Janssen Pharmaceutical K.K.*

Clinical Protocol

Protocol Title

A Phase 3, Multicenter, Open-label Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Generalized Pustular Psoriasis or Erythrodermic Psoriasis

Short Title

A Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Generalized Pustular Psoriasis or Erythrodermic Psoriasis

Protocol 77242113PSO3005**; Phase** 3
Version: Original

JNJ-77242113

*This study is being conducted by Janssen Pharmaceutical K.K. in Japan. The term "sponsor" is used throughout the protocol to represent Janssen Pharmaceutical K.K. in Japan.

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

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ABBREVIATIONS

β-hCG	β-human chorionic gonadotropin
ADA	anti-drug antibody
AE	adverse event
AESI	adverse event of special interest
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the plasma concentration versus time curve
AxMP	Auxiliary Medicinal Product (also known as NIMP)
BCG	Bacillus Calmette-Guérin
BID	twice daily
BSA	body surface area
CGI	Clinical Global Impression
ClinRO	clinician-reported outcome
C_{max}	maximum plasma concentration
COVID-19	Coronavirus disease 2019
CPK	creatine phosphokinase
CRF	case report form(s) (paper or electronic as appropriate for this study)
CRP	C-reactive protein
C-SSRS	Columbia-Suicide Severity Rating Scale
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DBL	database lock
DLQI	Dermatological Life Quality Index
ECG	Electrocardiogram
eDC	electronic data capture
eGFR	estimated glomerular filtration rate
EP	erythrodermic psoriasis
EQ-VAS	EuroQol visual analog scale
EQ-5D	EuroQol-5 Dimension
EQ-5D-5L	EuroQol-5 Dimension 5-level
E-R	exposure-response
ET	early termination
FAS	full analysis set
FDA	Food and Drug Administration (United States)
FIH	first-in-human
FOIA	Freedom of Information Act
FSH	follicle stimulating hormone
GCP	Good Clinical Practice
GPP	generalized pustular psoriasis
HBc	hepatitis B core antibody
HBs	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HRQoL	health-related quality of life
HRT	hormonal replacement therapy
IB	Investigator's Brochure
IC_{50}	half-maximal inhibitory concentration
ICE	intercurrent events
ICF	informed consent form
ICH	International Council on Harmonization
IEC	Independent Ethics Committee
IFN-γ	interferon gamma
IGA	Investigator Global Assessment
IGRA	interferon gamma release assay

IL	Interleukin
IL-12Rβ1	IL-12 receptor beta 1
IL-23R	IL-23 receptor
IMP	Investigational Medicinal Product
INR	international normalized ratio
IR	immediate-release
IRB	Institutional Review Board
IV	Intravenous
JAK	Janus kinase
JDA	Japanese Dermatological Association
LC-MS/MS	liquid chromatography/mass spectrometry/mass spectrometry
LDH	lactate dehydrogenase
LTE	Long-term extension
MCH	mean corpuscular hemoglobin
MCV	mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
MTX	Methotrexate
NOAEL	no-observed-adverse-effect-level
PASI	Psoriasis Area and Severity Index
PCR	polymerase chain reaction
PD	pharmacodynamic(s)
PDE4	phosphodiesterase 4
PHQ-9	Patient Health Questionnaire-9
PK	pharmacokinetic(s)
PQC	Product Quality Complaint
PRO	participant-reported outcome(s) (paper or electronic as appropriate for this study)
Qol	quality of life
RBC	red blood cells
SAE	serious adverse event
SAP	statistical analysis plan
SAS	safety analysis set
SD	standard deviation
SoA	Schedule of Activities
$t_{1/2}$	apparent elimination half-life calculated as $\log_e 2/\lambda z$
TB	Tuberculosis
Tbili	total bilirubin
t_{max}	time to reach the maximum observed plasma analyte concentration
TNF	tumor necrosis factor
ULN	upper limit of normal
VAS	visual analog scale
WBC	white blood cells

1. PROTOCOL SUMMARY

1.1. Synopsis

A Phase 3, Multicenter, Open-label Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Generalized Pustular Psoriasis or Erythrodermic Psoriasis

Short Title: A Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants With Generalized Pustular Psoriasis or Erythrodermic Psoriasis

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

BENEFIT-RISK ASSESSMENT

JNJ-77242113 has provided substantial efficacy in plaque psoriasis clearance in Phase 2b Study 77242113PSO2001. No risks associated with JNJ-77242113 have been identified in the previous studies; however, potential risks associated with other IL-23 inhibitors (hypersensitivity reactions, anti-drug antibody (ADA) production, infection) and study procedures could occur.

OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 in participants with generalized pustular psoriasis (GPP) or erythrodermic psoriasis (EP)	• Proportion of participants with GPP who experience treatment success (based on Clinical Global Impression [CGI] according to Japanese Dermatological Association [JDA] total score) at Week 16. • Proportion of participants with EP who experience treatment success (based on CGI) at Week 16.
Secondary	
• To further evaluate the efficacy of JNJ-77242113 in participants with GPP or EP	• Proportion of participants with GPP or EP who experience treatment success (for GPP: based on CGI scale according to JDA total score and for EP: based on CGI scale) over time. • Change from baseline in the total score of the JDA severity index for GPP over time. • Change from baseline in severity classification (mild, moderate, severe) of the JDA severity index for GPP over time. • Change from baseline in body surface area (BSA)

Objectives	Endpoints
	of involvement of lesion for EP over time. • Proportion of participants who achieve an Investigator's Global Assessment (IGA) score of cleared (0) or minimal (1) over time. • Proportion of participants who achieve an IGA score of cleared (0) over time. • Percent improvement from baseline in Psoriasis Area and Severity Index (PASI) over time.
• To evaluate the effect of JNJ-77242113 treatment on health-related quality of life (HRQoL) in participants with GPP or EP	• Change from baseline in Dermatology Life Quality Index (DLQI) score over time. • Proportion of participants who achieve a DLQI score of 0 or 1 over time. • Change from baseline in EQ-5D-5L (domain scores and visual analog scale [VAS]) over time.
• To assess the safety and tolerability of JNJ-77242113 in participants with GPP or EP	• Frequency and type of AEs and SAEs.
Exploratory	
• To further explore the efficacy of JNJ-77242113 in participants with GPP	• Change from baseline in components (skin symptoms, systemic symptoms/laboratory findings) of the JDA severity index for GPP over time.
• To further evaluate the effect of JNJ-77242113 on HRQoL in adolescent participants with GPP or EP	• Change from baseline in Children's DLQI (CDLQI) over time. • Change from baseline in Children's DLQI (CDLQI) score of 0 or 1 and over time.
• To evaluate the PK and immunogenicity of JNJ-77242113	• JNJ-77242113 PK parameters. • Incidence of anti-drug antibodies to JNJ-77242113.
• To explore biomarkers in participants with GPP or EP	• Change from baseline in levels of blood biomarkers.

Hypothesis

The primary hypothesis of this study is that JNJ-77242113 is efficacious in treating GPP or EP as assessed by the proportion of participants with GPP and EP who experience treatment success defined as at least "Minimally Improved" rating in the Clinical Global Impression (CGI) scale for GPP (according to Japanese Dermatological Association [JDA] total score) and EP, respectively, at Week 16.

OVERALL DESIGN

This is a Phase 3, open-label, multicenter study to evaluate the efficacy and safety of JNJ-77242113 for the treatment of participants with GPP or EP.

No Data Monitoring Committee will be commissioned for this study.

NUMBER OF PARTICIPANTS

A target of 16 (GPP, n=8; EP, n=8) participants will be enrolled in this study. All participants will take JNJ-77242113 from Week 0.

STUDY ARMS AND DURATION

The total duration of this study for each participant is approximately 165 weeks, which includes: a ~5-week screening period, a 52-week treatment period, a 104-week long-term extension treatment period (LTE), and a 4-week safety follow-up period. All the participants will receive JNJ-77242113 200 mg once daily for 52 weeks. Participants completing Week 52 visit may be eligible to enroll in the LTE. The LTE will begin at the end of Week 52 and will continue until Week 156. All the participants will have a 4-week safety follow-up period at the end of the treatment period or after the last dose of study intervention.

The first database lock (DBL) will occur when all patients complete Week 24 of the study. Additional DBLs may occur after Week 24 to support regulatory submissions and scientific disclosures.

EFFICACY EVALUATIONS

Investigator assessments (Clinician-reported Outcomes [ClinROs]) and PROs will be used to assess efficacy in this study per the Schedule of Activities (SoA) (Section 1.3) and are listed below.

ClinROs

- CGI scale
- JDA severity index (only for participants with GPP)
- Body surface area (BSA) of involvement of lesion (only for participants with EP)
- Investigator's Global Assessment (IGA)
- Psoriasis Area and Severity Index (PASI)

PROs

- Dermatology Life Quality Index (DLQI) for adult participants (≥18 years of age on the first date of the Screening Visit)
- Euro QoL-5 Dimension-5 Level Questionnaire (EQ-5D-5L) (domain scores and visual analog scale [VAS])
- Children's Dermatology Life Quality Index (CDLQI) for adolescent participants (≥12 years and <18 years of age on the first date of the Screening Visit)

Photographs (Optional)

Photography will be conducted to record skin lesions at each visit indicated in the SoA (Section 1.3). The details such as how to take photos of the lesion site are shown in the photography manual.

PHARMACOKINETIC EVALUATIONS

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

IMMUNOGENICITY EVALUATIONS

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

PHARMACODYNAMIC AND BIOMARKER EVALUATIONS

Biomarker assessments will be made to examine the biological response to treatment and to identify biomarkers that are relevant to JNJ-77242113 treatment response and/or psoriasis. Assessments will include the evaluation of relevant biomarkers in serum samples collected.

PHARMACOGENOMIC (DNA) EVALUATIONS

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

SAFETY EVALUATIONS

Safety assessments for all participants will include AEs, SAEs, AESIs, clinical laboratory assessments (hematology, chemistry including lipid panel, high-sensitivity C-reactive protein, pregnancy testing, and urinalysis), vital signs (including temperature, pulse/heart rate, respiratory rate, blood pressure), electrocardiograms, depression screening and symptoms monitoring (Patient Health Questionnaire-9 [PHQ-9]), suicidal ideation and behavioral risk monitoring (Columbia-Suicide Severity Rating Scale [C-SSRS]), and tuberculosis (TB) evaluations.

STATISTICAL METHODS

Descriptive summary statistics, such as n, mean, standard deviation, median, interquartile range, minimum, and maximum for continuous variables, and counts and percentages for discrete variables will be used to summarize the data by GPP and EP group wherever applicable.

Efficacy

For primary analysis, the full analysis set which is the population of participants who received at least 1 dose of study intervention will be used. The primary endpoint is the proportion of participants with GPP or EP who experience treatment success at Week 16. Frequencies, percentages, and 95% Clopper-Pearson exact confidence interval (CI) of percentages will be provided by GPP and EP group.

Secondary efficacy endpoints will be summarized descriptively by GPP and EP group. Descriptive statistics will include counts and proportions for categorical data, and median, mean, interquartile range, and range for continuous data. Graphical data displays may also be used to summarize the data.

Safety

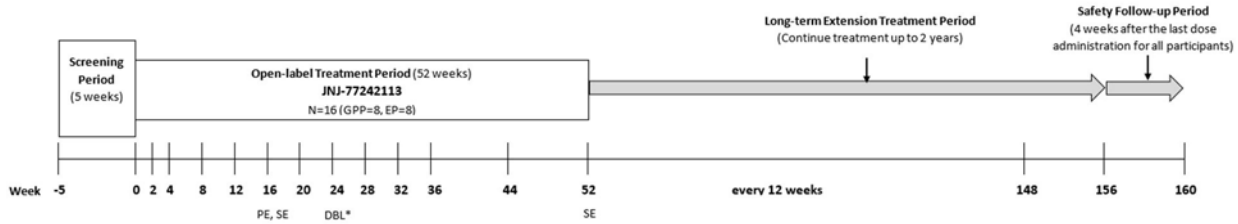
All safety analyses will be based on the population of participants who received at least 1 dose of study intervention. Safety data, including but not limited to, AEs, SAEs, AESIs (active TB, malignancy, possible Hy's Law cases), discontinuation of study intervention due to AEs, changes in laboratory assessments, vital signs, weight, changes in PHQ-9 scores, and changes in C-SSRS will be summarized. Treatment-emergent AEs will be summarized per MedDRA system organ class and preferred terms.

Other Analyses

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

1.2. Schema

Figure 1: Schematic Overview of the Study



*Additional DBLs may occur after Week 24 to support regulatory submissions and scientific disclosures.
DBL=database lock, EP=erythrodermic psoriasis, GPP=generalized pustular psoriasis, PE=primary endpoint, SE=secondary endpoints

1.3. Schedule of Activities (SoA)

1.3.1. Schedule of Activities – Screening Through Week 52

Period	Screening	Treatment Period													Notes
Week	-5-0[a]	0	2	4	8	12	16	20	24	28	32	36	44	52	
Visit Windows (Days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4	
Study Procedures															
Screening/Administrative															
ICF/assent	X														Must be signed before first study-related activity.
ICF/assent for optional photography substudy	X														ICF/assent for optional substudies can be signed at the Week 0 visit before any related substudy assessment are performed.
ICF/assent for optional pharmacogenomics (DNA) substudy	X														
ICF/assent for LTE[b]														X	
Demographics	X														
Medical history	X														Including GPP/EP diagnosis.
Prestudy therapy	X														Review of medication, including previous GPP/EP medications.
Inclusion/exclusion criteria[c]	X	X													
Chest imaging[d]	X														
IGRA	X														T-SPOT TB® or QuantiFERON-TB®.
HBV, HCV, and HIV testing	X														
FSH	X														If needed to confirm postmenopausal status.
Study Intervention Administration															
Dispense study intervention[e]		X	X	X	X	X	X	X	X	X	X	X	X	X[#]	[#]only for participants who enter LTE.
Administer study intervention[f]		Oral study intervention will be self-administered daily (Section 6.1).													
Study intervention accountability			X	X	X	X	X	X	X	X	X	X	X	X	
Efficacy Assessments															
PROs: Complete in the order shown before any tests, procedures, or consultations for all visits unless otherwise noted.															
DLQI (only for participants ≥18 years of age on the first date of Screening)		X	X	X	X	X	X	X	X	X	X	X	X	X	

Period	Screening	Treatment Period													Notes
Week	-5-0[a]	0	2	4	8	12	16	20	24	28	32	36	44	52	
Visit Windows (Days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4	
CDLQI (only for participants ≥12 to <18 years of age on the first date of Screening)		X	X	X	X	X	X	X	X	X	X	X	X	X	
EQ-5D-5L (domain scores and VAS)		X			X		X		X			X		X	
Clinician-reported Outcomes (ClinROs)															
CGI[g]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
JDA severity index for participants with GPP[h]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
BSA for participants with EP	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PASI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
IGA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Photography (optional substudy)		X		X			X							X	
Safety Assessments															
Full physical examination	X	X												X	
Targeted physical examination[i]			X	X	X	X	X	X	X	X	X	X	X		
Height[j]	X	X					X							X	
Weight	X	X					X							X	
Vital signs[k]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
12-lead ECG[l]	X						X							X	
PHQ-9[m]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
C-SSRS[m]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
TB evaluation[n]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy test for female participants of childbearing potential[o]	X (serum)	X	X	X	X	X	X	X	X	X	X	X	X	X	
Clinical Laboratory Tests[p]															
Hematology	X	X		X	X	X	X	X	X	X	X	X	X	X	
Chemistry	X	X		X	X	X	X	X	X	X	X	X	X	X	
Lipid panel[q]		X					X							X	
Urinalysis[r]		X		X	X	X	X	X	X	X	X	X	X	X	
Clinical Pharmacology Assessments[p]															
JNJ-77242113 concentration (plasma)[s]		X		X		X	X			X		X		X	
Antibodies to JNJ-77242113 (serum)		X		X		X	X			X		X		X	
Pharmacodynamics, Biomarkers, and Pharmacogenomics (DNA)[p]															
Serum biomarkers		X		X			X		X	X		X		X	Sample collection and testing will comply with local regulations.

Period	Screening	Treatment Period													Notes
Week	-5-0[a]	0	2	4	8	12	16	20	24	28	32	36	44	52	
Visit Windows (Days)			±2	±2	±4	±4	±4	±4	±4	±4	±4	±4	±4	±4	
Whole blood sample collection (optional substudy)		X													May be collected after Week 0 without constituting a protocol deviation.
Ongoing Participant Review[t]															
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

AE=adverse events, BSA=body surface area, CDLQI=Children Dermatology Life Quality Index, CGI=Clinical Global Impression, CRF=case report form, CRP=C-reactive Protein, C-SSRS=Columbia-Suicide Severity Rating Scale, CT=computed tomography, DLQI=Dermatology Life Quality Index, ECG=electrocardiogram, EP=erythrodermic psoriasis, ET=early termination, EQ-5D-5L=EuroQol-5 Dimension 5-level, FSH=follicle-stimulating hormone, GPP=generalized pustular psoriasis, HBV=hepatitis B virus, HCV=hepatitis C virus, HIV=human immunodeficiency virus, ICF=informed consent form, IGA=investigator's global assessment, IGRA=interferon-gamma release assay, JDA= Japanese Dermatological Association, LTE=long-term extension treatment period, PASI=Psoriasis Area and Severity Index, PHQ-9=Patient Health Questionnaire-9, PK=pharmacokinetics, PRO=participant-reported outcome, TB=tuberculosis, WBC=white blood cells

a. The screening window is 5 weeks. Minor extensions to the screening window can be granted with approval of the sponsor. All extensions must be documented.
b. LTE activities are to be initiated after ICF for LTE is obtained.
c. Minimum criteria for the availability of documentation supporting the eligibility criteria are described in Source Documents section of Appendix 2: Regulatory, Ethical, and Study Oversight Considerations. Check clinical status again before first dose of study intervention.
d. Chest radiograph (both posterior-anterior and lateral views, substitutable with chest CT) should have been performed ≤12 weeks before first administration of study intervention.
e. Study intervention will be dispensed after all other procedures. It may also be dispensed between visits.
f. Study intervention will be taken at the site during the baseline (Week 0), Week 4, and Week 16 visits, where both a pre- and post-dose PK sample will be drawn.
g. Criteria for CGI will differ between GPP and EP. Please see study manual. Evaluation for CGI will include comparison to the previous assessment at screening, comparison to screening assessment at Week 0, and comparison to Week 0 assessment for all other visits from Week 2.
h. Measurement required for JDA severity index such as fever, WBC, CRP, and serum albumin will be measured. If visit with no blood sample is taken, additional blood sample will be necessary.
i. Targeted physical examination should include skin and general examination with additional organ systems based on investigator's judgment.
j. For W16 and W52: Height will be measured only for participants <18 years on the first date of Screening.
k. Vital signs will include temperature, pulse/heart rate, respiratory rate, and blood pressure.
l. A 12-lead ECG will be performed locally. Participants should rest in a supine position for at least 5 minutes before ECG recording and should refrain from talking or moving arms or legs.
m. PHQ-9 and C-SSRS will be completed after PROs and before all other study procedures.
n. If TB is suspected at any time during the study, a chest radiograph or chest CT, and QuantiFERON-TB® or T-SPOT® test should be performed.
o. A negative urine test result is required at each visit prior to dispensing study intervention. A urine pregnancy test may be performed at any time during the visit, including before PRO collection.
p. At Week 0, all blood samples should be collected prior to study intervention administration, and the date and time of collection should be recorded as instructed in the Laboratory Manual. At all other study visits where applicable, the date and time of the dose prior to the PK sample should be recorded as instructed in the CRF completion guidelines.
q. Fasting requirement for lipid panel: ≥6 h unless medically contraindicated.

r. Urinalysis may be performed any time during the study visit including before PRO collection.
s. Collect 1 trough and 1 peak sample at Week 4 and Week 16. Details to be specified during training. If peak/trough collection at the Week 4 and Week 16 visits is not feasible, collection at an alternative visit is allowed.
t. All medications taken and new or worsening AEs reported after signing the ICF will be recorded. See CRF completion guidelines.

1.3.2. Schedule of Activities – Long-term Extension Treatment Period

Period	Long-term Extension Treatment Period									Safety follow-up[a]	Early Termination[b]	Notes
Week	64	76	88	100	112	124	136	148	156	160 or 4 weeks after the last dose		
Visit Windows (Days)	±6	±6	±6	±6	±6	±6	±6	±6	±6	±6		
Study Procedures												
Study Intervention Administration												
Dispense study intervention[c]	X	X	X	X	X	X	X	X				
Administer study intervention	Oral study intervention will be self-administered daily (Section 6.1).											
Study intervention accountability	X	X	X	X	X	X	X	X	X			
Efficacy Assessments												
PROs: Complete in the order shown before any tests, procedures, or consultations for all visits unless otherwise noted.												
DLQI (only for participants ≥18 years of age on the first date of Screening)	X	X	X	X	X	X	X	X	X		X	
CDLQI (only for participants ≥12 to <18 years of age on the first date of Screening)	X	X	X	X	X	X	X	X	X		X	
EQ-5D-5L	X			X			X		X		X	
Clinician-reported Outcomes (ClinROs)												
CGI[d]	X	X	X	X	X	X	X	X	X		X	
JDA severity index for participants with GPP[e]	X	X	X	X	X	X	X	X	X		X	
BSA for participants with EP	X	X	X	X	X	X	X	X	X		X	
PASI	X	X	X	X	X	X	X	X	X		X	
IGA	X	X	X	X	X	X	X	X	X		X	
Safety Assessments												
Full physical examination					X				X		X	
Targeted physical examination[f]	X	X	X	X		X	X	X		X		
Height[g]					X				X			
Weight					X				X		X	
Vital signs[h]	X	X	X	X	X	X	X	X	X	X	X	
12-lead ECG					X				X		X	
PHQ-9[i]	X	X	X	X	X	X	X	X	X	X	X	
C-SSRS[i]	X	X	X	X	X	X	X	X	X	X	X	

Period	Long-term Extension Treatment Period									Safety follow-up[a]	Early Termination[b]	Notes
Week	64	76	88	100	112	124	136	148	156	160 or 4 weeks after the last dose		
Visit Windows (Days)	±6	±6	±6	±6	±6	±6	±6	±6	±6	±6		
TB evaluation[j]	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy test for female participants of childbearing potential[k]	X	X	X	X	X	X	X	X	X	X	X	
Clinical Laboratory Tests												
Hematology	X		X		X		X		X	X[@]	X	[@]only required if clinically significant at the previous visit.
Chemistry	X		X		X		X		X	X[@]	X	
Urinalysis[l]	X		X		X		X		X		X	
Clinical Pharmacology Assessments												
JNJ-77242113 concentration (plasma)[m]	X				X				X		X	
Antibodies to JNJ-77242113 (serum)	X				X				X		X	
Pharmacodynamics and Biomarker Assessments[l]												
Serum biomarkers					X				X		X	Sample collection and testing will comply with local regulations.
Ongoing Participant Review[n]												
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	
Adverse events	X	X	X	X	X	X	X	X	X	X	X	

AE=adverse events, BSA=body surface area, CDLQI=Children Dermatology Life Quality Index, CGI=Clinical Global Impression, CRF=case report form, CRP=C-reactive protein, C-SSRS=Columbia-Suicide Severity Rating Scale, CT=computed tomography, DLQI=Dermatology Life Quality Index, ECG=electrocardiogram, EP=erythrodermic psoriasis, EQ-5D-5L=EuroQol-5 Dimension 5-level, GPP=generalized pustular psoriasis, IGA=investigator's global assessment, JDA= Japanese Dermatological Association, PASI=Psoriasis Area and Severity Index, PHQ-9=Patient Health Questionnaire-9, PK=pharmacokinetics, PRO=participant-reported outcome, TB=tuberculosis, WBC=white blood cells

a. Safety follow-up to be done approximately 4 weeks after the last administration of study intervention for all the participants.
b. Participants who terminate study intervention early should have an Early Termination Visit as soon as possible at the time of discontinuation and return approximately 4 weeks after the last administration of study intervention for safety follow-up.
c. Study intervention will be dispensed after all other procedures. It may also be dispensed between visits.
d. Criteria for CGI will differ between GPP and EP. Please see study manual. Evaluation for CGI will include comparison to Week 0 assessment for all other visits from Week 64.
e. Measurement required for JDA severity index such as fever, WBC, CRP, and serum albumin will be measured. If visit with no blood sample is taken, additional blood sample will be necessary.
f. Targeted physical examination should include skin and general examination with additional organ systems based on investigator's judgment.

g. Height will be measured only for participants <18 years on the first date of Screening.
h. Vital signs will include temperature, pulse/heart rate, respiratory rate, and blood pressure.
i. PHQ-9 and C-SSRS will be completed after PROs and before all other study procedures.
j. If TB is suspected at any time during the study, a chest radiograph or chest CT, and QuantiFERON-TB® or T-SPOT® test should be performed.
k. A negative urine test result is required at each visit prior to dispensing study intervention. A urine pregnancy test may be performed at any time during the visit, including before PRO collection.
l. Urinalysis may be performed any time during the study visit including before PRO collection.
m. At all study visits where applicable, the date and time of the dose prior to the PK sample should be recorded as instructed in the CRF completion guidelines.
n. All medications taken and new or worsening AEs reported will be recorded. See CRF completion guidelines.

2. INTRODUCTION

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

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

To date, JNJ-77242113 has been studied in several Phase 1 and Phase 2 studies. For the most comprehensive nonclinical and additional clinical information regarding JNJ-77242113, refer to the latest version of the Investigator's Brochure (IB) and Addenda 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 Protocol Supplementary Information page(s), which will be provided as a separate document.

2.1. Study Rationale

Generalized Pustular Psoriasis (GPP) is rare and represents active, unstable disease. The patient is pyrexial with red, painful, inflamed skin studded with monomorphic, sterile pustules which may coalesce to form sheets. Patients with GPP frequently need to be admitted to the hospital for management. Total or subtotal involvement of the skin by active psoriasis is known as Erythrodermic Psoriasis (EP). Chronic plaque psoriasis may gradually progress as plaques become confluent and extensive. EP may impair the thermoregulatory capacity of the skin, leading to hypothermia, high output cardiac failure, and metabolic changes including hypoalbuminaemia and anaemia due to loss of iron, vitamin B12, and folate (Langley 2005). Multiple therapies have been approved in Japan, however, there are still substantial unmet need for GPP and EP.

Targeting IL-23 is a highly effective approach for treating moderate to severe plaque psoriasis, GPP, and EP. GPP alone is associated with mutations in IL36RN (Sugiura 2014). However, increased expression of IL-36 is correlated with increased expression of cytokines that are known to be involved in the pathogenesis of psoriasis (IL-17A, IL-22, TNF-α, IL-23, and IFN-γ, but not IL-12 and IL-17F). The results indicate that the IL-36 cytokines are not only regulated by Th17 cytokines, but that they themselves can regulate the expression and enhance the function of Th17 cytokines (Carrier 2011). IL-23 is composed of a unique p19 subunit coupled with the common

p40 subunit shared with IL-12, and signals through the heterodimeric IL-23 receptor (IL-23R)/IL-12 receptor beta 1 (IL-12Rβ1) complex (Teng 2015). Binding of IL-23 to the IL-23R complex leads to phosphorylation of STAT3 and IL-23 induced expression of proinflammatory cytokines, such as IL-17A/F and IL-22. Existing highly successful biologic therapies targeting the p19 subunit of IL-23, such as guselkumab (Blauvelt 2017; Reich 2017) and risankizumab (Gordon 2018), act by preventing engagement of this ligand with the IL-23R ultimately causing reduced signaling. In addition, guselkumab and risankizumab have already been approved for the treatment of GPP and EP in Japan (Sano 2018; Yamanaka 2023).

JNJ-77242113 is a 13-amino acid peptide that binds directly to the IL-23R subunit and prevents IL-23, inhibiting proximal IL-23R signaling and downstream effector functions (eg, cytokine secretion). For those patients who prefer oral medication, oral therapies with high efficacy, long-term clinical remission, and good safety profile are more convenient and JNJ-77242113 may meet this unmet need. It has shown encouraging efficacy and safety results in Phase 2b study (77212113PSO2001) in participants with plaque psoriasis.

Based on the positive results observed in the Phase 2 study, JNJ-77242113 is being further assessed in this Phase 3 program. Study 77242113PSO3005 is a Phase 3, open-label, multicenter study to evaluate the efficacy and safety of JNJ-77242113 for the treatment of participants with GPP or EP.

2.2. Background

Two Phase 1 studies (PN-235-01 and 77242113PSO1002) in healthy participants have been completed and 1 Phase 1 study (77242113PSO1003) is ongoing in healthy participants. One Phase 2b study of JNJ-77242113 for the treatment of moderate to severe plaque psoriasis (77242113PSO2001) has also been completed and demonstrated a favorable efficacy and safety profile for JNJ-77242113.

Clinical Studies

Efficacy/Safety Studies

Phase 1

Overall, the safety data from 3 Phase 1 studies in healthy participants demonstrate that single and multiple oral doses of JNJ-77242113 administered as an oral solution (PN-235-01, final data) and single oral doses administered as immediate-release (IR) tablets or CCI [redacted] (77242113PSO1002 in Japanese and Chinese healthy participants, final data and 77242113PSO1003 in non-Japanese healthy participants, preliminary data) were generally well tolerated and with no safety signals.

Phase 2

Study 77242113PSO2001, was a Phase 2b multicenter, randomized, double-blind, placebo-controlled, dose-ranging, parallel-group, multicenter study to evaluate the efficacy and safety of JNJ-77242113 treatment in 255 adults with moderate to severe plaque psoriasis over 16 weeks. In

Study 77242113PSO2001, a dose response was observed for the primary endpoint (Psoriasis Area and Severity Index [PASI] 75 response at Week 16). A statistically significant higher proportion of participants in each JNJ-77242113 dose group achieved a PASI 75 response at Week 16 (37.2% for 25 mg once daily, 58.1% for 50 mg once daily, 51.2% for 25 mg twice daily, 65.1% for 100 mg once daily, 78.6% for 100 mg twice daily; nominal p=0.002 for 25 mg once daily; nominal p<0.001 for all other dose groups) than the placebo group (9.3%). All statistical testing was performed at the 2-sided 0.05 significance level.

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

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

- Overall, there was no clear evidence of a dose-dependent increase in the occurrence of specific adverse events (AEs) across the JNJ-772421113 groups.
- The proportions of participants who experienced 1 or more AEs were similar in the combined JNJ-77242113 (52.4%) and placebo (51.2%) groups.
- The most frequently reported AEs were in the Infections and infestations system organ class (SOC) and were similar between the combined JNJ-77242113 (30.2%) and placebo (27.9%) groups. The most common AEs by preferred term (PT) in this SOC were COVID-19 (10.8% and 11.6%), nasopharyngitis (7.1% and 4.7%), and upper respiratory tract infection (2.4% and 2.3%) in the combined JNJ-77242113 and placebo groups, respectively. In the Gastrointestinal disorders SOC, AEs were reported in 11.3% of participants in the combined JNJ-77242113 group and 11.6% in the placebo group. Other AEs by PT reported by at least 5% of participants included headache and cough.
- The percentage of participants with 1 or more serious adverse events (SAEs) through the end of study was small, with 3 participants (1.4%) experiencing 1 SAE each. All events were singular in nature and deemed not related to study intervention per the investigator.
- The proportion of participants who discontinued study intervention due to 1 or more AEs was small (n=6). Three out of the 6 events were in the Gastrointestinal SOC (n=1 each: abdominal pain, abdominal discomfort, and nausea). The other 3 events included suicide attempt, weight increase, and transaminases increase (n=1 each).
- Rates of abnormal laboratory test result were generally low and comparable between the treatment groups.
- There were no deaths or malignancies reported.

Human Pharmacokinetics and Immunogenicity

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

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

The PK results 77242113PSO1002 indicate that the exposure (C_{max} and AUC) of JNJ-77242113 increased with dose (100 to 300 mg) in Japanese participants, with no apparent difference in exposure between Japanese and Chinese participants (300 mg). The PK results from this study are also consistent with and comparable to the PK in predominantly white participants in both FIH Study PN-235-01 and the ongoing Study 77242113PSO1003.

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

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

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

Refer to the JNJ-77242113 IB for more information on clinical studies, pharmacokinetic, nonclinical pharmacology, and toxicology.

2.3. Benefit-risk Assessment

Detailed information about the known and expected benefits and risks of JNJ-77242113 may be found in the IB. The list provided in Section 2.3.1 describes the potential risks associated with the blockage of IL-23.

2.3.1. Risks for Study Participation

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
Potential Risks Due to Study Intervention JNJ-77242113		
Hypersensitivity reactions	Exogenous peptides administered orally or systemically have the potential to cause hypersensitivity reactions.	• This potential risk will be explained in the 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 JNJ-77242113 or its excipients will be excluded from the study. • Any participant who develops a serious hypersensitivity reaction such as anaphylaxis must discontinue study intervention (Section 7).
ADA production	Exogenous peptides administered orally or systemically have the potential to induce anti-drug antibodies (ADA) production, which may mediate untoward reactions such as reduced efficacy or hypersensitivity.	• This potential risk will be explained in the ICF and evaluated by measuring ADA and pharmacokinetics (PK) for analysis. • Participants are encouraged to consistently take their study intervention 24 hours apart, as directed.
Infection	Clinical experience with marketed IL-23 pathway blockers includes precautions for infections and tuberculosis (TB).	• This potential risk will be explained in the ICF. • Participants with evidence of active TB will be excluded from the study (Section 5.2). • Participants must agree not to receive a live viral or live bacterial vaccination 4 weeks prior to enrollment in the study or during the study and for 4 weeks after receiving the last dose of study intervention (Section 5.2). Additional guidance is provided for the BCG vaccine in Section 5.2. • Participants will be educated and instructed to seek medical attention if they develop signs or symptoms suggestive of an infection, and investigators are instructed to monitor for signs or symptoms of infections, including TB (Section 8.3.7). • Discontinuation of a participant's study intervention must be strongly considered if the participant develops a serious infection,

Potential Risks of Clinical Significance	Summary of Data/ Rationale for Risk	Mitigation Strategy
		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).

2.3.2. Benefits for Study Participation

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

2.3.3. Benefit-risk Assessment for Study Participation

Taking into account the measures taken to minimize risk to participants of this study, the potential risks identified in association with JNJ-77242113 are justified by the anticipated benefits that may be afforded to participants with GPP and EP.

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Objectives	Endpoints
Primary	
• To evaluate the efficacy of JNJ-77242113 in participants with GPP or EP	• Proportion of participants with GPP who experience treatment success (based on Clinical Global Impression CGI scale according to Japanese Dermatological Association [JDA] total score) at Week 16. • Proportion of participants with EP who experience treatment success (based on CGI scale) at Week 16.
Secondary	
• To further evaluate the efficacy of JNJ-77242113 in participants with GPP or EP	• Proportion of participants with GPP or EP who experience treatment success (for GPP: based on CGI scale according to JDA total score and for EP: based on CGI scale) over time. • Change from baseline in the total score of the JDA severity index for GPP over time. • Change in baseline in severity classification (mild, moderate, severe) of the JDA severity

Objectives	Endpoints
	index for GPP over time. • Change from baseline in body surface area (BSA) of involvement of lesion for EP over time. • Proportion of participants who achieve an Investigator's Global Assessment (IGA) score of cleared (0) or minimal (1) over time. • Proportion of participants who achieve an IGA score of cleared (0) over time. • Percent improvement from baseline in Psoriasis Area and Severity Index (PASI) over time.
• To evaluate the effect of JNJ-77242113 treatment on health-related quality of life (HRQoL) in participants with GPP or EP	• Change from baseline in Dermatology Life Quality Index (DLQI) score over time. • Proportion of participants who achieve a DLQI score of 0 or 1 over time. • Change from baseline in EQ-5D-5L (domain scores and visual analog scale [VAS]) over time.
• To assess the safety and tolerability of JNJ-77242113 in participants with GPP or EP	• Frequency and type of AEs and SAEs.
Exploratory	
• To further explore the efficacy of JNJ-77242113 in participants with GPP	• Change from baseline in components (skin symptoms, systemic symptoms/laboratory findings) of the JDA severity index for GPP over time.
• To further evaluate the effect of JNJ-77242113 on HRQoL in adolescent participants with GPP or EP	• Change from baseline in Children's DLQI (CDLQI) over time. • Change from baseline in Children's DLQI (CDLQI) score 0 or 1 over time.
• To evaluate the PK and immunogenicity of JNJ-77242113	• JNJ-77242113 PK parameters. • Incidence of anti-drug antibodies to JNJ-77242113.
• To explore biomarkers in participants with GPP or EP	• Change from baseline in levels of blood biomarkers.

ESTIMANDS

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

Study Intervention:

Experimental: JNJ-77242113

Population:

- Participants ≥12 years of age with GPP
- Participants ≥12 years of age with EP

Variable:

Binary response variables for the primary endpoints:

- Treatment success for GPP: a responder (participant with treatment success defined as at least "Minimally Improved" rating in CGI scale for GPP according to JDA total score) at Week 16.
- Treatment success for EP: a responder (participant with treatment success defined as at least "Minimally Improved" rating in CGI scale for EP) at Week 16.

Intercurrent Event (ICE):

Intercurrent event	Corresponding Strategy
Discontinuation of study intervention for any reason prior to Week 16.	Treatment Policy: observed data will be used regardless of whether or not this ICE had occurred.

Population Level Summary:

- Proportion of participants with GPP who experience treatment success at Week 16.
- Proportion of participants with EP who experience treatment success at Week 16.

Refer to Section 8 for evaluations related to endpoints.

HYPOTHESIS

The primary hypothesis of this study is that JNJ-77242113 is efficacious in treating GPP or EP as assessed by proportion of participants with GPP or EP who experience treatment success defined as at least "Minimally Improved" rating in CGI scale for GPP (according to JDA total score) and EP, respectively at Week 16.

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 3, open-label, multicenter study to evaluate the efficacy and safety of JNJ-77242113 for the treatment of participants with GPP or EP.

A target of 16 (GPP, n=8; EP, n=8) participants will be enrolled in this study. All participants will take JNJ-77242113 from Week 0.

The total duration of this study for each participant is approximately 165 weeks, which includes: a ~5-week screening period, a 52-week treatment period, a 104-week long-term extension treatment period (LTE), and a 4-week safety follow-up period.

All the participants will receive JNJ-77242113 200 mg once daily for 52 weeks. Participants completing Week 52 visit may be eligible to enroll in the LTE. The LTE will begin at the end of Week 52 and will continue until Week 156. All the participants will have a 4-week safety follow-up period at the end of the treatment period or after the last dose of study intervention.

Efficacy, safety, PK, immunogenicity, and biomarkers will be assessed according to the Schedule of Activities (SoA) (Section 1.3). In addition, there will be 2 optional substudies for participants who provide consent. Sample collections for these substudies include a pharmacogenomic blood sample and photograph collection.

The first database lock (DBL) will occur when all participants complete Week 24 of the study. Additional DBLs may occur after Week 24 to support regulatory submissions and scientific disclosures. Details of the DBLs will be described in the statistical analysis plan (SAP), as necessary.

No Data Monitoring Committee will be commissioned for this study.

A diagram of the study design is provided in Section 1.2.

4.2. Scientific Rationale for Study Design

Study Design

The open-label study design seems appropriate for this study considering GPP and EP are rare and severe forms of psoriasis that require continuous access of an effective treatment and frequent hospitalization for the management of complications. The endpoints and the treatment duration selected for the study are generally considered standard for GPP or EP studies (Imafuku 2016, Sano 2018, Yamanaka 2023).

DNA and Biomarker Collection

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

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

evaluate the PD of JNJ-77242113 and aid in evaluating the intervention-clinical response relationship.

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

Health Economics Data Collection

The EQ-5D-5L will be used in this study to evaluate health economics for participants with GPP or EP.

4.2.1. Participant Input into Design

In setting the strategy for the treatment of GPP and EP, patients were engaged early, systematically, and directly across important aspects of the drug development process.

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

- The once daily dose regimen was chosen to increase convenience compared with twice daily regimen.
- Lifestyle considerations were modified based on patient feedback related to sun exposure.
- The SoA was modeled to ensure the number of visits, frequency of visits, and tests within each visit were manageable for a patient with GPP or EP.

The results of the study may be made available to all the participants through a plain language summary. A technical summary of results will be made available on clinicaltrials.gov and/or clinicaltrialsregister.eu and/or other national registries at the conclusion of the study according to local standards/restrictions.

4.2.2. Study-specific Ethical Design Considerations

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

The primary ethical concern for the participants is that the study intervention may not provide benefit in relieving the signs and symptoms of GPP or EP as anticipated, in the absence of suitable alternative therapy. Participants will be discontinued from study intervention if the investigator considers it is in the best interest of the participant (Section 7.1).

The total blood volume to be collected (up to approximately 320 mL) 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 blood donation rule by Japanese Red Cross Society (400 mL of blood for donation). For more details regarding blood collection, see Blood Sample Collection in Section 8.

4.3. Justification for Dose

The JNJ-77242113 dose selection for the Phase 3 studies in psoriasis is CCI [redacted] Therefore, considering the CCI [redacted] a dose of JNJ-77242113 200 mg once daily has been selected for the Phase 3 efficacy and safety studies. The CCI [redacted] in the rat and monkey studies.

The dose and regimen of JNJ-77242113 selected for this Phase 3 study, CCI [redacted] will maximize the likelihood of a positive study outcome, and are supported by human safety and tolerability data from the Phase 1 and Phase 2 studies and the toxicology margins. Furthermore, the same dose of JNJ-77242113 is being evaluated in ongoing Phase 3 studies in participants with plaque psoriasis.

4.4. End of Study Definition

End of Study Definition

The end of study is considered as the last scheduled study assessment shown in the SoA (Section 1.3) for the last participant in the study. The final data from the study site will be sent to the sponsor (or designee) after completion of the final participant assessment at that study site, in the time frame specified in the Clinical Trial Agreement.

Participant Study Completion Definition

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

5. STUDY POPULATION

Screening for eligible participants will be performed within 5 weeks before first dose administration of the study intervention. Refer to Section 5.4 for conditions under which the repeat of any screening procedures is allowed.

The inclusion and exclusion criteria for enrolling participants in this study are described below. If there is a question about these criteria, the investigator must consult with the appropriate sponsor representative and resolve any issues before enrolling a participant in the study. Waivers are not allowed. For a discussion of the statistical considerations of participant selection, refer to Section 9.5.

5.1. Inclusion Criteria

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

Age

1. The study participant has ≥12 years of age at the Screening Visit.

Type of Participant and Disease Characteristic(s)

2. The study participant has a diagnosis of GPP or EP at screening.

    a. for GPP, a diagnosis must be classified based on the criteria for diagnosis of GPP by the Japanese Dermatological Association (Appendix 8: Diagnostic Criteria of Generalized Pustular Psoriasis)

    b. for EP, has a history of plaque-type psoriasis. In addition, has an involved BSA of lesion ≥80% at baseline.

3. Candidate for phototherapy or systemic treatment for psoriasis (either naïve or history of previous treatment).

Concomitant Therapy

4. a. In case of receiving methotrexate (MTX) or cyclosporine, the participant must be on stable dose from 2 weeks before the first administration of study intervention with doses of MTX <20 mg/week OR cyclosporine ≤5 mg/kg/day.

    Note: Participants must not be on both MTX and cyclosporine at the same time from 2 weeks before the first administration of study intervention.

    b. In case of receiving retinoid, the participant must be on stable dose from 2 weeks before the first administration of study intervention.

Weight

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

Sex and Contraceptive/Barrier Requirements

6. A female participant of childbearing potential must have a negative highly sensitive serum pregnancy test (β-human chorionic gonadotropin [β-hCG]) at screening and have a negative urine pregnancy test at Week 0 prior to administration of study intervention.

7. A female participant must agree not to be pregnant, breastfeeding, or planning to become pregnant while enrolled in this study or within 4 weeks after the last dose of study intervention.

8. A female participant must be

    a. not of childbearing potential

    OR

    b. of childbearing potential and

    - Practicing a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly) and agrees to remain on a highly effective method while receiving study intervention and until 4 weeks after last dose – the end of relevant systemic exposure. 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 Appendix 4: Contraceptive and Barrier Guidance.

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

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

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

11. 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, a condom [with spermicidal foam/gel/film/cream/suppository if available in their locale]), during the study and for at least 90 days after receiving the last administration of study intervention. Male participants must also be advised of the benefit for a female partner to use a highly effective method of contraception as condom may break or leak.

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

Informed Consent

13. The study participant must sign an ICF (or their legally acceptable representative must sign) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.

    For participants under the legal age of consent, parent(s) (preferably both if available or per local requirements) (or their legally acceptable representative) must sign an ICF indicating that they understand the purpose of, and procedures required for, the study and is/are willing to allow the child to participate in the study. Per local requirements, assent is also required of children capable of understanding the nature of the study and once children or minors have reached the legal age of consent, they may be required to sign the ICF as described in Informed Consent Process in Appendix 2: Regulatory, Ethical, and Study Oversight Considerations.

14. The study participant must sign the ICF (or their legally acceptable representative must sign) if the participant agrees to provide an optional DNA sample or photographs for research. Refusal to give consent for the optional DNA research sample does not exclude a participant from participation in the study.

    For participants under the legal age of consent, parent(s) (preferably both if available or per local requirements) (or their legally acceptable representative) must sign the ICF for the substudies if they agree to the child providing an optional DNA sample or photographs for research. Per local requirements, assent is also required of children capable of understanding the nature of the study and once children or minors have reached the legal age of consent, they may be required to sign the ICF as described in the Informed Consent Process and Assent in Appendix 2: Regulatory, Ethical, and Study Oversight Considerations.

15. The study participant 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:

Medical Conditions

1. The study participant has a total score of JDA severity index for GPP ≥14 at baseline if participants have a diagnosis of GPP.

2. The study participant has a differential diagnosis of the erythroderma (eg, erythroderma caused by lymphoma or drug eruption) other than EP.

3. The study participant has a history of or current diagnosis or signs or symptoms of severe, progressive, or uncontrolled liver, renal; cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances.

4. The study participant has a history of amyloidosis.

5. Known allergies, hypersensitivity, or intolerance to JNJ-77242113 or its excipients (refer to the IB).

6. The study participant had major surgery, (eg, requiring general anesthesia) within 8 weeks before screening, or will not have fully recovered from surgery, or has surgery planned during the time the participant is expected to participate in the study.

   Note: Participants with planned surgical procedures to be conducted under local anesthesia may participate.

7. The study participant had transplanted organ (with exception of a corneal transplant >12 weeks before the first dose administration of study intervention).

8. All participants with:

   - suicidal ideation in the 26 weeks prior to screening that may be defined as a C-SSRS rating of: Wish to be Dead, Non-Specific Active Suicidal Thoughts, or Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act and is considered to be at risk by the investigator.

   Participants ≥18 years if age with:

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

   Participants ≥12 to <18 years of age with:

   - suicidal ideation or non-suicidal self-injurious behavior in the 26 weeks prior to screening that may be defined as a C-SSRS rating of: Suicidal Ideation with Intention to Act, Suicidal Ideation with Specific Plan and Intent, or non-suicidal self-injurious behavior.

- any suicidal behavior in their lifetime that maybe defined as a C-SSRS rating at screening of: Actual suicide attempt, interrupted suicide attempt, aborted suicide attempt, or preparatory behaviors for making a suicide attempt.

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

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

Prior/Concomitant Therapy

11. The study participant has previously received JNJ-77242113.

12. The study participant has experienced primary efficacy failure (no response within 16 weeks) to 1 or more agents directly targeting IL-23 or has had a clinically significant AE to 1 or more agents directly targeted to IL-23.

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

	Prohibited Medication or Class of Medications or Therapy	**Restriction Duration** (See Section 6.9 for more information)
13.	Agents that deplete B-cells (eg, rituximab, alemtuzumab)	26 weeks prior to the first administration of study intervention
14.	Agents targeting TNFα (eg, infliximab etanercept, adalimumab, golimumab, certolizumab pegol)	8 weeks prior to the first administration of study intervention
15.	Any biologic therapy including (For agents targeting TNFα, please see Exclusion Criterion 14): a. IL-23-inhibitors: eg, guselkumab, tildrakizumab, risankizumab (Additional exclusions apply, see Exclusion Criteria 11 and 12). b. IL-17 inhibitors: eg, secukinumab, brodalumab, ixekizumab c. IL-12/23 inhibitors: eg, ustekinumab, briakinumab d. IL-36: eg, spesolimab e. natalizumab f. belimumab g. abatacept h. visilizumab	12 weeks prior to the first administration of study intervention

16.	Any experimental or investigational antibody or biological therapy	12 weeks or 5 half-lives, whichever is longer
17.	Granulocyte and monocyte apheresis (GMA)	12 weeks prior to the first administration of study intervention
18.	Systemic immunomodulating treatments including but not limited to: • azathioprine, corticosteroids, cyclophosphamide, tofacitinib, apremilast, deucravacitinib Other therapeutic procedures: • phototherapy Systemic medications that could affect psoriasis evaluations including, but not limited to: • herbal treatments, or traditional Taiwanese, Korean, or Chinese medicines Nonbiologic experimental therapies or investigational agents	4 weeks prior to the first administration of study intervention
19.	Topical medications/treatments that could affect psoriasis or efficacy evaluations including, but not limited to e.g., • Corticosteroids*, calcineurin inhibitors, tar, anthralin, calcipotriene, tazarotene, methoxsalen, trimethylpsoralen, fumarate, PDE4 inhibitors, topical JAK inhibitors, aryl hydrocarbon receptor-modulating agents • Shampoos that contain corticosteroids, coal, tar, or vitamin D3 analog • Herbal treatments or traditional Taiwanese, Korean, or Chinese medicines *Exception: Weak or medium ranked topical corticosteroid on face, palms, soles, and intertriginous areas is allowed with restriction use	2 weeks prior to the first administration of study intervention

within 24 hours prior to study visits.	
20. Live virus or bacterial vaccine	4 weeks (or longer if required per vaccine package insert) prior to first administration of study intervention
21. BCG vaccination	1 year prior to the first administration of study intervention

Diagnostic Assessments

22. Screening laboratory test results within the following parameters:

    a. Hemoglobin: <10 g/dL (SI: <100 g/L)
    b. White blood cells: $<3.5\times10^3/\mu L$ (SI: <3.5 GI/L)
    c. Neutrophils: $<1.5\times10^3/\mu L$ (SI: <1.5 GI/L)
    d. Platelets:$<100\times10^3/\mu L$ (SI: <100 GI)
    e. eGFR: <45 mL/min/1.73 m^2
    f. Aspartate aminotransferase (AST): >2×ULN
    g. Alanine aminotransferase (ALT): >2×ULN

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

23. The study participant tests positive for the following infections at screening:

    a. hepatitis B virus (HBV) tests (Appendix 7: Hepatitis B and Hepatitis C Virus Screening for instructions)
    b. hepatitis C antibody test (seropositive for antibodies and positive confirmatory test for hepatitis C virus (HCV), ie, HCV polymerase chain reaction (PCR) [Appendix 7: Hepatitis B and Hepatitis C Virus Screening])
    c. human immunodeficiency virus (HIV) antibody

Infections or Predisposition to Infections

24. History of chronic or recurrent infectious disease, including but not limited to chronic renal infection, chronic chest infection (eg, bronchiectasis), recurrent urinary tract infection (recurrent pyelonephritis or chronic non-remitting cystitis), severe fungal infection (mucocutaneous candidiasis), or open, draining, or infected skin wounds or ulcers.

25. History of an infected joint prosthesis or has received antibiotics for a suspected infection of a joint prosthesis, if that prosthesis has not been removed or replaced.

26. Known or suspected immunodeficiency, including history of invasive opportunistic infections (eg, active tuberculosis [TB], nontuberculous mycobacterial infection,

histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis, aspergillosis, HIV) or otherwise recurrent infections of abnormal frequency or prolonged duration, despite infection resolution, suggesting an immune-compromised status, as judged by the investigator.

27. Serious infection (eg, disseminated herpes zoster, sepsis, pneumonia, or pyelonephritis), or has been hospitalized or received intravenous (IV) antibiotics for an infection during the 8 weeks before screening.

28. The study participant has tested positive for or been exposed to COVID-19 within 4 weeks prior to the first dose of study intervention.

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

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

29. The study participant meets ANY of the following tuberculosis (TB) screening criteria.

    Note: Interferon gamma release assay (IGRA) testing with T-SPOT®TB (or QuantiFERON-TB®).

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

    b. have a history of untreated latent TB prior to screening. An exception is made for participants who are currently receiving treatment or will initiate treatment for latent TB at least 3 weeks prior to first administration of study intervention.

    Note: For participants with a history of treated latent TB, there must be documentation of appropriate treatment prior to the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous TB treatment and provide appropriate documentation. IGRA testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB.

    If the presence of latent TB is established, appropriate treatment has to be initiated at least 3 weeks before the first administration of study intervention.

    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 8 weeks 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 at least 3 weeks prior to the first administration of study intervention.

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

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

e. The study participant has a chest radiograph or chest computed tomography (CT) within 12 weeks prior to the first administration of study intervention that shows abnormalities suggestive of active or inactive TB.

Malignancy or Increased Potential of Malignancy

30. The study participant currently has a malignancy or history of malignancy within 5 years before screening (exceptions are a non-melanoma skin cancer or cervical carcinoma in situ that has been adequately treated with no evidence of recurrence for at least 12 weeks before the first study intervention administration).

31. The study participant has a history of lymphoproliferative disease, including lymphoma; a history of monoclonal gammopathy of undetermined significance; or signs and symptoms suggestive of possible lymphoproliferative disease, such as splenomegaly or significant lymphadenopathy.

Other Exclusions

32. 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.

33. 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 (eg, psychiatric disorders who cannot evaluate PRO properly).

NOTE: Investigators must ensure that all study enrollment criteria have been met at screening. If a participant's clinical status changes (including any available laboratory results or receipt of additional medical records) after screening but before the first dose of study intervention is given such that the participant no longer meets all eligibility criteria, then the participant must be

excluded from participation in the study. Section 5.4, describes options for retesting. The required source documentation to support meeting the enrollment criteria are noted in Appendix 2: Regulatory, Ethical, and Study Oversight Considerations.

5.3. Lifestyle Considerations

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

1. Recommended to be up to date on all age-appropriate vaccinations prior to screening per routine medical guidelines. It is strongly recommended that participants will have completed a locally approved (or emergency use-authorized) COVID-19 vaccination regimen at least 2 weeks prior to study-related visits or procedures. Study participants should follow applicable local vaccine labeling, guidelines, and standards-of-care for participants receiving immune-targeted therapy when determining an appropriate interval between vaccination and study enrollment (Section 6.9.1.3).
2. Refer to Section 6.9 for details regarding prohibited and restricted therapy during the study.
3. Agree to take study interventions and comply with fasting requirements (Section 6.1).
4. Agree to fast for at least 6 hours prior to lipid panel blood sample collection unless medically contraindicated (Section 1.3).
5. Strenuous exercise (eg, body building, long distance training [running/cycling]) may affect study specified assessments and safety laboratory results; for this reason, strenuous exercise should be avoided within 2 to 3 days before all planned study visits where laboratory tests are collected.
6. Agree to 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 study participation.
7. For adolescent participants, who are not of legal age of consent, a legal guardian or primary caregiver is recommended to:
    a. Accompany the participant to the study site on each assessment day according to the Section 1.3.
    b. Accurately and reliably dispense study intervention as directed.

5.4. Screen Failures

Participant Identification, Enrollment, and Screening Logs

The investigator agrees to complete a participant identification and enrollment log to permit easy identification of each participant during and after the study. This document will be reviewed by the sponsor study site contact for completeness. This study will not use Interactive Web Response System (IWRS).

The participant identification and enrollment log will be treated as confidential and will be filed by the investigator in the study file. To ensure participant confidentiality, no copy will be made. All reports and communications relating to the study will identify participants by participant

identification and age at initial informed consent. In cases where the participant is not 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 (screen failure) may be rescreened. Medical Monitor's approval is required prior to rescreening. Rescreened participants must be assigned new participant numbers, undergo the informed consent process, and meet all criteria as defined in Section 5.

Retesting

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

5.5. Criteria for Temporarily Delaying Enrollment/Administration of Study Intervention

Not applicable for this study.

6. STUDY INTERVENTION AND CONCOMITANT THERAPY

6.1. Study Intervention Administered

For adult participants:

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

For adolescent participants:

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

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

If adolescent participants have difficulty swallowing tablets, the study intervention may be CCI It may take CCI

CCI [redacted]

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

Designation	**Product**
Investigational Medicinal Product	JNJ-77242113
Non-investigational Medicinal Product(s) (NIMP)/Auxiliary Medicinal Product(s) (AxMP)	Not applicable

Study intervention administration must be captured in the source documents and the case report form (CRF). Study site personnel will instruct participants on how to store study intervention for at-home use as indicated for this protocol.

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

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

Description of Interventions

Intervention Name	JNJ-77242113
Intervention Description	film-coated tablet containing 200 mg JNJ-77242113
Type	Drug
Dose Formulation	Tablet
Unit Dose Strength	200 mg per tablet
Dosage Level	1×200 mg tablet once daily
Route of Administration	Oral
Use	Experimental
Investigational Medicinal Product (IMP)	Yes
Non-Investigational Medicinal Product/Auxiliary Medicinal Product (NIMP/AxMP)	No
Sourcing	Provided centrally by the sponsor
Packaging and Labeling (Labels will contain information to meet the applicable regulatory requirements)	Study intervention will be provided in blister packs. Each pack will be labeled as required per local requirements.
	The blisters are packaged in child resistant Dosepaks.
Delivery Instructions	Swallow tablet whole. Given with 240 mL water. The tablet should not be broken or crushed.
Fasting Requirement	At least 2 hours before taking the study intervention and for at least 30 minutes after taking the study intervention.
Current/Former Names or Aliases	JNJ-77242113 and previously referred to as aPi2915, PN21235, PN-21235, and PN-235.

6.2. Preparation/Handling/Storage/Accountability

Preparation/Handling/Storage

All study intervention must be stored at controlled temperatures ranging from 1°C to 30°C.

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

Accountability

The investigator is responsible for ensuring that all study intervention received at the site is inventoried and accounted for throughout the study. The dispensing of study intervention to the participant and the return of study intervention from the participant (if applicable), must be documented on the intervention accountability form. Participants, or their legally acceptable representatives where applicable, must be instructed to return all original containers, whether empty or containing study intervention. All study intervention will be stored and disposed of according to the sponsor's instructions. Study site personnel must not combine contents of the study intervention containers.

Study intervention must be handled in strict accordance with the protocol and as indicated on 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.

Study intervention must be dispensed under the supervision of the investigator or a qualified member of the study site personnel, or by a hospital/clinic pharmacist. Study intervention will be supplied only to participants or their legally acceptable representatives where applicable 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 Site Investigational Product Procedures Manual.

6.3. Assignment to Study Intervention

Intervention Allocation

Randomization will not be used in this study as this is a single-arm study. All the participants will be assigned to only JNJ-77242113.

6.4. Blinding, Masking

As this is an open-label study, blinding procedures are not applicable.

6.5. Study Intervention Compliance

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

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

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

Study intervention compliance will be further detailed in the SAP.

6.6. Dose Modification

Not applicable for this study.

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

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

6.8. Treatment of Overdose

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

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

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

- Contact the medical monitor immediately.
- Closely monitor the participant for AE/SAE and laboratory abnormalities.
- Document the quantity of the excess dose as well as the duration of the overdosing in the source documents.
- Evaluate the participant to determine, in consultation with the medical monitor, whether study intervention must be interrupted.

- Obtain a plasma sample for PK analysis if requested by the medical monitor (determined on a case-by-case basis).

6.9. Prior and Concomitant Therapy

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

Concomitant therapies must be recorded throughout the study beginning with signing of the ICF through the last study visit. Concomitant therapies must also be recorded beyond the last study visit in conjunction with SAEs that meet the criteria outlined in Section 8.4.1.

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

Any questions regarding treatment with concomitant medication during the study should be directed to the sponsor. The sponsor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered.

6.9.1. Prohibited Therapy

All experimental therapies or new investigational interventions (except for JNJ-77242113), including therapies for psoriasis or other conditions, must be discontinued prior to the first dose administration of study intervention per Exclusion Criteria (Section 5.2) and remain prohibited during the study (until ET Visit for participants who terminate early or until last study intervention administration visit). For guidance regarding the COVID-19 vaccine see Section 6.9.1.3.

The sponsor's medical monitor must be notified in advance (or as soon as possible thereafter) of any instances in which prohibited therapies are administered. The participant may be required to discontinue study intervention (Section 7.1.3).

6.9.1.1. GPP/EP Concomitant Medications

Topical Therapy

Shampoos (containing salicylic acid only) and bland emollients are allowed on all body regions but should not be used within 24 hours before any study visit. Non-medicated shampoos may be used on the day of the study visit.

Other topical therapies that could affect psoriasis evaluations including but not limited to (eg, topical corticosteroids*, topical calcineurin inhibitors, tar, anthralin, calcipotriene, tazarotene, methoxsalen, trimethylpsoralens, fumarate, PDE4 inhibitors, topical JAK inhibitors, aryl hydrocarbon receptor-modulating agents; shampoos that contain corticosteroids, coal, tar or vitamin D3 analogs; and herbal treatments and traditional Taiwanese, Korean, or Chinese medicines) are not permitted from Week 0 through Week 52.

*Exception: weak or medium ranked topical corticosteroid on face, palms, soles, and intertriginous areas with stable use is allowed with restriction use within 24 hours prior to study visits.

After Week 52, topical therapies are permitted for treatment of GPP or EP.

Phototherapy or Systemic Therapy

The use of phototherapy or systemic medications (other than MTX, retinoid, and cyclosporine) that could affect psoriasis or the efficacy evaluation, is not permitted at any time during the study (until ET Visit for participants who terminate early or until last study intervention administration visit).

These medications include, but are not limited to,

- those targeted for reducing TNFα (including but not limited to infliximab, etanercept, or adalimumab).
- drugs targeted for reducing IL-12/23, IL-17, IL-23, IL-36 (including but not limited to ustekinumab, guselkumab, tildrakizumab, secukinumab, risankizumab, ixekizumab, brodalumab, or spesolimab).
- 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 efficacy evaluation.
- antimalarial agents.
- herbal treatments.
- traditional Taiwanese, Korean, or Chinese medicines.

MTX, Retinoids, or Cyclosporine for Treatment of Psoriasis

In case of receiving retinoids, 2 weeks with stable dose before the first administration of study intervention is necessary, and any change in the dose should be avoided through Week 52. Dose can be reduced; however, it cannot be re-escalated once it is reduced. After Week 52, there is no limitation on retinoid.

In case of receiving MTX (<20 mg/week) or cyclosporine (≤5 mg/kg/day) at screening, at least 2 weeks with stable dose before the first administration of study intervention is necessary and this stable dose should continue through Week 16. In case of participants with confirmed clinical improvement, dose reduction is allowed before Week 16, but dose cannot be re-escalated. After Week 16, cyclosporine should be tapered off and discontinued by Week 32. If the condition of a participant worsens after tapering cyclosporine, the investigators should consider discontinuation of study drug and pursue alternative treatment options. After Week 16, MTX should be tapered off and an attempt should be made to discontinue MTX by Week 32. Minimal dose of MTX should

be maintained throughout the study if the participant is not able to discontinue MTX completely. Participants are not permitted to receive both MTX and cyclosporine at the same time during the study.

6.9.1.2. Concomitant Medications for Indications Other Than Psoriasis

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 must be recorded in the CRF.

The use of stable doses of nonsteroidal anti-inflammatory drugs (NSAIDs) is allowed during the treatment phase. However, disease modifying agents such as sulfasalazine, or intramuscular gold (MTX is excluded) are prohibited during the study (until ET Visit for participants who terminate early or until last study intervention administration visit).

The use of systemic corticosteroids for indications other than psoriasis should be limited to situations for which, there are no adequate alternatives in the opinion of the treating physician. Systemic corticosteroids should be used on a short-term basis, preferably for ≤2 weeks. Longer term and multiple use of corticosteroids should be discussed with the sponsor or designee and may require discontinuation of study intervention. Inhaled, otic, ocular, nasal, or other routes of mucosal delivery of corticosteroids are allowed throughout the study. After Week 52, intra-articular corticosteroids are allowed for indications other than psoriasis. Vitamin D3 and analogs for dietary supplementation are permitted.

6.9.1.3. Vaccines

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

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

If a participant discontinues study intervention for any reason before the end of the study, then the ET Visit assessments must be obtained (Section 1.3) as soon as possible. Study intervention assigned to the participant who discontinued study intervention may not be assigned to another participant (Section 6.2). Additional participants will not be entered in this study. Participants who discontinue study intervention but do not terminate study participation will continue to return for protocol specified procedures and evaluations. Discontinuation from study intervention does not mean that the participant is required to withdraw informed consent and leave the study.

7.1.1. Liver Chemistry Stopping Criteria

Stopping of study intervention for abnormal liver tests is required by the investigator when a participant meets one of the conditions outlined in Appendix 5: Liver Safety: Suggested Actions and Follow-up Assessments.

7.1.2. Temporary Interruption (Withholding) of Study Intervention

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

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

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

7.1.3. Permanent Discontinuation of Study Intervention

A participant's study intervention must be permanently discontinued if:

- The participant withdraws consent or assent to receive study intervention.
- The investigator believes that for safety reasons or tolerability reasons (eg, AE) it is in the best interest of the participant to discontinue study intervention.
- Participant meets the Sampson criteria for anaphylaxis (Sampson 2006) following study intervention administration.
- The participant becomes pregnant or plans a pregnancy during the study period. Refer to Appendix 4: Contraceptive and Barrier Guidance.
- Participant initiates protocol-prohibited medications, treatments, or interventions (outlined in Section 6.9) that have an impact on psoriasis efficacy evaluations at the discretion of the medical monitor.
- Participant develops a malignancy including squamous cell skin cancer. Consideration may be given to allow participants, who develop ≤2 basal cell skin cancers and who are adequately treated with no evidence of residual disease, to continue to receive study intervention.
- The participant develops a systemic opportunistic infection during the study period.
- Participant develops a recurrent or chronic serious infection during the study period.
- The participant is deemed ineligible according to the following TB screening criteria:
  - 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 a chest radiograph with evidence of current active TB and/or a positive IGRA 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 IGRA results should be handled as in Section 8.3.7. Participants with persistently indeterminate IGRA results may continue without treatment for latent TB if active TB is ruled out, their chest radiograph (both posterior-anterior and lateral views, substitutable with chest CT) shows no abnormality suggestive of TB (active or old, inactive TB) and the participant has no additional risk factors for TB as determined by the investigator and medical monitor.
  - A participant receiving treatment for latent TB discontinues this treatment prematurely or is noncompliant with the therapy.
- Substantial noncompliance with study visits schedule (Section 1.3) or study intervention administration (Section 6.5). Consideration for discontinuation must be discussed with the medical monitor.
- Hepatic or liver test abnormality outlined in Appendix 5: Liver Safety: Suggested Actions and Follow-up Assessments
- Participant reports suicidal ideation by answering "Yes" to Question 4 or 5 on the C-SSRS, or documents suicidal behavior on the C-SSRS at any time during the study and is considered at risk by the investigator after evaluation by a mental health professional. The investigator should contact the medical monitor for discussion.
- Sponsor decision.

7.2. Participant Discontinuation/Withdrawal From the Study

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

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

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

Withdrawal of Consent

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

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

7.2.1. Withdrawal From the Use of Research Sample

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 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 genetic (DNA) analyses 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 Sample While Remaining in the Main 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 Appendix 2: Regulatory, Ethical, and Study Oversight Considerations). In such a case, samples will be destroyed after they are no longer needed for the clinical study. Details of the sample retention for research are presented in the ICF for optional research samples.

7.3. Lost to Follow-up

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

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

- The study site personnel must attempt to contact the participant to reschedule the missed visit as soon as possible, to counsel the participant on the importance of maintaining the assigned visit schedule, to ascertain whether the participant wishes to or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee must make every reasonable effort to regain contact with the participant (where possible, 3 telephone calls, 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.
- Site personnel, or an independent third party, will attempt to collect the vital status of the participant within legal and ethical boundaries for all participants enrolled, including those who did not get study intervention. Public sources may be searched for vital status information.

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

8. STUDY ASSESSMENTS AND PROCEDURES

Overview

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

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

If multiple assessments are scheduled for the same timepoint, it is recommended that procedures be performed in the following sequence: ECGs should precede vital signs and both procedures should be completed prior to any invasive procedure. Vital signs should be recorded from the opposite arm from which blood samples are being taken.

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

Blood Sample Collection

The total blood volume to be collected from each participant through the duration of the study will be approximately 320 mL (this total includes the optional blood sampling).

Repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.

Sample Collection and Handling

The actual dates and times of sample collection must be recorded in the CRF or laboratory requisition form.

Refer to the SoA (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.

Study-Specific Materials

The investigator will be provided with the following supplies:

- Investigator site file (includes protocol and IB)
- Photography manual
- Laboratory kits
- ClinRO scales
- PRO scales
- eCRF completion instructions

8.1. Administrative and General/Baseline Procedures

8.1.1. Physical Examinations

Full or Targeted Physical Examination

Physical examinations will be performed by the investigator or designated physician, nurse practitioner or physician assistant as specified in the SoA (Section 1.3). Targeted physical exams will include a skin examination, general examination, and any other organ system examination based on clinical judgment of the participant's presenting complaints or symptoms. Any new, clinically significant finding (in the opinion of the investigator) must be captured as an AE. In addition, resolution of any abnormal findings during the study will be noted in the source document.

Height and Weight

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

8.2. Efficacy Assessments

Efficacy evaluations chosen for this study are consistent with those utilized to evaluate other therapies for psoriasis. Investigator assessments (ClinROs) and PROs will be used to assess efficacy in this study per the SoA (Section 1.3) and listed below.

ClinROs

- CGI scale
- JDA severity index (only for participants with GPP)
- BSA of involvement of lesion (only for participants with EP)
- IGA
- PASI

PROs

- DLQI for adult participants (≥18 years of age on the first date of the Screening Visit)
- EQ-5D-5L (domain scores and VAS)
- CDLQI for adolescent participants (≥12 years and <18 years of age on the first date of the Screening Visit)

The PRO instrument will be provided in the local language in accordance with local guidelines.

The PRO instrument will be available for regulators and for IRB/IEC submissions and will be provided separately in a companion manual with the instruments that will be submitted with the protocol.

The PRO and AE data will not be reconciled with each other.

Photographs (Optional)

Photography will be conducted to record skin lesions at each visit indicated in the SoA (Section 1.3). The details such as how to take photos of the lesion site are shown in the photography manual.

8.2.1. Clinician-reported Outcomes

8.2.1.1. Clinical Global Impression Scale

The CGI scale is a brief clinician-rated instrument. The CGI scale has proved to be a robust measure of efficacy in many clinical drug trials, and is easy and quick to administer, provided that the clinician knows the patient well. The CGI has 5 categories (Very much improved [1], Much improved [2], Minimally improved [3], No change [4], Worsened [5]) in this study. For GPP, the rating of the CGI scale is based on JDA severity index and for EP, the rating will be as provided in the study manual. Evaluation for CGI will include comparison to the previous assessment at screening, comparison to screening assessment at Week 0, and comparison to Week 0 assessment for all other visits from Week 2.

8.2.1.2. Japanese Dermatological Association Severity Index

The JDA severity index for GPP consists of area of erythema with pustules, area of erythema (total), area of edema, fever, WBC, CRP, and serum albumin (provided in the study manual). The total score of JDA severity index for GPP ranges between 0 and 17 (0=best, 17=worst). Area of

erythema with pustules, area of erythema (total), and area of edema are rated as 0 to 3. Fever, WBC, CRP, and serum albumin are rated as 0 to 2 (Iwatsuki 2010).

8.2.1.3. Body Surface Area

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

8.2.1.4. 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 (Fredriksson 1978) (provided in the study manual). In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities. Each of these areas is assessed and scored separately for erythema, induration, and scaling, which are each rated on a scale of 0 to 4 and extent of involvement on a scale of 0 to 6. The PASI produces a numeric score that can range from 0 to 72. A higher score indicates more severe disease.

8.2.1.5. 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) (provided in the study manual).

8.2.2. Participant-reported Outcomes

8.2.2.1. Dermatology Life Quality Index

The DLQI will be utilized in the adult population and is a dermatology specific health-related quality of life (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 (provided in the study manual). The total score ranges from 0 to 30 with a higher score indicating greater impact on HRQoL.

8.2.2.2. EuroQol 5-Dimension 5 Level Questionnaire

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

has endpoints labeled "best imaginable health state" and "worst imaginable health state" anchored at 100 and 0, respectively. Participants are asked to indicate how they rate their own health by indicating the point on the EQ-VAS which best represents their own health on that day (EuroQol 1990; Herdman 2011; Janssen 2013).

8.2.2.3. Children's Dermatology Life Quality Index

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

8.2.3. Endpoints

8.2.3.1. Primary Endpoints

- Proportion of participants with GPP who experience treatment success at Week 16. Treatment success for GPP is defined as at least "Minimally Improved" rating in CGI scale (according to JDA total score) at Week 16.
- Proportion of participants with EP who experience treatment success at Week 16. Treatment success for EP is defined as at least "Minimally Improved" rating in CGI scale at Week 16.

8.2.3.2. Secondary Endpoints

- Proportion of participants with GPP or EP who experience treatment success (for GPP: based on CGI scale according to JDA total score and for EP based on CGI scale) over time.
- Change from baseline in the total score of the JDA severity index for GPP over time.
- Change from baseline in in severity classification (mild, moderate, severe) of the JDA severity index for GPP over time.
- Change from baseline in BSA of involvement of lesion for EP over time.
- Proportion of participants who achieve an IGA score of cleared (0) or minimal (1) over time.
- Proportion of participants who achieve an IGA score of cleared (0) over time.
- Percent improvement from baseline in Psoriasis Area and Severity Index (PASI) over time.
- Change from baseline in DLQI score over time.
- Proportion of participants who achieve a DLQI score of 0 or 1 over time.
- Change from baseline in EQ-5D-5L (domain scores and VAS) over time.
- Frequency and type of AEs and SAEs.

8.2.3.3. Exploratory Endpoints

- Change from baseline in components (skin symptoms, systemic symptoms/laboratory findings) of the JDA severity index for GPP over time.
- Change from baseline in CDLQI over time.
- Change from baseline in CDLQI score 0 or 1 over time.
- JNJ-77242113 PK parameters.
- Incidence of anti-drug antibodies to JNJ-77242113.
- Change from baseline in levels of blood biomarkers.

8.3. Safety Assessments

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

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

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.

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

8.3.1. Vital Signs

Temperature (axillary), pulse/heart rate, respiratory rate, and blood pressure will be assessed.

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

8.3.2. Electrocardiograms

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

Details regarding collection of ECGs are available in the site manual.

8.3.3. Clinical Safety Laboratory Assessments

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

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

8.3.4. Pregnancy Testing

Both serum and urine pregnancy testing will be performed for all females of childbearing potential according to the SoA (Section 1.3). Additional serum or urine pregnancy tests may be performed, as determined necessary by the investigator, or required by local regulation, to establish the absence of pregnancy at any time during the participation in the study.

8.3.5. Depression Screening and Symptoms Monitoring

The PHQ-9 is a self-administered, 9-item questionnaire measuring symptoms and severity of depression. The recall period for all items is the past 2 weeks. The items include diminished interest or pleasure, depressed mood, insomnia/hypersomnia, fatigue or loss of energy, weight loss or weight gain/appetite loss or appetite gain, feelings of worthlessness, diminished concentration/indecisiveness, psychomotor agitation/retardation, and thoughts of death/suicide. Each item is rated on a 4-point Likert scale ranging from 0 “not at all” to 3 “nearly every day.” The PHQ-9 can generally be completed in 2 to 3 minutes (Kroenke 2001).

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

The PHQ-9 will be completed per the Section 1.3. The PHQ-9 result should be reviewed by the site staff prior to the participant leaving the visit to assess the level of depression.

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

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

8.3.6. Suicidal Ideation and Behavior Risk Monitoring

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

Two versions of C-SSRS will be used in this study: the 'Baseline/Screening' version of the C-SSRS will be conducted during the screening visit and the 'Since Last Visit' version of the C-SSRS will be completed at Week 0 and all other visits through the end of the study. The C-SSRS must be completed after performing PROs and before performing any other tests or study procedures.

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

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

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

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

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

8.3.7. Tuberculosis Evaluation

Initial Tuberculosis Evaluation

Participant medical history assessment must include specific questions about a history of TB or known occupational or other personal exposure to individuals with active TB. The participant should be asked about past testing for TB, including chest imaging results and responses to other TB testing. T-SPOT® may be processed at either the central or local laboratory.

Participants with a negative IGRA test result are eligible to continue with screening procedures. Participants with a newly identified positive IGRA test result must undergo an evaluation for active or latent TB, or suspected false-positive initial testing, and initiate appropriate treatment if needed

(see Section 5.2, Exclusion Criterion 29). Appropriate treatment for latent TB is defined according to Japan guidelines for immunocompromised patients.

Participants with indeterminate/borderline IGRA test results should have the test repeated. Participants with persistently indeterminate/borderline IGRA test results must undergo an evaluation for active or latent TB, or suspected false-positive initial testing, and initiate appropriate treatment if needed (see Section 5.2, Exclusion Criterion 29).

Ongoing Tuberculosis Evaluation

To aid in the early detection of TB infection or exposure during study participation, participants must be evaluated for TB signs, symptoms, and close contacts at scheduled visits during the initial 52 weeks of the study (refer to Section 1.3) or by telephone approximately every 2 to 12 weeks during the LTE. The following series of questions is suggested for use during the evaluation:

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

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

If the evaluation raises suspicion for TB infection or the participant has had a close contact exposure to TB, study intervention must be withheld and an immediate and thorough investigation must be undertaken (Section 7.1), consultation with a physician specializing in TB to determine if treatment is warranted prior to any further study intervention. Participants should be encouraged to return for all subsequent scheduled study visits according to the protocol.

During the study, a participant with confirmed latent TB must initiate appropriate treatment for latent TB as defined by Japan guidelines.

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

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

Timely, accurate, and complete reporting and analysis of safety information, including AEs, SAEs, and PQCs, from clinical studies are crucial for the protection of participants, investigators, and the sponsor, and are mandated by regulatory agencies worldwide. The sponsor has established Standard Operating Procedures in conformity with regulatory requirements worldwide to ensure

appropriate reporting of safety information; all clinical studies conducted by the sponsor, or its affiliates will be conducted in accordance with those procedures.

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

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

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

All Adverse Events

All AEs and special reporting situations, whether serious or non-serious, will be reported from the time a signed and dated ICF is obtained until completion of the participant's last study-related procedure, which may include contact for follow-up of safety. All AEs with an onset date after the signing of the ICF and up to 4 weeks after study intervention discontinuation must be recorded on specific AE pages of the eCRF.

Serious Adverse Events

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

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

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

Information regarding SAEs will be transmitted to the sponsor using the Serious Adverse Event Form, which must be completed and signed by a physician from the study site and transmitted to the sponsor immediately but no later than within 24 hours of their knowledge of the event. The initial and follow-up reports of an SAE should be transmitted 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.

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

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

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

8.4.3. Regulatory Reporting Requirements for Serious Adverse Events

The sponsor assumes responsibility for appropriate reporting of the safety information to the regulatory authorities/Independent Ethics Committee (IEC)/Institutional Review Board (IRB), as applicable.

8.4.4. 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 discontinue further study intervention.

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

8.4.5. Adverse Events of Special Interest

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

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

Any newly identified malignancy or case of active TB occurring after the first administration of study intervention must be reported by the investigator according to the procedures in Appendix 3: Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting. Investigators are also advised that active TB is considered a reportable disease in most countries/territories.

An AESI is considered serious only if it meets the definition of an SAE.

8.5. Pharmacokinetics

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

8.5.1. Evaluations

Venous blood samples of approximately 4 mL will be collected for measurement of plasma concentrations of JNJ-77242113 as indicated in the SoA (Section 1.3).

Samples collected for analyses of JNJ-77242113 plasma concentration may additionally be used to evaluate safety or efficacy aspects that address concerns arising during or after the study period. Genetic analyses will not be performed on these plasma samples. Participant confidentiality will be maintained. Additional information about the collection, handling, and shipment of biological samples can be found in the laboratory manual.

8.5.2. Analytical Procedures

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

8.6. Pharmacodynamics

Pharmacodynamic assessments are described in Section 8.8.

8.7. Genetics and Pharmacogenomics

Sample collection and testing will comply with local regulations.

A pharmacogenomic blood sample will be collected from participants who consent to this component of the study to allow for pharmacogenomic research, as necessary. Participant participation in pharmacogenomic research is optional. The sponsor will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.

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

8.8. Biomarkers

Biomarker assessments will be used to define and identify PD markers of therapeutic response to better understand the mechanism of action of JNJ-77242113 in participants with psoriasis, and aid in evaluating the drug exposure versus clinical response relationship, and the pathophysiology of psoriasis. This will include evaluation of relevant disease and pathway engagement biomarkers in serum. Serum will be collected from all participants. These assessments could also help explain interindividual 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 collection will be conducted at the timepoints indicated in the Section 1.3 and instruction for the collection and shipment of these samples can be found in the laboratory manual.

Sample collection and testing will comply with local regulations.

Serum Biomarkers

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

Stopping Analysis

Biomarker analyses are dependent upon the availability of appropriate biomarker assays and clinical response rates. Biomarker analysis may be deferred or not performed, if during or at the end of the study, it becomes clear that the analysis will not have sufficient scientific value for biomarker evaluation, or if there are not enough samples or responders to allow for adequate biomarker evaluation. In the event the study is terminated early or shows poor clinical efficacy, completion of biomarker assessments is based on justification and intended utility of the data.

8.9. Immunogenicity Assessments

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

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

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

Analytical Procedures

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

8.10. Health Economics/Medical Resource Utilization and Health Economics

Health Economics will be evaluated in this study utilizing the EQ-5D-5L (Refer to Section 8.2.2. for details). Medical Resource Utilization parameters will not be evaluated in this study.

9. STATISTICAL CONSIDERATIONS

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

9.1. Statistical Hypotheses

The primary hypothesis of this study is that JNJ-77242113 is efficacious in treating GPP or EP as assessed by proportion of participants with GPP and EP who experience treatment success defined as at least "Minimally Improved" rating in CGI scale for GPP (according to JDA total score) and EP, respectively at Week 16.

9.2. Analysis Sets

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

Analysis Sets	Description
Enrolled	All participants who sign the ICF.
Full Analysis Set (FAS)	All enrolled participants who received at least 1 dose of JNJ-77242113.
Safety Analysis Set (SAS)	All enrolled participants who received at least 1 dose of JNJ-77242113.
PK Analysis Set	All enrolled participants who received at least 1 dose of JNJ-77242113 and had at least 1 valid blood sample drawn for PK analysis after their first dose of JNJ-77242113.
Immunogenicity Analysis Set	All enrolled participants who received at least 1 dose of JNJ-77242113 and who had at least 1 sample obtained after the first dose of JNJ-77242113 for the detection of antibodies to JNJ-77242113.

9.3. Statistical Analyses

The SAP will be finalized prior to first DBL and it will include a more technical and detailed description of the statistical analyses described in this section. This section is a summary of the planned statistical analyses of the most important endpoints including primary and secondary endpoints.

9.3.1. General Considerations

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 data, as applicable.

9.3.2. Primary Efficacy Endpoints/Estimand Analysis

There are 2 primary endpoints for GPP and EP in this study as given below.

For GPP:

- Proportion of participants with GPP who experience GPP treatment success at Week 16. GPP treatment success is defined as at least "Minimally Improved" rating in CGI scale according to JDA total score for GPP at Week 16.

For EP:

- Proportion of participants with EP who experience EP treatment success at Week 16. EP treatment success is defined as at least "Minimally Improved" rating in CGI scale for EP at Week 16.

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

Study Intervention:

Experimental: JNJ-77242113

Population:

- Participants ≥12 years of age with GPP
- Participants ≥12 years of age with EP

Variable:

Binary response variables for the primary endpoints:

- Treatment success for GPP: a responder (participant with treatment success defined as at least "Minimally Improved" rating in CGI scale for GPP according to the JDA total score) at Week 16.
- Treatment success for EP: a responder (participant with treatment success defined as at least "Minimally Improved" rating in CGI scale for EP) at Week 16.

Intercurrent Event:

Intercurrent Event	Corresponding Strategy
Discontinuation of study intervention for any reason prior to Week 16.	Treatment Policy: observed data will be used regardless of whether or not this ICE had occurred.

Population Level Summary:

- Proportion of participants with GPP who experience treatment success at Week 16.
- Proportion of participants with EP who experience treatment success at Week 16.

Primary Endpoint Analyses

For the primary endpoint analyses, data from full analysis set (FAS) which is the population of participants who received at least 1 dose of study intervention will be analyzed. The number, proportion of participants with treatment success, and 95% Clopper-Pearson exact confidence interval (CI) will be provided for GPP and EP groups.

The primary endpoints will be analyzed using the primary estimand.

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

The detailed methods of analysis and the data-handling rules for primary endpoints will be described in the SAP.

9.3.3. Secondary Efficacy Endpoints/Estimand Analysis

The secondary efficacy endpoints are:

- Proportion of participants with GPP or EP (for GPP: based on CGI scale according to JDA total score and for EP based on CGI scale) who experience treatment success over time.
- Change from baseline in the total score of the JDA severity index for GPP over time.
- Change from baseline in severity classification (mild, moderate, severe) of the JDA severity index for GPP over time.
- Change from baseline in BSA of involvement of lesion for EP over time.
- Proportion of participants who achieve an IGA score of cleared (0) or minimal (1) over time.
- Proportion of participants who achieve an IGA score of cleared (0) over time.
- Percent improvement from baseline in PASI over time.
- Change from baseline in DLQI score over time.
- Proportion of participants who achieve a DLQI score of 0 or 1 over time.
- Change from baseline in EQ-5D-5L (domain scores and VAS) over time.

All the secondary efficacy endpoints will be summarized descriptively. Graphical data displays may also be used to summarize the data.

The detailed methods of analysis and the data-handling rules for the key secondary endpoints will be specified in the SAP.

9.3.4. Other Secondary and Exploratory Endpoints/Estimand Analysis

Other secondary and exploratory endpoints are listed in Section 3. The analyses for other secondary and exploratory efficacy endpoints at Week 16 and over time will be performed. A complete list of the planned analyses of other secondary and exploratory endpoints will be described in the SAP.

9.3.5. Safety Analyses

All safety analyses will be made on the Safety Analysis Set.

Safety data, including but not limited to, AEs, SAEs, AESIs (active TB, malignancy, possible Hy's Law cases), discontinuation of study intervention due to AEs, changes in laboratory assessments, changes in vital signs, changes in weight, changes in PHQ-9 scores, and changes in C-SSRS will be summarized. Treatment-emergent AEs will be summarized by MedDRA SOC and PT. Details will be specified in the SAP.

Adverse Events

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

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

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

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

Clinical Laboratory Tests

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

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

provided. A listing of participants with any markedly abnormal laboratory results will also be provided.

Vital Signs

Vital signs including temperature, pulse/heart rate, respiratory rate, and blood pressure (systolic and diastolic) will be summarized over time, using descriptive statistics and/or graphically. The percentage of participants with values beyond clinically important limits will be summarized.

Physical Examinations

Physical examination findings will be summarized at each scheduled time point. Descriptive statistics will be calculated at baseline and for observed values and changes from baseline at each scheduled time point. Frequency tabulations of the abnormalities will be made.

Weight

Descriptive statistics of weight will be summarized over time for adult participants. Descriptive statistics of weight and height will be summarized over time for adolescent participants.

PHQ-9

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

C-SSRS

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

9.3.6. Other Analyses

9.3.6.1. Pharmacokinetic Analyses

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

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

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, race) will be evaluated as potential covariates affecting PK parameters. Details will be given in a population PK analysis plan and the results of the population PK analysis will be presented in a separate report.

9.3.6.2. Biomarkers Analyses

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

Changes in serum biomarkers over time will be summarized by GPP and EP groups. Associations between baseline levels and changes from baseline in selected markers and clinical response to treatment will be explored. Biomarker analyses will be summarized in separate technical reports.

9.3.6.3. Immunogenicity Analyses

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

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

9.3.6.4. Pharmacokinetic/Pharmacodynamic Analyses

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

9.3.6.5. Pharmacogenomic Analyses

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

9.4. Interim Analysis/Analyses

No interim analyses are planned.

9.5. Sample Size Determination

The number of patients with GPP or those with EP is limited with 1.5% to 2.3% of the entire patients with psoriasis in Japan Therefore, based on the feasibility, approximately 16 participants (8 each for GPP and EP) will be targeted to enroll in the study.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Clinical Laboratory Tests

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

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

Protocol-Required Laboratory Assessments

<table>
<tr><th>Laboratory Assessments</th><th colspan="3">Parameters</th></tr>
<tr><td rowspan="2">Hematology</td><td>Platelet count
Red blood cell (RBC) count
Hemoglobin
Hematocrit</td><td><u>RBC Indices:</u>
Mean Corpuscular Volume (MCV)
Mean Corpuscular Hemoglobin (MCH)
% Reticulocytes</td><td><u>White blood cell (WBC) count with Differential:</u>
Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils</td></tr>
<tr><td colspan="3">Note: A WBC evaluation may include any abnormal cells, which will then be reported by the laboratory. An RBC evaluation may include abnormalities in the RBC count, RBC parameters, or RBC morphology, which will then be reported by the laboratory. In addition, any other abnormal cells in a blood smear will also be reported.</td></tr>
<tr><td rowspan="2">Clinical Chemistry</td><td colspan="2">Sodium
Potassium
Chloride
Bicarbonate
Blood urea nitrogen
Creatinine
Glucose (non-fasting)
Aspartate aminotransferase (AST)/Serum glutamic-oxaloacetic
Alanine aminotransferase (ALT)/Serum glutamic-oxaloacetic
Gamma-glutamyltransferase
estimated glomerular filtration rate (eGFR)
high-sensitivity C reactive protein (hsCRP)</td><td>Total bilirubin (Tbili) and Direct bilirubin
Alkaline phosphatase
Creatine phosphokinase (CPK)
Lactic acid dehydrogenase (LDH)
Uric acid
Calcium
Phosphate
Albumin
Total protein
Cholesterol
Triglycerides
Magnesium</td></tr>
<tr><td colspan="3">Details of liver chemistry stopping criteria and required actions and follow-up are given in Appendix 5: Liver Safety: Suggested Actions and Follow-up Assessments. Possible Hy's Law case (ALT or AST ≥3 x ULN and Tbili ≥2 x ULN) reporting requirements are defined in Section 8.4.1.</td></tr>
<tr><td rowspan="2">Lipid Panel</td><td colspan="3">Total cholesterol
High-density lipoprotein (HDL)
Low-density lipoprotein (LDL; calculated)
Triglycerides</td></tr>
<tr><td colspan="3">Note: Fasting requirements are described in the SoA (Section 1.3).</td></tr>
</table>

Laboratory Assessments	Parameters	
Routine Urinalysis	<u>Dipstick</u> Specific gravity pH Glucose Protein Blood Ketones Bilirubin Urobilinogen Nitrite Leukocyte esterase	<u>Sediment (if dipstick result is abnormal)</u> RBC WBC Epithelial cells Crystals Casts Bacteria
	If dipstick result is abnormal, microscopy will be used to measure sediment. In the microscopic examination, observations other than the presence of WBC, RBC and casts may also be reported by the laboratory.	
Other Laboratory Tests	• Serum (β-hCG) and Urine Pregnancy Testing for female participants of childbearing potential only • Serology (HIV antibody, hepatitis B surface antigen [HBsAg], and hepatitis C virus antibody) and or HCV RNA PCR test (only required if HCV antibody positive) • QuantiFERON® TB or T-SPOT® TB • Follicle stimulating hormone (FSH) as need to confirm postmenopausal status.	

Additional details will be provided in the laboratory manual.

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

10.2.1. Regulatory and Ethical Considerations

Investigator Responsibilities

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

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

Protocol Clarification Communications

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

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

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

Protocol Amendments

Neither the investigator nor the sponsor will modify this protocol without a formal amendment by the sponsor. All protocol amendments must be issued by the sponsor and signed and dated by the investigator. Protocol amendments must not be implemented without prior IEC/IRB approval, or when the relevant competent authority has raised any grounds for non-acceptance, except when necessary to eliminate immediate hazards to the participants, in which case the amendment must be promptly submitted to the IEC/IRB and relevant competent authority. Documentation of amendment approval by the investigator and IEC/IRB must be provided to the sponsor. When the change(s) 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 Protocol Supplementary Information page(s), which will be provided as a separate document. Except in emergency situations, this contact must be made before implementing any departure from the protocol. In all cases, contact with the sponsor must be made as soon as possible to discuss

the situation and agree on an appropriate course of action. The data recorded in the case report form (CRF) and source documents will reflect any departure from the protocol, and the source documents will describe this departure and the circumstances requiring it.

Regulatory Approval/Notification

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

Required Prestudy Documentation

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

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

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

- Completed investigator financial disclosure forms from all subinvestigators.
- Documentation of subinvestigator qualifications (eg, curriculum vitae).
- Name and address of any local laboratory conducting tests for the study, and a dated copy of current laboratory normal ranges for these tests, if applicable.

- Local laboratory documentation demonstrating competence and test reliability (eg, accreditation/license), if applicable.

Independent Ethics Committee or Institutional Review Board

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

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

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

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

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

- Protocol amendments (excluding the ones that are purely administrative, with no consequences for participants, data, or study conduct)
- Revision(s) to ICF and any other written materials to be provided to participants
- If applicable, new or revised participant recruiting materials approved by the sponsor
- Revisions to compensation for study-related injuries or payment to participants for participation in the study, if applicable
- New edition(s) of the IB and amendments/addenda

- Summaries of the status of the study at intervals stipulated in guidelines of the IEC/IRB (at least annually)
- Reports of AEs that are serious, unlisted/unexpected, and associated with the study intervention
- New information that may adversely affect the safety of the participants or the conduct of the study
- Deviations from or changes to the protocol to eliminate immediate hazards to the participants
- Report of deaths of participants under the investigator's care
- Notification if a new investigator is responsible for the study at the site
- Development Safety Update Report and Line Listings, where applicable
- Any other requirements of the IEC/IRB

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

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

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

Other Ethical Considerations

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

10.2.2. Financial Disclosure

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

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

10.2.3. Informed Consent Process and Assent Form

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

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

Before enrollment in the study, the investigator or an authorized member of the study site personnel must explain to potential participants or their legally acceptable representatives 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, which includes permission to obtain information about his or her survival status. It also denotes that the participant agrees to allow his or her study physician to recontact the participant for the purpose of obtaining consent for additional safety evaluations, and subsequent disease-related treatments, if needed. The physician may also recontact the participant for the purpose of obtaining consent to collect information about his or her survival status.

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

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

Participants will be asked for consent to provide optional samples for research. After informed consent for the study is appropriately obtained, the participant or his or her legally acceptable representative will be asked to sign and personally date the ICF indicating agreement to participate in the optional research component. Refusal to participate in the optional research will not result in ineligibility for the study. A copy of the signed ICF will be given to the participant.

If required, the ICF may be used for the required DNA component of the study.

Children (minors) or participants who are unable to comprehend the information provided can be enrolled only after obtaining consent of a legally acceptable representative. Assent must be obtained from children (minors) capable of understanding the nature of the study, typically participants 7 years of age and older, depending on the institutional policies. Assent must be obtained from participants who are able to write. A separate assent form in the language the participant can understand must be developed for adolescents. After having obtained the assent, a

copy of the assent form must be given to the participant, and to the participant's parent(s) or if applicable legally acceptable representative.

10.2.4. Recruitment Strategy

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

10.2.5. Data Protection

Privacy of Personal Data

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

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

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

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

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

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

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

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

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

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

10.2.7. Committees Structure

Adjudication Committee

The sponsor may perform adjudication on certain AEs during this study. If adjudication is required, the site will be required to provide medical records and other anonymized source documentation to the sponsor for this purpose. A separate adjudication charter will be available if the sponsor chooses to perform adjudication.

10.2.8. Publication Policy/Dissemination of Clinical Study Data

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

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

The results of the study will be reported in a Clinical Study Report generated by the sponsor and will contain data from all study sites that participated in the study per protocol. Recruitment performance or specific expertise related to the nature and the key assessment parameters of the study will be used to determine a coordinating investigator for the study. Results of pharmacogenomic and 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 the publication of results. Any work created in connection with performance of the study and contained in the data that can benefit from copyright protection (except any publication by the investigator as provided for below) shall be the property of the sponsor as author and owner of copyright in such work.

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

Registration of Clinical Studies and Disclosure of Results

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

10.2.9. Data Quality Assurance

Data Quality Assurance/Quality Control

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study sites, review of protocol procedures with the investigator and

study site personnel before the study, periodic monitoring visits by the sponsor, and direct transmission of clinical laboratory data from a central laboratory into the sponsor's database. Written instructions will be provided for collection, handling, storage, and shipment of samples.

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

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

10.2.10. Case Report Form Completion

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

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

Worksheets may be used for the capture of some data to facilitate completion of the CRF. Any such worksheets will become part of the participant's source documents. Data must be entered into the CRF in English. The CRF must be completed as soon as possible after a participant visit and the forms must be available for review at the next scheduled monitoring visit.

All participative measurements (eg, pain scale information or other questionnaires) will be completed by the same individual who made the initial baseline determinations whenever possible.

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

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

10.2.11. Source Documents

At a minimum, source documents consistent in the type and level of detail with that commonly recorded at the study site as a basis for standard medical care must be available for the following: participant identification, eligibility, and study identification; study discussion and date of signed informed consent; dates of visits; results of safety and efficacy parameters as required by the protocol; record of all AEs and follow-up of AEs; concomitant medication; intervention

receipt/dispensing/return records; study intervention administration information; and date of study completion and reason for early discontinuation of study intervention or withdrawal from the study, if applicable.

The author of an entry in the source documents must be identifiable. Given that participant-reported outcomes (PROs) are reports of a participant's health condition that come directly from the participant, without interpretation by a clinician or anyone else, the responses to PRO measures entered by study participants into source records cannot be overridden by site staff or investigators. In order to minimize inclusion bias, investigators participating in this study must agree not to change such PRO data items once entered and saved permanently into the source records for the following instruments (and visits) as set forth in the Data Management Plan for this study:

PROs

- Dermatology Life Quality Index (DLQI) for adult participants (≥18 years of age on the first date of the Screening Visit)
- Euro QoL-5 Dimension 5 Level Questionnaire (EQ-5D-5L)
- Children's Dermatology Life Quality Index (CDLQI) for adolescent participants (≥12 years and <18 years of age on the first date of the Screening Visit)
- Patient Health Questionnaire-9 (PHQ-9)

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

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

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

The minimum source documentation requirements for Sections 5.1 and 5.2 that specify a need for documented medical history are as follows:

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

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

An eSource system may be utilized, which contains data traditionally maintained in a hospital or clinic record to document medical care (eg, electronic source documents) as well as the clinical study-specific data fields as determined by the protocol. This data is electronically extracted for use by the sponsor. If eSource is utilized, references made to the CRF in the protocol include the eSource system, but information collected through eSource may not be limited to that found in the CRF.

10.2.12. Monitoring

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

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

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

In addition to on-site monitoring visits, remote contacts 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.

10.2.13. On-site Audits

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

Similar auditing procedures may also be conducted by agents of any regulatory body, either as part of a national GCP compliance program or to review the results of this study in support of a regulatory submission. The investigator must immediately notify the sponsor if he or she has been contacted by a regulatory agency concerning an upcoming inspection.

10.2.14. Record Retention

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

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

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

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

10.2.15. Study and Site Start and Closure

First Act of Recruitment

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

Study/Site Termination

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

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

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

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

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

10.3.1. Adverse Event Definitions and Classifications

Adverse Event

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

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

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

Serious Adverse Event

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

- Results in death
- Is life-threatening
  (The participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it 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 must be exercised in deciding whether expedited reporting is also appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above. These should usually be considered serious.

If a serious and unexpected AE occurs for which there is evidence suggesting a causal relationship between the study intervention and the event (eg, death from anaphylaxis), the event must be reported as a serious and unexpected suspected adverse reaction even if it is a component of the study endpoint (eg, all-cause mortality).

Unlisted (Unexpected) Adverse Event/Reference Safety Information

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

10.3.2. Attribution Definitions

Assessment of Causality

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

Related

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

Not Related

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

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

10.3.3. Severity Criteria

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

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

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

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

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

10.3.4. Special Reporting Situations

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

- Overdose of a sponsor study intervention

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

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

10.3.5. Procedures

All Adverse Events

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

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

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

Serious Adverse Events

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

- The event resolves
- The event stabilizes

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

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

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

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

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

10.3.6. Product Quality Complaint Handling

Definition

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

Procedures

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

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

10.3.7. Contacting Sponsor Regarding Safety, Including Product Quality

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

10.4. Appendix 4: Contraceptive and Barrier Guidance

Participants must follow contraceptive measures as outlined in Section 5.1. Pregnancy information will be collected and reported as noted in Section 8.4.4 and Appendix 3: Adverse Events, Serious Adverse Events, Product Quality Complaints, and Other Safety Reporting: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

Definitions

Female Participants of Childbearing Potential

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

Female Participants Not of Childbearing Potential

- **premenarchal**

  A premenarchal state is one in which menarche has not yet occurred.

- **postmenopausal**

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

- **permanently sterile (for the purpose of this study)**
  - Permanent sterilization methods include hysterectomy, or bilateral salpingectomy, or bilateral oophorectomy.
  - Has congenital abnormalities resulting in sterility.

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

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

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

Typical use failure rates may differ from those when used consistently and correctly.

Examples of Contraceptives

EXAMPLES OF CONTRACEPTIVES[a] ALLOWED FOR FEMALE PARTICIPANTS DURING THE STUDY INCLUDE:
USER INDEPENDENT **Highly Effective Methods That Are User Independent** *Failure rate of <1% per year when used consistently and correctly.*
• Intrauterine device (IUD)
• Intrauterine hormone-releasing system (IUS)
• Tubal closure (eg, bilateral tubal occlusion, bilateral tubal ligation)
• Azoospermic partner *(vasectomized or due to medical cause)* *(Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the female participant of childbearing potential and the absence of sperm has been confirmed. If not, additional highly effective method of contraception must be used. Spermatogenesis cycle is approximately 74 days)*
USER DEPENDENT **Highly Effective Methods That Are User Dependent** *Failure rate of <1% per year when used consistently and correctly.*
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation – oral
• Sexual abstinence *(Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.)*
NOT ALLOWED AS SOLE METHOD OF CONTRACEPTION DURING THE STUDY (not considered to be highly effective - failure rate of ≥1% per year)
• Progestogen-only oral hormonal contraception where inhibition of ovulation is not the primary mode of action
• Male condom with or without spermicide
• Periodic abstinence (calendar, symptothermal, post-ovulation methods)
• Withdrawal (coitus-interruptus)
• Lactational amenorrhea method (LAM)
a) Typical use failure rates may differ from those when used consistently and correctly.

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

10.5.1. Liver Chemistry Increased Monitoring With Continued Study Intervention

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

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

10.5.2. Liver Chemistry Stopping Criteria and Follow-up Assessments

Study intervention will be temporarily interrupted (withheld) for a participant if liver chemistry stopping criteria are met. Determination of temporary interruption (withheld) versus permanently discontinuation of study intervention is described below and should be discussed with the medical monitor.

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

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

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

a. New or worsening symptoms believed to be related to liver injury (such as fatigue, nausea, vomiting, right upper quadrant pain or tenderness, or jaundice) or hypersensitivity (such as fever, rash, or eosinophilia).

b. All events of ALT or AST ≥3×ULN and total bilirubin ≥2×ULN (or at least a doubling of direct bilirubin for known Gilbert's syndrome) or ALT or AST ≥3×ULN and INR >1.5 may indicate severe liver injury (possible 'Hy's Law') and must be reported to sponsor in an expedited manner and as an SAE if SAE criteria met (excluding studies of hepatic impairment or cirrhosis). The INR stated threshold value will not apply to participants receiving anticoagulants.
c. Includes: hepatitis A immunoglobulin M antibody; hepatitis B surface antigen and hepatitis B core antibody; hepatitis C RNA; cytomegalovirus IgM antibody; Epstein-Barr viral capsid antigen IgM antibody (or if unavailable, heterophile antibody or monospot testing); and hepatitis E IgM antibody. In participants with underlying chronic hepatitis B at study entry (identified by positive hepatitis B surface antigen) check quantitative hepatitis B DNA and hepatitis delta antibody. If hepatitis delta antibody assay cannot be performed, it can be replaced with a PCR of hepatitis D RNA virus (where needed) (Le Gal 2005).
d. PK sample may not be required for participants known to be receiving placebo or non-comparator interventions. Record the date/time of the PK blood sample draw and the date/time of the last dose of study intervention prior to the PK blood sample draw on the CRF. If the date or time of the last dose is unclear, provide the participant's best approximation. If the date/time of the last dose cannot be approximated OR a PK sample cannot be collected in the time period indicated above, do not obtain a PK sample. Instructions for sample handling and shipping are in the Study Reference Manual.
e. Serum bilirubin fractionation should be performed if testing is available. If serum bilirubin fractionation is not immediately available, stop study intervention if ALT or AST ≥3×ULN and total bilirubin ≥2×ULN. Additionally, if serum bilirubin fractionation testing is unavailable, record the absence/presence of detectable urinary bilirubin on dipstick which is indicative of direct bilirubin elevations suggesting liver injury.

References:

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

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

GUIDANCE ON STUDY CONDUCT DURING COVID-19 PANDEMIC

It is recognized that the COVID-19 may have an impact on the conduct of this clinical study due to, for example, isolation or quarantine of participants and study site personnel; travel restrictions/limited-access to public places, including hospitals; study site personnel being unavailable, isolated, 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 requirements or the clinical judgment of the investigator to protect the health and well-being of participants and site staff. If, at any time, a participant's travel to the study site is considered to be dangerous, study participation may be interrupted, and study follow-up conducted. If it becomes necessary to discontinue participation in the study, the procedures outlined in the protocol for discontinuing study intervention will be followed.

If, as a result of the COVID-19 scheduled 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 with the participant, investigator, and the sponsor.

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

The sponsor will continue to monitor the conduct and progress of the clinical study, and any changes will be communicated to the sites and to the health authorities according to local guidance. Modifications made to the study conduct as a result of the COVID-19 should be summarized in the Clinical Study Report.

- Certain protocol-mandated visits to the study site may not be possible during the major disruption events. Therefore, temporary measures may be implemented if considered appropriate by the sponsor and investigator to maintain continuity of participant care and study integrity. Certain measures, such as those listed below, may be necessary and should be instituted in accordance with applicable (including local) laws, regulations, guidelines, and procedures:

  - remote (eg, by phone/telehealth) or in-person, off-site (eg, in-home) interactions between site staff (or designees) and participants for study procedures, eg, those related to safety monitoring/efficacy evaluation/study intervention storage and administration (including training where pertinent)
  - procurement of study intervention by participants (or designee) or shipment of study intervention from the study site directly to participants for at-home administration (including the potential for self-administration of study intervention)
  - laboratory assessments using a suitably accredited local laboratory; for selected measures (eg, urine pregnancy), home testing may be employed
  - other procedures, eg, imaging, may be conducted at an appropriate facility
- Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Discontinuations of study interventions and withdrawal from the study should be documented in the CRF.
  - other relevant study data elements impacted by the major disruption, should also be documented in CRFs and/or other study systems, as directed by detailed sponsor guidance. These may include missed/delayed/modified study visits/assessments/dose, and instances where temporary measures such as those above are implemented.
- The sponsor will evaluate the totality of impact of major disruption events on collection of key study data and additional data analyses will be outlined in study SAP(s).

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

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

Eligibility Based on Hepatitis B Virus Test Results

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

a. If the HBV DNA is not detectable, the participant is eligible for this study. If HBV DNA is detectable, the participant is not eligible for this study. The participants who are eligible for this study (HBV DNA testing negative) will require HBV DNA quantitation to be monitored per local guidelines during the study. If HBV DNA testing cannot be performed, or there is evidence of chronic liver disease, the participant is not eligible for this study.

Eligibility based on HCV test results:

- Participants with negative anti-HCV antibody will be eligible to enroll.
- Participants with a positive anti-HCV antibody will require a negative HCV RNA PCR test before being eligible to participate in the study.

Reference:

Japan College of Rheumatology: Recommendations on Immunosuppressive Therapy in Patients with Rheumatic Disease and Hepatitis B Virus Infection, Revised Version; 18 October 2011.

10.8. Appendix 8: Diagnostic Criteria of Generalized Pustular Psoriasis

1. Definition of generalized pustular psoriasis and the primary signs parameters required for diagnosis (2006)

Generalized pustular psoriasis (GPP) is a rare disease in which acute fever, generalized skin rashes, and many sterile pustules develop. Histopathologically, GPP forms subcorneal pustules characterized by Kogoj's spongiform pustules. GPP may or may not be preceded by psoriasis vulgaris and is characterized by repeated disease recurrence. During the course of the disease, patients have abnormal clinical findings associated with systemic inflammation and often present with mucosal symptoms and arthritis as complications. Although rare, GPP may be accompanied by certain eye symptoms and secondary amyloidosis.

1) Primary parameters:

a. Systemic symptoms such as fever and fatigue;

b. Systemic or extensive flush accompanied by multiple sterile pustules that sometimes merge to form lakes of pus;

c. Neutrophilic subcorneal pustules histopathologically characterized by Kogoj's spongiform pustules;

d. The above clinical and histological features recur repeatedly. However, the diseases mentioned below can be excluded from initial-onset cases.

A definitive diagnosis of GPP can be made in patients with all four features above, and GPP would be suspected in those with features 2 and 3.

2. Parameters for reference in the diagnosis of GPP

1) Laboratory test findings necessary to assess the severity of the disease and complications*:

a. Leukocytosis, left shift;
b. Elevated erythrocyte sedimentation rate (ESR), positive for C-reactive protein (CRP);
c. Elevated immunoglobulin (Ig)G or IgA;
d. Hypoproteinemia, hypocalcemia;
e. Tonsillitis, elevated anti-streptolysin O antigens (ASLO), other infections;
f. Rheumatoid factor-negative polyarthritis, including ankylosing spondylitis;
g. Eye diseases (such as keratoconjunctivitis, uveitis, and iritis);

h. Hepatic, renal, and urinary findings: treatment choice and evaluation of secondary amyloidosis.

*The 3rd National Survey shows that specificity is 65% for leukocytosis, 67% for elevated erythrocyte sedimentation rate, 81% for a high level of CRP, and 12% for hypocalcemia. Due to insufficient data, anti-streptolysin O and Ig were not analyzed.

2) Diseases included in GPP

a. Acute GPP (von Zumbusch type): classical examples of GPP;

b. Impetigo herpetiformis: GPP associated with pregnancy and hormonal abnormalities;

c. Acrodermatitis continua of Hallopeau: strictly speaking, this disease is rare and therefore, requires careful diagnosis;

d. Pediatric GPP: circinate annular form is excluded.

3) In principle, cases involving transiently pustule formation are not included in this category; which however, does not apply to the cases where recurrence is suppressed by ongoing treatment.

3. Exclusion criteria for GPP

Three diagnoses of exclusion:

1) In principle, clear cases of psoriasis vulgaris with transient pustule formation after the application of corticosteroids are not included in this category. However, this does not apply to cases when pustules reoccur easily, and the dermatologists should decide whether to include the case in this category after careful observation for a certain period.

2) In general, the circinate annular form is excluded because of mild systemic symptoms; but the cases exhibiting in a clear transition into GPP are included.

3) Cases where the diagnosis of subcorneal pustular dermatosis or pustular drug eruptions (including acute generalized exanthematous pustulosis) is made after careful observation for a certain period are excluded.

Reference:

Fujita H, Terui T, Hyama K et al. Japanese guidelines for the management and treatment of generalized pustular psoriasis: The new pathogenesis and treatment of GPP. 2018; 45(11):1235-1270.

10.9. Appendix 9: Japanese Dermatological Association Severity Index

A. Evaluation of skin symptoms:	Erythema, pustule, edema (0-9)		
B. Evaluation of systemic symptoms/laboratory findings:	Fever, WBC count, serum CRP, serum albumin (0-8)		
○ Severity classification: (total score)	Mild (0-6)	Moderate (7-10)	Severe (11-17)

A. Evaluation of skin symptoms (0-9)

	Severe	Moderate	Mild	None
Area of erythema (whole)*	3	2	1	0
Area of erythema with pustules**	3	2	1	0
Area of edema**	3	2	1	0

* % relative to the body surface area (severe, ≥75%; moderate, <75%, ≥25%; mild, <25%)

** % relative to the body surface area (severe, ≥50%; moderate, <50%, ≥10%; mild, <10%)

B. Evaluation of systemic symptoms/laboratory findings (0-8)

Score	2	1	0
Fever (°C)	≥38.5	<38.5, ≥37	<37
WBC count (/μL)	≥15,000	<15,000, ≥10,000	<10,000
CRP (mg/dL)	≥7.0	<7.0, ≥0.3	<0.3
Serum albumin (g/dL)	<3.0	≥3.0, <3.8	≥3.8

Reference:

Fujita H, Terui T, Hyama K et al. Japanese guidelines for the management and treatment of generalized pustular psoriasis: The new pathogenesis and treatment of GPP. 2018; 45(11):1235-1270.

10.10. Appendix 10: Protocol Amendment History

This is an original protocol.

11. REFERENCES

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INVESTIGATOR AGREEMENT

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

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

Coordinating Investigator (where required):

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Signature: _____ Date: _____

(Day Month Year)

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____

(Day Month Year)

Sponsor's Responsible Medical Officer:

Name (typed or printed): PPD MD PhD

Institution: Janssen Pharmaceuticals K.K.

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	29-Aug-2023 02:58:19 (GMT)	Document Approval