A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BIMEKIZUMAB IN ADULT KOREAN STUDY PARTICIPANTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS

PROTOCOL PS0032 AMENDMENT 3

PHASE 3

SHORT TITLE:

A randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in adult Korean study participants with moderate to severe plaque psoriasis

Sponsor:
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PROTOCOL AMENDMENT SUMMARY OF CHANGES TABLE

Document History		
Document	**Date**	**Type of amendment**
Original Protocol	17 Dec 2020	Not applicable
PS0032 Protocol Amendment 1	24 Mar 2021	Substantial
PS0032 Protocol Amendment 2	12 May 2021	Substantial
PS0032 Protocol Amendment 3	16 Aug 2021	Substantial

SERIOUS ADVERSE EVENT REPORTING

Serious adverse event reporting (24h)	
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PROTOCOL AMENDMENT SUMMARY OF CHANGES

Amendment 3 (16 Aug 2021)

Overall rationale for the amendment

The purpose of this substantial amendment is to correct minor inconsistencies to be consistent within the protocol and across other psoriasis (PSO) studies in the development program.

Section # and Name	Description of Change	Brief Rationale
5.2 Exclusion criteria	Revised exclusion criterion 6.	Minor clarification for consistency with other PSO studies.
Section 4.4 End of study definition	Corrected the criteria for completion of the study.	Minor clarification for consistency with other PSO studies.
5.4 Screen failures	Revised the text to state that study participants with latent tuberculosis diagnosed at Screening who then complete a full course of prophylaxis treatment can be rescreened after completion of 4 weeks of prophylaxis.	Minor correction for consistency with Exclusion criterion #4.
8.2.7.2 Assessments at Screening	Revised the text to state that study participants with latent tuberculosis diagnosed at Screening who then complete a full course of prophylaxis treatment can be rescreened after completion of 4 weeks of prophylaxis.	Minor correction for consistency with Exclusion criterion #4.
8.2.7.2 Assessments at Screening	Corrected the footnote under Figure 8-1 to state that study participants with latent tuberculosis diagnosed at Screening who then complete a full course of prophylaxis treatment can be rescreened after completion of 4 weeks of prophylaxis.	Minor correction for consistency with Exclusion criterion #4.
8.2.7.3.5 Latent TB	Revised the text to state that study participants with latent tuberculosis diagnosed at Screening who then complete a full course of prophylaxis treatment can be rescreened after completion of 4 weeks of prophylaxis.	Minor correction for consistency with Exclusion criterion #4.

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1 PROTOCOL SUMMARY

1.1 Synopsis

Protocol title: A phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of bimekizumab in adult Korean study participants with moderate to severe plaque psoriasis

Short title: A randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in adult Korean study participants with moderate to severe plaque psoriasis

Rationale: The purpose of this study is to evaluate the efficacy and safety of bimekizumab in adult Korean study participants (aged at least 19 years) with moderate to severe plaque psoriasis (PSO). Following the completion of the pivotal global Phase 3 program of bimekizumab in moderate to severe PSO, the aim of this study is to bridge the existing evidence of efficacy and safety of bimekizumab from the Phase 3 program with limited Korean participation to a Korean population of study participants with moderate to severe PSO.

Objectives and endpoints

Objectives	**Endpoints**
Primary	**Co-Primary Endpoints**
To evaluate the efficacy of bimekizumab compared with placebo	**Co-Primary Endpoint 1**: • Participant-level outcome: Psoriasis Area and Severity Index (PASI)90 response at Week 16 **Co-Primary Endpoint 2:** • Participant-level outcome: Investigator's Global Assessment (IGA) 0/1 (clear or almost clear with at least a 2-category improvement from Baseline) response at Week 16
Secondary	
To evaluate the efficacy of bimekizumab compared with placebo at achieving complete skin clearance (PASI100/IGA 0)	• Participant-level outcome: PASI100 response at Week 16 • Participant-level outcome: IGA 0 (clear with at least a 2-category improvement from Baseline) response at Week 16
To evaluate the efficacy of bimekizumab compared with placebo at achieving rapid response (PASI75)	• Participant-level outcome: PASI75 response at Week 4

Objectives	Endpoints
To evaluate the efficacy of bimekizumab compared with placebo on itch, pain, and scaling	Reported by study participants using the patient symptom diary (PSD) (also published as Patient Symptom and Impact Measure [P-SIM] [Gottlieb et al, 2020]): • Participant-level outcome: PSD (P-SIM) response for itch at Week 16 • Participant-level outcome: PSD (P-SIM) response for pain at Week 16 • Participant-level outcome: PSD (P-SIM) response for scaling at Week 16
To evaluate the efficacy of bimekizumab compared with placebo on the change in psoriatic scalp disease in study participants with scalp psoriasis (PSO) at Baseline	• Participant-level outcome: Scalp IGA 0/1 (clear or almost clear with at least a 2-category improvement from Baseline) response at Week 16 for study participants with scalp PSO at Baseline
To assess the effect of bimekizumab compared with placebo on quality of life (QOL)	• Participant-level outcome: Dermatology Life Quality Index (DLQI) 0/1 response at Week 16
To evaluate the effect of bimekizumab compared with placebo on percent change from Baseline in body surface area (BSA) affected by PSO	• Participant-level outcome: Percent change from Baseline in BSA affected by PSO at Week 16
To evaluate the safety of bimekizumab	• Incidence of treatment-emergent adverse events (TEAEs) throughout the study • Incidence of treatment-emergent serious adverse events (TE-SAEs) throughout the study • Incidence of TEAEs leading to permanent discontinuation of investigational medicinal product (IMP) throughout the study
To assess the effect of bimekizumab on depression occurrence or worsening	• Change from Baseline in Patient Health Questionnaire (PHQ)-9 at Week 16
Tertiary	
To evaluate the pharmacokinetics (PK) of bimekizumab in study participants with moderate to severe PSO	• Plasma bimekizumab concentrations over the study duration
To evaluate the immunogenicity of bimekizumab	• Anti-bimekizumab antibody status over the study duration

Objectives	Endpoints
To assess the efficacy of bimekizumab compared with placebo over time	• PASI75 response over time • PASI90 response over time • PASI100 response over time • Absolute and percent change from Baseline in PASI score over time • Percentage of study participants with absolute PASI score ≤1, ≤2, ≤3, and ≤5 over time • Time to PASI50, PASI75, PASI90, and PASI100 response • IGA 0/1 response (with at least 2-category improvement from Baseline) over time • IGA 0 response (with at least 2-category improvement from Baseline) over time • Scalp-specific IGA (scalp IGA) 0/1 response (clear or almost clear with at least 2-category improvement from Baseline for participants with scalp PSO at Baseline) over time • Percentage of study participants with absolute BSA affected by PSO=0%, ≤1%, ≤3% and ≤5% over time • Percentage of study participants achieving a DLQI Total Score of 0 or 1 over time • Change from Baseline in DLQI Total Score over time • PSD (P-SIM) response rates over time • Change from Baseline in PSD (P-SIM) scores over time
To further evaluate the safety of bimekizumab compared with placebo over time	• Selected safety topics of interest TEAEs • Change from Baseline in laboratory variables (hematology and biochemistry) • Incidence of markedly abnormal laboratory values • Change from Baseline in vital signs • Incidence of markedly abnormal vital signs • Change from Baseline in electrocardiogram (ECG) parameters • ECG outliers • Change from Baseline in PHQ-9 • Incidence of PHQ-9 scores ≥15 and ≥20 • Incidence of suicidal ideation, suicidal behavior, or self-injurious behavior without suicidal intent (from Columbia Suicide Severity Rating Scale [C-SSRS])

Overall design

PS0032 is a Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of bimekizumab compared with placebo in adult Korean study participants with moderate to severe plaque PSO.

The study population consists of adult Korean study participants (≥19 years of age) with a diagnosis of moderate to severe plaque PSO (Baseline PASI ≥12 and BSA affected by PSO ≥10% and IGA score ≥3 on a 5-point scale) who are a candidate for systemic PSO therapy and/or phototherapy.

The Screening Period will last 2 weeks, but can be extended up to a total of 5 weeks in cases where a laboratory assessment needs to be repeated or to allow washout of prohibited medications. During the Screening Period, eligible study participants will be informed about the study and sign the Informed Consent Form (ICF). Following signed informed consent, all screening procedures and laboratory tests (hematology, urine, and biochemistry) will be performed per the Schedule of Activities (SoA) (Table 1-1). The Screening Period will also enable washout of any medications not permitted for use during the study. Study participants who require prophylaxis for latent tuberculosis (LTB) infection must be on treatment for at least 4 weeks prior to the first dose of IMP. These study participants may be rescreened after receiving prophylaxis treatment. One rescreening may be allowed after consultation with the Medical Monitor. Further details are provided in Section 5.4.

After completion of the Screening Period, eligible study participants will be allowed to enroll into the study. Approximately 45 adult Korean study participants will be randomized 2:1 to receive the following blinded IMP regimens during the Treatment Period:

- Bimekizumab 320mg every 4 weeks (Q4W) administered subcutaneous (sc) injection (30 study participants)
- Placebo Q4W administered sc injection (15 study participants)

During the Treatment Period, IMP will be administered at the study site.

All study participants choosing not to transition into a managed access program (MAP) (see Section 6.8) will have a Safety Follow-Up (SFU) Visit 20 weeks post last dose of IMP. Safety assessments will be made by ongoing monitoring and evaluation of adverse events (AEs) and other safety topics of interest specific to bimekizumab.

Study participants withdrawing early from IMP will undergo the Premature End of Treatment (PEOT) Visit assessments and be asked to continue in the SFU Period.

A study participant is considered to have completed the study if he/she has completed the Treatment Period of the study (Week 16) regardless of transfer into the MAP or completion of the SFU visit (see Section 6.8).

The end of the study is defined as the date of the last study participant's last visit (LPLV) in the study.

Number of participants

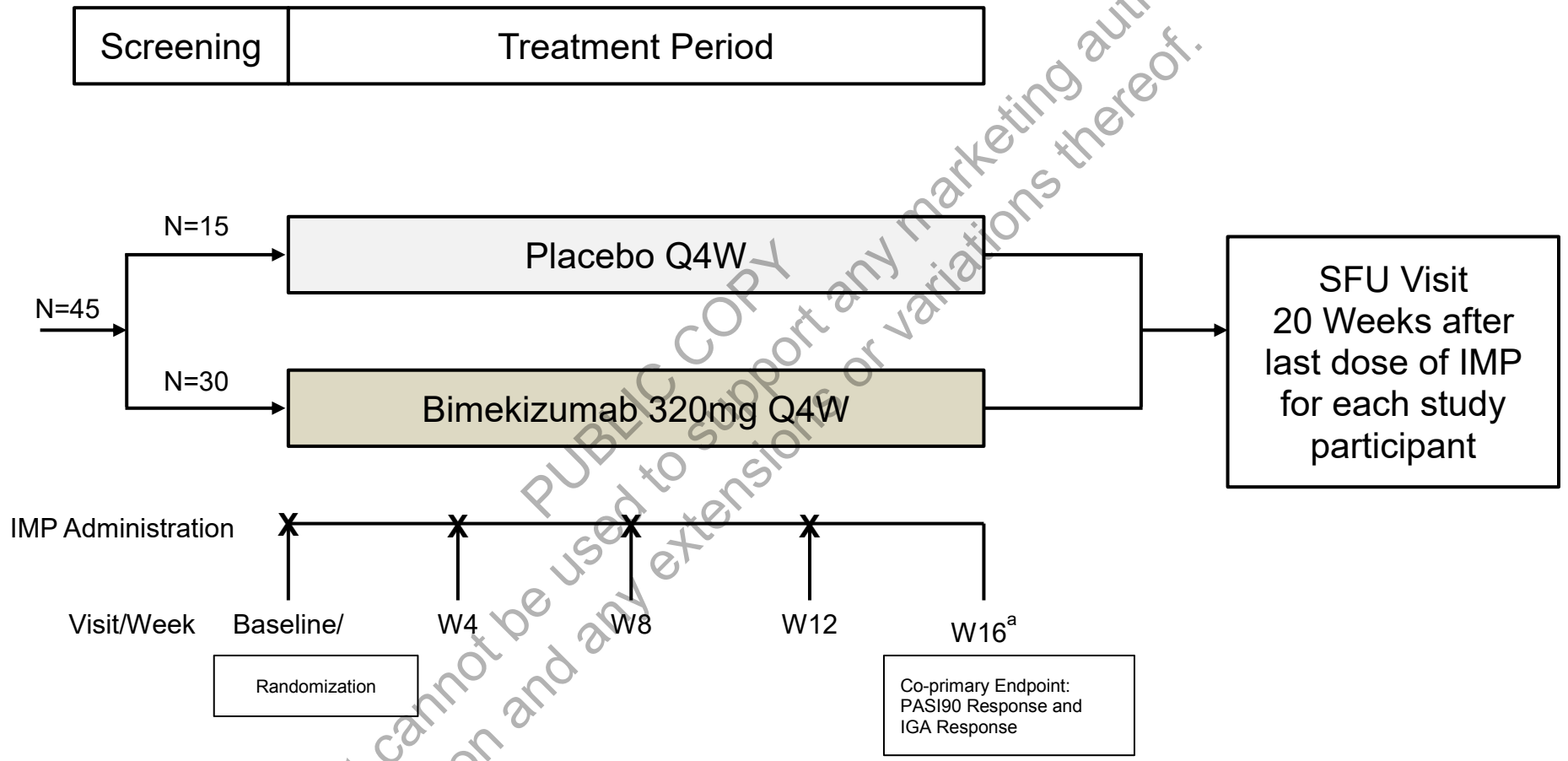
Approximately 45 adult Korean study participants will be randomly assigned to IMP for an estimated total of 30 evaluable study participants in the bimekizumab 320mg group and 15 study participants in the placebo group.

Treatment groups and duration

Study participants will be randomized 2:1 to 2 dose groups; bimekizumab 320mg Q4W or placebo. This study will include 3 periods: Screening Period (2 to 5 weeks), Treatment Period (16 weeks), and SFU Period (20 weeks after the last dose of IMP).

1.2 Schema

Figure 1-1: Study schematic



IGA= Investigator's Global Assessment; IMP=investigational medicinal product; MAP=managed access program; PASI=Psoriasis Area and Severity Index; PEOT=Premature End of Treatment; Q4W=every 4 weeks; SFU=Safety Follow-Up; W=Week

[a] If a participant completes Week16 and is provided the continued treatment with bimekizumab as part of the MAP, SFU is not required.

1.3 Schedule of activities

Table 1-1: Schedule of study assessments

Visit[a]/ Week / Protocol activity	Screening[b]	Treatment Period							SFU[c]
		Baseline (W0)	W1	W2	W4	W8	W12	W16/ PEOT	
Informed consent	X								
Inclusion/exclusion	X	X							
Urine drug screen	X								
Demographic data	X								
PSO history	X								
Significant past medical history and concomitant diseases	X	X[d]							
Physical examination [e, f]	X	X					X	X	X
Height		X							
Body weight		X						X	
Vital signs[g]	X	X	X	X	X	X	X	X	X
Hematology and biochemistry	X	X	X	X	X		X	X	X
Urinalysis	X	X						X	X
ECG	X							X	
Pregnancy testing[h]	X	X			X	X	X	X	X
Hepatitis B and C testing[i]	X								
HIV testing[j]	X								
Chest x-ray[k]	X								

Table 1-1: Schedule of study assessments

Visit[a]/ Week / Protocol activity	Screening[b]	Treatment Period							SFU[c]
		Baseline (W0)	W1	W2	W4	W8	W12	W16/ PEOT	
IGRA TB test	X								
TB questionnaire[l]	X	X					X[l]		X
PASI	X	X	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X	X	X
Scalp IGA[m]		X		X	X	X	X	X	X
Percentage of BSA	X	X	X	X	X	X	X	X	X
DLQI		X		X	X	X	X	X	
PHQ-9	X	X			X	X	X	X	X
C-SSRS	X	X			X	X	X	X	X
PSD (P-SIM) (daily)	X	X	X	X	X	X	X	X	
Concomitant medication	X	X	X	X	X	X	X	X	X
AEs	X	X	X	X	X	X	X	X	X
IRT[n, o]	X	X	X	X	X	X	X	X	X
Blood sample for PK plasma BKZ concentrations and anti-BKZ antibodies[p]		X			X	X	X	X	X
BKZ or placebo administration[n, o]		X			X	X	X		

AEs=adverse events; BKZ=bimekizumab; BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic Case Report Form; C-SSRS=Columbia Suicide Severity Rating Scale; HBcAb+=positive for anti-hepatitis B core antibody; HBsAg+=positive for hepatitis B surface antigen; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; MAP=Managed Access Program; PASI=Psoriasis Area Severity Index; PEOT=Premature End of Treatment; PHQ-9=Patient Health Questionnaire-9; PK=pharmacokinetic; PSD=patient symptom diary; P-SIM=Patient Symptom and Impact Measure; PSO=psoriasis; SFU=Safety Follow-Up; TB=tuberculosis; W=Week

[a] Visit windows of ±3 days from the first dose (W0) to the Week 16 visit. The SFU Visit window is ±7 days from last dose.
[b] The Screening Period will last 2 weeks, but can be extended up to a total of 5 weeks in cases where a laboratory assessment needs to be repeated or to allow washout of prohibited medications.
[c] For study participants not entering the MAP, the SFU Visit will occur 20 weeks after the final dose of IMP. No SFU will occur for study participants entering the MAP.
[d] Ensure no significant changes in medical history.
[e] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.
[f] The physical examination will be performed as per protocol.
[g] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and body temperature) are to be measured prior to blood sampling, and prior to IMP dosing, where applicable.
[h] Pregnancy testing will consist of serum testing at Screening. A urine pregnancy test will be administered at all other visits.
[i] Study participants who have evidence of or test positive for hepatitis B by any of the following criteria: 1) HBsAg+; 2) HBcAb+ are excluded. A positive test for HCV is defined as: 1) positive for hepatitis C antibody (anti-HCV Ab), and 2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction) are also excluded. Study participants will also be tested for antihepatitis B surface antibody.
[j] The HIV test results will not be recorded in the eCRF.
[k] Screening chest x-ray must occur within 3 months prior to the Screening Visit.
[l] Tuberculosis questionnaire will be required at PEOT.
[m] The scalp IGA will only be assessed for those study participants with scalp involvement (scalp IGA score >0) at Baseline.
[n] IMP administration is based on randomization.
[o] The dosing window is ±3 days relative to the scheduled dosing visit through Week 16.
[p] Samples will be collected prior to any IMP dosing at a visit.
[q] If an Unscheduled Visit is conducted due to safety or efficacy reasons, a C-SSRS assessment will be performed with the subject during the visit. If an Unscheduled Visit is conducted for reasons other than safety or efficacy concerns (eg, repeated collection of a laboratory specimen due to collection or analysis issues), a C-SSRS will not be required at these visits.

2 INTRODUCTION

2.1 Study rationale

Psoriasis is a common, chronic inflammatory disease characterized by a series of linked cellular changes in the skin: hyperplasia of epidermal keratinocytes, vascular hyperplasia and ectasia, and infiltration of T lymphocytes, neutrophils, and other types of leukocytes in affected skin. Therapy for patients with PSO varies according to the severity of disease. Limited or mild disease is often treated with topical therapies such as corticosteroids and vitamin D analogs. Patients with more severe disease are often treated with phototherapy, methotrexate, cyclosporine, the oral phosphodiesterase 4 inhibitor apremilast, or biologic agents, such as tumor necrosis factor (TNF) antagonists, interleukin (IL)-12/23 inhibitors, IL-23p19 inhibitors, and IL-17A inhibitors.

Though the pathophysiology of PSO is not fully understood, the importance of T-cells and inflammatory cytokines has been demonstrated by the clinical benefit provided by therapies directed at these targets (Krueger and Ellis, 2005). While antibodies targeting IL-17A cytokines have demonstrated efficacy in patients with PSO, psoriatic arthritis (PsA), and ankylosing spondylitis, as yet, no approved therapeutic approach selectively and potently inhibits the activity of both IL-17A and IL-17F (Krueger and Ellis, 2005).

Bimekizumab is a humanized, full-length monoclonal antibody (mAb) of the immunoglobulin G1 (IgG1) subclass with 2 identical antigen binding regions that potently and selectively bind and neutralize IL-17A, IL-17F, and IL-17AF cytokines. This property makes bimekizumab distinct from other IL-17-targeting agents, like secukinumab and ixekizumab (selective anti-IL-17A cytokine-targeting mAbs) or brodalumab (an-IL-17 receptor-targeting mAb). Bimekizumab is being developed for the treatment of adults with moderate to severe plaque PSO. Parallel programs in the inflammatory diseases of PsA, axial spondyloarthritis, and hidradenitis suppurativa are ongoing.

The purpose of this study is to evaluate the efficacy and safety of bimekizumab in adult Korean study participants with moderate to severe plaque PSO. Following the completion of the pivotal global Phase 3 program of bimekizumab in moderate to severe PSO, the aim of this study is to bridge the existing evidence of efficacy and safety of bimekizumab from the Phase 3 program with limited Korean participation to a Korean population of study participants with moderate to severe PSO.

2.2 Background

Psoriasis is a common, chronic inflammatory disease characterized by inflammation and keratinocyte proliferation. Plaque PSO, the most common form of the disease, is typified by areas of red, inflamed skin, often covered with thick, micaceous, silver-colored scales on extensor surfaces. Plaques may be pruritic and painful as the skin cracks and bleeds. In severe cases, plaques grow and merge into one another, covering large areas.

In addition to the impact on skin, PSO has a multitude of psychosocial and emotional effects on patients, including increased self-consciousness, frustration, fatigue, depression, and suicidal ideation. As a result, patients frequently report sleeping problems, difficulties at work, problems interacting with family members, disrupted leisure activities, and sexual difficulties

(Dowlatshahi et al, 2014; Gottlieb, 2005; Mukhtar et al, 2004; Ortonne, 2004; Krueger et al, 2001).

A number of comorbidities have been associated with PSO, especially with more severe PSO. Psoriatic arthritis, cardiovascular (CV) disease, metabolic syndrome, chronic pulmonary disease, peptic ulcer disease, renal disease, and diabetes have all been demonstrated to have an increased prevalence in PSO patients (Yeung et al, 2013; Christophers et al, 2010; Gisondi et al, 2007; Gelfand et al, 2006).

The reported prevalence of PSO in countries ranges between 0.09% and 11.43%, with at least 100 million individuals affected worldwide (WHO report on psoriasis, 2016). There are a variety of forms of PSO, including plaque, guttate, inverse, pustular, and erythrodermic. Plaque PSO (PSO vulgaris) is the most common, comprising approximately 80% to 90% of all cases. It is estimated that approximately 80% of patients with plaque PSO have mild to moderate disease, while 20% of patients have more severe disease, which affects either greater than 5% of BSA or is located on high impact areas including the scalp, genitals, hands, and nails (Boehncke and Schön, 2015; Menter et al, 2008).

Descriptions of nonclinical and clinical bimekizumab data, including the status of ongoing studies, are provided in the current version of the Investigator's Brochure (IB).

2.3 Benefit/risk assessment

Based on the limited data collected from Korean study participants in the completed Phase 3 pivotal program, the benefits and risks of bimekizumab administration in adult Korean study participants are expected to be similar to results in adult study participants with PSO to date.

In studies of bimekizumab in moderate to severe PSO, study participants achieved and maintained skin clearance across multiple efficacy variables, as assessed by PASI (change from Baseline and by various levels of response) and IGA responses, after up to 56 weeks of bimekizumab 320mg sc treatment administered Q4W or Q4W for an initial 16 weeks followed by every 8 weeks (Q8W) maintenance treatment. The observed safety data were as expected considering the mechanism of action of bimekizumab and the population under investigation. The vast majority of AEs were nonserious, mild to moderate, and did not lead to IMP discontinuation. The most commonly reported TEAEs in bimekizumab-treated study participants were nasopharyngitis, oral candidiasis, and upper respiratory tract infection.

Prespecified safety topics of interest for the study are: infections (serious, opportunistic, fungal, and TB), neutropenia, hypersensitivity, suicidal ideation and behavior, major CV events, liver function test (LFT) changes/enzyme elevations, malignancies, and inflammatory bowel diseases (IBD). This is based on findings from the bimekizumab clinical program to date, potential risks generally associated with biologic immunomodulators, or findings from other medicines with a related mechanism of action. There are no specific AE reporting requirements for these topics, however special monitoring, additional data collection activities, and/or enhanced signal detection activities (within UCB) are in place.

More detailed information about the known and expected benefits and risks and reasonably expected AEs of bimekizumab may be found in the IB.

3 OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	**Co-Primary Endpoints**
To evaluate the efficacy of bimekizumab compared with placebo	**Co-Primary Endpoint 1**: • Participant-level outcome: PASI90 response at Week 16 **Co-Primary Endpoint 2:** • Participant-level outcome: IGA 0/1 (clear or almost clear with at least a 2-category improvement from Baseline) response at Week 16
Secondary	
To evaluate the efficacy of bimekizumab compared with placebo at achieving complete skin clearance (PASI100/IGA 0)	• Participant-level outcome: PASI100 response at Week 16 • Participant-level outcome: IGA 0 (clear with at least a 2-category improvement from Baseline) response at Week 16
To evaluate the efficacy of bimekizumab compared with placebo at achieving rapid response (PASI75)	• Participant-level outcome: PASI75 response at Week 4
To evaluate the efficacy of bimekizumab compared with placebo on itch, pain, and scaling	Reported by study participants using the PSD (also published as P-SIM [Gottlieb et al, 2020]): • Participant-level outcome: PSD (P-SIM) response for itch at Week 16 • Participant-level outcome: PSD (P-SIM) response for pain at Week 16 • Participant-level outcome: PSD (P-SIM) response for scaling at Week 16
To evaluate the efficacy of bimekizumab compared with placebo on the change in psoriatic scalp disease in study participants with scalp PSO at Baseline	• Participant-level outcome: Scalp IGA 0/1 (clear or almost clear with at least a 2-category improvement from Baseline) response at Week 16 for study participants with scalp PSO at Baseline
To assess the effect of bimekizumab compared with placebo on QOL	• Participant-level outcome: DLQI 0/1 response at Week 16
To evaluate the effect of bimekizumab compared with placebo on percent change from Baseline in BSA affected by PSO	• Participant-level outcome: Percent change from Baseline in BSA affected by PSO at Week 16
To evaluate the safety of bimekizumab	• Incidence of TEAEs throughout the study • Incidence of TE-SAEs throughout the study • Incidence of TEAEs leading to permanent discontinuation of IMP throughout the study

Objectives	Endpoints
To assess the effect of bimekizumab on depression occurrence or worsening	• Change from Baseline in PHQ-9 at Week 16
Tertiary	
To evaluate the PK of bimekizumab in study participants with moderate to severe PSO	• Plasma bimekizumab concentrations over the study duration
To evaluate the immunogenicity of bimekizumab	• Anti-bimekizumab antibody status over the study duration
To assess the efficacy of bimekizumab compared with placebo over time	• PASI75 response over time • PASI90 response over time • PASI100 response over time • Absolute and percent change from Baseline in PASI score over time • Percentage of study participants with absolute PASI score ≤1, ≤2, ≤3, and ≤5 over time • Time to PASI50, PASI75, PASI90, and PASI100 response • IGA 0/1 response (with at least 2-category improvement from Baseline) over time • IGA 0 response (with at least 2-category improvement from Baseline) over time • Scalp-specific IGA (scalp IGA) 0/1 response (clear or almost clear with at least 2-category improvement from Baseline for participants with scalp PSO at Baseline) over time • Percentage of study participants with absolute BSA affected by PSO=0%, ≤1%, ≤3% and ≤5% over time • Percentage of study participants achieving a DLQI Total Score of 0 or 1 over time • Change from Baseline in DLQI Total Score over time • PSD (P-SIM) response rates over time • Change from Baseline in PSD (P-SIM) scores over time
To further evaluate the safety of bimekizumab compared with placebo over time	• Selected safety topics of interest TEAEs • Change from Baseline in laboratory variables (hematology and biochemistry) • Incidence of markedly abnormal laboratory values • Change from Baseline in vital signs • Incidence of markedly abnormal vital signs

Objectives	Endpoints
	• Change from Baseline in ECG parameters • ECG outliers • Change from Baseline in PHQ-9 • Incidence of PHQ-9 scores ≥15 and ≥20 • Incidence of suicidal ideation, suicidal behavior, or self-injurious behavior without suicidal intent (from C-SSRS)

4 STUDY DESIGN

4.1 Overall design

PS0032 is a Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of bimekizumab compared with placebo in adult Korean study participants with moderate to severe plaque PSO.

The study population consists of adult Korean study participants (≥19 years of age) with a diagnosis of moderate to severe plaque PSO (Baseline PASI ≥12 and BSA affected by PSO ≥10% and IGA score ≥3 on a 5-point scale) who are candidates for systemic PSO therapy and/or phototherapy.

This study will include 3 periods: Screening Period (2 to 5 weeks), Treatment Period (16 weeks), and SFU Period (20 weeks after the last dose of IMP [Figure 1-1]).

Study participants who have completed the 16-week Treatment Period may choose to enter into a MAP to receive open-label treatment with bimekizumab or enter the SFU.

The Screening Period will last 2 weeks, but can be extended up to a total of 5 weeks in cases where a laboratory assessment needs to be repeated or to allow washout of prohibited medications. During the Screening Period, eligible study participants will be informed about the study and sign the ICF. Following signed informed consent, all screening procedures and laboratory tests (hematology, urine, and biochemistry) will be performed per the SoA (Table 1-1). The Screening Period will also enable washout of any medications not permitted for use during the study. Study participants who require prophylaxis for LTB infection must be on treatment for at least 4 weeks prior to the first dose of IMP. These study participants may be rescreened after receiving prophylaxis treatment. One rescreening may be allowed after consultation with the Medical Monitor. Further details are provided in Section 5.4.

After completion of the Screening Period, eligible study participants will be allowed to enroll into the study. Approximately 45 adult Korean study participants will be randomized 2:1 to receive the following blinded IMP regimens during the Treatment Period:

- Bimekizumab 320mg Q4W administered sc injection (30 study participants)
- Placebo Q4W administered sc injection (15 study participants)

During the Treatment Period, IMP will be administered at the study site.

All study participants choosing not to transition into a MAP (see Section 6.8) will have a SFU Visit 20 weeks post last dose of IMP. Safety assessments will be made by ongoing monitoring and evaluation of AEs and other safety topics of interest specific to bimekizumab.

Study participants withdrawing early from IMP will undergo the PEOT Visit assessments and be asked to continue in the SFU Period.

IMP administration and all assessments to be performed during the study are presented in the SoA (Table 1-1).

4.2 Scientific rationale for study design

This bimekizumab Phase 3 local clinical study in Korean study participants with PSO is designed to support a bridging data submission package for approval of the PSO indication in Korea. Previously it was demonstrated in a dedicated Phase 1 PK study (UP0042) that the PK/PD profile of Caucasian and Asian study participants is largely comparable. In addition, subgroup analyses of the Phase 2 (PS0010 and PS0011) and Phase 3 (PS0009) PSO studies have indicated that results of the Asian population were comparable to those of the overall population. Population PK/PD analyses revealed a clear dose-response relationship and support the use of bimekizumab at an initial dose regimen of 320mg Q4W to ensure rapid and high skin clearance, followed by a less intense dose regimen (320mg Q8W) in the majority of study participants to maintain these initial responses beyond Week 16.

The clinical response obtained in the global PSO development program (PS0008, PS0009, and PS0013) at Week 16 was consistently maintained through one year in study participants receiving either bimekizumab 320mg Q4W or bimekizumab 320mg Q8W, supporting the rationale for a 16-week study. This study aims to demonstrate the superiority of clinical response to bimekizumab over placebo in Korean study participants to those of the overall population during the initial Treatment Period of 16 weeks, allowing for adequate extrapolation of results in the maintenance period.

4.3 Justification for dose

Bimekizumab 320mg Q4W treatment effects in the initial 16-week treatment period were rapid (PASI75 achieved after a single dose) and deep (complete PSO clearance demonstrated by PASI100 and IGA 0). Approximately 85% to 90% of study participants achieved a high level of response (PASI90) after 16 weeks of bimekizumab 320mg Q4W treatment.

Study PS0032 has been designed to mimic the initial Treatment Period of the 3 global Phase 3 studies (PS0008, PS0009, and PS0013) and evaluate the efficacy and safety of bimekizumab 320mg, administered sc Q4W, in Korean study participants to allow bridging to the global Phase 3 data.

4.4 End of study definition

A study participant is considered to have completed the study if he/she has completed the Treatment Period of the study (Week 16) regardless of transfer into the MAP or completion of the SFU visit (see Section 6.8).

The end of the study is defined as the date of the LPLV in the study.

5 STUDY POPULATION

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

5.1 Inclusion criteria

Study participants are eligible to be included in the study only if all of the following criteria are met at Screening and reconfirmed at the Baseline Visit:

Age

1. Study participant must be at least 19 years of age at the time of signing the informed consent.

Type of participant and disease characteristics

2. Study participant must be a Korean adult with a diagnosis of moderate to severe PSO.
3. Study participant must have had plaque PSO for at least 6 months prior to the Screening Visit.
4. Study participant must have PASI ≥12 and BSA affected by PSO ≥10% and IGA score ≥3 on a 5-point scale.
5. Study participant must be a candidate for systemic PSO therapy and/or phototherapy.
6. Study participant agrees not to change their usual sun exposure during the course of the study and to use ultraviolet A/ultraviolet B sunscreens if unavoidable exposure occurs.
7. Study participant is considered reliable and capable of adhering to the protocol (eg, able to understand and complete diaries), visit schedule, or medication intake according to the judgment of the Investigator.

Sex

8. A female study participant is eligible to participate if she is not pregnant (see Section 10.4 [Appendix 4]), not breastfeeding, and at least one of the following conditions applies:
   - Not a female of childbearing potential (FOCBP) as defined in Section 10.4 (Appendix 4)
     OR
     A FOCBP who agrees to follow the contraceptive guidance in Appendix 4 during the Treatment Period and for at least 20 weeks after the last dose of study treatment.

Informed consent

9. Study participant must be capable of giving signed informed consent as described in Section 10.1 (Appendix 1), which includes compliance with the requirements and restrictions listed in the ICF and in this protocol.

5.2 Exclusion criteria

Study participants are excluded from the study if any of the following criteria apply:

Medical conditions

1. Study participant has a form of PSO other than plaque-type (eg, pustular, erythrodermic and guttate PSO, or drug-induced PSO).
2. Study participant has an active infection or history of infections as follows:
   - Any active infection (except common cold) within 14 days prior to Baseline.
   - A serious infection, defined as requiring hospitalization or intravenous anti-infectives within 2 months prior to the Baseline Visit.
   - A history of opportunistic, recurrent, or infections that, in the opinion of the Investigator, might cause this study to be detrimental to the study participants. Opportunistic infections are infections caused by uncommon pathogens (eg, pneumocystis jirovecii, cryptococcosis) or unusually severe infections caused by common pathogens (eg, cytomegalovirus, herpes zoster).
3. Study participant has concurrent acute or chronic viral hepatitis B or C or human immunodeficiency virus (HIV) infection, or history of hepatitis B. Study participants who have evidence of, or tested positive for hepatitis B are excluded. A positive test for the hepatitis B virus (HBV) is defined as:
   - positive for hepatitis B surface antigen (HBsAg+) **or**
   - positive for anti-hepatitis B core antibody (HBcAb+).

   A positive test for the hepatitis C virus (HCV) is defined as:
   - positive for hepatitis C antibody (anti-HCV Ab) **and**
   - positive via a confirmatory test for HCV (eg, HCV polymerase chain reaction).
4. Study participant has a known tuberculosis (TB) infection, is at high risk of acquiring a TB infection, or has a current or history of nontuberculous mycobacterium (NTMB) infection. A study participant with LTB (a positive interferon-gamma release assay [IGRA] and diagnosis confirmed by a TB specialist) may be rescreened once and enrolled after receiving at least 4 weeks of appropriate LTB infection therapy and if no evidence of therapy-related hepatotoxicity has occurred prior to the first injection (alanine aminotransferase/aspartate aminotransferase [ALT/AST] remain ≤3×upper limit of normal [ULN]).

   Study participant has a past history of active TB involving any organ system unless adequately treated according to World Health Organization (WHO)/Centers for Disease Control (CDC) therapeutic guidance and proven to be fully recovered upon consult with a TB specialist.
5. Study participant has a history of a lymphoproliferative disorder, including lymphoma, or current signs and symptoms suggestive of lymphoproliferative disease.

6. Study participant has any active malignancy or history of malignancy within 5 years prior to the Screening Visit EXCEPT treated and considered cured cutaneous squamous or basal cell carcinoma, or in situ cervical cancer.
7. Study participant has a diagnosis of inflammatory conditions other than PSO or PsA, including but not limited to rheumatoid arthritis, sarcoidosis, or systemic lupus erythematosus. Study participants with a diagnosis of Crohn's disease or ulcerative colitis are allowed as long as they have no active symptomatic disease at Screening or Baseline.
8. Study participant has any systemic disease (ie, CV, neurological, renal, liver, metabolic, gastrointestinal, hematological, immunological, etc.) considered by the Investigator to be uncontrolled, unstable, or likely to progress to a clinically significant degree during the course of the study.
9. Study participant has had myocardial infarction or stroke within the 6 months prior to the Screening Visit.
10. Study participant has experienced primary failure (no response within 12 weeks) to 1 or more IL-17 biologic response modifier (eg, brodalumab, ixekizumab, secukinumab) **OR** more than 1 biologic response modifier other than an IL-17.
11. Study participant has a history of alcohol or drug abuse within 6 months prior to Screening as evaluated by the Investigator based on medical history, site interview, and/or results of the specified urine drug screen.
12. Study participant has a presence of active suicidal ideation, or positive suicidal behavior using the Columbia Suicide Severity Rating Scale (C-SSRS) and with either of the following criteria:
    - History of a suicide attempt within the 5 years prior to the Screening Visit. Study participants with a history of a suicide attempt more than 5 years ago should be evaluated by a mental healthcare practitioner (HCP) before enrolling into the study.
    - Suicidal ideation in the past month as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the C-SSRS.
13. Study participant has a presence of moderately severe major depression or severe major depression indicated by a score ≥15 using the Screening PHQ-9. Medication used to treat depression should be stable for 8 weeks prior to Baseline.
14. Study participant has a known hypersensitivity to any excipients of bimekizumab.
15. Study participant has any other condition, including medical or psychiatric, which, in the Investigator's judgment, would make the study participant unsuitable for inclusion in the study.

Prior/concomitant therapy

16. Study participant has received any live (includes attenuated) vaccination within the 8 weeks prior to the Baseline visit (eg, inactivated influenza and pneumococcal vaccines are allowed but nasal influenza vaccination is not permitted). Live vaccines are not allowed during the study, including the SFU Period (20 weeks after the final dose of IMP).

Administration of any other type of vaccine that is not a live or inactivated vaccine must be discussed with the study Medical Monitor or UCB Study Physician.

17. Study participant has received Bacillus Calmette-Guerin vaccinations within 1 year prior to the Baseline visit.
18. Study participant has had major surgery (including joint surgery) within the 3 months prior to the Baseline Visit or has planned major surgery within the duration of the study.
19. Study participant is taking or has taken prohibited PSO medications (Section 6.5.2) without meeting the mandatory washout period relative to the Baseline Visit.

Prior/concurrent clinical study experience

20. Study participant previously participated in a bimekizumab clinical study and received at least 1 dose of the IMP (including placebo).
21. Study participant previously participated in another study of a medication (systemic) under investigation within the 12 weeks or at least 5 half-lives prior to the Screening Visit, whichever is greater, or is currently participating in another study of a medication (systemic) under investigation.
22. Study participant previously participated in another study of a topical medication under investigation within the 4 weeks prior to the Screening Visit, or is currently participating in another study of a topical medication under investigation.
23. Study participant previously participated in another study of a medical device under investigation within the 4 weeks prior to the Screening Visit, or is currently participating in another study of a medical device under investigation.

Diagnostic assessments

24. Study participant has laboratory abnormalities at Screening, including any of the following:
    - ≥3×ULN of any of the following: ALT, AST, alkaline phosphatase (ALP); or >ULN total bilirubin (≥1.5×ULN total bilirubin if known Gilbert's syndrome)
    - White blood cell (WBC) count $<3.00\times10^3/\mu L$
    - Absolute neutrophil count $<1.5\times10^3/\mu L$
    - Lymphocyte count <500cells/µL
    - Hemoglobin <8.5g/dL
    - Any other laboratory abnormality, which, in the opinion of the Investigator, will prevent the study participant from completing the study or will interfere with the interpretation of the study results.

      Individual screening tests for which the results are in error, borderline, or indeterminate for inclusion in the study can be repeated once for confirmation during the Screening Period. Upon retesting, study participants whose results remain outside this threshold should not be randomized.

Other exclusions

25. Study participant is a member of Investigator site personnel directly affiliated with this study and/or their immediate families. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
26. Study participant is a UCB employee or an employee of third-party organizations involved in the study.

5.3 Lifestyle restrictions

Study participant agrees not to change his/her usual sun exposure during the course of the study and to use ultraviolet A/ultraviolet B sunscreens if unavoidable exposure occurs.

5.4 Screen failures

Screen failures are defined as study participants who consent to participate in the clinical study but are not subsequently randomized to study treatment. A minimal set of screen failure information is required to ensure transparent reporting of screen failure study participants to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any SAE.

One rescreening may be allowed after consultation with the Medical Monitor. Rescreened study participants should be assigned a new study participant number. Reasons for rescreening include, but are not limited to, the following:

- Study participant needs to complete a full course of antibiotic therapy for latent tuberculosis infection (LTBI) and can be rescreened after completion of 4 weeks of prophylaxis prior to Baseline as described in the exclusion criteria (Section 5.2).
- Individual laboratory screening tests for which the results are exclusionary can be retested. For example, tests that result in ALT, AST, or ALP up to 25% above the exclusion limit may be repeated once for confirmation; however, the Investigator will need to discuss with the Medical Monitor to help understand the elevation before the study participant can be enrolled. Tests can also be repeated during rescreening. Repetition of laboratory screening tests within the Screening Period for other than technical reasons (eg, frozen sample, expired laboratory kit) may not be performed without approval by Medical Monitor.
- Eligibility assessments could not be completed as planned (eg, for technical reasons) within the defined Screening Period of 5 weeks without approval by Medical Monitor.
- Participant does not meet the required washout period for concomitant medications (Section 6.5.2).

For randomized study participants with a Baseline result >ULN for ALT, AST, ALP, or total bilirubin, a Baseline diagnosis and/or the cause of any clinically meaningful elevation must be understood and recorded in the electronic Case Report form (eCRF).

If a participant has >ULN ALT, AST, or ALP that does not meet the exclusion limit at screening, repeat the tests, if possible, prior to dosing to ensure there is no further ongoing clinically

relevant increase. In case of a clinically relevant increase, inclusion of the study participant must be discussed with the Medical Monitor.

6 STUDY TREATMENTS

6.1 Treatments administered

Eligible study participants will be randomized 2:1 to receive the blinded study treatment regimens: bimekizumab 320mg Q4W or placebo (Table 6-1). Suitable areas for sc injections are the lateral abdominal wall, upper arm, and upper outer thigh. During each dosing visit, each of the injections should be administered at a separate injection site. Injection sites should be rotated at each visit, and injections should not be given into a PSO plaque or areas where the skin is tender, bruised, erythematous, or indurated. The injection should last approximately 10 to 15 seconds.

Further details of the IMPs and their specifications are provided in the IMP Handling Manual.

Table 6-1: Treatments administered

ARM Name	Bimekizumab	Placebo
IMP name	Bimekizumab 320mg Q4W	Placebo
Type	Biologic	N/A
Dose formulation	1mL PFS	1mL PFS
Unit dose strength(s)	160mg/mL	0.9% sodium chloride aqueous solution (physiological saline, preservative-free) of pharmacopoeia (USP/Ph.Eur) quality
Dosage level(s)	320mg Q4W	Placebo Q4W
Route of administration	sc injection	sc injection
Use	Bimekizumab = active	Placebo comparator
IMP	IMP	IMP
Sourcing	Provided centrally by the Sponsor	Provided centrally by the Sponsor
Packaging and labeling	Each PFS will be labeled as required by Korea.	Each PFS will be labeled as required by Korea.
Former name	UCB4940	N/A

IMP=investigational medicinal product; N/A=not applicable; PFS=prefilled syringe; Ph.Eur=European Pharmacopoeia; Q4W=every 4 weeks; sc=subcutaneous; USP=United States Pharmacopoeia

6.2 Preparation, handling, storage, and accountability requirements

Unblinded study staff will be responsible for preparation of the clinical study material, including recording the administration information on source documents, and administration of the IMP as sc injections. The unblinded personnel will not be involved in the study in any way other than

assuring the medication is taken from the correct kit and administering the IMP to the study participants.

Only study participants enrolled in the study may receive IMP, and only authorized site staff may supply or administer IMP. All IMP must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions, with access limited to the Investigator and authorized site staff.

The Investigator, institution, or the head of the medical institution (where applicable) is responsible for IMP accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records).

The Investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all IMP received and any discrepancies are reported and resolved before use of the IMP.

In case an out-of-range temperature is noted, it must be immediately reported as per instructions contained in the IMP Handling Manual.

Further guidance and information for the final disposition of unused IMP are provided in the IMP Handling Manual.

6.2.1 Drug accountability

During the Treatment Period of this study, the IMP will be administered in the clinic and compliance will be determined at the visit by study personnel.

The Drug Accountability Form will be used to record IMP dispensing and return information on a by-participant basis and will serve as source documentation during the course of the study. Details of any IMP lost, damaged (due to breakage or wastage), not used, partially used, disposed of at the study site, or returned to the Sponsor or designee must also be recorded on the appropriate forms. All supplies and pharmacy documentation must be made available throughout the study for UCB (or designee) to review.

In order to maintain the blind, all IMP documentation (eg, shipping receipts, drug accountability logs, interactive response technology (IRT) randomization materials) must be maintained and accessed by unblinded, trained site personnel only. Designated, unblinded site personnel must be appropriately trained and licensed (per country guidelines) to administer injections.

Unblinded study staff will be delegated the responsibility to receive, inventory, and destroy the used kits. The packaging identifies each kit by a unique number, but due to the open-label packaging, the unblinded study staff will be responsible in order to maintain the blind. Unblinded study staff will be responsible for preparation (breaking tamper proof sticker on kit, etc.) of the clinical study material, including recording the administration information on source documents.

The Investigator (or designee) is responsible for retaining all used, unused, and partially used containers of IMP until returned or destroyed.

The Investigator may assign some of the Investigator's duties for IMP accountability at the study site to an appropriate pharmacist/designee.

The Investigator must ensure that the IMP is used only in accordance with the protocol.

Periodically, and/or after completion of the clinical phase of the study, all used (including empty containers)/partially used, unused, damaged, and/or expired IMP must be reconciled and either destroyed at the site according to local laws, regulations, and UCB standard operating procedures, or returned to UCB (or designee). IMP intended for the study cannot be used for any other purpose than that described in this protocol.

6.3 Measures to minimize bias: randomization and blinding

An IRT will be used for assigning eligible study participants to a treatment regimen (as applicable) based on a predetermined production randomization and/or packaging schedule provided by UCB (or designee). The randomization schedule will be produced by the IRT vendor. The IRT will generate individual assignments for kits of IMP, as appropriate, according to the visit schedule.

At Screening, each study participant will be assigned a 5-digit number that serves as the study participant identifier throughout the study. The study participant number will be required in all communication between the Investigator or designee and the IRT regarding a particular participant.

At the Baseline Visit, a study participant will be randomized into the study. The Investigator or designee will use the IRT for randomization. The IRT will automatically inform the Investigator or designee of the study participant's identification number. The IRT will allocate kit numbers to the study participant based on the study participant number during the course of the study.

Study participant numbers and kit numbers will be tracked via the IRT.

6.3.1 Procedures for maintaining and breaking the treatment blind

6.3.1.1 Maintenance of study treatment blind

All study participant treatment details (bimekizumab or placebo) will be allocated and maintained by the IRT system.

In order to maintain the blind, all IMP documentation (eg, shipping receipts, drug accountability logs, IRT randomization materials) must be maintained and accessed by unblinded, trained site personnel only. Designated, unblinded site personnel must be appropriately trained and licensed (per Korea guidelines) to administer injections.

Unblinded study staff will be delegated the responsibility to receive, inventory, and destroy the used IMP. The packaging identifies each kit by a unique number. Unblinded study staff will be responsible for preparation (breaking tamper proof sticker on kit, etc.) of the IMP, including recording the administration information on source documents.

6.3.1.2 Breaking the treatment blind in an emergency situation

The integrity of this clinical study must be maintained by observing the treatment blind. In the event of an emergency for which the appropriate treatment for a study participant cannot be made without knowing the treatment assignment, it will be possible to determine to which treatment arm and dose the study participant has been allocated by contacting the IRT. All sites will be provided with details of how to contact the system for code breaking at the start of the study. The Medical Monitor or equivalent should be consulted prior to unblinding, whenever possible.

The Clinical Project Manager (CPM) will be informed immediately via the IRT when a code is broken, but will remain blinded to specific treatment information. Any unblinding of the IMP performed by the Investigator must be recorded in the source documents and on the Study Termination eCRF page.

6.4 Treatment compliance

During the Treatment Period of this study, the IMP will be administered in the clinic and compliance will be determined at the visit by study personnel. Drug accountability must be recorded on the Drug Accountability Form.

If a study participant is noncompliant with the study procedures or medications, in the opinion of the Investigator, then the study participant should be withdrawn as described in Section 7.2.

6.5 Concomitant medications/treatments

Any medications/treatment administered from the time of informed consent to the final study visit will be considered concomitant medication. This includes medications that were started before the study and are ongoing during the study.

6.5.1 Permitted concomitant treatments (medications and therapies)

The following concomitant medications are permitted during the study:

- Study participants may continue to use topical moisturizers or emollients, bath oils, or oatmeal bath preparations for skin conditions during the study, as needed (PRN).
- Mild and low potency topical steroids will be permitted for use limited to the face, axilla, and/or genitalia, PRN. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.
- Over-the-counter shampoos for the treatment of PSO of the scalp are permitted PRN. If this treatment contains a corticosteroid, it must adhere to the guidance for topical corticosteroids outlined in the above bullet.
- Study participants who are receiving an established regimen for depression should remain on stable dosing prior to Baseline and throughout the study. Medication used to treat depression should be stable for 8 weeks prior to Baseline.
- Study participants who are already receiving an established nonsteroidal anti-inflammatory drug (NSAID) regimen for PsA or symptoms of arthritis and have been on a stable dose for at least 1 week prior to the Screening Visit may continue their use during the study. However, initiation of, or increase in dosage of NSAIDs during the study (especially in study participants with a history of gastrointestinal (GI) intolerance to NSAIDs or a history of GI ulceration) should not occur prior to Week 16.
- Study participants may take mild pain relievers (acetaminophen/paracetamol, mild opiates) PRN for arthritis pain but preferably not within 24 hours of the Baseline Visit and the Week 16 Visit.
- Intra-articular steroid injections of any joint and hyaluronic acid injections are allowed after Week 16.

6.5.2 Prohibited concomitant treatments (medications and therapies)

For prohibited prior medications, refer to the exclusion criteria (Section 5.2).

The following concomitant medications and therapies are prohibited during the study:

Drug	Washout period relative to Baseline Visit
Topicals, except for those permitted	2 weeks
Systemic retinoids	1 month
Systemic treatment (nonbiological): systemic immunosuppressant agents (eg, methotrexate, cyclosporine, azathioprine, thioguanine) fumaric acid esters specifically used for the treatment of PSO systemic corticosteroids phototherapy	1 month
Anti-TNFs: etanercept (including biosimilar) infliximab (including biosimilar), golimumab, certolizumab pegol, adalimumab	 1 month for etanercept 3 months for infliximab (including biosimilar), golimumab, certolizumab pegol, adalimumab
Other biologics and other systemic therapies, eg,: apremilast, tofacitinib alefacept, efalizumab, guselkumab tildrakizumab, risankizumab ustekinumab, briakinumab rituximab	 2 weeks for apremilast and tofacitinib 3 months for alefacept, efalizumab, and guselkumab 5 months for tildrakizumab and risankizumab 6 months for ustekinumab and briakinumab 12 months for rituximab
Anti-IL-17 therapy: brodalumab ixekizumab secukinumab	3 months (bimekizumab is excluded per exclusion criteria)
Any other antipsoriatic agent (systemic) under investigation (or approved after the protocol is approved)	3 months or 5 half-lives, whichever is greater
Any other antipsoriatic agent (topical) under investigation	1 month

IL-17=interleukin 17; PSO=psoriasis; TNF=tumor necrosis factor

Study participants who take prohibited medications may be withdrawn from IMP but followed until the SFU Visit. The decision to withdraw a study participant for taking prohibited medications should be made in consultation with the Medical Monitor.

6.5.3 Vaccines

Administration of live (including attenuated) vaccines is not allowed during the conduct of the study and for 20 weeks after the last dose of IMP. Administration of inactivated vaccines is allowed during the study at the discretion of the Investigator in consultation with the Medical Monitor or UCB Study Physician.

Administration of any other type of vaccine that is not a live or inactivated vaccine must be discussed with the Medical Monitor or UCB Study Physician.

6.5.4 Rescue medication

No rescue medication is planned.

6.6 Dose modification

No dose modifications are allowed during the Treatment Period.

6.7 Criteria for study hold or dosing stoppage

UCB reserves the right to temporarily suspend or prematurely discontinue this study either at a single site, multiple sites, or at all sites at any time for reasons including, but not limited to, safety or ethical issues, inaccurate or incomplete data recording, noncompliance, or unsatisfactory enrollment with respect to quality or quantity.

If the study is prematurely terminated or suspended, UCB (or its representative) will inform the Investigators/institutions and the regulatory authority(ies) of the termination or suspension and the reason(s) for the termination or suspension, in accordance with applicable regulatory requirement(s). The Institutional Review Board (IRB)/Independent Ethics Committee (IEC) should also be informed and provided with the reason(s) for the termination or suspension by the Sponsor or by the Investigator/institution, as specified by the applicable regulatory requirement(s). In addition, arrangements will be made for the return or destruction of all unused IMP and other material in accordance with UCB procedures for the study.

6.8 Treatment after the end of the study

Study participants who have completed the 16-week Treatment Period may choose to enter into a MAP to receive open-label treatment with bimekizumab or enter the SFU.

7 DISCONTINUATION OF IMP AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 Discontinuation of IMP

A study participant should be withdrawn from IMP and will be asked to come back for the SFU Visit 20 weeks after last dose of IMP if any of the following events occur:

1. Study participant develops an illness that in the opinion of the Investigator would interfere with his/her continued participation if the risk of continuing participation outweighs the potential benefit.
2. Study participant develops erythrodermic, guttate, or pustular form of PSO.
3. Study participant is noncompliant with the study procedures or medications in the opinion of the Investigator.

4. Study participant uses prohibited concomitant medications, with the exception of topicals, that may present a risk to the safety of the study participant or the integrity of the study data, in the opinion of the Investigator and/or the Medical Monitor.
5. Study participant has a clinical laboratory value meeting any of the following criteria:
   - Hepatotoxicity as described in Section 7.1.1.
   - A laboratory value meeting any of the following criteria:
     - Absolute neutrophil count $<1.0\times10^3/\mu L$
     - Absolute lymphocyte count $<0.2\times10^3/\mu L$

   Study participants may remain in the study if the result is transient. A retest is required within 1 to 2 weeks at a scheduled or unscheduled visit. If the repeat absolute neutrophil count or absolute lymphocyte count is still below the allowable values, the study participant must be withdrawn. If the repeat absolute neutrophil count or absolute lymphocyte count is above the allowable values, the study participant may continue in the study.
6. The study participant experiences a severe AE, an SAE, or a clinically significant change in a laboratory value that, in the opinion of the Investigator, merits the discontinuation of IMP and appropriate measures being taken.
7. There is confirmation of a pregnancy during the study, as evidenced by a positive pregnancy test. Study participants with confirmed pregnancy must discontinue IMP and should remain in the study for safety follow-up (see Section 8.2.8.5).
8. A study participant considered as having either a suspected new LTBI or who develops an active TB or NTMB infection during the study must be immediately discontinued from IMP and a PEOT Visit must be scheduled as soon as possible, but not later than the next regular visit.

   The study participant must be permanently withdrawn if further examinations result in a diagnosis of active TB, or if the study participant is diagnosed with LTBI with no initiation of prophylactic treatment, prematurely discontinues prophylactic treatment, or, in the opinion of the Investigator or Sponsor, is noncompliant with prophylactic TB therapy.

   Confirmed active TB is an SAE and must be captured on an SAE Report Form and provided to the Sponsor in accordance with SAE reporting requirements. As with all SAEs, periodic follow-up reports should be completed as per protocol requirements until such time as the TB infection resolves.

   Additional information on TB policies is provided in Section 8.2.7.
9. Study participants with newly diagnosed IBD or IBD flares during the study must:
   - Be referred, as appropriate to a health care professional treating IBD, such as a gastroenterologist
   - Discontinue IMP and be followed-up until resolution of active IBD symptoms
   - If IBD flares increase in severity or frequency during the study, the Investigator should use clinical judgement in deciding whether the study participant should continue in the

study and contact the Medical Monitor and UCB Study Physician to confirm the study participant´s suitability for continued participation in the study.

10. Study participants **must be referred** immediately to a mental health care professional and may be withdrawn from the study based upon the Investigator's judgment of benefit/risk for:
    - Active suicidal ideation as indicated by a positive response ("Yes") to Question 4 of the "Since Last Visit" version of the C-SSRS.
    - Moderately severe major depression as indicated by a PHQ-9 score of 15 to 19 if this represents an increase of 3 points compared to last visit.
11. Study participants **must be referred** immediately to a mental health care professional and must be withdrawn from the study in case of:
    - Active suicidal ideation as indicated by a positive response ("Yes") to Question 5 of the "Since Last Visit" version of the C-SSRS.
    - Any suicidal behavior since last visit.
    - Severe major depression as indicated by a PHQ-9 score ≥20.

Study participants must be referred immediately to a mental health care professional for further assessment of any suicidal ideation/behavior (SIB) and/or any evidence of major depression. Investigators should contact the Medical Monitor, whenever possible, to discuss the withdrawal of a study participant in advance. Withdrawal is mandatory for suicidal behavior and/or a confirmed diagnosis of severe major depression. Otherwise, a withdrawal decision will be based on the Investigator's assessment of benefit/risk. The mental health consultation will be documented in source documentation.

7.1.1 Potential drug-induced liver injury IMP discontinuation criteria

Study participants with potential drug-induced liver injury (PDILI) must be assessed to determine if IMP must be discontinued. In addition, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued.

The PDILI criteria below require immediate and permanent discontinuation of IMP for study participants with either of the following:

- ALT or AST ≥8×ULN
- ALT or AST ≥3×ULN and coexisting total bilirubin ≥2×ULN

The PDILI criterion below requires immediate discontinuation of IMP for:

- Study participants with ALT or AST ≥3×ULN who exhibit temporally associated symptoms of hepatitis or hypersensitivity. Hepatitis symptoms include fatigue, nausea, vomiting, and right upper quadrant pain or tenderness. Hypersensitivity symptoms may include fever (without clear alternative cause), rash, or eosinophilia (ie, >5%).

  If a nondrug-related cause for the symptoms can be confirmed, these study participants may resume IMP administration after discussion with the responsible UCB Study Physician, but only when the requirements for rechallenge with IMP as provided in Section 10.6.2.1 are followed.

The PDILI criterion below allows for study participants to continue on IMP at the discretion of the Investigator.

- Study participants with ALT or AST ≥5×ULN and <8×ULN, total bilirubin <2×ULN, and no eosinophilia (ie, ≤5%), with no fever, rash, or symptoms of hepatitis (eg, fatigue, nausea, vomiting, right upper quadrant pain or tenderness).

Evaluation of PDILI must be initiated as described in Section 10.6.3, with repeat tests performed in 2 weeks. Upon retest, if ALT or AST values have reduced to <5×ULN, the study participant can continue with the study. However, if ALT or AST remains ≥5×ULN and <8×ULN after retest, IMP should be temporarily withheld and study participant should undergo a repeat test in two weeks. If ALT or AST values remain ≥5×ULN even after the second retest, then the study participant should be permanently withdrawn from the study and should be followed for possible drug-induced liver injury.

If study participants are unable to comply with the applicable monitoring schedule, IMP must be discontinued immediately.

Investigators should attempt to obtain information on study participants in the case of IMP discontinuation to complete the final evaluation. Study participants with PDILI should not be withdrawn from the study until investigation and monitoring are complete. All results of these evaluations and observations, as well as the reason(s) for IMP discontinuation and study participant withdrawal (if applicable), must be recorded in the source documents. The eCRF must document the primary reason for IMP discontinuation.

7.1.1.1 Follow-up evaluation

Potential drug-induced liver injury events require follow-up monitoring as described in Table 10-2. Monitoring should continue until liver chemistry values normalize, stabilize, or return to Baseline. Determination of stabilization is at the discretion of the Investigator in consultation with the hepatologist (as applicable) and UCB responsible physician, as needed.

7.1.2 Clinical laboratory criteria

Study participants should be monitored for absolute neutrophil count and/or absolute lymphocyte count as described in Section 7.1.

7.1.3 Treatment interruptions/temporary discontinuation of IMP

Doses of IMP that were missed due to a reasonable interfering AE or exceptional circumstance, which do not allow administration of IMP due to safety reasons, will not result in the study participant being considered noncompliant. The AE or exceptional circumstance should be discussed immediately with the Medical Monitor.

Any considerations related to restarting IMP should be discussed with the Medical Monitor.

The Investigator should not deviate from the protocol. However, the Investigator should take any measure necessary in deviation from, or not defined by, the protocol in order to protect clinical study participants from any immediate hazard to their health and safety. In this case, this action should be taken immediately, without prior notification of the regulatory authority, IRB/IEC, or Sponsor.

After implementation of such measure, the Investigator must notify the CPM of the Sponsor within 24 hours and follow any local regulatory requirements.

Any participant who develops a clinically important infection or recurrent infection not responsive to standard therapy during the study must discontinue IMP until resolution of the infection. The Investigator should use clinical judgement in deciding whether the participant should restart IMP, and contact the Medical Monitor and UCB study physician to confirm the participant's suitability for continued participation in the study.

7.2 Participant discontinuation/withdrawal from the study

If a study participant is unable to attend a visit due to the COVID-19 pandemic, study specific contingencies will be followed and the study participant should not be withdrawn.

Study participants are free to withdraw from the study at any time, without prejudice to their continued care.

Study participants should be withdrawn from the study and will be encouraged to come back for the SFU Visit 20 weeks after last dose of IMP if the study participant withdraws his/her consent or the Sponsor or a regulatory agency requests withdrawal of the study participant.

A study participant may withdraw from the study at any time at his/her own request, or may be withdrawn at any time at the discretion of the Investigator for safety, behavioral, compliance, or administrative reasons.

If the study participant withdraws consent for disclosure of future information, the Sponsor may retain and continue to use any data collected before such a withdrawal of consent.

If a study participant withdraws from the study, he/she may request destruction of any samples taken and not tested, and the Investigator must document this in the site study records.

See the SoA for data to be collected at the time of study discontinuation, follow-up, and any further evaluations that need to be completed (Table 1-1).

Refer to Section 7.1 for additional participant discontinuation/withdrawal criteria.

7.3 Lost to follow up

A study participant will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a study participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the study participant and reschedule the missed visit as soon as possible, counsel the study participant on the importance of maintaining the assigned visit schedule, and ascertain whether or not the study participant wishes to and/or should continue in the study.
- Before a study participant is deemed lost to follow up, the Investigator or designee must make every effort to regain contact with the study participant (at least 1 phone call and 1 written message to the study participant), and document his/her effort (date and summary of the phone call and copy of the written message in the source documents) to complete the final evaluation. All results of these evaluations and observations, together with a narrative

description of the reason(s) for removing the study participant, must be recorded in the source documents. The eCRF must document the primary reason for withdrawal.

Should the study participant continue to be unreachable, he/she will be considered to have withdrawn from the study with a primary reason of lost to follow up documented in the eCRF.

8 STUDY ASSESSMENTS AND PROCEDURES

Study procedures and their timing are summarized in the SoA (Table 1-1).

Some study-specific investigations may not be possible to be conducted according to the study protocol during a pandemic or other exceptional circumstances (eg, hurricanes) due to the need to implement safety measures and guidance from regulatory authorities. In such a situation, which may be accompanied by local or global containment or other measures, sites may need to prohibit access to study participants and study-related personnel. Study participants' visits to the study site may be replaced by contingency measures. These measures are primarily established to ensure the continued safety of study participants during the course of the study and to maintain the study participants' treatment schedule; if the Investigator considers it appropriate. The contingency measures will be described in a contingency plan which will be maintained by UCB for the respective study. The contingency measures are shared with the Investigator and the respective study-related personnel as soon as there are indications that it is necessary to implement any of the measures.

Protocol waivers or exemptions are not allowed.

Immediate safety concerns should be discussed with the Sponsor immediately upon occurrence or awareness to determine if the study participant should continue or discontinue IMP.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential study participants meet all eligibility criteria at the Baseline Visit for randomization. The Investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the study participant's routine clinical management (eg, blood count) and obtained before signing of the ICF may be utilized for Screening or Baseline purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the SoA (Table 1-1).

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

8.1 Efficacy assessments

8.1.1 PASI

The PASI is the most commonly used and validated assessment for grading the severity of PSO in clinical studies (Feldman, 2004). The PASI quantifies the severity and extent of the disease and weighs these with the percentage of BSA involvement. The PASI will be completed by the Investigator electronically at the visits specified in the SoA (Table 1-1).

The percent area of involvement (BSA%) is estimated across 4 body areas; head, upper extremities, trunk, and lower extremities. Assessors will enter the degree of involvement for a given region on a scale of 0 to 6 (0=none; 1=1% to <10% affected; 2=10% to <30% affected; 3=30% to <50% affected; 4=50% to <70% affected; 5=70% to <90% affected; 6=90% to 100% affected) (Table 8–1).

The Investigator assesses the average redness, thickness, and scaliness of lesions in each body area (each on a 5-point scale); 0=none, 1=slight, 2=moderate, 3=marked, and 4=very marked.

The PASI score ranges from 0 to 72, with a higher score indicating increased disease severity.

Table 8–1: Body areas for calculation of percent BSA for PASI

Body area	Details of area	BSA	Degree of involvement of body area[a]
Head	Face, back of head	10%	0 to 6
Upper extremities	Left, right, upper lower, flexor surface, extensor surface	20%	0 to 6
Trunk	Front, back, groin	30%	0 to 6
Lower extremities	Left, right, upper lower, flexor surface, extensor surface, including buttocks	40%	0 to 6
Total		100%	

BSA=body surface area; PASI=Psoriasis Area and Severity Index

[a] Where 0=none; 1=1% to <10% affected; 2=10% to <30% affected; 3=30% to <50% affected; 4=50% to <70% affected; 5=70% to <90% affected; 6=90% to 100% affected

The PASI50, PASI75, PASI90, and PASI100 responses are based on at least 50%, 75%, 90%, and 100% improvement in the PASI score, respectively. The total BSA affected by PSO will be entered as a percentage from 0 to 100.

8.1.2 IGA

A static IGA for PSO will be used to assess disease severity in all study participants during the study. The IGA will be completed at the visits specified in the SoA (Table 1-1).

The Investigator will assess the overall severity of PSO using the following 5-point scale presented in Table 8-2 below.

Table 8-2: Five-point IGA

Score	Short descriptor	Detailed descriptor
0	Clear	No signs of PSO; postinflammatory hyperpigmentation may be present
1	Almost clear	No thickening; normal to pink coloration; no to minimal focal scaling
2	Mild	Just detectable to mild thickening; pink to light red coloration; predominately fine scaling
3	Moderate	Clearly distinguishable to moderate thickening; dull to bright red, moderate scaling
4	Severe	Severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions

IGA=Investigator's Global Assessment; PSO=psoriasis

8.1.3 DLQI

The DLQI is a questionnaire designed for use in adult study participants with PSO. The DLQI is a skin disease-specific questionnaire aimed at the evaluation of how symptoms and treatment affect study participants' health related QOL. This instrument asks study participants about symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. It has been shown to be valid and reproducible in study participants with PSO. The DLQI score ranges from 0 to 30, with higher scores indicating lower health related QOL. A 4-point change in the DLQI score (DLQI response) has been reported to be meaningful for the study participant (within-subject minimal important difference); while a DLQI absolute score of 0 or 1 indicates no or small impact of the disease on health related QOL (Basra et al, 2015; Hongbo et al, 2005). Study participants will be asked to complete the DLQI as outlined in the SoA (Table 1-1).

8.1.4 Scalp IGA

A static IGA for scalp PSO will be used to assess disease severity on the scalp.

The scalp IGA will be assessed for all study participants at Baseline. The scalp IGA will be completed by the Investigator electronically. Only study participants with a scalp IGA score >0 at Baseline will have the scalp IGA assessed at later visits as specified in the SoA (Table 1-1).

Scalp lesions will be assessed in terms of clinical signs of redness, thickness, and scaliness using a 5-point scale (Table 8-3).

Table 8-3: Scalp IGA

Score	Short descriptor	Detailed descriptor
0	Clear	Scalp has no signs of PSO; postinflammatory hyperpigmentation may be present
1	Almost Clear	Scalp has no thickening; normal to pink coloration; no to minimal focal scaling
2	Mild	Scalp has just detectable to mild thickening; pink to light red coloration; predominately fine scaling

Table 8-3: Scalp IGA

Score	Short descriptor	Detailed descriptor
3	Moderate	Scalp has clearly distinguishable to moderate thickening; dull to bright red, moderate scaling
4	Severe	Scalp has severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions

PSO=psoriasis

8.1.5 PSD (P-SIM) responses

UCB developed a new electronic patient-reported outcome (ePRO) measure that will be used to assess key symptoms relevant to study participants with moderate to severe plaque PSO. PS0010 used the draft ePRO measure in selected countries to enable psychometric validation of the ePRO.

The PSD (P-SIM) consists of 14 items, measuring the following PSO-related signs, symptoms, and functional impacts: redness, scaling, cracking, lesions, thickening, itch, pain, burning, dryness, irritation, sensitivity, fatigue, embarrassment, and choice of clothing. Each item is assessed for severity/impact level over a recall period of the past 24 hours on a 0 to10 scale, where 0 means no symptoms or impact and 10 means very severe symptoms or worst impact.

Site staff will train study participants on the use of the ePRO diary at the Screening Visit, following which the device will be dispensed to the study participant for home use until the Week 16 Visit. The ePRO diary will be completed on a daily basis from Screening to the Week 16 Visit.

The ePRO diary software will be programmed such that the study participants will be given a window of opportunity to complete the ePRO diary. The data collected on the ePRO diary will be uploaded to a central server database and will be 21 CFR Part 11 compliant. Appropriate Good Clinical Practice (GCP) procedures (including study participant/site training and testing) will be performed at the study sites.

8.2 Safety assessments

Planned timepoints for all safety assessments are provided in the SoA (Table 1-1).

8.2.1 Physical examination

A physical examination will be performed at the visits specified in the SoA (Table 1-1). The physical examination will include general appearance; ear, nose, and throat; eyes, hair, and skin; respiratory; CV; GI; musculoskeletal; hepatic; neurological (including limb reflexes); and mental status. All physical examinations will also include evaluation of signs and symptoms of active TB and risk for exposure to TB (Section 8.2.7.3). Findings considered clinically significant changes since the physical examination at the Screening Visit will be recorded as AEs.

Investigators should pay special attention to clinical signs related to previous serious illnesses.

8.2.2 Vital signs

Vital signs will be collected at every visit and will include systolic and diastolic blood pressure (BP), pulse rate, and body temperature (oral, axillary, or otic). Study participants should be sitting for 5 minutes before and during vital signs assessments.

Vital signs should be assessed prior to IMP administration and prior to any blood collection.

8.2.3 12-lead ECGs

Twelve-lead standard ECGs will be recorded at the Screening and Week 16 visits and read by a central ECG reader. Full details of ECG recording will be provided in the ECG Manual.

8.2.4 PHQ-9

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression (Kroenke et al, 2001). The PHQ-9 scores for depression range from 0 to 27 with higher scores indicating a worse state. 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.

Refer to Section 7.1 for PHQ-9-related IMP discontinuation criteria.

8.2.5 Clinical safety laboratory assessments

All protocol-required laboratory assessments, as defined in Section 10.2 , must be conducted in accordance with the laboratory manual and the SoA (Table 1-1). See Section 10.2 and the SoA for the list, timing, and frequency of clinical laboratory tests to be performed.

The Investigator must review the laboratory report, document this review, and record any clinically significant changes occurring during the study in the AE section of the eCRF. The laboratory reports must be filed with the source documents. Clinically significant abnormal laboratory findings are those which are not associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the study participant's condition.

All laboratory tests with values considered clinically significantly abnormal during participation in the study or within 20 weeks after the last dose of IMP should be repeated until the values return to normal or Baseline or are no longer considered clinically significant by the Investigator or Medical Monitor. If such values do not return to normal/Baseline within a period of time judged reasonable by the Investigator, the etiology should be identified and the Sponsor notified.

If laboratory values from nonprotocol specified laboratory assessments performed at the institution's local laboratory require a change in study participant management or are considered clinically significant by the Investigator (eg, SAE or AE or dose modification), then the results must be recorded in the eCRF.

8.2.6 Neuropsychiatric AE monitoring/suicidal risk monitoring

Suicidal ideation and behavior will be assessed by using the C-SSRS. The questionnaire will be administered and assessed by trained study personnel. This scale will be used to assess suicidal ideation and behavior that may occur during the study. The visits at which the C-SSRS assessments will be performed are specified in the SoA (Table 1-1).

The C-SSRS is a standardized and validated instrument developed for the assessment of the severity and frequency of suicidal ideation and behavior (Posner et al, 2011; Mundt et al, 2010). Participants respond to standardized clinical questions that are presented in a uniform fashion. The C-SSRS defines 5 subtypes of suicidal ideation and behavior in addition to self-injurious behavior with no suicidal intent. The C-SSRS takes approximately 3 to 10 minutes to complete.

Refer to Section 7.1 for C-SSRS-related IMP discontinuation.

8.2.7 Assessment and management of TB and TB risk factors

All study participants will be assessed for TB through physical examination for signs and symptoms of TB (Section 8.2.7.3.1), laboratory testing (Section 8.2.5), chest x-ray (Section 8.2.7.3.2), and TB questionnaire (Section 8.2.7.3.3).

8.2.7.1 Definitions

Study participants with known active TB disease, at high risk of acquiring TB infection, or with untreated LTBI (ie, pending anti-TB prophylactic course) or current or history of NTMB infection are excluded from the study.

a. Known TB infection whether present or past is defined as:
   - Active TB disease or clinical signs and symptoms strongly suggestive of TB (pulmonary or extra pulmonary)
   - History of active TB disease involving any organ system or findings in other organ systems consistent with TB, unless adequately treated and proven to be fully recovered upon consult with a TB specialist
   - Any evidence by radiography or other imaging modalities consistent with previously active TB disease that is not reported in the study participant's medical history

b. High risk of acquiring TB infection is defined as:
   - Known close exposure (eg, sleeping in the same room) to another person with active TB infection within 3 months prior to Screening
   - Time spent within 3 months prior to Screening in a health care delivery setting or institution where individuals infected with TB are housed or where the risk of transmission of infection is high

c. Latent TB infection is defined as an infection by *Mycobacterium tuberculosis* with:
   - A positive IGRA (or 2 indeterminate IGRAs), AND
   - Chest imaging (or other imaging) negative for TB infection, AND
   - Absence of signs, symptoms (eg, evidence of organ-specific involvement), or physical findings suggestive of TB infection.

d. Pulmonary NTMB infection is defined as a group of lung or extrapulmonary infections caused by mycobacteria different from *M. tuberculosis* infections.

8.2.7.2 Assessments at Screening

At Screening, all study participants will have an IGRA test (QuantiFERON Gold Plus TB test is recommended), a chest x-ray (unless already performed within 3 months of Screening, a computed axial tomography [CAT] scan of the chest at Screening or within 3 months prior to Screening is acceptable, if available), and examination for signs and symptoms of TB. In addition, each study participant will complete a TB questionnaire directed at potential exposure to TB and symptoms of TB.

Study participants diagnosed with active TB during Screening will be excluded from the study. Study participants with LTBI diagnosed during Screening must complete a full course of prophylaxis and can be rescreened after completion of 4 weeks of prophylaxis prior to Baseline.

Study participant eligibility, retesting requirements, and treatment requirements at Screening are shown in Figure 8-1.

Figure 8-1: Decision tree for IGRA TB results at Screening

IGRA=interferon-gamma release assay; LTBI=latent tuberculosis infection; TB=tuberculosis
[a] IGRA retest must be done during the protocol-defined Screening window.
[b] Study participants with LTBI diagnosed during Screening must complete a course of prophylaxis. Study participants can be rescreened after completion of 4 weeks of prophylaxis prior to Baseline.

8.2.7.3 Assessment and reporting of TB and TB risk factors during the study

8.2.7.3.1 Physical examination

The Investigator should consider all potential sites of infection when assessing for TB during the physical examination, and other evaluations, and based on the study participant's medical or social history.

The most common primary focus of TB is the lung. Other sites may include gastrointestinal system, bone/joints, lymph glands, and meninges, etc. However, in immune-compromised patients, study participants, and/or patients treated with biologics, especially TNF inhibitors, extra pulmonary manifestations of TB are common compared to the normal population.

Some common symptoms that the study participant may present are dependent on the primary focus of infection and may include cough, blood in sputum, night sweats, lymphadenitis, joint pain/swelling, spinal deformity, headache/confusion, abdominal pain (mimicking IBD), etc. Unusual presentations should always be considered.

8.2.7.3.2 Chest x-ray for TB

Chest radiographic imaging is performed at Screening and results must be available at Baseline before first IMP administration unless a chest x-ray or CAT scan is available within 3 months prior to Screening.

Additional chest x-rays or other imaging tests should be performed when positive signs and symptoms indicate pulmonary infection, including potential TB infection, or when close exposure to persons with TB is documented.

8.2.7.3.3 TB questionnaire

The questionnaire "Evaluation of signs and symptoms of tuberculosis" should be used as a source document. The questionnaire will be completed as described in the SoA (Table 1-1). The questionnaire will assist with the identification of study participants who may require therapy for TB. A study participant who answers "Yes" to the question "Has the study participant been in close contact with an individual with active TB, or an individual who has recently been treated for TB?" at Screening is excluded. A "Yes" response to any of the other questions within the questionnaire at Screening should trigger further careful assessment to determine if the study participant has LTB or active TB (see Section 8.2.7.1). A "Yes" response to any of the questions during the study should trigger further assessments to determine if the study participant has either LTB or active TB infection.

8.2.7.3.4 IGRA test conversion

The IGRA is a whole blood testing methodology for diagnosing *M. tuberculosis* infection. It has become the gold standard, but does not help in differentiating LTBI from active TB disease.

Tuberculosis test conversion is defined as a positive or indeterminate (and confirmed indeterminate on repeat) IGRA result for the current test when previous IGRA test results were negative. All study participants with positive or indeterminate IGRA test results must immediately stop IMP administration. In case of an IGRA test conversion, the study participant must be considered as having either a suspected new latent or an active TB infection and be promptly referred to an appropriate specialist (eg, pulmonologist, infectious disease specialist) for further evaluation. However, the IGRA test conversion will not be detected since the IGRA

will be done at the Screening Visit only in this study. Additional assessments (eg, blood tests or IGRA, chest X-rays, or other imaging) should be performed where medically relevant and documented. Such conversions should be reported as AEs as described in the protocol. The AE term should be updated with the final diagnosis once available.

8.2.7.3.5 Latent TB

In case the evaluation by the appropriate specialist diagnoses a new LTBI, a TB prophylactic therapy in accordance with applicable clinical guidelines should be immediately initiated.

Study participants who initiate treatment for LTBI during the Screening Period must repeat initial screening laboratory parameters, all physical examinations, and questionnaires prior to randomization in the study, and must continue the full course of TB prophylactic therapy. Study participants can be rescreened after completion of 4 weeks of prophylaxis prior to Baseline

If no TB prophylactic therapy is initiated for the newly diagnosed LTBI during Screening, the study participant must not be enrolled into the study. Every related action should be discussed in advance with the Medical Monitor.

Any study participant who develops LTBI during the study must discontinue further administration of IMP and a PEOT Visit must be scheduled as soon as possible, but not later than the next regular visit. The study participant must be permanently withdrawn if the study participant is diagnosed with LTBI with no initiation of prophylactic treatment, prematurely discontinues prophylactic treatment, or, in the opinion of the Investigator or Sponsor, is noncompliant with prophylactic TB therapy. Once withdrawn, the PEOT Visit must be scheduled as soon as possible, and the study participant should be encouraged to keep the SFU Visit. Latent TB infection must be reported as an AE. Follow-up reports should be completed as per protocol requirement until such time as the LTBI resolves.

8.2.7.3.6 Active TB or nontuberculosis mycobacterium infection

Study participants who develop active TB or NTMB infection during the study must be withdrawn from the study. The study participant must be immediately permanently discontinued from IMP and a PEOT Visit must be scheduled as soon as possible, but no later than the next scheduled visit. The study participant should be encouraged to keep the SFU Visit as specified by the protocol. Treatment for active TB or NTMB should be started immediately.

Confirmed active TB is always considered an SAE. UCB's process requires that these must be captured on an SAE Report Form and provided to the Sponsor in accordance with SAE reporting requirements (Section 10.3 [Appendix 3]). Follow-up reports should be completed as per protocol requirement until such time as the TB infection resolves.

8.2.7.3.7 Tuberculosis management of LTBI, active TB, or other NTMB infection identified during study

During the study, study participants who develop evidence of LTBI, active TB, or NTMB infection must immediately stop further administration of IMP and will be referred to a TB specialist (pulmonologist or infectious disease specialist) for further evaluation. Study participants diagnosed with active TB or LTBI should receive appropriate TB or prophylaxis therapy. The study participant should be transferred to the care of his/her physician and managed according to the standard of care.

Study participants identified as having active TB during the study must be withdrawn and scheduled to return for the PEOT Visit as soon as possible, but no later than the next scheduled study visit, and complete all PEOT assessments. The study participant should be encouraged to complete a SFU Visit after the final dose of IMP.

If infection with NTMB is identified during the study, the same procedure as for active TB acquired during the study and compliant TB treatment shall be followed.

Additional details on TB detection and management are provided in the UCB TB Detection Procedure Guideline.

8.2.8 Adverse events and SAEs

Adverse events will be reported by the study participant.

The Investigator and any designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible for following up AEs that are serious, considered related to the study treatment or study procedures, or that caused the study participant to discontinue the IMP or the study (Section 7).

8.2.8.1 Time period and frequency for collecting AE and SAE information

All AEs and SAEs will be collected from the signing of the ICF until the SFU Visit at the time points specified in the SoA (Table 1-1).

In order to ensure complete safety data collection, all AEs occurring during the study (ie, after the signing of the ICF), including any pretreatment and post-treatment periods required by the protocol, must be reported in the CRF even if no IMP was taken but specific study procedures were conducted. This includes all AEs not present prior to the Screening Visit and all AEs that recurred or worsened after the Screening visit.

All SAEs will be recorded and reported to the Sponsor or designee within 24 hours, as indicated in Section 10.3. The Investigator will submit any updated SAE data to the Sponsor within 24 hours of it being available.

The Investigator is specifically requested to collect and report to UCB (or its representative) any SAEs (even if the Investigator is certain that they are in no way associated with the IMP), up to 20 weeks from the final dose of IMP for each study participant, and to also inform study participants of the need to inform the Investigator of any SAE within this period. Serious AEs that the Investigator thinks may be associated with the IMP must be reported to UCB regardless of the time between the event and the end of the study.

The method of recording, evaluating, and assessing causality of AEs, SAEs and the procedures for completing and transmitting SAE reports are provided in Section 10.3.

8.2.8.2 Method of detecting AEs and SAEs

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the study participant is the preferred method to inquire about AE occurrences.

8.2.8.3 Follow-up of AEs and SAEs

After the initial AE/SAE report, the Investigator is required to proactively follow each participant at subsequent visits/contacts. All will be followed until resolution, stabilization, the Investigator determines that it is no longer clinically significant, the event is otherwise explained, or the participant is lost to follow up (as defined in Section 7.3). Further information on follow-up procedures is given in Appendix 3 (Section 10.3).

8.2.8.4 Regulatory reporting requirements for SAEs

Prompt notification by the Investigator to the Sponsor of a SAE is essential so that legal obligations and ethical responsibilities towards the safety of study participants and the safety of a IMP under clinical investigation are met.

The Sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of IMP under clinical investigation. The Sponsor will comply with Korean regulatory requirements relating to safety reporting to the regulatory authority, IRB/IEC, and Investigators.

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions (SUSAR) according to local regulatory requirements and Sponsor policy, and forwarded to Investigators as necessary.

An Investigator who receives an Investigator safety report describing a SAE or other specific safety information (eg, summary or listing of SAEs) from the Sponsor will review and then file it along with the IB, and will notify the IRB/IEC, if appropriate according to local requirements.

8.2.8.5 Pregnancy

Details of all pregnancies in female study participants and female partners of male study participants will be collected after the start of study treatment and until the SFU Visit.

If a pregnancy is reported, the Investigator must immediately inform the Sponsor within 24 hours of learning of the pregnancy and should follow the procedures outlined in Appendix 4 (Section 10.4).

The female study participant should be discontinued from the IMP as soon as pregnancy is known (by positive pregnancy test), and the following should be completed:

- The study participant should return for a PEOT Visit.
- The study participant should immediately stop the intake of the IMP.
- A SFU Visit should be scheduled 20 weeks after the study participant has discontinued IMP.

Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered SAEs.

8.2.8.6 AEs of special interest

An adverse event of special interest (AESI) is any AE that a regulatory authority has mandated be reported on an expedited basis, regardless of the seriousness, expectedness, or relatedness of the AE to the administration of a UCB product/compound.For bimekizumab, the following events require immediate reporting (within 24 hours regardless of seriousness) to UCB:

- Hy's Law
  - Potential Hy's Law, defined as ALT or AST ≥3×ULN with coexisting total bilirubin ≥2×ULN in the absence of ALP ≥2×ULN, with no alternative explanation for the biochemical abnormality (ie, without waiting for any additional etiologic investigations to have been concluded). Follow-up information should be reported if an alternative etiology is identified during investigation and monitoring of the study participant.

8.2.8.7 Other safety topics of interest

Prespecified safety topics of interest for the study are: infections (serious, opportunistic, fungal, and TB), neutropenia, hypersensitivity, injection site reactions, neuropsychiatric AEs (including SIB-related AEs), depression, major CV events, LFT changes/enzyme elevations, malignancies, and IBD.

These are based on findings from the bimekizumab clinical program to date, potential risks generally associated with biologic immunomodulators, or findings from other medicines with a related mechanism of action. There are no specific AE reporting requirements for these topics, however, special monitoring, additional data collection activities, and/or enhanced signal detection activities within UCB are in place.

The reporting requirements for events relating to TB are as follows:

- The IGRA test conversions defined as a positive or indeterminate (and confirmed indeterminate on repeat) should be reported as AEs. The AE term would need to be updated with final diagnosis once available.
- Latent TB infection must be reported as an AE. Follow-up reports should be completed as per protocol requirement until the LTBI resolves.
- Confirmed active TB is always considered an SAE and must be reported per SAE reporting instructions in the study protocol. Follow-up reports should be completed as per protocol requirement until the TB infection resolves.

8.2.8.8 Anticipated SAEs

The following Anticipated SAEs are anticipated to occur in the population studied in this protocol at some frequency that is independent of drug exposure (Table 8-4).

This list does not change the Investigator's obligation to report all SAEs (including Anticipated SAEs) as detailed in Section 10.3.

Table 8-4: Anticipated SAEs for study participants with moderate to severe plaque PSO

MedDRA system organ class	MedDRA preferred term
Skin and subcutaneous tissue disorders	Any psoriatic condition HLT
Musculoskeletal and connective tissue disorders	Psoriatic arthropathy

HLT=high level term; MedDRA=Medical Dictionary for Regulatory Activities; SAE=serious adverse event
Note: Exception: Listed events will not be regarded as anticipated SAEs if they are life threatening or if they result in the death of the study participant.

8.3 Safety signal detection

Selected data from this study will be reviewed periodically to detect as early as possible any safety concern(s) related to the IMP so that Investigators, study participants, regulatory authorities, and IRBs/IECs will be informed appropriately and as early as possible.

The Study Physician or medically qualified designee/equivalent will conduct an ongoing review of SAEs and perform ongoing SAE reconciliations in collaboration with the Patient Safety (PS) representative.

As appropriate for the stage of development and accumulated experience with the IMP, medically qualified personnel at UCB may identify additional safety measures (eg, AEs, vital signs, laboratory results) for which data will be periodically reviewed during the course of the study.

8.4 Treatment of overdose

For this study, any dose of bimekizumab greater than that prescribed in the protocol will be considered an overdose. Overdose events are only considered AEs or SAEs if there are associated clinical signs and symptoms or if the act of taking the excess IMP itself is an AE or SAE (eg, suicide attempt).

UCB does not recommend specific treatment for an overdose. Any signs or symptoms of adverse reactions should be treated symptomatically as per standard care by the Investigator.

In the event of an overdose, the Investigator should:

1. Contact the Medical Monitor immediately
2. Closely monitor the study participant for any AE/SAE and laboratory abnormalities until bimekizumab can no longer be detected systemically (at least 90 days)
3. Obtain a plasma sample for PK analysis as soon as possible after the final dose of IMP if requested by the Medical Monitor (determined on a case-by-case basis)
4. Document the quantity of the excess dose as well as the duration of the overdose in the eCRF

8.5 Pharmacokinetics

Blood samples will be collected prior to dosing for measurement of plasma concentrations of bimekizumab at all timepoints described in Table 1-1.

Instructions for the collection and handling of biological samples will be provided by the Sponsor. The actual date and time (24-hour clock time) of each sample will be recorded.

Samples will be used to evaluate the PK of bimekizumab. Samples collected for analyses of bimekizumab plasma concentration may also be used to evaluate safety or efficacy aspects related to concerns arising during or after the study.

Study participant confidentiality will be maintained. At visits during which blood samples for the determination of plasma concentrations of bimekizumab will be taken, 1 sample of sufficient volume can be used.

Drug concentration information that may unblind the study will not be reported to any blinded study personnel as long as the study remains blinded.

8.6 Genetics

Genetics are not evaluated in this study.

8.7 Pharmacodynamics

Pharmacodynamic parameters are not evaluated in this study.

8.8 Biomarkers

Biomarkers are not evaluated in this study.

8.9 Immunogenicity assessments

Antibodies to bimekizumab will be evaluated in plasma samples collected from all study participants according to the SoA (Table 1-1). Additionally, plasma samples should also be collected at the final visit from study participants who discontinued IMP or withdrew from the study. These samples will be tested by the Sponsor or Sponsor's designee.

A tier-based approach will be used, consisting of consecutive screening, confirmatory and titration methods. Plasma samples will be screened for antibodies binding to bimekizumab and the titer of confirmed positive samples will be reported. Other analyses may be performed to verify the stability of antibodies to bimekizumab and/or further characterize the immunogenicity of bimekizumab.

The detection and characterization of antibodies to bimekizumab will be performed using validated assay methods by or under the supervision of the Sponsor. The procedures for sample analysis and the relevant validation results will be described in a separate bioanalytical report. All samples collected for detection of antibodies to IMP will also be evaluated for bimekizumab plasma concentration to enable interpretation of the antibody data. Confirmed positive antibody samples will be further characterized for their ability to neutralize the activity of bimekizumab. Samples may be stored for a maximum of 20 years (or according to local regulations) following the LPLV for the study at a facility selected by the Sponsor, to enable further analysis of immune responses to bimekizumab.

8.10 Health economics or medical resource utilization and health economics

Health economics/medical resource utilization and health economics parameters are not evaluated in this study.

9 STATISTICAL CONSIDERATIONS

A description of statistical methods is provided below and will be described in more detail in the Statistical Analysis Plan (SAP).

9.1 Definition of analysis sets

The Enrolled Set (ES) will consist of all study participants who have given informed consent.

The Randomized Set (RS) will consist of all randomized study participants.

The Safety Set (SS) will consist of all study participants that received at least 1 dose of the IMP.

The Full Analysis Set (FAS) will consist of all randomized study participants that received at least 1 dose of the IMP and have a valid measurement of the co-primary efficacy variables at Baseline.

The Per-Protocol Set (PPS) will consist of all study participants in the RS who had no important protocol deviations affecting the co-primary efficacy variables. Important protocol deviations will be predefined, and study participants with important protocol deviations will be evaluated during ongoing data cleaning meetings prior to unblinding the data (see Section 9.5).

The Pharmacokinetics Per-Protocol Set (PK-PPS) will consist of all randomized study participants who received at least 1 dose of the IMP and provided at least 1 quantifiable plasma concentration postdose without important protocol deviations that would affect the concentration.

9.2 General statistical considerations

Summary statistics will consist of frequency tables for categorical variables. For continuous variables, summary statistics will consist of the number of available observations, arithmetic mean, standard deviation, median, minimum, and maximum, unless stated otherwise.

All analyses will be performed using SAS® version 9.3 or later (SAS Institute, Cary, NC, US).

The statistical analysis of the co-primary efficacy variables will be performed using a Type I error rate at a 2-sided alpha level of 0.05.

9.3 Planned efficacy/outcome analyses

Efficacy variables will be analyzed for all study participants in the RS.

9.3.1 Efficacy estimands

The following 4 attributes describe the estimands (International Council for Harmonisation [ICH] Addendum, 2019) that will be used to define the treatment effect of interest for the co-primary endpoints of study participant-level outcomes:

PASI90 response at Week 16:

1. Treatment: 320mg bimekizumab Q4W for 16 weeks.
2. Target Population: adult Korean study participants meeting the protocol-specified inclusion/exclusion criteria.
3. Intercurrent event handling: An intercurrent event is defined as discontinuation of IMP prior to Week 16. A composite strategy will be implemented in which a positive clinical outcome is defined as achieving PASI90 response at Week 16 and not discontinuing IMP through Week 16.
4. Study participant-level summary measure: Odds ratio comparing bimekizumab to placebo.

Any missing data not associated with discontinuation of IMP will also be imputed as a nonresponse.

IGA 0/1 (clear or almost clear with at least a 2-category improvement from Baseline) response at Week 16:

1. Treatment: 320mg bimekizumab Q4W for 16 weeks.

2. Target Population: adult Korean study participants meeting the protocol-specified inclusion/exclusion criteria.
3. Intercurrent event handling: An intercurrent event is defined as discontinuation of IMP prior to Week 16. A composite strategy will be implemented in which a positive clinical outcome is defined as achieving IGA 0/1 response at Week 16 and not discontinuing IMP through Week 16.
4. Study participant-level summary measure: Odds ratio comparing bimekizumab to placebo.

Any missing data not associated with discontinuation of IMP will also be imputed as a nonresponse.

The secondary efficacy binary endpoints (PASI100 response at Week 16, IGA 0 response at Week 16, PASI75 response at Week 4, PSD [P-SIM] [itch, pain, and scaling] response at Week 16, Scalp IGA 0/1 response at Week 16, and DLQI Total Score 0/1 response at Week 16) will have the same estimand structure as for the primary estimands.

The following 4 attributes describe the estimand (ICH Addendum, 2019) that will be used to define the treatment effect of interest for the secondary efficacy endpoint percentage change from Baseline in BSA affected by PSO Week 16:

1. Target population: Study participants meeting the protocol-defined inclusion/exclusion criteria.
2. Study participant-level outcome: Percentage change from Baseline in BSA affected by PSO at Week 16
3. Intercurrent event handling: A hypothetical strategy will be implemented in which the estimand targets the treatment difference in a scenario where an intercurrent event does not occur, such that outcomes for study participants without an intercurrent event are as observed, and outcomes for study participants with an intercurrent event are treated as though they had completed the randomized study treatment through Week 16 by imputing data following an intercurrent event using multiple imputation (MI).
4. Study participant-level summary measure: Difference in the adjusted means between bimekizumab and placebo.

Any missing data not associated with discontinuation of IMP will also be imputed using MI.

9.3.2 Analysis of the primary efficacy/primary endpoint

The co-primary efficacy variables for this study will be PASI90 response and IGA 0/1 response at Week 16.

The primary analyses for these endpoints will be produced on the RS. In addition, sensitivity analyses for the co-primary endpoints will be produced on the FAS and PPS. Observed case summaries (excluding subjects with missing PASI/IGA data at Week 16) will also be provided.

Estimands related to primary efficacy analyses are described in Section 9.3.1.

An intercurrent event is defined as discontinuation of IMP prior to Week 16. A composite strategy will be implemented in which a positive clinical outcome is defined as achieving the primary endpoint (PASI90 or IGA 0/1) at Week 16 and not discontinuing IMP prior to Week 16.

The justification of this approach is that discontinuation of IMP for any reason is considered to be indicative of an ineffective response to the IMP. Therefore, a successful primary outcome depends both on achieving the response (PASI90 or IGA 0/1) and continuing study treatment through 16 weeks.

A study participant will be classified as a PASI90 responder if the PASI score at Week 16 has improved at least 90% from Baseline and the study participant has not discontinued IMP prior to Week 16.

A study participant will be classified as a IGA 0/1 responder if the IGA score at Week 16 is 0 or 1 (clear or almost clear) with at least a 2-category improvement from Baseline in the IGA score and the study participant has not discontinued IMP prior to Week 16.

The evaluation of superiority (bimekizumab vs placebo treatment comparison) will be based on the Cochran-Mantel-Haenszel (CMH) test. Odds ratios and 95% confidence intervals (CIs) based on the CMH method will also be presented.

9.3.3 Secondary efficacy endpoint analyses

The secondary efficacy variables will be analyzed for all study participants in the RS.

No formal statistical testing will be conducted for the secondary efficacy variables. Nominal p-values for the bimekizumab vs placebo treatment comparison will be described in the SAP.

The secondary efficacy endpoints will be derived as follows:

- PASI100 responder at Week 16: PASI score at Week 16 has improved by 100% from Baseline and the study participant has not discontinued IMP prior to Week 16.
- IGA 0 responder at Week 16: IGA score at Week 16 is 0 (Clear) with at least a 2-category improvement from Baseline in the IGA score and the study participant has not discontinued IMP prior to Week 16.
- PASI75 responder at Week 4: PASI score at Week 4 has improved by ≥75% from Baseline and the study participant has not discontinued IMP prior to Week 4.
- PSD (P-SIM) itch responder at Week 16: Itch score has improved (decreased) by ≥4 points from Baseline to Week 16 (using weekly averages) and the study participant has not discontinued IMP prior to Week 16. This will be assessed only in study participants with a Baseline itch score ≥4.
- PSD (P-SIM) pain responder at Week 16: Pain score has improved (decreased) by ≥4 points from Baseline to Week 16 (using weekly averages) and the study participant has not discontinued IMP prior to Week 16. This will be assessed only in study participants with a Baseline pain score ≥4.
- PSD (P-SIM) scaling responder at Week 16: Scaling score has improved (decreased) by ≥4 points from Baseline to Week 16 (using weekly averages) and the study participant has not discontinued IMP prior to Week 16. This will be assessed only in study participants with a Baseline scaling score ≥4.
- Scalp IGA 0/1 responder at Week 16 for study participants with scalp involvement at Baseline: Scalp IGA score at Week 16 is 0/1 (clear or almost clear) with at least a 2-category

improvement from Baseline in the IGA score and the study participant has not discontinued IMP prior to Week 16. Only study participants with a Scalp IGA score ≥2 at Baseline will be included.

- DLQI Total Score 0/1 at Week 16: DLQI Total score is equal to 0 or 1 at Week 16 and the study participant has not discontinued IMP prior to Week 16.

For the binary secondary efficacy endpoints assessing the superiority of bimekizumab vs placebo, the estimand structure as specified for the primary analysis will be implemented.

For the continuous change from Baseline efficacy endpoint, percent change from Baseline in BSA affected by PSO at Week 16, an analysis of covariance (ANCOVA) model will be used with fixed effects of treatment and Baseline value as a covariate. Missing data will be imputed via MI as outlined in the estimand structure (Section 9.3.1). If there are model convergence issues with MI, a last observation carried forward (LOCF) approach will be used.

For all secondary efficacy endpoints, observed data summaries will also be presented.

9.3.4 Tertiary efficacy endpoint analyses

The tertiary efficacy variables will be analyzed for all study participants in the RS.

Binary (responder) variables will be summarized using frequency tables by treatment group for each visit; nonresponder imputation (NRI) and observed case results will be displayed.

Continuous variables will be summarized using descriptive statistics by treatment group for each visit. No imputation will be applied to continuous variables, only observed data will be summarized.

Time to PASI50, PASI75, PASI90, and PASI100 response will be estimated using the Kaplan-Meier product-limit method for each treatment group. Time to a given response will be defined as the length in days from the first dose of IMP until the first date when the response is achieved. Study participants who discontinue IMP prior to achieving a response will be censored at the date of the last observed PASI assessment on or prior to the date of IMP discontinuation. Study participants who complete the study without achieving the given response will be censored at the date of the last observed PASI assessment.

Study participants will be censored at Baseline (Day 0) if there is no Baseline PASI assessment or no post-Baseline PASI assessment.

The median time to response, including the 2-sided 95% CI, will be calculated for each treatment group.

9.4 Planned safety and other analyses

Safety variables will be analyzed for all study participants in the SS.

9.4.1 Safety analyses

9.4.1.1 AEs

Adverse events will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA v19.0). Treatment-emergent AEs are defined as those AEs that have a start date on or following the first dose of IMP.

The frequency of all TEAEs will be presented for each treatment group separately by system organ class, high level term, and preferred term. The data will be displayed as number of study participants experiencing the TEAE, percentage of study participants, and number of TEAEs. Additional tables will summarize serious TEAEs, TEAEs leading to discontinuation, TEAEs by severity, and TEAEs categorized as safety topics of interest and AESIs. Definitions for categorizing TEAEs as safety topics of interest and AESIs will be provided in the SAP.

Further details of TEAE summaries will be provided in the SAP.

9.4.1.2 Vital signs

Vital signs will be summarized by visit. Absolute values and change from Baseline in systolic and diastolic BP and pulse rate will be presented descriptively by visit for each treatment group.

Markedly abnormal vital signs will be summarized. Definitions of markedly abnormal vital signs will be given in the SAP.

9.4.1.3 Hematology/biochemistry

Treatment-emergent markedly abnormal (TEMA) laboratory values are defined as those that have an assessment date on or following first dose of IMP.

Laboratory assessments will be analyzed by visit. Absolute values and change from Baseline in each laboratory parameter will be presented descriptively for each treatment group. The incidence rate of TEMA laboratory values at the parameter level will also be presented descriptively for each treatment group. Definitions for markedly abnormal laboratory values will be provided in the SAP.

9.4.1.4 Physical examination

Clinically significant changes from Baseline in physical examination findings will be reported as AEs and included in the TEAE summarization described in Section 9.4.1.1.

9.4.1.5 ECG

Changes from Baseline in ECG parameters will be summarized by treatment group. ECG outliers will be summarized as defined in the SAP.

9.4.1.6 PHQ-9

Change from Baseline in PHQ-9 score will be summarized over time by treatment group. The number of study participants with a PHQ-9 score ≥15 and ≥20 at any time will be summarized.

9.4.1.7 C-SSRS

The incidence of study participants with suicidal ideation, suicidal behavior, suicidal ideation or behavior, and self-injurious behavior will be summarized by visit and treatment group.

9.4.2 Pharmacokinetics and antidrug antibody analyses

Plasma bimekizumab concentrations will be summarized for the PK-PPS at each time point using descriptive statistics. In addition, PK model-based analyses may be performed and reported separately.

Antidrug antibody (ADAb) data will be evaluated for each study participant in the SS, and rates of ADAb-positive study participants will be calculated. Neutralizing antidrug antibody data will also be evaluated. Further details will be presented in the SAP.

9.5 Handling of protocol deviations

Important protocol deviations are deviations from the protocol which potentially could have a meaningful impact on study conduct, or on the primary efficacy, key safety, or PK outcomes for an individual study participant. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document at study start. Consistent with standard industry practice, the protocol deviation specification document may be refined during the study.

Important protocol deviations will be reviewed as part of the ongoing data cleaning process and all important deviations will be identified and documented prior to unblinding to confirm exclusion from analysis sets.

Important protocol deviations may lead to exclusion from the PPS or PK-PPS, but will not lead to exclusion from the RS or FAS (see Section 9.1).

In line with the studies that PS0032 will be bridged to, anticipated important protocol deviations will be categorized as follows:

- Inclusion criteria deviation
- Exclusion criteria deviation
- Incorrect treatment or dose
- Treatment noncompliance
- Withdrawal criteria deviation
- Procedural noncompliance
- Prohibited concomitant medication use

Deviations related to the Coronavirus Disease 2019 (COVID-19) global pandemic are unavoidable deviations from the protocol due to confirmed COVID-19 infection, suspected COVID-19 infection, general circumstances around COVID-19 without infection, or any other deviation from the protocol due to COVID-19. COVID-19 protocol deviations will be reviewed as part of the ongoing data cleaning process.

Summaries of all important protocol deviations will be produced. Deviations due to COVID-19 will also be summarized.

9.6 Handling of dropouts or missing data

Pharmacokinetic analyses will be based on observed data; no imputation will be used. However, if plasma concentration measurements are below the level of quantification, then for calculation of the derived statistics the result will be set to half of the lower level of quantification.

Study participants who prematurely discontinue IMP (intercurrent event) will have their data imputed under the estimand framework described in Section 9.3.1.

Missing data outside of an intercurrent event for the binary (responder) efficacy variables will be imputed; study participants with missing data will be considered as nonresponders for the respective time point. Missing data for the continuous secondary efficacy variable percentage change from Baseline in BSA affected by PSO will be imputed using MI. If the imputation model cannot converge, the LOCF method will be used. Further details will be provided in the SAP.

9.7 Planned interim analysis and data monitoring

After all study participants complete the Week 16 visit, an interim analysis may be performed. A final analysis and final CSR will be prepared once all data (through the SFU visit for study participants not entering the MAP) have been collected.

9.8 Determination of sample size

Sample size and power calculations are performed based on a total of 45 study participants being randomly assigned in a 2:1 ratio at Baseline to one of the following treatment groups:

- Bimekizumab 320mg Q4W (30 study participants)
- Placebo (15 study participants)

The primary efficacy analysis is based on the comparison of bimekizumab to placebo for the co-primary efficacy endpoints of PASI90 and IGA 0/1 response at Week 16. The assumed responder rates for PASI90 at Week 16 are 70% and 13.3% for bimekizumab and placebo, respectively. Based on the number of study participants planned, this equates to 21 and 2 responders in the bimekizumab and placebo treatment groups, respectively. In the global Phase 3 bimekizumab PSO program, the PASI90 responder rate ranged from 85% to 90%. The assumption here is relatively low to account for increased variability due to a small sample size and the possibility of missing data due to COVID-19. Additionally, the placebo PASI90 responder rate assumption is higher than observed in the Phase 3 program to account for potential variability due to small sample size. These assumptions are conservative against a bimekizumab treatment effect.

The power to show statistical superiority of bimekizumab relative to placebo at a 2-sided significance level of 0.05 under these assumptions is 95% for PASI90 at Week 16. As the Phase 3 studies demonstrated similar responder rates between PASI90 and IGA 0/1, this calculation is considered sufficient to justify the sample size. These calculations were performed using nQuery Advisor® 7.0 based on a two-group continuity corrected chi-square test of equal proportions (with unequal n).

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 Appendix 1: Regulatory, ethical, and study oversight considerations

10.1.1 Regulatory and ethical considerations

The study will be conducted under the auspices of an IRB/IEC, as defined in local regulations, ICH-GCP, and in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

The Investigator/UCB will ensure that an appropriately constituted IRB/IEC that complies with the requirements of the current ICH-GCP version or applicable country-specific regulations will be responsible for the initial and continuing review and approval of the clinical study. Prior to initiation of the study, the Investigator/UCB will forward copies of the protocol, ICF, IB, Investigator's curriculum vitae (if applicable), advertisement (if applicable), and all other study participant-related documents to be used for the study to the IRB/IEC for its review and approval.

Before initiating a study, the Investigator will have written and dated full approval from the responsible IRB/IEC for the protocol.

The Investigator will also promptly report to the IRB/IEC all changes in the study, all unanticipated problems involving risks to study participants or others, and any protocol deviations, to eliminate immediate hazards to study participants.

The Investigator will not make any changes in the study or study conduct without IRB/IEC approval, except where necessary to eliminate apparent immediate hazards to the study participants. For minor changes to a previously approved protocol during the period covered by the original approval, it may be possible for the Investigator to obtain an expedited review by the IRB/IEC as allowed.

As part of the IRB/IEC requirements for continuing review of approved studies, the Investigator will be responsible for submitting periodic progress reports to the IRB/IEC (based on IRB/IEC requirements), at intervals appropriate to the degree of study participant risk involved, but no less than once per year. The Investigator should provide a final report to the IRB/IEC following study completion.

UCB (or its representative) will communicate safety information to the appropriate regulatory authorities and all active Investigators in accordance with applicable regulatory requirements. The appropriate IRB/IEC will also be informed by the Investigator or the Sponsor, as specified by the applicable regulatory requirements in each concerned country. Where applicable, Investigators are to provide the Sponsor (or its representative) with evidence of such IRB/IEC notification.

10.1.2 Financial disclosure

Insurance coverage will be handled according to local requirements.

Finance and insurance are addressed in the Investigator and/or Contract Research Organization (CRO) agreements, as applicable.

10.1.3 Informed consent process

Study participant's informed consent must be obtained and documented in accordance with local regulations, ICH-GCP requirements, and the ethical principles that have their origin in the principles of the Declaration of Helsinki.

Prior to obtaining informed consent, information should be given in a language and at a level of complexity understandable to the study participant in both oral and written form by the Investigator (or designee). Each study participant will have the opportunity to discuss the study and its alternatives with the Investigator.

Prior to participation in the study, the ICF should be signed and personally dated by the study participant and by the person who conducted the informed consent discussion (Investigator or designee). The study participant must receive a copy of the signed and dated ICF. As part of the consent process, each study participant must consent to direct access to his/her medical records for study-related monitoring, auditing, IRB/IEC review, and regulatory inspection.

If the ICF is amended during the study, the Investigator (or the Sponsor, if applicable) must follow all applicable regulatory requirements pertaining to the approval of the amended ICF by the IRB/IEC and use of the amended form.

The study participant may withdraw consent to participate in the study at any time. A study participant is considered as enrolled in the study when he/she has signed the ICF. An eCRF must not be started, nor may any study specific procedure be performed for a given study participant, without having obtained written consent to participate in the study.

10.1.4 Data protection

UCB staff (or designee) will affirm and uphold the study participant's confidentiality. Throughout this study, all data forwarded to UCB (or designee) will be identified only by the study participant number assigned at Screening.

The Investigator agrees that representatives of UCB, its designee, representatives of the relevant IRB/IEC, or representatives of regulatory authorities will be allowed to review that portion of the study participant's primary medical records that directly concerns this study (including, but not limited to, laboratory test result reports, ECG reports, admission/discharge summaries for hospital admissions occurring during a study participant's study participation, and autopsy reports for deaths occurring during the study).

The study participant must be informed that personal study-related data will be used by the Sponsor in accordance with local data protection law. The level of disclosure must also be explained to the study participant.

The study participant must be informed that his/her medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the Sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.

10.1.5 Committee structure

Cardiovascular, Gastrointestinal, and Neuropsychiatric Adjudication Committees will periodically review data from this study. Details will be provided in the Cardiovascular, Gastrointestinal, and Neuropsychiatric Adjudication Committee charters.

Adjudication Committee members may not participate in the study as principal or co-Investigators, or as study participant care physicians, and must not be members of the study team at UCB or the conducting CRO. The duration of membership for the committees will be inclusive of planned analyses for this study.

10.1.6 Data quality assurance

All study participant data relating to the study will be recorded in the eCRF unless transmitted to the Sponsor or designee electronically (eg, laboratory data). The Investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the eCRF.

The Investigator must maintain accurate documentation (source data) that supports the information entered in the eCRF.

The Investigator must permit study-related monitoring, audits, IRB/IEC review, and regulatory agency inspections and provide direct access to source data documents.

The Sponsor or designee is responsible for the data management of this study including quality checking of the data.

Study monitors will perform ongoing source data verification to confirm that data entered into the eCRF by authorized site personnel are accurate, contemporaneous, original, and attributable from source documents; that the safety and rights of study participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH-GCP, and all applicable regulatory requirements.

All essential documents must be retained by the Investigator for the minimum retention period mandatory under the applicable local laws and regulations. The Investigator will contact UCB for authorization prior to the destruction of any study records or in the event of accidental loss or destruction of any study records. The Investigator will also notify UCB should he/she relocate or move the study-related files to a location other than that specified in the Sponsor's trial master file.

10.1.6.1 eCRF completion

The Investigator is responsible for prompt reporting of accurate and complete data in the eCRFs and in all required reports.

Any change or correction to the eCRF after saving must be accompanied by a reason for the change.

Corrections made after the Investigator's review and approval (by means of a password/electronic signature) will be reapproved by the Investigator.

The Investigator should maintain a list of personnel authorized to enter data into the eCRF.

Detailed instructions will be provided in the eCRF Completion Guidelines.

10.1.6.2 Apps

Each study participant will be provided with a mobile phone with a preinstalled application (app). The study-specific app will collect data from each participant throughout the study. The app will support the participant to complete study-specific activities, as follows:

- Receiving reminders and notifications
- Scheduling visits with the Investigator and/or authorized site representative(s)
- Completing PSD daily diary

The Investigator and authorized site representative(s) will have access to a secure website portal via unique access credentials to access the study data from the completed activities noted above.

Data will be reviewed by the Investigator via the website portal view of participant-entered data results.

Furthermore, this app is designed to only record data associated with the participant's disease state, and therefore it is neither designed nor intended to be used to collect or report safety-related information about the participant.

10.1.7 Source documents

All source documents must be accurate, clear, unambiguous, permanent, and capable of being audited. They should be made using some permanent form of recording (ink, typing, printing, optical disc). They should not be obscured by correction fluid or have temporary attachments (such as removable self-stick notes). Photocopies and/or printouts of eCRFs are not considered acceptable source documents.

Source documents are original records in which raw data are first recorded. These may include hospital/clinic/general practitioner records, charts, diaries, x-rays, laboratory results, printouts, pharmacy records, care records, ECG or other printouts, completed scales, QOL questionnaires, or video, for example. Source documents should be kept in a secure, limited access area.

Electronic PRO measures and the TB questionnaire will be completed by each study participant and will be collected via electronic device.

Source documents that are computer generated and stored electronically must be printed for review by the monitor. Once printed, these copies should be signed and dated by the Investigator and become a permanent part of the study participant's source documents. The Investigator will facilitate the process for enabling the monitor to compare the content of the printout and the data stored in the computer to ensure all data are consistent.

Electronic data records must be saved and stored as instructed by UCB (or designee).

10.1.8 Study and site closure

The Sponsor designee 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 IRB/IEC or local health authorities, the Sponsor's procedures, or GCP guidelines
- Inadequate recruitment of study participants by the Investigator
- Discontinuation of further study bimekizumab development

10.1.9 Publication policy

The results of this study may be published or presented at scientific meetings. If this is foreseen, the Investigator agrees to submit all manuscripts or abstracts to the Sponsor before submission. This allows the Sponsor to protect proprietary information and to provide comments.

The Sponsor will comply with the requirements for publication of study results. In accordance with standard editorial and ethical practice, the Sponsor will generally support publication of multicenter studies only in their entirety and not as individual site data. In this case, a coordinating Investigator will be designated by mutual agreement.

Authorship will be determined by mutual agreement and in line with International Committee of Medical Journal Editors authorship requirements.

10.1.10 Clinical trial registration and results disclosure

To comply with applicable laws, regulations and guidance, and provide information on the clinical study to the public in a timely manner, the sponsor will register this study on ClinicalTrials.gov or other publicly accessible websites on or before the start of the study, as defined by sponsor policies and applicable laws and/or regulations .

The sponsor will post the results of the study on ClinicalTrials.gov and other publicly accessible websites and registries as required by sponsor policies and applicable laws and/or regulations.

For results disclosure on public registries (eg, ClinicalTrials.gov), TEAEs and TE-SAEs will be published.

10.2 Appendix 2: Clinical laboratory tests

- The tests detailed in the table below will be performed by the central laboratory, with the exception of urine dipsticks and urine pregnancy tests, which will be performed locally at the site.
- Local laboratory results are only required in the event that the central laboratory results are not available in time for either IMP administration and/or response evaluation. If a local sample is required, it is important that the sample for central analysis is obtained at the same time. Additionally, if the local laboratory results are used to make either an IMP decision or response evaluation, the results must be entered into the eCRF.
- Protocol-specific requirements for inclusion or exclusion of study participants are detailed in Section 5.1 and Section 5.2 of the protocol.
- Additional tests may be performed at any time during the study as determined necessary by the Investigator or required by local regulations.

Table 10-1: Protocol-required safety laboratory assessments

Laboratory assessments	Parameters			
Hematology	Platelet count RBC count Hemoglobin Hematocrit	RBC indices: MCV MCH MCHC	WBC count with differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils	
Clinical chemistry[1]	BUN	Potassium	AST	Total bilirubin
	Creatinine	Sodium	ALT	Glucose (nonfasting)
	Calcium	Alkaline phosphatase	Lipid panel	Chloride
		GGT	LDH	
Routine urinalysis	• Specific gravity • pH, glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, and leukocyte esterase by dipstick • Microscopic examination (if protein, blood, nitrite or leukocyte esterase is abnormal)			
Other Screening tests	• Serum hCG pregnancy test (as needed for FOCBP) by central laboratory at Screening and urine pregnancy test locally for all assessments after Screening • IGRA testing • Urine drug screen • Serology (HIV antibody, HBsAg, and hepatitis C virus antibody) Specific details regarding the handling and processing of serum chemistry, hematology, and urinalysis samples are provided in the study laboratory manuals.			

ALT=alanine aminotransferase; AST=aspartate aminotransferase; BUN=blood urea nitrogen; eCRF=electronic Case Report Form; HBsAg=hepatitis B surface antigen; hCG=human chorionic gonadotropin; GGT=gamma glutamyltransferase; HIV=human immunodeficiency virus; IGRA= interferon-gamma release assay; INR=international normalized ratio; LDH=lactate dehydrogenase; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; MCV=mean corpuscular volume; RBC=red blood cell count; ULN=upper limit of normal; WBC=white blood cell count

[a] Details of liver chemistry stopping criteria and required actions and follow-up assessments after liver stopping or monitoring event are given in Section 7.1.1 and Appendix 6 (Section 10.6). All events of ALT ≥3×ULN and bilirubin ≥2×ULN (>35% direct bilirubin) or ALT ≥3×ULN and INR >1.5, if INR measured, may indicate severe liver injury (possible Hy's Law) and must be reported as an SAE.

Investigators must document their review of each laboratory safety report.

Laboratory/analyte results that could unblind the study will not be reported to investigative sites or other blinded personnel until the study has been unblinded.

10.3 Appendix 3: AEs – definitions and procedures for recording, evaluating, follow up, and reporting

Definition of AE

AE definition
• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of IMP, whether or not considered related to the IMP. • NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of IMP.

Events meeting the AE definition
• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital signs measurements), including those that worsen from Baseline, considered clinically significant in the medical and scientific judgment of the Investigator (ie, not related to progression of underlying disease). • Exacerbation of a chronic or intermittent preexisting condition including either an increase in frequency and/or intensity of the condition. • New conditions detected or diagnosed after IMP administration even though it may have been present before the start of the study. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction. • Signs, symptoms, or the clinical sequelae of a suspected overdose of either IMP or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae. • "Lack of efficacy" or "failure of expected pharmacological action" per se will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfill the definition of an AE or SAE.

Events NOT meeting the AE definition
• Any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the study participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the study participant's condition. • Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE. • Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital). • Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

Definition of SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (eg, hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

A SAE is defined as any untoward medical occurrence that, at any dose:
a. Results in death
b. Is life-threatening The term ”life-threatening” in the definition of 'serious' refers to an event in which the study participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the study participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician’s office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether “hospitalization” occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a preexisting condition that did not worsen from Baseline is not considered an AE.
d. Results in persistent disability/incapacity • The term disability means a substantial disruption of a person’s ability to conduct normal life functions. • This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.
e. Is a congenital anomaly/birth defect
f. Important medical events: • Medical or scientific judgment should be exercised in deciding whether SAE reporting is 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 study participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious. • Examples of such events include, but are not limited to, potential Hy’s law, invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

Recording and follow up of AE and/or SAE

AE and SAE recording

- When an AE/SAE occurs, it is the responsibility of the Investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostics reports) related to the event.
- The Investigator will then record all relevant AE/SAE information in the eCRF.
- It is **not** acceptable for the Investigator to send photocopies of the study participant's medical records to UCB in lieu of completion of the AE/SAE eCRF page.
- There may be instances when copies of medical records for certain cases are requested by UCB. In this case, all study participant identifiers, with the exception of the study participant number, will be redacted on the copies of the medical records before submission to UCB.
- The Investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE.

Assessment of intensity

The Investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Mild: An event that is easily tolerated by the study participant, causing minimal discomfort and not interfering with everyday activities.
- Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities.
- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with a SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.
- An event is defined as 'serious' when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe (eg, a severe AE may be either serious or not serious, depending on whether these criteria are also met).

The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) should be used as a supportive standardization instrument to evaluate AEs and SAEs, but the final intensity grading by the Investigator must be mild, moderate, or severe.

Assessment of causality

- The Investigator is obligated to assess the relationship between IMP and each occurrence of each AE/SAE.
- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- The Investigator will use clinical judgment to determine the relationship.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to IMP administration will be considered and investigated.
- The Investigator will also consult the IB and/or Product Information, for marketed products, in his/her assessment.
- For each AE/SAE, the Investigator **must** document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the Investigator has minimal information to include in the initial report to UCB. However, **it is very important that the Investigator always make an assessment of causality for every event before the initial transmission of the SAE data to UCB.**
- The Investigator may change his/her opinion of causality in light of follow-up information and send a SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.

Follow up of AEs and SAEs

- The Investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by UCB to elucidate the nature and/or 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.
- An AE should be followed until it has resolved, has a stable sequelae, the Investigator determines that it is no longer clinically significant, or the study participant is lost to follow up. This follow-up requirement applies to AEs, SAEs, and AEs of special interest.
- If a study participant dies during participation in the study or during a recognized follow-up period, the Investigator will provide UCB with a copy of any postmortem findings including histopathology.
- New or updated information will be recorded in the originally completed eCRF.
- The Investigator will submit any updated SAE data to the UCB within 24 hours of receipt of the information.

Reporting of SAEs

SAE reporting to UCB via an electronic data collection tool

- The primary mechanism for reporting an SAE to UCB will be the electronic data collection tool.
- If the electronic system is unavailable for more than 24 hours, then the site will use the paper SAE data collection tool (see next section).
- The site will enter the SAE data into the electronic system as soon as it becomes available.
- After the study is completed at a given site, the electronic data collection tool will be taken off-line to prevent the entry of new data or changes to existing data.
- If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic data collection tool has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to the UCB Study Physician by telephone.

Contacts for SAE reporting can be found in SERIOUS ADVERSE EVENT REPORTING

10.4 Appendix 4: Contraceptive guidance and collection of pregnancy information

Definitions

Female of childbearing potential (FOCBP)

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

Women in the following categories **are not considered FOCBP**:

1. Premenarchal
2. Premenopausal female with 1 of the following:
   - Documented hysterectomy
   - Documented bilateral salpingectomy
   - Documented bilateral oophorectomy

   Note: Documentation can come from the site personnel's review of the study participant's medical records, medical examination, or medical history interview.
3. Postmenopausal female
   - A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
   - Females on HRT and whose menopausal status is in doubt will be required to use one of the nonestrogen hormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

Contraception guidance

Female study participants

FOCBPs are eligible to participate if they agree to use a highly effective method of contraception consistently and correctly as described in the table below.

Highly effective contraceptive methods [a]

Highly effective contraceptive methods that are user dependent [b] Failure rate of <1% per year when used consistently and correctly.
Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation [c] • Oral • Intravaginal • Transdermal
Progestogen only hormonal contraception associated with inhibition of ovulation • Oral • Injectable
Highly effective methods that are user independent [c]
Implantable progestogen only hormonal contraception associated with inhibition of ovulation • Intrauterine device (IUD) • Intrauterine hormone-releasing system (IUS) • Bilateral tubal occlusion
Vasectomized partner A vasectomized partner is a highly effective contraception method provided that the partner is the sole male sexual partner of the FOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.
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 IMP. 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 study participant.

[a] In case of newly started contraception pills/IUDs, Investigator should consider the correct timing of starting/applying such methods in relation to the menstrual cycle and the manufacturing instruction as when these newly started methods would become effective.

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

[c] Hormonal contraception may be susceptible to interaction with the IMP, which may reduce the efficacy of the contraceptive method. In this case, two highly effective methods of contraception should be utilized during the treatment period and for at least 20 weeks after the final dose of IMP.

- Woman of child bearing potential should only be included after a confirmed menstrual period and a negative highly sensitive serum pregnancy test.
- Additional pregnancy testing should be performed as indicated in the SoA (Table 1-1) and as required locally.
- Pregnancy testing will be performed whenever a menstrual cycle is missed or when pregnancy is otherwise suspected.

Male study participants with partners who become pregnant

- The Investigator will attempt to collect pregnancy information on any male study participant's female partner who becomes pregnant while the male study participant is in this study. This applies only to male study participants who receive IMP. If the study participant is later found to be on placebo, then pregnancy data collection can stop.
- In cases where the partner of a male study participant enrolled in a clinical study becomes pregnant, the Investigator or designee is asked to contact the study participant to request consent of the partner via the Partner Pregnancy Consent Form that has been approved by the responsible IRB/IEC and should be available in the Investigator site file. In case of questions about the consent process, the Investigator may contact the UCB/CRO contract monitor for the study. The Investigator will complete the information in the eCRF only after the partner has agreed that additional information can be captured and has provided the signed Partner Pregnancy Consent form. UCB's PS department is also the primary contact for any questions related to the data collection for the partner pregnancy, eventual birth, and follow up.
- After obtaining the necessary signed Informed Consent from the pregnant female partner (and/or parent/legal representative), the Investigator will record pregnancy information on the appropriate form and submit it to the Sponsor within 1 working day of learning of the partner's pregnancy. The female partner will also be followed to determine the outcome of the pregnancy. Information on the status of the mother and child will be forwarded to the Sponsor. Generally, the follow up will be 30 days after the delivery date. Any termination of the pregnancy will be reported regardless of fetal status (presence or absence of anomalies) or indication for the procedure.

Female study participants who become pregnant

- Any female study participant who becomes pregnant while participating in the study will discontinue IMP (see Section 8.2.8.5).
- The Investigator will collect pregnancy information on any female study participant who becomes pregnant while participating in this study. Information will be recorded on the appropriate form and submitted to the Sponsor within 1 working day of learning of a study participant's pregnancy. The study participant will be followed to determine the outcome of the pregnancy. The Investigator will collect follow-up information on the study participant and the neonate and the information will be forwarded to the Sponsor. Generally, the follow up will be at least 30 days after the delivery date. Any termination of pregnancy will be reported, regardless of fetal status (presence or absence of anomalies) or indication for the procedure.
- While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy will be reported as an AE or SAE. A spontaneous abortion is always considered to be an SAE and will be reported as such. Any poststudy pregnancy-related SAE considered reasonably related to the IMP by the Investigator will be reported to the Sponsor as described in Section 8.2.8.5. While the Investigator is not obligated to actively seek this information in former study participants, he or she may learn of an SAE through spontaneous reporting.

10.5 Appendix 5: Genetics

Not applicable.

10.6 Appendix 6: Liver safety – suggested actions and follow-up assessments

The PDILI IMP discontinuation criteria for this study are provided in Section 7.1.1, with the accompanying required follow-up investigation and monitoring detailed below. All PDILI events must be reported as an AE and reported to the study site and Sponsor within 24 hours of learning of their occurrence. Any PDILI event that meets the criterion for potential Hy's Law must be reported as an AE of special interest (see Section 8.2.8.6), and, if applicable, also reported as an SAE (see Section 8.2.8.4).

Evaluation of PDILI consists of the diagnostic testing and continued monitoring included in Table 10-3 (specific tests dependent on laboratory results and corresponding symptoms) and consultation with a local hepatologist (if applicable; discussed in Section 10.6.1). The local hepatologist is the expert usually consulted by the treating physician for assessment and management of potential hepatic disease. This would usually be a hepatologist, but may be a gastroenterologist. Additional investigation and monitoring may be required and adapted based on the diagnosis after the cause of the liver injury/abnormality is confirmed (details in Section 7.1.1.1).

The results of all monitoring, including laboratory testing and other testing, should be made available to the study site and Sponsor.

All initial tests resulting in abnormal hepatic laboratory values need to be repeated, but appropriate medical action must not be delayed waiting for the repeat result.

If tests are done locally for more rapid results, a concurrent sample should also be sent to the central laboratory whenever possible. Medical care decisions are to be made initially using the most rapidly available results, and a conservative approach must be taken if the results from the 2 laboratory tests are significantly different. Data from the local and central laboratory are to be recorded on the applicable eCRF pages.

When IMP is discontinued, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued. In these cases, the Investigator should also consider dose reduction for medically necessary concomitant medication and consider changing any medically required concomitant medication known to be hepatotoxic to a suitable alternative.

When IMP is stopped due to PDILI (as described in Section 7.1.1), IMP must be permanently discontinued unless a subsequent alternative diagnosis fully explains the hepatic findings. If a subsequent alternative diagnosis fully explains the hepatic findings, and the requirements provided in Section 10.6.2.1 are met, rechallenge with IMP may be appropriate.

Table 10-2 summarizes the approach to investigate PDILI.

Table 10-2: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
≥3×ULN	≥2×ULN[b]	NA	Hepatology consult[c] Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and study participant discussed with Medical Monitor ASAP.	Immediate IMP discontinuation.[d]	Essential: Must have repeat liver chemistry values and additional testing completed ASAP (see Section 10.6.3); recommended to occur at the site with HCP.	Monitoring of liver chemistry values at least twice per week until values normalize, stabilize, or return to within Baseline values.[e]
≥3×ULN	NA	Yes				
≥8×ULN	NA	NA	Need for hepatology consult to be discussed (required if ALT or AST ≥8×ULN) Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and study participant discussed with Medical Monitor ASAP.			
≥5×ULN (and ≥2× Baseline) and <8×ULN	<2×ULN	No	Discussion with Medical Monitor required. Consider need for hepatology consult if there is no evidence of resolution (see	Further investigation – immediate IMP discontinuation not required (see Section 10.6.2).	Essential: Every attempt must be made to have repeat liver chemistry values and additional testing completed within 48 hours at the site with HCP (see Section 10.6.3).	Monitoring of liver chemistry values at least twice per week for 2 weeks.[e] • Immediate IMP discontinuation required if liver

Table 10-2: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
			follow-up requirements).[c]	IMP discontinuation required if any of the following occur: • Study participant cannot comply with monitoring schedule. • Liver chemistry values continue to increase. • Liver chemistry values remain ≥5×ULN (and ≥2× Baseline) after 4 weeks of monitoring without evidence of resolution.		chemistry values continue to increase. After 2 weeks of monitoring liver chemistry values: • ALT or AST remains ≥5×ULN <8×ULN, IMP should be temporarily withheld and study participant should undergo repeat test in 2 weeks. • Continue IMP if ALT or AST values <5×ULN; continue to monitor at least twice per week until values normalize, stabilize, or return to within Baseline values. • If ALT or AST remains ≥5×ULN after second re-test, immediate IMP discontinuation required. • Continue to monitor until values normalize, stabilize, or return to within Baseline values.[e]

ALP=alkaline phosphatase; ALT=alanine aminotransferase; ASAP=as soon as possible; AST=aspartate aminotransferase; HCP=health care practitioner; IMP=investigational medicinal product; NA=not applicable; PDILI=potential drug-induced liver injury; ULN=upper limit of normal

Table 10-2: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**

[a] Hepatitis symptoms include fatigue, nausea, vomiting, and right upper quadrant pain or tenderness; hypersensitivity symptoms include eosinophilia (>5%), rash, and fever (without clear alternative cause).
[b] If the study participant also has ≥2×ULN ALP, the possibility of an indication of biliary obstruction should be discussed with the Medical Monitor.
[c] Details provided in Section 10.6.1. The local hepatologist is the expert usually consulted by the treating physician for assessment and management of potential hepatic disease. This would usually be a hepatologist, but may be a gastroenterologist.
[d] Details are provided in Section 10.6.2.
[e] Unless an alternative monitoring schedule is agreed by the Investigator and UCB responsible physician. Determination of stabilization is at the discretion of the Investigator in consultation with the hepatologist (as applicable) and UCB responsible physician, as needed.

10.6.1 Consultation with Medical Monitor and local hepatologist

Potential drug-induced liver injury events require notification of the Medical Monitor or UCB Study Physician within 24 hours (eg, by laboratory alert), and the study participant must be discussed with the Medical Monitor or UCB Study Physician as soon as possible. If required, the study participant must also be discussed with the local hepatologist. The local hepatologist is the expert usually consulted by the treating physician for assessment and management of potential hepatic disease. This would usually be a hepatologist, but may be a gastroenterologist. If determined necessary, this discussion should be followed by a full hepatology assessment (see Section 10.6.3) and SAE report (if applicable).

10.6.2 Immediate action: determination of IMP discontinuation

All PDILI events require immediate action, testing, and monitoring.

The immediate action is dependent on the laboratory values and symptoms of hepatitis or hypersensitivity and ranges from continuation of IMP (followed by immediate investigation) to immediate and permanent discontinuation (see Section 7.1.1 for details).

When IMP is discontinued, all concomitant medications and herbal supplements that are not medically necessary should also be discontinued. The Investigator should also consider dose reduction for medically necessary concomitant medication and consider changing any medically required concomitant medication known to be hepatotoxic to a suitable alternative.

10.6.2.1 IMP restart/rechallenge

Study participants who are immediately discontinued from IMP due to having met certain criteria for PDILI (as described in Section 7.1.1), but for whom an alternative diagnosis is confirmed, ie, DILI is excluded, can rarely restart IMP. Rechallenge with IMP can occur only if ALL of the following requirements are met:

- The results of additional testing and monitoring described in Section 10.6.3 and Section 7.1.1.1 confirm a nondrug-related cause for the abnormal hepatic laboratory parameters and any associated symptoms (ie, a subsequent alternative diagnosis fully explains the hepatic findings).
- No alternative treatment options are available to the study participant.
- The study participant has shown clear therapeutic benefit from the IMP.
- Study participant's ALT or AST elevations do not exceed ≥5×ULN.
- Study participant's total bilirubin is <2×ULN.
- Study participant has no signs or symptoms of hypersensitivity.
- The rechallenge is approved by the UCB Study Physician and a hepatologist. The hepatologist must be external to UCB. It is recommended that the hepatologist be a local hepatology expert or the hepatologist treating the study participant.
- Study participant agrees to the Investigator-recommended monitoring plan and understands his/her individual benefit/risk for restarting IMP and this is adequately documented.

10.6.3 Testing: identification/exclusion of alternative etiology

The measurements and additional information required for the assessment of PDILI events when there is a reasonable possibility that they may have been caused by the IMP are detailed in Table 10-3 (laboratory measurements) and Table 10-4 (additional information). Results of the laboratory measurements and information collected are to be submitted to the Sponsor on the corresponding eCRF. If the medical history of the study participant indicates a requirement for other assessments not included below, these additional assessments should be completed and submitted, as applicable.

All blood samples should be stored, if possible. If tests are done locally for more rapid results, a concurrent sample must also be sent to the central laboratory.

Table 10-3: PDILI laboratory measurements

Virology-related	Hepatitis A IgM antibody
	HBsAg
	Hepatitis E IgM antibody
	HBcAb-IgM
	Hepatitis C RNA
	Cytomegalovirus IgM antibody
	Epstein-Barr viral capsid antigen IgM antibody (if unavailable, obtain heterophile antibody or monospot testing)
Immunology	Anti-nuclear antibody (qualitative and quantitative)
	Anti-smooth muscle antibody (qualitative and quantitative)
	Type 1 anti-liver kidney microsomal antibodies (qualitative and quantitative)
Hematology	Eosinophil count
Urinalysis	Urine drug screen[a]
Chemistry	Amylase
	Sodium, potassium, chloride, glucose, blood urea nitrogen, creatinine
	Total bilirubin, ALP, AST, ALT, gamma-glutamyltransferase, total cholesterol, albumin
	If total bilirubin ≥1.5×ULN, obtain fractionated bilirubin to obtain % direct bilirubin
	Serum creatine phosphokinase and lactate dehydrogenase to evaluate possible muscle injury causing transaminase elevation
Additional	Prothrombin time/INR[b]
	Serum pregnancy test[c]
	PK sample

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; FOCBP= female of childbearing potential; HBcAb-IgM=hepatitis B core antibody-IgM; HBsAg=hepatitis B surface antigen;

IgM=immunoglobulin M; INR=international normalized ratio; PDILI=potential drug-induced liver injury; PK=pharmacokinetics; RNA=ribonucleic acid; ULN=upper limit of normal

[a] Tests in addition to the specified analytes may be performed based on the Investigator's medical judgment and study participant history.

[b] Measured only for study participants with ALT >8×ULN, elevations in total bilirubin, and symptoms of hepatitis or hypersensitivity. Hepatitis symptoms include fatigue, nausea, vomiting, and right upper quadrant pain or tenderness; hypersensitivity symptoms include eosinophilia (>5%), rash, and fever (without clear alternative cause).

[c] For FOCBPs.

The following additional information is to be collected:

Table 10-4: PDILI information to be collected

New or updated information
• Concomitant prescriptions and over-the-counter medications (eg, acetaminophen, herbal remedies, vitamins); dosages and dates should be included.
• Pertinent medical history, including the following: – History of liver disease (eg, autoimmune hepatitis, nonalcoholic steatohepatitis, or other "fatty liver disease") – Adverse reactions to drugs – Allergies – Relevant family history or inheritable disorders (eg, Gilbert's syndrome, alpha-1 antitrypsin deficiency) – Recent travel – Progression of malignancy involving the liver (Note: Metastatic disease to the liver, by itself, should not be used as an explanation for significant AST and/or ALT elevations.)
• The appearance or worsening of clinical symptoms of hepatitis or hypersensitivity (eg, fatigue, nausea, vomiting, right upper quadrant pain or tenderness, decreased appetite, abdominal pain, jaundice, fever, or rash)
• Recent clinically significant hypotension or hypoxemia with compromised cardiopulmonary function
• Alcohol and illicit drug use
• Results of liver imaging or liver biopsy, if done
• Results of any specialist or hepatology consult, if done
• Any postmortem/pathology reports

ALT=alanine aminotransferase; AST=aspartate aminotransferase; PDILI=potential drug-induced liver injury

10.7 Appendix 7: Medical device AEs, adverse device effects, SAEs, and device deficiencies: definition and procedures for recording, evaluating, follow up, and reporting

Not applicable.

10.8 Appendix 8: Rapid alert procedures

Not applicable.

10.9 Appendix 9: Country-specific requirements

Not applicable.

10.10 Appendix 10: Abbreviations and trademarks

ADAb	antidrug antibodies
AE	adverse event
AESI	adverse event of special interest
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BP	blood pressure
BSA	body surface area
CAT	computed axial tomography
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CPM	Clinical Project Manager
CRO	Contract Research Organization
CTCAE	Common Terminology Criteria for Adverse Events
CV	cardiovascular
DLQI	Dermatology Life Quality Index
ECG	electrocardiogram
eCRF	electronic Case Report Form
C-SSRS	Columbia Suicide Severity Rating Scale
ePRO	electronic patient-reported outcome
FOCBP	Female of child bearing potential
GCP	Good Clinical Practice
GI	gastrointestinal
HBcAb	anti-hepatitis B core antibody
HBsAg	hepatitis B surface antigen
HCP	healthcare practitioner
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IB	Investigator's Brochure
IBD	inflammatory bowel disease
ICF	Informed Consent Form

ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
Ig	immunoglobulin
IGA	Investigator's Global Assessment
IGRA	interferon-gamma release assay
IL	interleukin
IMP	investigational medicinal product
IRB	Institutional Review Board
IRT	interactive response technology
LFT	liver function test
LOCF	last observation carried forward
LPLV	last study participant's last visit
LTB	latent tuberculosis
LTBI	latent tuberculosis infection
mAb	monoclonal antibody
MAP	Managed Access Program
MI	multiple imputation
NSAID	nonsteroidal anti-inflammatory drug
NTMB	nontuberculous mycobacterium
PASI	Psoriasis Area and Severity Index
PDILI	potential drug-induced liver injury
PEOT	Premature End of Treatment
PHQ-9	Patient Health Questionnaire 9
PK	pharmacokinetics
PK-PPS	Pharmacokinetics Per-Protocol Set
PPS	Per-Protocol Set
PRN	As needed, pro re nata
PS	Patient Safety
PsA	psoriatic arthritis
P-SIM	Patient Symptom and Impact Measure
PSD	patient symptom diary
PSO	psoriasis

Q4W	every 4 weeks
Q8W	every 8 weeks
QOL	quality of life
RS	Randomized Set
SAE	serious adverse event
SAP	Statistical Analysis Plan
sc	subcutaneous
SFU	Safety Follow-Up
SIB	suicidal ideation/behavior
SoA	Schedule of Activities
SS	Safety Set
TB	tuberculosis
TEAE	treatment-emergent adverse event
TNF	tumor necrosis factor
ULN	upper limit of normal
WBC	white blood cell

10.11 Appendix 11: Protocol amendment history

Amendment 1 (24 Mar 2021)

Overall rationale for the amendment

The purpose of this substantial amendment is to add text describing the option for participating in the Managed Access Program (MAP), add new withdrawal criterion for infections, revise wording for Pregnancy Followup Period, and to add text regarding adjudication committees.

Section # and Name	Description of Change	Brief Rationale
Section 1.1 Synopsis Figure 1.2 Schema Table 1.1 Schedule of Activities Section 4.1 Overall design Section 4.4 End of study definition Section 6.8 Treatment after the end of the study	Added text to describe the option for a Managed Access Program	Clarification
Section 7.1.3 Treatment interuptions/temporary discontinued	Added specific infection-related treatment interruptions to ensure that participants with serious or recurrent infections not responding to standard therapies are not exposed to immunomodulatory therapies until their infection is resolved. This is in line with most biologic therapies, including other anti-IL17s	Clarification
Section 9.7 Planned interim analysis and data monitoring	Added text regarding interim analysis	Clarification
Section 10.1.5 Committee structure	Added text regarding Adjudication Committees	Clarification
10.4 Appendix 4: Contraceptive guidance and collection of pregnancy information	Changed the pregnancy follow up to 30 days after the delivery date	For consistency across other study related documents
Throughout	Minor editorial and document formatting revisions	Minor and for clarity, therefore have not been summarized

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Amendment 2 (12 May 2021)

Overall rationale for the amendment

The purpose of this substantial amendment is in response to Korean Regulatory Authorities feedback regarding clarification of analysis sets and important protocol deviations. For consistency across other study related documents mean corpuscular hemoglobin concentrations (MCHC), chloride, gamma glutamyltransferase (GGT), lactate dehydrogenase (LDH), and lipid panel were added to the clinical chemistry assessments.

The Managed Access Plan (MAP) is provided in this version of the protocol. The MAP was added in PS0032 Amendment 1 which was not submitted.

Section # and Name	Description of Change	Brief Rationale
Table 10-1: Protocol-required safety laboratory assessments	Added, mean corpuscular hemoglobin concentrations (MCHC), chloride, gamma glutamyltransferase (GGT), lactate dehydrogenase (LDH), and lipid panel to clinical chemistry assessments	For consistency across other study related documents
Section 9.3.2 Analysis of the primary efficacy/primary endpoint	Added more detail on the analysis sets to be used for primary endpoints.	Updated per Agency feedback/request
Section 9.3.3 Secondary efficacy endpoint analysis	Added more detail on the analysis sets to be used for secondary endpoints.	Updated per Agency feedback/request
Section 9.5 Handling of protocol deviations	Included detail of the process to be used to identify protocol deviations and exclusions from analysis sets. Added categories for the classification of important protocol deviations.	Updated per Agency feedback/request
Throughout	Minor editorial and document formatting revisions	Minor and for clarity, therefore have not been summarized

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SPONSOR DECLARATION

I confirm that I have carefully read and understand this protocol and agree to conduct this clinical study as outlined in this protocol and according to current Good Clinical Practice.

Approval Signatures

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