PROTOCOL PS0014 AMENDMENT 3.3

A MULTICENTER, OPEN-LABEL STUDY TO ASSESS THE LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF BIMEKIZUMAB IN ADULT SUBJECTS WITH MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

PHASE 3

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SERIOUS ADVERSE EVENT REPORTING

Serious adverse event reporting (24h)	
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AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BA	bioavailability
BSA	body surface area
cAMP	cyclic adenosine monophosphate
CDMS	clinical data management system
CI	confidence interval
CPMP	Committee for Proprietary Medicinal Products
CRO	contract research organization
CSR	Clinical Study Report
DBP	diastolic blood pressure
DLQI	Dermatology Life Quality Index
EAIR	exposure adjusted incidence rate
EAER	exposure adjusted event rate
ECG	electrocardiogram
eCRF	electronic Case Report Form
eC-SSRS	electronic Columbia Suicide Severity Rating Scale
EQ-5D-3L	Euro-Quality of Life 5-Dimensions, 3 levels
FAS	Full Analysis Set
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HLT	high level term
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
iv	intravenous
LTBI	latent tuberculosis infection
mAb	monoclonal antibody
MCS	Mental Component Summary
MedDRA	Medical Dictionary for Regulatory Activities
mNAPSI	Modified Nail Psoriasis Severity Index Score
NTMB	nontuberculous mycobacterium
OLE	Open-label extension
PASE	Psoriatic Arthritis Screening and Evaluation
PASI	Psoriasis Area Severity Index
PCS	Physical Component Summary
PD	pharmacodynamic(s)
PDE	phosphodiesterase
PDILI	potential drug-induced liver injury
PEOT	Premature End of Treatment
PGA	Patient Global Assessment
PGADA	Patient's Global Assessment of Disease Activity
PHQ-9	Patient Health Questionnaire-9
PK	pharmacokinetic(s)
PK-PPS	Pharmacokinetics Per-Protocol Set
pp-IGA	palmoplantar Investigator's Global Assessment
PS	Patient Safety
PsA	psoriatic arthritis
PSO	psoriasis
PT	preferred term
Q4W	every 4 weeks
Q8W	every 8 weeks

QOL	quality of life
SAE	serious adverse event
SAP	Statistical Analysis Plan
SBP	systolic blood pressure
sc	subcutaneous(ly)
SD	standard deviation
SF-36	Short Form 36-item Health Survey
SFU	Safety Follow-Up
SOC	System Organ Class
SOP	Standard Operating Procedure(s)
SS	Safety Set
TB	tuberculosis
TEAE	treatment-emergent adverse event
TNF	tumor necrosis factor
TSQM-9	Treatment Satisfaction Questionnaire for Medication
ULN	upper limit of normal
VAS	visual analog scale
WPAI-SHP	Work Productivity and Activity Impairment Questionnaire-specific health problem

1 SUMMARY

This is a Phase 3, multicenter, open-label study to assess the long-term safety, tolerability, and efficacy of bimekizumab in adult subjects with moderate to severe chronic plaque psoriasis (PSO) who complete 1 of the Phase 3 feeder studies.

The study population consists of adult subjects (≥18 years of age) who have completed 1 of the Phase 3 feeder studies and had an initial diagnosis of moderate to severe chronic plaque PSO (Baseline Psoriasis Area and Severity Index [PASI] ≥12, body surface area [BSA] affected by PSO ≥10%, and Investigator's Global Assessment [IGA] score ≥3 [on a 5-point scale]). Subjects must have achieved a PASI50 response by the designated time in the feeder study to be eligible for PS0014.

Approximately 1120 subjects are expected to enroll in PS0014. For each subject, the study will last a maximum of 192 weeks and will consist of a Treatment Period (144 weeks) and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP] depending on subject's participation in the Open-Label Extension (OLE2) Period; see paragraph below).

Subjects participating in the OLE2 (implemented as part of Protocol Amendment #3.3) will enter the OLE2 Period after completing the Treatment Period (at Week 144), including subjects in the SFU period and subjects who have completed the SFU Period. The OLE2 Period will be a 48-week open-label treatment period with final visit at OLE2 Week 48, followed by an SFU Period (SFU2, 20 weeks after the final dose of IMP administered in the OLE2 Period).

During the Treatment Period (up to Week 144), eligible subjects will receive the following IMP regimens as determined by the subject's treatment regimen and PASI response in the feeder study. Subjects receiving:

- Bimekizumab 320mg Q4W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg every 4 weeks (Q4W).
- Bimekizumab 320mg Q4W who achieve PASI90 in the feeder study will be randomized 4:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Bimekizumab 320mg every 8 weeks (Q8W) who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg every 4 weeks (Q4W).
- Bimekizumab 320mg Q8W who achieve PASI90 in the feeder study will receive bimekizumab 320mg Q8W.
- Ustekinumab who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Ustekinumab who achieve PASI90 in the feeder study will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Placebo (after a Week 16 response [≥PASI90] on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study) who complete the Randomized Withdrawal Period of the feeder study will receive bimekizumab 320mg Q4W.

At the final study visit in the feeder studies, eligible subjects continuing into PS0014 will complete the final study visit assessments and any additional PS0014 Baseline assessments, and will then receive their first dose of open-label bimekizumab in PS0014. During Year 1 of the Treatment Period (Weeks 0 to 44), all subjects will attend study visits at the study site Q4W for study assessments and IMP will be administered in the clinic by subcutaneous (sc) injection. During Years 2 and 3 of the Treatment Period (Weeks 48 to 144), all subjects will attend study visits at the study site every 12 weeks for study assessments and subjects may self-inject IMP at home.

At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit after implementation of Protocol Amendment #2 if the subject has already completed the Week 48 visit.

Subjects withdrawing early from the study will undergo the Premature End of Treatment (PEOT) Visit assessments and will enter the SFU Period.

After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate bimekizumab treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).
- OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.

During the OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48), all subjects will attend visits at the site every 12 weeks for study assessments and subjects may self-inject IMP at home.

Following completion or early withdrawal from the OLE2 Period, subjects will return for the SFU of the OLE2 Period (SFU2) Visit 20 weeks after the last dose of IMP administration.

The primary objective of the study is to assess the long-term safety and tolerability of bimekizumab administered sc in the treatment of adult subjects with moderate to severe chronic plaque PSO. The secondary objectives of the study are listed in Section 3.2.

The primary safety variable is the incidence of treatment-emergent adverse events (TEAEs) adjusted by duration of subject exposure to treatment. The secondary safety variables are the incidence of serious adverse events (SAEs) adjusted by duration of subject exposure to treatment and TEAEs leading to withdrawal adjusted by duration of subject exposure to treatment (see Section 4.2).

Efficacy variables are listed in Section 4.2.2 and Section 4.3.2.

Pharmacokinetic (PK) variables are listed in Section 4.3.3 and the immunological variable is listed in Section 4.3.4.

Pharmacokinetic and immunological variables will be evaluated to assess their relationship to treatment response.

In addition, subjects may consent to participate in a PS0014 sub-study designed to evaluate the safe and effective use of self-injecting device presentations (ie, prefilled safety syringe and auto-injector presentations) for sc self-injection of bimekizumab by subjects in select sites in Europe, Japan, Canada, and the US.

2 INTRODUCTION

2.1 Psoriasis

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. 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).

There are a variety of forms of PSO including plaque, guttate, inverse, pustular, and erythrodermic. Plaque PSO is the most common, comprising approximately 80% to 90% of all cases. Approximately 17% of those with PSO have moderate to severe disease (Kurd et al, 2008).

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 (PsA), cardiovascular 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).

2.1.1 Global epidemiology of PSO

Psoriasis affects approximately 3% of the US adult population (Rachakonda et al, 2014; Kurd and Gelfand, 2009) and its onset can begin at any age (Augustin et al, 2010; Icen et al, 2009). The reported worldwide incidence and prevalence of PSO varies greatly depending on age, gender, ethnicity, and geography, primarily due to genetic and environmental factors. Estimates of incidence and prevalence include all types of PSO. Plaque PSO is the most common form of the disease; therefore, reported estimates of the magnitude of this condition are likely weighted heavily by this subtype. Both the incidence and prevalence of PSO are higher among Caucasians and those living in higher latitudes. Psoriasis affects approximately 2% to 4% of the population of western countries. Geographical differences are also influenced by case definition, study design, and the definition of prevalence (Parisi et al, 2013; Langley et al, 2005; Raychaudhuri and Gross, 2000).

2.1.2 Current treatments for PSO

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 (PDE) 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. The effectiveness of TNF inhibitors in the treatment of PSO has been demonstrated in many Phase 3 clinical studies and has led to the approval of multiple TNF inhibitors for use in patients with moderate to severe PSO. Interleukin inhibitors approved for this indication include the IL-12/23 antagonist ustekinumab, the IL-23p19 antagonist guselkumab, the IL-17A inhibitors secukinumab and ixekizumab, and the IL-17 receptor antagonist brodalumab.

Standard therapies for PSO are listed below:

- Topical steroids (eg, triamcinolone, mometasone, clobetasol, betamethasone, hydrocortisone) are generally used as first-line treatment of PSO. High-strength steroids are typically reserved for use on the arms and legs. Areas such as the face and skin folds (axillary, inguinal regions, etc) are usually treated with a low potency steroid. Chronic use of topical steroids can lead to corticosteroid-related side effects and is generally discouraged.
- Vitamin D analogs (eg, calcipotriol and tacalcitol) are commonly used to treat mild-to-moderate PSO, and work best within the mild patients. They are safe but lack efficacy for more severe disease.
- Phototherapy is a frequent option for moderate to severe patients, but the inconvenience of multiple treatment visits and varying efficacy limits its use in the market.
- Methotrexate is a systemic immunosuppressant and is used in moderate to severe PSO patients. Toxicity concerns, particularly in older patients, are a major drawback.
- Cyclosporine is a systemic immunosuppressant used in patients with severe, recalcitrant, PSO who have failed at least one systemic therapy or in whom other systemic therapies are contraindicated. In recommended dosages cyclosporine can cause systemic hypertension and nephrotoxicity, therefore, renal function must be monitored during therapy.

- Apremilast is an oral small-molecule inhibitor of PDE4 that is also approved for treatment of adults with moderate to severe plaque PSO. Phosphodiesterase 4 inhibitors work intracellularly to modulate a network of proinflammatory and anti-inflammatory mediators. Phosphodiesterase 4 is a cyclic adenosine monophosphate (cAMP)-specific PDE and the dominant PDE in inflammatory cells. Phosphodiesterase 4 inhibition elevates intracellular cAMP levels, which in turn down-regulates the inflammatory response by modulating the expression of TNFα, IL-23, IL-17, and other inflammatory cytokines.
- Biologics, including TNFα inhibitors (adalimumab, etanercept, and infliximab), IL-12/23 inhibitors (ustekinumab), the IL-23p19 antagonist (guselkumab), the IL-17A inhibitors (secukinumab and ixekizumab), and the IL-17 receptor antagonist brodalumab are the treatment options of choice for patients with moderate to severe plaque PSO who are candidates for systemic therapy or phototherapy. These products are injected sc or delivered via intravenous (iv) infusion. Different from the traditional systemic drugs that impact the entire immune system, biologics target specific parts of the immune system and offer reduced multi-organ toxicity and adverse effects associated with traditional treatments.
  - TNFα inhibitors, while effective, come with boxed warnings including the risk of serious infections and reports of lymphoma and malignancy in children and adolescent patients. The efficacy of TNFα inhibitors in treating PSO is attributed to their inhibition of T-helper 17 cells.
  - Ustekinumab has been approved in the US and the EU for the treatment of patients with moderate to severe plaque PSO who are candidates for phototherapy or systemic therapy. Ustekinumab is a human immunoglobulin (Ig) G1κ monoclonal antibody (mAb) that binds with specificity to the p40 protein subunit used by both the IL-12 and IL-23 cytokines, naturally occurring cytokines that are involved in inflammatory and immune responses, such as natural killer cell activation and cluster of differentiation 4+ T-cell differentiation and activation.
  - Secukinumab and ixekizumab have been approved in the US and the EU for the treatment of moderate to severe plaque PSO in adult patients who are candidates for systemic therapy or phototherapy. Secukinumab is a human IgG1 mAb that selectively binds to the IL-17A cytokine and inhibits its interaction with the IL-17 receptor. Ixekizumab is a humanized IgG4 mAb that selectively binds with the IL-17A cytokine and inhibits its interaction with the IL-17 receptor. Interleukin-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Both drugs inhibit the release of proinflammatory cytokines and chemokines.
  - Guselkumab has been approved in the US and EU for the treatment of adult patients with moderate to severe plaque PSO who are candidates for systemic therapy or phototherapy. It is a human monoclonal IgG1λ antibody that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. Interleukin-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of proinflammatory cytokines and chemokines.
  - Brodalumab has been approved in the EU for the treatment of moderate to severe plaque PSO in adult patients who are candidates for systemic therapy and in the US for the treatment of moderate to severe plaque PSO in adult patients who are candidates for

systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies. Brodalumab is a human monoclonal IgG2 antibody that selectively binds to human IL-17RA and inhibits its interactions with cytokines IL-17A, IL-17F, IL-17C, IL-17A/F heterodimer, and IL-25. Blocking IL-17RA inhibits IL-17 cytokine-induced responses including the release of proinflammatory cytokines and chemokines. Brodalumab has a black box warning regarding suicidal ideation and behavior.

2.2 Bimekizumab

Bimekizumab is an engineered, humanized, full length mAb of IgG1 subclass of approximately 150,000 Daltons which is expressed in a genetically engineered Chinese hamster ovary cell line. Bimekizumab has high affinity for human IL-17A and human IL-17F and selectively and potently inhibits the activity of both isoforms in vitro. Interleukin-17A and IL-17F are key proinflammatory cytokines believed to play important roles in autoimmune and inflammatory diseases. Bimekizumab is being developed for the treatment of patients with inflammatory diseases such as PsA, PSO, and axial spondyloarthritis (axSpA).

While anti-IL-17A antibodies have demonstrated efficacy in patients with PSO, PsA, and ankylosing spondylitis, as yet, no therapeutic approach selectively and potently inhibits the activity of both IL-17A and IL-17F isoforms in vitro. Bimekizumab has been designed to inhibit the activity of IL-17A and IL-17F subtypes of IL-17. This property makes bimekizumab distinctly different from the other IL-17-targeting agents, like secukinumab and ixekizumab (selective anti-IL-17-A mAb) or brodalumab (anti-IL-17 receptor mAb).

Overexpression of IL-17A, IL-17C, and IL-17F in lesion tissue suggests that broader IL-17 blockade may be more beneficial in the treatment of plaque PSO. However, blocking all IL-17 isoforms (including the IL-17E isoform, also known as IL-25) may not be the optimal approach. The role of IL-25 in PSO and other IL-17 mediated diseases has not been well established; however, it has been suggested that IL-25 may play a beneficial role in inflammatory conditions associated with type 1 T-helper mediated immune responses, such as PSO (as opposed to type 2 T-helper mediated) (Valizadeh et al, 2015).Thus, it can be hypothesized that inhibition of both IL-17A and IL-17F is associated with additional benefits in PSO compared with the selective IL-17A inhibition or a broader IL-17 blockade.

2.2.1 Clinical

2.2.1.1 Completed studies

Five clinical studies of bimekizumab have been completed: UP0008 in 39 subjects with mild to moderate plaque PSO, RA0124 in 30 healthy volunteers, PA0007 in 53 subjects with PsA, UP0031 in 12 healthy volunteers, and UP0042 in 48 healthy volunteers.

UP0008 was a Phase 1, single ascending dose study in adults with mild-to-moderate PSO affecting ≤5% BSA. In this blinded study, single doses of up to 640mg (approximately 8mg/kg in an 80kg adult) were evaluated without any safety concerns. A total of 26 subjects with PSO with less than 5% of body surface involvement were treated with a range of single iv doses from 8 to 640mg. There were no clinically relevant safety findings identified at any dose and all doses were well tolerated. The pre-specified exploratory assessment of disease activity showed clinically relevant and statistically significant improvements at the higher doses studied.

RA0124 was a Phase 1, open-label, parallel-group, single-dose study in healthy subjects. The primary objective of this study was to determine the absolute bioavailability (BA) of single sc doses of bimekizumab (80mg and 160mg). The secondary objectives were to evaluate the dose proportionality of bimekizumab 80mg and 160mg sc, and to evaluate the safety and tolerability of these sc doses and 160mg given by iv infusion. In RA0124, the absolute BA was similar for the 2 doses tested (0.656 and 0.631 for the bimekizumab 80mg and 160mg sc doses, respectively). The PK of bimekizumab was linear in the tested dose range and the median $t_{1/2}$ following sc administration was similar to that following iv administration (27.81 days and 28.25 days for bimekizumab 160mg sc and 160mg iv, respectively).

Bimekizumab has also been investigated in a Phase 1b, proof of concept, randomized, placebo controlled, multiple dose study (PA0007). The primary objective of PA0007 was to assess the safety and PK of multiple dose administration of iv bimekizumab in subjects with PsA. Four active doses and a placebo were tested. Drug was administered as a loading dose at Week 0, and 2 additional doses were administered at Week 3 and Week 6. In each treatment group, subjects received a total of 3 doses of bimekizumab, administered every 3 weeks as shown below:

- 80mg loading dose followed by 40mg at Week 3 and Week 6
- 160mg loading dose followed by 80mg at Week 3 and Week 6
- 240mg loading dose followed by 160mg at Week 3 and Week 6
- 560mg loading dose followed by 320mg at Week 3 and Week 6

The results of this study demonstrated that all doses of bimekizumab were well tolerated and there were no unexpected clinically relevant safety findings.

Infections (mostly nasopharyngitis) were the most commonly reported events in both the active treatment and the placebo group. None of the infections were considered serious or required treatment with antibiotics. Two subjects in the active treatment group experienced 1 local candida infection each (oropharhyngitis and vulvovaginitis, respectively) that were nonserious and resolved with topical therapy. There was a potential reduction in mean neutrophil count in the active treatment group, although this drop was not clinically relevant and a clear relationship with dose or time was not evident. Some increases in liver function tests were reported, but none had a convincing relationship to exposure to IMP. The exploratory analysis showed clinically relevant improvement in activity of PsA and in skin involvement in those subjects with concomitant active psoriatic lesions.

UP0031 was a Phase 1, open-label, parallel-group, randomized, single-dose study to evaluate the BA, PK, and tolerability of 2 different formulations of bimekizumab in healthy subjects. Subjects receiving Formulation A (histidine-based) were administered 2x1mL injections of [redacted] each of bimekizumab and subjects receiving Formulation B (acetate-based) were administered a single injection of bimekizumab 160mg given as a 1mL injection. Six subjects were randomized to each bimekizumab formulation. The geometric means for area under the curve were similar between bimekizumab 2x80mg and 1x160mg groups and the relative BA for Formulation B vs Formulation A was 96.1% (95% confidence interval [CI]: 72.7%, 127.0%). Administration of the 2 formulations of bimekizumab used in this study identified no new safety issues. There were no TEAEs leading to discontinuation, and no SAEs or fatalities were reported. The only adverse event (AE) experienced by more than 1 subject in either treatment group was injection site pain

(5 subjects [83.3%] and 3 subjects [50.0%] in the 2x80mg and 1x160mg groups, respectively). The most frequently reported TEAE considered related to the IMP was injection site pain, experienced by 5 subjects (83.3%) and 3 subjects (50.0%) in the 2x80mg and 1x160mg groups, respectively. There were no clinically significant laboratory values reported in the study.

UP0042 was a randomized double-blind, placebo-controlled, single-dose, parallel-group study to evaluate the safety, tolerability, and PK of bimekizumab administered as an sc injection to Japanese and Caucasian healthy subjects. This study demonstrated that the PK profiles following single administration of 80mg, 160mg, and 320mg with sc injection were dose proportional with a linear elimination in both Japanese and Caucasian subjects and that the PK profiles of Japanese and Caucasian subjects were considered to be generally similar. A single dose of bimekizumab (80mg, 160mg, or 320mg) administered as sc injection was generally safe and well tolerated in healthy Japanese and Caucasian subjects and no major differences in safety findings were observed between Japanese and Caucasian subjects.

Additional information on completed studies is available in the Investigator's Brochure (IB).

2.2.1.2 Ongoing studies

All ongoing studies at the time of Protocol Amendment #3.3 implementation are presented and described in the current version of the IB

2.2.1.3 Feeder studies

Eligible subjects who complete the feeder studies are eligible for enrollment into PS0014. These studies include:

- PS0008 is a Phase 3, multicenter, randomized, double-blind, parallel-group study with an active comparator-controlled initial treatment period followed by a dose-blind maintenance period to evaluate the efficacy, safety, and PK of bimekizumab administered as an sc injection of 320mg Q4W and 320mg Q8W compared with adalimumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0009 is a Phase 3, multicenter, randomized, double-blind, placebo- and active comparator-controlled, parallel-group study to evaluate the efficacy, safety, PK, and PD of bimekizumab administered as an sc injection of 320mg Q4W compared with placebo and ustekinumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0013 is a Phase 3, multicenter, double-blind, placebo-controlled study with an initial treatment period followed by a randomized withdrawal period to evaluate the efficacy, safety, and PK of bimekizumab administered as an sc injection of 320mg Q4W and 320mg Q8W compared with placebo in adult subjects with moderate to severe chronic plaque PSO.

2.2.2 Nonclinical

Parallel inhibition of IL-17A and IL-17F has been shown to be efficacious in a variety of animal models of inflammatory disease. Intravenously administered bimekizumab was well tolerated in repeat dose toxicology studies in Cynomolgus monkeys with a no adverse effect level of 200mg/kg/week. The findings of note in toxicity studies were diarrhea related to infectious enteritis (observed in the single dose study) and asymptomatic mild colonic ulceration in a proportion of animals (in the repeat dose study); this latter finding was not associated with hematology abnormalities. Data suggest that bimekizumab has induced primary lesions to the

mucosa associated lymphoid tissue via a pharmacologically-related mechanism. In a second repeat-dose study, none of the minor apoptosis or necrosis findings observed in gut associated lymph nodes were revealed. In animals given the highest dose of bimekizumab in the study (20mg/kg/week), a slightly higher number of protozoa (*Balantidium coli*) was observed in the cecum and colon as compared to the control animals and low dose animals. Therefore, gut associated lymph node lesions observed in the first study are considered to be accidental and/or linked to exaggerated pharmacology and proliferation of *Balantidium coli* and is considered the consequence of a change in local mucosal immunity. To date, similar findings have not been seen in studies in humans.

Additional information on the nonclinical data for bimekizumab is available in the current version of the IB.

3 STUDY OBJECTIVES

3.1 Primary objective

The primary objective of the study is to assess the long-term safety and tolerability of bimekizumab administered sc in adult subjects with moderate to severe chronic plaque PSO.

3.2 Secondary objectives

The secondary objectives of the study are to:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over 144 weeks as measured by SAEs and TEAEs leading to study withdrawal
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over 144 weeks as measured by PASI90 (defined as a subject who achieves 90% reduction in the PASI score from the feeder study Baseline) and IGA response (Clear or Almost Clear with at least a 2 category improvement from Baseline on a 5-point scale)

3.3 Other objectives

The other objectives of the study are to:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over 144 weeks
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over 144 weeks
- Assess the impact of initiating bimekizumab therapy in subjects who received ustekinumab in PS0009
- Assess the PK of bimekizumab
- Assess the immunogenicity of bimekizumab
- Assess the change in psoriatic nail disease in subjects with nail disease at Baseline in the feeder studies
- Assess the change in psoriatic scalp disease over time for subjects with scalp PSO at Baseline in the feeder studies

- Assess the change in palmoplantar PSO for subjects who have palmoplantar PSO at Baseline in the feeder studies
- Assess the symptoms of PsA as measured by the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire
- Assess general health-related quality of life (QOL), including the change in skin-related QOL and treatment satisfaction
- Assess the safety of bimekizumab manufactured using Process 5

4 STUDY VARIABLES

4.1 Primary safety variable

The primary safety variable is the incidence of TEAEs adjusted by duration of subject exposure to treatment.

4.2 Secondary variables

4.2.1 Secondary safety variables

The secondary safety variables are:

- Incidence of SAEs adjusted by duration of subject exposure to treatment
- Incidence of TEAEs leading to withdrawal adjusted by duration of subject exposure to treatment

4.2.2 Secondary efficacy variables

The secondary efficacy variables are:

- PASI90 at Week 144
- IGA 0/1 response at Week 144

4.3 Other variables

The other variables are listed below and will be evaluated according to the schedule of study assessments in Table 5-1 and Table 5-2. Variables evaluated in the OLE2 Period are listed in Table 5-3.

4.3.1 Other safety variables

Change from Baseline variables for safety will be defined relative to the Baseline entry measurement from PS0014.

The other safety variables to be assessed are:

- Severity and frequency of TEAEs
- Change from Baseline in clinical laboratory variables (chemistry and hematology)
- Change from Baseline in vital signs
- Change from Baseline in 12-lead electrocardiogram (ECG) results
- Change from Baseline in the Patient Health Questionnaire 9 (PHQ-9)

Physical examination findings considered to be clinically significant changes since the physical examination at the Baseline Visit will be recorded as AEs.

4.3.2 Other efficacy variables

Change from Baseline efficacy variables will be defined relative to the Baseline measurement from the feeder study. The other efficacy variables are listed below:

- PASI75, PASI90, and PASI100 response
- Percentage of subjects with PASI ≤1, ≤2, ≤3 and ≤5
- IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline)
- IGA response (Clear with at least 2 category improvement relative to Baseline)
- Absolute and percent change from Baseline in PASI score
- Absolute and percent change from Baseline in the BSA affected by PSO
- Absolute and percent change from Baseline in the product of IGA and BSA (IGAxBSA)
- Change from Baseline in Dermatology Life Quality Index (DLQI)
- Percentage of subjects achieving a DLQI total score of 0 or 1
- Percentage of subjects achieving a minimal clinically important difference (improvement from Baseline of 4 or more) in the DLQI
- Change from Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) score for subjects with nail disease at Baseline
- mNAPSI75, mNAPSI90 and mNAPSI100 response
- Change from Baseline in the Patient's Global Assessment of Disease Activity (PGADA) for the arthritis visual analog scale (VAS) for subjects with PsA at Baseline
- Change from Baseline in Patient Global Assessment (PGA) of PSO score
- Scalp-specific IGA (Scalp IGA) response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with scalp PSO at Baseline
- Palmoplantar Investigator's Global Assessment (pp-IGA) response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with palmoplantar PSO at Baseline
- Change from Baseline in the PASE questionnaire scores (function score, symptom score, and total score)
- Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47)
- Change from Baseline in Short Form 36-item Health Survey (SF-36), Physical Component Summary (PCS) score, Mental Component Summary (MCS) score, and individual domains
- Responses to Euro-Quality of Life 5-Dimensions, 3 levels (EQ-5D-3L)
- Changes from Baseline in EQ-5D-3L VAS scores and all dimensions

- Change from Baseline in Work Productivity and Activity Impairment Questionnaire-specific health problem (WPAI-SHP) V2.0 adapted to PSO scores
- Treatment Satisfaction Questionnaire for Medication (TSQM-9)

4.3.3 Pharmacokinetic variables

The PK variable is plasma concentrations of bimekizumab.

4.3.4 Immunological variable

The immunological variable is anti-bimekizumab antibody levels prior to and following IMP administration.

5 STUDY DESIGN

5.1 Study description

PS0014 is a multicenter, open-label study to assess the long-term safety, tolerability, and efficacy of bimekizumab in eligible adult subjects with moderate to severe chronic plaque PSO who complete 1 of the Phase 3 feeder studies. At the final study visit in the feeder studies, eligible subjects continuing into PS0014 will complete the final study visit assessments and any additional PS0014 Baseline assessments, and will then receive their first dose of open-label bimekizumab in PS0014. Subjects will receive IMP (bimekizumab 320mg Q4W or bimekizumab 320mg Q8W) based on their treatment regimen and PASI response in the feeder study (see Section 5.2.1).

An additional open-label cohort will be added in Japan to allow enrollment of subjects with PSO including moderate to severe chronic plaque PSO, generalized pustular PSO, and erythrodermic PSO. The details of this cohort are included in the country-specific protocol amendment.

An OLE2 Period will be added in Canada and the US after the country-specific Protocol Amendment #3.3 implementation (addition of a 48-week open-label treatment period, ie, the OLE2 Period), and subjects will be invited to continue or reinitiate bimekizumab treatment for an additional 40 weeks.

In addition, subjects may consent to participate in a PS0014 sub-study designed to evaluate the safe and effective use of self-injecting device presentations (ie, prefilled safety syringe and auto-injector presentations) for sc self-injection of bimekizumab by subjects in select sites in Europe, Japan, Canada, and the US.

5.2 Study periods

PS0014 will include a Treatment Period of 144 weeks (from Baseline/Feeder Study Final Visit to Week 144 Visit) followed by a SFU Period of 20 weeks after the last dose of IMP in the Treatment Period. After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), PS0014 will be prolonged by an OLE2 Period, during which eligible subjects will be invited to continue or reinitiate bimekizumab treatment for 40 weeks (from Week 144/OLE2 Baseline to OLE2 Week 48) and will be followed in a second

SFU Period of 20 weeks after the final dose of IMP (SFU2 Period), as appropriate. Subjects will be invited to continue or reinitiate bimekizumab treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).
- OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.

5.2.1 Treatment Period

During the Treatment Period, eligible subjects will receive the following IMP regimens as determined by the subject's treatment regimen and PASI response in the feeder study. Subjects receiving:

- Bimekizumab 320mg Q4W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q4W who achieve PASI90 in the feeder study will be randomized 4:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Bimekizumab 320mg Q8W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who achieve PASI90 in the feeder study will receive bimekizumab 320mg Q8W.
- Ustekinumab who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Ustekinumab who achieve PASI90 in the feeder study will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Placebo (after a Week 16 response [≥PASI90] on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study) who complete the Randomized Withdrawal Period of the feeder study will receive bimekizumab 320mg Q4W.

During Year 1 of the Treatment Period (Weeks 0 to 44), all subjects will attend study visits at the study site Q4W for study assessments. During Years 2 and 3 of the Treatment Period (Weeks 48 to 144), all subjects will attend study visits at the study site Q12W for study assessments.

At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit. The last dose bimekizumab 320mg Q8W in the Treatment Period will be administered at Week 136. The End of Treatment Visit of the Treatment Period will be the Week 144 Visit.

The assessments to be performed at each Treatment Period Visit are presented in Table 5-1 and Table 5-2.

5.2.2 OLE2 Period

Subjects enrolled as per Protocol Amendment #3 will be treated in the Treatment Period until Week 136 (last dose of bimekizumab 320mg Q8W) and will be followed in a SFU Period for 20 weeks after their last dose of IMP. After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), study subjects will be invited to continue or reinitiate bimekizumab treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).
- OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.

During the OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48), subjects may self-inject IMP at home (described in Section 7.2) at the time points specified in the schedule of assessments (Table 5-3).

5.2.3 Safety Follow-Up Periods

Two SFU Periods are considered since Protocol Amendment #3.3 implementation. A first SFU following the Treatment Period and a second SFU (SFU2) following the OLE2 Period (added as per Protocol Amendment #3.3).

Following completion or early withdrawal from the Treatment Period, subjects will return for a SFU Visit 20 weeks after their final dose of bimekizumab.

The assessments for the SFU are presented in Table 5-2.

Subjects still in the Treatment Period (not having attended Week 144 yet; OLE2 Group A) will have the opportunity to directly roll over in the OLE2. Subjects having attended Week 144 Visit and who are participating in the SFU or have completed the SFU (OLE2 Group B) will be invited to reinitiate treatment in the OLE2 Period.

All subjects who have completed treatment in the OLE2 Period (ie, have completed the OLE2 Week 48 Visit), or have withdrawn from IMP during the OLE2 Period before OLE2 Week 48, will return for a SFU2 Visit 20 weeks after their final dose of IMP.

The assessments for the SFU2 are presented in Table 5-3.

5.2.4 Premature End of Treatment

Subjects withdrawing early from the study will undergo the PEOT Visit assessments (see Section 8.2) and will enter the SFU or SFU2 Period, depending on when subjects withdraw.

5.3 Study duration per subject

For each subject, prior to Protocol Amendment 3.3 implementation, the study will last a maximum of 160 weeks and will consist of:

- A Treatment Period during which subjects will continue to receive open-label bimekizumab in PS0014 for up to 144 weeks (the last dose will be administered at Week 136 and Week 144 will be the End of Treatment Visit).
- An SFU Period 20 weeks after the final dose of bimekizumab administered during the Treatment Period (subjects will enter the SFU after Week 144 Visit or after withdrawal).

Subjects eligible for the OLE2 Period (added as part of Protocol Amendment #3.3) will enter the OLE2 after completing Week 144 of the Treatment Period. The OLE2 Period includes a 48-week open-label treatment period with a final visit at OLE2 Week 48, and an SFU Period (SFU2) of 20 weeks after the final dose of IMP administered in the OLE2 Period.

For subjects participating in the OLE2 Period, the maximum study duration will depend on the time between their participation in the Treatment Period until Week 144 and the start of the OLE2 Period:

- 204 weeks for subjects still being treated in the Treatment Period and who will directly roll over to the OLE2 Period at Week 144.
- 224 weeks for subjects who have attended Week 144 and who will have completed the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 Period.

- Between 204 and 224 weeks for subjects who will have attended Week 144 and are participating the in the SFU. For these subjects, the maximum study duration will depend upon when they will stop the 20-week SFU period to enter the 4-week Screening Period of the OLE2 Period.

The end of the study is defined as the date of the last visit of the last subject in the study.

5.4 Planned number of subjects and sites

Approximately 1120 subjects (including approximately 60 subjects from the Japanese-specific local amendment) will be enrolled in the study. The anticipated enrollment in the feeder studies is 1250 subjects (450 subjects from PS0008, 480 subjects from PS0009, and 320 subjects from PS0013) and approximately 85% are expected to roll into PS0014.

5.5 Anticipated regions and countries

The regions planned for the study conduct are North America, Western Europe, Central/Eastern Europe, and Asia/Australia, with possible extension to other regions and countries.

5.6 Schedule of study assessments

The schedule of study assessments for Year 1 (Weeks 0 to 44) is presented in Table 5-1. The schedule of study assessments for Years 2 and 3 (Weeks 48 to 144) is presented in Table 5-2. The schedule of study assessments for OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48) is presented in Table 5-3. At each visit, all study assessments should be performed prior to administration of IMP.

Table 5-1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Visit [a] / Week / Protocol activity	Treatment Period-Year 1											
	Stable Dosing							Flexible Dosing [b]				
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44
Informed consent	X											
Inclusion/exclusion	X											
Physical exam [c,d]	X			X			X			X		
Body weight	X											
Vital signs [e]	X	X	X		X		X		X		X	
Hematology and chemistry	X	X	X		X		X		X		X	
Urinalysis	X	X	X		X		X		X		X	
Urine drug screen	X											
ECG	X											
Pregnancy testing [f]	X	X	X	X	X	X	X	X	X	X	X	X
IGRA TB test [g]												
TB questionnaire	X			X			X			X		
Blood sample for bimekizumab plasma concentrations [h]	X				X		X				X	
Blood sample for anti-bimekizumab antibodies [h]	X				X		X				X	
PASI	X	X	X	X	X	X	X	X	X	X	X	X
Percentage of BSA	X	X	X	X	X	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X	X	X	X	X	X
DLQI	X						X					
PHQ-9	X	X	X		X		X		X		X	
eC-SSRS	X	X	X		X		X		X		X	

Table 5-1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity \ Visit [a]/ Week	Treatment Period-Year 1											
	Stable Dosing							Flexible Dosing [b]				
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44
mNAPSI [i]	X						X					
Scalp IGA [j]	X						X					
pp-IGA[k]	X						X					
EQ-5D-3L	X						X					
SF-36	X						X					
PGA of PSO	X						X					
PASE [l]	X											
PGADA[l]	X						X					
WPAI-SHP V2.0	X						X					
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X
IRT	X	X	X	X	X	X	X	X	X	X	X	X
Bimekizumab administration Q4W[m, n]	X	X	X	X	X	X	X	X	X	X	X	X
Bimekizumab administration Q8W[m, n]	X		X		X		X		X		X	
Subject training on self-injection[o]											X	X

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire 9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; SF-36=Short Form 36-item Health Survey; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; TB=tuberculosis; W=Week; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from the first dose at all visits.

[b] At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).

[c] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

Table 5-1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity \ Visit [a]/ Week	Treatment Period-Year 1											
	Stable Dosing							Flexible Dosing [b]				
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44

[d] The physical examination will be performed as per Section 9.3.5.
[e] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.
[f] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.
[g] Ensure that results for the latest IGRA test performed in the feeder study are negative.
[h] All blood samples taken prior to dosing.
[i] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.
[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.
[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.
[l] The PGADA and the PASE are assessed only for subjects with PsA at Baseline in the feeder studies.
[m] The dosing window is ±7 days relative to the scheduled dosing visit.
[n] Only subjects receiving IMP Q4W are dosed on Weeks 4, 12, 20, 28, 36, and 44. Subjects who are switched from IMP Q4W to IMP Q8W at Week 24 are dosed on Weeks 32 and 40 in the Flexible Dosing Period.
[o] Subject training on self-injection to be performed as described in Section 7.2.

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Visit [a] / Week / Protocol activity	Treatment Period – Years 2 and 3 [b]																							W144 / PEOT	SFU[c]
	48 C	52 C/H	56 C/H	60 C	64 C/H	68 C/H	72 C	76 C/H	80 C/H	84 C	88 C/H	92 C/H	96 C	100 C/H	104 C/H	108 C	112 C/H	116 C/H	120 C	124 C/H	128 C/H	132 C	136 C/H	140 C/H		
Physical exam [d,e]	X			X			X			X			X			X			X			X			X	X
Body weight	X												X												X	X
Vital signs [f]	X			X			X			X			X			X			X			X			X	X
Hematology and chemistry	X			X			X			X			X			X			X			X			X	X
Urinalysis	X			X			X			X			X			X			X			X			X	X
ECG	X												X												X	
Urine pregnancy testing [g]	X			X			X			X			X			X			X			X			X	X
IGRA TB test	X												X												X	
TB questionnaire	X			X			X			X			X			X			X			X			X	
Blood sample for bimekizumab plasma concentrations [h]	X						X						X						X						X	X
Blood sample for anti-bimekizumab antibodies [h]	X						X						X						X						X	X
PASI	X			X			X			X			X			X			X			X			X	
Percentage of BSA	X			X			X			X			X			X			X			X			X	
IGA	X			X			X			X			X			X			X			X			X	
DLQI	X						X						X						X						X	
PHQ-9	X			X			X			X			X			X			X			X			X	X
eC-SSRS	X			X			X			X			X			X			X			X			X	X

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Visit [a] / Week / Protocol activity	Treatment Period – Years 2 and 3 [b]																								W144 / PEOT	SFU[c]
	48 C	52 C/H	56 C/H	60 C	64 C/H	68 C/H	72 C	76 C/H	80 C/H	84 C	88 C/H	92 C/H	96 C	100 C/H	104 C/H	108 C	112 C/H	116 C/H	120 C	124 C/H	128 C/H	132 C	136 C/H	140 C/H		
mNAPSI [i]	X						X						X						X						X	
Scalp IGA [j]	X						X						X						X						X	
pp-IGA [k]	X						X						X						X						X	
EQ-5D-3L	X						X						X						X						X	
SF-36	X						X						X						X						X	
PGA of PSO	X						X						X						X						X	
PASE[l]	X												X												X	
PGADA[l]	X												X												X	
WPAI-SHP V2.0	X												X									X			X	
TSQM-9	X																									
Concomitant medication	X			X			X			X			X			X			X			X			X	X
Adverse events	X			X			X			X			X			X			X			X			X	X
IRT	X			X			X			X			X			X			X			X			X	X
Bimekizumab self-injection Q4W [m,n,q]	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X		
Bimekizumab self-injection Q8W [m,n]	X[o]		X		X		X		X		X		X		X		X		X		X		X			
IMP accountability for self-injection at home[p]				X			X			X			X			X			X			X			X	

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; H=home; IGRA=interferon-gamma release assay; IMP=investigational

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Protocol activity \ Visit [a] / Week	Treatment Period – Years 2 and 3 [b]																							W144 / PEOT	SFU[c]
	48 C	52 C/H	56 C/H	60 C	64 C/H	68 C/H	72 C	76 C/H	80 C/H	84 C	88 C/H	92 C/H	96 C	100 C/H	104 C/H	108 C	112 C/H	116 C/H	120 C	124 C/H	128 C/H	132 C	136 C/H	140 C/H		

medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PEOT=Premature End of Treatment; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire-9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; SFU=Safety Follow-Up; TB=tuberculosis; TSQM-9=Treatment Satisfaction Questionnaire for Medication; W=Week; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Note: Starting at Week 48 of the Treatment Period, subjects may self-inject IMP at home; self-injection training will be provided to the subject/caregivers by qualified site personnel (see Section 7.2).

[a] Visit windows of ±7 days from the first dose at all visits except SFU. The Safety Follow-Up Visit window is ±7 days from final dose.

[b] Starting at Week 48 of the Treatment Period, subjects will attend site visits every 12 weeks.

[c] The SFU Visit will occur 20 weeks after the final dose.

[d] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[e] The physical examination will be performed as per Section 9.3.5.

[f] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[g] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.

[h] All blood samples taken prior to dosing.

[i] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.

[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.

[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.

[l] The PGADA and the PASE are assessed only for subjects with PsA at Baseline in the feeder studies.

[m] The dosing window is ±7 days relative to the scheduled dose.

[n] The last dose for subjects receiving bimekizumab 320mg Q8W will be Week 136.

[o] The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48, or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit.

[p] If self-injected at home, the subject/caregiver will document the date, body location, kit number and time point of administration of study medication. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

[q] Q4W IMP administration only applies to those subjects who have not yet changed to Q8W at Week 48, or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit.

Table 5-3: Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W32	OLE2 W36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
	C	C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity		OLE2 Groups A + B										
Informed consent	Group B	Group A										
Eligibility	Group B	Group A+B										
Urine drug screen	Group B											
Significant past medical history and concomitant diseases [d]	Group B[d]											
Physical exam [e]	Group B	Group A[f] + B			X		X		X		X	X
Body weight		Group A[f] + B									X	
Vital signs [g]	Group B	Group A[f] + B			X		X		X		X	X
Hematology and chemistry	Group B	Group A[f] + B					X				X	X
Urinalysis	Group B	Group A[f] + B					X				X	X
Pregnancy testing (urine) [h]	Group B	Group A[f] + B			X		X		X		X	X
Hepatitis B and C testing	Group B											
HIV testing [i]	Group B											
IGRA TB test		Group A[f]									X	
Tuberculosis questionnaire	Group B	Group A[f] + B			X		X		X		X	
PASI	Group B	Group A[f] + B			X		X		X		X	
Percentage of BSA	Group B	Group A[f] + B			X		X		X		X	

Table 5-3: Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W32	OLE2 W36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
	C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity		OLE2 Groups A + B										
IGA	Group B	Group A[f] + B			X		X		X		X	
DLQI		Group A[f] + B					X				X	
PHQ-9	Group B	Group A[f] + B			X		X		X		X	X
ECG		Group A[f]										
Blood sample for bimekizumab plasma concentrations [j]		Group A[f]										
Blood sample for anti-bimekizumab antibodies [j]		Group A[f]										
scalp IGA		Group A[f]										
mNAPSI		Group A[f]										
pp-IGA		Group A[f]										
EQ-5D-3L		Group A[f]										
PASE		Group A[f]										
PGADA		Group A[f]										
WPAI-SHP V2.0		Group A[f]										
eC-SSRS	Group B	Group A[f] + B			X		X		X		X	X
Concomitant medication	Group B	Group A[f] + B			X		X		X		X	X

Table 5-3: Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W32	OLE2 W36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
		C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity			**OLE2 Groups A + B**									
Adverse events	Group B [k]	Group A[f] + B			X		X		X		X	X
IRT	Group B	Group A[f] + B			X		X		X		X	X
Bimekizumab administration Q4W/Q8W [l, m, n]		Group B [l]	X	X	X	X	X	X		X		
Bimekizumab administration Q8W [m, n]		Group A+B [l]		X		X	X	X		X		
IMP accountability for self-injection at home					X		X		X		X	

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; H=home; HIV= human immunodeficiency virus; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; OLE=open label extension; PASI=Psoriasis Area Severity Index; PEOT=Premature End of Treatment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire-9; pp-IGA=palmoplantar Investigator's Global Assessment; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU=Safety Follow-Up; SFU2=Safety Follow-Up #2; TB=tuberculosis; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem; W=Week.

Note: Subjects may self-inject IMP at home; self-injection training will be provided to the subject/caregivers by qualified site personnel.

[a] Visit windows of ±14 days relative to the Week 144/OLE2 Baseline Visit all visits except SFU2. The SFU2 Visit window is ±7 days from final dose.

[b] Assessment for the OLE2 Screening is applicable to subjects in OLE2 Group B, ie, subjects who agreed to reinitiate bimekizumab treatment after having completed the Week 144 Visit.

[c] The SFU2 Visit will occur 20 weeks after the final dose.

[d] Only applicable for subjects who completed the SFU period; only new or modified medical history since completing SFU will be entered in eCRF.

[e] The physical examination will be performed as per Section 9.3.5.

[f] These tests are performed as part of the Week 144 visit (the Week 144 Visit coincides with the Week 144/OLE2 Baseline Visit for subjects in Group A, ie, direct enrollers from Treatment Period to OLE2 Period).

[g] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[h] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.

[i] The HIV test results will not be recorded in the eCRF.

Table 5-3: Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

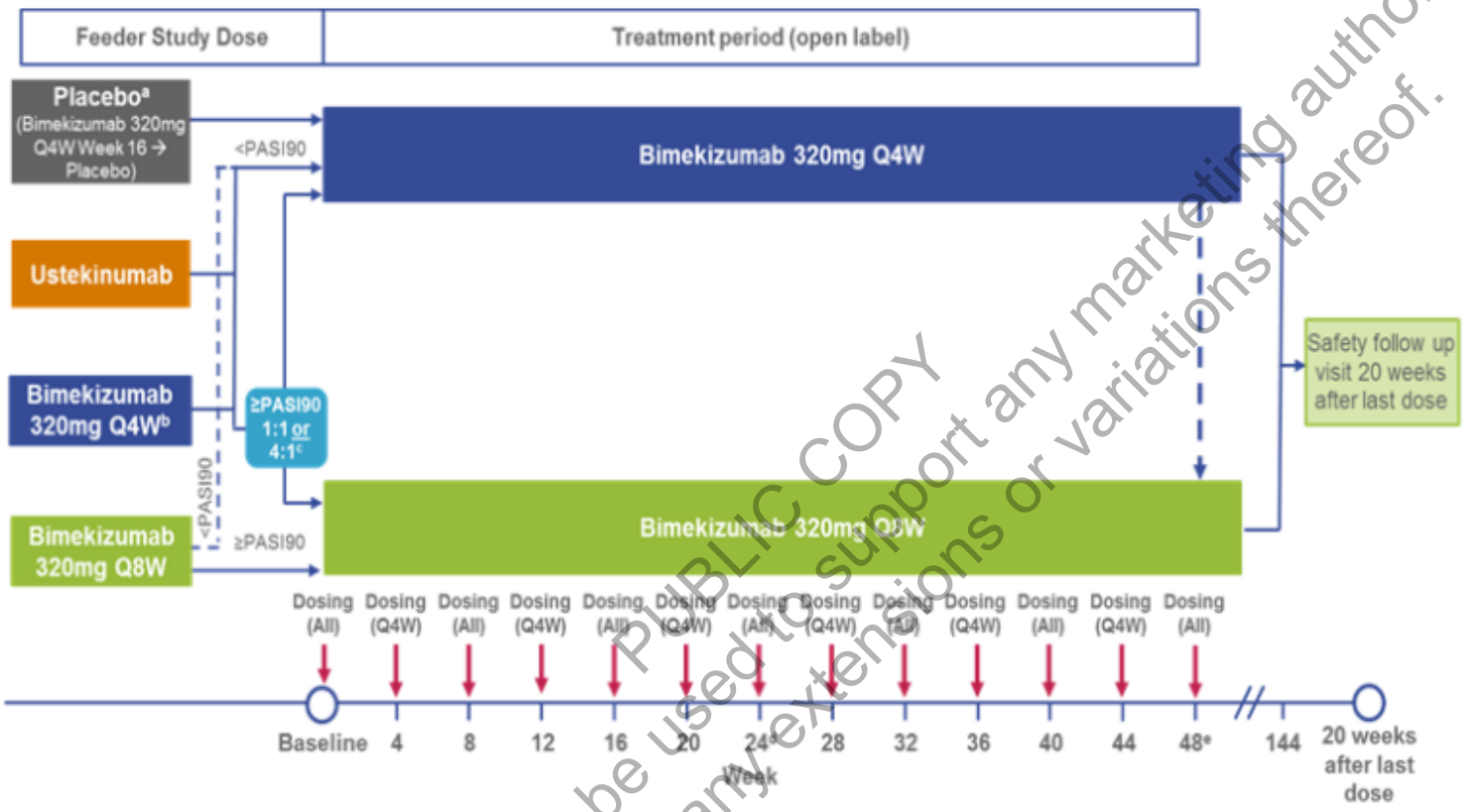
Visit [a]/ Week	OLE2 Period[b]										OLE2 W48/ PEOT	SFU2[c]
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W32	OLE2 W36	OLE2 W 40		
		C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity			OLE2 Groups A + B									

[j] All blood samples taken prior to dosing.
[k] Collected only from subjects in the SFU Period.
[l] Q4W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B and had an IGA ≥3 upon entry of OLE2 Period. These subjects will receive Q4W dosing for 16 weeks, then will change from Q4W to Q8W dosing. Subjects who have entered the OLE2 Period as part of Group B with an IGA <3 upon entry of OLE2 Period will receive Q8W dosing from the OLE2 Screening Visit onwards.
[m] The dosing window is ±14 days relative to the Week 144/OLE2 Baseline Visit.
[n] If self-injected at home, the subject/caregiver will document the date, body location, kit number, and time point of administration of study medication. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

5.7 Schematic diagram

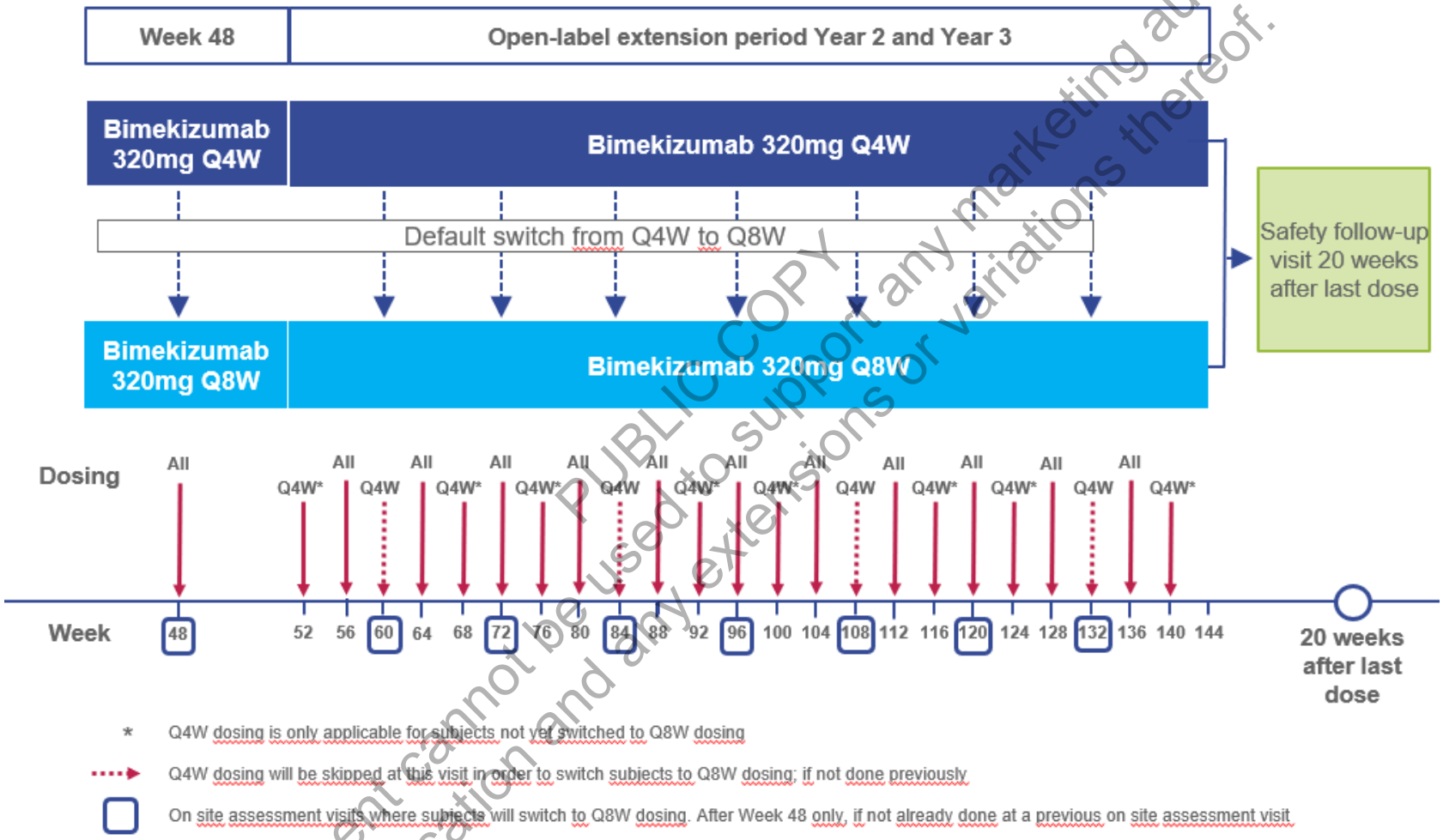
The study schematic diagram for PS0014 from Screening through Week 48 is presented in Figure 5–1, from Week 48 through Week 144 is presented in Figure 5-2, and from OLE2 Screening to the OLE2 Week 48 Visit is presented in Figure 5-3.

Figure 5–1: Schematic diagram, Screening through Week 48



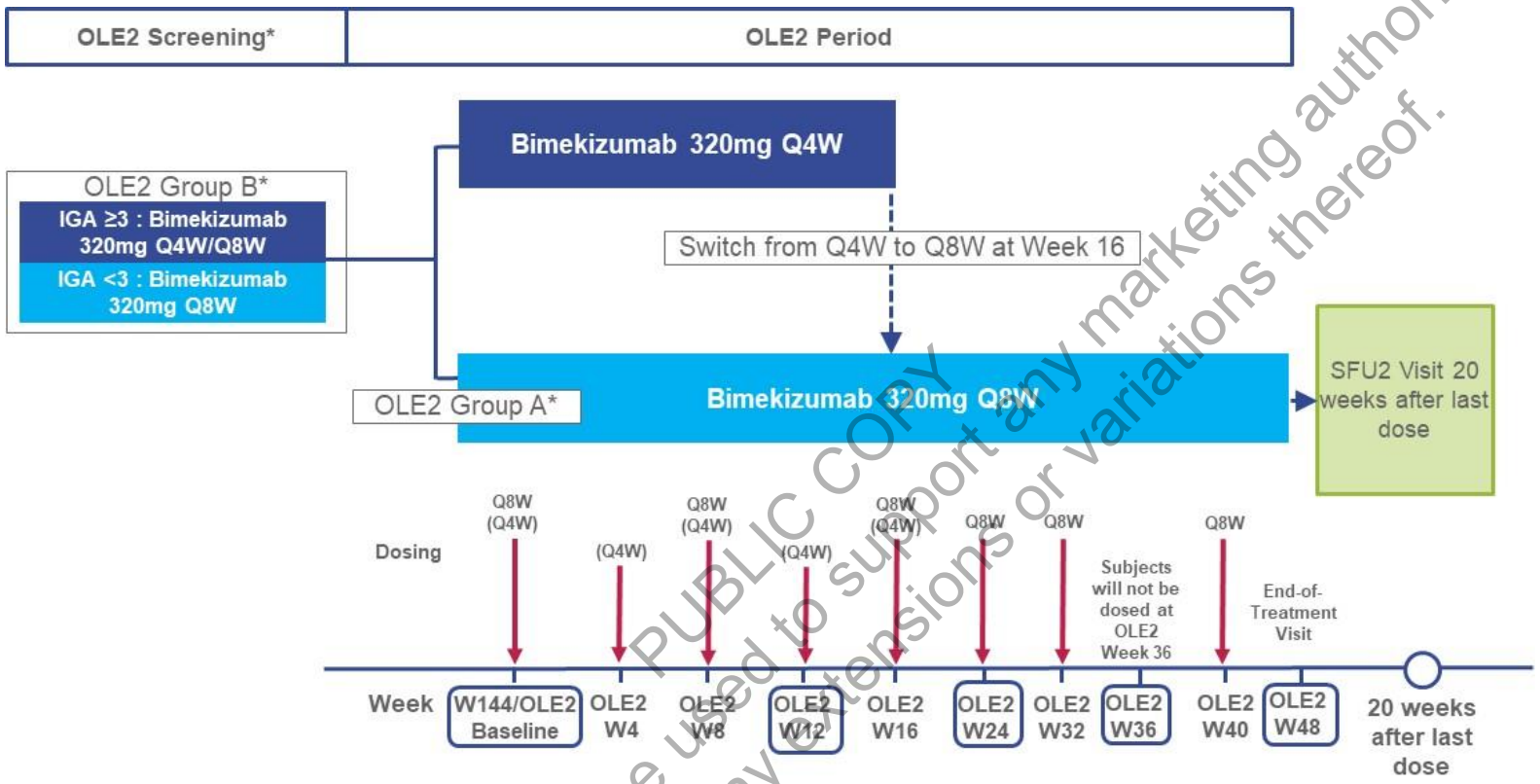
IMP=investigational medicinal product; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Self-injection will be allowed from Week 48 onward.
Note: At Week 28 and all following visits, subjects on continuous treatment with the same IMP for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.
[a] Subjects on placebo after a Week 16 response (≥PASI90) on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study may enroll in PS0014.
[b] Subjects on bimekizumab 320mg Q4W who achieved a PASI50 at Week 12 in the escape arm of the feeder study may enroll in PS0014.
[c] Subjects on ustekinumab or bimekizumab 320mg Q4W in feeder studies who achieved PASI90 will be randomized, respectively, 1:1 or 4:1 to bimekizumab 320mg Q4W or 320mg Q8W.
[d] At Week 24, if PASI90 is achieved, Investigator may change the dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W (optional).
[e] The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #3.

Figure 5-2: Schematic diagram, Years 2 and 3 (Week 48 through Week 144)



Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Self-injection will be allowed from Week 48 onward.
Note: The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #3.

Figure 5-3: Schematic diagram, OLE2 Period (From OLE2 Screening through OLE2 Week 48)



IGA=Investigator's Global Assessment; IMP=investigational medicinal product; OLE=Open Label Extension; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU2=Safety follow-up; W=week

Note: Q4W/Q8W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B, and had an IGA ≥3 upon entry of OLE2 Period. These subjects will receive Q4W dosing for 16 weeks, then will change from Q4W to Q8W dosing.

5.8 Rationale for study design and selection of dose

PS0014 is an open-label study designed to assess the long-term safety, tolerability, and efficacy of bimekizumab over a 144-week Treatment Period. Doses used in this study are based on the dosing regimens (Q4W and Q8W) of the feeder studies, as well as the subjects' PASI score upon entering the study. Subjects who do not achieve a PASI90 response in the feeder studies may be enrolled in PS0014 at the discretion of the Investigator. In the PS0011 study, a multicenter, 48-week, double-blind, placebo-controlled, parallel-group extension study to assess the long-term safety, tolerability, and efficacy of bimekizumab in adult subjects with moderate to severe chronic plaque PSO, 97% of subjects receiving 320mg Q4W were PASI90 responders at Week 52 (full analysis set, observed case). In addition, all subjects (100%) achieved a PASI75 response by Week 52.

In PS0014, doses can be adjusted at Week 24 for subjects receiving bimekizumab 320mg Q4W at the discretion of the Investigator (optional).

Based on pooled data from the Phase 3 studies (PS0008, PS0009, and PS0013), during the maintenance period bimekizumab 320mg Q8W provided efficacy results similar to bimekizumab 320mg Q4W. Therefore, at Week 48, subjects receiving bimekizumab 320mg Q4W will switch to receive bimekizumab 320mg Q8W. Subjects who are receiving bimekizumab 320mg Q4W treatment who already completed the Week 48 visit at the time of implementation of Protocol Amendment #3 will be switched to bimekizumab 320mg Q8W at the next scheduled clinic visit. This change in dosing interval will reduce subject and site burden, while allowing collection of more long-term safety data on the bimekizumab 320mg Q8W dosing regimen.

Subjects in the feeder studies who responded without biologic intervention are not eligible for PS0014.

Subjects who are participating in the Treatment Period can directly roll over to the OLE2 Period and continue receiving bimekizumab 320mg Q8W (OLE2 Group A). Subjects who have attended Week 144 Visit and are participating in the SFU of the Treatment Period or have completed the SFU at the time of Protocol Amendment #3.3 implementation (OLE2 Group B) can reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. For eligible subjects reinitiating treatment with bimekizumab, treatment regimen will be based on current disease activity, as measured by IGA: subjects with IGA score <3 will receive bimekizumab 320mg Q8W, whereas subjects with IGA score ≥3 will receive 16 weeks of bimekizumab 320mg Q4W, followed by 320mg Q8W for the remaining dosing timepoints of the OLE2 Period.

The OLE2 Period will 1) collect additional long-term safety data; 2) explore safety data in subjects who have temporarily stopped bimekizumab and could have been exposed to other treatments; and 3) provide an additional 48-week open-label treatment period for subjects continuing their current treatment or reinitiating treatment at the Week 144/OLE2 Baseline Visit.

6 SELECTION AND WITHDRAWAL OF SUBJECTS

6.1 Inclusion criteria

To be eligible to participate in this study prior to the OLE2 Period (eligibility criteria for the OLE2 Period are listed in Section 6.3), all of the following inclusion criteria must be confirmed at the Baseline Visit:

1. Subject has provided informed consent.
2. Subject is considered reliable and capable of adhering to the protocol (eg, able to understand and complete diaries), visit schedule, and medication intake according to the judgment of the Investigator.
3. Subject completes the feeder study without meeting any withdrawal criteria.
4. Female subjects must be:
   - Postmenopausal: Menopause is defined as 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause.
   - Permanently sterilized (eg, tubal occlusion, hysterectomy, bilateral salpingectomy)
   - Or, if of childbearing potential (and engaged in sexual activity that could result in procreation), must be willing to use a highly effective method of contraception throughout the duration of the study until 20 weeks after last administration of IMP, and have a negative pregnancy test at the Baseline/feeder study final visit in PS0014. The following methods are considered highly effective when used consistently and correctly:
     - Combined (estrogen and progestogen) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal)
     - Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
     - Intrauterine device
     - Intrauterine hormone-releasing system
     - Vasectomized partner
     - Abstinence as a form of birth control is generally not allowed in the study unless abstinence is in accordance with a subject's preferred and common lifestyle. Study personnel must confirm the continued use of abstinence is still in accordance with the subject's lifestyle at regular intervals during the study.

6.2 Exclusion criteria

Subjects are not permitted to enroll in the study if any of the following exclusion criteria is met:

1. Subject has previously participated in this study.
2. Female subjects who plan to become pregnant during the study or within 20 weeks following final dose of study medication.
3. Subject has any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the subject's ability to participate in this study.

   Note: For any subject with an ongoing SAE, or a history of serious infections in the feeder study, the Medical Monitor must be consulted prior to the subject's entry into PS0014, although the decision on whether to enroll the subject remains with the Investigator.
4. Subject has a positive or indeterminate interferon gamma release assay (IGRA) in a feeder study, unless appropriately evaluated and treated as per Section 9.3.1.
5. Subject may not participate in another study of a medicinal product or device under investigation other than the substudy described in Section 5.1.
6. Subject has a history of chronic alcohol or drug abuse within 6 months prior to Baseline as assessed by medical history, site interview, and/or results of the specified urine drug screen.

6.3 Eligibility criteria for the OLE2 Period

Prior to initiating the OLE2 Period assessments, all subjects will be asked to read and sign a separate Informed Consent Form (ICF).

6.3.1 All subjects (OLE2 Groups A and B)

To be eligible to participate in the OLE2 Period, all of the following inclusion criteria must be confirmed for all subjects:

1. Subject provided informed consent.
2. Subject is considered reliable and capable of adhering to the protocol (eg, able to understand and complete diaries), visit schedule, and medication intake according to the judgment of the Investigator.
3. Subject completes the Treatment Period to Week 144 without meeting any withdrawal criteria defined in Section 6.4.

6.3.2 OLE2 Period Group A subjects

To participate in the OLE2 Period, subjects still treated and who completed the Week 144 Visit by the time of Protocol Amendment #3.3 implementation will not need to fulfil other eligibility criteria than those listed in Section 6.3.1 and will continue treatment from the Week 144/OLE2 Baseline Visit if they do not meet any of the withdrawal criteria defined in Section 6.4.

6.3.3 OLE2 Period Group B subjects

Inclusion criteria

To be eligible to participate in the OLE2 Period, all of the additional following inclusion criteria must be confirmed during the OLE2 Screening Period for subjects who have attended Week 144 and are in the SFU or have completed the SFU before Protocol Amendment #3.3 implementation (OLE2 Group B subjects):

1. Female subjects must be:
   - Postmenopausal: Menopause is defined as 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause.
   - Permanently sterilized (eg, tubal occlusion, hysterectomy, bilateral salpingectomy)
   - Or, if of childbearing potential (and engaged in sexual activity that could result in procreation), must be willing to use a highly effective method of contraception throughout the duration of the study until 20 weeks after last administration of IMP, and have a negative pregnancy test at OLE2 Screening. The following methods are considered highly effective when used consistently and correctly
     - Combined (estrogen and progestogen) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal)
     - Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
     - Intrauterine device
     - Intrauterine hormone-releasing system
     - Vasectomized partner
     - Abstinence as a form of birth control is generally not allowed in the study unless abstinence is in accordance with a subject's preferred and common lifestyle. Study personnel must confirm the continued use of abstinence is still in accordance with the subject's lifestyle at regular intervals during the study.
2. Subjects with a diagnosis of Crohn's disease or ulcerative colitis are allowed as long as they have no active symptomatic disease.

Exclusion criteria

Subjects in the OLE2 Group B are not permitted to enroll in the OLE2 Period if any of the following exclusion criteria are met:

1. Female subjects who plan to become pregnant during the OLE2 Period or within 20 weeks following final dose of study medication.
2. Subject has developed any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the subject's ability to participate in the OLE2 Period.

3. Any subjects with an ongoing SAE, or a history of serious infections, the Medical Monitor must be consulted prior to the subject's entry in the OLE2 Period, although the decision on whether to enroll the subject remains with the Investigator.
4. Subject had a positive or indeterminate IGRA in the Treatment Period to Week 144, unless appropriately evaluated and treated as per Section 12.3.1.
5. Subject may not participate in another study of a medicinal product or device under investigation
6. Subject has a history of chronic alcohol or drug abuse within 6 months prior to reentry as assessed by medical history, site interview, and/or results of the urine drug screen.
7. Subjects who have used systemic treatments for PSO after Week 144 must have stopped this treatment 1 month prior to receiving the first bimekizumab injection in the OLE2 Period (See Section 7.8.2 regarding prohibited medications).
8. Subject has erythrodermic, guttate, or pustular form of PSO.
9. Subject is noncompliant with the study procedures or medications in the opinion of the Investigator.
10. Subject has a clinical laboratory value meeting any of the following criteria:
    a. ≥3.0x ULN of any of the following: ALT, AST, alkaline phosphatase (ALP); or >ULN total bilirubin (≥1.5xULN total bilirubin if known Gilbert's syndrome)
    b. A laboratory value meeting any of the following criteria:
        - Absolute neutrophil count $<1.0x10^3/\mu L$
        - Absolute lymphocyte count $<0.2x10^3/\mu L$

    Subjects may enter the OLE2 Period if the result is transient. If a retest is required, it must be done within 1 to 2 weeks.
11. Subject has concurrent acute or chronic viral hepatitis B or C or HIV infection. Subjects who have evidence of, or tested positive for hepatitis B or hepatitis C are excluded. A positive test for the hepatitis B virus is defined as: (1) positive for hepatitis B surface antigen, or (2) positive for anti-hepatitis B core antibody. A positive test for the hepatitis C virus is defined as: (1) positive for hepatitis C antibody, and (2) positive via a confirmatory test for hepatitis C virus (for example, hepatitis C virus polymerase chain reaction).
12. There is confirmation of a pregnancy, as evidenced by a positive pregnancy test (see Section 9.1.4 for more information regarding pregnancies).

13. Subjects showing:
    - Suicidal ideation in the past month prior to the OLE2 Screening Visit as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the electronic Columbia Suicide Severity Rating Scale (eC SSRS).
    - Any suicidal behavior since last visit.
14. Subject has presence of moderately severe or severe major depression, indicated by a score ≥15 on the PHQ-9. Medication used to treat depression should be stable for 4 weeks prior to Week 144/OLE2 Baseline.
15. Subject has developed any active malignancy or history of malignancy prior to the OLE2 Screening Visit EXCEPT treated and considered cured cutaneous squamous or basal cell carcinoma, or in situ cervical cancer.
16. Subject has received any live (includes attenuated) vaccination within the 8 weeks prior to the Week 144/OLE2 Baseline Visit.

6.4 Withdrawal criteria

Subjects are free to withdraw from the study at any time, without prejudice to their continued care. Subjects who withdraw from the study should complete the PEOT Visit (see Section 8.2).

Subjects should be withdrawn from the study and will be encouraged to come back for the SFU and/or SFU2 Visit 20 weeks after final dose of IMP if the subject withdraws his/her consent or the Sponsor or a regulatory agency requests withdrawal of the subject.

A subject must be withdrawn from IMP and will be asked to come back for the SFU and/or SFU2 Visit 20 weeks after final dose of IMP if any of the following events occur:

1. Subject develops an illness that in the opinion of the Investigator would interfere with his/her continued participation if the risk of continuing IMP outweighs the potential benefit.
2. Subject develops erythrodermic, guttate, or pustular form of PSO.
3. Subject is noncompliant with the study procedures or medications in the opinion of the Investigator.
4. Subject uses prohibited concomitant medications, with the exception of topicals, as defined in this protocol (Section 7.8.2), that may present a risk to the safety of the subject or the integrity of the study data, in the opinion of the Investigator and/or the Medical Monitor.
5. Subject has a clinical laboratory value meeting any of the following criteria:

   c. Hepatotoxicity as described in Section 6.4.1.

   d. A laboratory value meeting any of the following criteria:
      - Absolute neutrophil count <$1.0x10^3/\mu L$
      - Absolute lymphocyte count <$0.2x10^3/\mu L$

   Subjects 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 subject must be

withdrawn. If the repeat absolute neutrophil count or absolute lymphocyte count is above the allowable values, the subject may continue in the study.

6. The subject experiences a severe AE, an SAE, or a clinically significant change in a laboratory value occurs that, in the opinion of the Investigator, merits the discontinuation of the IMP.
7. There is confirmation of a pregnancy during the study, as evidenced by a positive pregnancy test (see Section 9.1.4 for more information regarding pregnancies).
8. At Week 28 and all following visits, subjects on continuous treatment with the same IMP for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.
9. A subject considered as having either a suspected new latent tuberculosis infection (LTBI) or who develops active tuberculosis (TB) or nontuberculosis mycobacterium (NTMB) infection during the study (including but not limited to, conversion demonstrated by IGRA or other diagnostic means) must be immediately discontinued from IMP, a PEOT Visit must be scheduled as soon as possible, but not later than the next regular visit.

   The subject must be permanently withdrawn if further examinations result in a diagnosis of active TB, or if the subject 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 9.3.1.
10. Subjects with newly diagnosed inflammatory bowel disease (IBD) or with 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 subject should continue in the study and contact the Medical Monitor and UCB study physician to confirm the subject's suitability for continued participation in the study.
11. Subjects **must be referred** immediately to a mental health care professional (ie, locally licensed psychiatrist, psychologist, or master's level therapist) 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 eC-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.

12. Subjects must be referred immediately to a mental healthcare professional (ie, locally licensed psychiatrist, psychologist, or master's level therapist) and must be withdrawn for:
    - Active suicidal ideation as indicated by a positive response ("Yes") to Question 5 of the "Since Last Visit" version of the eC-SSRS.
    - Any suicidal behavior since last visit.
    - Severe major depression as indicated by a PHQ-9 score ≥20.

    The mental health consultation must be recorded in source documentation.

Investigators should attempt to obtain information on subjects in the case of withdrawal or discontinuation. For subjects considered as lost to follow-up, the Investigator should make an effort (at least 1 phone call and 1 written message to the subject), 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 subject, must be recorded in the source documents. The electronic Case Report Form (eCRF) must document the primary reason for withdrawal or discontinuation.

Investigators should contact the Medical Monitor, whenever possible, to discuss the withdrawal of a subject in advance.

6.4.1 Potential drug-induced liver injury IMP discontinuation criteria

Subjects 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 subjects with either of the following:

- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥8x upper limit of normal (ULN).
- Alanine aminotransferase or AST ≥3xULN and coexisting total bilirubin ≥2xULN.

The PDILI criterion below requires immediate discontinuation of IMP for:

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

  If a nondrug-related cause for the symptoms can be confirmed, these subjects may resume IMP administration after discussion with the responsible UCB physician, but only when the requirements for rechallenge with IMP as provided in Section 9.2.1.2.1 are followed.

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

- Subjects with ALT or AST ≥5xULN and <8xULN, total bilirubin <2xULN, 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 9.2.1 with repeat tests performed in two weeks. Upon re-test, if ALT or AST values have reduced to <5xULN, the subject can continue with the study. However, if ALT or AST remains ≥5xULN <8xULN after re-test, IMP should be temporarily withheld and subject should undergo a repeat test in 2 weeks. If ALT or AST values remain ≥5xULN even after the second re-test, then the subject should be permanently withdrawn from the study and should be followed for possible PDILI.

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

Investigators should attempt to obtain information on subjects in the case of IMP discontinuation to complete the final evaluation. Subjects 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 subject withdrawal (if applicable), must be recorded in the source documents. The eCRF must document the primary reason for IMP discontinuation.

7 STUDY TREATMENT

7.1 Description of IMP

The IMP used in this study is bimekizumab. Bimekizumab will be manufactured using 2 manufacturing processes: Process 4 (Phase 3 clinical supply manufacturing process) and Process 5 (planned commercial manufacturing process). Bimekizumab will be supplied in a 1mL prefilled syringe or a 1ml prefilled auto-injector (only in some countries) at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection.

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

7.2 Treatments to be administered

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.

Suitable areas for sc injections are the lateral abdominal wall, upper outer thigh, or upper arm. 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.

An IMP Handling Manual will be provided to each site containing instructions regarding drug preparation and dosing.

Treatment Period dosing

The initial dose of bimekizumab administered in PS0014 will be based on the subject's PASI response and previous dose regimen in the feeder study. Subjects receiving:

- Bimekizumab 320mg Q4W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q4W who achieve PASI90 in the feeder study will be randomized 4:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Bimekizumab 320mg Q8W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who achieve PASI90 in the feeder study will receive bimekizumab 320mg Q8W.
- Ustekinumab who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Ustekinumab who achieve PASI90 in the feeder study will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Placebo (after a Week 16 response [≥PASI90] on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study) who complete the Randomized Withdrawal Period of the feeder study will receive bimekizumab 320mg Q4W.

At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W (optional).

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit.

After Week 48 and in between the scheduled study visits at the site, subjects will have the option to perform self-injection at home. All other injections will be administered preferably by self-injection during scheduled visits. Self-injection training will be provided to the subject/caregivers by qualified site personnel at Week 40 and Week 44. After Week 48, the subject/caregiver will perform administration under the supervision of the site staff to ensure that study medication is being properly and safely injected.

OLE2 Period dosing

After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and

data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).

- OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.

During the OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48), all subjects will attend study visits at the study site every 12 weeks for study assessments and subjects may self-inject IMP at home.

Once subjects/caregivers as determined by the Investigator (or designee) have been trained, the study medication may be administered at home. The subject will receive the required number of syringes for injections at each visit needed to perform the Q4W or Q8W administrations at home. Subjects who are unable to or decide not to self-inject IMP or those without a family member/friend/caregiver who can help, will not be discontinued, but may continue to visit the site for unscheduled visits for IMP administration only.

If administered at home, the subject/caregiver will document the date, body location, kit number and time point of administration of study medication.

All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

7.3 Packaging

Bimekizumab will be packaged and labeled according to Good Manufacturing Practice (GMP) guidelines and applicable laws or regulations. It will be suitably packaged in such a way as to protect the product from deterioration during transport and storage. Further information regarding storage and transport conditions are provided in the IMP Handling Manual.

7.4 Labeling

Bimekizumab will be labeled in accordance with the current International Council for Harmonisation (ICH) guidelines on Good Clinical Practice (GCP) and GMP and will include any locally required statements. If necessary, labels will be translated into the local language.

7.5 Handling and storage requirements

Refer to the IMP Handling Manual for the storage conditions of the IMP.

The Investigator (or designee) is responsible for the safe and proper storage of IMP at the site. Investigational medicinal product stored by the Investigator is to be kept in a secured area with limited access according to the storage conditions mentioned on the label.

Appropriate storage conditions must be ensured either by controlling the temperature (eg, room, refrigeration unit) or by completion of a temperature log in accordance with local requirements on a regular basis (eg, once a week), showing actual and minimum/maximum temperatures reached over the time interval.

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

The IMP will be shipped to the study sites in temperature-controlled containers. Out-of-range shipping or storage conditions must be brought to the attention of the Sponsor or designee, immediately. Authorization to use any out-of-range IMP must be documented and received prior to dispensing or administering the IMP at the study site.

In addition, the Investigator (or designee) will instruct the subject on how to handle the IMP during the transport and how to store the IMP following the instruction guide. Cooler bags with freezer packs will be provided to the subjects. Specific attention will be put on the transport from site to home using cold bags, and the subject will be instructed to put the IMP as quickly as possible into his/her refrigerator. In case of broken refrigerator, or broken or lost syringes, the subject will inform the site immediately and new IMP will be prepared. All efforts should be made to follow the treatment scheme as per protocol.

7.6 Drug accountability

A Drug Accountability form will be used to record IMP dispensing and return information on a by-subject 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.

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 drug 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 (SOPs) or returned to UCB (or designee). Investigational medicinal product intended for the study cannot be used for any other purpose than that described in this protocol.

7.7 Procedures for monitoring subject compliance

During Year 1 of 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.

After Week 48, self-injection at home will be possible at the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, 140, and at the OLE2 Weeks 4, 8, 16, 32, and 40. Dates, locations, kit numbers and time of self-injection will be captured using a home administration form. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit. Completed home administration forms should be reviewed by the Investigator.

If a subject is noncompliant with the study procedures or medications that may present a risk to the safety of the subject in the opinion of the Investigator, then the subject should be withdrawn as described in Section 6.4.

7.8 Concomitant medications/treatments

Any 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.

7.8.1 Permitted concomitant treatments (medications and therapies)

The following concomitant medications are permitted during the study.

7.8.1.1 Topical medications

Subjects may continue to use topical moisturizers or emollients, bath oils, or oatmeal bath preparations for skin conditions during the study, as needed. Over-the-counter shampoos for the treatment of PSO of the scalp are also permitted.

Topical steroids and vitamin D analogue ointment will be permitted for use, as needed.

7.8.1.2 Other medications

Subjects may take pain relievers (acetaminophen/paracetamol, non-steroidal anti-inflammatory drugs, opiates) as needed for pain but not within 24 hours of the Baseline and Week 144 Visits. Intra-articular injections (eg, steroids, hyaluronic acid) are permitted and must be carefully recorded in the eCRF.

Subjects who are receiving an established regimen for depression during the feeder study should continue treatment.

7.8.2 Prohibited concomitant treatments (medications and therapies)

Table 7-1 presents the list of prohibited PSO medications.

Table 7-1: Prohibited PSO medications

Drug
Systemic retinoids
Systemic treatment (nonbiological): systemic immunosuppressant agents (eg, methotrexate, cyclosporine, azathioprine, thioguanine) fumaric acid esters specifically used for the treatment of PSO systemic corticosteroids phototherapy
Anti-TNFs: infliximab (including biosimilar), golimumab etanercept (including biosimilar) certolizumab pegol adalimumab (including biosimilar)
Other biologics and other systemic therapies, eg: alefacept efalizumab apremilast rituximab ustekinumab briakinumab tofacitinib guselkumab tildrakizumab risankizumab
Anti-IL-17 therapy secukinumab ixekizumab brodalumab
Any other antipsoriatic agent (systemic or topical) under investigation (or approved after the protocol is approved)

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

Up to Week 144

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

Post Week 144 (OLE2 Period)

Subjects who have used systemic treatments for PSO after Week 144 must have stopped this treatment 1 month prior to receiving the first bimekizumab injection in the OLE2 Period. Subjects receiving systemic immunomodulatory medications for an indication other than PSO must have their eligibility confirmed by the Medical Monitor prior to enrollment in the OLE2 Period.

Subjects who take prohibited medications during the OLE2 Period may be withdrawn from IMP but followed until the SFU2 Visit. The decision to withdraw a subject for taking prohibited medications should be made in consultation with the Medical Monitor.

7.8.2.1 Vaccines

Administration of live (including attenuated) vaccines is not allowed during the conduct of the study and for 20 weeks after the final dose of IMP. Administration of inactivated vaccines is allowed during the study at the discretion of the Investigator.

7.9 Blinding

PS0014 is an open-label study; thus, there will be no blinding.

7.10 Randomization and numbering of subjects

Subjects who received ustekinumab and achieved PASI90 in the feeder study will be randomized 1:1 to a treatment regimen using an interactive response technology (IRT). Subjects who received bimekizumab 320mg Q4W and who achieved PASI90 in the feeder study will be randomized 4:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. All other subjects will be assigned to a treatment regimen based on the PASI90 status and dosing regimen from their feeder study. The same unique 5-digit identification number used in the feeder study will be used in PS0014. This subject number will be used to identify the subject throughout the study and to maintain subject confidentiality. At study visits, an IRT will assign the applicable subject kits of IMP. Further instructions will be provided in the IRT manual.

Subjects who roll over directly from the Treatment Period into the OLE2 Period will continue receiving bimekizumab 320mg Q8W and will keep their unique 5-digit identification number. Subjects who reinitiate bimekizumab after having completed treatment (subjects in the SFU of the Treatment Period or who have completed the SFU of the Treatment Period) will receive either bimekizumab 320mg Q4W/Q8W or bimekizumab 320mg Q8W depending on their disease activity at time of reentry (bimekizumab 320mg Q4W/Q8W for subjects with IGA score ≥3 or bimekizumab 320mg Q8W for subjects with IGA score <3). For these subjects, the same unique 5-digit identification number used in the study will be reused.

8 STUDY PROCEDURES BY VISIT

Table 5-1 (Schedule of study assessments) provides a general overview of study assessments in Year 1 (Weeks 0 to 44). Table 5-2 (Schedule of study assessments) provides a general overview of study assessments in Years 2 and 3 (Weeks 48 to 144). Table 5-3 (Schedule of study

assessments) provides a general overview of study assessments in OLE2 Period (from OLE2 Screening or Week 144/OLE2 Baseline to OLE2 Week 48).

A list of procedures to be completed at each visit up to Week 144 is described below.

- Visit windows of ±7 days on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. The window of ±7 days is relative to Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside of the visit window must be discussed with the Medical Monitor.
- The dosing window is ±7 days relative to the scheduled dosing visit.
- For the SFU Visit (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.

A list of procedures to be completed at each visit of the OLE2 Period is described below.

- Visit windows of ±14 days on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. The window of ±14 days is relative to Week 144/OLE2 Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside of the visit window must be discussed with the Medical Monitor.
- The dosing window is ±14 days relative to the scheduled dosing visit.
- For the SFU2 Visit (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.

8.1 Treatment Period

8.1.1 Stable Dosing

8.1.1.1 Baseline/Feeder Study Final Visit

The following procedures/assessments will be performed/recorded on the last visit of the feeder study and prior to administration of IMP in PS0014:

- Informed consent
- Inclusion/exclusion
- Physical exam
- Body weight
- Vital signs (sitting systolic blood pressure [SBP], sitting diastolic blood pressure [DBP], pulse rate, and body temperature) should be obtained prior to blood sampling

- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine drug screen
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- ECG
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline in the feeder study
- Scalp IGA for subjects with scalp involvement at Baseline in the feeder study
- pp-IGA for subjects with palmoplantar involvement at Baseline in the feeder study
- EQ-5D-3L
- SF-36
- PGA of PSO
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration will occur.

8.1.1.2 Week 4 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur.

8.1.1.3 Week 8 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS

- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration will occur.

8.1.1.4 Week 12 and Week 20 Visits (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam (Week 12 only)
- Urine pregnancy test
- PASI
- Percentage of BSA
- IGA
- TB questionnaire (Week 12 only)
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur.

8.1.1.5 Week 16 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- PASI
- Percentage of BSA
- IGA

- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration will occur.

8.1.1.6 Week 24 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam
- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- PGADA

- WPAI-SHP V2.0
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration will occur.

At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).

8.1.2 Flexible Dosing

8.1.2.1 Week 28 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- PASI
- Percentage of BSA
- IGA
- Urine pregnancy test
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur.

8.1.2.2 Week 32 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- PASI
- Percentage of BSA
- IGA

- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration will occur.

8.1.2.3 Week 36 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam
- Urine pregnancy test
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur.

8.1.2.4 Week 40 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- PASI
- Percentage of BSA

- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration will occur.

Self-injection training will be provided to the subject/caregivers by qualified site personnel to allow self-injection to be performed at home after Week 48 (see Section 7.2).

8.1.2.5 Week 44 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- PASI
- Percentage of BSA
- IGA
- Urine pregnancy test
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur.

Self-injection training will be provided to the subject/caregivers by qualified site personnel to allow self-injection to be performed at home after Week 48 (see Section 7.2).

8.1.2.6 Week 48 Visit (±7 days relative to Baseline)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48, or at the next scheduled clinic visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #3.

Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 48 should be dosed at this visit and should receive kits for home administration 8 weeks later (Table 8-1).

Table 8-1: Dosing scheme, Years 2 and 3 (Weeks 48 to 144)

		Year 2												Year 3										
Week	**48 [a,b]**	**52**	**56**	**60[a,c]**	**64**	**68**	**72[a,b]**	**76**	**80**	**84[a,c]**	**88**	**92**	**96[a,b]**	**100**	**104**	**108[a,c]**	**112**	**116**	**120[a,b]**	**124**	**128**	**132[a,c]**	**136**	**140**
Dose Assignment	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**	**C**	**C/ H**	**C/ H**
Bimekizumab 320mg Q4W	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Bimekizumab 320mg Q8W	●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●	

C=Clinic; H=home; Q4W=every 4 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●).

[a] The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #3.

[b] Subjects whose dosing interval is changed to bimekizumab 320mg Q8W should be dosed at this visit and should receive kits for home administration 8 weeks later.

[c] Subjects whose dosing interval is changed to bimekizumab 320mg Q8W should NOT be dosed at this visit and should receive kits for home administration 4 weeks later.

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam
- Body weight
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
  - IGRA TB test
- ECG
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- TSQM-9

- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, subjects will be given the opportunity for self-injection of bimekizumab (see Section 7.2).

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.2.7 Self-injection at home (Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140)

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. This only applies to those subjects who have not yet changed to bimekizumab 320mg Q8W.

Subjects receiving bimekizumab 320mg Q8W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 56, 64, 80, 88, 104, 112, 128, and 136.

- Adverse events will be captured spontaneously if the subject decides to visit the site to receive the bimekizumab administration.
- All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit (Section 7.2).

8.1.2.8 Week 60, Week 84, Week 108, and Week 132 Visit (±7 days relative to Baseline)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W as follows:

- At Week 60 if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #3.
- At Week 84 if the subject has already completed the Week 72 visit prior to implementation of Protocol Amendment #3.
- At Week 108 if the subject has already completed the Week 96 visit prior to implementation of Protocol Amendment #3.
- At Week 132 if the subject has already completed the Week 120 visit prior to implementation of Protocol Amendment #3.

As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at one of these visits should NOT be dosed at that visit, and should receive kits for home administration 4 weeks later.

The following procedures/assessments will be performed/recorded at this visit. If IMP is administered at this visit, they should be performed/recorded prior to administration of IMP:

- Physical exam
- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- WPAI-SHP V2.0 (Week 132 only)
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection. This only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #3.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.2.9 Week 72 Visit (±7 days relative to Baseline)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 72 if the subject has already completed the Week 48 and Week 60 visits prior to implementation of Protocol Amendment #3. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 72 should be dosed at this visit and should receive kits for home administration 8 weeks later.

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam
- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W or Q8W dosing will occur, preferably by self-injection. The Q4W dosing only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #3.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.2.10 Week 96 Visit (±7 days relative to Baseline)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 96 if the subject had already completed the Week 84 visit prior to implementation of Protocol Amendment #3. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 96 should be dosed at this visit, and should receive kits for home administration 8 weeks later.

The following procedures/assessments will be performed/recorded:

- Physical exam
- Body weight
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
  - IGRA TB test
- ECG
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO

- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W or Q8W dosing will occur, preferably by self-injection. The Q4W dosing only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #3.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.2.11 Week 120 Visit (±7 days relative to Baseline)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 120 if the subject had already completed the Week 108 visit prior to implementation of Protocol Amendment #3. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 120 should be dosed at this visit, and should receive kits for home administration 8 weeks later.

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam
- Vital signs
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9

- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W or Q8W dosing will occur, preferably by self-injection. The Q4W dosing only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #3.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.2.12 Week 144 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded:

- Physical exam
- Body weight
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
  - IGRA TB test
- ECG
- TB questionnaire
- PASI

- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Concomitant medication
- AEs
- Contact IRT

Return of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

If Protocol Amendment #3.3 is implemented at the time study subjects are treated in the Treatment Period (ie, up to Week 144; OLE2 Group A subjects), these subjects will be invited to participate in the OLE2 Period and may directly roll over and continue bimekizumab treatment from the Week 144/OLE2 Baseline Visit as long as they do not meet any of the withdrawal criteria and have provided informed consent.

If Protocol Amendment #3.3 is implemented at the time subjects have completed the Week 144 Visit and are in the SFU Period of the Treatment Period or have completed the SFU of the Treatment Period (Group B subjects), these subjects will be invited to enter the OLE2 Period to reinitiate bimekizumab treatment in the OLE2 Period. However, before receiving the first dose at the Week 144/OLE2 Baseline Visit, they will first undergo screening during the 4-week OLE2 Screening Period (see Section 8.1.3.1 for the procedures that will apply for the Screening of the OLE2 Period).

8.1.3 OLE2 Period

8.1.3.1 OLE2 Screening (up to 4 weeks) – applicable for OLE2 Group B only

Prior to any study specific activities of the OLE2 Period, subjects who completed the Week 144 Visit and are in the SFU or have completed the SFU of the Treatment Period (OLE2 Group B) will undergo screening. Subjects who have used systemic treatments for PSO after Week 144 must have stopped this treatment 1 month prior to receiving the first bimekizumab injection in the OLE2 Period. Screening procedures may be performed during this time. Subjects receiving systemic immunomodulatory medications for an indication other than PSO must have their eligibility confirmed by the Medical Monitor prior to enrollment in the OLE2 Period.

At the Screening Visit of the OLE2 Period (OLE2 Screening Visit), subjects will be asked to read, sign, and date an ICF that has been approved by the Sponsor and an IRB/IEC and that complies with regulatory requirements. Subjects will be given adequate time to consider any information concerning the study given to them by the Investigator or designee. As part of the informed consent procedure, subjects will be given the opportunity to ask the Investigator any questions regarding potential risks and benefits of continued participation in the study.

The following procedures/assessments will be performed at the OLE2 Screening Visit for subjects in the OLE2 Group B:

- Informed consent
- Inclusion/exclusion
- Urine drug screen
- Significant past medical history including clinically relevant past or coexisting medical conditions and surgeries (only applicable for subjects who completed the SFU; only new or modified medical history since completing the SFU should be entered in eCRF)
- Physical exam
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Hepatitis B and Hepatitis C
  - HIV
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA

- PHQ-9
- eC-SSRS
- Prior and concomitant medication (including new or modified medications initiated after SFU)
- AE (only for subjects in the SFU)
- Contact IRT

8.1.3.2 Dosing in the OLE2 Period

Subjects will be dosed in the OLE2 Period according to the dosing schedule presented in Table 8-2.

Table 8-2: Dosing scheme, OLE2 Period

	OLE2 Period								
Visits/Week	**Week 144/OLE2 Baseline**	**OLE2 W4**	**OLE2 W8**	**OLE2 W12 [a]**	**OLE2 W16**	**OLE2 W24 [b]**	**OLE2 W32**	**OLE2 W36 [c]**	**OLE2 W40**
Dose Assignment	**C**	**H**	**H**	**C**	**H**	**C**	**H**	**C**	**H**
Bimekizumab 320mg Q4W/Q8W [d]	●●	●●	●●	●●	●●	●●	●●		●●
Bimekizumab 320mg Q8W	●●		●●		●●	●●	●●		●●

C=Clinic; H=home; IGA= Investigator's Global Assessment; IMP=investigational medicinal product; OLE=open label extension; Q4W/Q8W=every 4 weeks for 16 weeks, followed by every 8 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●).

[a] Subjects will receive kits for home administration 4 weeks later.

[b] Subjects will receive kits for home administration 8 weeks later.

[c] Subjects should NOT be dosed at this visit and will receive kits for home administration 4 weeks later.

[d] Q4W/Q8W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B and had an IGA ≥3 upon entry of the OLE2 Period. These subjects will receive Q4W dosing for 16 weeks until OLE2 Week 16, then will change from Q4W to Q8W and will receive their next dose at the scheduled clinic visit OLE2 Week 24.

8.1.3.2.1 Week 144/OLE2 Baseline Visit

Subjects who will still be treated in the Treatment Period at the time of implementing Protocol Amendment #3.3 (OLE2 Group A subjects) will attend Week 144 Visit and directly roll over to the OLE2 Period to continue treatment (bimekizumab 320mg Q8W). They will undergo all study assessments of the Week 144 Visit and will receive bimekizumab 320mg Q8W at this visit, which will also coincide with the first visit of the OLE2 Period, ie, the Week 144/OLE2 Baseline Visit.

Subjects who have completed Week 144 Visit and are in the SFU of the Treatment Period or have completed the SFU Period at the time of Protocol Amendment #3.3 implementation (OLE2

Group B subjects) will reinitiate bimekizumab treatment at the Week 144/OLE2 Baseline Visit, and will be assigned a treatment regimen based on disease severity at the Week 144/OLE2 Baseline Visit (bimekizumab 320mg Q4W/Q8W for subjects with IGA score ≥3 or bimekizumab 320mg Q8W for subjects with IGA score <3).

Applicable for OLE2 Groups A and B:

- Confirmation of eligibility
- Physical exam
- Body weight
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- eC-SSRS
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- DLQI
- Concomitant medication
- AEs
- Contact IRT

Additional Procedures/assessments applicable for OLE2 Group A

- Informed Consent
- ECG
- Blood sample for bimekizumab plasma concentrations
- Blood sample for anti-bimekizumab antibodies
- IGRA TB test
- scalp IGA
- mNAPSI

- pp-IGA
- EQ-5D-3L
- PASE
- PGADA
- WPAI-SHP V2.0

At the Week 144/OLE2 Baseline Visit, after completion of the above-mentioned procedures, administration of IMP will occur, preferably by self-injection under supervision of the site personnel.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.3.2.2 Self-injection at home (OLE2 Weeks 4, 8, 16, 32, and 40)

Subjects receiving bimekizumab 320mg Q8W will be given the opportunity for self-injection of bimekizumab at home on the following weeks: OLE2 Weeks 8, 16, 32, and 40.

Subjects receiving bimekizumab 320mg Q4W/Q8W will be given the opportunity for self-injection of bimekizumab at home on the following weeks: OLE2 Weeks 4, 8, and 16. At OLE2 Week 16, subjects receiving bimekizumab 320mg Q4W/Q8W will switch to bimekizumab 320mg Q8W regimen and will be given the opportunity for self-injection of bimekizumab at home at OLE2 Weeks 32 and 40.

Adverse events will be captured spontaneously if the subject decides to visit the site to receive the bimekizumab administration.

All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

8.1.3.2.3 OLE2 Week 12, Week 24, and Week 36 Visits (±14 days relative to OLE2 Baseline)

As depicted in Table 8-2, subjects receiving bimekizumab 320mg Q4W/Q8W should receive IMP at the OLE2 Week 12 Visit, and all subjects will receive kits for home administration 4 weeks later at OLE2 Week 16. All subjects will receive IMP administration at the OLE2 Week 24 Visit, and will receive kits for home administration 8 weeks later. At the OLE2 Week 36 Visit, subjects will not be dosed and will receive kits for home administration 4 weeks later at OLE2 Week 40.

The following procedures/assessments will be performed/recorded at every clinic visit prior to administration of IMP:

- Physical exam
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling

- Urine pregnancy test, for applicable subjects
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

The following additional assessments will be performed / recorded every 24 weeks (ie, at OLE2 Week 24 Visit) prior to administration of IMP:

- Collection of blood and urine samples for the following tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
- DLQI

At the OLE2 Week 12 (OLE2 Group B subjects on Q4W/Q8W dosing only) and Week 24 Visit, after completion of the above-mentioned procedures, administration of IMP will occur, preferably by self-injection under supervision of the site personnel.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.3.3 OLE2 Week 48 Visit (±14 days relative to OLE2 Baseline)

The following procedures/assessments will be performed/recorded:

- Physical exam
- Body weight
- Vital signs (sitting systolic BP and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis

  - Urine pregnancy test
  - IGRA TB test
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

Return of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.2 Premature End of Treatment Visit

If a subject is withdrawn from the study during the Treatment Period (up to Week 144):

- The subject will be withdrawn from IMP, will undergo the same assessments as the Week 144 visit (see Section 8.1.2.12), and will enter the SFU Period.
- The subject will be encouraged to return for the SFU Visit (20 weeks after the last received dose; see Section 8.3).

If a subject is withdrawn from the study during the OLE2 Period:

- The subject will be withdrawn from IMP, will undergo the same assessments as the OLE2 Week 48 visit (see Section 8.1.3.3), and will enter the SFU2 Period.
- The subject will be encouraged to return for the SFU2 Visit (20 weeks after the last received dose; see Section 8.4).

8.3 Safety Follow-Up Visit (20 weeks after final dose up to Week 144, ±7 days)

All subjects, including those withdrawn from IMP, will have a SFU Visit 20 weeks after their final dose of IMP.

The following procedures/assessments will be performed/recorded:

- Physical exam
- Body weight
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling

- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

8.4 Safety Follow-Up Visit 2 (20 weeks after final dose of the OLE2 Period, ±7 days)

The following procedures/assessments will be performed/recorded:

- Physical exam
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following tests should be obtained at this visit:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

8.5 Unscheduled Visit

At the Investigator's discretion, an Unscheduled Visit may be completed at any time during the study, but prior to the SFU Visit or SFU2 Visit (depending on which period [Treatment Period or OLE2 Period] the subject is in), if deemed necessary for the subject's safety and well-being.

If an Unscheduled Visit is conducted due to safety or efficacy reasons, an eC-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, injection for subjects not making use of home self-injections), an eC-SSRS will not be required at these visits.

At this visit, any assessment may be performed, as needed, depending on the reason for the visit.

9 ASSESSMENT OF SAFETY

9.1 Adverse events

9.1.1 Definitions

9.1.1.1 Adverse event

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

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

Signs or symptoms of the condition/disease for which the IMP is being studied should be recorded as AEs only if their nature changes considerably or their frequency or intensity increases in a clinically significant manner as compared to the clinical profile known to the Investigator from the subject's history or the Baseline Period.

9.1.1.2 Serious adverse event

Once it is determined that a subject experienced an AE, the seriousness of the AE must be determined. An SAE must meet 1 or more of the following criteria:

- Death
- Life-threatening

  (Life-threatening does not include a reaction that might have caused death had it occurred in a more severe form.)
- Significant or persistent disability/incapacity
- Congenital anomaly/birth defect (including that occurring in a fetus)
- Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or subject and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious

  (Important medical events may include, but are not limited to, potential Hy's Law [see Section 9.1.1.3], allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.)

- Initial inpatient hospitalization or prolongation of hospitalization

  (A patient admitted to a hospital, even if he/she is released on the same day, meets the criteria for the initial inpatient hospitalization. An emergency room visit that results in admission to the hospital would also qualify for the initial inpatient hospitalization criteria. However, emergency room visits that do not result in admission to the hospital would not qualify for this criteria and, instead, should be evaluated for 1 of the other criteria in the definition of serious [eg, life-threatening adverse experience, important medical event].

  Hospitalizations for reasons not associated with the occurrence of an AE [eg, preplanned surgery or elective surgery for a pre-existing condition that has not worsened or manifested in an unusual or uncharacteristic manner] do not qualify for reporting. For example, if a subject has a condition recorded on his/her medical history and later has a preplanned surgery for this condition, it is not appropriate to record the surgery or hospitalization as an SAE, since there is no AE upon which to assess the serious criteria. Please note that, if the pre-existing condition has worsened or manifested in an unusual or uncharacteristic manner, this would then qualify as an AE and, if necessary, the seriousness of the event would need to be determined.)

9.1.1.2.1 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.

This list does not change the Investigator's obligation to report all SAEs (including Anticipated SAEs) as detailed in Section 9.1.2.3.

Table 9–1: Anticipated SAEs for the population of subjects with moderate to severe chronic plaque PSO

MedDRA system order 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; PSO=psoriasis; 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 subject.

9.1.1.3 Adverse events of special interest

An AE of special interest 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.

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

9.1.1.4 Other safety topics of interest

Pre-specified safety topics of interest for the study are: infections (serious, opportunistic, fungal, and TB), neutropenia, hypersensitivity, suicidal ideation and behavior, depression, major cardiovascular events, liver function test changes/enzyme elevations, malignancies, and IBDs (with gastroenterology referral, as appropriate). This is based on findings from the IMP 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.

9.1.2 Procedures for reporting and recording AEs

The subject will be given the opportunity to report AEs spontaneously. A general prompt will also be given at each study assessment to detect AEs. For example:

"Did you notice anything unusual about your health (since your last visit)?"

In addition, the Investigator should review any self-assessment procedures (eg, diary cards) employed in the study.

9.1.2.1 Description of AEs

When recording an AE, the Investigator should use the overall diagnosis or syndrome using standard medical terminology, rather than recording individual symptoms or signs. The eCRF and source documents should be consistent. Any discrepancies between the subject's own words on his/her own records (eg, diary card) and the corresponding medical terminology should be clarified in the source documentation.

When recording the severity of an AE in the eCRF (ie, mild, moderate, or severe), the Investigator may refer to the Common Terminology Criteria for Adverse Events Version 4 (http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm) for additional guidance as needed. Details for completion of the Adverse Event eCRF (including judgment of relationship to IMP) are described in the eCRF Completion Guidelines.

9.1.2.2 Rule for repetition of an AE

An increase in the intensity of an AE should lead to the repetition of the AE being reported with:

- The outcome date of the first AE that is not related to the natural course of the disease being the same as the start date of the repeated AE, and the outcome of "worsening"
- The AE verbatim term being the same for the first and repeated AE, so that the repeated AE can be easily identified as the worsening of the first one

9.1.2.3 Additional procedures for reporting SAEs

If an SAE is reported, UCB must be informed within 24 hours of receipt of this information by the site (see contact information for SAE reporting listed in the SAE Reporting section at the front of the protocol). The Investigator must forward to UCB (or its representative) a duly completed "Investigator SAE Report Form for Development Drug" (SAE report form) provided by UCB, even if the data are incomplete, or if it is obvious that more data will be needed in order

to draw any conclusions. Information recorded on this form will be entered into the global safety database.

An Investigator SAE report form will be provided to the Investigator. The Investigator SAE Report form must be completed in English.

It is important for the Investigator, when completing the SAE report form, to include the assessment as to a causal relationship between the SAE and the IMP administration. This insight from the Investigator is very important for UCB to consider in assessing the safety of the IMP and in determining whether the SAE requires reporting to the regulatory authorities in an expedited manner.

Additional information (eg, autopsy or laboratory reports) received by the Investigator must be provided within 24 hours. All documents in the local language must be accompanied by a translation in English, or the relevant information included in the same document must be summarized in the Investigator SAE report form.

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 30 days from the end of the study for each subject, and to also inform participating subjects 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.

Upon receipt of the SAE report form, UCB will perform an assessment of expectedness of the reported SAE. The assessment of the expectedness of the SAE is based on the IB.

9.1.3 Follow up of AEs

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 subject is lost to follow up. This follow-up requirement applies to AEs, SAEs, and AEs of special interest; further details regarding follow up of PDILI events is provided in Section 9.2.1.4.

If an AE is ongoing at the end of the study for a subject, follow up should be provided until resolution/stable level of sequelae is achieved, or until the Investigator no longer deems that it is clinically significant, or until the subject is lost to follow up. If no follow up is provided, the Investigator must provide a justification. The follow up will usually be continued for 20 weeks after the subject has discontinued his/her IMP.

Information on SAEs obtained after clinical database lock will be captured through the Patient Safety (PS) database without limitation of time.

9.1.4 Pregnancy

If an Investigator is notified that a subject has become pregnant after the first intake of any IMP, the Investigator must immediately notify UCB's PS department by providing the completed Pregnancy Report and Outcome form (for contact details see SAE reporting information at the beginning of this protocol). The subject should be withdrawn from the study as soon as pregnancy is known (by positive pregnancy test), and the following should be completed:

- The subject should return for a PEOT Visit.

- The subject should immediately stop the intake of the IMP.
- A SFU Visit should be scheduled 20 weeks after the subject has discontinued her IMP.

The Investigator must inform the subject of information currently known about potential risks and about available treatment alternatives.

The pregnancy will be documented on the Pregnancy Report and Outcome form provided to the Investigator. The progression of the pregnancy and the eventual birth (if applicable) must be followed up using the Pregnancy Report and Outcome form in which the Investigator has to report on the health of the mother and of the child. Every reasonable attempt should be made to follow the health of the child for 30 days after birth for any significant medical issues. In certain circumstances, UCB may request that follow up is continued for a period longer than 30 days. If the subject is lost to follow up and/or refuses to give information, written documentation of attempts to contact the subject needs to be provided by the Investigator and filed at the site. UCB's PS department is the primary contact for any questions related to the data collection for the pregnancy, eventual birth, and follow up.

In cases where the partner of a male subject enrolled in a clinical study becomes pregnant, the Investigator or designee is asked to contact the subject to request consent of the partner via the Partner Pregnancy Consent form that has been approved by the responsible Institutional Review Board (IRB)/Independent Ethics Committee (IEC) and should be available in the Investigator site file. In case of questions about the consent process, the Investigator may contact the UCB or the Contract Research Organization (CRO) contract monitor for the study. The Investigator will complete the Pregnancy Report and Outcome form and send it to UCB's PS department (for contact details see SAE reporting information at the beginning of this protocol) 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.

A pregnancy becomes an SAE in the following circumstances: miscarriage, elective abortion when medically indicated (eg, when pregnancy is endangering life or health of woman or when fetus will be born with severe abnormalities), unintended pregnancy after hormonal contraceptive failure (if the hormonal contraceptive was correctly used), ectopic pregnancy, fetal demise, or any congenital anomaly/birth defect of the baby. Those SAEs must be additionally reported using the Investigator SAE Report form.

Should a subject become pregnant while participating in the study, the subject may be offered the option to enroll in a separate observational pregnancy follow-up study sponsored by UCB and conducted independently from study PS0014. If the study is available locally, the PS0014 Investigator will be provided with the locally approved information about the observational pregnancy follow-up study to inform the subject at the time the pregnancy is reported. Participation in this separate study will be voluntary and will not impact therapeutic management of the subject nor interfere with termination and follow-up procedures as described in PS0014.

9.1.5 Suspected transmission of an infectious agent via a medicinal product

For the purposes of reporting, any suspected transmission of an infectious agent via a medicinal product should be considered as an SAE; such cases must be reported immediately, recorded in

the AE module of the eCRF, and followed as any other SAE. Any organism, virus, or infectious particle (eg, prion protein transmitting transmissible spongiform encephalopathy), pathogenic or nonpathogenic, is considered an infectious agent.

9.1.6 Overdose of IMP

Excessive dosing (beyond that prescribed in the protocol and including overdose) should be recorded in the eCRF. Any SAE or nonserious AE associated with excessive dosing must be followed as any other SAE or nonserious AE. These events are only considered AEs or SAEs if there are associated clinical signs and symptoms or if the act of taking the excess medicine itself is an AE or SAE (eg, suicide attempt).

9.1.7 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, clinical study subjects, 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 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 or ECG results) for which data will be periodically reviewed during the course of the study.

9.2 Laboratory measurements

Clinical laboratory assessments consist of serum chemistry, hematology, and urinalysis at visits specified in Table 5-1, Table 5-2, and Table 5-3. A centralized laboratory will be used to supply all laboratory test supplies and analyze all blood and urine samples for hematology, chemistry, and urinalysis measurements. Any unscheduled laboratory testing should also be collected using the central laboratory. If tests are done locally, a concurrent sample should also be sent to the central laboratory whenever possible.

Specific details regarding the handling and processing of serum chemistry, hematology, and urinalysis samples are provided in the study laboratory manuals.

The following laboratory parameters will be measured:

Table 9–2: Laboratory measurements

Hematology	Chemistry	Urinalysis dipstick[a]
Basophils	Calcium	pH
Eosinophils	Chloride	Albumin (protein)
Lymphocytes	Magnesium	Glucose
Monocytes	Potassium	Blood
Neutrophils	Sodium	Leukocyte esterase
Hematocrit	Glucose	Nitrite
Hemoglobin	BUN	Drug screen[b]
MCH	Creatinine	Urine dipstick for pregnancy testing[c]
MCHC	ALP	
MCV	AST	
Platelet count	ALT	
RBC count	GGT	
WBC count	Total bilirubin	
	HIV [d]	
	Hepatitis B and C [d]	

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BUN=blood urea nitrogen; GGT=gamma glutamyltransferase; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; MCV=mean corpuscular volume; RBC=red blood cell; WBC=white blood cell

[a] A urine microscopic examination will be performed if the result for albumin (protein), leukocyte esterase, blood or nitrite is abnormal. A urine microscopic examination will include: WBC, RBC, epithelial cells (squamous, transitional and renal tubular), hyaline casts, WBC casts, RBC casts, waxy casts, granular casts, calcium oxalate crystals, uric acid crystals, triphosphate crystals, yeast, bacteria, amorphous urates, and amorphous phosphates.

[b] Only at Baseline/Feeder Study Final Visit and OLE2 Screening Visit.

[c] Urine pregnancy testing will be performed at all visits.

[d] Only for Group B; only at the OLE2 Screening Visit.

9.2.1 Evaluation of PDILI

The PDILI IMP discontinuation criteria for this study are provided in Section 6.4.1, 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 9.1.1.3), and, if applicable, also reported as an SAE (see Section 9.1.1.2).

Evaluation of PDILI consists of the diagnostic testing and continued monitoring included in Table 9–3 (specific tests dependent on laboratory results and corresponding symptoms) and consultation with a local hepatologist (if applicable; discussed in Section 9.2.1.1). 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 9.2.1.4).

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 6.4.1), 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 9.2.1.2.1 are met, rechallenge with IMP may be appropriate.

Table 9–3 summarizes the approach to investigate PDILI.

Table 9–3: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
≥3xULN	≥2xULN[b]	NA	Hepatology consult[c]. Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and subject discussed with Medical Monitor ASAP.	Immediate, permanent IMP discontinuation [e]	Essential: Must have repeat liver chemistry values and additional testing completed ASAP (see Section 9.2.1.2.1); 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.[d]
≥3xULN	NA	Yes				
≥8xULN	NA	NA	Hepatology consult. Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and subject discussed with Medical Monitor ASAP.	Immediate, permanent IMP discontinuation		

≥5xULN and <8xULN	<2xULN	No	Discussion with Medical Monitor required. Consider need for hepatology consult if there is no evidence of resolution (see Follow up requirements). [c]	Further investigation – immediate IMP discontinuation not required (see Section 9.2.1.2) IMP discontinuation required if any of the following occur: • Subject cannot comply with monitoring schedule. • Liver chemistry values continue to increase • Liver chemistry values remain ≥5xULN after 4 weeks of monitoring without evidence of resolution	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 9.2.1.2.1).	Monitoring of liver chemistry values at least twice per week for 2 weeks.[d] • Immediate IMP discontinuation required if liver chemistry values continue to increase. After 2 weeks of monitoring liver chemistry values: • ALT or AST remains ≥5xULN <8xULN, IMP should be temporarily withheld and subject should undergo repeat test in 2 weeks. Continue IMP if ALT or AST values <5xULN; continue to monitor at least twice per week until values normalize, stabilize, or return to within Baseline values. If ALT or AST remains ≥5xULN after second re-test, immediate, permanent IMP discontinuation required.

Table 9–3: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
						Continue to monitor until values normalize, stabilize, or return to within baseline values.[d]

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

[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 subject also has ≥2xULN ALP, the possibility of an indication of biliary obstruction should be discussed with the Medical Monitor.

[c] Details provided in Section 9.2.1.1. 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] 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.

[e] Details provided in Section 9.2.1.2.1.

9.2.1.1 Consultation with Medical Monitor and local hepatologist

Potential drug-induced liver injury events require notification of the Medical Monitor within 24 hours (eg, by laboratory alert), and the subject must be discussed with the Medical Monitor as soon as possible. If required, the subject 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 9.2.1.3) and SAE report (if applicable).

9.2.1.2 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 6.4.1 and Table 9–3 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.

9.2.1.2.1 Investigational medicinal product restart/rechallenge

Subjects who are immediately discontinued from IMP due to having met certain criteria for PDILI (as described in Section 6.4.1 and Table 9–3), but for whom an alternative diagnosis is confirmed, ie, drug-induced liver injury is excluded, can rarely restart IMP.

Rechallenge with IMP can occur only if ALL of the following requirements are met at the time of the rechallenge:

- The results of additional testing and monitoring described Section 9.2.1.3 and Section 9.2.1.4 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).
- The subject has shown clear therapeutic benefit from the IMP.
- Subject's ALT or AST elevations do not exceed ≥5xULN.
- Subject's total bilirubin is <2xULN.
- Subject has no signs or symptoms of hypersensitivity or hepatitis.
- The rechallenge is approved by the UCB responsible physician.
- Subject agrees to the Investigator-recommended monitoring plan.

9.2.1.3 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 9–4 (laboratory measurements) and Table 9–5 (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 subject 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.

The following measurements are to be assessed:

Table 9–4: 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, BUN, creatinine
	Total bilirubin, ALP, AST, ALT, GGT, total cholesterol, albumin
	If total bilirubin ≥1.5xULN, obtain fractionated bilirubin to obtain % direct bilirubin
	Serum CPK and LDH 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; BUN=blood urea nitrogen; CPK=creatine phosphokinase; GGT=gamma glutamyltransferase; HBcAb-IgM=hepatitis B core antibody-IgM; HBsAg=hepatitis B surface antigen; IgM=immunoglobulin M; INR=international normalized ratio; LDH=lactate dehydrogenase; PDILI=potential drug-induced liver injury; PK=pharmacokinetic; 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 subject history.

[b] Measured only for subjects with ALT >8xULN, 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 women of childbearing potential.

The following additional information is to be collected:

Table 9–5: PDILI information to be collected

New or updated information
Concomitant prescription 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

9.2.1.4 Follow-up evaluation

Potential drug-induced liver injury events require follow-up monitoring as described in Table 9–3. 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.

9.3 Other safety measurements

9.3.1 Assessment and management of TB and TB risk factors

All subjects will be assessed for TB at the time points specified in the Schedule of study assessments Table 5-1, Table 5-2, and Table 5-3 through physical examination for signs and symptoms of TB, laboratory testing (Section 9.3.1.1), and subject questionnaire (Section 9.3.1.2).

For the purposes of this study, TB definitions are as follows:

a. Known TB infection:

   – Active TB infection or clinical signs and symptoms suspicious for TB (pulmonary or extra-pulmonary).

   – History of active TB infection involving any organ system or findings in other organ systems consistent with TB infection, 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 infection that is not reported in the subject's medical history.

b. High risk of acquiring TB infection:

   – Known close exposure to another person with active TB infection within the 3 months prior to Baseline.

   – Time spent in a healthcare delivery setting or institution where individuals infected with TB are housed and where the risk of transmission of infection is high.

c. Latent TB infection (unless appropriate prophylaxis is initiated at least 8 weeks prior to IMP dosing and continued to completion of prophylaxis):

   – The absence of signs, symptoms, or physical findings suggestive of TB infection with a positive IGRA test (or 2 indeterminate IGRA test results) and a chest x-ray (or other imaging) without evidence of TB infection. If the result of the IGRA test is indeterminate, the particular IGRA test previously performed may be repeated once; if positive or indeterminate on retest, the subject may not be randomized to IMP without further evaluation by a TB specialist and discussion with the Study Physician, if LTBI is identified. The retest must be done during the protocol-defined Baseline window.

Note: If available, respiratory or other specimens must also be smear and culture negative for TB (Centers for Disease Control diagnosis of LTBI) http://www.cdc.gov/TB/topic /testing/default.htm).

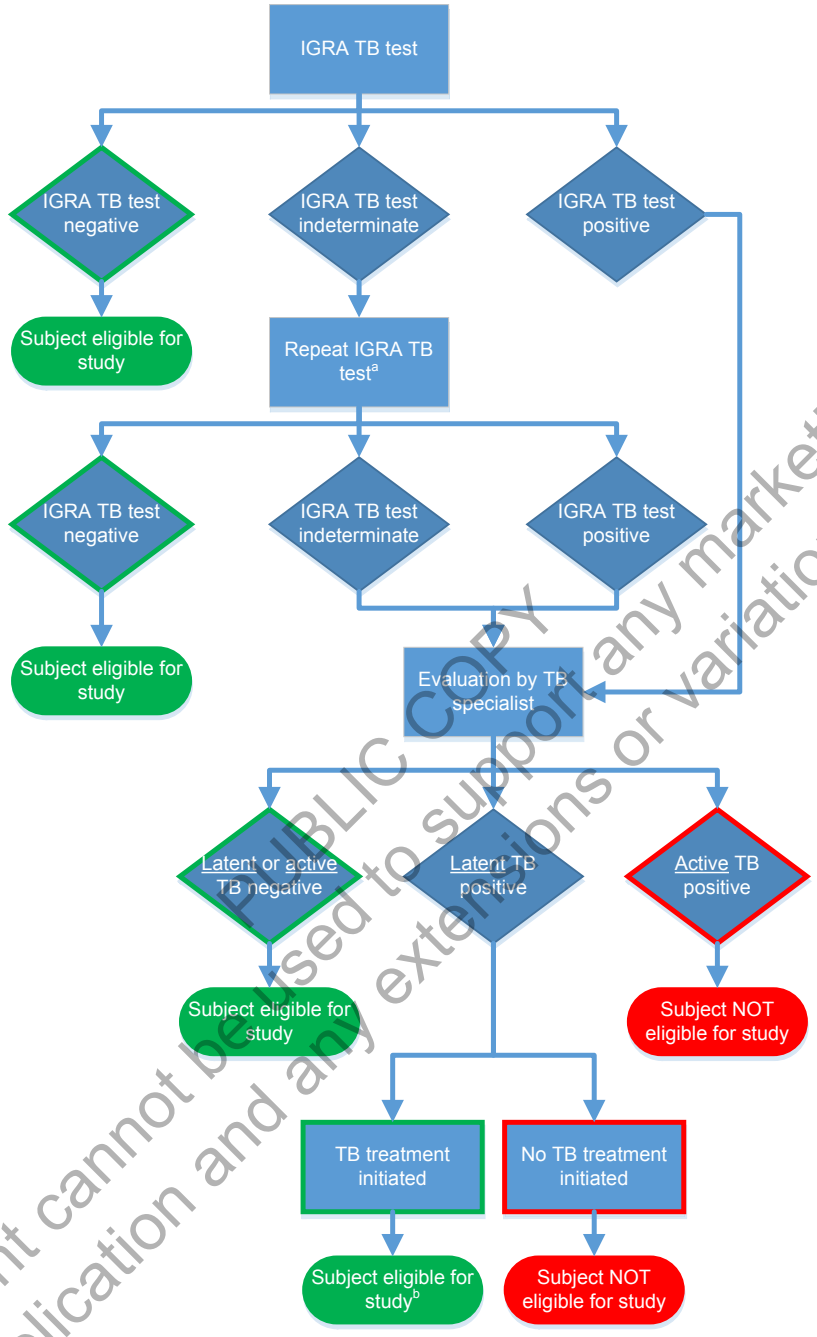
d. A NTMB infection is defined as a clinical infection caused by mycobacterial species other than those belonging to the Mycobacterium tuberculosis complex.

e. Tuberculosis test conversion:

   – A positive IGRA result for the current test when previous IGRA test results were negative. All subjects with TB test conversion must immediately stop IMP administration and be referred to a TB specialist for further evaluation. Confirmed TB test conversions should be classified as due to LTBI, active TB infection, or NTMB, and reported to the UCB PS function.

Subject eligibility, retesting requirements, and treatment requirements are depicted in Figure 9-1.

Figure 9-1: Schematic diagram of TB test results and study eligibility



IGRA=interferon-gamma release assay; TB=tuberculosis
[a] IGRA retest must be done during the protocol-defined Screening window
[b] Subjects with LTBI may enter the study only after they have completed at least 8 weeks of appropriate prophylactic therapy and thereafter, will continue and complete the entire regimen.

9.3.1.1 Tuberculosis assessment by IGRA

During conduct of the study, the TB assessment by IGRA (QuantiFERON TB test) will be performed as described in Table 5-1, Table 5-2, and Table 5-3 for all subjects. The test results will be reported as positive, negative, or indeterminate. Positive and indeterminate TB test results must be reported as an AE and appropriately updated once the final diagnosis is known (eg, active TB, LTBI, or false positive TB test). UCB also recommends that a TB specialist be consulted where TB (latent or active) is suspected or if there are doubts regarding test results. If latent or active TB is identified, subject must undergo appropriate study-specified withdrawal procedures.

9.3.1.2 Tuberculosis 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 Table 5-1, Table 5-2, and Table 5-3. The questionnaire will assist with the identification of subjects who may require therapy for TB.

9.3.1.3 Tuberculosis management

LTBI and active TB identified during study

During the study, subjects who develop evidence of LTBI or active TB must immediately stop further administration of IMP and will be referred to an appropriate TB specialist (pulmonologist or infectious disease specialist) for further evaluation. Evidence of LTBI is defined as subject's IGRA test converts to positive or indeterminate (and confirmed indeterminate on repeat), or the subject's questionnaire or history and physical indicates that TB infection or exposure may have occurred. Evidence of active TB includes, in addition to the aforementioned tests, signs and symptoms of organ involvement. In either situation, the subject should be carefully assessed by a TB specialist for active TB. Subjects diagnosed with active TB should be withdrawn from the study and receive appropriate TB or prophylaxis therapy.

If a TB specialist excludes an active TB infection, the subject can proceed with the IMP no earlier than 4 weeks after the start of an appropriate prophylactic therapy.

Any presumptive diagnosis or diagnosis of a TB infection is a reportable event. Confirmed active TB must be reported as an SAE. The Investigator is to complete and submit the TB Follow-Up Form provided.

The subject should be transferred to the care of his/her physician and managed according to the best available standard of care. Subjects identified as having converted to 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 Visit assessments (Section 8.2).

The subject should be encouraged to complete a SFU Visit (20 weeks after the final dose of IMP, Section 8.3).

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

9.3.2 Pregnancy testing

Urine pregnancy testing will be performed at all visits as specified in Table 5-1, Table 5-2, and Table 5-3. The Baseline Visit pregnancy testing results must be negative, and received and reviewed prior to administration of IMP. A negative urine pregnancy test result must be obtained immediately prior to each administration of IMP at the visits specified in Table 5-1, Table 5-2, and Table 5-3. Pregnancy tests should be administered to all female subjects of childbearing potential, regardless of their use of birth control.

9.3.3 Vital signs

Vital signs will be collected the time points specified in Table 5-1, Table 5-2, and Table 5-3 and will include SBP, DBP, pulse rate, and body temperature (oral, axillary, or otic). Subjects should be sitting for 5 minutes before and during vital signs assessments.

Vital signs are to be measured prior to blood sampling, and prior to dosing, where applicable.

9.3.4 12-lead ECGs

Twelve-lead standard ECGs will be recorded at the visits specified in Table 5-1 and Table 5-2, and read by a central ECG reader.

Full details of ECG recording will be provided in the ECG Manual.

9.3.5 Physical examination

A physical examination will be performed at visits specified in Table 5-1, Table 5-2, and Table 5-3. The physical examination will include general appearance; ear, nose, and throat; eyes, hair, and skin; respiratory; cardiovascular; gastrointestinal; 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. Findings considered clinically significant changes since the physical examination at Baseline will be recorded as AEs.

9.3.6 Body weight

Body weight will be measured at visits specified in Table 5-1, Table 5-2, and Table 5-3.

9.3.7 Assessment of suicidal ideation and behavior

Suicidal ideation and behavior will be assessed by using the eC-SSRS; the questionnaire will be self-administered by the subject 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 eC-SSRS assessments will be performed are specified in the schedule of study assessments (Table 5-1, Table 5-2, and Table 5-3).

The eC-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). Subjects respond to standardized clinical questions that are presented in a uniform fashion. The eC-SSRS defines 5 subtypes of suicidal ideation and behavior in addition to self-injurious behavior with no suicidal intent. The eC-SSRS takes approximately 3 to 10 minutes to complete.

Refer to Section 6.4 for eC-SSRS-related withdrawal criteria.

9.3.8 Patient Health Questionnaire 9

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression. The PHQ-9 scores for depression range from 0 to 27, with higher scores indicating 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.

The PHQ-9 will be assessed at the visits specified in Table 5-1, Table 5-2, and Table 5-3.

Refer to Section 6.4 for PHQ-9-related withdrawal criteria.

10 ASSESSMENT OF EFFICACY

The PASI, BSA, IGA, scalp IGA, pp-IGA, and mNAPSI should be performed by the Investigator, another delegated physician, or an appropriately qualified medical professional (based on local requirements) who has had documented training on how to perform these assessments correctly. The same assessor should evaluate the subject at each assessment.

10.1 Psoriasis Area and Severity Index

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 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 10–1).

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 10–1: 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 PASI75, PASI90, and PASI100 responses are based on at least 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.

The PASI will be completed at the visits specified in Table 5-1, Table 5-2, and Table 5-3.

10.2 IGA

A static IGA for PSO will be used to assess disease severity in all subjects during the study. The IGA will be completed at the visits specified in Table 5-1, Table 5-2, and Table 5-3.

The Investigator will assess the overall severity of PSO using the following 5-point scale presented in Table 10–2.

Table 10–2: Five-point IGA

Score	Short Descriptor	Detailed Descriptor
0	Clear	No signs of PSO; post-inflammatory 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 coloration; 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

10.3 Dermatology Life Quality Index

The DLQI is a questionnaire designed for use in adult subjects with PSO. The DLQI is a skin disease-specific questionnaire aimed at the evaluation of how symptoms and treatment affect subjects' health related quality of life (QOL). This instrument asks subjects about symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. It has been shown to be valid and reproducible in subjects 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 subject (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. Subjects will be asked to complete the DLQI as outlined in the Schedule of study assessments (Table 5-1, Table 5-2, and Table 5-3).

10.4 mNAPSI Score

Psoriatic nail disease will be evaluated using the mNAPSI. All affected nails will be scored (0 to 3) for onycholysis/oil drop dyschromia, nail plate crumbling, and pitting and will be scored (0 for "no" or 1 for "yes") for leukonychia, nail bed hyperkeratosis, splinter hemorrhages, and red spots in the lunula. The score for an individual nail ranges from 0 to 13 with higher scores indicative of more severe nail disease. The total mNAPSI score is the sum of the scores for each individual nail. If a nail is unaffected, it will be recorded as such and will not contribute to the total mNAPSI score. Subjects with nail disease at Baseline are defined as those with an mNAPSI score >0 at Baseline.

The mNAPSI will be assessed at the visits specified in Table 5-1 and Table 5-2.

10.5 Scalp IGA

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

All subjects will complete the scalp IGA at Baseline. Only subjects with scalp involvement at Baseline in the feeder study will complete the scalp IGA at the visits specified in Table 5-1 and Table 5-2. Subjects with scalp involvement at Baseline are defined as those with a scalp IGA score >0 at Baseline.

Scalp lesions will be assessed in terms of clinical signs of redness, thickness, and scaliness using a 5-point scale (Table 10–3).

Table 10–3: Scalp IGA

Score	Short Descriptor	Detailed Descriptor
0	Clear	Scalp has no signs of PSO; post-inflammatory 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
3	Moderate	Scalp has clearly distinguishable to moderate thickening; dull to bright red coloration; 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

IGA=Investigator's Global Assessment; PSO=psoriasis

10.6 pp-IGA

A static IGA for palmoplantar PSO will be used to assess palmoplantar disease severity.

All subjects will complete the pp-IGA at Baseline. Only subjects with palmoplantar involvement at Baseline in the feeder study will complete the pp-IGA at the other visits specified in Table 5-1 and Table 5-2. Subjects with palmoplantar involvement at Baseline are defined as those with a pp-IGA score >0 at Baseline.

Palmoplantar disease will be assessed in terms of clinical signs of redness, thickness, and scaliness using a 5-point scale (Table 10–4).

Table 10–4: pp-IGA

Score	Short Descriptor	Detailed Descriptor
0	Clear	Palmoplantar areas have no signs of PSO; post-inflammatory hyperpigmentation may be present
1	Almost clear	Palmoplantar areas have no thickening; normal to pink coloration; no to minimal focal scaling
2	Mild	Palmoplantar areas have just detectable to mild thickening; pink to light red coloration; predominately fine scaling
3	Moderate	Palmoplantar areas have clearly distinguishable to moderate thickening; dull to bright red and clearly distinguishable coloration; moderate scaling
4	Severe	Palmoplantar areas have severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions; numerous fissures

pp-IGA=palmoplantar Investigator's Global Assessment; PSO=psoriasis

10.7 Euro-Quality of Life 5-Dimensions, 3 levels

The EQ-5D-3L health questionnaire provides a descriptive profile and a single index value for health status. The instrument is comprised of a 5-item health status measure and a VAS. The EQ-5D-3L VAS records the respondent's self-rated health status on a vertical 20cm scale, graduated from 0 to 100 (0=worst imaginable health status, 100=best imaginable health status).

The EQ-5D-3L will be assessed at the visits specified in Table 5-1 and Table 5-2.

10.8 Short Form 36-Item Health Survey

The SF-36 (Version 2, standard recall) is a 36-item generic health related QOL instrument that uses a recall period of 4 weeks. Items are grouped into 8 domains as follows: Physical Functioning (10 items), Role Physical (4 items), Bodily Pain (2 items), General Health (5 items), Vitality (4 items), Social Functioning (2 items), Role Emotional (3 items), Mental Health (5 items), and 1 item for perceived stability or change in health (Health Transition) during the last year. The concepts represented by these domains contribute to physical, mental, and social aspects of health-related QOL. In addition to domain scores, the PCS and MCS scores are calculated from the 8 domains (excluding the Health Transition item). Component scores appreciate the impact of each domain on physical and mental health status (Maruish, 2011). Each of the 8 domain scores and the component summary scores range from 0 to 100, with a higher score indicating a better health status. The domains and the 2 component summary scores are standardized with a mean of 50 and a standard deviation (SD) of 10 in the general US population. The minimally important differences, in terms of T-score points at a group level, for SF-36 domains and component summaries are the following: PCS, 2; MCS, 3; Physical Functioning, 3; Role Physical, 3; Bodily Pain, 3; General Health, 2; Vitality, 2; Social Functioning, 3; Role Emotional, 4; and Mental Health, 3.

The SF-36 will be completed by the subject at the visits specified in Table 5-1 and Table 5-2.

10.9 Patient Global Assessment of PSO

The PGA of PSO is a PSO-specific item in which the patient responds to the multiple-choice question, "How severe are your psoriasis-related symptoms right now?" Possible responses to the question are "no symptoms," "mild symptoms," "moderate symptoms," "severe symptoms," or "very severe symptoms."

The PGA of PSO will be completed at the visits specified in Table 5-1 and Table 5-2.

10.10 Psoriatic Arthritis Screening and Evaluation questionnaire

The PASE questionnaire is a self-administered tool to screen for active PsA in patients with PSO (Husni et al, 2014). The questionnaire consists of 15 items that are divided into a 7-item symptoms subscale and an 8-item functions subscale. Standardized responses are based on 5 categories relating to agreement (strongly agree [5], agree [4], no idea [3], disagree [2], and strongly disagree [1]). The total maximum score is 75 points (symptom score: 35 points and function score: 40 points). Psoriatic Arthritis Screening and Evaluation questionnaire scores ≥47 points are indicative of active PsA.

If a subject with a PASE score ≥47 points is referred to a rheumatologist, the referral will be recorded in the eCRF. Subjects with PsA, defined as a past medical history of PsA or PASE ≥47, are required to receive the additional PsA assessment (PGADA) as noted in Section 10.11.

The PASE questionnaire will be completed at the visits specified in Table 5-1 and Table 5-2.

10.11 Patient's Global Assessment of Disease Activity for arthritis VAS

The PGADA for the arthritis VAS will be used to provide an overall evaluation of arthritis disease symptoms. Subjects will respond to the question, "Considering all the ways your arthritis affects you, please mark a vertical line on the scale below to show how you are feeling today," using a VAS where 0 is "very good, no symptoms" and 100 is "very poor, severe symptoms.

Only subjects with PsA will complete the PGADA at the visits specified in Table 5-1 and Table 5-2.

10.12 WPAI-SHP V2.0

The WPAI-SHP V2.0 is a patient-reported questionnaire that assesses subject's employment status, work absenteeism, work impairment while working (presenteeism), overall work, and daily activity impairment attributable to a specific health problem (Reilly et al, 1993). It has been used in several clinical studies of biologic therapy in subjects with plaque PSO (Kimball et al, 2012; Vender et al, 2012).

Five out of 6 items of the WPAI-SHP are regrouped into the 4 dimensions, with scores expressed as percentage, where higher numbers indicate greater impairment and less productivity, ie, worse outcomes, as described in the WPAI-SHP scoring rules.

The WPAI-SHP V2.0 will be assessed at the visits specified in Table 5-1 and Table 5-2.

10.13 Treatment Satisfaction Questionnaire for Medication (TSQM-9)

The TSQM-9 (Bharmal et al, 2009) is a 9-item measure developed to provide a suitable measure of treatment satisfaction with medication. It has 5 to 7 Likert response options per item and consists of 3 subscales: effectiveness (3 items), convenience (3 items), and a global satisfaction scale (3 items). The TSQM-9 was developed from the TSQM 1.4 (Atkinson et al, 2004) which has an additional subscale which measures side effects (3 items). The estimated completion time for this measure is less than 5 minutes. Scores range from 0 (worst) to 100 (best).

The TSQM will be performed at Week 48.

11 ASSESSMENT OF PHARMACOKINETIC VARIABLES

11.1 Pharmacokinetic variables

Blood samples for measurement of PK assessments (Section 4.3.3) will be collected at the time points specified in the Schedule of study assessments (Table 5-1 and Table 5-2). Blood samples for the measurement of PK assessments will not be collected in the OLE2 Period.

At dosing visits, blood samples will be drawn prior to dosing, and will be drawn at the same time of the sampling for clinical laboratory tests. The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the Laboratory Manual for this study. Detailed information on sample analysis will be provided in a bioanalytical report.

12 ASSESSMENT OF IMMUNOLOGICAL VARIABLES

Blood samples for measurement of antibodies to bimekizumab will be collected at the visits specified in Table 5-1 and Table 5-2. The threshold for antibody positivity will be defined prior to analysis. Blood samples for the measurement of antibodies to bimekizumab will not be collected in the OLE2 Period.

At dosing visits, blood samples will be drawn prior to dosing, and will be drawn at the same time of the sampling for clinical laboratory tests. The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the Laboratory Manual for this study. The presence of antibodies to bimekizumab will be determined using a validated bioanalytical method. Detailed information on sample analysis will be provided in a bioanalytical report.

13 STUDY MANAGEMENT AND ADMINISTRATION

13.1 Adherence to protocol

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 subjects 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 Clinical Project Manager of the Sponsor within 24 hours and follow any local regulatory requirements.

13.2 Monitoring

UCB (or designee) will monitor the study to meet the Sponsor's monitoring SOPs, ICH-GCP guideline, and applicable regulatory requirements, and to ensure that study initiation, conduct, and closure are adequate. Monitoring of the study may be delegated by UCB to a CRO or a contract monitor.

The Investigator and his/her staff are expected to cooperate with UCB (or designee) and to be available during the monitoring visits to answer questions sufficiently and to provide any missing information. The Investigator(s)/institution(s) will permit direct access to source data/documents for study-related monitoring, audits, IRB/IEC review, and regulatory inspection(s).

The Investigator will allow UCB (or designee) to periodically review all eCRFs and corresponding source documents (eg, hospital and laboratory records for each subject). Monitoring visits will provide UCB (or designee) with the opportunity to evaluate the progress of the study, verify the accuracy and completeness of eCRFs, ensure that all protocol requirements, applicable authorities regulations, and Investigator's obligations are being fulfilled, and resolve any inconsistencies in the study records.

13.2.1 Definition of source data

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, or QOL questionnaires, for example. Source documents should be kept in a secure, limited access area.

Source documents that are computer generated and stored electronically must be printed for review by the monitor (eg, ECG reports). Once printed, these copies should be signed and dated by the Investigator and become a permanent part of the subject'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, such as Holter monitor records or electroencephalogram records, must be saved and stored as instructed by UCB (or designee).

Patient-Reported Outcome measures (eg, DLQI, EQ-5D-3L, SF-36, PGA of PSO, and PGADA) will be entered electronically by the subject.

13.2.2 Source data verification

Source data verification ensures accuracy and credibility of the data obtained. During monitoring visits, reported data are reviewed with regard to being accurate, complete, and verifiable from source documents (eg, subject files, recordings from automated instruments, tracings [ECG], x-ray films, laboratory notes). All data reported on the eCRF should be supported by source documents, unless otherwise specified in Section 13.2.1.

13.3 Data handling

13.3.1 Case Report form completion

The Investigator is responsible for prompt reporting of accurate, complete, and legible 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 electronic eCRF.

Detailed instructions will be provided in the eCRF Completion Guidelines.

13.3.2 Database entry and reconciliation

Case Report forms/external electronic data will be entered/loaded into a validated electronic database using a clinical data management system (CDMS). Computerized data cleaning checks will be used in addition to manual review to check for discrepancies and to ensure consistency of the data. Case Report form data are entered into the clinical database using independent, double-data entry, with the exception of comment fields, which are verified by a second person. The data are entered into the eCRFs once and are subsequently verified if the study is performed using electronic data capture.

An electronic audit trail system will be maintained within the CDMS to track all data changes in the database once the data have been saved initially into the system or electronically loaded. Regular backups of the electronic data will be performed.

13.3.3 Subject Baseline and Enrollment Log/Subject Identification Code list

The subject's Baseline and enrollment will be recorded in the Subject Baseline and Enrollment Log.

The Investigator will keep a Subject Identification Code list. This list remains with the Investigator and is used for unambiguous identification of each subject.

The subject's consent and enrollment in the study must be recorded in the subject's medical record. These data should identify the study and document the dates of the subject's participation.

13.4 Termination of the study

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 IRB/IEC should also be informed and provided with 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 of all unused IMP and other material in accordance with UCB procedures for the study.

13.5 Archiving and data retention

The Investigator will maintain adequate records for the study, including eCRFs, medical records, laboratory results, Informed Consent documents, drug dispensing and disposition records, safety reports, information regarding subjects who discontinued, and other pertinent data.

All essential documents are to be retained by the Investigator until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region, or at least 2 years have elapsed since the formal discontinuation of clinical development of the IMP. These documents should be retained for a longer period; however, if required by the applicable regulatory requirement(s) or by an agreement with UCB (Committee for Proprietary Medicinal Products [CPMP]/ICH/135/95, 2002

[Section 4.9.5]). 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.

13.6 Audit and inspection

The Investigator will permit study-related audits mandated by UCB, after reasonable notice, and inspections by domestic or foreign regulatory authorities.

The main purposes of an audit or inspection are to confirm that the rights and well-being of the subjects enrolled have been protected, that enrolled subjects (ie, signing consent and undergoing study procedures) are appropriate for the study, and that all data relevant for the evaluation of the IMP have been processed and reported in compliance with the planned arrangements, the protocol, investigational site, and IRB/IEC SOPs, ICH-GCP, and applicable regulatory requirements.

The Investigator will provide direct access to all study documents, source records, and source data. If an inspection by a regulatory authority is announced, the Investigator will immediately inform UCB (or designee).

13.7 Good Clinical Practice

Noncompliance with the protocol, ICH-GCP, or local regulatory requirements by the Investigator, institution, institution staff, or designees of the Sponsor will lead to prompt action by UCB to secure compliance. Continued noncompliance may result in the termination of the site's involvement in the study.

14 STATISTICS

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

14.1 Definition of analysis sets

The Enrolled Set (ES) will consist of all subjects who have given informed consent for PS0014.

The Safety Set (SS) will consist of all subjects who receive at least 1 dose of the IMP in PS0014.

The Full Analysis Set (FAS) will consist of all enrolled subjects who receive at least 1 dose of the IMP and have a valid efficacy measurement for PASI at Baseline of the Feeder Study and Baseline of PS0014.

The OLE2 Period Set (OL2S) will consist of all subjects that receive at least 1 dose of IMP at Week 144/OLE2 or later in the OLE2 Period (including the Week 144/OLE2 Baseline dose).

The Pharmacokinetics Per-Protocol Set (PK-PPS) will consist of all enrolled subjects who receive at least 1 dose of the IMP and provide at least 1 quantifiable plasma concentration postdose without protocol deviations that would affect the concentration in PS0014.

14.2 General statistical considerations

Descriptive statistics will be used to provide an overview of the safety and efficacy results. For categorical parameters, the number and percentage of subjects in each category will be presented. The denominator for percentages will be based on the number of subjects appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will include n, mean, SD, median, minimum, and maximum. No statistical hypothesis testing will be performed. Baseline values for safety and efficacy variables will be determined from Baseline values of the primary study.

Further methods pertaining to the summary and analysis of the efficacy and safety data are presented in the following sections, and will be described in more detail in the SAP.

14.3 Planned safety analyses

Safety variables will be analyzed for all subjects in the SS and selected summaries will be provided for subjects in the OLE2 period (OL2S).

Adverse events will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA®). Treatment-emergent AEs will be defined as events that have a start date on or following the first administration of study treatment in PS0014 through the final administration of study treatment + 140 days (covering the 20-week SFU Period). Treatment-emergent AEs will be categorized to treatment group based on the dose being received at the time of onset of the event. Tables will include columns for bimekizumab 320mg Q4W, bimekizumab 320mg Q8W, and All bimekizumab (any dose of bimekizumab).

For all safety analyses, change from Baseline variables will be defined relative to the Baseline entry measurement in PS0014.

14.3.1 Primary safety analysis

All TEAEs will be summarized descriptively by treatment group, primary System Organ Class (SOC), high level term (HLT), and preferred term (PT). This summary will include the exposure adjusted incidence rate (EAIR) with associated 95% CI and the exposure adjusted event rate (EAER).

For EAIR, the numerator will be the total number of subjects experiencing the AE. The denominator will be 100 subject-years; that is, the total summation of individual subject-years at risk up to the first occurrence of the AE for subjects with that AE, and the total subject-years at risk for those subjects not experiencing that AE, divided by 100. Exposure adjusted incidence rates will be presented with a 95% exact CI based upon the Chi-Square distribution (Ulm, 1990).

For EAERs, the numerator will be the number of AEs including repeat occurrences in individual subjects; the denominator will be 100 subject-years. That is, the total summation of individual subject-years at risk divided by 100. No CI will be computed for EAER.

Patient exposure at risk in days will be defined as date of last administration of study medication – date of first administration of study medication + 140 days (ie, the duration of the SFU Period). If a subject dies, patient exposure at risk is censored at the date of death. The sum of these exposure days at risk across subjects is converted to years for the EAIR and EAER calculations described above.

14.3.2 Other safety analysis

Additional tables will summarize TEAEs by intensity and relationship to study medication, TEAEs leading to withdrawal from the study, treatment-emergent SAEs, and deaths. In addition to summaries that characterize events that occur during PS0014, for TEAEs and SAEs, additional summaries will be produced summarizing feeder study and PS0014 combined, where treatment emergence and exposure at risk are relative to the first dose of study drug in the feeder study. In the case of a subject that switches study treatment when starting PS0014, exposure at risk to feeder study treatment will end the day prior to the first PS0014 dose.

In order to evaluate if there is any difference in the TEAE profile of subjects who have dose adjustments, additional summaries will be generated. With respect to dose adjustments, for the Week 48 interim analysis, subjects will be classified into 1 of 2 groups:

- Nonadjusters – This group consists of subjects who do not experience a dose adjustment prior to Week 48.
- Adjusters – This group consists of subjects who experience a dose regimen adjustment at Week 24. This means that the subjects in this group had a dose adjustment from 320mg Q4W to 320mg Q8W at Week 24.

For the full analysis, subjects will be categorized into those who did not experience a dose regimen adjustment during the study and those that experienced a dose regimen adjustment at any time.

Summaries based on these groups will be done for the TEAE overview, incidence of TEAEs (by SOC, HLT, and PT), and incidence of treatment-emergent SAEs.

Extent of exposure to study medication in PS0014 will be summarized using descriptive statistics. As with the primary summaries of TEAEs, extent of exposure will be presented with columns for bimekizumab 320mg Q4W, bimekizumab 320 Q8W, and All bimekizumab.

Change from Baseline in laboratory values, ECGs, and vital signs will be presented using descriptive statistics by the treatment received in PS0014 and overall.

Additional summaries to assess the safety of bimekizumab manufactured using Process 5 will be described further in the SAP.

14.4 Planned efficacy analyses

Efficacy analyses will be summarized based on the FAS during the Treatment Period. The summaries described in this section will provide data on maintenance of effect of open-label bimekizumab over 144 weeks and beyond. Additionally, it will allow an assessment of the impact of dose adjustments on efficacy results. As these variables are summarized over time and the initial values can be impacted by the treatment in the feeder study, the presentation using a combination of feeder/extension study treatment groups is intended to provide perspective on the change in these values from the feeder study through the Treatment Period of PS0014. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline study results by scheduled visit for PS0014. Selected efficacy summaries during the OLE2 Period may also be provided for selected efficacy variables.

Responder efficacy variables (PASI75, PASI90, PASI100, IGA, DLQI score of 0 or 1, mNAPSI75, mNAPSI90, mNAPSI100, pp-IGA and scalp IGA) will be summarized descriptively. The PASI responder variables are derived relative to the Baseline in the feeder study.

Continuous efficacy variables based on the change from Baseline (PASI, DLQI, BSA affected by PSO, PGADA, SF-36, the EQ-5D-3L PCS, MCS and domain scores, WPAI-SHP, PGA of PSO, and PASE) will be summarized using descriptive statistics by scheduled visit. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline results by scheduled visit for PS0014. Figures for selected variables will also be generated in order to demonstrate the kinetics of response over time.

In addition to the summaries described above, the impact of dose regimen adjustment on efficacy will be considered. This will be done primarily by summarizing efficacy variables by the adjuster groups described above, for the Week 48 interim analysis and for the full analysis.

14.5 Pharmacokinetic analyses

Pharmacokinetic variables will be analyzed for all subjects in the PK-PPS.

Bimekizumab plasma concentrations will be summarized for each treatment group at each visit specified in Table 5-1 and Table 5-2. Treatment groups presented will be relative to the treatment received in PS0014.

14.6 Immunogenicity analyses

Anti-bimekizumab antibodies (including positivity) will be summarized by treatment at each scheduled visit at which samples are collected. Treatment groups presented will be relative to both the treatment received in the feeder study, as well PS0014 treatment.

14.7 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 key efficacy, key safety, or PK outcomes for an individual subject. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document at study start. 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.

14.8 Handling of dropouts or missing data

For responder efficacy variables (PASI75, PASI90, PASI100, IGA, DLQI score of 0 or 1, mNAPSI75, mNAPSI90, mNAPSI100, pp-IGA and scalp IGA), missing data will be handled by nonresponder imputation, meaning that subjects that discontinue early or who have missing data at a given time point are imputed as though they did not achieve the given response. Supportive summaries will be based on observed case data.

For continuous efficacy variables based on the change from Baseline (PASI, DLQI, BSA affected by PSO, PGADA, SF-36, the EQ-5D-3L PCS, MCS and domain scores, WPAI-SHP, PGA of PSO, and PASE), missing data will be handled by using multiple imputation via the Markov-Chain Monte Carlo method. Supportive summaries will be based on observed case data.

Additional methods of missing data imputation may be explored, and will be outlined in the SAP.

14.9 Planned interim analysis and data monitoring

An interim analysis is planned at Week 48 and Week 144, details of which will be documented in the SAP. Additional interim analyses may be performed (details of which will be documented in the SAP). Corresponding interim Clinical Study Reports (CSRs) may be written. A final analysis and updated final CSR will be prepared once all data through the OLE2 Period and SFU2 Visit have been collected.

14.10 Determination of sample size

As the primary objective of this study is to assess the long-term safety and tolerability of bimekizumab, the number of subjects anticipated is based on the number of subjects recruited into and completing the feeder studies and meeting the eligibility requirements for PS0014.

15 ETHICS AND REGULATORY REQUIREMENTS

15.1 Informed consent

Subject'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 subject in both oral and written form by the Investigator (or designee). Each subject will have the opportunity to discuss the study and its alternatives with the Investigator.

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

All subjects enrolling in the OLE2 Period will sign a new ICF.

If the Informed Consent form 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 Informed Consent form by the IRB/IEC and use of the amended form.

All studies conducted at centers in the United States must include the use of a Health Insurance Portability and Accountability Act Authorization form.

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

15.2 Subject identification cards

Upon signing the Informed Consent and Assent form (as applicable), the subject or legal representative will be provided with a subject identification card in the language of the subject. The Investigator will fill in the subject identifying information and medical emergency contact information. The Investigator will instruct the subject to keep the card with him/her at all times.

15.3 Institutional Review Boards and Independent Ethics Committees

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, Informed Consent form, IB, Investigator's curriculum vitae (if applicable), advertisement (if applicable), and all other subject-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 human subjects or others, and any protocol deviations, to eliminate immediate hazards to subjects.

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 subjects. 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 subject 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.

15.4 Subject privacy

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

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 subject'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 subject's study participation, and autopsy reports for deaths occurring during the study).

15.5 Protocol amendments

Protocol changes may affect the legal and ethical status of the study and may also affect the statistical evaluations of sample size and the likelihood of the study fulfilling its primary objective.

Significant changes to the protocol will only be made as an amendment to the protocol and must be approved by UCB, the IRB/IEC, and the regulatory authorities (if required), prior to being implemented.

16 FINANCE, INSURANCE, AND PUBLICATION

Insurance coverage will be handled according to local requirements.

Finance, insurance, and publication rights are addressed in the Investigator and/or CRO agreements, as applicable.

17 REFERENCES

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18 APPENDICES

18.1 Protocol Amendment 1

Rationale for the amendment

The protocol has been amended for the following reasons:

- Extended the study duration for an additional 2 years. Changes include addition of a new schedule of assessments for years 2 and 3, and updates to Section 8, Study procedures by visit.
- Modified the text in Section 7 to include guidance for allowing subjects the option to self-inject study drug at home after Week 48.
- Modified guidance to the Investigator regarding changing a subject's dosing interval from 320mg Q4W to 320mg Q8W if PASI90 is achieved at Week 24, to clarify this is optional. Added a requirement that a subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) if PASI90 is achieved at Week 48 unless, based on medical judgement, the Investigator decides differently.
- Provided rationale (Section 5.8) why subjects who received bimekizumab 320mg Q4W, but did not achieve PASI90 in the feeder study, should continue receiving bimekizumab 320mg Q4W in PS0014 requested by the Medicines and Healthcare products Regulatory Agency).
- Amended Inclusion Criterion #4 to add contraceptive measures according to the feeder studies PS0009 and PS0013 (requested by the Medicines and Healthcare products Regulatory Agency).
- Amended Exclusion Criterion #3 to clarify that the Investigator will have the ultimate decision regarding whether a subject with an ongoing SAE, or a history of serious infections in the feeder study, can continue receiving bimekizumab in PS0014 (requested by the Medicines and Healthcare products Regulatory Agency).
- Amended Exclusion Criterion #4 to clarify that subjects who have a positive or indeterminate IGRA test result in a feeder study are excluded from PS0014 unless they are appropriately evaluated and treated.
- Updated the lists of efficacy, safety, and PK variables; added the Treatment Satisfaction Questionnaire for Medication (TSQM-9) to the study as an "other" efficacy variable; and updated the corresponding description of statistical methods in Section 14).
- Changed the pregnancy testing assessment to urine pregnancy testing at all study visits.
- Updated Section 9.2.1 (Evaluation of PDILI) for improved clarity.
- Added plans for interim analyses at Week 24 and Week 48 (Section 14.9).
- Updated study contact details for the clinical trial biostatistician.

Modifications and changes

Global changes:

The following changes were made throughout the protocol:

- The duration of the open-label Treatment Period has been changed from 48 weeks to 144 weeks throughout the document.
- The maximum duration of the study has been changed from 64 weeks to 160 weeks throughout the document.
- Cross references to the new schedule of assessments (Table 5-2) for the 2-year extension have been made throughout the document.
- The list of abbreviations was updated accordingly.
- Minor spelling, editorial, and formatting changes were made throughout the document.

Specific changes:

Change #1

Clinical Trial Biostatistician

Name:	[redacted]
Address:	UCB Biosciences, 8010 Arco Corporation Drive, Raleigh, NC 27617
Phone:	[redacted]
Fax:	

Has been changed to:

Clinical Trial Biostatistician

Name:	[redacted]
Address:	UCB Biosciences, 8010 Arco Corporation Drive, Raleigh, NC 27617
Phone:	[redacted]
Fax:	

Change #2

Section 1 Summary, paragraph 3

Approximately 1120 subjects are expected to enroll in PS0014. For each subject, the study will last a maximum of 64 weeks and will consist of a Treatment Period (48 weeks) and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]).

Has been changed to:

Approximately 1120 subjects are expected to enroll in PS0014. For each subject, the study will last a maximum of ~~64~~**160** weeks and will consist of a Treatment Period (~~48~~**144** weeks) and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]).

And paragraph 5

At the final study visit in the feeder studies, eligible subjects continuing into PS0014 will complete the final study visit assessments and any additional PS0014 Baseline assessments, and will then receive their first dose of open-label bimekizumab in PS0014. During the Treatment Period, all subjects will attend study visits at the study site Q4W for study assessments. Following completion or early withdrawal from the Treatment Period, subjects will return for a SFU Visit 20 weeks after their final dose of bimekizumab.

Has been changed to:

At the final study visit in the feeder studies, eligible subjects continuing into PS0014 will complete the final study visit assessments and any additional PS0014 Baseline assessments, and will then receive their first dose of open-label bimekizumab in PS0014. During **Year 1 of** the Treatment Period **(Weeks 0 to 44),** all subjects will attend study visits at the study site Q4W for study assessments **and IMP will be administered in the clinic by subcutaneous (sc) injection**. **During Years 2 and 3 of the Treatment Period (Weeks 48 to 144), all subjects will attend study visits at the study site Q12W for study assessments and subjects may self-inject IMP at home.**

At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional). At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

Following completion or early withdrawal from the Treatment Period, subjects will return for a SFU Visit 20 weeks after their final dose of bimekizumab.

Change #3

Section 2.2.1.2 Ongoing studies

Four additional studies of bimekizumab for the treatment of PSO are ongoing.

- PS0010 is a Phase 2b, double-blind, placebo-controlled, dose ranging study to evaluate the safety, efficacy, PK, and pharmacodynamics (PD) of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0011 is a long-term extension study for subjects who completed PS0010 to assess the long-term safety, tolerability, and efficacy of bimekizumab.
- PS0016 is a Phase 2a, subject-blind, Investigator-blind study to evaluate the time course of PD response, safety, and PK of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.

- PS0018 is a long-term extension study for eligible subjects from PS0016 to assess the safety, tolerability, and efficacy of bimekizumab.

Has been changed to:

~~Four~~ **Five** additional studies of bimekizumab for the treatment of PSO are ongoing.

- PS0010 is a Phase 2b, double-blind, placebo-controlled, dose ranging study to evaluate the safety, efficacy, PK, and pharmacodynamics (PD) of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0011 is a long-term extension study for subjects who completed PS0010 to assess the long-term safety, tolerability, and efficacy of bimekizumab.
- PS0016 is a Phase 2a, subject-blind, Investigator-blind study to evaluate the time course of PD response, safety, and PK of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0018 is a long-term extension study for eligible subjects from PS0016 to assess the safety, tolerability, and efficacy of bimekizumab.
- **PS0015 is a Phase 3b, double-blind, active comparator controlled, parallel group study to evaluate the efficacy and safety of bimekizumab compared with secukinumab in adult subjects with moderate to severe chronic PSO.**

Change #4

Section 3.2 Secondary objectives

The secondary objectives of the study are to:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over 48 weeks as measured by SAEs and TEAEs leading to study withdrawal
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over 48 weeks as measured by PASI90 (defined as a subject who achieves 90% reduction in the PASI score from the feeder study Baseline) and IGA response (Clear or Almost Clear with at least a 2 category improvement from Baseline on a 5-point scale)

Has been changed to:

The secondary objectives of the study are to:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over ~~48~~**144** weeks as measured by SAEs and TEAEs leading to study withdrawal
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over ~~48~~**144** weeks as measured by PASI90 (defined as a subject who achieves 90% reduction in the PASI score from the feeder study Baseline) and IGA response (Clear or Almost Clear with at least a 2 category improvement from Baseline on a 5-point scale)

Change #5

Section 3.3 Other objectives

The first 2 bullets have been revised:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over ~~48~~**144** weeks
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over ~~48~~**144** weeks

And a new bullet has been added to the list:

- **Assess general health-related quality of life (QOL), including the change of skin-related QOL and treatment satisfaction**

Change #6

Section 4.2.2 Secondary efficacy variables

The secondary efficacy variables are:

- PASI90 at Week 48
- IGA response at Week 48

Has been changed to:

The secondary efficacy variables are:

- PASI90 at Week ~~48~~**144**
- IGA response at Week ~~48~~**144**

Change #7

Section 4.3.1 Other safety variables

The following bullet has been added:

- **Change from Baseline in the Patient Health Questionnaire 9 (PHQ-9)**

Change #8

Section 4.3.2 Other efficacy variables

Change from Baseline efficacy variables will be defined relative to the Baseline measurement from the feeder study. The other efficacy variables are listed below:

- PASI75, PASI90, and PASI100 response
- IGA response
- Absolute and percent change from Baseline in PASI score
- Change from Baseline in IGA score
- Absolute and percent change from Baseline in the product of IGA and BSA (IGAxBSA)
- Change from Baseline in Dermatology Life Quality Index (DLQI)

- Percentage of subjects achieving a DLQI total score of 0 or 1
- Percentage of subjects achieving a minimal clinically important difference (improvement from Baseline of 4 or more) in the DLQI
- Change from Baseline in the Patient Health Questionnaire 9 (PHQ-9)
- Change from Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) score for subjects with nail disease at Baseline
- Change from Baseline in the Patient's Global Assessment of Disease Activity (PGADA) for the arthritis visual analog scale (VAS) for subjects with PsA at Baseline
- Change from Baseline in Patient Global Assessment (PGA) of PSO score
- Change from Baseline in the scalp IGA for subjects with scalp PSO at Baseline
- Palmoplantar Investigator's Global Assessment (pp-IGA) response (Clear or Almost Clear) for subjects with palmoplantar PSO at Baseline
- Change from Baseline in the PASE questionnaire scores (function score, symptom score, and total score)
- Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47)
- Change from Baseline in Short Form 36-item Health Survey (SF-36), Physical Component Summary (PCS) score, Mental Component Summary (MCS) score, and individual domains
- Responses to Euro-Quality of Life 5-Dimensions, 3 levels (EQ-5D-3L)
- Changes from Baseline in EQ-5D-3L VAS scores and all dimensions
- Change from Baseline in Work Productivity and Activity Impairment Questionnaire-specific health problem (WPAI-SHP) V2.0 adapted to PSO scores

Has been changed to:

Change from Baseline efficacy variables will be defined relative to the Baseline measurement from the feeder study. The other efficacy variables are listed below:

- PASI75, PASI90, and PASI100 response
- **Percentage of subjects with PASI ≤1, ≤2, ≤3 and ≤5**
- IGA response
- Absolute and percent change from Baseline in PASI score
- Change from Baseline in IGA score
- **Absolute and percent change from Baseline in the body surface area (BSA) affected by PSO**
- Absolute and percent change from Baseline in the product of IGA and BSA (IGAxBSA)
- Change from Baseline in Dermatology Life Quality Index (DLQI)
- Percentage of subjects achieving a DLQI total score of 0 or 1

- Percentage of subjects achieving a minimal clinically important difference (improvement from Baseline of 4 or more) in the DLQI
- ~~Change from Baseline in the Patient Health Questionnaire 9 (PHQ-9)~~
- Change from Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) score for subjects with nail disease at Baseline
- **mNAPSI75, mNAPSI90 and mNAPSI100 response**
- Change from Baseline in the Patient's Global Assessment of Disease Activity (PGADA) for the arthritis visual analog scale (VAS) for subjects with PsA at Baseline
- Change from Baseline in Patient Global Assessment (PGA) of PSO score
- ~~Change from Baseline in the scalp IGA for subjects with scalp PSO at Baseline~~
- **Scalp-specific IGA (Scalp IGA) response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with scalp PSO at Baseline**
- Palmoplantar Investigator's Global Assessment (pp-IGA) response (Clear or Almost Clear **with at least 2 category improvement relative to Baseline**) for subjects with palmoplantar PSO at Baseline
- Change from Baseline in the PASE questionnaire scores (function score, symptom score, and total score)
- Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47)
- Change from Baseline in Short Form 36-item Health Survey (SF-36), Physical Component Summary (PCS) score, Mental Component Summary (MCS) score, and individual domains
- Responses to Euro-Quality of Life 5-Dimensions, 3 levels (EQ-5D-3L)
- Changes from Baseline in EQ-5D-3L VAS scores and all dimensions
- Change from Baseline in Work Productivity and Activity Impairment Questionnaire-specific health problem (WPAI-SHP) V2.0 adapted to PSO scores
- Treatment Satisfaction Questionnaire for Medication (TSQM-9)

Change #9

Section 4.3.3 Pharmacokinetic variables

The PK variables are plasma concentrations of bimekizumab and population PK including:

- Total body clearance (CL/F)
- Apparent volume of distribution (V/F)

Has been changed to:

The PK variable~~s are~~ **is** plasma concentrations of bimekizumab. ~~and population PK including:~~

- ~~Total body clearance (CL/F)~~
- ~~Apparent volume of distribution (V/F)~~

Change #10

Section 5.2 Study periods

PS0014 will include 2 periods, a Treatment Period (48 weeks) and a SFU Period (20 weeks after the final dose of IMP).

Has been changed to:

PS0014 will include 2 periods, a Treatment Period (~~48~~**144** weeks) and a SFU Period (20 weeks after the final dose of IMP).

Change #11

Section 5.2.1 Treatment Period; paragraphs 2, 3, 4, and 5

During the Treatment Period, all subjects will attend study visits at the study site Q4W for study assessments.

At Week 24 only, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W.

Investigational medicinal product will be administered in the clinic by sc injection at the time points specified in the schedule of assessments (Table 5-1).

The assessments to be performed at each Treatment Period Visit are presented in Table 5-1.

Has been changed to:

During **Year 1 of** the Treatment Period **(Weeks 0 to 44),** all subjects will attend study visits at the study site Q4W for study assessments. **During Years 2 and 3 of the Treatment Period (Weeks 48 to 144), all subjects will attend study visits at the study site Q12W for study assessments.**

At Week 24 ~~only~~, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W **(optional). At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.**

During Year 1 of the Treatment Period (Weeks 0 to 44), IMP ~~Investigational medicinal product~~ will be administered in the clinic by sc injection at the time points specified in the schedule of assessments (**Table 5-1**). **During Years 2 and 3 of the Treatment Period (Weeks 48 to 144), subjects may self-administer IMP at home (described in Section 7.2) at the time points specified in the schedule of assessments (Table 5-2)**.

The assessments to be performed at each Treatment Period Visit are presented in Table 5-1 **and Table 5-2**.

Change #12

Section 5.2.2 Safety Follow-Up; second sentence

The assessments for the SFU are presented in Table 5-1.

Has been changed to:

The assessments for the SFU are presented in ~~Table 5-1~~ **Table 5-2**.

Change #13

Section 5.3 Study duration per subject; first sentence

Eligible subjects will continue to receive open-label bimekizumab in PS0014 for up to 48 weeks or until the Sponsor decides to discontinue the study

Has been changed to:

Eligible subjects will continue to receive open-label bimekizumab in PS0014 for up to ~~48~~**144** weeks or until the Sponsor decides to discontinue the study.

Change #14

Section 5.6 Schedule of study assessments

The schedule of study assessments is presented in Table 5-1. At each visit, all study assessments should be performed prior to administration of IMP.

Has been changed to:

The schedule of study assessments **for Year 1 (Weeks 0 to 44)** is presented in Table 5-1. **The schedule of study assessments for Years 2 and 3 (Weeks 48 to 144) is presented in Table 5-2**. At each visit, all study assessments should be performed prior to administration of IMP.

Change #15

Table 5 1: Schedule of study assessments

Protocol activity / Visit [a] / Week	Treatment Period												W48/ PEOT	SFU [c]
	Stable Dosing							Flexible Dosing [b]						
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44		
Informed consent	X													
Inclusion/exclusion	X													
Physical exam [d,e]	X			X			X						X	X
Body weight	X												X	
Vital signs [f]	X	X	X		X		X		X		X		X	X
Hematology and chemistry	X	X	X		X		X		X		X		X	X
Urinalysis	X	X	X		X		X		X		X		X	X
Urine drug screen	X													
ECG	X												X	
Pregnancy testing [g]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IGRA TB test [h]													X	
TB questionnaire	X			X			X			X			X	X
Blood sample for bimekizumab plasma concentrations [i]	X				X		X				X		X	X
Blood sample for anti-bimekizumab antibodies [i]	X				X		X				X		X	X
PASI	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Percentage of BSA	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DLQI	X						X						X	
PHQ-9	X	X	X		X		X		X		X		X	X

Table 5 1: Schedule of study assessments

Protocol activity / Visit [a]/ Week	Treatment Period												W48/ PEOT	SFU [c]
	Stable Dosing							Flexible Dosing [b]						
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44		
eC-SSRS	X	X	X		X		X		X		X		X	X
mNAPSI [j]	X						X						X	
Scalp IGA [k]	X						X						X	
pp-IGA [l]	X						X						X	
EQ-5D-3L	X						X						X	
SF-36	X						X						X	
PGA of PSO	X						X						X	
PASE[m]	X												X	
PGADA[m]	X						X						X	
WPAI-SHP V2.0	X						X						X	
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IRT	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Bimekizumab administration [n]	X	X	X	X	X	X	X	X	X	X	X	X		

Table 5 1: Schedule of study assessments

Protocol activity \ Visit [a]/ Week	Treatment Period												W48/ PEOT	SFU [c]
	Stable Dosing							Flexible Dosing [b]						
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44		

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PEOT=Premature End of Treatment; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire 9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; SF-36=Short Form 36-item Health Survey; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU=Safety Follow-Up; TB=tuberculosis; W=Week; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from the first dose at all visits except SFU. The Safety Follow-Up Visit window is ±7 days from final dose.

[b] At Week 24 only, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W.

[c] The SFU Visit will occur 20 weeks after the final dose.

[d] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[e] The physical examination will be performed as per Section 9.3.5.

[f] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[g] Pregnancy testing will consist of serum testing at Baseline and Week 48/PEOT. Urine pregnancy tests will be performed at all other visits. Pregnancy test results must be negative prior to administering IMP.

[h] Ensure that an IGRA test was performed during the last dosing visit of the feeder study and the result was negative.

[i] All blood samples taken prior to dosing.

[j] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.

[k] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.

[l] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.

[m] The PGADA is assessed only for subjects with PsA at Baseline in the feeder studies.

n The dosing window is ±7 days relative to the scheduled dosing visit.

Has been changed to:

Table 5 1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity / Visit [a] / Week	Treatment Period-Year 1												~~W48/ PEOT~~	~~SFU~~ [e]
	Stable Dosing							Flexible Dosing [b]						
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44		
Informed consent	X													
Inclusion/exclusion	X													
Physical exam [c,d]	X			X			X			X			~~X~~	~~X~~
Body weight	X												~~X~~	
Vital signs [e]	X	X	X		X		X		X		X		~~X~~	~~X~~
Hematology and chemistry	X	X	X		X		X		X		X		~~X~~	~~X~~
Urinalysis	X	X	X		X		X		X		X		~~X~~	~~X~~
Urine drug screen	X													
ECG	X												~~X~~	
Pregnancy testing [f]	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
IGRA TB test [g]													~~X~~	
TB questionnaire	X			X			X			X			~~X~~	~~X~~
Blood sample for bimekizumab plasma concentrations [h]	X				X		X				X		~~X~~	~~X~~
Blood sample for anti-bimekizumab antibodies [h]	X				X		X				X		~~X~~	~~X~~
PASI	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
Percentage of BSA	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
IGA	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
DLQI	X						X						~~X~~	
PHQ-9	X	X	X		X		X		X		X		~~X~~	~~X~~

Table 5 1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity \ Visit [a]/ Week	Treatment Period-Year 1												~~W48/ PEOT~~	~~SFU~~ [e]
	Stable Dosing							Flexible Dosing [b]						
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44		
eC-SSRS	X	X	X		X		X		X		X		~~X~~	~~X~~
mNAPSI [i]	X						X						~~X~~	
Scalp IGA [j]	X						X						~~X~~	
pp-IGA[k]	X						X						~~X~~	
EQ-5D-3L	X						X						~~X~~	
SF-36	X						X						~~X~~	
PGA of PSO	X						X						~~X~~	
PASE [l]	X												~~X~~	
PGADA[l]	X						X						~~X~~	
WPAI-SHP V2.0	X						X						~~X~~	
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
IRT	X	X	X	X	X	X	X	X	X	X	X	X	~~X~~	~~X~~
Bimekizumab administration[m, n]	X	X	X	X	X	X	X	X	X	X	X	X		
Subject training on self-injection[o]											X	X		

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; ~~PEOT=Premature End of Treatment;~~ PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire 9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; SF-36=Short Form 36-item Health Survey; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks~~; SFU=Safety Follow-Up;~~ TB=tuberculosis; W=Week; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from the first dose at all visits ~~except SFU. The Safety Follow-Up Visit window is ±7 days from final dose~~.

Table 5 1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity / Visit [a] / Week	Treatment Period-Year 1												~~W48/ PEOT~~	~~SFU~~ [e]
	Stable Dosing							Flexible Dosing [b]						
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44		

[b] At Week 24 ~~only,~~ for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).
[e] ~~The SFU Visit will occur 20 weeks after the final dose.~~
[c] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.
[d] The physical examination will be performed as per Section 9.3.5.
e Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.
[f] Urine pregnancy testing will be performed at all visits ~~Pregnancy testing will consist of serum testing at Baseline and Week 48/PEOT. Urine pregnancy tests will be performed at all other visits~~. Pregnancy test results must be negative prior to administering IMP.
[g] Ensure that results for the latest IGRA test performed in the feeder study are negative ~~an IGRA test was performed during the last dosing visit of the feeder study and the result was negative~~.
[h] All blood samples taken prior to dosing.
i The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.
[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.
[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.
[l] The PGADA and the PASE are assessed only for subjects with PsA at Baseline in the feeder studies.
[m] The dosing window is ±7 days relative to the scheduled dosing visit.
[n] Only subjects receiving IMP Q4W are dosed on Week s 4, 12, 20, 28, 36, and 44.
[o] Subject training on self-injection to be performed as described in Section 7.2.

Change #16

A new schedule of assessments (Table 5-2) has been added for years 2 and 3.

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Visit [a]/ Week / Protocol activity	Treatment Period – Years 2 and 3 [b]																							W144 / PEOT	SFU[c]
	48	52H	56H	60	64H	68H	72	76H	80H	84	88H	92H	96	100H	104H	108	112H	116H	120	124H	128H	132	136H	140H	
Physical exam [d,e]	X			X			X			X			X			X			X			X			X	X
Body weight	X												X												X	X
Vital signs [f]	X			X			X			X			X			X			X			X			X	X
Hematology and chemistry	X			X			X			X			X			X			X			X			X	X
Urinalysis	X			X			X			X			X			X			X			X			X	X
ECG	X												X												X	
Urine pregnancy testing [g]	X			X			X			X			X			X			X			X			X	X
IGRA TB test	X												X												X	
TB questionnaire	X			X			X			X			X			X			X			X			X	
Blood sample for bimekizumab plasma concentrations [h]	X						X						X						X						X	X
Blood sample for anti-bimekizumab antibodies [h]	X						X						X						X						X	X
PASI	X			X			X			X			X			X			X			X			X	
Percentage of BSA	X			X			X			X			X			X			X			X			X	
IGA	X			X			X			X			X			X			X			X			X	
DLQI	X						X						X									X			X	

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Visit [a] / Week / Protocol activity	Treatment Period – Years 2 and 3 [b]																								W144 / PEOT	SFU[c]
	48	52H	56H	60	64H	68H	72	76H	80H	84	88H	92H	96	100H	104H	108	112H	116H	120	124H	128H	132	136H	140H		
PHQ-9	X			X			X			X			X			X			X			X			X	X
eC-SSRS	X			X			X			X			X			X			X			X			X	X
mNAPSI [i]	X						X						X						X						X	
Scalp IGA [j]	X						X						X						X						X	
pp-IGA [k]	X						X						X						X						X	
EQ-5D-3L	X						X						X						X						X	
SF-36	X						X						X						X						X	
PGA of PSO	X						X						X						X						X	
PASE[l]	X												X												X	
PGADA[l]	X												X												X	
WPAI-SHP V2.0	X												X									X			X	
TSQM-9	X																									
Concomitant medication	X			X			X			X			X			X			X			X			X	X
Adverse events	X			X			X			X			X			X			X			X			X	X
IRT	X			X			X			X			X			X			X			X			X	X
Bimekizumab self-injection [m,n]	X[o]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
IMP accountability for self-injection at home[p]				X			X			X			X			X			X			X			X	

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; H=home; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Visit [a] / Week / Protocol activity	Treatment Period – Years 2 and 3 [b]																							W144 / PEOT	SFU[c]
	48	52H	56H	60	64H	68H	72	76H	80H	84	88H	92H	96	100H	104H	108	112H	116H	120	124H	128H	132	136H	140H	

Index; PEOT=Premature End of Treatment; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire-9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; SFU=Safety Follow-Up; TB=tuberculosis; TSQM-9=Treatment Satisfaction Questionnaire for Medication; W=Week; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Note: Starting at Week 48 of the Treatment Period, subjects may self-inject IMP at home; self-injection training will be provided to the subject/caregivers by qualified site personnel (see Section 7.2).

[a] Visit windows of ±7 days from the first dose at all visits except SFU. The Safety Follow-Up Visit window is ±7 days from final dose.

[b] Starting at Week 48 of the Treatment Period, subjects will attend site visits every 12 weeks.

[c] The SFU Visit will occur 20 weeks after the final dose.

[d] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[e] The physical examination will be performed as per Section 9.3.5.

[f] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[g] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.

[h] All blood samples taken prior to dosing.

[i] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.

[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.

[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.

[l] The PGADA and the PASE are assessed only for subjects with PsA at Baseline in the feeder studies.

[m] The dosing window is ±7 days relative to the scheduled dose.

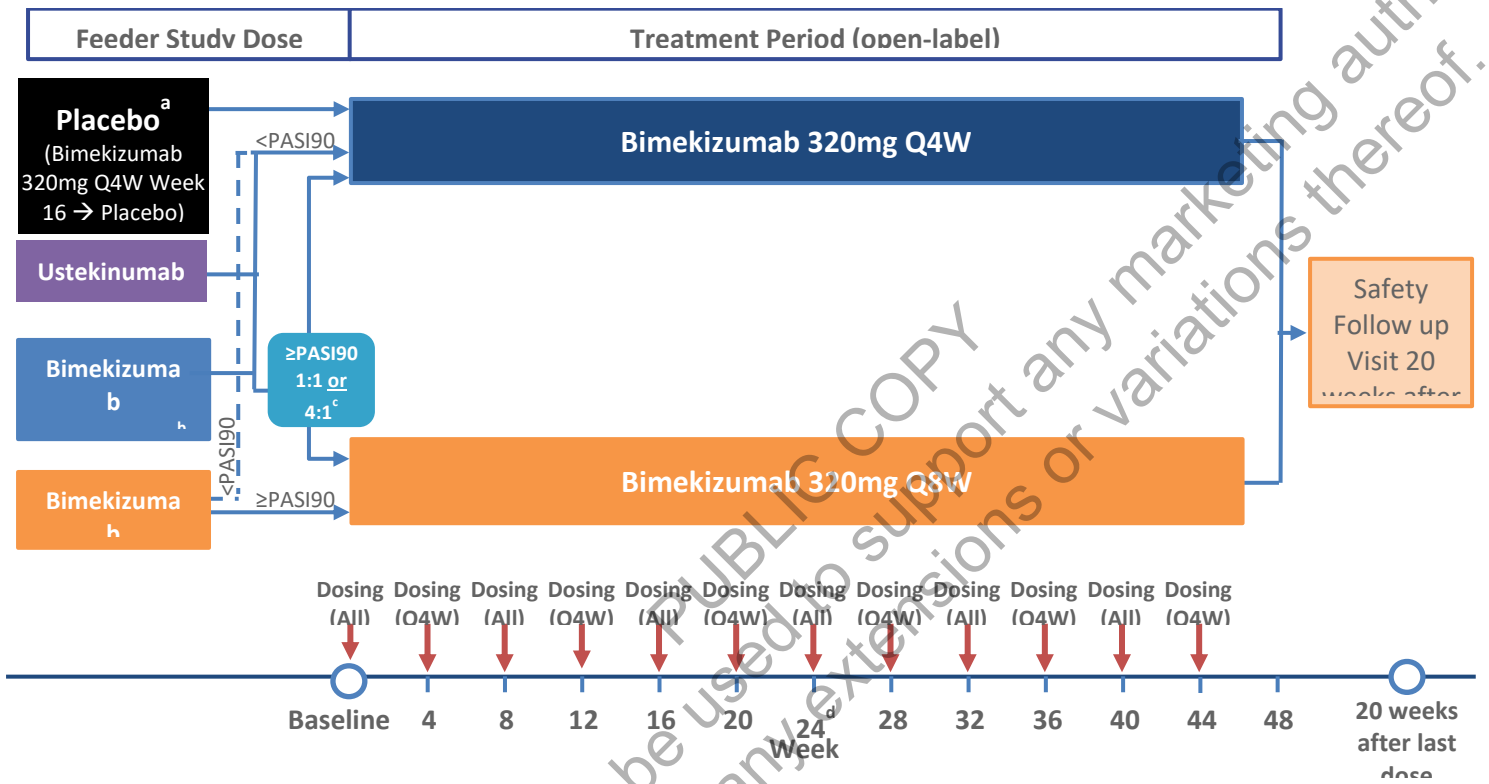
[n] The last dose for subjects receiving bimekizumab 320mg Q4W will be Week 140 and the last dose for subjects receiving bimekizumab 320mg Q8W will be Week 136.

[o] At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

[p] If self-injected at home, the subject/caregiver will document the date, body location, kit number and time point of administration of study medication. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

Change #17

Figure 5–1: Schematic diagram



PASI= Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks

Note: At Week 28 and all following visits, subjects on continuous treatment with the same IMP for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.

a Subjects on placebo after a Week 16 response (≥PASI90) on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study may enroll in PS0014.

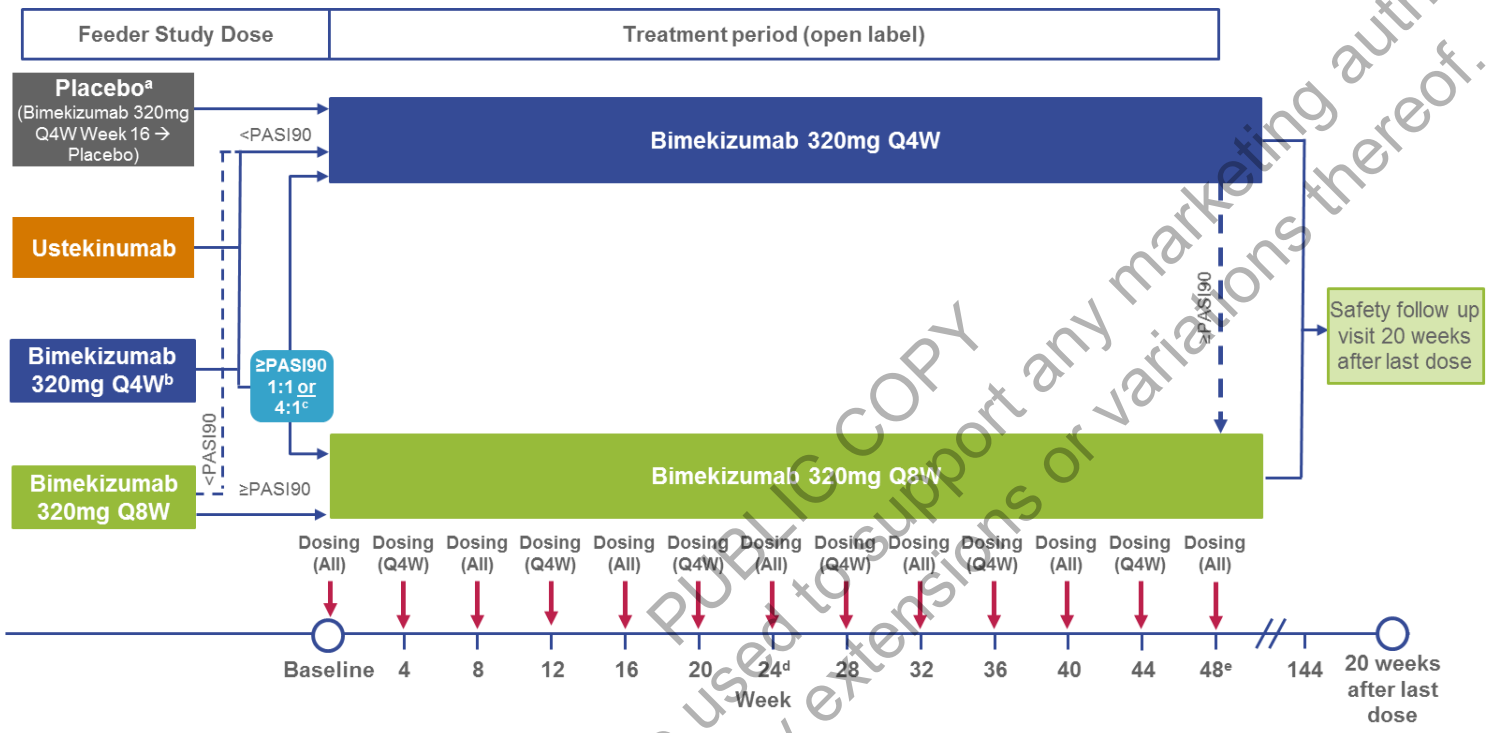
b Subjects on bimekizumab 320mg Q4W who achieved a PASI50 at Week 12 in the escape arm of the feeder study may enroll in PS0014.

c Subjects on ustekinumab or bimekizumab 320mg Q4W in feeder studies who achieved PASI90 will be randomized, respectively, 1:1 or 4:1 to bimekizumab 320mg Q4W or 320mg Q8W.

d At Week 24 only, if PASI90 is achieved, Investigator may change the dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W.

Has been changed to:

Figure 5–1: Schematic diagram



IMP=investigational medicinal product; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks

Note: Self-injection will be allowed from Week 48 onward.

Note: At Week 28 and all following visits, subjects on continuous treatment with the same IMP for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.

[a] Subjects on placebo after a Week 16 response (≥PASI90) on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study may enroll in PS0014.

[b] Subjects on bimekizumab 320mg Q4W who achieved a PASI50 at Week 12 in the escape arm of the feeder study may enroll in PS0014.

[c] Subjects on ustekinumab or bimekizumab 320mg Q4W in feeder studies who achieved PASI90 will be randomized, respectively, 1:1 or 4:1 to bimekizumab 320mg Q4W or 320mg Q8W.

[d] At Week 24 ~~only~~, if PASI90 is achieved, Investigator may change the dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W (optional).

[e] At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

Change #18

Section 5.8 Rationale for study design and selection of dose

PS0014 is an open-label study designed to assess the long-term safety, tolerability, and efficacy of bimekizumab over a 48-week Treatment Period. Doses used in this study are based on the dosing regimens (Q4W and Q8W) of the feeder studies, as well as the subjects' PASI score upon entering the study, and can be adjusted at Week 24 only for subjects receiving bimekizumab 320mg Q4W at the discretion of the Investigator. Subjects in the feeder studies who responded without biologic intervention are not eligible for PS0014.

Has been changed to:

PS0014 is an open-label study designed to assess the long-term safety, tolerability, and efficacy of bimekizumab over a 144 ~~48~~-week Treatment Period. Doses used in this study are based on the dosing regimens (Q4W and Q8W) of the feeder studies, as well as the subjects' PASI score upon entering the study. **Subjects who do not achieve a PASI90 response in the feeder studies may be enrolled in PS0014 at the discretion of the Investigator. In the PS0011 study, a multicenter, 48-week, double-blind, placebo-controlled, parallel-group extension study to assess the long-term safety, tolerability, and efficacy of bimekizumab in adult subjects with moderate to severe chronic plaque PSO, 97% of subjects receiving 320mg Q4W were PASI90 responders at Week 52 (full analysis set, observed case). In addition, all subjects (100%) achieved a PASI75 response by Week 52.** ~~, and~~

In PS0014, doses can be adjusted at Week 24 ~~only~~ for subjects receiving bimekizumab 320mg Q4W at the discretion of the Investigator **(optional). At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.**

Subjects in the feeder studies who responded without biologic intervention are not eligible for PS0014.

Change #19

Section 6.1 Inclusion criteria

4. Female subjects of childbearing potential must continue to use an acceptable method of contraception (as detailed in the feeder study) for up to 20 weeks after the final dose of bimekizumab in PS0014.

Has been changed to:

4. Female subjects must be:~~Female subjects of childbearing potential must continue to use an acceptable method of contraception (as detailed in the feeder study) for up to 20 weeks after the final dose of bimekizumab in PS0014.~~

- **Postmenopausal: Menopause is defined as 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause.**
- **Permanently sterilized (eg, tubal occlusion, hysterectomy, bilateral salpingectomy)**

- **Or, if of childbearing potential (and engaged in sexual activity that could result in procreation), must be willing to use a highly effective method of contraception throughout the duration of the study until 20 weeks after last administration of IMP, and have a negative pregnancy test at the Baseline/Feeder study final visit in PS0014. The following methods are considered highly effective when used consistently and correctly:**
  - **Combined (estrogen and progestogen) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal)**
  - **Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)**
  - **Intrauterine device**
  - **Intrauterine hormone-releasing system**
  - **Vasectomized partner**
  - **Abstinence as a form of birth control is generally not allowed in the study unless abstinence is in accordance with a subject's preferred and common lifestyle. Study personnel must confirm the continued use of abstinence is still in accordance with the subject's lifestyle at regular intervals during the study.**

Change #20

Section 6.2 Exclusion criteria; criterion 3

3. Subject has any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the subject's ability to participate in this study.

   Note: For any subject with an ongoing SAE, or a history of serious infections in the feeder study, the Medical Monitor must be consulted prior to the subject's entry into PS0014.

Has been changed to:

3. Subject has any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the subject's ability to participate in this study.

   Note: For any subject with an ongoing SAE, or a history of serious infections in the feeder study, the Medical Monitor must be consulted prior to the subject's entry into PS0014, **although the decision on whether to enroll the subject remains with the Investigator**.

And criterion 4:

4. Subject must have a negative interferon gamma release assay (IGRA) as measured at the final dosing visit of the feeder study.

Has been changed to:

4. ~~Subject must have a negative interferon gamma release assay (IGRA) as measured at the final dosing visit of the feeder study.~~ **Subject has a positive or indeterminate interferon gamma release assay (IGRA) in a feeder study, unless appropriately evaluated and treated as per Section 9.3.1.**

Change #21

Section 6.3 Withdrawal criteria; criterion 11, first sentence

11. Subjects **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:

Has been changed to:

11. Subjects **must be referred** immediately to a mental health care professional **(ie, locally licensed psychiatrist, psychologist, or master's level therapist)** and may be withdrawn from the study based upon the Investigator's judgment of benefit/risk for:

And criterion 12, first sentence

12. Subjects must be referred immediately to a mental healthcare professional and must be withdrawn for:

Has been changed to:

12. Subjects must be referred immediately to a mental healthcare professional **(ie, locally licensed psychiatrist, psychologist, or master's level therapist)** and must be withdrawn for:

Change #22

Section 6.3.1 Potential drug-induced liver injury IMP discontinuation criteria; paragraph 3, fist bullet:

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

Has been changed to:

- Subjects with ALT or AST ≥3xULN who exhibit temporally associated symptoms of hepatitis or hypersensitivity. Hepatitis symptoms include fatigue, nausea, vomiting, right upper quadrant pain or tenderness. Hypersensitivity symptoms **could** include fever ~~(without clear alternative cause)~~, rash, or eosinophilia (ie, >5%) **(without clear alternative cause)**.

Change #23

Section 7.1 Description of IMP, paragraph 1

The IMP used in this study is bimekizumab. Bimekizumab will be manufactured using 2 manufacturing processes: Process 4 (Phase 3 clinical supply manufacturing process) and Process 5 (planned commercial manufacturing process). Bimekizumab will be supplied in a 1mL prefilled syringe at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection.

Has been changed to:

The IMP used in this study is bimekizumab. Bimekizumab will be manufactured using 2 manufacturing processes: Process 4 (Phase 3 clinical supply manufacturing process) and Process 5 (planned commercial manufacturing process). Bimekizumab will be supplied in a 1mL

prefilled syringe or a 1ml prefilled auto-injector (only in some countries) at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection.

Change #24

Section 7.2 Treatments to be administered, paragraphs 5, 6, 7, 8, 9

At Week 24 only, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W.

Has been changed to:

At Week 24 ~~only~~, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W (**optional).At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.**

After Week 48 and in between the scheduled study visits at the site, subjects will have the option to perform self-injection at home. All other injections will be administered preferably by self-injection during scheduled visits. Self-injection training will be provided to the subject/caregivers by qualified site personnel at Week 40 and Week 44. After Week 48, the subject/caregiver will perform administration under the supervision of the site staff to ensure that study medication is being properly and safely injected.

Once subjects/caregivers as determined by the Investigator (or designee) have been trained, the study medication may be administered at home. The subject will receive the required number of syringes for injections at each visit needed to perform the Q4W or Q8W administrations at home. Subjects who are unable to or decide not to self-inject IMP or those without a family member/friend/caregiver who can help, will not be discontinued, but may continue to visit the site for unscheduled visits for IMP administration only.

If administered at home, the subject/caregiver will document the date, body location, kit number and time point of administration of study medication.

All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

Change #25

Section 7.5 Handling and storage requirements

The following paragraph has been added:

In addition, the Investigator (or designee) will instruct the subject on how to handle the IMP during the transport and how to store the IMP following the instruction guide. Cooler bags with freezer packs will be provided to the subjects. Specific attention will be put on the transport from site to home using cold bags, and the subject will be instructed to put

the IMP as quickly as possible into his/her refrigerator. In case of broken refrigerator, or broken or lost syringes, the subject will inform the site immediately and new IMP will be prepared. All efforts should be made to follow the treatment scheme as per protocol.

Change #26

Section 7.7 Procedures for monitoring subject 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.

Has been changed to:

During **Year 1 of** 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.

After Week 48, self-injection at home will be possible at the following weeks: Weeks 52,56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. Dates, locations, kit numbers and time of self-injection will be captured using a home administration form. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit. Completed home administration forms should be reviewed by the Investigator.

If a subject is noncompliant with the study procedures or medications that may present a risk to the safety of the subject in the opinion of the Investigator, then the subject should be withdrawn as described in Section 6.3.

Change #27

Section 7.8.1.2 Other medications, paragraph 1

Subjects may take pain relievers (acetaminophen/paracetamol, non-steroidal anti-inflammatory drugs, opiates) as needed for pain but not within 24 hours of the Baseline and Week 48 Visits. Intra-articular injections (eg, steroids, hyaluronic acid) are permitted and must be carefully recorded in the eCRF.

Has been changed to:

Subjects may take pain relievers (acetaminophen/paracetamol, non-steroidal anti-inflammatory drugs, opiates) as needed for pain but not within 24 hours of the Baseline and Week ~~48~~**144** Visits. Intra-articular injections (eg, steroids, hyaluronic acid) are permitted and must be carefully recorded in the eCRF.

Change #28

Section 8 Study procedures by visit

Table 5-1 (Schedule of study assessments) provides a general overview of study assessments. A list of procedures to be completed at each visit is described below.

Has been changed to:

Table 5-1 (Schedule of study assessments) provides a general overview of study assessments **in Year 1 (Weeks 0 to 44). Table 5-2 (Schedule of study assessments) provides a general overview of study assessments in Years 2 and 3 (Weeks 48 to 144).** A list of procedures to be completed at each visit is described below.

Change #29

Section 8.1.1.1 Baseline/Feeder Study Final Visit

The following bullet:

- Serum pregnancy test

Has been changed to:

- ~~Serum~~ **Urine pregnancy test**

Change #30

Section 8.1.1.2 Week 4 Visit (±7 days relative to Baseline)

The first bullet has been deleted from the list:

- ~~Physical exam~~

Change #31

Section 8.1.1.6 Week 24 Visit (±7 days relative to Baseline); last paragraph

At Week 24 only, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W.

Has been changed to:

At Week 24 ~~only~~, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).

Change #32

Section 8.1.2.1 Week 28 and Week 44 Visits (±7 days relative to Baseline)

Has been changed to:

Section 8.1.2.1 Week 28 Visit ~~and Week 44 Visits~~ (±7 days relative to Baseline)

Change #33

Section 8.1.2.3 Week 36 Visit (±7 days relative to Baseline)

A new bullet has been added to the list:

- **Physical exam**

Change #34

Section 8.1.2.4 Week 40 Visit (±7 days relative to Baseline)

A new paragraph has been added:

Self-injection training will be provided to the subject/caregivers by qualified site personnel to allow self-injection to be performed at home after Week 48 (see Section 7-2).

Change #35

A new subsection has been added and subsequent subsections were renumbered accordingly:

Section 8.1.2.5 Week 44 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- **PASI**
- **Percentage of BSA**
- **IGA**
- **Urine pregnancy test**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur.

Self-injection training will be provided to the subject/caregivers by qualified site personnel to allow self-injection to be performed at home after Week 48 (see Section 7.2).

Change #36

Section 8.1.2.6 Week 48 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded:

- Physical exam
- Body weight
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Serum pregnancy test

  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- ECG
- IGRA TB test
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Concomitant medication
- AEs
- Contact IRT

Has been changed to:

Section 8.1.2.6 Week 48 Visit (±7 days relative to Baseline)

At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- Physical exam
- Body weight

- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - ~~Serum~~ **Urine** pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
  - **IGRA TB test**
- ECG
- ~~IGRA TB test~~
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- mNAPSI for subjects with nail involvement at Baseline
- Scalp IGA for subjects with scalp involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L
- SF-36
- PGA of PSO
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- **TSQM-9**
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, subjects will be given the opportunity for self-injection of bimekizumab (see Section 7.2).

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Change #37

The following new subsections have been added:

Section 8.1.2.7 Self-injection at home injection (Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136 and 140)

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136 and 140.

Subjects receiving bimekizumab 320mg Q8W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 56, 64, 80, 88, 104, 112, 128, and 136.

- Adverse events will be captured spontaneously if the subject decides to visit the site to receive the bimekizumab administration.
- **All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit (Section 7.2).**

Section 8.1.2.8 Week 60, Week 84, Week 108, and Week 132 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- **Physical exam**
- **Vital signs**
- **Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:**
  - **Hematology and chemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
- **TB questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **DLQI (Week 132 only)**

- **PHQ-9**
- **WPAI-SHP V2.0 (Week 132 only)**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Section 8.1.2.9 Week 72 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- **Physical exam**
- **Vital signs**
- **Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:**
  - **Hematology and chemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**
- **TB questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **DLQI**
- **PHQ-9**
- **eC-SSRS**
- **mNAPSI for subjects with nail involvement at Baseline**
- **Scalp IGA for subjects with scalp involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **EQ-5D-3L**

- **SF-36**
- **PGA of PSO**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4Wor Q8W dosing will occur, preferably by self-injection.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Section 8.1.2.10 Week 96 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded:

- **Physical exam**
- **Body weight**
- **Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling**
- **Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:**
  - **Hematology and chemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**
  - **IGRA TB test**
- **ECG**
- ~~IGRA TB test~~
- **TB questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **DLQI**
- **PHQ-9**
- **eC-SSRS**
- **mNAPSI for subjects with nail involvement at Baseline**

- **Scalp IGA for subjects with scalp involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **EQ-5D-3L**
- **SF-36**
- **PGA of PSO**
- **PASE**
- **PGADA (only for subjects with PsA)**
- **WPAI-SHP V2.0**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Section 8.1.2.11 Week 120 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

- **Physical exam**
- **Vital signs**
- **Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:**
  - **Hematology and chemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**
- **TB questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **PHQ-9**
- **eC-SSRS**

- **mNAPSI for subjects with nail involvement at Baseline**
- **Scalp IGA for subjects with scalp involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **EQ-5D-3L**
- **SF-36**
- **PGA of PSO**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W or Q8W dosing will occur, preferably by self-injection.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Section 8.1.2.12 Week 144 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded:

- **Physical exam**
- **Body weight**
- **Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling**
- **Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:**
  - **Hematology and chemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**
  - **IGRA TB test**
- **ECG**
- ~~**IGRA TB test**~~
- **TB questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**

- **DLQI**
- **PHQ-9**
- **eC-SSRS**
- **mNAPSI for subjects with nail involvement at Baseline**
- **Scalp IGA for subjects with scalp involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **EQ-5D-3L**
- **SF-36**
- **PGA of PSO**
- **PASE**
- **PGADA (only for subjects with PsA)**
- **WPAI-SHP V2.0**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

Return of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Change #38

Section 8.2 Premature End of Treatment Visit; first bullet

- The subject will be withdrawn from IMP, will undergo the same assessments as the Week 48 visit (see Section 8.1.2.5), and will enter the SFU Period.

Has been changed to:

- The subject will be withdrawn from IMP, will undergo the same assessments as the Week **144** visit (see ~~Section 8.1.2.5~~**Section 8.1.2.12**), and will enter the SFU Period.

Change #39

Section 8.3 Safety Follow-Up Visit (20 weeks after final dose, ±7 days)

All subjects, including those withdrawn from IMP, will have a SFU Visit 20 weeks after their final dose of IMP.

The following procedures/assessments will be performed/recorded:

- Physical exam
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling

- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- TB questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

Has been changed to:

All subjects, including those withdrawn from IMP, will have a SFU Visit 20 weeks after their final dose of IMP.

The following procedures/assessments will be performed/recorded:

- Physical exam
- **Body weight**
- Vital signs (sitting SBP and DBP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- ~~TB questionnaire~~
- ~~PASI~~
- ~~Percentage of BSA~~

- ~~IGA~~
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

Change #40

Section 8.4 Unscheduled Visit

At the Investigator's discretion, an Unscheduled Visit may be completed at any time during the study, but prior to the SFU Visit, if deemed necessary for the subject's safety and well-being.

If an Unscheduled Visit is conducted due to safety or efficacy reasons, an eC-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), an eC-SSRS will not be required at these visits.

At this visit, any assessment may be performed, as needed, depending on the reason for the visit.

Has been changed to:

At the Investigator's discretion, an Unscheduled Visit may be completed at any time during the study, but prior to the SFU Visit, if deemed necessary for the subject's safety and well-being.

If an Unscheduled Visit is conducted due to safety or efficacy reasons, an eC-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, **injection for subjects not making use of home self-injections**), an eC-SSRS will not be required at these visits.

At this visit, any assessment may be performed, as needed, depending on the reason for the visit.

Change #41

Table 9-2; the following has been removed from the table:

~~Serum pregnancy testing~~

And footnote c:

Urine pregnancy testing will be performed at all visits consist of serum testing at Baseline and Week 48/PEOT Visit. Urine pregnancy tests will be performed at all other visits.

Has been changed to:

Urine pregnancy testing will be performed at all visits ~~consist of serum testing at Baseline and Week 48/PEOT Visit. Urine pregnancy tests will be performed at all other visits.~~

Change #42

Table 9 3: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
≥3xULN	≥2xULN[b]	NA	Hepatology consult[c]. Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and subject discussed with Medical Monitor ASAP.	Immediate, permanent IMP discontinuation.	Essential: Must have repeat liver chemistry values and additional testing completed ASAP (see Section 9.2.1.2.1); 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.[d]
≥3xULN	NA	Yes				
≥8xULN	NA	NA	Need for hepatology consult to be discussed (required if ALT or AST ≥8xULN). Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and subject discussed with Medical Monitor ASAP.	Immediate, permanent IMP discontinuation		

≥5xULN (and ≥2x baseline) and <8xULN	<2xULN	No	Discussion with Medical Monitor required. Consider need for hepatology consult if there is no evidence of resolution (see Follow up requirements). [c]	Further investigation – immediate IMP discontinuation not required (see Section 9.2.1.2). IMP discontinuation required if any of the following occur: • Subject cannot comply with monitoring schedule. • Liver chemistry values continue to increase • Liver chemistry values remain ≥5xULN (and ≥2x Baseline) after 4 weeks of monitoring without evidence of resolution	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 9.2.1.2.1).	Monitoring of liver chemistry values at least twice per week for 2 weeks.[d] • Immediate IMP discontinuation required if liver chemistry values continue to increase. After 2 weeks of monitoring liver chemistry values: • ALT or AST remains ≥5xULN <8xULN, IMP should be temporarily withheld and subject should undergo repeat test in 2 weeks. Continue IMP if ALT or AST values <5xULN; continue to monitor at least twice per week until values normalize, stabilize, or return to within Baseline values. If ALT or AST remains ≥5xULN after second re-test, immediate, permanent IMP discontinuation required.

Table 9 3: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
						Continue to monitor until values normalize, stabilize, or return to within baseline values.[d]

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

[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 subject also has ≥2xULN ALP, the possibility of an indication of biliary obstruction should be discussed with the Medical Monitor.

[c] Details provided in Section 9.2.1.1. 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] 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.

Has been changed to:

Table 9-5: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
≥3xULN	≥2xULN[b]	NA	Hepatology consult[c]. Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and subject discussed with	Immediate, permanent IMP discontinuation.[e]	Essential: Must have repeat liver chemistry values and additional testing completed ASAP (see Section	Monitoring of liver chemistry values at least twice per week until values normalize,
≥3xULN	NA	Yes				

Table 9-5: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
			Medical Monitor ASAP.		9.2.1.2.1); recommended to occur at the site with HCP.	stabilize, or return to within baseline values.[d]
≥8xULN	NA	NA	Hepatology consult. ~~Need for hepatology consult to be discussed (required if ALT or AST ≥8xULN).~~ Medical Monitor must be notified within 24 hours (eg, by laboratory alert) and subject discussed with Medical Monitor ASAP.	Immediate, permanent IMP discontinuation		

≥5xULN ~~(and ≥2x baseline)~~ and <8xULN	<2xULN	No	Discussion with Medical Monitor required. Consider need for hepatology consult if there is no evidence of resolution (see Follow up requirements). [c]	Further investigation – immediate IMP discontinuation not required (see Section 9.2.1.2). IMP discontinuation required if any of the following occur: • Subject cannot comply with monitoring schedule. • Liver chemistry values continue to increase • Liver chemistry values remain ≥5xULN ~~(and ≥2x Baseline)~~ after 4 weeks of monitoring without evidence of resolution	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 9.2.1.2.1).	Monitoring of liver chemistry values at least twice per week for 2 weeks.[d] • Immediate IMP discontinuation required if liver chemistry values continue to increase. After 2 weeks of monitoring liver chemistry values: • ALT or AST remains ≥5xULN <8xULN, IMP should be temporarily withheld and subject should undergo repeat test in 2 weeks. Continue IMP if ALT or AST values <5xULN; continue to monitor at least twice per week until values normalize, stabilize, or return to within Baseline values. If ALT or AST remains ≥5xULN after second re-test, immediate, permanent IMP discontinuation required.

Table 9-5: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis of hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
						Continue to monitor until values normalize, stabilize, or return to within baseline values.[d]

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

[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 subject also has ≥2xULN ALP, the possibility of an indication of biliary obstruction should be discussed with the Medical Monitor.

[c] Details provided in Section 9.2.1.1. 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] 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.

[e] Details provided in Section 9.2.1.2.1.

Change #43

Section 9.2.1.2.1 Investigational medicinal product restart/rechallenge

Rechallenge with IMP can occur only if ALL of the following requirements are met:

- The results of additional testing and monitoring described Section 9.2.1.3 and Section 9.2.1.4 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).
- The subject has shown clear therapeutic benefit from the IMP.
- Subject's ALT or AST elevations do not exceed ≥5xULN.
- Subject's total bilirubin is <2xULN.
- Subject has no signs or symptoms of hypersensitivity or hepatitis
- The rechallenge is approved by the UCB responsible physician, Data Monitoring Committee (DMC), and a hepatologist. The hepatologist must be external to UCB but may be a member of the DMC. It is recommended that the hepatologist be a local hepatology expert or the hepatologist treating the subject.
- Subject agrees to the Investigator-recommended monitoring plan.

Has been changed to:

Subjects who are immediately discontinued from IMP due to having met certain criteria for PDILI (as described in Section 6.3.1 and Table 9-3), but for whom an alternative diagnosis is confirmed, ie, drug-induced liver injury is excluded, can rarely restart IMP.

Rechallenge with IMP can occur only if ALL of the following requirements are met **at the time of the rechallenge**:

- The results of additional testing and monitoring described Section 9.2.1.3and Section 9.2.1.4confirm a nondrug-related cause for the abnormal hepatic laboratory parameters and any associated symptoms (ie, a subsequent alternative diagnosis fully explains the hepatic findings).
- The subject has shown clear therapeutic benefit from the IMP.
- Subject's ALT or AST elevations do not exceed ≥5xULN.
- Subject's total bilirubin is <2xULN.
- Subject has no signs or symptoms of hypersensitivity or hepatitis
- The rechallenge is approved by the UCB responsible physician~~, Data Monitoring Committee (DMC), and a hepatologist. The hepatologist must be external to UCB but may be a member of the DMC. It is recommended that the hepatologist be a local hepatology expert or the hepatologist treating the subject~~.
- Subject agrees to the Investigator-recommended monitoring plan.

Change #44

Section 9.3.1.2 Tuberculosis 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 Table 5-1. The questionnaire will assist with the identification of subjects who may require therapy for TB. A subject who answers "Yes" to the question "Has the subject been in close contact with an individual with active TB, or an individual who has recently been treated for TB?" at Baseline is excluded (see Exclusion Criterion #4, Section 6.2). A "Yes" response to any of the other questions within the questionnaire at Baseline should trigger further careful assessment to determine if subject has LTBI or active TB. A "Yes" response to any of the questions during the study should trigger further assessments to determine if the subject has either LTBI or active TB infection.

Has been changed to:

The questionnaire "Evaluation of signs and symptoms of tuberculosis" should be used as a source document. The questionnaire will be completed as described in Table 5-1 **and Table 5-2**. The questionnaire will assist with the identification of subjects who may require therapy for TB. ~~A subject who answers "Yes" to the question "Has the subject been in close contact with an individual with active TB, or an individual who has recently been treated for TB?" at Baseline is excluded (see Criterion #4, Section 6.2). A "Yes" response to any of the other questions within the questionnaire at Baseline should trigger further careful assessment to determine if subject has LTBI or active TB.~~ A "Yes" response to any of the questions during the study should trigger further assessments to determine if the subject has either LTBI or active TB infection.

Change #45

Section 9.3.2 Pregnancy testing

Pregnancy testing will consist of serum testing at Baseline and Week 48/PEOT, and urine pregnancy testing at all other visits as specified in Table 5-1.

The Baseline Visit serum pregnancy testing results must be negative, and received and reviewed prior to administration of IMP. A negative urine pregnancy test result must be obtained immediately prior to each administration of IMP at the visits specified in Table 5-1. Pregnancy tests should be administered to all female subjects of childbearing potential, regardless of their use of birth control.

Has been changed to:

Urine pregnancy testing will be performed at all visits ~~Pregnancy testing will consist of serum testing at Baseline and Week 48/PEOT, and urine pregnancy testing at all other visits~~ as specified in Table 5-1 **and Table 5-2**.

The Baseline Visit ~~serum~~ pregnancy testing results must be negative, and received and reviewed prior to administration of IMP. A negative urine pregnancy test result must be obtained immediately prior to each administration of IMP at the visits specified in Table 5-1 **and Table 5-2**. Pregnancy tests should be administered to all female subjects of childbearing potential, regardless of their use of birth control.

Change #46

Section 9.3.6 Body weight

Body weight will be measured at Baseline and at the Week 48/PEOT Visit.

Has been changed to:

Body weight will be measured at Baseline and ~~at the Week 48/PEOT Visit~~ **at the visits specified in Table 5-1 and Table 5-2**.

Change #47

Section 9.3.8 Patient Health Questionnaire 9

A new subsection has been added (moved from Section 10.4):

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression. The PHQ-9 scores for depression range from 0 to 27, with higher scores indicating 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.

The PHQ-9 will be assessed at the visits specified in Table 5-1 and Table 5-2.

Refer to Section 6.3 for PHQ-9-related withdrawal criteria.

Change #48

Section 10.4 Patient Health Questionnaire 9

This subsection has been moved to Section 9.3.8

Change #49

Section 10.11 Psoriatic Arthritis Screening and Evaluation questionnaire

The last sentence of the first paragraph has been deleted:

~~Subjects with scores ≥47 should be referred to a rheumatologist for evaluation.~~

Change #50

Section 10.14 Treatment Satisfaction Questionnaire for Medication (TSQM-9)

A new subsection has been added:

The TSQM-9 (Bharmal et al, 2009) is a 9-item measure developed to provide a suitable measure of treatment satisfaction with medication. It has 5 to 7 Likert response options per item and consists of 3 subscales: effectiveness (3 items), convenience (3 items), and a global satisfaction scale (3 items). The TSQM-9 was developed from the TSQM 1.4 (Atkinson et al, 2004) which has an additional subscale which measures side effects (3 items). The estimated completion time for this measure is less than 5 minutes. Scores range from 0 (worst) to 100 (best).

The TSQM will be performed at Week 48.

Change #51

Section 14.1 Definition of analysis sets, paragraph 4

The Pharmacokinetics Per-Protocol Set (PK-PPS) will consist of all enrolled subjects who receive at least 1 dose of the IMP and provide at least 1 quantifiable plasma concentration postdose in PS0014.

Has been changed to:

The Pharmacokinetics Per-Protocol Set (PK-PPS) will consist of all enrolled subjects who receive at least 1 dose of the IMP and provide at least 1 quantifiable plasma concentration postdose **without protocol deviations that would affect the concentration** in PS0014.

Change #52

Section 14.3.2 Other safety analyses; paragraph 2, second bullet:

- Adjusters – This group consists of subjects who experience a dose regimen adjustment at Week 24 only during the study. This means that the subjects in this group had a dose adjustment from 320mg Q4W to 320mg Q8W at Week 24.

Has been changed to:

- Adjusters – This group consists of subjects who experience a dose regimen adjustment at Week 24 **or Week 48** ~~only~~ during the study. This means that the subjects in this group had a dose adjustment from 320mg Q4W to 320mg Q8W at Week 24 **or Week 48**.

Change #53

Section 14.4 Planned efficacy analyses

Efficacy analyses will be summarized based on the FAS. The summaries described in this section will provide data on maintenance of effect of open-label bimekizumab over 48 weeks and beyond. Additionally, it will allow an assessment of the impact of dose adjustments on efficacy results. As these variables are summarized over time and the initial values can be impacted by the treatment in the feeder study, the presentation by the randomized treatment group (feeder study) is intended to provide perspective on the change in these values starting with the initial study randomization (feeder study) through the Treatment Period of PS0014. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline study results by scheduled visit for PS0014.

Responder efficacy variables (PASI75, PASI90, PASI100, IGA, DLQI score of 0 or 1, mNAPSI, and scalp IGA) will be summarized descriptively in the feeder study and overall. The PASI responder variables are derived relative to the Baseline in the feeder study.

Continuous efficacy variables based on the change from Baseline (PASI, DLQI, PHQ-9, PGADA, SF-36, the EQ-5D-3L PCS, MCS and domain scores, WPAI-SHP, PGA of PSO, and PASE) will be summarized using descriptive statistics by scheduled visit and the randomized treatment group in the feeder study and overall. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline results by scheduled visit for PS0014. Figures for selected variables will also be generated in order to demonstrate the kinetics of response over time.

In addition to the summaries described above, the impact of dose regimen adjustment on efficacy will be considered. This will be done primarily by summarizing efficacy variables by the 2 adjuster groups described above. Furthermore, a supportive analysis specifically for dose adjusters will be performed in which PASI score will be summarized by visit, where Baseline is recalibrated for each individual subject and defined as the visit where the bimekizumab 320mg Q8W is initiated. The visits summarized will be in weeks relative to when the dosing regimen is decreased to Q8W, as opposed to the scheduled week of the PS0014 assessment. These summaries will be based on observed case only.

Has been changed to:

Efficacy analyses will be summarized based on the FAS. The summaries described in this section will provide data on maintenance of effect of open-label bimekizumab over **48144 weeks** and beyond. Additionally, it will allow an assessment of the impact of dose adjustments on efficacy results. As these variables are summarized over time and the initial values can be impacted by the treatment in the feeder study, the **presentation using a combination of feeder/extension study treatment groups** ~~by the randomized treatment group (feeder study)~~ is intended to provide perspective on the change in these values **from the feeder study** ~~starting with the initial study randomization (feeder study)~~ through the Treatment Period of PS0014. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline study results by scheduled visit for PS0014.

Responder efficacy variables (PASI75, PASI90, PASI100, IGA, DLQI score of 0 or 1, ~~mNAPSI~~ **mNAPSI75, mNAPSI90, mNAPSI100, pp-IGA** and scalp IGA) will be summarized descriptively ~~in the feeder study and overall~~. The PASI responder variables are derived relative to the Baseline in the feeder study.

Continuous efficacy variables based on the change from Baseline (PASI, DLQI, BSA affected by PSO, ~~PHQ-9~~, PGADA, SF-36, the EQ-5D-3L PCS, MCS and domain scores, WPAI-SHP, PGA of PSO, and PASE) will be summarized using descriptive statistics by scheduled visit ~~and the randomized treatment group in the feeder study and overall~~. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline results by scheduled visit for PS0014. Figures for selected variables will also be generated in order to demonstrate the kinetics of response over time.

In addition to the summaries described above, the impact of dose regimen adjustment on efficacy will be considered. This will be done primarily by summarizing efficacy variables by the ~~2~~ adjuster groups described above. Furthermore, a supportive analysis specifically for dose adjusters will be performed in which PASI score will be summarized by visit, where Baseline is recalibrated for each individual subject and defined as the visit where the bimekizumab 320mg Q8W is initiated. The visits summarized will be in weeks relative to when the dosing regimen is decreased to Q8W, as opposed to the scheduled week of the PS0014 assessment. These summaries will be based on observed case only.

Change #54

Section 14.8 Handling of dropouts or missing data; paragraph 1 and 2

For responder efficacy variables (PASI75, PASI90, PASI100, IGA, DLQI score of 0 or 1, mNAPSI, and scalp IGA), missing data will be handled by nonresponder imputation, meaning

that subjects that discontinue early or who have missing data at a given time point are imputed as though they did not achieve the given response. Supportive summaries will be based on observed case data.

For continuous efficacy variables based on the change from Baseline (PASI, DLQI, PHQ-9, PGADA, SF-36, the EQ-5D-3L PCS, MCS and domain scores, WPAI-SHP, PGA of PSO, and PASE), missing data will be handled by using multiple imputation via the Markov-Chain Monte Carlo method. Supportive summaries will be based on observed case data.

Has been changed to:

For responder efficacy variables (PASI75, PASI90, PASI100, IGA, DLQI score of 0 or 1, ~~mNAPSI~~**mNAPSI75, mNAPSI90, mNAPSI100, pp-IGA** and scalp IGA), missing data will be handled by nonresponder imputation, meaning that subjects that discontinue early or who have missing data at a given time point are imputed as though they did not achieve the given response. Supportive summaries will be based on observed case data.

For continuous efficacy variables based on the change from Baseline (PASI, DLQI, **BSA affected by PSO**, ~~PHQ-9,~~ PGADA, SF-36, the EQ-5D-3L PCS, MCS and domain scores, WPAI-SHP, PGA of PSO, and PASE), missing data will be handled by using multiple imputation via the Markov-Chain Monte Carlo method. Supportive summaries will be based on observed case data.

Change #55

Section 14.9 Planned interim analysis and data monitoring

After the final Week 48 visit, an interim analysis may be performed and a corresponding interim Clinical Study Report (CSR) may be written. A final analysis and updated final CSR will be prepared once all data (through the SFU visit) have been collected.

Has been changed to:

Interim analyses are planned at Week 24 and Week 48, details of which will be documented in the SAP. After the final Week ~~48~~144 visit, an interim analysis may be performed and a corresponding interim Clinical Study Report (CSR) may be written. A final analysis and updated final CSR will be prepared once all data (through the SFU visit) have been collected.

Change #56

Section 17 References

The following references were added:

Atkinson MJ, Sinha A, Hass SL, Colman SS, Kumar RN, Brod M, Rowland CR. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire

for Medication (TSQM), using a national panel study of chronic disease. Health Qual Life Outcomes. 2004;26;2:12.

Bharmal M, Payne K, Atkinson MJ, Desrosiers MP, Morisky DE, Gemmen E. Validation of an abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9) among patients on antihypertensive medications. Health Qual Life Outcomes. 2009; 7:36.

18.2 Protocol Amendment 2

Rationale for the amendment

Change the dose regimen at Week 48 (or at the next scheduled clinic visit after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit) from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W, based on pooled data from the Phase 3 studies (PS0008, PS0009, and PS0013), which demonstrated that during the maintenance period bimekizumab 320mg Q8W provided essentially the same efficacy as bimekizumab 320mg Q4W.

Correct the omission of Canada from the list of countries where the PS0014 substudy evaluating the safe and effective use of self-injecting device presentations will be conducted. Correction of this error ensures consistency with the substudy protocol (DV0002).

Added provision for collecting a concurrent sample for central laboratory testing if laboratory tests are performed locally.

Align text pertaining to secondary efficacy variables, other safety variables, other efficacy variables, and statistical analyses with SAP.

Change the sponsor company name from "UCB Biopharma SPRL" to "UCB Biopharma SRL" since the name of the legal form of the entity UCB Biopharma has changed into "société à responsabilité limitée" abbreviated "SRL."

In addition, minor corrections, including typographical/grammatical errors, have been made.

Modifications and changes

Global changes

No global changes have been made.

Specific changes

Change #1

Sponsor name on the title page and in the study contact information

Sponsor

UCB Biopharma SPRL

Allée de la Recherche 60

1070 Brussels

BELGIUM

Has been changed to:

Sponsor

UCB Biopharma **SRL**

Allée de la Recherche 60

1070 Brussels

BELGIUM

Change #2

Section 1, Summary; Section 5.2.1, Treatment Period; and Section 7.2, Treatments to be administered

At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

Has been changed to:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit after implementation of Protocol Amendment #2 if the subject has already completed the Week 48 visit.

Change #3

Section 1, Summary, and Section 5.1, Study description, paragraph 3

In addition, subjects may consent to participate in a PS0014 sub-study designed to evaluate the safe and effective use of self-injecting device presentations (ie, prefilled safety syringe and auto-injector presentations) for sc self-injection of bimekizumab by subjects in select sites in Europe, Japan, and the US.

Has been changed to:

In addition, subjects may consent to participate in a PS0014 sub-study designed to evaluate the safe and effective use of self-injecting device presentations (ie, prefilled safety syringe and auto-injector presentations) for sc self-injection of bimekizumab by subjects in select sites in Europe, Japan, **Canada,** and the US.

Change #4

Section 4.2.2, Secondary efficacy variables

- IGA response at Week 144

Has been changed to:

- IGA **0/1** response at Week 144

Change #5

Section 4.3.1, other safety variables

- Change from Baseline in clinical laboratory variables (chemistry, hematology, and urinalysis)

Has been changed to:

- Change from Baseline in clinical laboratory variables **(chemistry and hematology)**

Change #6

Section 4.3.2, other efficacy variables

- Percentage of subjects with PASI ≤1, ≤2, ≤3 and ≤5
- IGA response
- Absolute and percent change from Baseline in PASI score
- Change from Baseline in IGA score
- Absolute and percent change from Baseline in the BSA affected by PSO

Has been changed to:

- Percentage of subjects with PASI ≤1, ≤2, ≤3 and ≤5
- **IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline)**
- **IGA response (Clear with at least 2 category improvement relative to Baseline)**
- Absolute and percent change from Baseline in PASI score
- Absolute and percent change from Baseline in the BSA affected by PSO

Change #7

Section 5.6, schedule of study assessments

Table 5-1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity / Visit [a] / Week	Treatment Period-Year 1											
	Stable Dosing							Flexible Dosing [b]				
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44
Bimekizumab administration[m, n]	X	X	X	X	X	X	X	X	X	X	X	X

[n] Only subjects receiving IMP Q4W are dosed on Week s 4, 12, 20, 28, 36, and 44.

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Protocol activity / Visit [a] / Week	Treatment Period – Years 2 and 3 [b]																						W144 / PEOT	SFU[c]
	48	52H	56H	60	64H	68H	72	76H	80H	84	88H	92H	96	100H	104H	108	112H	116H	120	124H	128H	132	136H	140H		
DLQI	X						X						X									X			X	
Bimekizumab self-injection [m,n]	X[o]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

[n] The last dose for subjects receiving bimekizumab 320mg Q4W will be Week 140 and the last dose for subjects receiving bimekizumab 320mg Q8W will be Week 136.

[o] At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

[p] If self-injected at home, the subject/caregiver will document the date, body location, kit number and time point of administration of study medication. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

Has been changed to:

Table 5-1: Schedule of study assessments – Year 1 (Weeks 0 to 44)

Protocol activity / Visit [a] / Week	Treatment Period-Year 1											
	Stable Dosing							Flexible Dosing [b]				
	Baseline/Feeder Study Final Visit	4	8	12	16	20	24	28	32	36	40	44
Bimekizumab administration **Q4W**[m, n]	X	X	X	X	X	X	X	X	X	X	X	X
Bimekizumab administration Q8W[m, n]	**X**		**X**		**X**		**X**		**X**		**X**	

[n] Only subjects receiving IMP Q4W are dosed on Weeks 4, 12, 20, 28, 36, and 44. **Subjects who are switched from IMP Q4W to IMP Q8W at Week 24 are dosed on Weeks 32 and 40 in the Flexible Dosing Period.**

Table 5-2: Schedule of study assessments – Years 2 and 3 (Weeks 48 to 144)

Protocol activity / Visit [a] / Week	Treatment Period – Years 2 and 3 [b]																							W144 / PEOT	SFU[c]
	48 C	52 H	56 H	60 C	64 H	68 H	72 C	76 H	80 H	84 C	88 H	92 H	96 C	100 H	104 H	108 C	112 H	116 H	120 C	124 H	128 H	132 C	136 H	140 H		
DLQI	X						X						X						**X**			~~X~~			X	
Bimekizumab self-injection **Q4W** [m,n,q]	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X	X[o]	X	X		
Bimekizumab self-injection Q8W [m,n]	**X[o]**		**X**		**X**		**X**		**X**		**X**		**X**		**X**		**X**		**X**		**X**		**X**			

[n] The last dose for subjects receiving **bimekizumab 320mg Q8W will be Week 136**.

[o] **The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48, or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #2 if the subject has already completed the Week 48 visit.**

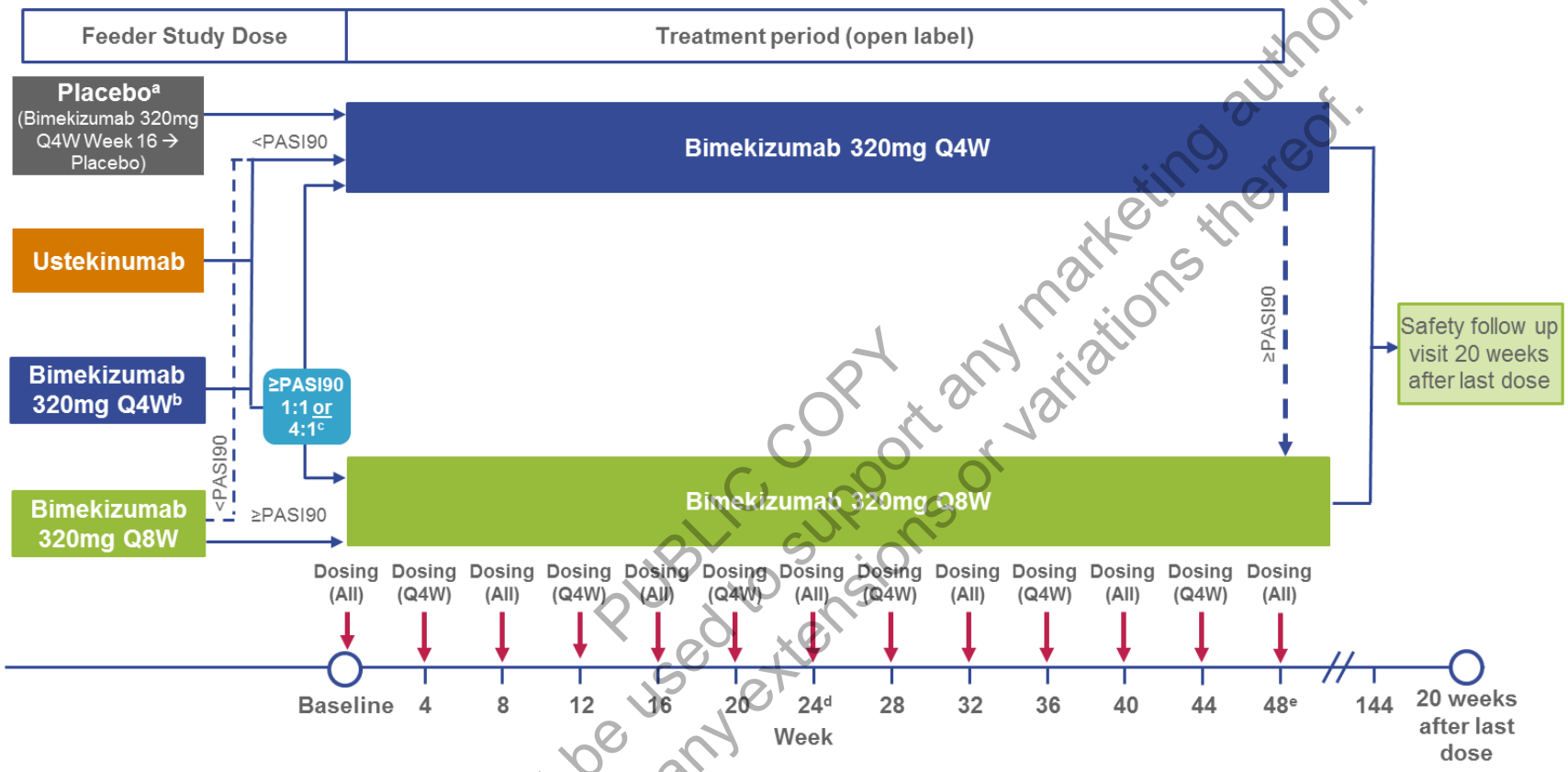
[q] **Q4W IMP administration only applies to those subjects who have not yet changed to Q8W at Week 48, or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #2 if the subject has already completed the Week 48 visit.**

Change #8

Section 5.7, Schematic diagram

The study schematic diagram for PS0014 is presented in Figure 5-1.

Figure 5-1: Schematic diagram

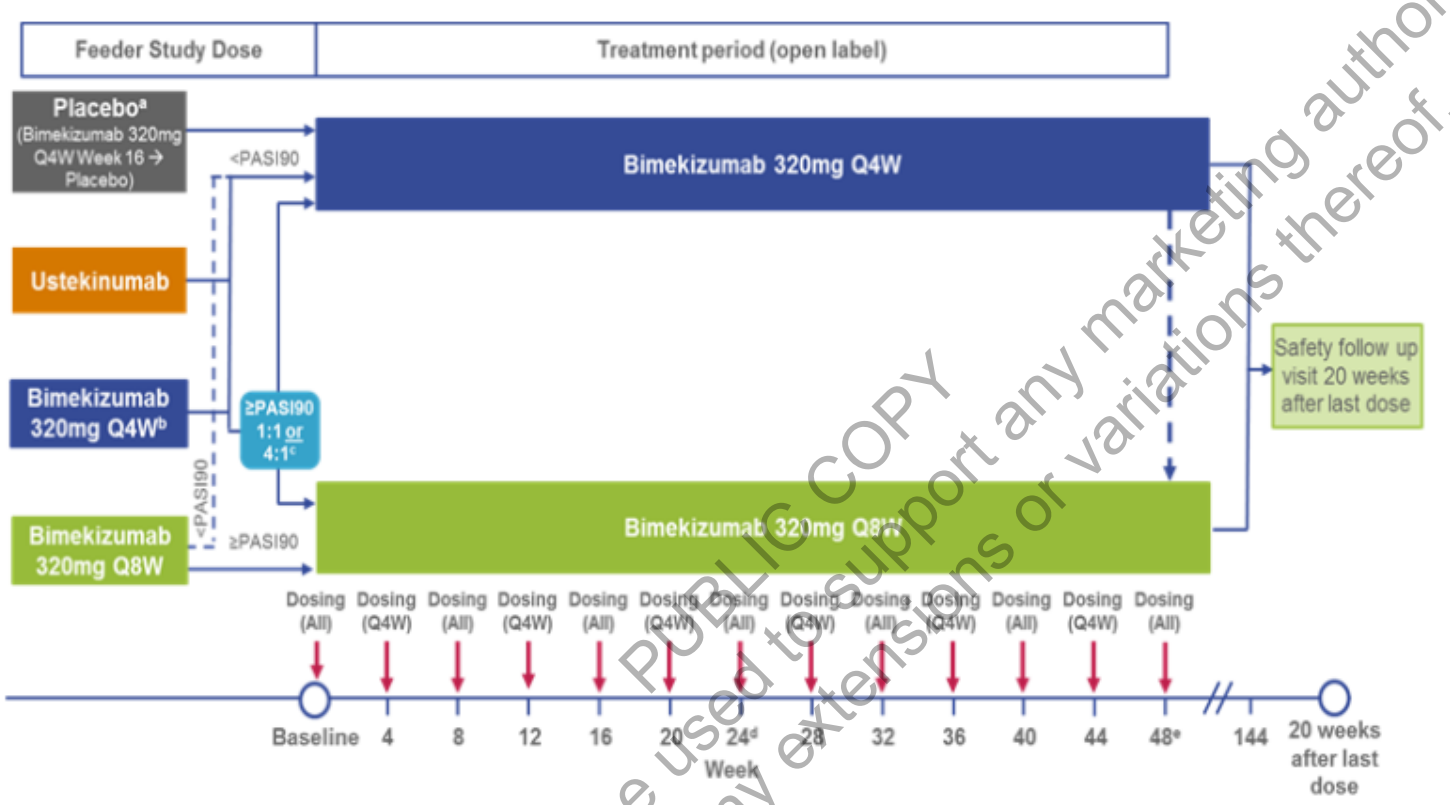


IMP=investigational medicinal product; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Self-injection will be allowed from Week 48 onward.
Note: At Week 28 and all following visits, subjects on continuous treatment with the same IMP for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.
[a] Subjects on placebo after a Week 16 response (≥PASI90) on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study may enroll in PS0014.
[b] Subjects on bimekizumab 320mg Q4W who achieved a PASI50 at Week 12 in the escape arm of the feeder study may enroll in PS0014.
[c] Subjects on ustekinumab or bimekizumab 320mg Q4W in feeder studies who achieved PASI90 will be randomized, respectively, 1:1 or 4:1 to bimekizumab 320mg Q4W or 320mg Q8W.
[d] At Week 24, if PASI90 is achieved, Investigator may change the dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W (optional).

Has been changed to:

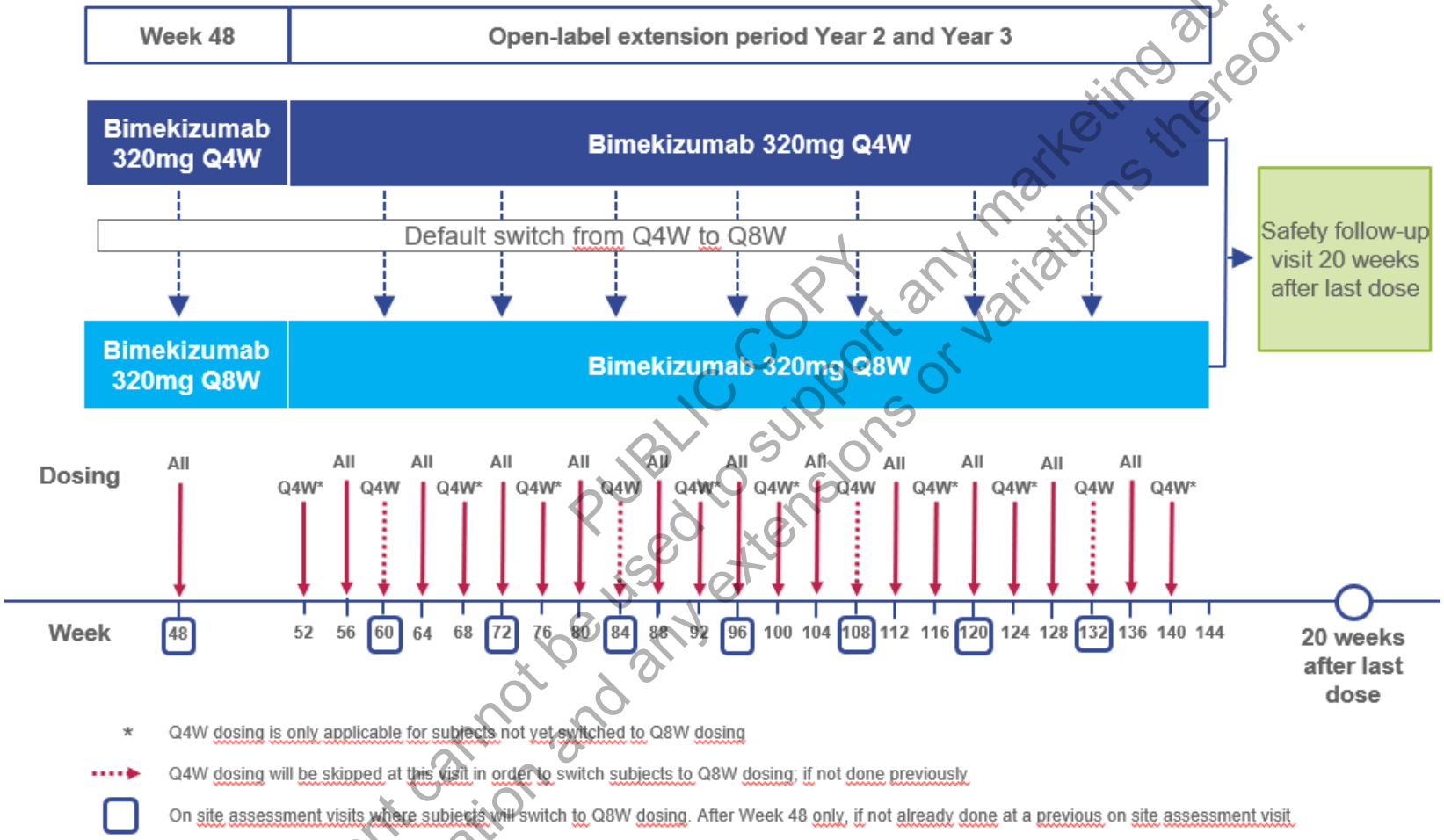
The study schematic diagram for PS0014 from Screening through Week 48 is presented in Figure 5-1, and from Week 48 through Week 144 is presented in Figure 5-2.

Figure 5-1: Schematic diagram, Screening through Week 48



IMP=investigational medicinal product; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Self-injection will be allowed from Week 48 onward.
Note: At Week 28 and all following visits, subjects on continuous treatment with the same IMP for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.
[a] Subjects on placebo after a Week 16 response (≥PASI90) on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study may enroll in PS0014.
[b] Subjects on bimekizumab 320mg Q4W who achieved a PASI50 at Week 12 in the escape arm of the feeder study may enroll in PS0014.
[c] Subjects on ustekinumab or bimekizumab 320mg Q4W in feeder studies who achieved PASI90 will be randomized, respectively, 1:1 or 4:1 to bimekizumab 320mg Q4W or 320mg Q8W.
[d] At Week 24, if PASI90 is achieved, Investigator may change the dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W (optional).
[e] **The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.**

Figure 5-2: Schematic diagram, Years 2 and 3 (Week 48 through Week 144)



Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Self-injection will be allowed from Week 48 onward.
Note: The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.

Change #9

Section 5.8, Rational for study design and selection of dose

In PS0014, doses can be adjusted at Week 24 for subjects receiving bimekizumab 320mg Q4W at the discretion of the Investigator (optional). At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

Has been changed to:

In PS0014, doses can be adjusted at Week 24 for subjects receiving bimekizumab 320mg Q4W at the discretion of the Investigator (optional).

Based on pooled data from the Phase 3 studies (PS0008, PS0009, and PS0013), during the maintenance period bimekizumab 320mg Q8W provided efficacy results similar to bimekizumab 320mg Q4W. Therefore, at Week 48, subjects receiving bimekizumab 320mg Q4W will switch to receive bimekizumab 320mg Q8W. Subjects who are receiving bimekizumab 320mg Q4W treatment who already completed the Week 48 visit at the time of implementation of Protocol Amendment #2 will be switched to bimekizumab 320mg Q8W at the next scheduled clinic visit. This change in dosing interval will reduce subject and site burden, while allowing collection of more long-term safety data on the bimekizumab 320mg Q8W dosing regimen.

Change #10

Section 7.2, Treatments to be administered

The subject will receive the required number of syringes for injections at each visit needed to perform the Q4W or Q8W administrations at home.

Has been changed to:

The subject will receive the required number of syringes for injections at each visit needed to perform **the Q8W administrations** at home.

Change #11

Section 8.1.2.6, Week 48 Visit (±7 days relative to Baseline)

At Week 48, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the subject's dosing interval will change from 320mg Q4W to 320mg Q8W (default) unless, based on medical judgement, the investigator decides differently.

Has been changed to:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48, or at the next scheduled clinic visit if the subject

has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.

Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 48 should be dosed at this visit and should receive kits for home administration 8 weeks later (Table 8-1).

Table 8-1: Dosing scheme, Years 2 and 3 (Weeks 48 to 144)

Week	48 [a,b]	Year 2												Year 3										
		52	56	60[a,c]	64	68	72[a,b]	76	80	84[a,c]	88	92	96[a,b]	100	104	108[a,c]	112	116	120[a,b]	124	128	132[a,c]	136	140
Dose Assignment	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**	**C**	**C/H**	**C/H**
Bimekizumab 320mg Q4W	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Bimekizumab 320mg Q8W	●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●	

C=Clinic; H=home; Q4W=every 4 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●).

[a] The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.

[b] Subjects whose dosing interval is changed to bimekizumab 320mg Q8W should be dosed at this visit and should receive kits for home administration 8 weeks later.

[c] Subjects whose dosing interval is changed to bimekizumab 320mg Q8W should NOT be dosed at this visit and should receive kits for home administration 4 weeks later.

Change #12

Section 8.1.2.7, Self-injection at home injection (Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136 and 140)

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136 and 140.

Has been changed to:

Section 8.1.2.7, Self-injection at home (Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. **This only applies to those subjects who have not yet changed to bimekizumab 320mg Q8W.**

Change #13

Section 8.1.2.8, Week 60, Week 84, Week 108, and Week 132 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded prior to administration of IMP:

The following text has been changed to:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W as follows:

- **At Week 60 if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.**
- **At Week 84 if the subject has already completed the Week 72 visit prior to implementation of Protocol Amendment #2.**
- **At Week 108 if the subject has already completed the Week 96 visit prior to implementation of Protocol Amendment #2.**
- **At Week 132 if the subject has already completed the Week 120 visit prior to implementation of Protocol Amendment #2.**

As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at one of these visits should NOT be dosed at that visit, and should receive kits for home administration 4 weeks later.

The following procedures/assessments will **be performed/recorded at this visit. If IMP is administered at this visit, they should** be performed/recorded prior to administration of IMP:

And the following text:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection.

Has been changed to:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection. **This only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #2.**

Change #14

Section 8.1.2.9, Week 72 Visit (±7 days relative to Baseline)

The following text has been added:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 72 if the subject had already completed the Week 48 and Week 60 visits prior to implementation of Protocol Amendment #2. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 72 should NOT be dosed at this visit, and should receive kits for home administration 8 weeks later.

And the following text:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection.

Has been changed to:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W or Q8W dosing will occur, preferably by self-injection. **The Q4W dosing only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #2.**

Change #15

Section 8.1.2.10, Week 96 Visit (±7 days relative to Baseline)

The following text has been added:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 96 if the subject had already completed the Week 84 visit prior to implementation of Protocol Amendment #2. As depicted in Table 8-1, subjects

whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 96 should be dosed at this visit, and should receive kits for home administration 8 weeks later.

And the following text:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection.

Has been changed to:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection. **The Q4W dosing only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #2.**

Change #16

Section 8.1.2.11, Week 120 Visit (±7 days relative to Baseline)

The following text has been added:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 120 if the subject had already completed the Week 108 visit prior to implementation of Protocol Amendment #2. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 120 should be dosed at this visit, and should receive kits for home administration 8 weeks later.

And the following text:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection.

Has been changed to:

After completion of the above-mentioned procedures, bimekizumab administration for subjects receiving Q4W dosing will occur, preferably by self-injection. **The Q4W dosing only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #2.**

Change #17

Section 9.2, Laboratory measurements

The following text has been added:

If tests are done locally, a concurrent sample should also be sent to the central laboratory whenever possible.

Change #18

Section 14.1, Definition of analysis sets

The Full Analysis Set (FAS) will consist of all enrolled subjects who receive at least 1 dose of the IMP and have a valid efficacy measurement for PASI at Baseline of PS0014.

Has been changed to:

The Full Analysis Set (FAS) will consist of all enrolled subjects who receive at least 1 dose of the IMP and have a valid efficacy measurement for PASI at Baseline of **the Feeder Study and Baseline of** PS0014.

Change #19

Section 14.3.2, Other safety analyses

In order to evaluate if there is any difference in the TEAE profile of subjects who have dose adjustments, additional summaries will be generated and are described further here. With respect to dose adjustments, subjects will be classified into 1 of 2 groups:

- Nonadjusters – This group consists of subjects who do not experience a dose adjustment during the study.
- Adjusters – This group consists of subjects who experience a dose regimen adjustment at Week 24 or Week 48 during the study. This means that the subjects in this group had a dose adjustment from 320mg Q4W to 320mg Q8W at Week 24 or Week 48.

Summaries based on these 2 groups will be done for the TEAE overview, incidence of TEAEs (by SOC, HLT, and PT), and incidence of treatment-emergent SAEs.

Has been changed to:

In order to evaluate if there is any difference in the TEAE profile of subjects who have dose adjustments, additional summaries will be **generated.** With respect to dose adjustments, **for the Week 48 interim analysis,** subjects will be classified into 1 of 2 groups:

- Nonadjusters – This group consists of subjects who do not experience a dose adjustment **prior to Week 48**.
- Adjusters – This group consists of subjects who experience a dose regimen adjustment at **Week 24**. This means that the subjects in this group had a dose adjustment from 320mg Q4W to 320mg Q8W at **Week 24**.

For the full analysis, subjects will be categorized into those who did not experience a dose regimen adjustment during the study and those that experienced a dose regimen adjustment at any time.

Summaries based on **these groups** will be done for the TEAE overview, incidence of TEAEs (by SOC, HLT, and PT), and incidence of treatment-emergent SAEs.

Change #20

Section 14.4, Planned efficacy analyses

In addition to the summaries described above, the impact of dose regimen adjustment on efficacy will be considered. This will be done primarily by summarizing efficacy variables by the adjuster groups described above. Furthermore, a supportive analysis specifically for dose adjusters will be performed in which PASI score will be summarized by visit, where Baseline is recalibrated for each individual subject and defined as the visit where the bimekizumab 320mg Q8W is initiated. The visits summarized will be in weeks relative to when the dosing regimen is decreased to Q8W, as opposed to the scheduled week of the PS0014 assessment. These summaries will be based on observed case only.

Has been changed to:

In addition to the summaries described above, the impact of dose regimen adjustment on efficacy will be considered. This will be done primarily by summarizing efficacy variables by the adjuster groups described above**, for the Week 48 interim analysis and for the full analysis.**

Change #21

Section 14.7, 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 subject. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document at study start. 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.

Has been changed to:

Important protocol deviations are deviations from the protocol which potentially could have a meaningful impact on study conduct, or on the **key** efficacy, key safety, or PK outcomes for an individual subject. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document at study start. 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.

Change #22

Section 14.9, Planned interim analysis and data monitoring

Interim analyses are planned at Week 24 and Week 48, details of which will be documented in the SAP. After the final Week 144 visit, an interim analysis may be performed and a corresponding interim Clinical Study Report (CSR) may be written. A final analysis and updated final CSR will be prepared once all data (through the SFU visit) have been collected.

Has been changed to:

An interim analysis is planned **at Week 48**, details of which will be documented in the SAP. **Additional interim analyses** may be performed and corresponding interim CSRs may be written. A final analysis and updated final CSR will be prepared once all data (through the SFU visit) have been collected.

18.3 Protocol Amendment 3

Rationale for the amendment

Correct statement from "study subjects should NOT be dosed at this visit" to "study subjects should be dosed at this visit" in the description of study procedures by visit for Week 72 to align with change made in Protocol Amendment 2.

Add DLQI at Week 120 and delete DLQI at Week 132 in description of study procedures by visit for consistency with the change made in Protocol Amendment 2.

Removed statement regarding dosing interval change from the description of study procedures by visit for Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140, in order to reduce potential for confusion if study subjects go to sites for injections instead of performing injections at home.

In addition, minor corrections, including typographical and grammatical errors, changes to abbreviations, and administrative changes have been made.

Modifications and changes

Global changes

No global changes have been made.

Specific changes

Change #1

Section 8.1.2.7, Self-injection at home (Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. This only applies to those subjects who have not yet changed to bimekizumab 320mg Q8W.

Has been changed to:

~~**The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit if the subject has already completed the Week 48 visit prior to implementation of Protocol Amendment #2.**~~

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home (described in Section 7.2) on the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. This only applies to those subjects who have not yet changed to bimekizumab 320mg Q8W.

Change #2

Section 8.1.2.8, Week 60, Week 84, Week 108, and Week 132 Visit (±7 days relative to Baseline)

The following bullet has been deleted:

- DLQI (Week 132 only)

Change #3

Section 8.1.2.9, Week 72 Visit (±7 days relative to Baseline)

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 72 if the subject had already completed the Week 48 and Week 60 visits prior to implementation of Protocol Amendment #2. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 72 should NOT be dosed at this visit, and should receive kits for home administration 8 weeks later.

Has been changed to:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 72 if the subject had already completed the Week 48 and Week 60 visits prior to implementation of **Protocol Amendment #3**. As depicted in Table 8-1, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 72 should ~~**NOT**~~ be dosed at this visit, and should receive kits for home administration 8 weeks later.

Change #4

Section 8.1.2.11, Week 120 Visit (±7 days relative to Baseline)

The following bullet has been added:

- DLQI

18.4 Protocol Amendment 3.3

Rationale for the amendment

The protocol has been amended for the following reasons:

- To collect additional long-term safety data,
- To explore safety data with subjects who have temporarily stopped bimekizumab and could have been exposed to other treatments, and
- To provide an additional 48-week open-label treatment period for subjects continuing their current treatment or reinitiating treatment at Week 144/OLE2 Baseline.

Modifications and changes

Global changes

The following global changes were made throughout the protocol:

- An additional 48-week open label treatment period was added (OLE2 Period).

The maximum duration of the study has been changed. For subjects participating in the OLE2 Period, the maximum study duration will depend on the time between their participation in the Treatment Period until Week 144 and the start of the OLE2 Period: 204 weeks for subjects still being treated in the Treatment Period and who will directly roll over to the OLE2 Period at Week 144; 224 weeks for subjects who have attended Week 144 and who will have completed the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 Period; between 204 and 224 weeks for subjects who will have attended Week 144 and are participating in the SFU. For these subjects, the maximum study duration will depend upon when they will stop the 20-week SFU period to enter the 4-week Screening Period of the OLE2 Period.

- Implementation of a new schedule of assessments (Table 5-3) for the OLE2 Period has been made. Schematic diagram (Figure 5-3) for the for the OLE2 Period has been made.
- A list of inclusion and exclusion criteria has been added for participating in the OLE2 Period.
- The description of the treatment to be administered has been adapted to take into account the treatment to be administered in the OLE2 Period.
- Addition of the study procedures by visit has been made for the OLE2 Period (Section 8.1.3).

Specific changes

Change #1

Section 1 Summary

Approximately 1120 subjects are expected to enroll in PS0014. For each subject, the study will last a maximum of 160 weeks and will consist of a Treatment Period (144 weeks) and a Safety

Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]

Was changes to

Approximately 1120 subjects are expected to enroll in PS0014. For each subject, the study will last a maximum of **192** weeks and will consist of a Treatment Period (144 weeks) and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP] **depending on subject's participation in the Open-Label Extension (OLE2) Period; see paragraph below).**

Subjects participating in the OLE2 (implemented as part of Protocol Amendment #3.3) will enter the OLE2 Period after completing the Treatment Period (at Week 144), including subjects in the SFU period and subjects who have completed the SFU Period. The OLE2 Period will be a 48-week open-label treatment period with final visit at OLE2 Week 48, followed by an SFU Period (SFU2, 20 weeks after the final dose of IMP administered in the OLE2 Period).

Change #2

Section 1 Summary

The following text was added:

After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate bimekizumab treatment as per the following OLE2 Groups:

- **OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).**
- **OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.**

During the OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48), all subjects will attend visits at the site every 12 weeks for study assessments and subjects may self-inject IMP at home.

Following completion or early withdrawal from the OLE2 Period, subjects will return for the SFU of the OLE2 Period (SFU2) Visit 20 weeks after the last dose of IMP administration.

Change #3

Section 2.2.1.2 Ongoing studies

Five additional studies of bimekizumab for the treatment of PSO are ongoing.

- PS0010 is a Phase 2b, double-blind, placebo-controlled, dose ranging study to evaluate the safety, efficacy, PK, and pharmacodynamics (PD) of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0011 is a long-term extension study for subjects who completed PS0010 to assess the long-term safety, tolerability, and efficacy of bimekizumab.
- PS0016 is a Phase 2a, subject-blind, Investigator-blind study to evaluate the time course of PD response, safety, and PK of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0018 is a long-term extension study for eligible subjects from PS0016 to assess the safety, tolerability, and efficacy of bimekizumab.
- PS0015 is a Phase 3b, double-blind, active comparator controlled, parallel group study to evaluate the efficacy and safety of bimekizumab compared with secukinumab in adult subjects with moderate to severe chronic PSO.

Bimekizumab is also being evaluated in the treatment of other indications (eg, PsA, axSpA, hidradenitis suppurativa). Additional information on the clinical data for bimekizumab is available in the current version of the IB

Was changed to

All ongoing studies at the time of Protocol Amendment #3.3 implementation are presented and described in the current version of the IB

Change #4

Section 5.1 Study description

The following paragraph was added:

An OLE2 Period will be added in Canada and the US after the country-specific Protocol Amendment #3.3 implementation (addition of a 48-week open-label treatment period, ie, the OLE2 Period), and subjects will be invited to continue or reinitiate bimekizumab treatment for an additional 40 weeks.

Change #5

Section 5.2.1 Study periods

PS0014 will include 2 periods, a Treatment Period (144 weeks) and a SFU Period (20 weeks after the final dose of IMP).

Was changed to:

PS0014 will include a Treatment Period of 144 weeks (from Baseline/Feeder Study Final Visit to Week 144 Visit) followed by a SFU Period of 20 weeks after the last dose of IMP in the Treatment Period. After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), PS0014 will be prolonged by an OLE2 Period, during which eligible subjects will be invited to continue or reinitiate bimekizumab treatment for 40 weeks (from Week 144/OLE2 Baseline to OLE2 Week 48) and will be followed in a second SFU Period of 20 weeks after the final dose of IMP (SFU2 Period), as appropriate. Subjects will be invited to continue or reinitiate bimekizumab treatment as per the following OLE2 Groups:

- **OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).**
- **OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.**

Change #6

Section 5.2.1 Treatment period

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit.

During Year 1 of the Treatment Period (Weeks 0 to 44), IMP will be administered in the clinic by sc injection at the time points specified in the schedule of assessments (Table 5-1). During

Years 2 and 3 of the Treatment Period (Weeks 48 to 144), subjects may self-inject IMP at home (described in Section 7.2) at the time points specified in the schedule of assessments (Table 5-2).

The assessments to be performed at each Treatment Period Visit are presented in Table 5-1 and Table 5-2.

Was changed to

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit after implementation of Protocol Amendment #3 if the subject has already completed the Week 48 visit. **The last dose bimekizumab 320mg Q8W in the Treatment Period will be administered at Week 136. The End of Treatment Visit of the Treatment Period will be the Week 144 Visit.**

The assessments to be performed at each Treatment Period Visit are presented in Table 5-1 and Table 5-2.

Change #7

The following section was added:

5.2.2 OLE2 Period

Subjects enrolled as per Protocol Amendment #3 will be treated in the Treatment Period until Week 136 (last dose of bimekizumab 320mg Q8W) and will be followed in a SFU Period for 20 weeks after their last dose of IMP. After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), study subjects will be invited to continue or reinitiate bimekizumab treatment as per the following OLE2 Groups:

- **OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).**
- **OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.**

During the OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48), subjects may self-inject IMP at home (described in Section 7.2) at the time points specified in the schedule of assessments (Table 5-3).

Change #8

Section 5.2.3 Safety Follow-up Periods

The following text was added:

Two SFU Periods are considered since Protocol Amendment #3.3 implementation. A first SFU following the Treatment Period and a second SFU (SFU2) following the OLE2 Period (added as per Protocol Amendment #3.3).

….

Subjects still in the Treatment Period (not having attended Week 144 yet; OLE2 Group A) will have the opportunity to directly roll over in the OLE2. Subjects having attended Week 144 Visit and who are participating in the SFU or have completed the SFU (OLE2 Group B) will be invited to reinitiate treatment in the OLE2 Period.

All subjects who have completed treatment in the OLE2 Period (ie, have completed the OLE2 Week 48 Visit), or have withdrawn from IMP during the OLE2 Period before OLE2 Week 48, will return for a SFU2 Visit 20 weeks after their final dose of IMP.

The assessments for the SFU2 are presented in Table 5-3.

Change #9

Section 5.2.4 Premature enrolment

Subjects withdrawing early from the study will undergo the PEOT Visit assessments (see Section 8.2) and will enter the SFU.

Was changed to:

Subjects withdrawing early from the study will undergo the PEOT Visit assessments (see Section 8.2) and will enter the **SFU or SFU2 Period depending on when subjects withdraw**.

Change #10

Section 5.3 Study duration per subject

Eligible subjects will continue to receive open-label bimekizumab in PS0014 for up to 144 weeks or until the Sponsor decides to discontinue the study. The SFU Visit will be conducted 20 weeks after the final dose of bimekizumabThe end of the study is defined as the date of the last visit of the last subject in the study.

Was changed to:

For each subject, prior to Protocol Amendment 3.3 implementation, the study will last a maximum of 160 weeks and will consist of:

- **A Treatment Period during which** subjects will continue to receive open-label bimekizumab in PS0014 for up to 144 weeks **(the last dose will be administered at Week 136 and Week 144 will be the End of Treatment Visit).**
- **An SFU Period** 20 weeks after the final dose of bimekizumab **administered during the Treatment Period (subjects will enter the SFU after Week 144 Visit or after withdrawal).**

Subjects eligible for the OLE2 Period (added as part of Protocol Amendment #3.3) will enter the OLE2 after completing Week 144 of the Treatment Period. The OLE2 Period includes a 48-week open-label treatment period with a final visit at OLE2 Week 48, and an SFU Period (SFU2) of 20 weeks after the final dose of IMP administered in the OLE2 Period.

For subjects participating in the OLE2 Period, the maximum study duration will depend on the time between their participation in the Treatment Period until Week 144 and the start of the OLE2 Period:

- **204 weeks for subjects still being treated in the Treatment Period and who will directly roll over to the OLE2 Period at Week 144.**
- **224 weeks for subjects who have attended Week 144 and who will have completed the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 Period.**
- **Between 204 and 224 weeks for subjects who will have attended Week 144 and are participating the in the SFU. For these subjects, the maximum study duration will depend upon when they will stop the 20-week SFU period to enter the 4-week Screening Period of the OLE2 Period.**

The end of the study is defined as the date of the last visit of the last subject in the study.

Change #11

A table for study procedures for the OLE22 Period was added

Table 5-3 Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W 32	OLE2 W 36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
		C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity			**OLE2 Groups A + B**									
Informed consent	Group B	Group A										
Eligibility	Group B	Group A+B										
Urine drug screen	Group B											
Significant past medical history and concomitant diseases [d]	Group B [d]											
Physical exam [e]	Group B	Group A[f] + B			X		X		X		X	X
Body weight		Group A[f] + B									X	
Vital signs [g]	Group B	Group A[f] + B			X		X		X		X	X
Hematology and chemistry	Group B	Group A[f] + B					X				X	X
Urinalysis	Group B	Group A[f] + B					X				X	X
Pregnancy testing (urine) [h]	Group B	Group A[f] + B			X		X		X		X	X
Hepatitis B and C testing	Group B											
HIV testing [i]	Group B											
IGRA TB test		Group A [f]									X	
Tuberculosis questionnaire	Group B	Group A[f] + B			X		X		X		X	
PASI	Group B	Group A[f] + B			X		X		X		X	

Table 5-3 Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W 32	OLE2 W 36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
		C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity			OLE2 Groups A + B									
Percentage of BSA	Group B	Group A[f] + B			X		X		X		X	
IGA	Group B	Group A[f] + B			X		X		X		X	
DLQI		Group A[f] + B					X				X	
PHQ-9	Group B	Group A[f] + B			X		X		X		X	X
ECG		Group A[f]										
Blood sample for bimekizumab plasma concentrations [j]		Group A[f]										
Blood sample for anti-bimekizumab antibodies [j]		Group A[f]										
scalp IGA		Group A[f]										
mNAPSI		Group A[f]										
pp-IGA		Group A[f]										
EQ-5D-3L		Group A[f]										
PASE		Group A[f]										
PGADA		Group A[f]										
WPAI-SHP V2.0		Group A[f]										

Table 5-3 Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W 32	OLE2 W 36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
		C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity			**OLE2 Groups A + B**									
eC-SSRS	Group B	Group A[f] + B			X		X		X		X	X
Concomitant medication	Group B	Group A[f] + B			X		X		X		X	X
Adverse events	Group B [k]	Group A[f] + B			X		X		X		X	X
IRT	Group B	Group A[f] + B			X		X		X		X	X
Bimekizumab administration Q4W/Q8W [l, m, n]		Group B [l]	X	X	X	X	X	X		X		
Bimekizumab administration Q8W [m, n]		Group A+B [l]		X		X	X	X		X		
IMP accountability for self-injection at home					X		X		X		X	

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; H=home; HIV= human immunodeficiency virus; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; OLE=open label extension; PASI=Psoriasis Area Severity Index; PEOT=Premature End of Treatment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire-9; pp-IGA=palmoplantar Investigator's Global Assessment; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU=Safety Follow-Up; SFU2=Safety Follow-Up #2; TB=tuberculosis; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem; W=Week.

Note: Subjects may self-inject IMP at home; self-injection training will be provided to the subject/caregivers by qualified site personnel.

[a] Visit windows of ±14 days relative to the Week 144/OLE2 Baseline Visit all visits except SFU2. The SFU2 Visit window is ±7 days from final dose.

[b] Assessment for the OLE2 Screening is applicable to subjects in OLE2 Group B, ie, subjects who agreed to reinitiate bimekizumab treatment after having completed the Week 144 Visit.

[c] The SFU2 Visit will occur 20 weeks after the final dose.

[d] Only applicable for subjects who completed the SFU period; only new or modified medical history since completing SFU will be entered in eCRF.

[e] The physical examination will be performed as per Section 9.3.5.

Table 5-3 Schedule of study assessments – OLE2 Period (from OLE2 Screening Visit or from Week 144/OLE2 Visit to Week 48)

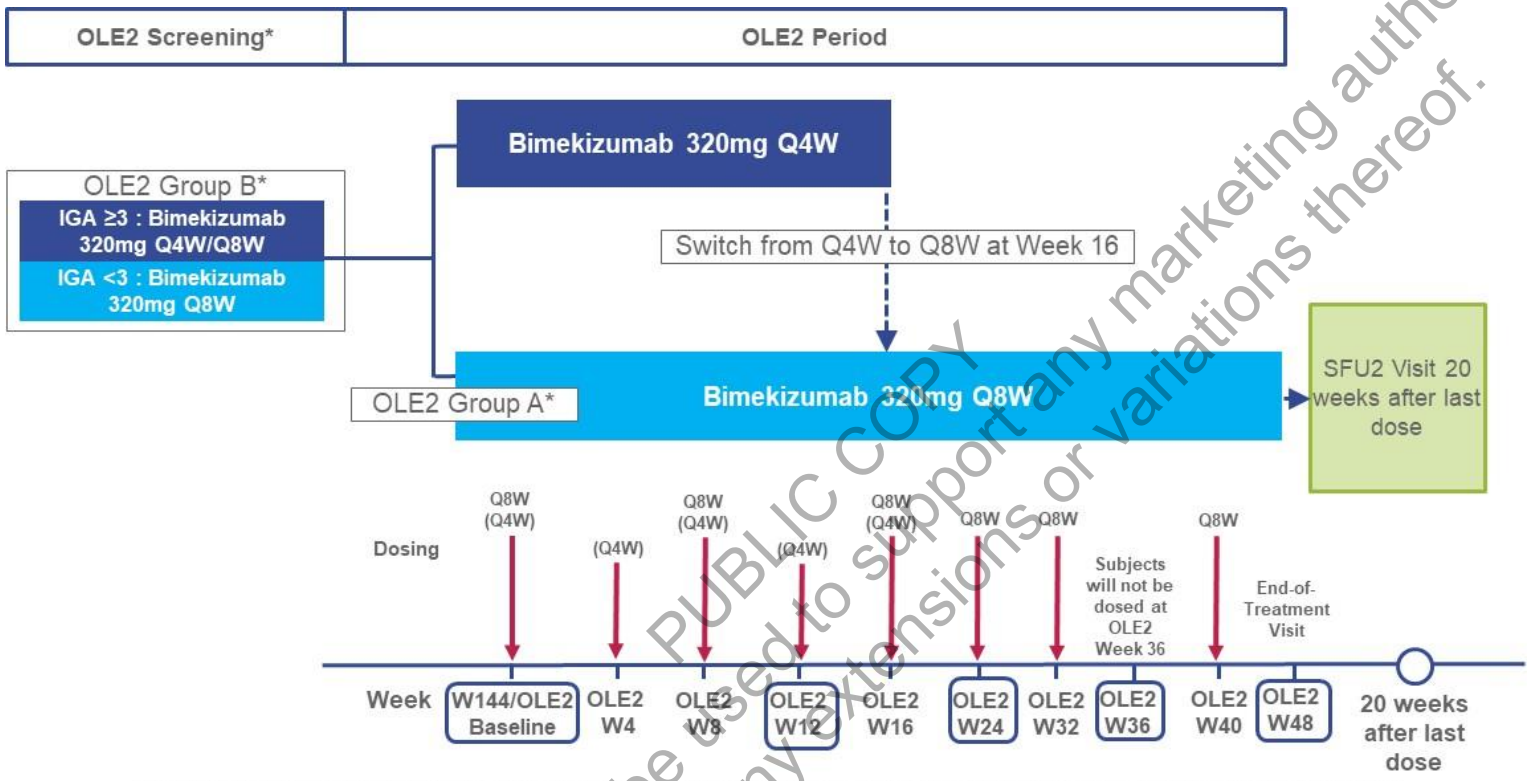
Visit [a]/ Week	OLE2 Period[b]											
	OLE2 Screening	W144/OLE2 Baseline	OLE2 W4	OLE2 W 8	OLE2 W 12	OLE2 W 16	OLE2 W 24	OLE2 W 32	OLE2 W 36	OLE2 W 40	OLE2 W48/ PEOT	SFU2[c]
		C	C/H	C/H	C	C/H	C	C/H	C	C/H	C	
Protocol activity			**OLE2 Groups A + B**									

[f] These tests are performed as part of the Week 144 visit (the Week 144 Visit coincides with the Week 144/OLE2 Baseline Visit for subjects in Group A, ie, direct enrollers from Treatment Period to OLE2 Period).
[g] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.
[h] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.
[i] The HIV test results will not be recorded in the eCRF.
[j] All blood samples taken prior to dosing.
[k] Collected only from subjects in the SFU Period.
[l] Q4W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B and had an IGA ≥3 upon entry of OLE2 Period. These subjects will receive Q4W dosing for 16 weeks, then will change from Q4W to Q8W dosing. Subjects who have entered the OLE2 Period as part of Group B with an IGA <3 upon entry of OLE2 Period will receive Q8W dosing from the OLE2 Screening Visit onwards.
[m] The dosing window is ±14 days relative to the Week 144/OLE2 Baseline Visit.
[n] If self-injected at home, the subject/caregiver will document the date, body location, kit number, and time point of administration of study medication. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

Change #12

A new schematic diagram was made for the OLE2 Period.

Figure 5-3 Schematic diagram, OLE2 Period (From OLE2 Screening through OLE2 Week 48)



IGA=Investigator's Global Assessment; IMP=investigational medicinal product; OLE=Open Label Extension; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU2=Safety follow-up; W=week

Note: Q4W/Q8W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B, and had an IGA ≥3 upon entry of OLE2 Period. These subjects will receive Q4W dosing for 16 weeks, then will change from Q4W to Q8W dosing.

Change #13

The following sections were added:

6.3 Eligibility criteria for the OLE2 Period

Prior to initiating the OLE2 Period assessments, all subjects will be asked to read and sign a separate Informed Consent Form (ICF).

6.3.1 All subjects (OLE2 Groups A and B)

To be eligible to participate in the OLE2 Period, all of the following inclusion criteria must be confirmed for all subjects:

13. Subject provided informed consent.
14. Subject is considered reliable and capable of adhering to the protocol (eg, able to understand and complete diaries), visit schedule, and medication intake according to the judgment of the Investigator.
15. Subject completes the Treatment Period to Week 144 without meeting any withdrawal criteria defined in Section 6.4.

6.3.2 OLE2 Period Group A subjects

To participate in the OLE2 Period, subjects still treated and who completed the Week 144 Visit by the time of Protocol Amendment #3.3 implementation will not need to fulfil other eligibility criteria than those listed in Section 6.3.1 and will continue treatment from the Week 144/OLE2 Baseline Visit if they do not meet any of the withdrawal criteria defined in Section 6.4.

6.3.3 OLE2 Period Group B subjects

Inclusion criteria

To be eligible to participate in the OLE2 Period, all of the additional following inclusion criteria must be confirmed during the OLE2 Screening Period for subjects who have attended Week 144 and are in the SFU or have completed the SFU before Protocol Amendment #3.3 implementation (OLE2 Group B subjects):

16. Female subjects must be:
    - Postmenopausal: Menopause is defined as 12 consecutive months of amenorrhea, for which there is no other obvious pathological or physiological cause.
    - Permanently sterilized (eg, tubal occlusion, hysterectomy, bilateral salpingectomy)
    - Or, if of childbearing potential (and engaged in sexual activity that could result in procreation), must be willing to use a highly effective method of contraception throughout the duration of the study until 20 weeks after last administration of IMP, and have a negative pregnancy test at OLE2 Screening. The following methods are considered highly effective when used consistently and correctly
        - Combined (estrogen and progestogen) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal)

- Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
- Intrauterine device
- Intrauterine hormone-releasing system
- Vasectomized partner
- Abstinence as a form of birth control is generally not allowed in the study unless abstinence is in accordance with a subject's preferred and common lifestyle. Study personnel must confirm the continued use of abstinence is still in accordance with the subject's lifestyle at regular intervals during the study.

17. Subjects with a diagnosis of Crohn's disease or ulcerative colitis are allowed as long as they have no active symptomatic disease.

Exclusion criteria

Subjects in the OLE2 Group B are not permitted to enroll in the OLE2 Period if any of the following exclusion criteria are met:

18. Female subjects who plan to become pregnant during the OLE2 Period or within 20 weeks following final dose of study medication.
19. Subject has developed any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the subject's ability to participate in the OLE2 Period.
20. Any subjects with an ongoing SAE, or a history of serious infections, the Medical Monitor must be consulted prior to the subject's entry in the OLE2 Period, although the decision on whether to enroll the subject remains with the Investigator.
21. Subject had a positive or indeterminate IGRA in the Treatment Period to Week 144, unless appropriately evaluated and treated as per Section 12.3.1.
22. Subject may not participate in another study of a medicinal product or device under investigation
23. Subject has a history of chronic alcohol or drug abuse within 6 months prior to reentry as assessed by medical history, site interview, and/or results of the urine drug screen.
24. Subjects who have used systemic treatments for PSO after Week 144 must have stopped this treatment 1 month prior to receiving the first bimekizumab injection in the OLE2 Period (See Section 7.8.2 regarding prohibited medications).
25. Subject has erythrodermic, guttate, or pustular form of PSO.
26. Subject is noncompliant with the study procedures or medications in the opinion of the Investigator.
27. Subject has a clinical laboratory value meeting any of the following criteria:

f. ≥3.0x ULN of any of the following: ALT, AST, alkaline phosphatase (ALP); or >ULN total bilirubin (≥1.5xULN total bilirubin if known Gilbert's syndrome)

g. A laboratory value meeting any of the following criteria:

- Absolute neutrophil count <1.0x10^3/µL
- Absolute lymphocyte count <0.2x10^3/µL

Subjects may enter the OLE2 Period if the result is transient. If a retest is required, it must be done within 1 to 2 weeks.

28. Subject has concurrent acute or chronic viral hepatitis B or C or HIV infection. Subjects who have evidence of, or tested positive for hepatitis B or hepatitis C are excluded. A positive test for the hepatitis B virus is defined as: (1) positive for hepatitis B surface antigen, or (2) positive for anti-hepatitis B core antibody. A positive test for the hepatitis C virus is defined as: (1) positive for hepatitis C antibody, and (2) positive via a confirmatory test for hepatitis C virus (for example, hepatitis C virus polymerase chain reaction).
29. There is confirmation of a pregnancy, as evidenced by a positive pregnancy test (see Section 9.1.4 for more information regarding pregnancies).
30. Subjects showing:
    - Suicidal ideation in the past month prior to the OLE2 Screening Visit as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the electronic Columbia Suicide Severity Rating Scale (eC SSRS).
    - Any suicidal behavior since last visit.
31. Subject has presence of moderately severe or severe major depression, indicated by a score ≥15 on the PHQ-9. Medication used to treat depression should be stable for 4 weeks prior to Week 144/OLE2 Baseline.
32. Subject has developed any active malignancy or history of malignancy prior to the OLE2 Screening Visit EXCEPT treated and considered cured cutaneous squamous or basal cell carcinoma, or in situ cervical cancer.
33. Subject has received any live (includes attenuated) vaccination within the 8 weeks prior to the Week 144/OLE2 Baseline Visit.

Change #14

Section 7.2 Treatment to be administered

OLE2 Period dosing

After the implementation of Protocol Amendment #3.3 (addition of a 48-week open-label treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3 implementation will attend the Week 144 Visit and may directly roll over to the OLE2 Period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional

weeks, starting from the first treatment visit of the OLE2 Period (ie, Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for subjects entering the OLE2 Period).

- OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are in the SFU or have completed the SFU at the time of Protocol Amendment #3.3 implementation may reinitiate bimekizumab treatment in the OLE2 Period after having undergone Screening assessments during a 4-week OLE2 Screening Period. The first dose will be administered at the Week 144/OLE2 Baseline Visit; data collected at this visit will be used as baseline data. Subjects with an IGA score ≥3 upon entry in the OLE2 Period will be treated with bimekizumab Q4W for the first 16 weeks, and will then switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 upon entry will be treated with bimekizumab Q8W from the Week 144/OLE2 Baseline Visit.

During the OLE2 Period (Week 144/OLE2 Baseline to OLE2 Week 48), all subjects will attend study visits at the study site every 12 weeks for study assessments and subjects may self-inject IMP at home.

Change #15

Section 7.7 Procedures for monitoring subject compliance

After Week 48, self-injection at home will be possible at the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140.

Was changed to:

After Week 48, self-injection at home will be possible at the following weeks: Weeks 52, 56, 64, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, 140, **and at the OLE2 Weeks 4, 8, 16, 32, and 40.**

Change #16

Section 7.8.2 Prohibited concomitant treatments (medications and therapies)

Table 7 1: Prohibited PSO medications

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

Was changed to:

Up to Week 144

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

Post Week 144 (OLE2 Period)

Subjects who have used systemic treatments for PSO after Week 144 must have stopped this treatment 1 month prior to receiving the first bimekizumab injection in the OLE2 Period. Subjects receiving systemic immunomodulatory medications for an indication other than PSO must have their eligibility confirmed by the Medical Monitor prior to enrollment in the OLE2 Period.

Subjects who take prohibited medications during the OLE2 Period may be withdrawn from IMP but followed until the SFU2 Visit. The decision to withdraw a subject for taking prohibited medications should be made in consultation with the Medical Monitor.

Change #17

Section 7.10 Randomization and numbering of subjects

The following paragraph was added

Subjects who roll over directly from the Treatment Period into the OLE2 Period will continue receiving bimekizumab 320mg Q8W and will keep their unique 5-digit identification number. Subjects who reinitiate bimekizumab after having completed treatment (subjects in the SFU of the Treatment Period or who have completed the SFU of the Treatment Period) will receive either bimekizumab 320mg Q4W/Q8W or bimekizumab 320mg Q8W depending on their disease activity at time of reentry (bimekizumab 320mg Q4W/Q8W for subjects with IGA score ≥3 or bimekizumab 320mg Q8W for subjects with IGA score <3). For these subjects, the same unique 5-digit identification number used in the study will be reused.

Change #18

Section 8 STUDY PROCEDURES BY VISIT

Table 5-1 (Schedule of study assessments) provides a general overview of study assessments in Year 1 (Weeks 0 to 44). Table 5-2 (Schedule of study assessments) provides a general overview of study assessments in Years 2 and 3 (Weeks 48 to 144). A list of procedures to be completed at each visit is described below.

- Visit windows of ±7 days on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. The window of ±7 days is relative to Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside of the visit window must be discussed with the Medical Monitor.
- The dosing window is ±7 days relative to the scheduled dosing visit.
- Visit (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.

Was changed to

Table 5-1 (Schedule of study assessments) provides a general overview of study assessments in Year 1 (Weeks 0 to 44). Table 5-2 (Schedule of study assessments) provides a general overview of study assessments in Years 2 and 3 (Weeks 48 to 144). Table 5-3 **(Schedule of study**

assessments) provides a general overview of study assessments in OLE2 Period (from OLE2 Screening or Week 144/OLE2 Baseline to OLE2 Week 48).

A list of procedures to be completed at each visit up to Week 144 is described below.

- Visit windows of ±7 days on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. The window of ±7 days is relative to Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside of the visit window must be discussed with the Medical Monitor.
- The dosing window is ±7 days relative to the scheduled dosing visit.
- **For the SFU Visit (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.**

A list of procedures to be completed at each visit of the OLE2 Period is described below.

- **Visit windows of ±14 days on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. The window of ±14 days is relative to Week 144/OLE2 Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside of the visit window must be discussed with the Medical Monitor.**
- **The dosing window is ±14 days relative to the scheduled dosing visit.**
- **For the SFU2** Visit (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.

Change #19

Section 8.1.2.12 Week 144 Visit (±7 days relative to Baseline)

The following text was added:

If Protocol Amendment #3.3 is implemented at the time study subjects are treated in the Treatment Period (ie, up to Week 144; OLE2 Group A subjects), these subjects will be invited to participate in the OLE2 Period and may directly roll over and continue bimekizumab treatment from the Week 144/OLE2 Baseline Visit as long as they do not meet any of the withdrawal criteria and have provided informed consent.

If Protocol Amendment #3.3 is implemented at the time subjects have completed the Week 144 Visit and are in the SFU Period of the Treatment Period or have completed the SFU of the Treatment Period (Group B subjects), these subjects will be invited to enter the OLE2 Period to reinitiate bimekizumab treatment in the OLE2 Period. However, before receiving the first dose at the Week 144/OLE2 Baseline Visit, they will first undergo screening during the 4-week OLE2 Screening Period (see Section 8.1.3.1 for the procedures that will apply for the Screening of the OLE2 Period).

Change #20

The following sections were added:

8.1.3 OLE2 Period

8.1.3.1 OLE2 Screening (up to 4 weeks) – applicable for OLE2 Group B only

Prior to any study specific activities of the OLE2 Period, subjects who completed the Week 144 Visit and are in the SFU or have completed the SFU of the Treatment Period (OLE2 Group B) will undergo screening. Subjects who have used systemic treatments for PSO after Week 144 must have stopped this treatment 1 month prior to receiving the first bimekizumab injection in the OLE2 Period. Screening procedures may be performed during this time. Subjects receiving systemic immunomodulatory medications for an indication other than PSO must have their eligibility confirmed by the Medical Monitor prior to enrollment in the OLE2 Period.

At the Screening Visit of the OLE2 Period (OLE2 Screening Visit), subjects will be asked to read, sign, and date an ICF that has been approved by the Sponsor and an IRB/IEC and that complies with regulatory requirements. Subjects will be given adequate time to consider any information concerning the study given to them by the Investigator or designee. As part of the informed consent procedure, subjects will be given the opportunity to ask the Investigator any questions regarding potential risks and benefits of continued participation in the study.

The following procedures/assessments will be performed at the OLE2 Screening Visit for subjects in the OLE2 Group B:

- Informed consent
- Inclusion/exclusion
- Urine drug screen
- Significant past medical history including clinically relevant past or coexisting medical conditions and surgeries (only applicable for subjects who completed the SFU; only new or modified medical history since completing the SFU should be entered in eCRF)
- Physical exam
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - Hepatitis B and Hepatitis C
  - HIV
- Tuberculosis questionnaire
- PASI

- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Prior and concomitant medication (including new or modified medications initiated after SFU)
- AE (only for subjects in the SFU)
- Contact IRT

8.1.3.2 Dosing in the OLE2 Period

Subjects will be dosed in the OLE2 Period according to the dosing schedule presented in Table 8-2.

Table 8-2 Dosing scheme, OLE2 Period

	OLE2 Period								
Visits/Week	**Week 144/OLE2 Baseline**	**OLE2 W4**	**OLE2 W8**	**OLE2 W12 [a]**	**OLE2 W16**	**OLE2 W24 [b]**	**OLE2 W32**	**OLE2 W36 [c]**	**OLE2 W40**
Dose Assignment	**C**	**H**	**H**	**C**	**H**	**C**	**H**	**C**	**H**
Bimekizumab 320mg Q4W/Q8W [d]	●●	●●	●●	●●	●●	●●	●●		●●
Bimekizumab 320mg Q8W	●●		●●		●●	●●	●●		●●

C=Clinic; H=home; IGA= Investigator's Global Assessment; IMP=investigational medicinal product; OLE=open label extension; Q4W/Q8W=every 4 weeks for 16 weeks, followed by every 8 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●).

[a] Subjects will receive kits for home administration 4 weeks later.

[b] Subjects will receive kits for home administration 8 weeks later.

[c] Subjects should NOT be dosed at this visit and will receive kits for home administration 4 weeks later.

[d] Q4W/Q8W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B and had an IGA ≥3 upon entry of the OLE2 Period. These subjects will receive Q4W dosing for 16 weeks until OLE2 Week 16, then will change from Q4W to Q8W and will receive their next dose at the scheduled clinic visit OLE2 Week 24.

8.1.3.2.1 Week 144/OLE2 Baseline Visit

Subjects who will still be treated in the Treatment Period at the time of implementing Protocol Amendment #3.3 (OLE2 Group A subjects) will attend Week 144 Visit and directly roll over to the OLE2 Period to continue treatment (bimekizumab 320mg Q8W). They will undergo all study assessments of the Week 144 Visit and will receive bimekizumab 320mg Q8W at this visit,

which will also coincide with the first visit of the OLE2 Period, ie, the Week 144/OLE2 Baseline Visit.

Subjects who have completed Week 144 Visit and are in the SFU of the Treatment Period or have completed the SFU Period at the time of Protocol Amendment #3.3 implementation (OLE2 Group B subjects) will reinitiate bimekizumab treatment at the Week 144/OLE2 Baseline Visit, and will be assigned a treatment regimen based on disease severity at the Week 144/OLE2 Baseline Visit (bimekizumab 320mg Q4W/Q8W for subjects with IGA score ≥3 or bimekizumab 320mg Q8W for subjects with IGA score <3).

Applicable for OLE2 Groups A and B:

- Confirmation of eligibility
- Physical exam
- Body weight
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- eC-SSRS
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- DLQI
- Concomitant medication
- AEs
- Contact IRT

Additional Procedures/assessments applicable for OLE2 Group A

- Informed Consent
- ECG
- Blood sample for bimekizumab plasma concentrations
- Blood sample for anti-bimekizumab antibodies

- IGRA TB test
- scalp IGA
- mNAPSI
- pp-IGA
- EQ-5D-3L
- PASE
- PGADA
- WPAI-SHP V2.0

At the Week 144/OLE2 Baseline Visit, after completion of the above-mentioned procedures, administration of IMP will occur, preferably by self-injection under supervision of the site personnel.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.3.2.2 Self-injection at home (OLE2 Weeks 4, 8, 16, 32, and 40)

Subjects receiving bimekizumab 320mg Q8W will be given the opportunity for self-injection of bimekizumab at home on the following weeks: OLE2 Weeks 8, 16, 32, and 40.

Subjects receiving bimekizumab 320mg Q4W/Q8W will be given the opportunity for self-injection of bimekizumab at home on the following weeks: OLE2 Weeks 4, 8, and 16. At OLE2 Week 16, subjects receiving bimekizumab 320mg Q4W/Q8W will switch to bimekizumab 320mg Q8W regimen and will be given the opportunity for self-injection of bimekizumab at home at OLE2 Weeks 32 and 40.

Adverse events will be captured spontaneously if the subject decides to visit the site to receive the bimekizumab administration.

All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly after the administration. The subjects/caregivers return the documentation together with any used/unused containers at the next scheduled clinic visit.

8.1.3.2.3 OLE2 Week 12, Week 24, and Week 36 Visits (±14 days relative to OLE2 Baseline)

As depicted in Table 8-2, subjects receiving bimekizumab 320mg Q4W/Q8W should receive IMP at the OLE2 Week 12 Visit, and all subjects will receive kits for home administration 4 weeks later at OLE2 Week 16. All subjects will receive IMP administration at the OLE2 Week 24 Visit, and will receive kits for home administration 8 weeks later. At the OLE2 Week 36 Visit, subjects will not be dosed and will receive kits for home administration 4 weeks later at OLE2 Week 40.

The following procedures/assessments will be performed/recorded at every clinic visit prior to administration of IMP:

- Physical exam
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Urine pregnancy test, for applicable subjects
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

The following additional assessments will be performed / recorded every 24 weeks (ie, at OLE2 Week 24 Visit) prior to administration of IMP:

- Collection of blood and urine samples for the following tests should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
- DLQI

At the OLE2 Week 12 (OLE2 Group B subjects on Q4W/Q8W dosing only) and Week 24 Visit, after completion of the above-mentioned procedures, administration of IMP will occur, preferably by self-injection under supervision of the site personnel.

Distribution of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

8.1.3.3 OLE2 Week 48 Visit (±14 days relative to OLE2 Baseline)

The following procedures/assessments will be performed/recorded:

- Physical exam
- Body weight

- Vital signs (sitting systolic BP and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following clinical laboratory tests:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - IGRA TB test
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

Return of IMP and accountability activities for home administration to be performed as described in Section 7.2, Section 7.5, and Section 7.7.

Change #21

Section 8.2Premature End of Treatment Visit

The following text was added:

If a subject is withdrawn from the study during the OLE2 Period:

- **The subject will be withdrawn from IMP, will undergo the same assessments as the OLE2 Week 48 visit (see Section 8.1.3.3), and will enter the SFU2 Period.**
- **The subject will be encouraged to return for the SFU2 Visit (20 weeks after the last received dose; see Section 8.4).**

Change #22

8.4 Safety Follow-Up Visit 2 (20 weeks after final dose of the OLE2 Period, ±7 days)

The following procedures/assessments will be performed/recorded:

- Physical exam
- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood and urine samples for the following tests should be obtained at this visit:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

Change #23

Section 18.5 Laboratory measurements

The following test were added

Table 9-2 Laboratory measurements

Hematology	Chemistry	Urinalysis dipstick[a]
	HIV [d]	
	Hepatitis B and C [d]	

[d] Only for Group B; only at the OLE2 Screening Visit.

Change #24

Section 18.5 Unscheduled Visit

At the Investigator's discretion, an Unscheduled Visit may be completed at any time during the study, but prior to the SFU Visit, if deemed necessary for the subject's safety and well-being.

Was changed to

At the Investigator's discretion, an Unscheduled Visit may be completed at any time during the study, but prior to the SFU Visit **or SFU2 Visit (depending on which period [Treatment Period or OLE2 Period] the subject is in)**, if deemed necessary for the subject's safety and well-being.

Change #25

11 ASSESSMENT OF PHARMACOKINETIC VARIABLES

11.1 Pharmacokinetic variables

The following sentence was added:

Blood samples for the measurement of PK assessments will not be collected in the OLE2 Period.

Change #26

12 ASSESSMENT OF IMMUNOLOGICAL VARIABLES

The following sentence was added:

Blood samples for the measurement of antibodies to bimekizumab will not be collected in the OLE2 Period.

Change #27

Section 14.1 Definition of analysis sets

The following sentence was added:

The OLE2 Period Set (OL2S) will consist of all subjects that receive at least 1 dose of IMP at Week 144/OLE2 or later in the OLE2 Period (including the Week 144/OLE2 Baseline dose).

Change #28

14.3 Planned safety analyses

Safety variables will be analyzed for all subjects in the SS.

Was changed to

Safety variables will be analyzed for all subjects in the SS **and selected summaries will be provided for subjects in the OLE2 Period (OL2S).**

Change #29

14.4 Planned efficacy analyses

Efficacy analyses will be summarized based on the FAS. The summaries described in this section will provide data on maintenance of effect of open-label bimekizumab over 144 weeks and beyond. Additionally, it will allow an assessment of the impact of dose adjustments on efficacy results. As these variables are summarized over time and the initial values can be impacted by the treatment in the feeder study, the presentation using a combination of feeder/extension study treatment groups is intended to provide perspective on the change in these values from the feeder study through the Treatment Period of PS0014. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline study results by scheduled visit for PS0014.

Was changed to

Efficacy analyses will be summarized based on the FAS **during the Treatment Period**. The summaries described in this section will provide data on maintenance of effect of open-label bimekizumab over 144 weeks and beyond. Additionally, it will allow an assessment of the impact of dose adjustments on efficacy results. As these variables are summarized over time and the initial values can be impacted by the treatment in the feeder study, the presentation using a combination of feeder/extension study treatment groups is intended to provide perspective on the change in these values from the feeder study through the Treatment Period of PS0014. The table presentations will display descriptive statistics for the Baseline of the feeder study and the observed and change from Baseline study results by scheduled visit for PS0014. **Selected efficacy summaries during the OLE2 Period may also be provided for selected efficacy variables.**

Change #30

14.9 Planned interim analysis and data monitoring

An interim analysis is planned at Week 48, details of which will be documented in the SAP. Additional interim analyses may be performed and corresponding interim Clinical Study Reports (CSRs) may be written. A final analysis and updated final CSR will be prepared once all data through the SFU visit) have been collected.

Was changed to

An interim analysis is planned at Week 48 **and Week 144**, details of which will be documented in the SAP. Additional interim analyses may be performed **(details of which will be documented in the SAP). Corresponding** interim Clinical Study Reports (CSRs) may be written. A final analysis and updated final CSR will be prepared once all data through the **SFU visit) OLE2 Period and SFU2 Visit** have been collected.

19 DECLARATION AND SIGNATURE OF INVESTIGATOR

I confirm that I have carefully read and understood this protocol and agree to conduct this clinical study as outlined in this protocol, according to current Good Clinical Practice and local laws and requirements.

I will ensure that all subinvestigators and other staff members read and understand all aspects of this protocol.

I have received and read all study-related information provided to me.

The objectives and content of this protocol as well as the results deriving from it will be treated confidentially, and will not be made available to third parties without prior authorization by UCB.

All rights of publication of the results reside with UCB, unless other agreements were made in a separate contract.

Investigator:

Printed name	Date/Signature

20 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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