCRF. Every effort should be made to keep participants on stable concomitant medications. If a medication is temporarily discontinued because of abnormal

laboratory values, side effects, concurrent illness, or the performance of a procedure, the change and reason for it should be clearly documented in the participant's medical records.

Any questions regarding treatment with concomitant medication during the study should be directed to the medical monitor.

The sponsor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered.

Prohibited Therapy

All experimental therapies or new investigational interventions (except for JNJ-77242113), including therapies for psoriasis or other conditions, are prohibited during the trial. For guidance regarding the COVID-19 vaccine see Section 6.8.1.

If a prohibited therapy is administered during the active treatment phase (ie, Week 0 to Week 36), the medical monitor should be notified, and the participant may be required to discontinue from the study treatment per medical monitor's discretion. If a prohibited therapy is initiated during the safety follow-up period, the participant should still complete his or her final study visit, and the medication should be recorded as a concomitant medication.

The sponsor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered.

Psoriasis Concomitant Medications

Topical Therapy

Topical therapies that could affect psoriasis or the PASI/IGA evaluation (eg, corticosteroids, tar, anthralin, calcipotriene, tazarotene, methoxsalen, pimecrolimus, tacrolimus, and traditional Taiwanese, Korean, or Chinese medicines) are not permitted during the study. The only allowable concomitant treatments throughout the study are shampoos (containing salicylic acid only) and topical moisturizers. Participants should not use these topical agents (shampoos and moisturizers) the day of a study visit. Nonmedicated shampoos may be used on the day of the study visit.

Phototherapy or Systemic Therapy

The use of phototherapy or systemic medications that could affect psoriasis or the PASI/IGA evaluation is not permitted at any time during the study. These medications include, but are not limited to, those targeted for reducing TNF (including but not limited to infliximab or etanercept), drugs targeted for reducing IL-12/23, IL-17, or IL-23 (including but not limited to ustekinumab, guselkumab, tildrakizumab [MK3222], secukinumab, risankizumab [BI-655066], ixekizumab [LY2439821], or brodalumab [AMG827]), alpha-4 integrin antagonists (including but not limited to natalizumab), JAK inhibitors (including but not limited to tyrosine kinase 2 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 or the PASI/IGA evaluation (including but not limited to methotrexate, cyclosporine, acitretin, or

other retinoids), 1,25-dihydroxy vitamin D3 and analogues, antimalarial agents, herbal treatments, or traditional Taiwanese, Korean, or Chinese medicines, and any other biological agent or other systemic medication that could affect psoriasis or the PASI/IGA evaluation.

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. They 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.

6.8.1. Vaccinations (including COVID-19)

Live attenuated vaccines are prohibited for the duration of study participation.

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.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

A participant's study intervention must be discontinued if:

- The 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.
- The participant meets the Sampson criteria for anaphylaxis ([Sampson 2006](#)) following study intervention administration (see Section [10.10](#)).
- The participant has a reaction resulting in myalgia and/or arthralgia with fever and/or rash (suggestive of serum sickness and not representative of signs and symptoms of other recognized clinical syndromes) occurring 1 to 14 days after an administration of study intervention. These may be accompanied by other events including pruritus, facial, hand, or lip edema, dysphagia, urticaria, sore throat, and/or headache.
- The participant becomes pregnant or plans a pregnancy during the study period. Refer to Section [10.7](#).
- The initiation of protocol-prohibited medications, treatments, or interventions (outlined in Section [6.8](#)) that have an impact on psoriasis efficacy evaluations at the discretion of the medical monitor.
- The participant has a malignancy including squamous cell skin cancer. Consideration may be given to allow participants, who develop ≤ 2 basal cell skin cancers and who are adequately treated with no evidence of residual disease, to continue to receive study intervention.
- The participant develops a systemic opportunistic infection during the study period.

- The participant develops a recurrent or chronic serious infection during the study period.
- The 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 undergoing evaluation has chest imaging with evidence of current active TB and/or a positive IGRA test result, unless active TB can be ruled out and appropriate treatment for latent TB can be initiated prior to the next administration of study intervention and continued to completion. Indeterminate/borderline results should be handled as outlined in Section 8.2.8.
 - A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy.
- The participant is unable to adhere to the study visit schedule or comply with protocol requirements.
- The participant has a possible Hy's Law case, as defined by the occurrence of alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $\geq 3\times$ upper limit of normal (ULN), together with total bilirubin $\geq 2\times$ ULN or International Normalized Ratio (INR) >1.5 (if measured) without an identifiable cause (Section 10.8).
- The participant has his/her treatment assignment unblinded by the investigator.
- Sponsor decision.

Discontinuation of a participant's study intervention should be considered for participants with any type of suicidal ideation or behavior, or any self-injurious behavior, who are deemed to be at risk by the investigator. Discussion of such participants with the medical monitor or designee is required.

For participants who report Suicidal Ideation with Intention to Act ("Ideation level 4"), suicidal ideation with specific plan and intent ("Ideation level 5"), suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt) or any self-injurious behavior on a C-SSRS assessment, the investigator risk assessment must be based upon evaluation by a mental health professional (see Section 10.6).

Participants who decide to discontinue study intervention administration for reasons other than those outlined above must be interviewed by the investigator to determine if a specific reason for discontinuing study intervention can be identified. Participants should be explicitly asked about the possible contribution of AEs to their decision to discontinue study intervention; investigators should confirm that any AE information elicited has been documented. If a participant elects to discontinue study intervention due to an AE, the event should be recorded as the reason for study intervention discontinuation, even if the investigator's assessment is that the AE would not require study intervention discontinuation. The reason for study intervention discontinuation must be

documented in the eCRF and in source documents. Study intervention assigned to a participant who discontinues may not be assigned to another participant.

A participant will not be automatically withdrawn from the study if he or she must discontinue treatment before the end of the treatment regimen. Participants who discontinue study intervention but do not terminate study participation will continue to return for protocol-specified procedures and evaluations for approximately 4 weeks following the last administration of study intervention. The procedures and evaluations listed for the Early Termination Visit should also be performed approximately 4 weeks after the last administration of study intervention.

All procedures and evaluations must be conducted prior to a participant's withdrawal of consent.

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
- The participant is not in compliance with requirements of the study, including prohibitions and restrictions
- Death

When a participant withdraws before study completion, the reason for withdrawal is to be documented in the eCRF 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.

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 sample:

- The collected sample 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 sample, in which case the sample 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 sample has 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 sample 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 Section 10.3.5). 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.

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 he or she 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, emails, 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.

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 (Section 1.3) summarizes the frequency and timing of efficacy, PK, immunogenicity, biomarker, and safety measurements applicable to this study. It is strongly recommended that the same investigator perform the efficacy assessments at every visit.

Participants will be provided with an electronic device to enter patient-reported outcome (PRO) data at each study visit. Study-site personnel will train participants on how to use the electronic PRO device.

All visit-specific PRO assessments should be conducted/completed before any tests, procedures or other clinical assessments, with the exception of the urine pregnancy test and urinalysis, to prevent influencing participant perceptions. Refer to the site manual for instructions on the administration of PROs.

Electrocardiograms 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.

All samples (including safety, efficacy, PK, and biomarkers) must be obtained after the PRO assessment. Blood collections for PK and biomarker assessments should be kept as close to the specified time as possible. Actual dates of all assessments and blood collections will be recorded in the source documentation; in addition, times of all blood collections will be recorded in the source documentation (laboratory requisition form).

Additional serum or urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulations, to establish the absence of pregnancy at any time during the participation in the study. Results of all pregnancy testing should be documented in the participants' source documents.

Guidelines for handling of assessments affected by the COVID-19 pandemic are found in Section 10.9.

Blood Sample Collection

The total blood volume to be collected from each participant through Week 40 of the study will be approximately 141 mL. In addition, repeat or unscheduled samples may be collected for safety reasons or for technical issues with the samples. Total blood volume may vary slightly per region.

Sample Collection and Handling

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

Instructions for the collection, handling, storage, and shipment of samples are found in the laboratory manual that will be provided. Collection, handling, storage, and shipment of samples must be under the specified, and where applicable, controlled temperature conditions as indicated in the laboratory manual.

Study-Specific Materials

The investigator will be provided with the following supplies:

- Protocol
- Investigator's Brochure for JNJ-77242113
- Site Investigational Product and Procedures Manual
- Laboratory manual
- Laboratory kits
- Interactive Web Response System Manual
- Sample eCRF
- Electronic case report form Completion Guidelines
- Electronic PRO equipment (tablet device questionnaires, completion instructions)
- Participant Study Participation Card
- Investigative Site File
- Recruitment materials, as needed

8.1. Efficacy Assessments

Investigator assessments and PROs of efficacy are included in this section.

- The PRO instrument will be provided in the local language in accordance with local guidelines.
- The PRO instrument must be available for regulators and for IEC/IRB submissions.
- The PRO and AE data will not be reconciled with one another.

8.1.1. Psoriasis Area and Severity Index

The PASI is a system used for assessing and grading the severity of psoriatic lesions and their response to therapy (Section 10.4; 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.

8.1.2. Investigator's Global Assessment

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

8.1.3. Body Surface Area

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

8.1.4. Nail Psoriasis Area and Severity Index

The NAPSI is an index used for assessing and grading the severity of nail psoriasis (Rich 2003). Each of the participant's 20 nails (fingernails and toenails) is divided into quadrants and is assessed for any presence of nail psoriasis in the nail matrix (pitting, leukonychia, red spots in the lunula, and nail plate crumbling) and any presence of nail psoriasis in the nail bed (onycholysis, splinter hemorrhages, oil drop discoloration, and nail bed hyperkeratosis). Both the nail matrix (score 0-4) and nail bed (score 0-4) scores equal the number of quadrants affected by nail/nailbed psoriasis. The total individual nail score is the sum of the nail matrix and nail bed score and ranges from 0 to 8. The sum of all 20 individual nail scores is the total NAPSI score (0 to 160).

8.1.5. 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 similar to the IGA (clear [0], minimal [1], mild [2], moderate [3], or severe [4]).

8.1.6. Static Physician's Global Assessment of Genitalia

The static s-PGA of genitalia is a 6-point numerical rating scale to assess the severity of genital psoriasis at a given time point (Merola 2017). The s-PGA of genitalia 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].

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

The severity of hand and foot psoriasis has been assessed in various clinical studies using a hf-PGA instrument (Leonardi 2011; Goldblum 2013). The plaques on the hands and feet are scored on a 5-point scale as: clear [0], almost clear [1], mild [2], moderate [3], and severe [4].

8.1.8. 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).

8.1.9. Psoriasis Symptom and Sign Diary

The PSSD includes PRO questionnaires designed to measure the severity of psoriasis symptoms and signs for the assessment of treatment benefit ([Feldman 2016](#)). This study will use a 7-day recall version of the PSSD that asks the participant to answer the questions thinking about the last 7 days. The PSSD is a self-administered PRO instrument and includes 11 items covering symptoms (itch, pain, stinging, burning, and skin tightness) and patient-observable signs (skin dryness, cracking, scaling, shedding or flaking, redness, and bleeding) using 0 to 10 numerical rating scales for severity. Two subscores will be derived each ranging from 0 to 100: the psoriasis symptoms score and the psoriasis signs score. A higher score indicates more severe disease.

8.1.10. Dermatological 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.

8.1.11. 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](#)).

8.1.12. Genital Psoriasis Sexual Frequency Questionnaire

The GenPs-SFQ is a 2-item patient-reported instrument used to assess the impact of genital psoriasis on the frequency of sexual activity in the last 7-days ([Gottlieb 2018](#)). 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]).

8.1.13. Patient Global Impression- Severity and Change

Interpreting meaningful change in scores on PRO instruments is an important step in evaluating results and is included in Food and Drug Administration (FDA) guidelines ([FDA 2018](#)). The methods for interpreting meaningful change have evolved over time and various approaches exist. Anchor-based methods are often preferred. Anchor-based methods link scores on the PRO to an external criterion that identifies participants who have experienced an important change in their condition. The Patient Global Impression-Severity (PGI-S) and Change (PGI-C) will be used as anchors, external criteria, to determine meaningful change in scores for other PROs in this population. The PGI-S contains 1 question on how the participant would currently rate severity of disease in the past 7 days, with responses ranging from 1="None" to 5="Very severe." The PGI-C contains 1 question on how the participant would rate the change from their first treatment in this

study. The response options are presented on a 7-point scale from 1=“A lot better now” to 7=“A lot worse now.”

8.1.14. Treatment Satisfaction Questionnaire for Medications – 9 Items

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

8.2. Safety Assessments

Details regarding the iDMC are provided in Section [10.3.6](#)

Adverse events will be reported and followed by the investigator as specified in Section [8.3](#) and Section [10.5](#).

Any clinically relevant changes occurring during the study must be recorded on the AE section of the eCRF.

Any clinically significant abnormalities persisting at the end of the study/early withdrawal will be followed by the investigator until resolution or until a clinically stable condition is reached, if possible.

The study will include the following evaluations of safety and tolerability according to the time points provided in the SoA (Section [1.3](#)).

8.2.1. Physical Examinations

Physical Examination

Physical examinations will be performed by the investigator or designated physician, nurse practitioner or physician assistant as specified in the SoA (Section [1.3](#)). A full physical examination will be completed at Week 0 and either the final safety visit or the Early Termination Visit. A targeted physical examination will be completed at all other visits as specified in the SoA (Section [1.3](#)). 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 and in the eCRF.

Weight

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.

8.2.2. Vital Signs

Vital signs (including temperature, pulse/heart rate, respiratory rate, and blood pressure) will be obtained at visits specified in the SoA (Section [1.3](#)).

8.2.3. Electrocardiogram

Triplicate 12-lead ECGs will be performed as specified in the SoA (Section 1.3). The 3 individual ECG tracings should be obtained as closely as possible in succession about 2 minutes apart. The full set of triplicates should be completed in about 5 minutes. Details regarding collection of ECGs are available in the site manual.

8.2.4. Clinical Safety Laboratory Assessments

Blood samples for serum chemistry and hematology and urine samples for urinalysis will be collected as noted in Section 10.2. 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 eCRF. 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 study manual or approved by the medical monitor are specified in Section 10.2.

8.2.5. Pregnancy Testing

Pregnancy testing (urine) is planned at times indicated in the SoA (Section 1.3).

Additional serum or urine pregnancy tests may be performed, as determined necessary by the investigator or required by local regulations, to establish the absence of pregnancy at any time during the participation in the study.

8.2.6. Columbia-Suicide Severity Rating Scale

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 tool to prospectively evaluate suicidal ideation and behavior in this study, as part of a comprehensive evaluation of safety. The C-SSRS is an investigator-administered questionnaire and will be conducted on the electronic clinical outcomes assessment (eCOA) device provided to the site.

The ‘Since Last Visit’ version of the C-SSRS (Section 10.6) will be completed at all 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.

At Week 0, participants with a C-SSRS rating of Suicidal Ideation with Intention to Act (“Ideation level 4”), Suicidal Ideation with Specific Plan and Intent (“Ideation level 5”), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt), must be determined to not be at risk by the investigator

based on an evaluation by a mental health professional (eg, psychiatrist, psychologist, or appropriately trained social worker or nurse) in order to be eligible for study participation (Section 5.2). Participants with C-SSRS ratings of Wish to be Dead (“Ideation level 1”), Non-Specific Active Suicidal Thoughts (“Ideation level 2”), Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act (“Ideation level 3”) or non-suicidal self-injurious behavior must be determined not to be at risk by the investigator in order to be eligible for study participation (Section 5.2). Any questions regarding eligibility of such participants should be discussed with the medical monitor or designee.

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

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

Interruption or the discontinuation of study intervention should be considered for any participant who reports Suicidal Ideation with Intention to Act (“Ideation level 4”), Suicidal Ideation with Specific Plan and Intent (“Ideation level 5”), or suicidal behavior (actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt) on a C-SSRS assessment and who is deemed to be at risk by the investigator based upon evaluation by a mental health professional. If a participant can be adequately treated with psychotherapy and/or pharmacotherapy then the participant, at the discretion of the investigator, may be continued with treatment if agreed to by the medical monitor or designee. Discussion of such participants with the medical monitor or designee is required (Section 10.6).

Any C-SSRS finding, which in the opinion of the investigator is new or considered to be worsening and clinically significant, should be reported on the AE eCRF (Section 10.5).

8.2.7. Concomitant Medication

Concomitant medications will be reviewed at each visit and recorded in the source documents and eCRF.

8.2.8. Tuberculosis Evaluation(s)

Ongoing TB Evaluation

To aid in the early detection of TB infection or exposure during study participation, participants must be evaluated for TB signs, symptoms, and close contacts at scheduled visits or by telephone approximately every 8 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, 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.

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

IGRA Testing

NOTE: Formal screening for TB using IGRA testing will not take place in protocol 77242113PSO2002, unless the investigator considers it necessary after performing an ongoing TB evaluation as described above.

Participants with a negative IGRA test result are eligible to continue in the study. 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 (Section 5.2). 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 may continue in the study without treatment for latent TB, if active TB is ruled out, chest imaging shows no abnormality suggestive of TB (active or inactive), and the participant has no additional risk factors for TB as determined by the investigator. This determination must be promptly reported to the sponsor’s medical monitor and recorded in the participant’s source documents and initialed by the investigator.

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

Timely, accurate, and complete reporting and analysis of safety information, including AEs, SAEs, and product quality complaints (PQCs), from clinical studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide.

The sponsor has established Standard Operating Procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of safety information; all clinical studies conducted by the sponsor or its affiliates will be conducted in accordance with those procedures.

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally acceptable representative) for the duration of the study. Collection of additional medical records may be requested by the medical monitor or the sponsor to support safety monitoring and reporting.

Further details on AEs, SAEs, and PQCs can be found in Section [10.5](#).

8.3.1. Time Period and Frequency for Collecting AE and SAE 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. Any clinically relevant changes during the study must be recorded in the AE section of the eCRF.

Serious Adverse Events

All SAEs, as well as PQC, occurring during the study must be reported to the appropriate sponsor contact person by study-site personnel within 24 hours of their knowledge of the event.

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

Information regarding SAEs will be transmitted to the sponsor using the SAE Form, which must be completed and signed by a physician from the study site and transmitted to the sponsor within 24 hours. 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.

8.3.2. Method of Detecting AEs and SAEs

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 AEs

Solicited AEs are predefined local and systemic events for which the participant is specifically questioned.

Unsolicited AEs

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

8.3.3. Follow-up of AEs and SAEs

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, SAE, or PQC as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

Adverse events, including pregnancy, will be followed by the investigator as specified in Section 10.5.

8.3.4. Regulatory Reporting Requirements for Serious Adverse Events

The sponsor assumes responsibility for appropriate reporting of AEs to the regulatory authorities. The sponsor will also report to the investigator (and the head of the investigational institute where required) all suspected unexpected serious adverse reactions (SUSARs). The investigator (or sponsor where required) must report SUSARs to the appropriate IEC/IRB that approved the protocol unless otherwise required and documented by the IEC/IRB. A SUSAR will be reported to regulatory authorities unblinded. Participating investigators and IEC/IRB will receive a blinded SUSAR summary, unless otherwise specified.

8.3.5. Pregnancy

All initial reports 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 an SAE reporting form. Any participant who becomes pregnant during the study must promptly discontinue further study intervention. Participants who are found to be pregnant in between study visits should immediately stop taking the study intervention and contact the investigator.

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

8.3.6. Disease-Related Events and Disease-Related Outcomes Not Qualifying as AEs or SAEs

All events that meet the definition of an SAE will be reported as SAEs, regardless of whether they are protocol-specific assessments.

8.3.7. Adverse Events of Special Interest

An adverse event of special interest (AESI; serious or non-serious) is one 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 potential Hy's Law cases.

Any newly identified malignancy, case of active TB, or potential Hy's Law case occurring after the first study intervention administration(s) must be reported by the investigator according to the

procedures in Section 10.5. Investigators are also advised that active TB is considered a reportable disease in most countries.

These events are to be considered serious only if they meet the definition of an SAE.

8.4. 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. Genetic analyses will not be performed on these plasma samples. Participant confidentiality will be maintained.

8.4.1. Evaluations

Venous blood samples for determination of JNJ-77242113 plasma concentrations will be collected at the time points indicated in the SoA (Section 1.3). During the study, the nominal sample collection times may be changed by the sponsor with clear communication to the investigator, but the total blood volume will not exceed 450 mL every 8 weeks. The exact dates and times of blood sample collection must be recorded in the eCRF or on the laboratory requisition form.

The laboratory manual contains further information regarding the collection, handling, labeling, and shipment of plasma samples.

8.4.2. Analytical Procedures

Pharmacokinetics

Plasma samples will be analyzed to determine concentrations of JNJ-77242113 using a validated, specific, and sensitive liquid chromatography-tandem mass spectrometry (LC-MS/MS) method by or under the supervision of the sponsor. The sponsor, or its designee, under conditions in which the participants' identity remains blinded, will assay these samples.

8.4.3. Pharmacokinetic Parameters and Evaluations

Parameters

Pharmacokinetic analysis will be performed by or under the responsibility of the sponsor.

Using the actual sampling times (see the SoA [Section 1.3]), if feasible, the following PK parameters will be estimated for JNJ-77242113 using a population PK approach:

C_{max}	Maximum observed plasma analyte concentration.
t_{max}	Actual sampling time to reach the maximum observed plasma analyte concentration.
AUC_{24h}	Area under the plasma analyte concentration-time curve from time 0 to 24 hours postdose, calculated by linear-linear trapezoidal summation.
AUC_{last}	Area under the plasma analyte concentration vs time curve from time 0 to time of the last measurable (non-below quantification limit [BQL]) concentration calculated by linear-linear trapezoidal summation.
AUC_{∞}	Area under the analyte concentration vs. time curve from time 0 to infinite time, calculated as $AUC_{last} + C_{last}/\lambda_z$, where C_{last} is the last observed measurable (non-BQL)

	plasma analyte concentration; extrapolations of more than 20.00% of the total AUC are reported as approximations.
$t_{1/2}$	Apparent elimination half-life calculated as $0.693/\lambda_z$
λ_z	Apparent terminal elimination rate constant, estimated by linear regression using the terminal log-linear phase of the log transformed concentration-time curve.

8.5. Genetics and Pharmacogenomics

Genetics and pharmacogenomics are not evaluated in this study.

8.6. Biomarkers

Biomarker assessments will be used to define and identify PD markers of therapeutic response to better understand the mechanism of action of JNJ-77242113 in participants with psoriasis, and aid in evaluating the drug exposure clinical response relationship, and the pathophysiology of psoriasis. This will include evaluation of relevant disease and pathway engagement biomarkers in serum. These assessments could also help explain inter-individual variability including differences between responders and non-responders 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 will be collected per the SoA (Section 1.3). Instructions for collection and shipment of samples will be outlined in the laboratory reference manual.

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.

8.6.1. Serum Psoriasis Pharmacodynamic Changes

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

8.7. Immunogenicity Assessments

Antibodies to JNJ-77242113 will be evaluated in serum samples collected from all participants according to the SoA (Section 1.3). 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 verify the stability of antibodies to JNJ-77242113 and/or further characterize the immunogenicity of JNJ-77242113.

Serum samples will be used to evaluate the immunogenicity of anti-JNJ-77242113 antibodies. 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

The detection and characterization of antibodies to JNJ-77242113 will be performed using a validated assay method by or under the supervision of the sponsor. All samples collected for detection of antibodies to JNJ-77242113 will also be evaluated for corresponding JNJ-77242113 plasma concentration to enable interpretation of the antibody data. Antibodies may be further characterized and/or evaluated for their ability to neutralize the activity of the study intervention(s). Samples may be stored up to 15 years (or according to local regulations) following the last participant's last visit for the study at a facility selected by the sponsor to enable further analysis of immune responses to JNJ-77242113.

8.8. Medical Resource Utilization and Health Economics

Health Economics/Medical Resource Utilization and Health Economics parameters are not 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 objective of this LTE study is to evaluate the long-term clinical response and safety of JNJ-77242113 treatment in participants with moderate-to-severe psoriasis. All of the analyses will be descriptive in order to evaluate the longer-term effects of efficacy and safety and no statistical hypothesis is specified.

9.2. Sample Size Determination

Protocol 77242113PSO2002 is the LTE study of Protocol 77242113PSO2001, therefore there is no formal calculation of the sample size for study 77242113PSO2002. The sample size of this LTE study will be determined by the number of participants who enroll in study 77242113PSO2001 and are eligible to enter and choose to participate in this LTE study. The 77242113PSO2001 study is designed to enroll approximately 240 participants and a detailed sample size determination for the study is described in Section 9.2 of the 77242113PSO2001 protocol.

9.3. Populations for Analysis Sets

Since this study (77242113PSO2002) is the LTE for study 77242113PSO2001, to more accurately evaluate long-term clinical response to JNJ-77242113, the full analysis set (FAS) for 77242113PSO2002 will consist of randomized participants who received at least one dose of study intervention in the originating study (77242113PSO2001) for participants initially randomized to JNJ-77242113. This is consistent with the analysis set for the originating study. For participants randomized to placebo in the originating study, only those who crossed over and received JNJ-77242113 during the LTE will be included in the FAS for the LTE study.

For the efficacy analyses in this study, participants in the FAS will be presented according to the participants' assigned treatment to which they were randomized in study 77242113PSO2001. The FAS will be used for all efficacy analyses.

Similarly, safety analyses will include all randomized participants in 77242113PSO2001 who received at least 1 dose 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. Pharmacokinetics analyses for JNJ-77242113 will include participants who receive at least one dose of JNJ-77242113 in 77242113PSO2001 or 77242113PSO2002 and have at least one sample collection after taking JNJ-77242113. Antibodies to JNJ-77242113 will be analyzed for participants who receive at least one dose of JNJ-77242113 in 77242113PSO2001 or 77242113PSO2002 and have at least one sample collection after taking JNJ-77242113.

See [Table 3](#) for populations for analyses.

Table 3: Populations for Analyses

Population	Description
Enrolled	All participants who sign the ICF in the 77242113PSO2001 study
Randomized	All participants who were randomized in the 77242113PSO2001 study
Full Analysis Set	Randomized participants who received at least one dose of study intervention in the originating study (77242113PSO2001) for participants initially randomized to JNJ-77242113, and participants who crossed over and received JNJ-77242113 for participants initially randomized to placebo
Safety Analysis Set	All randomized participants in 77242113PSO2001 who received at least 1 dose of study intervention from Week 0 of 77242113PSO2001
Pharmacokinetics Analysis Set	All participants in 77242113PSO2001 or 77242113PSO2002 who received at least 1 complete dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113
Immunogenicity Analysis Set	All participants in 77242113PSO2001 or 77242113PSO2002 who received at least 1 dose of JNJ-77242113 and who had at least 1 sample obtained after the first dose of JNJ-77242113 for the detection of antibodies to JNJ-77242113

9.4. Statistical Analyses

9.4.1. Statistical Methods

This study is an LTE study following the originating study 77242113PSO2001 and no formal hypothesis testing will be performed for the primary and secondary endpoints. Simple descriptive summary statistics, such as n, mean, standard deviation (SD), median, interquartile range,

minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data. The baseline data from the originating study (77242113PSO2001) will be used to calculate the change-from-baseline-related endpoints.

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

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

9.4.2. Efficacy Analysis

9.4.2.1. Primary Endpoint(s)

The primary efficacy endpoint is the proportion of participants achieving PASI 75 at Week 36, defined as at least a 75% improvement in PASI from baseline of the originating study.

9.4.2.1.1. Primary Estimand

The primary estimand is defined by the following 5 attributes:

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

Population: Adult participants with moderate-to-severe plaque psoriasis

Intercurrent events (ICEs) and their corresponding strategies: See [Table 4](#).

Variable/endpoint: Response binary variable, where a responder is defined as a participant achieving a PASI 75 response at Week 36 who does not have ICEs in categories 1 and 2.

Population level summary: The proportions of participants achieving a PASI 75 response at Week 36.

Table 4: Intercurrent Events and their Corresponding Strategies

Intercurrent Events	Analysis Strategy for Addressing ICEs
1. Discontinuation of study intervention due to lack of efficacy, or due to an AE of worsening of psoriasis prior to Week 36 2. Initiation of a protocol-prohibited medication or therapy during the study that could improve psoriasis prior to Week 36	Composite Strategy: Participants with these ICEs are considered as PASI 75 non-responders after these events. The occurrence of these ICEs is captured in the variable definition.

Table 4: Intercurrent Events and their Corresponding Strategies

Intercurrent Events	Analysis Strategy for Addressing ICEs
3. Discontinuation of study intervention for reasons other than ICE 1 prior to Week 36	Treatment Policy: observed data will be used regardless of whether or not this ICE had occurred.

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

9.4.2.2. Secondary Endpoint(s)

In addition to the primary endpoint analysis, the analyses for secondary efficacy endpoints listed below will be performed to support the primary endpoint analysis.

- Proportion of participants achieving PASI 90 ($\geq 90\%$ improvement in PASI from baseline of the originating study) at Week 36.
- Proportion of participants achieving PASI 100 (100% improvement in PASI from baseline of the originating study) at Week 36.
- Change from baseline of the originating study in PASI total score at Week 36.
- Proportion of participants achieving an IGA score of cleared (0) or minimal (1) at Week 36.
- Change from baseline of the originating study in PSSD symptoms score at Week 36.
- Change from baseline of the originating study in PSSD signs score at Week 36.
- Proportion of participants achieving PSSD symptoms score=0 at Week 36 among participants with a baseline (in the originating study) symptoms score ≥ 1 .
- Proportion of participants achieving PSSD signs score=0 at Week 36 among participants with a baseline (in the originating study) signs score ≥ 1 .

9.4.2.3. Exploratory Endpoint(s)

The following endpoints will be analyzed over time through Week 36 as exploratory endpoints. Detailed analyses will be specified in the SAP.

- The proportions of participants achieving PASI 100% improvement, $\geq 90\%$ improvement, and $\geq 75\%$ improvement from baseline of the originating study.
- The change from baseline of the originating study in PASI score.
- The proportions of participants achieving an IGA score of cleared (0), an IGA score of cleared (0) or minimal (1), and an IGA score of mild or better (≤ 2), respectively.
- The change from baseline of the originating study in BSA.
- The proportion of participants with DLQI score of 0 and 1 among participants with a baseline (from the originating study) DLQI score > 1 .
- The change from baseline of the originating study in PSSD symptoms score.
- The change from baseline of the originating study in PSSD signs score.

- The proportion of participants who achieve a PSSD symptoms score =0 among participants with a baseline (from the originating study) symptoms score that is ≥ 1 .
- The proportion of participants who achieve a PSSD signs score =0, among participants with a baseline (from the originating study) signs score that is ≥ 1 .
- The change from baseline of the originating study in domain scores of the PROMIS-29.
- Proportion of participants who achieve 5-point improvement or higher in each PROMIS-29 domain from baseline of the originating study.
- Assessment of treatment satisfaction domains through Week 36 using the TSQM-9.
- The proportion of participants who achieve an ss-IGA score of absence of disease (0) or very mild disease (1) and at least a 2-grade improvement from baseline of the originating study among participants with scalp psoriasis and an ss-IGA score ≥ 2 at baseline of the originating study.
- Percent change from baseline of the originating study in NAPSI among participants with a NAPSI score >0 at baseline of the originating study.
- The proportion of participants who achieve an f-PGA score of clear (0) or minimal (1) among participants with nail psoriasis and an f-PGA score ≥ 2 at baseline of the originating study.
- The proportion of participants who achieve an hf-PGA score of clear (0) or almost clear (1) and a reduction of at least 2 grades on the hf-PGA scale from baseline of originating study among participants with hand and/or foot psoriasis and an hf-PGA score ≥ 2 at baseline of the originating study.
- The proportion of participants who achieve an s-PGA of genitalia score of clear (0) or minimal (1) among participants with genital psoriasis and an s-PGA of genitalia score ≥ 3 at baseline of the originating study.
- Proportion of participants achieving a score of never (0) or rarely (1) in GenPs-SFQ item 2 among participants with a GenPs-SFQ item 2 score ≥ 2 at baseline of the originating study.

9.4.3. Safety Analyses

Safety data, including but not limited to, AEs, SAEs, discontinuation of study intervention due to AEs, changes in laboratory assessments, changes in vital signs, and changes in weight will be summarized. Intervention-emergent AEs will be summarized by treatment group and Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred terms. Details will be specified in the SAP.

Adverse Events

The verbatim terms used in the eCRF by investigators to identify AEs will be coded using the MedDRA. Intervention-emergent AEs are AEs with onset during the intervention period or that are a consequence of a preexisting condition that has worsened since baseline. All intervention-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. In addition, comparisons between intervention groups will be provided if appropriate.

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

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

Listings of participants with SAEs, severe AEs, AEs for psoriasis, AEs leading to discontinuation of study, and anaphylactic reaction/serum sickness reactions will also be provided. All safety analyses will be based on the population of participants who received at least 1 dose of study intervention in the originating study (77242113PSO2001); participants will be summarized by the intervention they received.

Clinical Laboratory Tests

Laboratory data will be summarized by type of laboratory test (eg, hematology, clinical chemistry). Selected laboratory parameters will be summarized by treatment groups. Common Terminology Criteria for Adverse Events (CTCAE) and ULN will be used to identify abnormal laboratory test results, and the incidence and severity of abnormal laboratory parameters (hematology and chemistry) will be summarized by treatment group.

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

Columbia-Suicide Severity Rating Scale

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

Vital Signs

Descriptive statistics of heart rate and blood pressure (systolic and diastolic) values and changes from baseline will be summarized at each scheduled time point.

Weight

Descriptive statistics of changes from baseline will be summarized at selected scheduled time points.

9.4.4. Other Analyses

Pharmacokinetic Analyses

The PK evaluable population is defined as all the participants who received at least 1 complete dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113 (in 77242113PSO2001 or 77242113PSO2002).

Plasma JNJ-77242113 concentrations will be summarized by visit and treatment group. Descriptive statistics will be calculated at each sampling timepoint. Concentrations below the lowest quantifiable concentration will be treated as zero in the summary statistics. All plasma concentrations below the lowest quantifiable concentration or missing data will be labeled as such in the concentration database. Pharmacokinetic data may also be displayed graphically.

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

Pharmacokinetic/PD Analyses

If data permit, the relationships between plasma JNJ-77242113 concentration and efficacy may be examined when appropriate. If a relationship is observed, a suitable PK/PD model may be developed to describe the exposure-response relationship and will be presented in a separate technical report.

Immunogenicity Analyses

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) in 77242113PSO2001 or 77242113PSO2002.

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

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

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

Biomarkers Analyses

Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information. Any biomarker samples received by the contract vendor or sponsor after the cutoff date will not be analyzed, and therefore, excluded from the biomarker analysis.

Changes in biomarkers over time will be summarized by treatment group. Associations between baseline levels and changes from baseline in select markers and response to treatment will be

explored. The analyses will aim to identify biomarker relevant to treatment. Results of biomarker analyses will be reported in separate technical reports.

9.5. Interim Analysis

No formal interim analyses are planned for this study. However, selected efficacy, safety, and other data through Week 36 of this LTE study may be included in the interim analyses of the originating study (77242113PSO2001) for those participants who have entered the LTE study when the interim analyses occur. In addition, selected efficacy, safety, and other data from this LTE study may be used to support regulatory discussions and Phase 3 planning.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS**10.1. Appendix 1: Abbreviations**

ADA	anti-drug antibodies
AE	adverse event
AESI	adverse event of special interest
ALT	alanine aminotransferase
anti-HCV	hepatitis C antibody
AST	aspartate aminotransferase
AUC	area under the plasma concentration versus time curve
AUC ₀₋₂₄	area under the plasma analyte concentration-time curve from time 0 to 24 hours postdose
BCG	bacille Calmette-Guerin
BID	twice daily
BSA	body surface area
ClinRO	clinician-reported outcome
C _{max}	maximum observed plasma concentration
COVID-19	Coronavirus Disease 2019
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events
C _{trough}	plasma concentration just prior to the beginning or at the end of the dosing interval
DBL	database lock
DILI	drug-induced liver injury
DLQI	Dermatological Life Quality Index
ECG	Electrocardiogram
eCOA	electronic clinical outcomes assessment
eCRF	electronic case report form(s)
eDC	electronic data capture
EU	European Union
FAS	full analysis set
FDA	Food and Drug Administration
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
HDL	high-density lipoprotein
hf-PGA	Physician's Global Assessment of Hands and/or Feet
HIV	human immunodeficiency virus
HRQoL	Health-Related Quality of Life
HRT	hormone replacement therapy
IB	Investigator's Brochure
IC ₅₀	half maximal inhibitory concentration
ICEs	intercurrent events
ICF	informed consent form
ICH	International Council for Harmonisation
ICMJE	International Committee of Medical Journal Editors
iDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
Ig	Immunoglobulin
IGA	Investigator Global Assessment
IGRA	Interferon gamma release assay
IL	Interleukin
IL-12Rβ1	interleukin 12 receptor beta 1
IL-23R	interleukin 23 receptor
IMP	Investigational Medicinal Product

IND	Investigational New Drug
INR	International Normalized Ratio
IRB	Institutional Review Board
IWRS	interactive web response system
JAK	Janus kinase
LC-MS/MS	liquid chromatography/mass spectrometry/mass spectrometry
LDL	low-density lipoprotein
LSmeans	Least Square means
LTE	long-term extension
MAD	multiple ascending doses
MedDRA	Medical Dictionary for Regulatory Activities
NAbs	neutralizing antibodies
NAPSI	Nail Psoriasis Area and Severity Index
NIMP	Non-Investigational Medicinal Product
NK	natural killer
NOAEL	no-observed-adverse-effect-level
PASI	Psoriasis Area and Severity Index
PCC	protocol clarification communication
PD	pharmacodynamic(s)
PDE	Phosphodiesterase
PGI-C	Patient Global Impression-Change
PGI-S	Patient Global Impression-Severity
PK	pharmacokinetic(s)
PQC	product quality complaint
PRO	patient-reported outcome(s)
PROMIS-29	Patient-Reported Outcomes Measurement Information System-29
PSSD	Psoriasis Symptom and Sign Diary
QD	once daily
RBC	red blood cell
SAD	single ascending doses
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SoA	Schedule of Activities
s-PGA	Static Physician's Global Assessment
ss-IGA	Scalp Specific Investigator Global Assessment
STAT	signal transducers and activators of transcription
SUSAR	suspected unexpected serious adverse reaction
TB	Tuberculosis
t _{max}	time to maximum plasma concentration
TNBS	2,4,6-trinitrobenzene sulfonic acid
TNF	tumor necrosis factor
TSQM-9	Treatment Satisfaction Questionnaire for Medications-9 items
TYK	tyrosine kinase
ULN	upper limit of normal
US	United States
WBC	white blood cell

10.2. Appendix 2: Clinical Laboratory Tests

The following tests will be performed according to the SoA (Section 1.3):

Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters		
Hematology	Platelet count Red blood cell (RBC) count Hemoglobin Hematocrit	<u>Red Blood Cell Indices:</u> Mean corpuscular volume Mean corpuscular hemoglobin Reticulocytes	<u>White Blood Cell (WBC) count with Differential:</u> Neutrophils Lymphocytes Monocytes Eosinophils Basophils
	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.		
Clinical Chemistry	Sodium Potassium Chloride Bicarbonate Blood urea nitrogen Creatinine Glucose (nonfasting) Aspartate aminotransferase/Serum glutamic-oxaloacetic Alanine aminotransferase/Serum glutamic-oxaloacetic Gamma-glutamyltransferase Estimated glomerular filtration rate (eGFR)	Total and Direct bilirubin Alkaline phosphatase Creatine phosphokinase Lactic acid dehydrogenase Uric acid Calcium Phosphate Albumin Total protein Cholesterol Triglycerides Magnesium	
	Note: Details of liver chemistry stopping criteria and required actions and follow-up are given in Section 10.8: Liver Safety. Potential Hy’s Law case (ALT or AST ≥3 x ULN and Tbili ≥2 x ULN) reporting requirements are defined in Section 8.3.1.		
Lipid Panel	Total cholesterol High-density lipoprotein (HDL) Low-density lipoprotein (LDL) [calculated] Triglycerides		
	Note: Fasting lipid panel at Week 0 and Week 36. Nonfasting lipid panel at the Early Termination Visit. Fasting is recommended for at least 6 hours unless medically contraindicated.		

Laboratory Assessments	Parameters	
Routine Urinalysis	<u>Dipstick</u> Specific gravity pH Glucose Protein Blood Ketones Bilirubin Urobilinogen Nitrite Leukocyte esterase	<u>Sediment</u> Red blood cells White blood cells Epithelial cells Crystals Casts Bacteria
	<p>If dipstick result is abnormal, microscopy will be used to measure sediment.</p> <p>In the microscopic examination, observations other than the presence of WBC, RBC and casts may also be reported by the laboratory.</p> <p>Specific gravity, pH, glucose, protein, blood, ketones, bilirubin, and urobilinogen will be determined using a dipstick. Red blood cells, WBCs, epithelial cells, crystals, casts, and bacteria will be measured using microscopy. If there is discordance between the dipstick results, the sediment will be examined microscopically.</p>	
Other Tests	<ul style="list-style-type: none"> • Urine Pregnancy Testing for women of childbearing potential only • High sensitivity C-reactive protein 	

10.3. Appendix 3: Regulatory, Ethical, and Study Oversight Considerations

10.3.1. 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-specific requirements.

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

Protocol Clarification Communications

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

The PCC Document may be shared by the sites with 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) involve 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 should 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 eCRF 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, 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).
- Investigator's Brochure (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).

Country Selection

This study will only be conducted in those countries where the intent is to launch or otherwise help ensure access to the developed product if the need for the product persists, unless explicitly addressed as a specific ethical consideration in Section 4.2.1, Study-Specific Ethical Design Considerations.

Other Ethical Considerations

For study-specific ethical design considerations, refer to Section 4.2.1.

10.3.2. 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.

10.3.3. Informed Consent Process

Each participant (or a legally acceptable representative) must give written 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 should be in accordance with principles that originated in

the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy.

Informed consent may be obtained remotely. Refer to the Monitoring Guideline.

Before enrollment in the study, the investigator or an authorized member of the study-site personnel must explain to potential participants or their legally acceptable representatives the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort participation in the study may entail. Participants will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive for the treatment of his or her disease. Participants will be told that alternative treatments are available if they refuse to take part and that such refusal will not prejudice future treatment. Finally, they will be told that the investigator will maintain a participant identification register for the purposes of long-term follow-up if needed and that their records may be accessed by health authorities and authorized sponsor personnel without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations. By signing the ICF the participant or legally acceptable representative is authorizing such access. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed. The physician may also recontact the participant for the purpose of obtaining consent to collect information about his or her survival status.

The participant or legally acceptable representative 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 should be appropriately recorded by means of either the participant's or his or her legally acceptable representative'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.

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

If the participant or legally acceptable representative is unable to read or write, an impartial witness should be present for the entire informed consent process (which includes reading and explaining all written information) and should personally date and sign the ICF after the oral consent of the participant or legally acceptable representative is obtained.

10.3.4. Data Protection

Privacy of Personal Data

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

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

The informed consent obtained from the participant (or his or her legally acceptable representative) includes 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. This consent also addresses the transfer of the data to other entities and to other countries.

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. 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.

Exploratory PD biomarker, PK, and immunogenicity 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.

10.3.5. Long-Term Retention of Samples for Additional Future Research

Samples collected in this study may be stored for up to 15 years (or according to local regulations) for additional research. Samples will only be used to understand JNJ-77242113, to understand psoriasis, to understand differential intervention responders, and to develop tests/assays related to JNJ-77242113 and psoriasis. The research may begin at any time during the study or 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 (Section 7.2.1).

10.3.6. Committees Structure

Data Monitoring Committee

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

not involved in the conduct of the study. The iDMC responsibilities, authorities, and procedures will be documented in the iDMC charter.

10.3.7. 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 biomarker 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 this study and will not use it for other purposes without the sponsor's prior written consent.

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

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

Study participant identifiers will not be used in publication of results. Any work created in connection with performance of the study and contained in the data that can benefit from copyright protection (except any publication by the investigator as provided for below) shall be the property of the sponsor as author and owner of copyright in such work.

Consistent with Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines, the sponsor shall have the right to publish such primary (multicenter) data and information without approval from the investigator. The investigator has the right to publish study site-specific data after the primary data are published. If an investigator wishes to publish information from the study, a copy of the manuscript must be provided to the sponsor for review at least 60 days before submission for publication or presentation. Expedited reviews will be arranged for abstracts, poster presentations, or other materials. If requested by the sponsor in writing, the investigator will withhold such publication for up to an additional 60 days to allow for filing of a patent application. In the event that issues arise regarding scientific integrity or regulatory compliance, the sponsor will review these issues with the investigator. The sponsor will not mandate modifications to scientific content and does not have the right to suppress information. For multicenter study designs and sub-study approaches, secondary results generally should not be published before the primary endpoints of a study have been published. Similarly, investigators

will recognize the integrity of a multicenter study by not submitting for publication data derived from the individual study site until the combined results from the completed study have been submitted for publication, within 18 months after the study end date, or the sponsor confirms there will be no multicenter study publication. Authorship of publications resulting from this study will be based on the guidelines on authorship, such as those described in the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals, which state that the named authors must have made a significant contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of the data for the work; and drafted the work or revised it critically for important intellectual content; and given final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Registration of Clinical Studies and Disclosure of Results

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

10.3.8. 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, and 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 eCRF completion will be provided and reviewed with study-site personnel before the start of the study. The sponsor may review the eCRF 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.

10.3.9. Case Report Form Completion

Electronic 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 eCRF. All eCRF 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 eCRF are accurate and correct.

The study data will be transcribed by study-site personnel from the source documents onto an eCRF, 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 eCRF. Any such worksheets will become part of the participant's source documents. Data must be entered into

the eCRF in English. The eCRF must be completed as soon as possible after a participant visit and the forms should 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 electronic data capture (eDC) tool. If corrections to an eCRF are needed after the initial entry into the eCRF, 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.

10.3.10. 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 should be identifiable. Given that 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.

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 eCRF and will be considered source data:

- Race
- History of smoking, all nicotine use, eg, cigarettes (including e-cigarettes or the equivalent of e-cigarettes), cigars, chewing tobacco, patch, gum
- Blood pressure and pulse/heart rate
- Height and weight
- Details of physical examination
- Investigator-completed scales and assessments and PROs

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
- 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 eCRF in the protocol include the eSource system but information collected through eSource may not be limited to that found in the eCRF.

10.3.11. 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. 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 enrollment has begun. At these visits, the monitor may compare the data entered into the eCRF with the source documents (eg, hospital/clinic/physician's office medical records). The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the eCRF 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 can occur. 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.

10.3.12. 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 should immediately notify the sponsor if he or she has been contacted by a regulatory agency concerning an upcoming inspection.

10.3.13. Record Retention

In compliance with the ICH/GCP guidelines, the investigator/institution will maintain all eCRF 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.

10.3.14. Study and Site Start and Closure

First Act of Recruitment

The first site open 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

10.4. Appendix 4: Psoriasis Area and Severity Index

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

In the PASI system, the body is divided into 4 regions: the head (h), trunk (t), upper extremities (u), and lower extremities (l), which account for 10%, 30%, 20%, and 40% of the total BSA, respectively. Each of these areas is assessed separately for erythema, induration and scaling, which are each rated on a scale of 0 to 4.

The scoring system for the signs of the disease (erythema, induration, and scaling) are: 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:

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

The PASI formula is:

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

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

10.5. Appendix 5: Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

10.5.1. 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 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 Section 8.3, 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 were 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 should 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.

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 standard-of-care background therapies 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.

10.5.2. Attribution Definitions

Assessment of Causality

The causal relationship to study intervention is determined by the investigator. The following selection should 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.

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

10.5.4. 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
- 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

Special reporting situations should be recorded in the eCRF. Any special reporting situation that meets the criteria of an SAE should be recorded on the SAE page of the eCRF.

10.5.5. Procedures

All AEs

All AEs, regardless of seriousness, severity, or presumed relationship to study intervention, must be recorded using medical terminology in the source document and the eCRF. 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 eCRF 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:

- Hospitalizations not intended to treat an acute illness or AE (eg, social reasons such as pending placement in long-term care facility).
- Surgery or procedure planned before entry into the study (must be documented in the eCRF). 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.
- For convenience the investigator may choose to hospitalize the participant for the duration of the intervention period.

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 eCRF, which must be completed and reviewed by a physician from the study site and transmitted in a secure manner to the sponsor within 24 hours. 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.

10.5.6. Product Quality Complaint Handling

Definition

A 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.

10.5.7. Contacting Sponsor Regarding Safety, Including Product Quality

The names (and corresponding telephone numbers) of the individuals who should 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.

10.6. Appendix 6: Columbia-Suicide Severity Rating Scale**Appendix 6a: Columbia-Suicide Severity Rating Scale (Since Last Visit)**

SUICIDAL IDEATION	
<p>Ask questions 1 and 2. If both are negative, proceed to the "Suicidal Behaviour" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete the "Intensity of Ideation" section below.</p>	Since Last Visit
<p>1. Wish to be Dead Subject endorses thoughts about a wish to be dead or not alive anymore, or a wish to fall asleep and not wake up. <i>Have you wished you were dead or wished you could go to sleep and not wake up?</i></p> <p>If yes, describe:</p>	<p>Yes No</p> <p><input type="checkbox"/> <input type="checkbox"/></p>
<p>2. Non-Specific Active Suicidal Thoughts General non-specific thoughts of wanting to end one's life / commit suicide (e.g. "I've thought about killing myself") without thoughts of ways to kill oneself / associated methods, intent, or plan during the assessment period. <i>Have you actually had any thoughts of killing yourself?</i></p> <p>If yes, describe:</p>	<p>Yes No</p> <p><input type="checkbox"/> <input type="checkbox"/></p>
<p>3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different from a specific plan with time, place or method details worked out (e.g. thought of method to kill self but not a specific plan). Includes person who would say, "I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it... and I would never go through with it". <i>Have you been thinking about how you might do this?</i></p> <p>If yes, describe:</p>	<p>Yes No</p> <p><input type="checkbox"/> <input type="checkbox"/></p>
<p>4. Active Suicidal Ideation with Some Intent to Act, Without Specific Plan Active suicidal thoughts of killing one self and subject reports having <u>some intent to act on such thoughts</u>, as opposed to "I have the thoughts but I definitely will not do anything about them". <i>Have you had these thoughts and had some intention of acting on them?</i></p> <p>If yes, describe:</p>	<p>Yes No</p> <p><input type="checkbox"/> <input type="checkbox"/></p>
<p>5. Active Suicidal Ideation with Specific Plan and Intent Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out. <i>Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?</i></p> <p>If yes, describe:</p>	<p>Yes No</p> <p><input type="checkbox"/> <input type="checkbox"/></p>
INTENSITY OF IDEATION	
<p>The following features should be rated with respect to the most severe type of ideation (i.e. 1-5 from above, with 1 being the least severe and 5 being the most severe).</p> <p>Most Severe Ideation: _____</p>	Most Severe
<p>Frequency <i>How many times have you had these thoughts?</i></p> <p>(1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day</p>	
<p>Duration <i>When you have the thoughts, how long do they last?</i></p> <p>(1) Fleeting - few seconds or minutes (4) 4-8 hours/most of day (2) Less than 1 hour/some of the time (5) More than 8 hours/persistent or continuous (3) 1-4 hours/a lot of time</p>	
<p>Controllability <i>Could/can you stop thinking about killing yourself or wanting to die if you want to?</i></p> <p>(1) Easily able to control thoughts (4) Can control thoughts with a lot of difficulty (2) Can control thoughts with little difficulty (5) Unable to control thoughts (3) Can control thoughts with some difficulty (6) Does not attempt to control thoughts</p>	
Deterrents	

<p>Are there things - anyone or anything (e.g. family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?</p> <p>(1) Deterrents definitely stopped you from attempting suicide (2) Deterrents probably stopped you (3) Uncertain that deterrents stopped you</p> <p>(4) Deterrents most likely did not stop you (5) Deterrents definitely did not stop you (0) Does not apply</p>	
<p>Reasons for Ideation What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?</p> <p>(1) Completely to get attention, revenge or a reaction from others. (2) Mostly to get attention, revenge or a reaction from others. (3) Equally to get attention, revenge or a reaction from others and to end/stop the pain.</p> <p>(4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling). (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling). (0) Does not apply</p>	

SUICIDAL BEHAVIOUR (Tick all that apply, so long as these are separate events; must ask about all types)	Since Last Visit
<p>Actual Attempt: A potentially self-injurious act committed with at least some wish to die, as a result of act. Behaviour was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is any intent/desire to die associated with the act, then it can be considered an actual suicide attempt. There does not have to be any injury or harm, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behaviour or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g. gunshot to head, jumping from window of a high floor/storey). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. Have you made a suicide attempt? Have you done anything to harm yourself? Have you done anything dangerous where you could have died? What did you do? Did you _____ as a way to end your life? Did you want to die (even a little) when you _____? Were you trying to end your life when you _____? Or did you think it was possible you could have died from _____? Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)? (Self-Injurious Behaviour without suicidal intent) If yes, describe:</p>	<p>Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>Total # of Attempts _____</p> <p>Yes No <input type="checkbox"/> <input type="checkbox"/></p>
<p>Has subject engaged in Non-Suicidal Self-Injurious Behaviour?</p> <p>Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act (if not for that, actual attempt would have occurred). Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed towards self, gun is taken away by someone else, or he/she is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything? If yes, describe:</p>	<p>Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>Total # of Interrupted _____</p>
<p>Aborted Attempt: When person begins to take steps towards making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behaviour. Examples are similar to interrupted attempts, except that the individual stops him/herself instead of being stopped by something else. Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything? If yes, describe:</p>	<p>Yes No <input type="checkbox"/> <input type="checkbox"/></p> <p>Total # of Aborted _____</p>
<p>Preparatory Acts or Behaviour:</p>	

Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalisation or thought, such as assembling a specific method (e.g. buying pills, purchasing a gun) or preparing for one's death by suicide (e.g. giving things away, writing a suicide note). <i>Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)?</i> If yes, describe:	Yes No <input type="checkbox"/> <input type="checkbox"/>
Suicidal Behaviour: Suicidal behaviour was present during the assessment period?	Yes No <input type="checkbox"/> <input type="checkbox"/>
Suicide:	Yes No <input type="checkbox"/> <input type="checkbox"/>
<i>Answer for Actual Attempts Only</i>	Most Lethal Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g. surface scratches). 1. Minor physical damage (e.g. lethargic speech, first degree burns, mild bleeding, sprains). 2. Moderate physical damage; medical attention needed (e.g. conscious but sleepy, somewhat responsive, second degree burns, bleeding of major vessel). 3. Moderately severe physical damage; <i>medical</i> hospitalisation and likely intensive care required (e.g. comatose with reflexes intact, third degree burns less than 20% of body, extensive blood loss but can recover, major fractures). 4. Severe physical damage; <i>medical</i> hospitalisation with intensive care required (e.g. comatose without reflexes, third degree burns over 20% of body, extensive blood loss with unstable vital signs, major damage to a vital area). 5. Death	Enter Code _____
Potential Lethality: Only Answer if Actual Lethality = 0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun failed to fire so no medical damage; lay on train tracks with oncoming train but pulled away before run over). 0 = Behaviour not likely to result in injury 1 = Behaviour likely to result in injury but not likely to cause death 2 = Behaviour likely to result in death despite available medical care	Enter Code _____

10.7. Appendix 7: Contraceptive and Barrier Guidance

Participants must follow contraceptive measures as outlined in Section 5.1. Pregnancy information will be collected and reported as noted in Section 8.3.5 and Section 10.3.

Definitions

Woman of Childbearing Potential

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

Woman 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 12 months 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 women not using hormonal contraception or hormonal replacement therapy (HRT), however in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient. If there is a question about menopausal status in women on HRT, the woman will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if she wishes to continue HRT during the study.
- **permanently sterile (for the purpose of this study)**
Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy.

Note: If the childbearing potential changes after start of the study (eg, a premenarchal woman experiences menarche) or the risk of pregnancy changes (eg, a woman who is not heterosexually active becomes active), a woman 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 men or women should 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 should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.

Examples of Contraceptives

EXAMPLES OF CONTRACEPTIVES^a ALLOWED DURING THE STUDY FOR FEMALE PARTICIPANTS INCLUDE:
USER INDEPENDENT Highly Effective Methods That Are User Independent <i>Failure rate of <1% per year when used consistently and correctly.</i>
<ul style="list-style-type: none"> • Implantable progestogen-only hormone contraception associated with inhibition of ovulation^b • Intrauterine device • Intrauterine hormone-releasing system • Tubal closure (eg, bilateral tubal occlusion, bilateral tubal ligation) • Azoospermic partner (<i>vasectomized or due to medical cause</i>) <i>(Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the woman of childbearing potential and the absence of sperm has been confirmed. If not, additional highly effective method of contraception should be used. Spermatogenesis cycle is approximately 74 days.)</i>
USER DEPENDENT Highly Effective Methods That Are User Dependent <i>Failure rate of <1% per year when used consistently and correctly.</i>
<ul style="list-style-type: none"> • Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation^b <ul style="list-style-type: none"> – oral – intravaginal – transdermal – injectable • Progestogen-only hormone contraception associated with inhibition of ovulation^b <ul style="list-style-type: none"> – oral – injectable • Sexual abstinence <i>(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.)</i>
NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION DURING THE STUDY FOR FEMALE PARTICIPANTS^d (not considered to be highly effective - failure rate of ≥1% per year)
<ul style="list-style-type: none"> • Progestogen-only oral hormonal contraception where inhibition of ovulation is not the primary mode of action. • Male or female condom with or without spermicide^e • Cap, diaphragm, or sponge with spermicide • A combination of male condom with either cap, diaphragm, or sponge with spermicide (double-barrier methods)^e • Periodic abstinence (calendar, symptothermal, post-ovulation methods) • Withdrawal (coitus-interruptus) • Spermicides alone • Lactational amenorrhea method

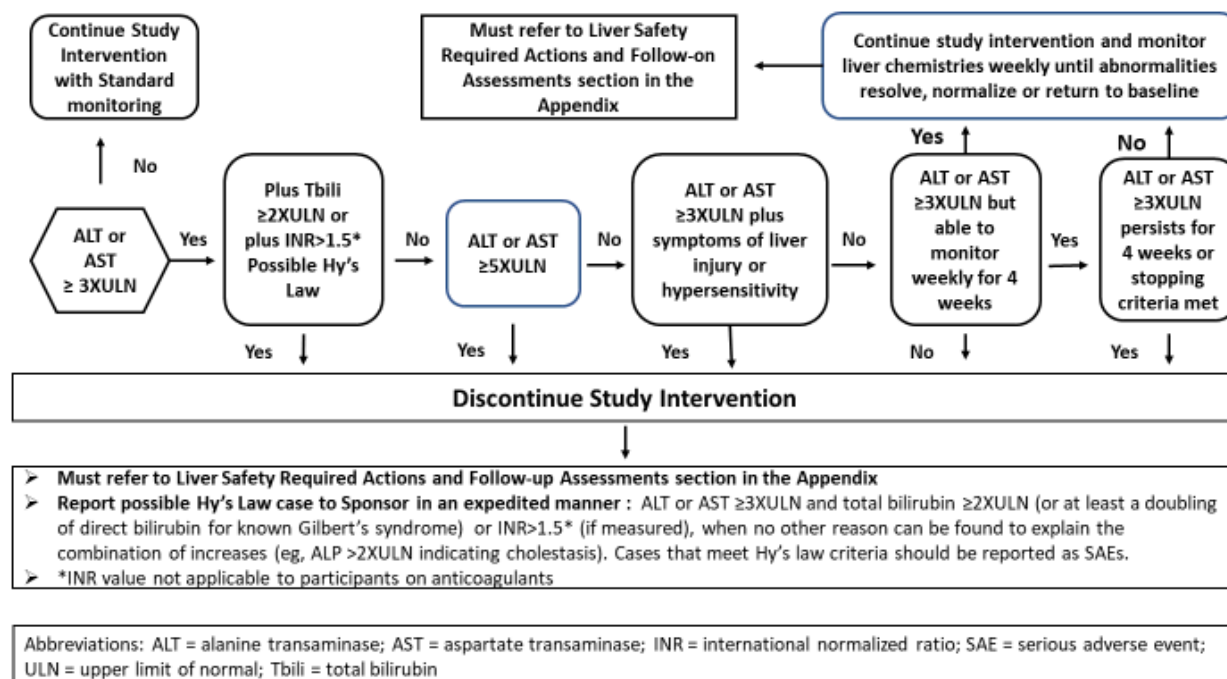
- a) Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies.
- b) Hormonal contraception may be susceptible to interaction with the study intervention, which may reduce the efficacy of the contraceptive method. In addition, consider if the hormonal contraception may interact with the study intervention.
- c) Male condom and female condom should not be used together (due to risk of failure with friction).
- d) May only be used in combination with a highly effective method of birth control (Failure rate of <1% per year when used consistently and correctly).

10.8. Appendix 8: Liver Safety: Suggested Actions and Follow-up Assessments

10.8.1. Stopping Algorithm

Study intervention will be discontinued for a participant if liver chemistry stopping criteria are met.

Phase 2 Liver Chemistry Stopping Criteria and Increased Monitoring Algorithm (no preexisting liver disease)



10.8.2. Follow-up Assessments**10.8.2.1. Phase 2 Liver Chemistry Stopping Criteria and Follow-up Assessments**

Phase 2 liver chemistry stopping criteria are designed to assure participant safety and to evaluate liver event etiology.

Liver Chemistry Stopping Criteria	
ALT/AST-absolute	ALT or AST- $\geq 5 \times \text{ULN}$
ALT/AST-Increase	<p>If cannot monitor: ALT or AST- $\geq 3 \times \text{ULN}$ and cannot be monitored weekly for 4 weeks</p> <p>Or if able to monitor: ALT or AST- $\geq 3 \times \text{ULN}$ persists for ≥ 4 weeks</p>
Total bilirubin^{1, 2}	ALT or AST- $\geq 3 \times \text{ULN}$ and total bilirubin $\geq 2 \times \text{ULN}$ (or at least a doubling of direct bilirubin in known Gilbert's syndrome)
INR²	ALT or AST- $\geq 3 \times \text{ULN}$ and INR > 1.5 , if INR measured
Symptomatic³	ALT or AST- $\geq 3 \times \text{ULN}$ associated with symptoms (new or worsening) believed to be related to liver injury or hypersensitivity
Suggested Actions, Monitoring and Follow-up Assessments	
Actions	Follow-up Assessments
<ul style="list-style-type: none"> • Immediately stop study intervention • Report the event to the sponsor within 24 hours • Complete the eCRF according to eCRF completion guidelines, and complete an SAE data collection tool if the event also met the criteria for an SAE² • Perform follow-up assessments as described in the Follow-Up Assessment column • Monitor the participant until liver chemistry test abnormalities resolve, stabilize, or return to baseline (see MONITORING) <p>MONITORING: If ALP $< 2 \times \text{ULN}$, ALT or AST- $\geq 3 \times \text{ULN}$ AND total bilirubin $\geq 2 \times \text{ULN}$ (or at least a doubling of direct bilirubin in known Gilbert's syndrome) or INR > 1.5 (if measured):</p> <ul style="list-style-type: none"> • Repeat liver chemistry tests (include ALT, aspartate transaminase [AST], alkaline phosphatase, total and direct bilirubin and INR) and perform liver event follow-up assessments within 24 hours 	<ul style="list-style-type: none"> • Viral hepatitis serology⁴ • Obtain INR and recheck with each liver chemistry assessment until the transaminases values show downward trend • Obtain blood sample for PK analysis within 48 hours after the most recent dose⁵ • Obtain serum creatine phosphokinase, lactate dehydrogenase, gamma-glutamyltransferase, glutamate dehydrogenase, and serum albumin • Fractionate bilirubin • Obtain complete blood count with differential to assess eosinophilia • Record the appearance or worsening of clinical symptoms of liver injury, or hypersensitivity, on the eCRF as per eCRF completion guidelines • Record use of concomitant medications (including acetaminophen, herbal remedies,

- Monitor participant twice weekly until liver chemistry test abnormalities resolve, stabilize, or return to baseline
- A specialist or hepatology consultation is recommended

If ALT or AST- $\geq 3 \times \text{ULN}$ AND total bilirubin $< 2 \times \text{ULN}$ and INR ≤ 1.5 :

- Repeat liver chemistry tests (include ALT, AST, alkaline phosphatase, total and direct bilirubin and INR) and perform liver chemistry follow-up assessments within **24 to 72 hours**
- Monitor participants weekly until liver chemistry abnormalities resolve, stabilize, or return to baseline

RESTART/RECHALLENGE

- **Do not restart/rechallenge** participant with study intervention. **PERMANENTLY DISCONTINUE STUDY INTERVENTION AND CONTINUE PARTICIPANT IN THE STUDY FOR ANY PROTOCOL-SPECIFIED FOLLOW-UP ASSESSMENTS**

recreational drugs and other over-the-counter medications)

- Record alcohol use on the eCRF as per eCRF completion guidelines

If ALT or AST $\geq 3 \times \text{ULN}$ AND total bilirubin $\geq 2 \times \text{ULN}$ or INR > 1.5 (if measured) obtain the following in

addition to the assessments listed above:

- 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) and/or liver biopsy to evaluate liver disease; complete eCRF as per eCRF completion guidelines
- Liver biopsy may be considered and discussed with local specialist if available:
 - In participants when serology raises the possibility of autoimmune hepatitis
 - In participants when suspected drug-induced liver injury (DILI) progresses or fails to resolve on withdrawal of study intervention
 - In participants with acute or chronic atypical presentation
- If liver biopsy conducted complete eCRF as per eCRF completion guidelines

1. Serum bilirubin fractionation should be performed if testing is available. If serum bilirubin fractionation is not immediately available, discontinue study intervention if ALT $\geq 3 \times \text{ULN}$ **and** total bilirubin $\geq 2 \times \text{ULN}$. 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.
2. All events of ALP $< 2 \times \text{ULN}$, ALT **or** AST- $\geq 3 \times \text{ULN}$ **and** total bilirubin $\geq 2 \times \text{ULN}$ (or at least a doubling of direct bilirubin in known Gilbert's syndrome) or ALP $< 2 \times \text{ULN}$, ALT **or** AST- $\geq 3 \times \text{ULN}$ **and** INR > 1.5 (if measured) 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 are met (excluding studies of hepatic impairment or cirrhosis). The INR stated threshold value will not apply to participants receiving anticoagulants.

3. 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).
4. Includes: hepatitis A immunoglobulin M antibody; HBsAg and hepatitis B core antibody; hepatitis C ribonucleic acid; cytomegalovirus IgM antibody; Epstein-Barr viral capsid antigen IgM antibody (or if unavailable, heterophile antibody or monospot testing); and hepatitis E IgM antibody.
5. Pharmacokinetic 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 blood sample draw on the eCRF. 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.

10.8.2.2. Phase 2 Liver Chemistry Increased Monitoring Criteria with Continued Study Intervention

Liver Chemistry Increased Monitoring Criterion and Actions with Continued Study Intervention	
Criterion	Actions
ALT or AST- $\geq 3 \times \text{ULN}$ and $< 5 \times \text{ULN}$ and total bilirubin $< 2 \times \text{ULN}$ or INR < 1.5 (if measured), without symptoms believed to be related to liver injury or hypersensitivity, and who can be monitored weekly for 4 weeks	<ul style="list-style-type: none"> • Notify the sponsor within 24 hours of learning of the abnormality to discuss participant safety • Participant must return weekly for repeat liver chemistry tests (ALT, AST, alkaline phosphatase, total bilirubin) until the abnormalities resolve, stabilize or return to baseline • If at any time, the participant meets liver chemistry stopping criteria, proceed as described in Section 10.8 • If, after 4 weeks of monitoring, ALT or AST-$< 3 \times \text{ULN}$ and total bilirubin $< 2 \times \text{ULN}$, monitor participants twice monthly until liver chemistry tests resolve, stabilize, or return to baseline

10.9. Appendix 9: Guidance on Study Conduct During the COVID-19 Pandemic

It is recognized that the COVID-19 pandemic may have an impact on the conduct of this clinical study due to, for example, self-isolation/quarantine by participants and study-site personnel; travel restrictions/limited access to public places, including hospitals; study-site personnel being unavailable, isolated, 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 safety is considered to be at unacceptable risk, study intervention will be discontinued, and study follow-up will be conducted.

If, as a result of the COVID-19 pandemic, visits cannot be conducted in-person at the study site, they 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 between the participant and investigator and with the agreement of the sponsor.

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.

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. Modifications made to the study conduct as a result of the COVID-19 pandemic should be summarized in the Clinical Study Report.

ADDITIONAL ELEMENTS, WHERE APPLICABLE:

- Certain protocol-mandated visits to the study site may not be possible during the COVID-19 outbreak. Therefore, temporary measures may be implemented if considered appropriate by the sponsor and investigator to maintain continuity of patient 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 / telemedicine) or in-person, off-site (eg, in-home) interactions between site staff (or designees) and patients 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 patients (or designee) or shipment of study drug from the study site directly to patients for at-home administration

- laboratory assessments using a suitably accredited local laboratory; for selected measures (eg, urine pregnancy), home testing may be employed
 - other procedures 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 with the prefix “COVID-19-related” in the eCRF.
 - other relevant study data elements impacted by the pandemic should also be documented / labeled as “COVID-19-related” in eCRFs and / or other study systems, as directed by detailed sponsor guidance. These may include missed / delayed / modified study visits / assessments / dosing, and instances where temporary measures such as those above are implemented.
- The sponsor will evaluate the totality of impact of COVID-19 on collection of key study data and additional data analyses will be outlined in study SAP(s).

10.10. Appendix 10: Criteria for Assessing Potential Cases of Anaphylaxis

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled (Sampson 2006):

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
AND AT LEAST ONE OF THE FOLLOWING:
 - a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that participant (minutes to several hours):
 - a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
 - b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
 - d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced BP after exposure to known allergen for that participant (minutes to several hours):
 - a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP*
 - b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

Key: PEF=Peak expiratory flow; BP=blood pressure.

*Low systolic blood pressure for children is defined as less than 70 mm Hg from 1 month to 1 year, less than (70 mm Hg + [2 x age]) from 1 to 10 years, and less than 90 mm Hg from 11 to 17 years.

10.11. Appendix 11: Protocol Amendment History

This is an original protocol.

11. REFERENCES

- Armstrong AW (2020), Puig L, Joshi A, et al. Comparison of biologics and oral treatments for plaque psoriasis: A meta-analysis. *JAMA Dermatol.* 2020;156(3):258–269.
- Bharmal M (2009), Payne K, Atkinson MJ, Desrosiers M-P, Morisky DE, Gemmen E. Validation of an abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9) among patients on antihypertensive medications. *Health Qual Life Outcomes.* 2009;7:36.
- Blauvelt A (2017), Papp KA, Griffiths CEM, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. *J Am Acad Dermatol.* 2017;76(3):405–417.
- Bloch Y (2018), Bouchareychas L, Merceron R, et al. Structural activation of pro-inflammatory human cytokine IL-23 by cognate IL-23 receptor enables recruitment of the shared receptor IL-12Rβ1. *Immunity.* 2018;48(1):45-58.e6.
- Cella D (2010), Riley W, Stone A, et al. Initial adult health item banks and first wave testing of the Patient-Reported Outcomes Measurement Information System (PROMIS™) Network: 2005–2008. *J Clin Epidemiol.* 2010;63(11):1179-1194.
- Feldman SR (2016), Mathias SD, Schenkel B, et al. Development of a patient-reported outcome questionnaire for use in adults with moderate-to-severe plaque psoriasis: The psoriasis Symptoms and Signs Diary. *J Dermatology & Dermatology Surgery.* 2016;20(1):19-26.
- Finlay AY (1994), Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. *Clin Exp Dermatol.* 1994;19(3):210-216.
- Food and Drug Administration (2018). Methods to identify what is important to patients and select, develop or modify fit-for-purpose clinical outcomes assessments. 2018. Discussion Document for Patient-Focused Drug Development Public Workshop on Guidance 3. Available from: <https://www.fda.gov/media/116277/download>. Accessed 07 September 2021.
- Fredriksson T (1978), Pettersson U. Severe psoriasis--oral therapy with a new retinoid. *Dermatologica.* 1978;157(4):238-244.
- Goldblum O (2013), Thomason D, Yang M, Sundaram M. Validation of the physician's global assessment of psoriasis of the hands and/or feet as a clinical endpoint. *J Am Acad Dermatol.* 2013;68(4)Supplement1:AB218.
- Gordon KB (2018), Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet.* 2018;392(10148):650–661.
- Gottlieb AB (2018), Kirby B, Ryan C, et al. The development of the Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) to assess the impact of genital psoriasis on sexual health. *Dermatol Ther (Heidelb).* 2018;8(1):33-44.
- International Council for Harmonisation (2011). ICH guideline S6 (R1)-preclinical safety evaluation of biotechnology-derived pharmaceuticals. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-s6r1-preclinical-safety-evaluation-biotechnology-derived-pharmaceuticals-step-5_en.pdf. 2011. Accessed 07 September 2021.
- International Council for Harmonisation (2020). ICH S5 (R3) guideline on reproductive toxicology: detection of toxicity to reproduction for human pharmaceuticals. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-s5-r3-guideline-reproductive-toxicology-detection-toxicity-reproduction-human-pharmaceuticals_en.pdf. 2020. Accessed 07 September 2021.
- Leonardi C (2011), Langley RG, Papp K, et al. Adalimumab for treatment of moderate to severe chronic plaque psoriasis of the hands and feet: efficacy and safety results from REACH, a randomized, placebo-controlled, double-blind trial. *Arch. Dermatol.* 2011;147(4):429-436.
- Long CC (1992), Finlay AY, Averill RW. The rule of hand: 4 hand areas = 2 FTU = 1 g. *Arch Dermatol.* 1992;128(8):1129–1130.

Merola JF (2017), Bleakman AP, Gottlieb AB, et al. The Static Physician's Global Assessment of Genitalia: a clinical outcome measure for the severity of genital psoriasis. *J Drugs Dermatol*. 2017;16(8):793-799.

Nasa M (2019). Psoriasis-unmet need- detailed, expanded analysis (US & EU). Decisions Resource Group. 2019;1-73.

Otezla (apremilast) US Package Insert (dated June 2020). Available from:
https://www.pi.amgen.com/~/-/media/amgen/repositorysites/pi-amgen-com/otezla/otezla_pi_english.ashx.

Reich K (2017), Armstrong AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. *J Am Acad Dermatol*. 2017;76(3):418–431.

Rich P (2003), Scher RK. Nail Psoriasis Severity Index: a useful tool for evaluation of nail psoriasis. *J Am Acad Dermatol* 2003;49(2):206-212.

Rossiter ND (1996), Chapman P, Haywood IA. How big is a hand? *Burns* 1996;22(3):230–231.

Sampson HA (2006), Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol*. 2006;117(2):391-397.

Sherlock JP (2012), Joyce-Shaikh B, Turner SP, et al. IL-23 induces spondyloarthritis by acting on ROR- γ t+ CD3+CD4-CD8- enthesal resident T cells. *Nat Med*. 2012;18(7):1069–1076.

Teng MWL (2015), Bowman EP, McElwee JJ, et al. IL-12 and IL-23 cytokines: from discovery to targeted therapies for immune-mediated inflammatory diseases. *Nat Med*. 2015;21(7):719–729.

Thomas CL (2007), Finlay AY. The “handprint” approximates to 1% of the total body surface area whereas the “palm minus the fingers” does not. *Br J Dermatol*. 2007;157(5):1080-1081.

INVESTIGATOR AGREEMENT

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

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

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

Signature: _____ Date: _____

(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

Telephone Number: _____

Signature: _____ Date: _____

(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): PPD MD

Institution: Janssen Research & Development

Signature: electronic signature appended at the end of the protocol Date: _____

(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	07-Apr-2022 03:02:27 (GMT)	Document Approval