PROTOCOL PS0015 AMENDMENT 5.4

A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, SECUKINUMAB-CONTROLLED, PARALLEL-GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BIMEKIZUMAB IN ADULT SUBJECTS WITH MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

PHASE 3b

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SERIOUS ADVERSE EVENT REPORTING

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AE	adverse event
AESI	adverse event of special interest
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the curve
axSpA	axial spondyloarthritis
BA	bioavailability
BCG	Bacillus Calmette-Guerin
BP	blood pressure
BSA	body surface area
cAMP	cyclic adenosine monophosphate
CDC	Centers for Disease Control
CDMS	clinical data management system
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CPM	Clinical Project Manager
CPMP	Committee for Proprietary Medicinal Products
CRO	contract research organization
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
ECG	electrocardiogram
eCRF	electronic Case Report Form
eC-SSRS	electronic Columbia Suicide Severity Rating Scale
ePRO	Electronic Patient-Reported Outcome
EQ-5D-3L	European Quality-of-Life 5-Dimensions 3-Level
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FAS	Full Analysis Set
GCP	Good Clinical Practice

GMP	Good Manufacturing Practice
HCV	hepatitis C virus
HCV Ab	hepatitis C antibody
HIV	human immunodeficiency virus
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
IND	Investigational New Drug
IRB	Institutional Review Board
IRT	interactive response technology
iv	intravenous(ly)
LOCF	last observation carried forward
LTB	latent tuberculosis
LTBI	latent tuberculosis infection
mAb	monoclonal antibody
MI	multiple imputation
mNAPSI	Modified Nail Psoriasis Severity Index
MS	Maintenance Set
NRI	nonresponder imputation
NSAID	nonsteroidal anti-inflammatory drug
NTMB	nontuberculous mycobacterium
OLE	open-label extension
OL2S	OLE2 Period Set
OLS	Open-Label Set

PASE	Psoriatic Arthritis Screening and Evaluation
PASI	Psoriasis Area Severity Index
PD	pharmacodynamic(s)
PDE	phosphodiesterase
PDILI	potential drug-induced liver injury
PEOT	Premature End of Treatment
PFS	prefilled syringe
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
PPS	Per-Protocol Set
PS	Patient Safety
PsA	psoriatic arthritis
PSO	psoriasis
PT	preferred term
Q4W	every 4 weeks
Q8W	every 8 weeks
QOL	quality of life
RS	Randomized Set
SAE	serious adverse event
SAP	Statistical Analysis Plan
sc	subcutaneous(ly)
scalp IGA	scalp-specific Investigator's Global Assessment
SFU	Safety Follow-Up
SOP	Standard Operating Procedure
SS	Safety Set
TB	tuberculosis
TEAE	treatment-emergent adverse event
TNF	tumor necrosis factor
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 3b, multicenter, randomized, 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 plaque psoriasis (PSO).

The study population consists of adult subjects (≥18 years of age) with a diagnosis of moderate to severe chronic plaque PSO (Baseline Psoriasis Area Severity Index [PASI] score ≥12 and body surface area [BSA] affected by PSO ≥10% and Investigator's Global Assessment [IGA] score ≥3 [on a 5-point scale]) who are a candidate for secukinumab, or for systemic PSO therapy and/or phototherapy.

Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. For each subject, the study will last a maximum of 165 weeks and will consist of 5 periods: a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at Week 44), an Open-Label Extension (OLE) Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W) followed by a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP] depending on subject's participation in the second OLE Period [OLE2 Period]; see paragraph below).

Subjects participating in the OLE2 Period (implemented as part of Protocol Amendment #5.4) will enter the OLE2 Period after completing the OLE 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 treatment period with final visit at OLE2 Week 48, followed by a SFU Period (SFU2, 20 weeks after the final dose of IMP administered in the OLE2 Period).

During the first 16 weeks of the double-blind Treatment Period, eligible subjects will be randomized 1:1 to receive one of the following blinded IMP regimens:

- Bimekizumab 320mg administered subcutaneously (sc) every 4 weeks (Q4W)
- Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W

Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.

Approximately 350 subjects will be randomized to bimekizumab 320mg and approximately 350 subjects will be randomized to secukinumab. Investigational medicinal product will be administered at Baseline, Weeks 1, 2, 3, and 4 and then Q4W thereafter, until Week 44 (double-blind Treatment Period). All doses will be administered in the clinic.

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg every 8 weeks (Q8W). To maintain the blind after re-randomization, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Subjects in the secukinumab arm will continue to receive secukinumab 300mg Q4W.

At the completion of the Week 48 visit assessments, subjects may receive open-label bimekizumab treatment for an additional 96 weeks during the OLE Period. All subjects enrolling

in the OLE Period will, after signing a new ICF, be evaluated for eligibility, be randomized, and receive their first dose of bimekizumab in the OLE Period.

During the OLE Period, eligible subjects will receive the following IMP regimens as determined by the subject's treatment regimen and PASI response in the double-blind Treatment Period.

At Week 48, subjects receiving:

- Bimekizumab 320mg Q4W who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Bimekizumab 320mg Q4W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q8W.
- Secukinumab who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Secukinumab who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

During the OLE Period, subjects will attend study visits at Weeks 52, 56, 64, and 72, and then every 12 weeks.

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64 or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed Week 64.

All subjects not enrolling in the OLE Period will have the Week 48 study assessments and will enter the SFU Period.

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 #5.4 (addition of a 48-week treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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 Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4

implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit will be treated with bimekizumab Q4W for the first 16 weeks, and then will switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

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

The primary objective of the study is to compare the efficacy of bimekizumab administered sc for 16 weeks versus secukinumab at achieving complete clearance (PASI100) in subjects with moderate to severe chronic plaque PSO. The secondary objectives of the study are listed in Section 3.2.

The primary efficacy variable is the PASI100 response, defined as complete clearance from Baseline in the PASI score, at Week 16. The secondary efficacy variables are listed in Section 4.2.

Pharmacokinetic variables are listed in Section 4.3.3. The immunological variable is listed in Section 4.3.4.

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

Safety variables to be assessed are adverse events (AEs), vital signs, electrocardiograms (ECGs), and measurements of laboratory parameters.

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 psoriasis

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 at 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 psoriasis

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, and 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 pro-inflammatory 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), 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 Th17-T cells.
  - Ustekinumab has been approved in the US and the EU for the treatment of patients with moderate to severe plaque psoriasis 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 CD4+ 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 pro-inflammatory 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 pro-inflammatory cytokines and chemokines.
- Brodalumab has been approved in the US for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies. In the EU, brodalumab is indicated for the treatment of moderate to severe plaque PSO in adult patients who are candidates for systemic therapy. 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 pro-inflammatory cytokines and chemokines. Brodalumab has a black box warning regarding suicidal ideation and behavior.

2.2 Bimekizumab

Bimekizumab (UCB4940) 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 pro-inflammatory 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 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 8mg 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 pharmacokinetics (PK) of bimekizumab was linear in the tested dose range and the median half-life 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 Weeks 3 and 6
- 160mg loading dose followed by 80mg at Weeks 3 and 6
- 240mg loading dose followed by 160mg at Weeks 3 and 6
- 560mg loading dose followed by 320mg at Weeks 3 and 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 (oropharyngitis 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 two 1mL injections of 80mg 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 (AUC) 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 treatment-emergent adverse events (TEAEs) leading to discontinuation, and no serious adverse events (SAEs) or fatalities were reported. The only preferred term (PT) experienced by more than 1 subject in either treatment group was injection site pain (5 subjects [83.3%] and 3 subjects [50%] 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 pharmacokinetics of bimekizumab administered as subcutaneous 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 [redacted] 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 #5.4 implementation are presented and described in the current version of the IB.

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/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 are 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 this study is to compare the efficacy of bimekizumab administered sc for 16 weeks versus secukinumab at achieving complete clearance (PASI100) in subjects with moderate to severe chronic plaque PSO.

3.2 Secondary objectives

The secondary objectives of the study are to:

- Evaluate the efficacy of bimekizumab compared with secukinumab after 4 weeks, 16 weeks, and 48 weeks of treatment.
- Assess TEAEs, SAEs, and TEAEs leading to withdrawal adjusted by duration of subject exposure to IMP.

3.3 Other objectives

The other objectives of the study are to demonstrate the effects of bimekizumab on the following aspects of the disease:

- Assess the efficacy of bimekizumab over time
- Assess the change of skin-related quality of life (QOL)
- Assess the change of general health-related QOL
- Assess the change in nail PSO over time in subjects with nail PSO at Baseline
- Assess the change in psoriatic scalp disease over time in subjects with scalp PSO at Baseline
- Assess the change in psoriatic palmoplantar disease over time in subjects with palmoplantar PSO at Baseline
- Assess the change in patient global assessment PSO score
- Assess the change in symptoms of PSO (itch, pain, and scaling) as reported by subjects
- Assess work productivity status
- Assess the safety and tolerability of bimekizumab
- Assess the PK of bimekizumab

- Assess the immunogenicity of bimekizumab
- Assess the maintenance of efficacy of bimekizumab dosing Q4W versus Q8W
- Assess the safety and efficacy of initiating bimekizumab therapy in subjects who received secukinumab in the double-blind Treatment Period

4 STUDY VARIABLES

4.1 Primary efficacy variable

The primary efficacy variable is the PASI100 response, defined as complete clearance from Baseline in the PASI score, at Week 16.

4.2 Secondary variables

4.2.1 Secondary efficacy variables

The secondary efficacy variables are:

- PASI75 response at Week 4
- PASI90 response at Week 16
- PASI100 response at Week 48
- IGA response (0/1) (defined as Clear or Almost Clear with at least a 2-category improvement relative to Baseline) at Week 16

4.2.2 Secondary safety variables

The secondary safety variables are:

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

4.3 Other variables

The other variables are listed below and will be evaluated according to the planned assessments (Table 5–1, Table 5–2, and Table 5-3).

4.3.1 Other efficacy variables

The other efficacy variables are listed below and will be evaluated according to the planned assessments (Table 5–1, Table 5–2, and Table 5-3). This excludes the time points for the primary and secondary variables specified above in Section 4.1 and Section 4.2.1, respectively.

The other efficacy variables are:

- PASI75, PASI90, and PASI100 response
- Time to PASI75, PASI90, and PASI100 response
- Absolute and percent change from Baseline in PASI
- Percentage of subjects with PASI ≤1, ≤2, ≤3, and ≤5

- IGA response (Clear)
- IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline)
- Shift from Baseline in IGA 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)
- Percent of subjects achieving a DLQI total score of 0 or 1
- Percent of subjects achieving a minimal clinically important difference (improvement from Baseline of 4 or more) in the DLQI
- Change from Baseline in the Patient's Global Assessment of Disease Activity (PGADA) for the arthritis visual analog scale (VAS) in subjects with PsA at Baseline
- Change from Baseline in Patient Global Assessment of PSO score
- Change from Baseline in symptoms of PSO (itch, pain, and scaling)
- Change from Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) score for subjects with nail PSO at Baseline
- Percent of subjects achieving mNAPSI75, mNAPSI90, and mNAPSI100 for subjects with nail PSO at Baseline
- Scalp-specific Investigator's Global Assessment (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
- Responses to the European Quality-of-Life 5-Dimensions 3-Level (EQ-5D-3L) dimensions, absolute and changes from Baseline in EQ-5D-3L VAS scores
- Change from Baseline in Work Productivity and Activity Impairment Questionnaire-specific health problem (WPAI-SHP) V2.0 adapted to PSO scores
- Change from Baseline in the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire scores (function score, symptom score, and total score)
- Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47)

4.3.2 Other safety variables

Other safety variables to be assessed are:

- Severity and frequency of AEs
- Change from Baseline in vital signs

- ECG results
- Change from Baseline in clinical laboratory values (chemistry, hematology, and urinalysis)
- Change from Baseline in Patient Health Questionnaire-9 (PHQ-9) scores

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

4.3.3 Pharmacokinetic variable

The PK variable is the plasma concentration of bimekizumab.

4.3.4 Immunological variable

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

5 STUDY DESIGN

5.1 Study description

PS0015 is a randomized, double-blind, secukinumab-controlled, parallel-group study to evaluate the efficacy and safety of bimekizumab administered sc to subjects with moderate to severe chronic plaque PSO. To be eligible to participate in this study, subjects must be adults with a diagnosis of moderate to severe plaque PSO (PASI ≥12 and BSA ≥10% and IGA score ≥3 [on a 5-point scale]) who are candidates for secukinumab, or for systemic PSO therapy and/or phototherapy.

5.2 Study periods

This study will include the following periods:

- A Screening Period (2 to 5 weeks)
- A double-blind Treatment Period (48 weeks; final dose at Week 44)
- An optional OLE Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W) followed by a SFU Period (20 weeks after the final dose of IMP administered in the OLE Period depending upon subject's participation in the OLE2 Period), and
- An optional 48-week OLE2 Period followed by a SFU Period (SFU2, 20 weeks after the final dose of IMP administered in the OLE2 Period).

The OLE2 Period was added as per Protocol Amendment #5.4 at the time when subjects will still be treated in the OLE (prior to Week 144 Visit) or will have finished treatment in the OLE (after completing Week 144 Visit):

- Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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).

- Eligible subjects who have completed the Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit 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 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

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

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

5.2.1 Screening Period

The Screening Period will last 2 weeks, but can be extended up to a total of 5 weeks in cases where a laboratory assessment needs to be repeated or to allow washout of prohibited medications. During this time, eligible subjects will be informed about the study and sign the Informed Consent Form (ICF), laboratory data (hematology, urine, and biochemistry tests) will be obtained, and the doses of medications used to treat PsA (if applicable) will be verified as stable. The Screening Period will also enable washout of any medications not permitted for use during the study. Subjects who require prophylaxis for latent tuberculosis (LTB) infection must be on treatment for at least 8 weeks prior to their first dose of IMP. These subjects may be rescreened once they have completed the first 8 weeks of prophylaxis treatment.

One rescreening may be allowed after consultation with the Medical Monitor.

The assessments to be performed at the Screening Visit are presented in Table 5–1.

5.2.2 Treatment Period

During the first 16 weeks of the 48-week double-blind Treatment Period, approximately 700 subjects will be randomized 1:1 to receive the following blinded IMP regimens:

- Bimekizumab 320mg administered sc Q4W (350 subjects)
- Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W (350 subjects)

Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. To maintain the blind after re-

randomization, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Subjects in the secukinumab arm will continue to receive secukinumab 300mg Q4W.

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).

Subjects withdrawing early from the study will undergo the PEOT Visit assessments and will enter the SFU Period.

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

5.2.3 OLE Period

After completion of the Week 48 visit assessments, subjects will be allowed to enroll in the OLE Period. All subjects enrolling in the OLE Period will sign a new ICF, and then receive the following IMP regimens as determined by the subject's treatment regimen and PASI response in the double-blind Treatment Period.

At Week 48, subjects receiving:

- Bimekizumab 320mg Q4W who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Bimekizumab 320mg Q4W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q8W.
- Secukinumab who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Secukinumab who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

During the OLE Period, subjects will attend study visits at Weeks 52, 56, 64, and 72, and then every 12 weeks. At study visits, IMP will be administered in the clinic by sc injection as applicable. In between study visits, subjects will self-inject IMP at home.

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64, or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed Week 64.

The last dose bimekizumab 320mg Q8W in the OLE Period will be administered at Week 136. The End of Treatment Visit of the OLE Period will be the Week 144 Visit.

All subjects not enrolling in the open-label study will have the Week 48 study assessments and will enter the SFU Period.

The assessments to be performed at each OLE Period visit are presented in Table 5–2.

5.2.4 OLE2 Period

Subjects enrolled as per Protocol Amendment #5.1 will be treated in the OLE Period until Week 136 (last dose of bimekizumab 320mg Q8W) and will be followed in a SFU Period for 20 weeks after attending the Week 144 Visit (see Section 5.2.3). After the implementation of Protocol Amendment #5.4 (addition of a 48-week treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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 Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit will be treated with bimekizumab Q4W for the first 16 weeks, and then will switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

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

The assessments to be performed at each visit of the OLE2 Period are presented in Table 5-3.

5.2.5 Safety Follow-Up Periods

The assessments for the SFU Visits are presented in Table 5–1, Table 5–2, and Table 5-3.

Two SFU Periods are considered since Protocol Amendment #5.4 implementation: a first SFU following the OLE Period and a second SFU (SFU2) following the OLE2 Period (added as per Protocol Amendment #5.4 implementation).

Subjects having completed Week 144 Visit and who are in the SFU or have completed the SFU will be invited to reinitiate their treatment in the OLE2 Period.

Subjects still being treated in the OLE Period (not having attended Week 144 yet) will have the opportunity to directly roll over in the OLE2 Period without participating in the first SFU.

Subjects who decide not to participate in OLE2 Period will undergo the first SFU period for 20 weeks after their last dose in the OLE 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 have a SFU2 Visit 20 weeks after their final dose of IMP administered up to OLE2 Week 48.

5.2.6 Premature End of Treatment

Subjects withdrawing early from the study will undergo PEOT Visit assessments (see Section 8.5) and will enter the SFU or SFU2 Period depending on when subjects withdraw.

5.3 Study duration per subject

For each subject, the study will last a maximum of up to 165 weeks, as follows:

- Screening Period: 2 to 5 weeks
- Double-blind Treatment Period: 48 weeks (final dose at Week 44)
- OLE Period: 96 weeks (final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W) followed by a Safety Follow-Up Period: a SFU Visit is planned 20 weeks after the final dose of IMP visit in the OLE Period (this SFU will not apply to subjects directly rolling over from the OLE to the OLE2 Period [see Section 5.2.5])

Subjects eligible for the OLE2 Period (added as part of Protocol Amendment #5.4) will enter the OLE2 Period after completing Week 144 of the OLE Period. The OLE2 Period will include a 48-week treatment period with a final visit at OLE2 Week 48 and a SFU Period (SFU2) of 20 weeks after the final dose of IMP administered in the OLE2 Period.

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

- 209 weeks for subjects still being treated in the OLE Period and who will directly roll over to the OLE2 Period at Week 144
- 225 weeks for subjects who have completed Week 144 and the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 Period. Note: for these subjects, the study duration will not be continuous.
- Between 209 and 225 weeks for subjects who have completed Week 144 and are participating the in the SFU. For these subjects, the maximum study duration will depend upon when they stop the 20-week SFU period to enter the 4-week OLE2 Screening Period.

5.4 Planned number of subjects and sites

Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. There will be approximately 350 subjects in the bimekizumab 320mg treatment arm and 350 subjects in the secukinumab 300mg treatment arm. The planned number of study sites is approximately 86. Every eligible subject who signs an ICF will be randomized.

5.5 Anticipated regions and countries

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

5.6 Schedule of study assessments

The schedule of study assessments is presented in Table 5–1 for the Screening and double-blind Treatment Periods, in Table 5–2 for the OLE Period, and in Table 5-3 for the OLE2 Period. At each visit, all study assessments should be performed prior to administration of IMP.

Table 5–1: Schedule of study assessments, Screening and double-blind Treatment Periods

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first dose)	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Informed consent	X																	
Inclusion/exclusion	X	X[c]																
Urine drug screen	X																	
Demographic data	X																	
Psoriasis history	X																	
eC-SSRS	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Significant past medical history and concomitant diseases	X	X[d]																
Physical exam[c, e]	X							X			X			X			X	X
Height		X																
Body weight		X							X		X			X			X	
Vital signs[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology and biochemistry	X	X	X	X		X	X	X	X		X		X		X		X	X
Urinalysis	X	X							X		X		X		X		X	X
ECG	X								X				X				X	
Pregnancy testing[g]	X	X				X	X	X	X	X	X	X	X	X	X	X	X	X
Hepatitis B and C testing[h]	X																	
HIV testing[i]	X																	
Chest x-ray[j]	X																	
IGRA tuberculosis test	X															X		

Table 5–1: Schedule of study assessments, Screening and double-blind Treatment Periods

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first dose)	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Tuberculosis questionnaire	X	X						X			X			X			X	X
PASI	X	X	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	X	X	
Blood sample for bimekizumab/secukinumab plasma concentrations[k]		X	X	X		X	X	X	X	X	X			X			X	X
Blood sample for anti-bimekizumab antibodies[k]		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	X	X	
DLQI		X				X	X	X	X				X				X	
Patient Symptoms (itch, pain, and scaling)		X				X	X	X	X				X				X	
PHQ-9	X	X				X	X	X	X	X	X	X	X	X	X	X	X	
scalp IGA[l]		X	X[l]	X[l]		X[l]	X[l]	X[l]	X[l]				X[l]				X[l]	
mNAPSI[m]		X							X[m]				X[m]				X[m]	
pp-IGA[n]		X							X[n]				X[n]				X[n]	
Patient Global Assessment of psoriasis		X				X	X	X	X				X				X	
PASE		X															X	
PGADA		X							X[o]				X[o]				X[o]	
WPAI-SHP V2.0		X							X				X				X	

Table 5–1: Schedule of study assessments, Screening and double-blind Treatment Periods

Protocol activity \ Visit[a]/ Week	Screening	Treatment Period																SFU[b]
		Baseline (first dose)	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Photographs of skin and nails (subset of sites)		X	X	X		X	X	X	X				X				X	
EQ-5D-3L		X				X			X				X				X	
Concomitant medication	X	X	X	X	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	X	X	X	X
Randomization		X							X									
IRT[p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
IMP administration[q]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic Case Report Form; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=European Quality-of-Life 5-Dimensions 3-Level; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=Modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; 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; PsA=psoriatic arthritis; scalp IGA=scalp-specific Investigator's Global Assessment; SFU=Safety Follow-Up; TB=tuberculosis; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Table 5–1: Schedule of study assessments, Screening and double-blind Treatment Periods

Protocol activity \ Visit[a]/ Week	Screening	Treatment Period																SFU[b]
		Baseline (first dose)	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	

[a] Visit windows of ±3 days from the first dose from the Week 1 visit to the Week 24 visit. Visit windows of ±7 days from Week 28 through Week 48/PEOT. The SFU Visit window is ±7 days relative to the scheduled visit date.
[b] The SFU Visit will occur 20 weeks after the final dose if subject does not enroll in the OLE Period.
[c] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.
[d] Ensure no significant changes in medical history.
[e] The physical examination will be performed as per Section 12.3.5.
[f] Vital signs (blood pressures, 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 the Screening. Urine pregnancy testing will be performed at all other visits.
[h] Subjects who have evidence of or test positive for hepatitis B by any of the following criteria: 1) positive for hepatitis B surface antigen; 2) positive for anti-hepatitis B core antibody are excluded. A positive test for HCV is defined as: 1) positive for hepatitis C antibody, and 2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction) are also excluded. Subjects will also be tested for anti-hepatitis B surface antibody.
[i] The HIV test results will not be recorded in the eCRF.
[j] Screening chest x-ray must occur within 3 months prior to Screening Visit.
[k] All blood samples taken prior to dosing.
[l] The scalp IGA will be assessed only for those subjects with scalp involvement (scalp IGA score >0) at Baseline.
[m] The mNAPSI will be assessed only in subjects with nail involvement (mNAPSI score >0) at Baseline.
[n] The pp-IGA will be assessed only in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline.
[o] The PGADA is assessed for all subjects at Baseline. At all subsequent visits, the PGADA is only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).
[p] IMP administration is based on randomization.
[q] The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through Week 48, the dosing window is ±7 days relative to the scheduled dosing visit.

Table 5–2: Schedule of study assessments, OLE Period

Visit[a]/ Week / Protocol activity	48 (1st OLE dose)	Year 2												Year 3													SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT	
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C
Informed consent	X																									
Eligibility[c]	X																									
eC-SSRS		X	X		X		X			X			X			X			X			X			X	X
Physical exam[d,e]					X		X			X			X			X			X			X			X	X
Body weight													X												X	
Vital signs[f]		X	X		X		X			X			X			X			X			X			X	X
Hematology and biochemistry		X	X		X		X			X			X			X			X			X			X	X
Urinalysis					X		X			X			X			X			X			X			X	X
ECG													X												X	
Pregnancy testing (urine)[g]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IGRA tuberculosis test													X												X	
Tuberculosis questionnaire			X		X		X			X			X			X			X			X			X	X
PASI		X	X		X		X			X			X			X			X			X			X	
Percentage of BSA		X	X		X		X			X			X			X			X			X			X	
Blood sample for bimekizumab plasma concentrations[h]							X						X						X						X	X
Blood sample for anti-bimekizumab antibodies[h]							X						X						X						X	X
IGA		X	X		X		X			X			X			X			X			X			X	
DLQI							X						X						X						X	
Patient Symptoms (itch, pain, and scaling)			X		X		X			X			X			X			X			X			X	
PHQ-9		X	X		X		X			X			X			X			X			X			X	
scalp IGA[i]							X						X						X						X	
mNAPSI[j]							X						X						X						X	

Table 5–2: Schedule of study assessments, OLE Period

Protocol activity \ Visit[a]/ Week	48 (1st OLE dose)	Year 2												Year 3												SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT	
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C
pp-IGA[k]							X						X						X						X	
EQ-5D-3L							X						X						X						X	
PASE													X												X	
PGADA[l]													X												X	
WPAI-SHP V2.0													X												X	
Concomitant medication		X	X		X		X			X			X			X			X			X			X	X
Adverse events		X	X		X		X			X			X			X			X			X			X	X
Randomization	X																									
IRT[m]	X	X	X		X		X			X			X			X			X			X			X	X
IMP administration – Q4W [n, o, p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
IMP administration – Q8W [n, o]	X		X		X		X		X		X		X		X		X		X		X		X			

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic Case Report Form; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=European Quality-of-Life 5-Dimensions 3-Level; H=home; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=Modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; 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; PsA=psoriatic arthritis; scalp IGA=scalp-specific Investigator's Global Assessment; SFU=Safety Follow-Up; TB=tuberculosis; WPAI SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from Week 48 through Week 72. Visit windows of ±14 days from Week 76 through Week 144. The SFU Visit window is ±7 days relative to the scheduled visit date.

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

[c] Criteria for OLE Period, Section 6.3.

[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 12.3.5.

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

[g] Pregnancy testing will consist of urine pregnancy testing at all visits. Home pregnancy test kits will be provided to participants for use between clinic visits.

Table 5–2: Schedule of study assessments, OLE Period

Visit[a]/ Week	48 (1st OLE dose)	Year 2												Year 3													SFU[b]
Protocol activity		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT		
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C	

[h] All blood samples taken prior to dosing.
[i] The scalp IGA will be assessed only for those subjects with scalp involvement (scalp IGA score >0) at Baseline.
[j] The mNAPSI will be assessed only in subjects with nail involvement (mNAPSI score >0) at Baseline.
[k] The pp-IGA will be assessed only in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline.
[l] The PGADA is assessed only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).
[m] IMP administration is based on randomization.
[n] From Week 48 through Week 72, the dosing window is ±7 days relative to the scheduled dosing visit. From Week 76 through the Week 140 Visit, the dosing window is ±14 days relative to the scheduled dosing visit.
[o] 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.
[p] Q4W IMP administration only applies to those subjects who have not yet changed to Q8W at Week 64, or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 64 visit after implementation of Protocol Amendment #5.

Table 5-3: Schedule of study assessments, OLE2 Period

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	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											
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	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	
IGA	Group B	Group A[f] + B			X		X		X		X	
DLQI		Group A[f] + B					X				X	X

Table 5-3: Schedule of study assessments, OLE2 Period

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	C
Protocol activity			OLE2 Groups A + B									
Patient Symptoms (itch, pain, and scaling)		Group A[f] + B			X		X		X		X	
PHQ-9	Group B	Group A[f] + B			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
Adverse events	Group B [k]	Group A[f] + B			X		X		X		X	X
IRT	X	Group A[f] + B			X		X		X		X	X

Table 5-3: Schedule of study assessments, OLE2 Period

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	C
Protocol activity			**OLE2 Groups A + B**									
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		

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; IGA=Investigator's Global Assessment; H=home; IMP=investigational medicinal product; IRT=interactive response technology; OLE=open label extension; PASI=Psoriasis Area Severity Index; PHQ-9=Patient Health Questionnaire-9; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU2=Safety Follow-Up #2; TB=tuberculosis; 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 from the first dose at 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 their 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 12.3.5.

[f] These tests are performed as part of Week 144 visit (the Week 144 Visit coincides with the Week 144/OLE2 Baseline Visit for subjects in Group A, ie, direct enroller from OLE 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. Home pregnancy test kits will be provided to participants for use between clinic visits.

[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.

Table 5-3: Schedule of study assessments, OLE2 Period

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	C
Protocol activity			OLE2 Groups A + B									

[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 W144/OLE2 Screening Visit onwards.

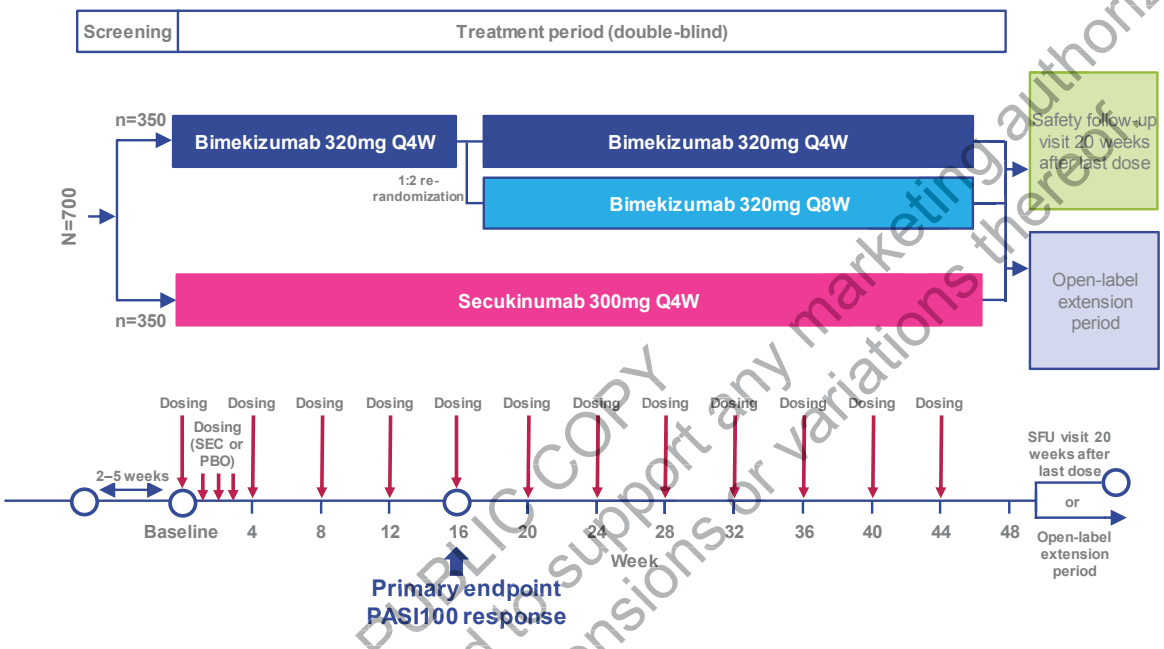
[m] The dosing window is ±14 days relative to the Week 144/OLE2 Baseline Visit.

[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 PS0015 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 Week OLE2 Screening to the OLE2 Week 48 Visit is presented in Figure 5–3.

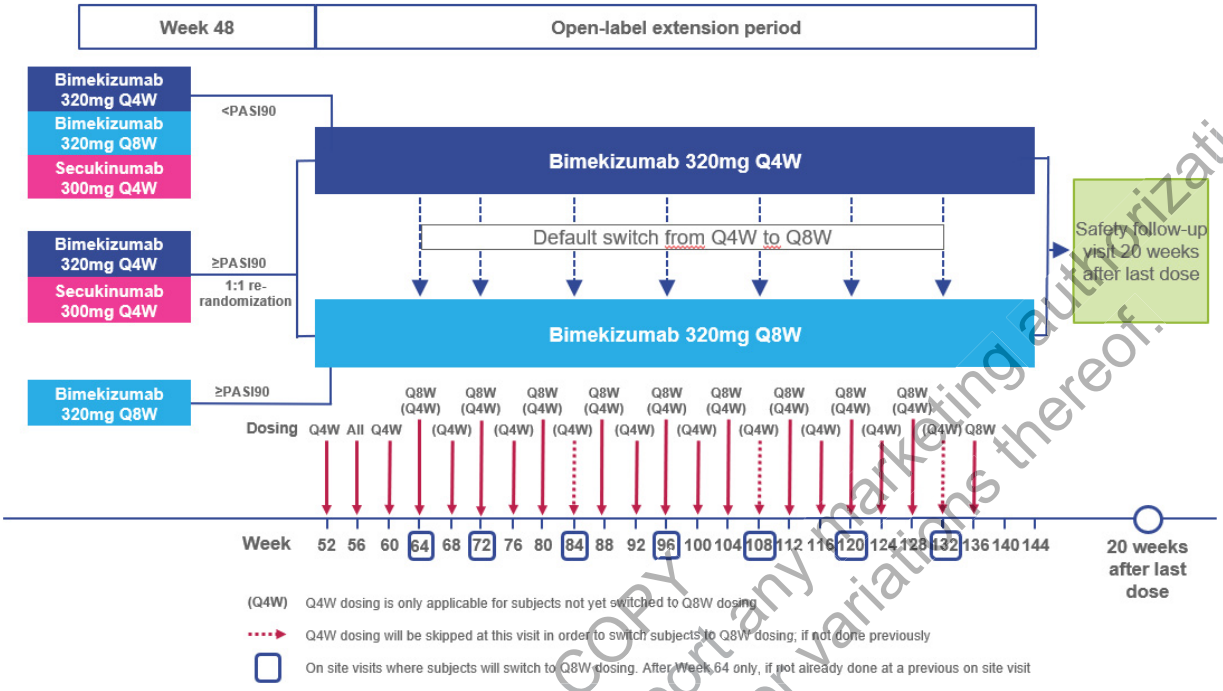
Figure 5–1: Schematic diagram, Screening and double-blind Treatment Period (through Week 48)



IGA=Investigator's Global Assessment; IMP=investigational medicinal product; PASI100=Psoriasis Area Severity Index complete response; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks; SEC=secukinumab; SFU=safety follow-up

Note: At Week 28 and all following visits, subjects on continuous treatment 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.

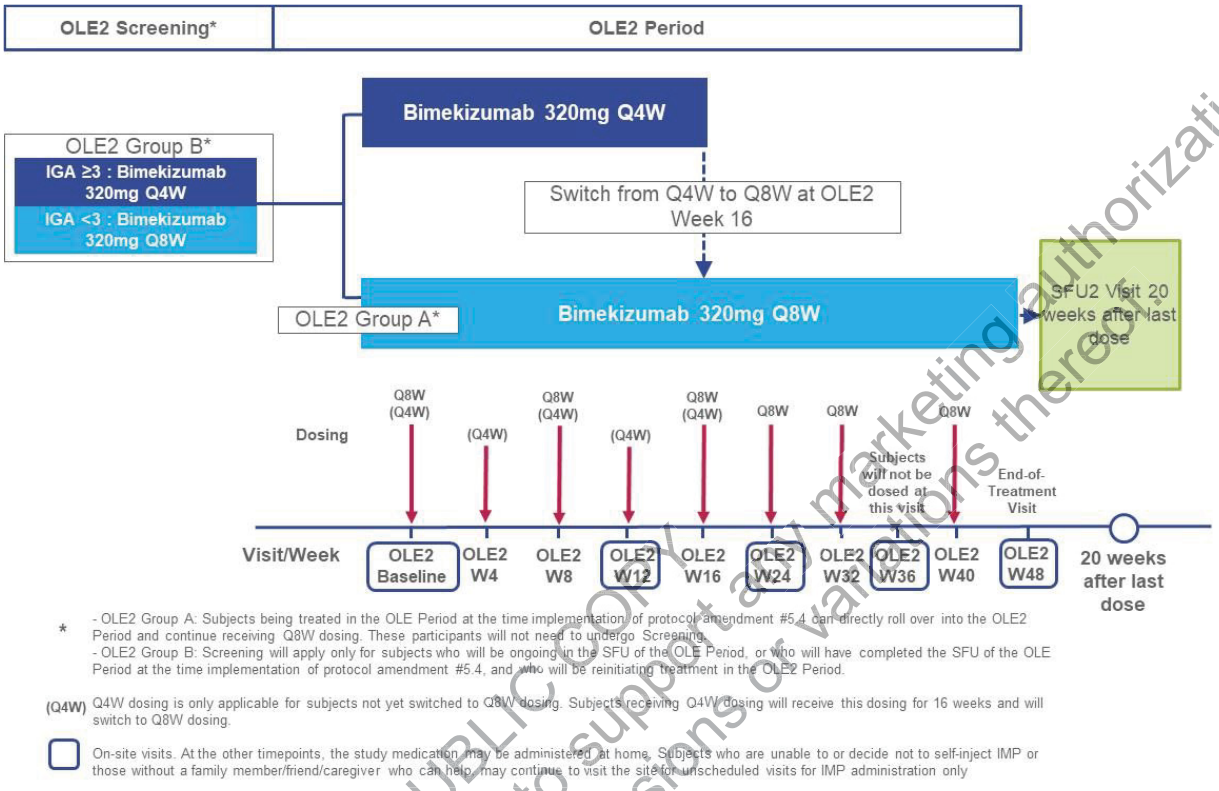
Figure 5–2: Schematic diagram, OLE Period (Week 48 through Week 144)



PASI=Psoriasis Area Severity Index; PASI90=90% improvement in the PASI score; Q4W=every 4 weeks; Q8W=every 8 weeks

Note: The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64, or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 64 visit prior to implementation of Protocol Amendment #5.1.

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

5.8.1 Study design

A randomized, double-blind, active comparator-controlled study design has been selected to demonstrate efficacy and safety of bimekizumab relative to secukinumab. The study population will include adults with moderate to severe chronic plaque PSO and allow subjects who have received previous biologic treatment as well as those who are biologic treatment naïve. The primary efficacy outcome measure (based on PASI) and other efficacy assessments included in this study are consistent with those used for other PSO studies and are considered appropriate for establishing efficacy of bimekizumab. A treatment period of 48 weeks (final dose at Week 44) will be used to demonstrate the superiority of bimekizumab versus secukinumab based on PASI100 at Week 16, along with the maintenance of efficacy of bimekizumab at Week 48.

The addition of the OLE Period will allow collection of long-term efficacy and safety data from eligible subjects on open-label bimekizumab for an additional 96 weeks.

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 treatment period for subjects continuing their current treatment or reinitiating treatment at the Week 144/OLE2 Baseline Visit.

5.8.2 Dose selection

Bimekizumab doses ranging from 64mg to 480mg were evaluated in the Phase 2b multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study PS0010. Bimekizumab 320mg was found to have an acceptable safety profile, only required 2 injections per treatment administration, and achieved significant PASI responses at Week 12 (summarized in the IB). Furthermore, data from the Phase 2a multicenter, randomized, subject-blind, investigator-blind study PS0016 and PK/PD modeling in this PSO population indicates improved responses through Week 16. Therefore, a bimekizumab dose of 320mg Q4W through Week 16 was selected for this study.

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 64, 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 64 visit at the time of implementation of Protocol Amendment #5.1 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 who are participating in the OLE Period can directly roll over to the OLE2 Period and continue receiving bimekizumab 320mg Q8W. Eligible subjects who are in the SFU of the OLE Period or who have completed the SFU at the time of Protocol Amendment #5.4 implementation can reinitiate their treatment in the OLE2 Period based on their 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, in line with the original initial treatment period, followed by 320mg Q8W for the remaining dosing timepoints of the OLE2 Period.

6 SELECTION AND WITHDRAWAL OF SUBJECTS

6.1 Inclusion criteria

To be eligible to participate in this study, all of the following criteria must be met at Screening and be reconfirmed 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, or medication intake according to the judgment of the Investigator.
3. Male or female at least 18 years of age.
4. Subject must have had chronic plaque PSO for at least 6 months prior to the Screening visit.

5. Subject must have PASI ≥12 and BSA affected by PSO ≥10% and IGA score ≥3 on a 5-point scale.
6. Subject must be a candidate for systemic PSO therapy and/or phototherapy.
7. Subject must be considered, in the opinion of the Investigator, to be a suitable candidate for treatment with secukinumab per regional labeling and has no contraindications to receive secukinumab as per the local label.
8. 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.
   - Or, 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 Visit 1 (Screening) and immediately prior to first dose. 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.
9. Subject agrees not to change their usual sun exposure during the course of the study and to use ultraviolet A/ultraviolet B (UVA/UVB) sunscreens if unavoidable exposure occurs.

6.2 Exclusion criteria

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

1. Female subject who is breastfeeding, pregnant, or plans to become pregnant during the study or within 20 weeks following the final dose of IMP.
2. Subject previously participated in a bimekizumab clinical study and received at least 1 dose of the IMP (including placebo).
3. Subject is currently participating in another study of a medication (systemic) under investigation. Subject must be washed out of the medication for 12 weeks or at least 5 half-lives prior to the Baseline Visit, whichever is greater.

4. Subject is currently participating in another study of a topical medication under investigation. Subject must be washed out of the medication for 4 weeks prior to the Baseline Visit.
5. Subject is currently, or was within the 4 weeks prior to the Baseline Visit, participating in another study of a medical device under investigation.
6. Subject has a known hypersensitivity to any excipients of bimekizumab or secukinumab.
7. Subject has a form of PSO other than chronic plaque-type (eg, pustular, erythrodermic and guttate PSO or drug-induced PSO).
8. Subject has an active infection or history of infection(s) as follows:
   - Any active infection (except common cold) within 14 days prior to Baseline
   - A serious infection, defined as requiring hospitalization or iv anti-infective(s) within 2 months prior to the Baseline visit
   - A history of opportunistic, recurrent, or chronic infections that, in the opinion of the Investigator, might cause this study to be detrimental to the subject. Opportunistic infections are infections caused by uncommon pathogens (eg, pneumocystis jirovecii, cryptococcosis) or unusually severe infections caused by common pathogens (eg, cytomegalovirus, herpes zoster)
9. Subject has concurrent acute or chronic viral hepatitis B or C or human immunodeficiency virus (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 (HCV) is defined as: (1) positive for hepatitis C antibody (HCV Ab) and (2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction).
10. Subject has received any live (includes attenuated) vaccination within the 8 weeks prior to the Baseline visit (eg, inactivated influenza and pneumococcal vaccines are allowed, but nasal influenza vaccination is not permitted).
11. Subject has received Bacillus Calmette-Guerin (BCG) vaccinations within 1 year prior to the Baseline Visit.
12. Subject has known tuberculosis (TB) infection, is at high risk of acquiring TB infection, or has current or history of nontuberculous mycobacterium (NTMB) infection. A subject with LTB (a positive interferon-gamma release assay [IGRA] and diagnosis confirmed by TB specialist) may be rescreened once and enrolled after receiving at least 8 weeks of appropriate LTB infection therapy and if no evidence of therapy-related hepatotoxicity has occurred prior to the first injection (alanine aminotransferase [ALT]/aspartate aminotransferase [AST] remain ≤3 times the upper limit of normal [ULN]).

    Subject has a past history of active TB involving any organ system unless adequately treated according to World Health Organization/Centers for Disease Control (CDC) therapeutic guidance and proven to be fully recovered upon consult with a TB specialist.

    Refer to Section 12.3.1 for details on determining full TB exclusion criteria.

13. Subject has a history of a lymphoproliferative disorder including lymphoma or current signs and symptoms suggestive of lymphoproliferative disease.
14. Subject has any active malignancy or history of malignancy within 5 years prior to the Screening Visit EXCEPT treated and considered cured cutaneous squamous or basal cell carcinoma, or in situ cervical cancer.
15. Subject has a diagnosis of inflammatory conditions other than PSO or PsA, including but not limited to rheumatoid arthritis, sarcoidosis, or systemic lupus erythematosus. Subjects with a diagnosis of Crohn's disease or ulcerative colitis are allowed as long as they have no active symptomatic disease at Screening or Baseline.
16. Subject has had major surgery (including joint surgery) within the 3 months prior to the Baseline Visit, or has planned major surgery within 6 months after entering the study.
17. Subject has any systemic disease (ie, cardiovascular, neurological, renal, liver, metabolic, gastrointestinal, hematological, immunological, etc) considered by the Investigator to be uncontrolled, unstable, or likely to progress to a clinically significant degree during the course of the study.
18. Subject has had myocardial infarction or stroke within the 6 months prior to the Screening Visit.
19. Subject has laboratory abnormalities at Screening, including any of the following:
    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. White blood cell count $<3.00x10^3/\mu L$
    c. Absolute neutrophil count $<1.5x10^3/\mu L$
    d. Lymphocyte count <500 cells/μL
    e. Hemoglobin <8.5g/dL
    f. Any other laboratory abnormality, which, in the opinion of the Investigator, will prevent the subject from completing the study or will interfere with the interpretation of the study results.

    Individual screening tests for which the results are in error, borderline, or indeterminate for inclusion in the study can be repeated once for confirmation during the Screening Period. Upon retesting, subjects whose results remain outside this threshold should not be randomized.
20. Subject has any other condition, including medical or psychiatric, which, in the Investigator's judgment, would make the subject unsuitable for inclusion in the study.
21. Subject has previous exposure to secukinumab.
22. Subject has experienced primary failure (no response within 12 weeks) to one or more IL-17 biologic response modifiers (ie, brodalumab, ixekizumab), or to more than one biologic response modifier other than an IL-17.

23. Subject is taking PsA medications other than stable doses (ie, stable for at least 1 week prior to the Screening Visit) of nonsteroidal anti-inflammatory drugs (NSAIDs) or analgesics (see Section 7.8.1.2).
24. Subject has a history of chronic alcohol or drug abuse within 6 months prior to Screening as evaluated by the Investigator based on medical history, site interview, and/or results of the specified urine drug screen.

25a. Presence of active suicidal ideation, or positive suicide behavior using the "Screening" version of the electronic Columbia Suicide Severity Rating Scale (eC-SSRS) and with either of the following criteria:

- History of a suicide attempt within the 5 years prior to the Screening Visit. Subjects with a history of a suicide attempt more than 5 years ago should be evaluated by a mental healthcare professional (eg, locally licensed psychiatrist, psychologist, or master's level therapist) before enrolling into the study.
- Suicidal ideation in the past month prior to the Screening Visit as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the "Screening" version of the eC-SSRS.

26. Subject has presence of moderately severe major depression or severe major depression, indicated by a score ≥15 using the screening PHQ-9. Medication used to treat depression should be stable for 8 weeks prior to baseline.
27. Subject is a member of Investigator site personnel directly affiliated with this study and/or their immediate families. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
28. Subject is a UCB employee or employee of third-party organizations involved in the study.
29. Subject is taking or has taken prohibited psoriasis medications without meeting the mandatory washout period relative to the Baseline Visit (Table 7–2).

6.3 Eligibility for the OLE Period

Prior to entering the OLE Period, subjects on double-blind study treatment must complete all of the Week 48 visit assessments. Prior to initiating the OLE Period assessments, all subjects will be asked to read and sign a separate ICF. To be eligible to participate in the OLE Period of this study, the subject must have completed the double-blind Treatment Period without meeting any withdrawal criteria and have been compliant with the ongoing clinical study requirements.

6.4 Eligibility for the OLE2 Period

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

6.4.1 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 OLE Period to Week 144 without meeting any withdrawal criteria defined in Section 6.5.

6.4.2 OLE2 Period Group A subjects

To participate in the OLE2 Period, subjects still treated in the OLE Period and who completed the Week 144 Visit by the time of the implementation of Protocol Amendment #5.4 will not need to fulfil other eligibility criteria than those listed in Section 6.4.1 and will continue their treatment from the Week 144/OLE2 Baseline Visit if they do not meet any of the withdrawal criteria defined in Section 6.5.

6.4.3 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 #5.4 implementation:

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 is 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 OLE study 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 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/µL

- 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 (HCV) is defined as: (1) positive for hepatitis C antibody (HCV Ab) and (2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction).
12. There is confirmation of a pregnancy, as evidenced by a positive pregnancy test (see Section 12.1.4 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 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.

6.5 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 8.5).

Subjects should be withdrawn from the study and will be encouraged to come back for the SFU 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 should be withdrawn from IMP and will be asked to come back for the SFU 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:
   a. Hepatotoxicity as described in Section 6.5.1
   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 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 that, in the opinion of the Investigator, merits the discontinuation of the investigational product and appropriate measures being taken.
7. There is confirmation of a pregnancy during the study, as evidenced by a positive pregnancy test (see Section 12.1.4 for more information regarding pregnancies).

8b. At Week 28 and all following visits, subjects on continuous treatment 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.

9a. A subject considered as having either a suspected new latent tuberculosis infection (LTBI) or who develops active TB or pulmonary NTMB infection during the study (including but not limited to, conversion demonstrated by IGRA or other diagnostic means) must be immediately discontinued from IMP.

The subject must be permanently withdrawn if further examinations result in a diagnosis of pulmonary NTMB, 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 12.3.1.

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.

11a. Subjects **must be referred** immediately to a mental healthcare professional (eg, 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.

12a. Subjects must be referred immediately to a mental healthcare professional (eg, 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.

6.5.1 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:

- ALT or AST ≥ 8xULN
- ALT 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 12.2.1.2.1 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 12.2.1 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 and <8xULN after re-test, IMP should be temporarily withheld and subject should undergo a repeat test in two 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 drug-induced liver injury.

  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 TREATMENTS

7.1 Description of investigational medicinal products

The IMPs used in this study are bimekizumab, secukinumab, and placebo.

- Bimekizumab will be supplied in a 1mL prefilled syringe (PFS) at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection.
- Secukinumab is commercially available and will be supplied as a 150mg/mL single-use PFS for sc injection.
- Placebo will be supplied as 0.9% sodium chloride aqueous solution (physiological saline, preservative free) of pharmacopeia (US Pharmacopeia/European Pharmacopeia) quality in a 1mL PFS for sc injection.

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

7.2 Treatments to be administered

Unblinded study staff will be responsible for preparation of the clinical trial material, including recording the administration information on source documents, and administration of the IMP as sc injections. The unblinded personnel will not be involved in the study in any way other than assuring the medication is taken from the correct kit and administering the drug to the subjects.

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.

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64 or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 visit.

The dosing scheme for Baseline through Week 44 is depicted in Table 7–1. The dosing scheme from Week 48 through Week 140 is depicted in Table 7–2.

Table 7–1: Dosing scheme, double-blind Treatment Period

Week Dose Assignment	Baseline (first dose)	1	2	3	4	8	12	16[a]	20	24	28	32	36	40	44
Bimekizumab 320mg	●●	○○	○○	○○	●●	●●	●●	Q4W ●●	●●	●●	●●	●●	●●	●●	●●
								Q8W ●●	○○	●●	○○	●●	○○	●●	○○
Secukinumab 300mg	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲

Q4W=every 4 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●). A placebo injection is depicted by a white circle (○). A secukinumab 150mg injection is depicted by a black triangle (▲).

[a] Subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

Table 7–2: Dosing scheme, OLE Period

Week	48 (1st OLE)	Year 2												Year 3										
		52	56	60	64[a,b]	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**	**C**	**H**	**C**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**
Bimekizumab 320mg Q4W	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Bimekizumab 320mg Q8W	●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●	

C=clinic; H=home; OLE=Open-Label Extension; 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 64 or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 visit.

[b] Subjects whose dosing interval is changed to bimekizumab 320mg Q8W should be dosed at this visit and will 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 will receive kits for home administration 4 weeks later.

During the OLE Period, IMP administration on weeks with no scheduled clinic visit should primarily be performed by subjects at home. Self-injection training will be provided to the subject/caregiver by qualified site personnel at Week 48 (upon signature of the ICF). Additional training may be provided by site staff at subsequent clinic visits as needed. At Week 48 and subsequent clinic visits, the subject/caregiver will perform self-administration under the supervision of the site staff to ensure that study medication is being properly and safely injected.

After the implementation of Protocol Amendment #5.4 (addition of a 48-week treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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 Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit will be treated with bimekizumab Q4W for the first 16 weeks, then will switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

The dosing scheme from Week 144/OLE2 Baseline through OLE2 Week 40 is depicted in Table 7–3.

Table 7–3: Dosing scheme, OLE2 Period

Visits/Week / Dose Assignment	OLE2 Period								
	Week 144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12 [a]	OLE2 W16	OLE2 W24 [b]	OLE2 W32	OLE2 W36 [c]	OLE2 W40
	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; Q4W/Q8W=every 4 weeks for 16 weeks, followed by every 8 weeks; Q8W=every 8 weeks; OLE=Open Label Extension; W=week

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 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.

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

The IMPs will be packaged and labeled according to Good Manufacturing Practice (GMP) guidelines and applicable laws or regulations. They 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

The IMPs 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/caregiver on how to handle the IMP during transport, and how to store the IMP following the instruction guide. Cooler bags with freezer packs will be provided to the subjects/caregivers. Specific attention will be put on the transport from site to home using cold bags, and the subject/caregiver 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 supplied. 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 (eg, due to breakage or wastage), not used, partially used, disposed of at the study site, or returned to the sponsor or designee must also be recorded on the appropriate forms. All supplies and pharmacy documentation must be made available throughout the study for UCB (or designee) to review.

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

Unblinded study staff will be responsible for receipt, inventory, and destruction of used kits. The packaging identifies each kit by a unique number, but due to the commercial packaging of the comparator, the unblinded study staff will be responsible to maintain the blind. Unblinded study staff will be responsible for preparation (breaking tamper proof sticker on kit, etc) of the clinical trial material, including recording the administration information on source document.

The OLE2 Period will be unblinded and blinding precautions will not be applicable.

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

The Investigator should 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 the double-blind Treatment Period (up to Week 44), investigational medicinal product 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 60, 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, body 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 with the subject. 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 6.5.

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.

In the double-blind Treatment Period, mild and low potency topical steroids will be permitted for use limited to the face, axilla, and/or genitalia, as needed. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.

In the OLE and OLE2 Periods, the medications listed as permitted for the double-blind Treatment Period will be allowed. In addition, any topical steroids and vitamin D analog ointment will be permitted for use, as needed. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.

7.8.1.2 Other medications

Subjects may take pain relievers (acetaminophen/paracetamol, NSAIDs, opiates) as needed for pain but preferably not within 24 hours of the Baseline and Week 48 Visits. Intraarticular injections (eg, steroids or hyaluronic acid) are permitted and must be carefully recorded in the eCRF.

Subjects who are receiving an established regimen for depression should remain on stable dosing prior to Baseline and throughout the study.

7.8.2 Prohibited concomitant treatments (medications and therapies)

Table 7–4 presents the list of prohibited PSO medications.

Table 7–4: Prohibited psoriasis medications

Drug	Washout period relative to Baseline Visit
Topicals except for those permitted (Section 7.8.1.1)	2 weeks
Systemic retinoids	1 month
Systemic treatment (non-biological), eg: systemic immunosuppressant agents (eg, methotrexate, cyclosporine, azathioprine, thioguanine) fumaric acid esters specifically used for the treatment of PSO systemic corticosteroids phototherapy	1 month
Anti-TNFs, eg: etanercept (including biosimilar) infliximab (including biosimilar), golimumab, certolizumab pegol, adalimumab (including biosimilar)	 1 month for etanercept 3 months for everything other than etanercept
Other biologics and other systemic therapies, eg: ustekinumab apremilast, tofacitinib alefacept, efalizumab, guselkumab tildrakizumab, risankizumab briakinumab rituximab	 6 months for ustekinumab 2 weeks for apremilast and tofacitinib 3 months for alefacept, efalizumab, and guselkumab 5 months for tildrakizumab, risankizumab 6 months for briakinumab 12 months for rituximab
Anti-IL-17 therapies, eg: brodalumab ixekizumab	3 months (any prior exposure to secukinumab or bimekizumab is excluded [see Section 6.2])
Any other antipsoriatic agent (systemic) under investigation (or approved after the protocol is approved)	3 months or 5 half-lives, whichever is greater
Any other antipsoriatic agent (topical) under investigation	1 month

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

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 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.

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 (see Exclusion Criterion #10, Section 6.2). Administration of inactivated vaccines is allowed during the study at the discretion of the Investigator.

7.9 Blinding

Due to differences in presentation between the bimekizumab and secukinumab, special precautions will be taken to ensure study blinding during the double-blind Treatment Period and study sites will have blinded and unblinded personnel.

For subjects receiving bimekizumab, bimekizumab will be administered at Baseline; placebo will be administered at Week 1, Week 2, and Week 3; their second dose of bimekizumab will be at Week 4; and bimekizumab doses Q4W through Week 16. At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. To maintain the blind, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Secukinumab subjects will receive secukinumab at Baseline, Week 1, Week 2, Week 3, Week 4, and Q4W thereafter.

All Sponsor and Investigator site personnel involved in the study will be blinded to the randomized IMP assignment with the following exceptions:

- Unblinded study staff will be responsible for preparation (breaking tamper proof sticker on kit, etc) of the clinical trial material, including recording the administration information on source documents, and administration of the IMP as sc injections. The unblinded personnel will not be involved in the study in any way other than assuring the medication is taken from the correct kit and administering the drug to the subjects.
- Bioanalytical staff analyzing blood samples for bimekizumab and anti-bimekizumab antibody determination.

During the double-blind Treatment Period of the study, the Sponsor will provide blinded and unblinded site monitors for the purposes of verifying safety, efficacy, and drug administration and documentation records. Unblinded study site personnel need to be available in order to resolve queries. Study monitors and study site personnel, blinded to treatment assignment, will not discuss or have access to any drug related information. This will continue at least until all subjects have completed the double-blind Treatment Period of the study.

Study sites will be required to have a written blinding plan in place, signed by the Principal Investigator, which will detail the site's steps for ensuring that the double-blind nature of the study is maintained. Sites will be instructed to keep study subjects blind to the IMP as detailed in the site blinding plan.

After all subjects have completed the double-blind Treatment Period of the study and the interim analysis has occurred, unblinded study site personnel can perform assessments in the OLE and OLE2 Period(s) of the study.

Further details are provided in the study manual and site blinding plan.

7.9.1 Procedures for maintaining and breaking the treatment blind

7.9.1.1 Maintenance of IMP blind

All subject treatment details (bimekizumab or secukinumab) will be allocated and maintained by the IRT system.

7.9.1.2 Breaking the treatment blind in an emergency situation

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

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

7.10 Randomization and numbering of subjects

An IRT will be used for assigning eligible subjects to a treatment regimen based on a predetermined production randomization and/or packaging schedule provided by UCB (or designee). The randomization schedule will be produced by the IRT vendor. The IRT will generate individual assignments for subject kits of IMP, as appropriate, according to the visit schedule. Subject treatment assignment will be stratified by region and prior biologic exposure (yes/no). The IRT will generate individual assignments for subject kits of IMP, as appropriate, according to the visit schedule.

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

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

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. To maintain the blind after re-randomization, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Subjects in the secukinumab arm will continue to receive secukinumab 300mg Q4W.

In the OLE Period, subjects:

- Who received bimekizumab 320mg Q4W and achieved PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

- Who received bimekizumab 320mg Q4W and who did not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Who received bimekizumab 320mg Q8W and who did not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Who received bimekizumab 320mg Q8W and who achieved PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q8W.
- Who received secukinumab and who did not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.
- Who received secukinumab and who achieved PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64, or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed Week 64.

Subjects who roll over directly from the OLE 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 OLE Period or who have completed the SFU of the OLE 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.

Subject numbers and kit numbers will be tracked via the IRT during the double-blind Treatment Period, the OLE Period, and the OLE2 Period.

8 STUDY PROCEDURES BY VISIT

Table 5–1, Table 5–2, and Table 5-3 provide a general overview of study assessments during the double-blind Treatment Period, the OLE Period, and the OLE2 Period, respectively. A list of procedures to be completed at each visit is described below.

- Visit windows of ±3 days on either side of the scheduled dosing are permitted up to and including Week 24; however, the Investigator should try to keep the subjects on the original dosing schedule. From the Week 28 Visit through the Week 72 Visit, 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. From the Week 76 Visit through the Week 144/PEOT Visit, 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 visit window is relative to Baseline and applicable for all subsequent visits up to Week 144/OLE2 Baseline Visit. From the Week 144/OLE2 Baseline Visit through the OLE2 Week 48/PEOT Visit, visit windows of ±14 days relative to the Week 144/OLE2 Baseline Visit on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. Changes to the dosing schedule outside the visit window must be discussed with the Medical Monitor.

- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the Week 72 Visit, the dosing window is ±7 days relative to the scheduled dosing visit. From the Week 76 Visit through the OLE2 Week 40 Visit, the dosing window is ±14 days relative to the scheduled dosing visit.
- For the SFU and SFU2 Visits (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.

8.1 Screening Visit (2 to 5 weeks)

Prior to any study specific activities, subjects will be asked to read, sign, and date an ICF that has been approved by the Sponsor and an Institutional Review Board (IRB)/Independent Ethics Committee (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 participation in the study.

The following procedures/assessments will be performed at the Screening Visit:

- Informed consent
- Inclusion/exclusion
- Urine drug screen
- Demographic data (age, gender, race and ethnicity [according to local regulations])
- Psoriasis history including the date of onset and past treatments
- Significant past medical history including clinically relevant past or coexisting medical conditions and surgeries
- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- Vital signs (sitting systolic and diastolic blood pressure [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 biochemistry
  - Urinalysis
  - Serum pregnancy test
  - Hepatitis B and Hepatitis C
  - HIV
  - IGRA tuberculosis test
- Record 12-lead ECG

- Chest x-ray (not necessary if performed within 3 months prior to Screening Visit and report is available)
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

8.2 Treatment Period

8.2.1 Baseline Visit

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

- Inclusion/exclusion (includes evaluation of signs and symptoms of active TB and risk for exposure to TB)
- Significant past medical history and concomitant diseases to ensure no significant changes since Screening
- Height
- 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 tests should be obtained prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- Tuberculosis questionnaire
- PASI
- Percentage of BSA

- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- eC-SSRS
- scalp IGA
- mNAPSI
- pp-IGA
- Patient Global Assessment of psoriasis
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)
- EQ-5D-3L
- Concomitant medication
- AEs
- Upon confirmation of subject's eligibility, randomization will occur
- Contact IRT

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

8.2.2 Week 1 and Week 2 Visits (±3 days relative to Baseline)

The following procedures/assessments will be performed/recorded:

- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Collection of blood samples for the following tests should be obtained prior to dosing:
  - Hematology and biochemistry
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- PASI
- Percentage of BSA
- IGA
- scalp IGA for subjects with scalp involvement at Baseline

- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

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

8.2.3 Week 3 Visit (±3 days relative to Baseline)

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

- Vital signs (sitting systolic and diastolic BP, pulse rate, and body temperature) should be obtained prior to blood sampling
- Concomitant medication
- AEs
- Contact IRT

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

8.2.4 Week 4 Visit (±3 days relative to Baseline)

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

- 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 prior to dosing:
  - Hematology and biochemistry
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)

- eC-SSRS
- scalp IGA for subjects with scalp involvement at Baseline
- Patient Global Assessment of psoriasis
- EQ-5D-3L
- Concomitant medication
- AEs
- Contact IRT

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

8.2.5 Week 8 and Week 12 Visits (±3 days relative to Baseline)

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

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB (Week 12 only)
- 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 prior to dosing:
  - Hematology and biochemistry
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- Tuberculosis questionnaire (Week 12 only)
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- Patient Global Assessment of psoriasis
- PHQ-9
- eC-SSRS
- scalp IGA for subjects with scalp involvement at Baseline
- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)
- Concomitant medication

- AEs
- Contact IRT

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

8.2.6 Week 16 Visit (±3 days relative to Baseline)

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

- 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 tests should be obtained prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- Record 12-lead ECG
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- eC-SSRS
- scalp IGA for subjects with scalp involvement at Baseline
- mNAPSI for subjects with nail involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- Patient Global Assessment of psoriasis
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)
- EQ-5D-3L

- Concomitant medication
- AEs
- Contact IRT

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. After completion of the above-mentioned procedures, administration of IMP will occur.

8.2.7 Week 20 (±3 days relative to Baseline) and Week 28 Visits (±7 days relative to Baseline)

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

- 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 prior to dosing:
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations (Week 20 only)
  - Anti-bimekizumab antibodies (Week 20 only)
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

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

8.2.8 Week 24 Visit (±3 days relative to Baseline)

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

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 tests should be obtained prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

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

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

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

- 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 prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
- Record 12-lead ECG
- PASI
- Percentage of BSA
- IGA
- DLQI

- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- eC-SSRS
- scalp IGA for subjects with scalp involvement at Baseline
- mNAPSI for subjects with nail involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- Patient Global Assessment of psoriasis
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)
- EQ-5D-3L
- Concomitant medication
- AEs
- Contact IRT

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

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

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

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 tests should be obtained prior to dosing:
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9

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

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

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

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

- 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 prior to dosing:
  - Hematology and biochemistry
  - 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, administration of IMP will occur.

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

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

- 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:
  - Urine pregnancy test
  - IGRA tuberculosis test

- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

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

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

The following procedures/assessments will be performed/recorded:

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 tests should be obtained at this visit:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab/secukinumab plasma concentrations
  - Anti-bimekizumab antibodies
- Record 12-lead ECG
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- scalp IGA for subjects with scalp involvement at Baseline
- mNAPSI for subjects with nail involvement at Baseline

- pp-IGA for subjects with palmoplantar involvement at Baseline
- Patient Global Assessment of psoriasis
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- Photographs of skin and nails (subjects consenting to sub-study in participating centers only)
- EQ-5D-3L
- eC-SSRS
- Concomitant medication
- AEs

8.3 OLE Period

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

The following procedures/assessments will be performed/recorded after completion of assessments listed for Week 48 (Section 8.2.13) and prior to administration of IMP:

- Sign a separate ICF for the OLE Period
- Inclusion/exclusion: Confirm that subject completed the double-blind Treatment Period without meeting any withdrawal criteria and has been compliant with the ongoing clinical study requirements
- Upon confirmation of subject's eligibility, randomization will occur
- Contact IRT

Self-injection training will be provided to the subject/caregiver by qualified site personnel to allow self-injection to be performed at home after Week 48. Additional training may be provided by site staff at subsequent clinic visits as needed (see Section 7.2).

After completion of the above-mentioned procedures, IMP administration will occur, preferably by self-injection under supervision of the site personnel.

8.3.2 Week 52 Visit (±7 days relative to Baseline)

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

- 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 prior to dosing:
  - Hematology and biochemistry
  - Urine pregnancy test

- PASI
- Percentage of BSA
- IGA
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, administration of IMP will occur for subjects on bimekizumab 320mg Q4W dosing only, preferably by self-injection under supervision of the site personnel.

8.3.3 Week 56 Visit (±7 days relative to Baseline)

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

- 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 prior to dosing:
  - Hematology and biochemistry
  - Urine pregnancy test
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

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.

8.3.4 Self-injection at home (Weeks 60, 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 64 or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 visit.

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home on the following weeks: Weeks 60, 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 on the following weeks: Weeks 80, 88, 104, 112, 128, and 136.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. In case of a scheduled home self-injection the pregnancy test needs to be performed immediately prior to self-injecting bimekizumab at home. If the pregnancy test result is positive, IMP should not be administered and the site should be contacted.

- 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.

8.3.5 Week 64 (±7 days relative to Baseline), Week 84, Week 108, Week 132 Visits (±14 days relative to Baseline)

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

- At Week 64 if the subject has not completed the Week 64 visit prior to implementation of Protocol Amendment #5.1.
- At Week 84 if the subject has already completed the Week 72 visit prior to implementation of Protocol Amendment #5.1.
- At Week 108 if the subject has already completed the Week 96 visit prior to implementation of Protocol Amendment #5.1.
- At Week 132 if the subject has already completed the Week 120 visit prior to implementation of Protocol Amendment #5.1.

Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W will receive kits for home administration as follows:

- Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 64 should be dosed at this visit, and will receive kits for home administration 8 weeks later (Table 7–2).

- Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 84, Week 108, or Week 132 should NOT be dosed at that visit, and will receive kits for home administration 4 weeks later (Table 7–2).

The following procedures/assessments will be performed/recorded. If IMP is administered on site during this visit, they need to be performed/recorded prior to administration of IMP:

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

After completion of the above-mentioned procedures, administration of IMP will occur:

- At each of these visits for subjects on bimekizumab 320mg Q4W dosing, preferably by self-injection under supervision of the site personnel. This only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #5.1.
- At Week 64 only for those subjects on bimekizumab 320mg Q8W dosing, 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. Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2).

8.3.6 Week 72 (±7 days relative to Baseline) and Week 120 Visits (±14 days relative to Baseline)

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

- At Week 72 if the subject has already completed the Week 64 visit prior to implementation of Protocol Amendment #5.1.
- At Week 120 if the subject has already completed the Week 108 visit prior to implementation of Protocol Amendment #5.1.

As depicted in Table 7–2, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at one of these visits should be dosed at this visit and will receive kits for home administration 8 weeks later.

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

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- scalp IGA for subjects with scalp involvement at Baseline
- mNAPSI for subjects with nail involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- EQ-5D-3L

- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT
- 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. Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2).

8.3.7 Week 96 Visit (±14 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 has already completed the Week 84 visit prior to implementation of Protocol Amendment #5.1. As depicted in Table 7–2, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 96 should be dosed at this visit, and will receive kits for home administration 8 weeks later.

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

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 tests should be obtained prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - IGRA tuberculosis test
  - Bimekizumab plasma concentrations
  - Anti-bimekizumab antibodies
- Record 12-lead ECG
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA

- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- scalp IGA for subjects with scalp involvement at Baseline
- mNAPSI for subjects with nail involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- EQ-5D-3L
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

At Week 96, 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. Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2).

8.3.8 Week 144 Visit (±14 days relative to Baseline)

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

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 tests should be obtained prior to dosing:
  - Hematology and biochemistry
  - Urinalysis
  - Urine pregnancy test
  - IGRA tuberculosis test
  - Bimekizumab plasma concentrations

  - Anti-bimekizumab antibodies
- Record 12-lead ECG
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- scalp IGA for subjects with scalp involvement at Baseline
- mNAPSI for subjects with nail involvement at Baseline
- pp-IGA for subjects with palmoplantar involvement at Baseline
- PASE
- PGADA (only for subjects with PsA)
- WPAI-SHP V2.0
- EQ-5D-3L
- 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.

If Protocol Amendment #5.4 is implemented at the time subjects are treated in the OLE 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 their 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 #5.4 is implemented at the time subjects have completed the Week 144 Visit and are in the SFU Period of the OLE Period or have completed the SFU of the OLE Period (Group B subjects), these subjects will be invited to enter the OLE2 Period to reinitiate their 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 (Section 8.4.1).

8.4 OLE2 Period

8.4.1 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 OLE Period (OLE2 Group B subjects) will undergo screening. Subjects who have used systemic treatments 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)
- AEs (only for subjects in the SFU)
- 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 biochemistry
  - 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)
- Contact IRT

8.4.2 OLE2 Baseline Visit

Subjects who will still be treated in the OLE Period at the time of implementing Protocol Amendment #5.4 (OLE2 Group A subjects) will attend Week 144 Visit and directly roll over to the OLE2 Period to continue their 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 OLE or have completed the SFU Period at the time of Protocol Amendment #5.4 implementation (OLE2 Group B subjects) will reinitiate their treatment at the Week 144/OLE2 Baseline Visit, and will be assigned a treatment regimen based on their 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:

- 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 biochemistry
  - Urinalysis
  - Urine pregnancy test
- eC-SSRS
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- PHQ-9
- DLQI

- Patient symptoms (itch, pain, and scaling)
- 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.

8.4.3 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 dosed at OLE2 Weeks 32 and 40.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. In case of a scheduled home self-injection the pregnancy test needs to be performed immediately prior to self-injecting bimekizumab at home. If the pregnancy test result is positive, IMP should not be administered and the site should be contacted.

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.

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

As depicted in Table 7–3, 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
- Patient symptoms (itch, pain, and scaling)
- PHQ-9
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

The following will be additional assessments will be performed / recorded every 24 weeks (ie, OLE2Weeks 24 and 48) prior to administration of IMP

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

  - Urinalysis
- DLQI

At the OLE2 Week 12 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. Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2 and Table 5-3).

8.4.5 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 should be obtained prior to dosing:
  - Hematology and chemistry
  - Urinalysis
  - Urine pregnancy test
  - IGRA TB test
- Tuberculosis questionnaire
- PASI
- Percentage of BSA
- IGA
- DLQI
- Patient symptoms (itch, pain, and scaling)
- 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.

8.5 Premature End of Treatment Visit

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

- If the subject will be withdrawn from IMP prior to the Week 48 visit of the double-blind Treatment Period, the subject will undergo the same assessments as the Week 48 visit (see Section 8.2.13), and will enter the SFU Period.
- If the subject will be withdrawn from IMP prior to the Week 144 visit of the OLE Period, the subject will undergo the same assessments as the Week 144 visit (see Section 8.3.8), 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 8.6).

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 8.4.5) 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 8.7).

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

The following procedures/assessments will be performed/recorded:

- Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB
- 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 biochemistry
  - Urinalysis
  - Urine pregnancy test
  - Bimekizumab (secukinumab for subjects not entering the OLE Period) plasma concentrations
  - Anti-bimekizumab antibodies
- Tuberculosis questionnaire
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

8.7 Safety Follow-Up Visit 2 (20 weeks after final dose in 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 biochemistry
  - Urinalysis
  - Urine pregnancy test
- eC-SSRS
- Concomitant medication
- AEs
- Contact IRT

8.8 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, OLE or OLE2, the participant 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 EFFICACY

The PASI, BSA, IGA, scalp IGA, mNAPSI, and pp-IGA 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.

9.1 Psoriasis Area 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 9–1).

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 9–1: 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.

9.2 Investigator's Global Assessment

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 9–2.

Table 9–2: 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; 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

9.3 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 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).

9.4 Scalp IGA

A static IGA for scalp 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 will complete the scalp IGA at the other 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 9–3).

Table 9–3: 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, moderate scaling
4	Severe	Scalp has severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions

PSO=psoriasis; scalp IGA=scalp-specific Investigator's Global Assessment

9.5 mNAPSI

Nail PSO 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 PSO. 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 PSO at Baseline are defined as those with a mNAPSI score >0 at Baseline.

Only subjects with nail involvement at Baseline will complete the mNAPSI at the other visits specified in Table 5–1 and Table 5–2.

9.6 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 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 9–4).

Table 9–4: 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

9.7 European Quality-of-Life 5-Dimensions 3-Level Questionnaire

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.

9.8 Patient Global Assessment of psoriasis

The Patient Global Assessment 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 Patient Global Assessment of psoriasis will be performed at the visits specified in Table 5–1.

9.9 Itch, pain, and scaling numerical rating scale

UCB developed and validated a new Patient Reported Outcome measure, in the form of a patient symptom diary, which is used to assess key symptoms relevant to subjects with moderate to severe chronic plaque PSO. In this study itch, pain, and scaling items from the diary will be used to assess the patient-reported level of these symptoms over time. The items will be administered on an electronic site tablet, during visits, as specified in Table 5–1, Table 5–2, and Table 5-3).

9.10 PASE questionnaire

The Psoriatic Arthritis Screening and Evaluation (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 assessments (PGADA) as noted in Section 9.11.

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

9.11 PGADA for arthritis visual analog scale

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.

All subjects will complete the PGADA at Baseline. Subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47) will complete the PGADA at the visits specified in Table 5–1 and Table 5–2.

9.12 Photographs

At certain clinical sites, representative photographs of the changes in skin and nail appearance will be captured. Subjects who consent to the procedure will have full body (anterior and posterior views) photographs taken. Only those subjects with nail disease at Baseline will have nail photographs taken. Only those subjects with palmoplantar disease at Baseline will have photographs of their palms or soles of their feet taken. Only those subjects with scalp disease at Baseline will have scalp photographs taken. Photographs will be anonymized and will be used for publication purposes.

Study sites selected for photography will be trained and receive standardized photographic equipment by a centralized photographic vendor. Photographs will be electronically transferred from the site to the vendor.

At the end of the study, the site will receive an electronic file of all subject photographs for archiving.

The central photography vendor will tabulate and transfer all subject photos to the Sponsor at the end of the study.

9.13 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 (WPAI-SHP) (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 ASSESSMENT OF PHARMACOKINETIC VARIABLES

10.1 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.

Pharmacokinetic samples from subjects receiving secukinumab will not be analyzed, but stored for potential future PK analysis and anti-drug antibody determination.

11 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.

12 ASSESSMENT OF SAFETY

12.1 Adverse events

12.1.1 Definitions

12.1.1.1 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 ICF), 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.

12.1.1.2 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 12.1.1.3], 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)

Confirmed active TB must be reported as an SAE. The Investigator is to complete and submit the TB Follow-Up Form provided.

12.1.1.2.1 Anticipated serious adverse events

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 12.1.2.3.

Table 12–1: Anticipated serious adverse events for the population of subjects with moderate to severe chronic plaque psoriasis

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; 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.

12.1.1.3 Adverse events of special interest

An AE of special interest (AESI) is any AE that a regulatory authority has mandated be reported on an expedited basis, regardless of the seriousness, expectedness, or relatedness of the AE to the administration of a UCB product/compound.

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 AESI (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.

12.1.1.4 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 inflammatory bowel diseases (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.

12.1.2 Procedures for reporting and recording adverse events

The subject will be given the opportunity to report AEs spontaneously. A general prompt will also be given at each study visit 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.

12.1.2.1 Description of adverse events

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 (CTCAE) 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.

12.1.2.2 Rule for repetition of an adverse event

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

12.1.2.3 Additional procedures for reporting serious adverse events

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 Serious Adverse Event 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.

12.1.3 Follow up of adverse events

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 AESIs; further details regarding follow up of PDILI events is provided in Section 12.2.1.4.

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.

12.1.4 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 Serious Adverse Event 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 an early discontinuation 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 need 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 IRB/IEC and should be available in the Investigator site file. In case of questions about the consent process, the Investigator may contact the UCB/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 Serious Adverse Event 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 a 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 PS0015. If the study is available locally, the PS0015 PI 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 study protocol PS0015.

12.1.5 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.

12.1.6 Overdose of investigational medicinal product

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).

12.1.7 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.

In addition, an independent Data Monitoring Committee (DMC) will periodically review and monitor safety data from this study and advise UCB. Details are provided in the DMC Charter.

Cardiovascular and Neuropsychiatric Adjudication Committees will also periodically review and monitor safety data from this study and advise UCB. Details are provided in the Adjudication Committee Charters.

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.

12.2 Laboratory measurements

Clinical laboratory assessments consist of serum chemistry, hematology, and urinalysis. A centralized laboratory will be used to supply all laboratory test supplies and analyze all blood and urine samples for hematology, biochemistry, 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. Testing to rule out hepatitis B, hepatitis C, and HIV (see Exclusion Criterion #9, Section 6.2) and a urine drug screen will be performed at Screening in addition to those measurements listed in Table 12–2.

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 12–2: 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	Urine dipstick for pregnancy testing[c]
MCH	Creatinine	Urine drug screen
MCHC	ALP	
MCV	AST	
Platelet count	ALT	
RBC count	GGT	
WBC count	Total bilirubin	
	LDH	
	CRP[b]	
	Lipid panel[b]	
	NT-proBNP[b]	
	Serum pregnancy testing[c]	

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BUN=blood urea nitrogen; CRP=C-reactive protein; GGT=gamma glutamyltransferase; LDH=lactate dehydrogenase; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; MCV=mean corpuscular volume; NT-proBNP=N-terminal pro B-type natriuretic peptide; 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] Assessments of NT-proBNP and CRP will not be performed during any OLE Period; in addition, lipid panel will not be performed during OLE2 Period.

[c] Pregnancy testing will consist of serum testing at the initial Screening. Urine pregnancy testing will be performed at all other visits.

12.2.1 Evaluation of PDILI

The PDILI IMP discontinuation criteria for this study are provided in Section 6.5.1, 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 AESI (see Section 12.1.1.3), and, if applicable, also reported as an SAE (see Section 12.1.1.2).

Evaluation of PDILI consists of the diagnostic testing and continued monitoring included in Table 12–3 (specific tests dependent on laboratory results and corresponding symptoms) and consultation with a local hepatologist (if applicable; discussed in Section 12.2.1.1). 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 12.2.1.4).

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 6.5.1), 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 12.2.1.2.1 are met, rechallenge with IMP may be appropriate.

Table 12–3 summarizes the approach to investigate PDILI.

Table 12–3: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
≥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 12.2.1.3); recommended to occur at the site with HCP.	Monitoring of liver chemistry values at least twice per week until values normalize, stabilize, or return to within baseline values. [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 12.2.1.2). 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	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 12.2.1.3).	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.

Table 12–3: Required investigations and follow up for PDILI

Laboratory value			Immediate		Follow up	
ALT or AST	**Total bilirubin**	**Symptoms[a] of hepatitis or hypersensitivity**	**Consultation requirements**	**Actions**	**Testing**	**Evaluation**
				4 weeks of monitoring without evidence of resolution		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. 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 12.2.1.1. 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 12.2.1.2.1.

12.2.1.1 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 12.2.1.3) and SAE report (if applicable).

12.2.1.2 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 6.5.1 and Table 12–3 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.

12.2.1.2.1 IMP restart/rechallenge

Subjects who are immediately discontinued from IMP due to having met certain criteria for PDILI (as described in Section 6.5.1 and Table 12–3), 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 in Section 12.2.1.3 and Section 12.2.1.4 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.
- During the double-blind Treatment Period, the rechallenge is approved by the UCB responsible physician, DMC, and a hepatologist.
- During the OLE and OLE2 Periods, the rechallenge is approved by the UCB responsible physician.
- Subject agrees to the Investigator-recommended monitoring plan.

12.2.1.3 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 12–4 (laboratory measurements) and Table 12–5 (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 12–4: 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

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 12–5: 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

12.2.1.4 Follow-up evaluation

Potential drug-induced liver injury events require follow-up monitoring as described in Table 12–3. 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.

12.3 Other safety measurements

12.3.1 Assessment and management of TB and TB risk factors

All subjects will be assessed for TB at Screening and at the time points specified in the Schedule of Assessments (Table 5–1, Table 5–2, and Table 5-3) through physical examination for signs and symptoms of TB, chest x-ray (Section 12.3.1.2), laboratory testing (Section 12.3.1.1), and subject questionnaire (Section 12.3.1.3).

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

c. 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.

d. High risk of acquiring TB infection:

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

e. 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 Screening window.

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

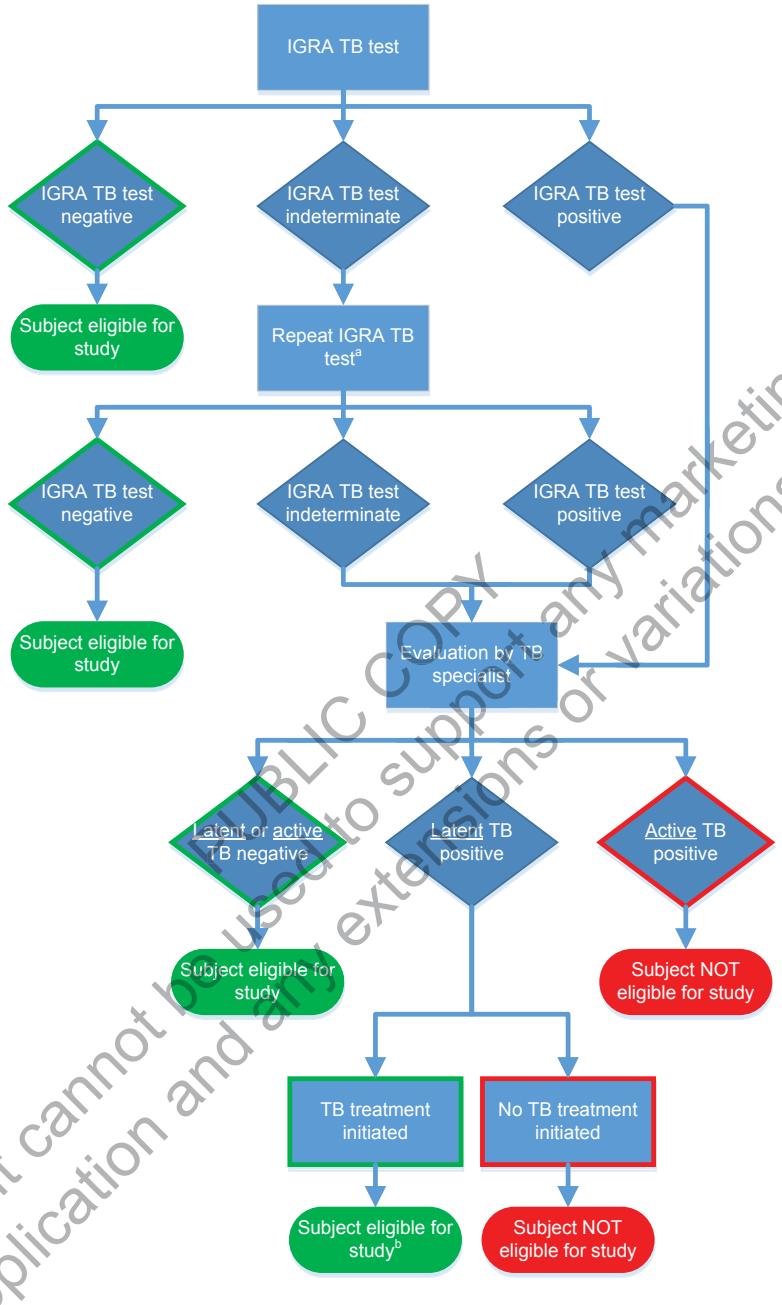
f. NTMB infection is defined as a clinical infection caused by mycobacterial species other than those belonging to the Mycobacterium tuberculosis complex.

g. 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 12-1.

Figure 12-1: 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.

12.3.1.1 Tuberculosis assessment by IGRA

During conduct of the study, the TB assessment by IGRA (QuantiFERON TB test is recommended) 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, latent TB, 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 active TB is identified, subject must undergo appropriate study-specified withdrawal procedures. The retest during Screening must be done during the protocol-defined Screening window.

12.3.1.2 Chest x-ray for tuberculosis

A plain posteroanterior chest x-ray must be performed in the Screening Period unless one has been performed within 3 months prior to the Screening Visit. The chest x-ray (or, if done, computed axial tomography of the chest) must be clear of signs of TB infection (previous or current) before first IMP administration. All chest imaging (particularly x-rays) should be available for review by the Investigator before randomization of the subject. The chest x-ray reading should be repeated if the TB test was confirmed positive. If the second read of the pretreatment chest x-ray is confirmed to be clear, the patient may be included in the study 8 weeks after the start of the TB prophylactic treatment. If the pretreatment chest x-ray is not available for a re-read, it should be repeated after notification to the radiologist that this patient is IGRA positive, and confirmed to be clear for signs of TB.

The chest imaging must be negative for any old or recent TB infection as determined by a qualified radiologist and/or pulmonary physician. Any new clinically significant findings post Baseline on chest x-ray must be documented in the source documents and the eCRF as an AE.

12.3.1.3 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. 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 Screening is excluded. A “Yes” response to any of the other questions within the questionnaire at Screening should trigger further careful assessment to determine if subject has LTB or active TB (see Exclusion Criterion #12, Section 6.2). A “Yes” response to any of the questions during the study should trigger further assessments to determine if the subject has either LTB or active TB infection.

12.3.1.4 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 must be withdrawn from the study and receive appropriate TB 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.

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

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

12.3.2 Pregnancy testing

Pregnancy testing will consist of serum testing at the initial Screening. The pregnancy test will be urine at other visits, including at the OLE2 Screening Visit.

The Screening Visit serum pregnancy testing results must be negative and received and reviewed prior to randomization.

A negative urine pregnancy test result should 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.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. Home pregnancy tests will be provided to participants for use at Weeks 60, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, 140, and at the OLE2 Weeks 4, 8, 16, 32, and 40. At weeks on which IMP dosing is scheduled (specified in Table 5–1, Table 5–2, and Table 5-3), a negative urine pregnancy test result should be obtained immediately prior to the administration of IMP. In the case of a positive pregnancy test result, IMP should not be administered and the site should be contacted.

12.3.3 Vital signs

Vital signs will be collected at every visit and will include systolic and diastolic BP, 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.

12.3.4 12-lead electrocardiograms

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.

12.3.5 Physical examination

A physical examination will be performed at the 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; and hepatic. Findings considered clinically significant changes since the physical examination at the Screening Visit will be recorded as AEs.

12.3.6 Height and body weight

Height will be measured at Baseline only.

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

12.3.7 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 6.5 for eC-SSRS-related withdrawal criteria.

12.3.8 Patient Health Questionnaire-9

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression (Kroenke et al, 2001). The PHQ-9 scores for depression range from 0 to 27, with higher scores indicating 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 Section 6.5 for PHQ-9-related withdrawal criteria.

12.4 Other study measurements

12.4.1 Demographic information

Demographic information will be collected in all subjects and include age, gender, race and ethnicity. Information on demographics will be collected according to local rules and regulations. Demographic information will be recorded in the eCRF.

12.4.2 Medical history

A complete medical history will be collected as part of the initial Screening assessment and include all clinically relevant past or coexisting medical conditions and surgeries. Findings will be recorded in the eCRF.

For OLE2 Group B, only new or modified medical history since completing the SFU will be collected at OLE2 Screening and entered in eCRF.

12.4.3 Psoriasis history

A detailed history of each subject's PSO history will be collected and include the date of onset and past treatments for PSO.

12.4.4 Data Monitoring and Adjudication Committees

The DMC membership includes experienced clinicians and a statistician, all of whom have expertise in clinical trials. Cardiovascular and Neuropsychiatric Adjudication Committees will also periodically review data from this trial. Both Data Monitoring and Adjudication Committee members may not participate in the study as principal or co-Investigators, or as study subject care physicians. The DMC will monitor the study through the last subject completing the Week 48 and SFU visit (for subjects not participating in the OLE period).

The Cardiovascular and Neuropsychiatric Adjudication Committees will monitor the study through the last subject completing the OLE, SFU, OLE2, and SFU2 Periods for PS0015. Detailed role, scope, responsibilities, and complete procedures, as well as the identity of members, are described in the separate committee charters.

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 CPM 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).

Electronic Patient-Reported Outcome (ePRO) measures (eg, DLQI, EQ-5D-3L, Patient Global Assessment of PSO, and PGADA) will be completed by each subject and will be collected electronically.

The data collection and database management system will be supplied by a vendor and will be compliant with the relevant regulations. The data collected on the ePROs will be uploaded to a central server database and will be sent electronically to UCB (or a designated CRO).

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 electronic 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. This study is performed using Electronic Data Capture: the data are entered into the eCRFs once and are subsequently verified. 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 Screening and Enrollment log/Subject Identification Code list

The subject's screening and enrollment will be recorded in the Subject Screening 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 will consist of all subjects who have given informed consent.

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

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

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

The Full Analysis Set (FAS) will consist of all subjects in the RS that receive at least 1 dose of the IMP and have a valid PASI measurement at Baseline.

The Maintenance Set (MS) will consist of all subjects that receive at least 1 dose of IMP at Week 16 or later in the double-blind Treatment Period (including the Week 16 dose).

The Open-label Set (OLS) will consist of all subjects that receive at least 1 dose of IMP at Week 48 or later in the OLE Period (including the Week 48 dose).

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

The Per-Protocol Set (PPS) will consist of all subjects in the RS who had no important protocol deviations affecting the primary efficacy variable. Important protocol deviations will be predefined and subjects with important protocol deviations will be evaluated during ongoing data cleaning meetings prior to unblinding of the data.

14.2 General statistical considerations

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

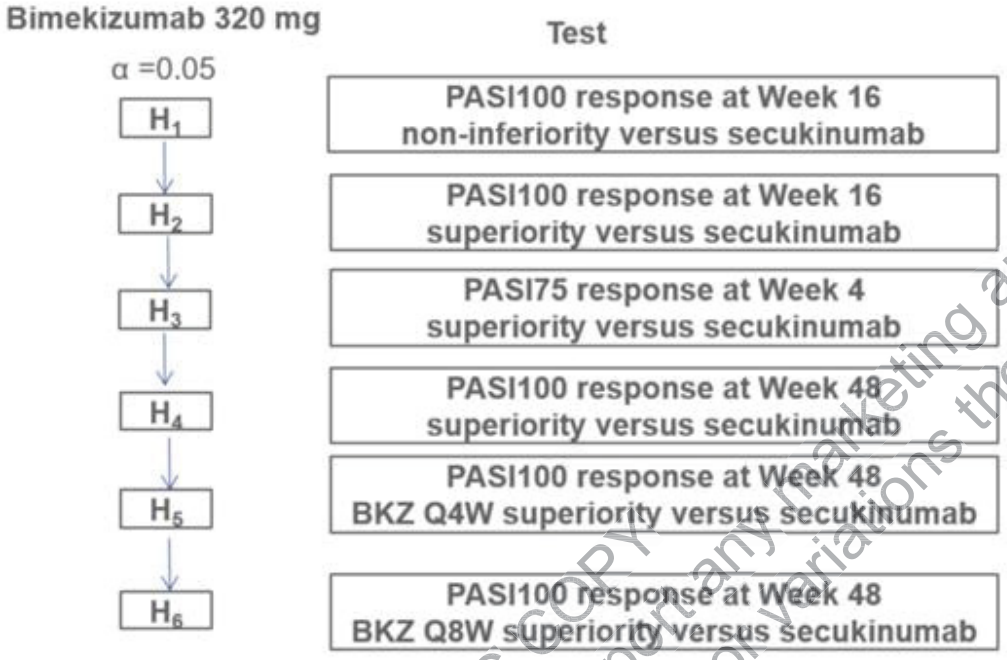
The statistical analysis of the primary efficacy variable and selected secondary efficacy variables will account for multiplicity and control the familywise Type I error rate at a 2-sided alpha level of 0.05 by using a fixed sequence testing procedure.

The hypotheses (H_1, H_2, H_3, H_4, H_5, and H_6) comparing bimekizumab vs secukinumab will be tested at a 2-sided alpha level of 0.05.

The first 2 hypotheses (H_1 and H_2) test whether bimekizumab is non-inferior and superior, respectively, to secukinumab for PASI100 response at Week 16. These are the hypothesis tests corresponding to the primary endpoint. If these hypotheses are rejected at a 2-sided alpha level of 0.05, that alpha will be passed to the next test in the sequence, allowing the testing procedure to proceed.

The hypotheses associated with the subsequent tests are for selected secondary efficacy endpoints and are based on testing for superiority relative to secukinumab. Figure 14–1 presents the details on this procedure.

Figure 14–1: Hypothesis testing



BKZ=bimekizumab; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Tests for H_1, H_2, H_3, and H_4 are based on all subjects initially randomized to bimekizumab compared to secukinumab. For H_5 and H_6, testing is based on the subjects re-randomized at Week 16 to bimekizumab 320mg Q4W, and bimekizumab 320mg Q8W, respectively, compared to secukinumab.

14.3 Planned efficacy analyses

14.3.1 Analysis of the primary efficacy variable

The analysis of the primary efficacy variable (PASI100 at Week 16) will be based on the RS. A stratified Cochran-Mantel-Haenszel (CMH) test will be performed, where region and prior biologic exposure (yes/no) will be used as stratification variables. Region and prior biologic exposure have been selected as stratification variables in the analysis because they are stratification variables in the randomization and because they may have an impact on efficacy. Treatment comparisons between bimekizumab and secukinumab will be made based on the CMH test using the p-value for the general association. For the assessment of non-inferiority, a non-inferiority margin of 10% will be used and evaluated based on the CI for the stratified Mantel-Haenszel risk difference between bimekizumab and secukinumab. A non-inferiority margin of 10% has been selected as this is considered to be a clinically relevant difference that could influence the choice of interventions used to treat chronic plaque PSO. Therefore, a difference within the 10% non-inferiority margin would suggest a similar impact on efficacy between the treatments.

Nonresponder imputation (NRI) will be used to account for missing data in the primary analysis. Specifically, any subject who withdraws from IMP prior to Week 16 or who has missing data for the primary efficacy variables at the Week 16 time point will be considered a nonresponder. Based on previous studies of biologics in subjects with moderate to severe chronic plaque PSO,

it is expected that the number of subjects who discontinue prior to Week 16 will be low. For the small percentage of subjects for whom primary endpoint data are unavailable at Week 16, this lack of data is suggestive of an ineffective IMP, thereby supporting the imputation of nonresponse. Therefore, NRI is considered an appropriate method for handling missing data since achieving the clinical response and making it through 16 weeks of IMP are both critical components of the primary outcome.

14.3.1.1 Sensitivity analyses

The primary efficacy analysis described in Section 14.3.1 will be repeated based on the FAS and the PPS.

As a sensitivity analysis to the primary analysis method, logistic regression based on the RS will be used. The odds ratio of the responder rates at Week 16 will be estimated and tested between treatment groups using a logistic regression model with factors of treatment group, region, and prior biologic exposure (yes/no). The odds ratio, associated CI, and p-value based on the Wald test will be presented. If the logistic regression model is unable to converge, then prior biologic exposure may be dropped from the model to facilitate convergence. If the model is still unable to converge, then region may be removed from the model as well. As with the primary analysis, missing data will be handled using NRI.

The center-by-treatment interaction will be tested by replacing region with center in the logistic regression model described above and adding a center-by-treatment interaction term. In the model, center will be based on the original centers prior to pooling. However, if the model is unable to converge due to a low number of subjects at a given center, a pooling (to be further described in the SAP) will be applied in order to allow the model to converge.

In order to obtain reasonable estimates of variability for a treatment arm at a given center, a minimum of 10 subjects will be considered acceptable for a center to be included in the model without pooling. Given the 1:1 randomization allocation scheme at the start of the study, this should provide a minimum of about 5 subjects in the bimekizumab arm and 5 subjects in the secukinumab arm. Centers with fewer than 10 subjects will be eligible for pooling. The following center pooling algorithm will be used for each geographic region:

- If a center has 10 or more subjects, then no pooling will be done for that center.
- Centers with fewer than 10 subjects will be ordered from largest to smallest with pooling proceeding in the following manner:
  - Two or more centers will be combined until the cumulative subject total is at least 10.
  - Once a pooled center has at least 10 subjects, the process will continue in an iterative fashion for the subsequent centers in the ordered list, where a new pooled center begins each time at least 10 subjects has been reached in the previous pool.
  - If this iterative process reaches the end of the ordered list of centers where the final pooled center has fewer than 10 subjects, then the subjects from the centers in that pool will be combined with the pooled center formed in the previous iteration.

This procedure is only to be performed within a geographic region – there will be no pooling of centers across regions.

If the center-by-treatment interaction is not found to be significant (α=0.10), then no further analyses will be performed. On the other hand, if the interaction is significant, further analyses will be conducted to determine which center or centers may be the source of the interaction. This will be done by running the logistic regression model (including the interaction term) where each center will be systematically removed from the model. The impact of a given center will be based on the change in the interaction p-value when that center is removed. The center or centers that appear to be driving the significant interaction effect will then be removed from the model to verify that conclusions remain the same with or without the influential center(s).

Additional sensitivity analyses to evaluate varying assumptions related to the handling of missing data will also be performed and are described in greater detail in Section 14.7.

14.3.2 Other efficacy analyses

14.3.2.1 Analysis of the secondary efficacy variables

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

All secondary efficacy variables are binary. Therefore, the stratified CMH test (as specified for the primary analysis) will be implemented to test for superiority. As in the primary analysis, NRI will be used to account for missing data. Sensitivity analyses for handling missing data on secondary endpoints are outlined in Section 14.7.

PASI75 response at Week 4 will be analyzed for all subjects in the RS based on the randomized treatment group at Baseline.

Additionally, PASI100 at Week 48 will be evaluated as a secondary efficacy variable. The way the analysis for this variable is conducted will depend on which comparison is being made. The planned comparisons are as follows:

- Compare all subjects initially randomized to bimekizumab (regardless of re-randomization assignment at Week 16) to all subjects initially randomized to secukinumab based on the RS (H_4)
- Compare subjects who were assigned to bimekizumab 320mg Q4W at Week 16 to secukinumab based on the MS (H_5)
- Compare subjects who were assigned to bimekizumab 320mg Q8W at Week 16 to secukinumab based on the MS (H_6)

14.3.2.2 Analysis of the other efficacy variables

Other efficacy variables will be summarized by treatment and visit and will generally be summarized based on imputed data (NRI and multiple imputation [MI] for binary and continuous variables, respectively, unless otherwise stated in the SAP). In some cases, variables may also be summarized based on observed case data (ie, subjects with missing data or who have prematurely discontinued IMP are treated as missing). There may be cases where the multiple imputation model fails to converge. In such situations, the last observation carried forward (LOCF) approach will instead be used to impute the missing data. If LOCF is used instead of multiple imputation for this reason, this will be clearly specified in the corresponding table summary. Should there be no missing data for a study variable, then only observed case data will be presented. Note that for LOCF imputation, any missing data or data collected following

discontinuation of IMP will be imputed with the most recent previous value. See Section 14.7 for further details.

Time to PASI75/90/100 response will be estimated and presented using the Kaplan-Meier product-limit method based on the RS by initially randomized treatment groups (Bimekizumab vs secukinumab). This could make the interpretation of the data challenging given that there are two different bimekizumab dosing regimens starting at Week 16, but it is anticipated that most responses will be observed by Week 16 when all bimekizumab subjects are on the same regimen. Time to a given response will be defined as the length in days from the first dose of IMP until the first date when the response is achieved. Subjects who discontinue IMP prior to achieving a response will be censored at the date of IMP discontinuation. Subjects who reach the Week 48 Visit without achieving the given PASI response will be censored at the date of the Week 48 Visit. The median time to response, including the 2-sided 95% CI, will be calculated for each treatment. Between group differences (bimekizumab vs secukinumab) will be analyzed with the log-rank statistic.

In general, data will be summarized by visit through Week 48 in the double-blind Treatment Period and then by visit in the OLE Period and OLE2 Period separately. All summaries of data up to Week 16 will be based on the RS for the 2 randomized treatment groups (bimekizumab and secukinumab). For visits after Week 16 in the double-blind Treatment Period, by-visit summaries will be prepared for the following 3 groups of subjects:

1. Subjects in the MS summarized by the 3 maintenance treatment groups (bimekizumab 320mg Q4W, bimekizumab 320mg Q8W, and secukinumab). Note that while the MS is primarily defined for the evaluation of data after Week 16, these summary tables will include data at all visits (Baseline to Week 48) to provide a comprehensive summary of subjects by maintenance treatment group for the MS.
2. A subset of Group 1 above. Specifically, this will include only those subjects who are responders at Week 16 for the variable being summarized. This will provide an assessment of how efficacy is maintained among Week 16 responders.
3. Subjects in the RS summarized by the 2 randomized treatment groups (bimekizumab and secukinumab). Data from Baseline to Week 48 will be included in these tables. This provides an intent-to-treat analysis among all randomized subjects in the study through Week 48.

All efficacy variables in the double-blind Treatment Period will be summarized in the manner described for Group 1 and 3 above. Summaries for Groups 2 will be done only for a subset of efficacy variables, namely, PASI75/90/100, IGA Clear or Almost Clear, Scalp IGA Clear or Almost Clear, pp-IGA Clear or Almost Clear, mNAPSI75/90/100, and DLQI 0/1.

In the OLE Period, efficacy variables of interest generally will be summarized descriptively by the combined treatment regimen in the double-blind Treatment Period and re-randomized treatment in the OLE.

In general, efficacy variables will be summarized using descriptive statistics by treatment group and scheduled visit during the OLE Period based on Baseline at beginning of the study unless otherwise specified.

In the OLE2 Period, selected efficacy variables of interest will be summarized descriptively by OLE2 Period Treatment Group during the OLE2 Period.

Further details on the above analyses including analysis in the OLE Period and OLE2 Period will be provided in the SAP.

14.4 Subgroup analyses

Subgroup analyses will be performed on the primary and secondary efficacy variables that are part of the fixed sequence testing procedure described in Section 14.2. The following variables for subgroup analyses will be defined: age, gender, disease duration, region, weight, body mass index, prior systemic chemotherapy or phototherapy, prior biologic exposure, prior primary failure to biologics, prior systemic therapy of any kind, Baseline disease severity, and antibody positivity. These summaries will be based on imputed data (NRI) and will include descriptive statistics only.

14.5 Planned safety and other analyses

14.5.1 Safety analyses

Safety variables will be analyzed for all subjects in the SS. This will include all subjects who took at least one dose of study medication. Selected analyses will also be presented for MS, OLS, and OL2S. Adverse events will be coded according to the Medical Dictionary for Regulatory Activities. Adverse events will be summarized descriptively by treatment group, primary system organ class, High Level Term (HLT), and PT. Additional tables will summarize AEs by intensity and relationship to IMP, AEs leading to withdrawal from the study, SAEs, and deaths. Safety topics of interest will be summarized and will be described in greater detail in the SAP.

Laboratory values (including markedly abnormal laboratory values), urinary values, vital signs, and extent of exposure will be presented descriptively by treatment group. Definitions for markedly abnormal laboratory values will be provided in the SAP.

14.5.2 Pharmacokinetic analyses

Pharmacokinetic variables will be analyzed for all subjects in the PK-PPS. Bimekizumab plasma concentrations will be summarized for each treatment at each scheduled visit where samples are collected.

14.5.3 Immunogenicity analyses

Anti-bimekizumab antibodies will be assessed using a tiered approach: screening, confirmatory, and titer assays will be used. Anti-bimekizumab antibodies (including positivity) will be summarized by treatment at each scheduled visit at which samples are collected.

14.6 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/PD 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.

14.7 Handling of dropouts or missing data

Study variables with multiple components may have rules to account for partial missing data of 1 or more components. Such rules will be defined in the SAP. The following rules are outlined for cases where variables are completely missing, including partial missing data where the data handling rules conclude that the variable should be treated as completely missing.

The analysis of the primary efficacy variable will use NRI for handling of missing data. That is, subjects with missing data or who have discontinued IMP prior to Week 16 will be considered as nonresponders for the primary analysis.

The following sensitivity analyses for the primary efficacy variable will be performed:

1. Missing data will be addressed by using MI (Markov-Chain Monte Carlo method for intermittent missing data, followed by monotone regression for monotone missing data) to evaluate the effect of the method for handling missing data on the analysis. The actual PASI scores will be imputed and then dichotomized to obtain the response status. The treatment differences for each imputed data set will subsequently be evaluated using the stratified CMH test as used in the primary analysis. The results from each of the imputed data sets will be combined for overall inference using Rubin's rules, which account for the uncertainty associated with the imputed values (Rubin, 1987). This will be done using SAS PROC MIANALYZE. This procedure assumes a missing at random pattern of missingness and corresponds to an estimand of the difference in outcome improvement if all subjects tolerated or adhered to treatment (Mallinckrodt et al, 2012). This is an estimand of efficacy to evaluate the de jure hypothesis.
2. Another sensitivity analysis will be based on observed data at Week 16. Subjects with missing data or who have prematurely discontinued IMP will be treated as missing. The same stratified CMH test as in the primary efficacy analysis will be used.

Further details on the MI procedures will be provided in the SAP.

Missing data for the secondary efficacy variables (which are all binary) will be imputed using NRI. Additionally, the 2 missing data-handling approaches described above for the primary efficacy variable will be used for the secondary efficacy variables. Additional missing data handling approaches may be described in the SAP.

For other continuous efficacy variables, MI will be used to impute missing data when possible. If the imputation model cannot converge, LOCF will be used. The MI procedure will be similar to sensitivity analysis #1 described above with the following differences: (1) the imputation model will use the change from Baseline (instead of actual) values by visit and no dichotomization will be necessary; (2) instead of using the stratified CMH test, the imputed data sets will be combined and simple means and standard errors will be calculated using Rubin's rules (via SAS PROC MIANALYZE). For calculation of other descriptive statistics such as the median, minimum and maximum, Rubin's rules do not apply. Multiple imputation estimates will be computed by simply averaging the estimates from the multiple repetitions of the imputation algorithm.

14.8 Planned interim analysis

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.

14.9 Determination of sample size

A total of 700 subjects will be randomly assigned in a 1:1 ratio at Baseline to one of the following treatment groups:

- Bimekizumab 320mg (350 subjects)
- Secukinumab (350 subjects)

The primary efficacy analysis is based on the comparison of bimekizumab to secukinumab for the primary efficacy variable of PASI100 response at Week 16. The assumed responder rates for PASI100 at Week 16 are 60% and 44% for bimekizumab and secukinumab, respectively. The assumed responder rate for bimekizumab is based on the Phase 2b PS0010 data. The assumptions related to the responder rates for secukinumab are based on those observed in the CLEAR study (Thaçi et al, 2015). The power to show statistical superiority of bimekizumab relative to secukinumab under these assumptions is 98% for the primary endpoint. The power for the non-inferiority comparison (with 10% non-inferiority margin) under these assumptions is >99%.

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 ICF should be signed and personally dated by the subject and by the person who conducted the informed consent discussion (Investigator or designee). The subject must receive a copy of the signed and dated ICF. 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 OLE Period will sign a new ICF. Similarly, all subjects enrolling in the OLE2 Period will sign a new ICF.

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

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 ICF. 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 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, ICF, 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 Screening.

The Investigator agrees that representatives of UCB, its designee, representatives of the relevant IRB/IEC, or representatives of regulatory authorities will be allowed to review that portion of the 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 primary rationale for this amendment was to incorporate a re-randomization at Week 16 for subjects in the bimekizumab 320mg treatment arm. At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

The following additional changes were also made:

- Add the number of subjects included in the summary of the completed study UP0042
- Clarify the scalp IGA and pp-IGA efficacy response criteria
- Move the PHQ-9 variable from an other safety variable to an other efficacy variable
- Added percent of subjects achieving mNAPSI75, mNAPSI90, and mNAPSI100 for subjects with nail PSO at Baseline as an other efficacy variable
- Clarify that all study assessments should be performed prior to administration of IMP
- Clarify the study visit windows
- Clarify that the PGADA should be performed on all subjects at Baseline
- Define mental healthcare professional
- Clarify the assessment and management of TB wording
- Clarify the drug accountability wording
- Revise the systemic retinoid washout period
- Clarify that the same assessor should evaluate the subject at each assessment
- Remove the requirement for a rheumatologist evaluation for subjects with a PASE ≥47
- Clarify the IMP restart/rechallenge requirements in case of PDILI
- Add the definition of the Enrolled Set and Maintenance Set
- Revise the statistical analysis based on the addition of re-randomization at Week 16

Minor spelling, editorial, and formatting changes were also made, and the List of Abbreviations was updated.

Modifications and changes

Change #1

Section 1 Summary

During the Treatment Period, eligible subjects will be randomized 1:1 to receive one of the following blinded IMP regimens:

- Bimekizumab 320mg administered subcutaneously (sc) every 4 weeks (Q4W)

- Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W

Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.

Approximately 350 subjects will be randomized to bimekizumab 320mg and approximately 350 subjects will be randomized to secukinumab. Investigational medicinal product will be administered at Baseline, Weeks 1, 2, 3, and 4 and then Q4W thereafter, until Week 44 (Treatment Period). All doses will be administered in the clinic.

Has been changed to:

During the **first 16 weeks of the** Treatment Period, eligible subjects will be randomized 1:1 to receive one of the following blinded IMP regimens:

- Bimekizumab 320mg administered subcutaneously (sc) every 4 weeks (Q4W)
- Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W

Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.

Approximately 350 subjects will be randomized to bimekizumab 320mg and approximately 350 subjects will be randomized to secukinumab. Investigational medicinal product will be administered at Baseline, Weeks 1, 2, 3, and 4 and then Q4W thereafter, until Week 44 (Treatment Period). All doses will be administered in the clinic.

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg every 8 weeks (Q8W). To maintain the blind after re-randomization, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Subjects in the secukinumab arm will continue to receive secukinumab 300mg Q4W.

Change #2

Section 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 healthy volunteers.

Has been changed to:

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.

Change #3

Section 2.2.1.2 Ongoing studies

Seven additional studies of bimekizumab in the treatment of PSO are ongoing.

- PS0008 is a Phase 3, multicenter, randomized, double-blind, parallel-group, active-comparator-controlled study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0009 is a Phase 3 randomized, double-blind, placebo- and active comparator-controlled study to evaluate the efficacy and safety of bimekizumab administered sc to adult subjects with moderate to severe plaque PSO.
- 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.
- PS0013 is a Phase 3, multicenter, randomized withdrawal, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- 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.
- PS0014 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.

Has been changed to:

Eight~~**seven**~~ additional studies of bimekizumab in the treatment of PSO are ongoing.

- PS0008 is a Phase 3, multicenter, randomized, double-blind, parallel-group, active-comparator-controlled study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0009 is a Phase 3 randomized, double-blind, placebo- and active comparator-controlled study to evaluate the efficacy and safety of bimekizumab administered sc to adult subjects with moderate to severe plaque PSO.
- 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.
- PS0013 is a Phase 3, multicenter, randomized withdrawal, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.

- **PS0014 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.**
- 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.

Change #4

Section 4.3.1 Other efficacy variables

The following bullet has been added:

- Percent of subjects achieving mNAPSI75, mNAPSI90, and mNAPSI100 for subjects with nail PSO at Baseline

Change #5

Section 4.3.1 Other efficacy variables

- Scalp-specific Investigator's Global Assessment (scalp IGA) response (0/1 and 0) at Week 16 for subjects with scalp PSO at Baseline
- Scalp IGA response (0/1 and 0) for subjects with scalp PSO at Baseline
- Palmoplantar Investigator's Global Assessment (pp-IGA) response (0/1 and 0) for subjects with palmoplantar PSO at Baseline

Has been changed to:

- Scalp-specific Investigator's Global Assessment (scalp IGA) response (~~**0/1 and 0**~~**Clear or Almost Clear with at least 2 category improvement relative to Baseline**) ~~**at Week 16**~~ for subjects with scalp PSO at Baseline
- ~~**Scalp IGA response (0/1 and 0) for subjects with scalp PSO at Baseline**~~
- Palmoplantar Investigator's Global Assessment (pp-IGA) response (~~**0/1 and 0**~~ **Clear or Almost Clear with at least 2 category improvement relative to Baseline**) for subjects with palmoplantar PSO at Baseline

Change #6

Section 4.3.1 Other efficacy variables

The following bullet has been added:

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

Change #7

Section 4.3.2 Other safety variables

The following bullet has been removed:

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

Change #8

Section 5.2.2 Treatment Period

During the 48-week Treatment Period, approximately 700 subjects will be randomized 1:1 to receive the following blinded IMP regimens:

- Bimekizumab 320mg administered sc Q4W (350 subjects)
- Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W (350 subjects)

Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.

Has been changed to:

During the **first 16 weeks of the** 48-week Treatment Period, approximately 700 subjects will be randomized 1:1 to receive the following blinded IMP regimens:

- Bimekizumab 320mg administered sc Q4W (350 subjects)
- Secukinumab 300mg administered sc at Baseline and Weeks 1, 2, 3, and 4 followed by dosing Q4W (350 subjects)

Subjects receiving bimekizumab 320mg will receive placebo sc on Weeks 1, 2, and 3 in order to maintain the blind.

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. To maintain the blind after re-randomization, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Subjects in the secukinumab arm will continue to receive secukinumab 300mg Q4W.

Change #9

Section 5.6 Schedule of study assessments

The schedule of study assessments is presented in Table 5–1.

Has been changed to:

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.**

Change #10

Table 5–1 Schedule of study assessments

Inclusion/exclusion	X	X																
Significant past medical history and concomitant diseases	X	X[c]																

Physical exam[d, e]	X							X			X			X			X	X
scalp IGA[l]		X	X	X		X[l]	X[l]	X[l]	X[l]				X[l]				X[l]	
Randomization		X																

Has been changed to:

Inclusion/exclusion	X	X[c]																
Significant past medical history and concomitant diseases	X	X[d]																
Physical exam[c, e]	X							X			X			X			X	X
scalp IGA[l]		X	X[l]	X[l]		X[l]	X[l]	X[l]	X[l]				X[l]				X[l]	
Randomization		X							**X**									

Change #11

Table 5–1 Schedule of study assessments, footnotes a through d, o, and q

[a] Visit windows of ±3 days from the first dose from the Week 1 visit to the Week 24 visit. Visit windows of ±7 days from Week 28 through Week 48/PEOT. The SFU Visit window is -3 and +7 days from the last dose.

[b] The SFU Visit will occur 20 weeks after the last dose.

[c] Ensure no significant changes in medical history.

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

[o] The PGADA is assessed only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).

[q] The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the end of the study, including the SFU visit, the dosing window is ±7 days relative to the scheduled dosing visit.

Have been changed to:

[a] Visit windows of ±3 days from the first dose from the Week 1 visit to the Week 24 visit. Visit windows of ±7 days from Week 28 through Week 48/PEOT. The SFU Visit window is ~~**-3 and +**~~ ±7 days ~~**from the last dose**~~**relative to the scheduled visit date**.

[b] The SFU Visit will occur 20 weeks after the ~~**last**~~**final** dose.

[c] ~~**Ensure no significant changes in medical history**~~.**Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.**

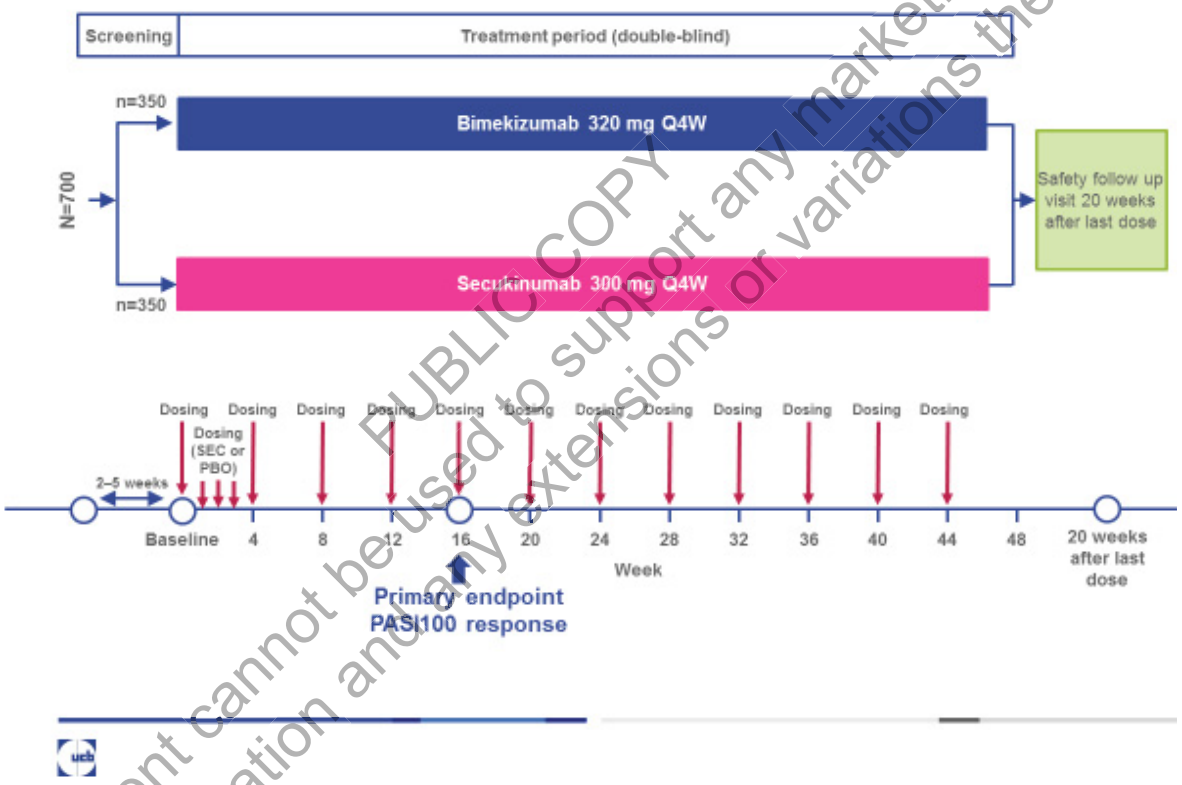
[d] ~~**Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.**~~**Ensure no significant changes in medical history.**

[o] The PGADA is assessed ~~only~~for **all** subjects ~~**with PsA**~~at Baseline ~~**(defined as a past medical history of PsA or PASE ≥47)**~~**. At all subsequent visits, the PGADA is only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).**

[q] The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the end of the study, ~~**including the SFU visit**~~,the dosing window is ±7 days relative to the scheduled dosing visit.

Change #12

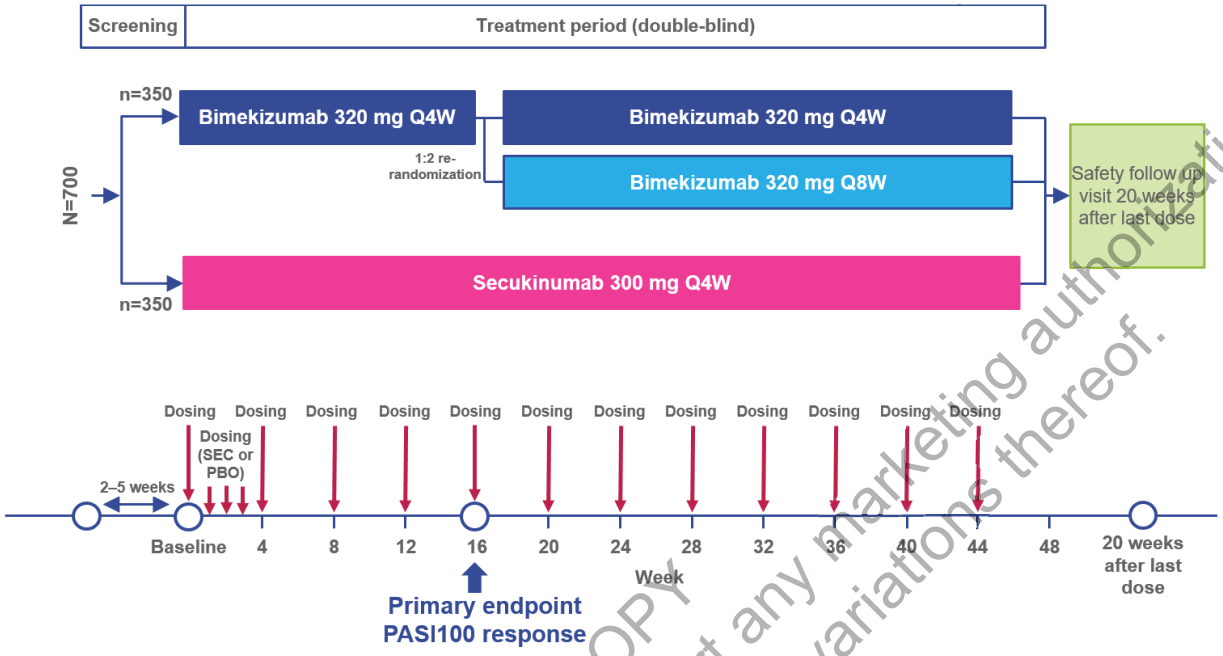
Figure 5–1: Schematic diagram



PASI100=Psoriasis Area Severity Index complete response; PBO=placebo; Q4W=every 4 weeks; SEC=secukinumab; w=Week

Note: At Week 28 and all following visits, subjects on continuous treatment 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.

Has been changed to:



IGA=Investigator's Global Assessment; IMP=investigational medicinal product; PASI100=Psoriasis Area Severity Index complete response; PBO=placebo; Q4W=every 4 weeks; **Q8W=every 8 weeks;** SEC=secukinumab~~; w=Week~~

Note: At Week 28 and all following visits, subjects on continuous treatment 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.

Change #13

Section 5.8.2 Dose selection

Bimekizumab doses ranging from 64mg to 480mg were evaluated in the Phase 2b multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study PS0010. Bimekizumab 320mg was found to have an acceptable safety profile, only required 2 injections per treatment administration, and achieved significant PASI responses at Week 12 (summarized in the IB). Furthermore, data from the Phase 2a multicenter, randomized, subject-blind, investigator-blind study PS0016 and PK/PD modeling in this PSO population indicates improved responses through Week 16. Therefore, a bimekizumab dose of 320mg Q4W was selected for this study.

Has been changed to:

Bimekizumab doses ranging from 64mg to 480mg were evaluated in the Phase 2b multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study PS0010. Bimekizumab 320mg was found to have an acceptable safety profile, only required 2 injections per treatment administration, and achieved significant PASI responses at Week 12 (summarized in the IB). Furthermore, data from the Phase 2a multicenter, randomized, subject-blind, investigator-blind study PS0016 and PK/PD modeling in this PSO population indicates improved responses through Week 16. Therefore, a bimekizumab dose of 320mg Q4W **through Week 16 and 320mg Q4W or Q8W thereafter** was selected for this study.

Change #14

Section 6.2 Exclusion criteria

25. Presence of active suicidal ideation, or positive suicide behavior using the "Screening" version of the electronic Columbia Suicide Severity Rating Scale (eC-SSRS) and with either of the following criteria:

    – History of a suicide attempt within the 5 years prior to the Screening Visit. Subjects with a history of a suicide attempt more than 5 years ago should be evaluated by a mental healthcare practitioner before enrolling into the study.

    – Suicidal ideation in the past month prior to the Screening Visit as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the "Screening" version of the eC-SSRS.

Has been changed to:

25**a**. Presence of active suicidal ideation, or positive suicide behavior using the "Screening" version of the electronic Columbia Suicide Severity Rating Scale (eC-SSRS) and with either of the following criteria:

    – History of a suicide attempt within the 5 years prior to the Screening Visit. Subjects with a history of a suicide attempt more than 5 years ago should be evaluated by a mental healthcare ~~**practitioner**~~**professional (eg, locally licensed psychiatrist, psychologist, or master's level therapist)** before enrolling into the study.

    – Suicidal ideation in the past month prior to the Screening Visit as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the "Screening" version of the eC-SSRS.

Change #15

Section 6.3 Withdrawal criteria

9. A subject considered as having either a suspected new latent tuberculosis infection (LTBI) or who develops active TB or NTMB infection during the study (including but not limited to, conversion demonstrated by IGRA or other diagnostic means) must be immediately discontinued from IMP and a PEOT Visit must be scheduled as soon as possible, but not later than the next regular visit.

    The 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 12.3.1.

Has been changed to:

9**a**. A subject considered as having either a suspected new latent tuberculosis infection (LTBI) or who develops active TB or **pulmonary** NTMB infection during the study (including but not limited to, conversion demonstrated by IGRA or other diagnostic means) must be immediately discontinued from IMP ~~**and a PEOT Visit must be scheduled as soon as possible, but not later than the next regular visit**~~.

The subject must be permanently withdrawn if further examinations result in a diagnosis of **pulmonary NTMB**, 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 12.3.1.

Change #16

Section 6.3 Withdrawal criteria

11. Subjects **must be referred** immediately to a mental healthcare professional and may be withdrawn from the study based upon the Investigator's judgment of benefit/risk for:

- Active suicidal ideation as indicated by a positive response ("Yes") to Question 4 of the "Since Last Visit" version of the 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.

Has been changed to:

11**a**. Subjects **must be referred** immediately to a mental healthcare professional **(eg, 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.

Change #17

Section 6.3 Withdrawal criteria

12. Subjects must be referred immediately to a mental healthcare professional 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

Has been changed to:

12**a**. Subjects must be referred immediately to a mental healthcare professional **(eg, 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

Change #18

Table 7–1: Dosing scheme

Week Dose Assignment	Baseline (first dose)	1	2	3	4	8	12	16	20	24	28	32	36	40	44
Bimekizumab 320mg	●●	○○	○○	○○	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Secukinumab 300mg	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲

Notes: A bimekizumab 160mg injection is depicted by a black circle (●). A placebo injection is depicted by a white circle (○). A secukinumab 150mg injection is depicted by a black triangle (▲).

Has been changed to:

Week Dose Assignment	Baseline (first dose)	1	2	3	4	8	12	16[a]	20	24	28	32	36	40	44
Bimekizumab 320mg	●●	○○	○○	○○	●●	●●	●●	Q4W ●●	●●	●●	●●	●●	●●	●●	●●
								Q8W ●●	○○	●●	○○	●●	○○	●●	○○
Secukinumab 300mg	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲

Q4W=every 4 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●). A placebo injection is depicted by a white circle (○). A secukinumab 150mg injection is depicted by a black triangle (▲).

[a] **Subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**

Change #19

Section 7.6 Drug accountability

Blinded study staff may be delegated the responsibility to receive, inventory, and destroy the used kits. The packaging identifies each kit by a unique number that does not correlate to the contents and therefore, does not unblind study site staff. Unblinded study staff will be responsible for preparation (breaking tamper proof sticker on kit, etc) of the clinical trial material, including recording the administration information on source document.

Has been changed to:

~~**Blinded study staff may be delegated the responsibility to receive, inventory, and destroy the used kits.**~~ **Unblinded study staff will be responsible for receipt, inventory, and destruction of used kits.** The packaging identifies each kit by a unique number ~~**that does not correlate to the contents and therefore, does not unblind study site staff**~~**, but due to the commercial packaging of the comparator, the unblinded study staff will be responsible to maintain the blind**. Unblinded study staff will be responsible for preparation (breaking tamper proof sticker on kit, etc) of the clinical trial material, including recording the administration information on source document.

Change #20

Section 7.6 Drug accountability

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

Has been changed to:

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

Change #21

Table 7-2 Prohibited psoriasis medications

Systemic retinoids	3 months

Has been changed to:

Systemic retinoids	~~**3**~~**1** month~~s~~

Change #22

Section 7.9 Blinding

For subjects receiving bimekizumab, bimekizumab will be administered at Baseline; placebo will be administered at Week 1, Week 2, and Week 3; their second dose of bimekizumab will be at Week 4; and bimekizumab doses Q4W thereafter. Secukinumab subjects will receive secukinumab at Baseline, Week 1, Week 2, Week 3, Week 4, and Q4W thereafter.

Has been changed to:

For subjects receiving bimekizumab, bimekizumab will be administered at Baseline; placebo will be administered at Week 1, Week 2, and Week 3; their second dose of bimekizumab will be at

Week 4; and bimekizumab doses Q4W ~~thereafter~~**through Week 16. At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W**. **To maintain the blind, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44.** Secukinumab subjects will receive secukinumab at Baseline, Week 1, Week 2, Week 3, Week 4, and Q4W thereafter.

Change #23

Section 7.10 Randomization and numbering of subjects

The following was added:

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. To maintain the blind after re-randomization, subjects in the bimekizumab 320mg Q8W treatment arm will receive placebo at Weeks 20, 28, 36, and 44. Subjects in the secukinumab arm will continue to receive secukinumab 300mg Q4W.

Change #24

Section 8 Study procedures by visit

- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the end of the study, including the SFU visit, the dosing window is ±7 days relative to the scheduled dosing visit.
- For the SFU Visit (20 weeks after the final dose), the visit should occur no more than 3 days prior to the scheduled visit date and within 7 days after the scheduled visit date (-3 days/+7 days).

Has been changed to:

- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the end of the study, ~~**including the SFU visit,**~~ the dosing window is ±7 days relative to the scheduled dosing visit.
- For the SFU Visit (20 weeks after the final dose), the visit ~~**should occur no more than 3 days prior to the scheduled visit date and within 7 days after the scheduled visit date (-3 days/+7 days)**~~**window is ±7 days relative to the scheduled visit date**.

Change #25

Section 8.2.1 Baseline Visit

- Inclusion/exclusion

Has been changed to:

- Inclusion/exclusion **(includes evaluation of signs and symptoms of active TB and risk for exposure to TB)**

Change #26

Section 8.2.1 Baseline Visit

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

Has been changed to:

After completion of the above-mentioned procedures, ~~**bimekizumab or secukinumab**~~**IMP** administration will occur.

Change #27

Section 8.2.2 Week 1 and Week 2 Visits (±3 days relative to Baseline)

After completion of the above-mentioned procedures, placebo or secukinumab administration will occur.

Has been changed to:

After completion of the above-mentioned procedures, **IMP**~~**placebo or secukinumab**~~ administration will occur.

Change #28

Section 8.2.3 Week 4 Visit (±3 days relative to Baseline)

After completion of the above-mentioned procedures, administration of placebo or secukinumab will occur.

Has been changed to:

After completion of the above-mentioned procedures, administration of **IMP**~~**placebo or secukinumab**~~ will occur.

Change #29

Sections 8.2.4 Week 4 Visit (±3 days relative to Baseline), 8.2.5 Week 8 and Week 12 Visits (±3 days relative to Baseline), 8.2.7 Week 20 (±3 days relative to Baseline) and Week 28 Visits (±7 days relative to Baseline), 8.2.8 Week 24 Visit (±7 days relative to Baseline), 8.2.9 Week 32 Visit (±7 days relative to Baseline), 8.2.10 Week 36 Visit (±7 days relative to Baseline), 8.2.11 Week 40 Visit (±7 days relative to Baseline), 8.2.12 Week 44 Visit (±7 days relative to Baseline)

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

Has been changed to:

After completion of the above-mentioned procedures, administration of **IMP**~~**bimekizumab or secukinumab**~~ will occur.

Change #30

Section 8.2.6 Week 16 Visit (±3 days relative to Baseline)

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

Has been changed to:

At Week 16 subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W. After completion of the above-mentioned procedures, administration of **IMP~~bimekizumab or secukinumab~~** will occur.

Change #31

Section 8.4 Safety Follow-Up Visit (20 weeks after final dose, -3 days/+7 days), section title

8.4 Safety Follow-Up Visit (20 weeks after final dose, -3 days/+7 days)

Has been changed to:

8.4 Safety Follow-Up Visit (20 weeks after final dose, ~~**-3 days/+**~~7 days)

Change #32

Section 9 Assessment of efficacy

The PASI, BSA, IGA, scalp IGA, mNAPSI, and pp-IGA 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. Preferably the same assessor should evaluate the subject at each assessment.

Has been changed to:

The PASI, BSA, IGA, scalp IGA, mNAPSI, and pp-IGA 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. ~~**Preferably t**~~The same assessor should evaluate the subject at each assessment.

Change #33

Section 9.11 PASE questionnaire

The Psoriatic Arthritis Screening and Evaluation (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. Subjects with scores ≥47 should be referred to a rheumatologist for evaluation.

Has been changed to:

The Psoriatic Arthritis Screening and Evaluation (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. ~~**Subjects with scores ≥47 should be referred to a rheumatologist for evaluation.**~~

Change #34

Section 12.2.1.2.1 IMP restart/rechallenge

- The rechallenge is approved by the UCB responsible physician, 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.

Has been changed to:

The rechallenge is approved by the UCB responsible physician, 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.**~~

Change #35

Section 12.3.1 Assessment and management of TB and TB risk factors

b. High risk of acquiring TB infection:

  - Known exposure to another person with active TB infection within the 3 months prior to Screening.
  - 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 specialize and discussion with the Study Physician, if LTBI is identified. The retest must be done during the protocol-defined Screening window.

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

Has been changed to:

b. High risk of acquiring TB infection:

  - Known **close** exposure to another person with active TB infection within the 3 months prior to Screening.

- 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~~ze~~ and discussion with the Study Physician, if LTBI is identified. The retest must be done during the protocol-defined Screening window.

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

Change #36

Section 12.3.1.1 Tuberculosis assessment by IGRA

If latent or active TB is identified, subject must undergo appropriate study-specified withdrawal procedures.

Has been changed to:

If ~~**latent or**~~ active TB is identified, subject must undergo appropriate study-specified withdrawal procedures.

Change #37

Section 12.3.1.3 Tuberculosis questionnaire

The following sentence was deleted:

Subjects with a latent or active TB infection must be withdrawn from the study.

Change #38

Section 12.3.1.4 Tuberculosis management

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 or LTBI should be withdrawn from the study and receive appropriate TB or prophylaxis therapy.

Has been changed to:

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 ~~**or LTBI should**~~ **must** be withdrawn from the study and receive appropriate TB ~~**or prophylaxis**~~therapy.

Change #39

Section 14.1 Definition of analysis sets

The following sentence has been added:

The Enrolled Set will consist of all subjects who have given informed consent.

Change #40

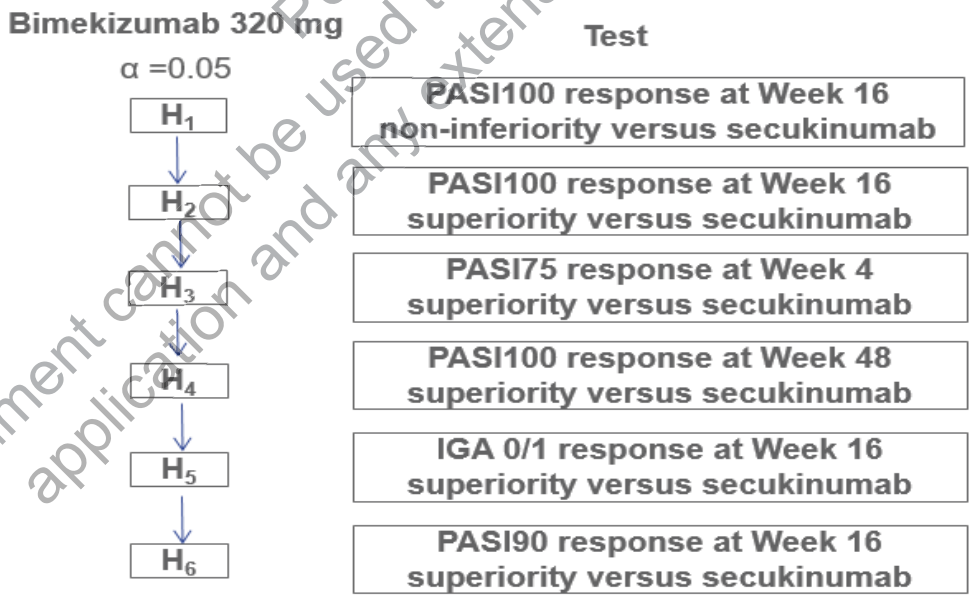
Section 14.1 Definition of analysis sets

The following sentence has been added:

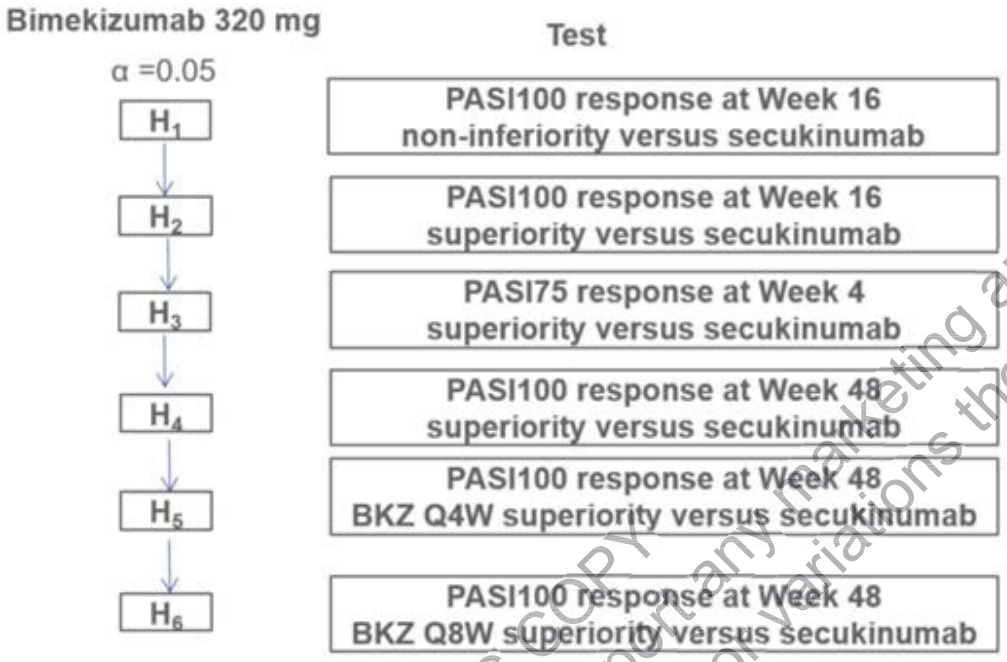
The Maintenance Set (MS) will consist of all subjects that receive at least 1 dose of IMP at Week 16 or later in the Treatment Period (including the Week 16 dose).

Change #41

Figure 14-1 Hypotheses testing of secondary efficacy endpoints



Has been changed to:



BKZ=bimekizumab; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Tests for H_1, H_2, H_3, and H_4 are based on all subjects initially randomized to bimekizumab compared to secukinumab. For H_5 and H_6, testing is based on the subjects re-randomized at Week 16 to bimekizumab 320mg Q4W, and bimekizumaba 320mg Q8W, respectively, compared to secukinumab.

Change #42

Section 14.3.1.1 Sensitivity analysis

In order to obtain reasonable estimates of variability for a treatment arm at a given center, a minimum of 10 subjects will be considered acceptable for a center to be included in the model without pooling. Given the 1:1 randomization allocation scheme, this should provide a minimum of about 5 subjects in the bimekizumab arm and 5 subjects in the secukinumab arm. Centers with fewer than 10 subjects will be eligible for pooling. The following center pooling algorithm will be used for each geographic region:

Has been changed to:

In order to obtain reasonable estimates of variability for a treatment arm at a given center, a minimum of 10 subjects will be considered acceptable for a center to be included in the model without pooling. Given the 1:1 randomization allocation scheme **at the start of the study**, this should provide a minimum of about 5 subjects in the bimekizumab arm and 5 subjects in the secukinumab arm. Centers with fewer than 10 subjects will be eligible for pooling. The following center pooling algorithm will be used for each geographic region:

Change #43

Section 14.3.2.1 Analysis of the secondary efficacy variables

The following has been added:

PASI75 response at Week 4 will be analyzed for all subjects in the RS based on the randomized treatment group at Baseline.

Additionally, PASI100 at Week 48 will be evaluated as a secondary efficacy variable. The way the analysis for this variable is conducted will depend on which comparison is being made. The planned comparisons are as follows:

- Compare all subjects initially randomized to bimekizumab (regardless of re-randomization assignment at Week 16) to all subjects initially randomized to secukinumab based on the RS (H_4)
- Compare subjects who were assigned to bimekizumab 320mg Q4W at Week 16 to secukinumab based on the MS (H_5)
- Compare subjects who were assigned to bimekizumab 320mg Q8W at Week 16 to secukinumab based on the MS (H6)

Change #44

Section 14.3.2.2 Analysis of the other efficacy variables

Other efficacy variables will be summarized by treatment and visit and will generally be summarized based on imputed data (NRI and multiple imputation [MI] for binary and continuous variables, respectively, unless otherwise stated in the SAP). In some cases, variables may also be summarized based on observed case data (ie, subjects with missing data or who have prematurely discontinued IMP are treated as missing). There may be cases where the multiple imputation model fails to converge. In such situations, the last observation carried forward (LOCF) approach will instead be used to impute the missing data. If LOCF is used instead of multiple imputation for this reason, this will be clearly specified in the corresponding table summary. Should there be no missing data for a study variable, then only observed case data will be presented. Note that for LOCF imputation, any missing data or data collected following discontinuation of IMP will be imputed with the most recent previous value. See Section 14.7 for further details.

Time to PASI75/90/100 response will be estimated and presented using the Kaplan-Meier product-limit method for each treatment. Time to a given response will be defined as the length in days from the first dose of IMP until the first date when the response is achieved. Subjects who discontinue IMP prior to achieving a response will be censored at the date of IMP discontinuation. Subjects who reach the Week 48 Visit without achieving the given PASI response will be censored at the date of the Week 48 Visit. The median time to response, including the 2-sided 95% CI, will be calculated for each treatment. Between group differences (bimekizumab vs secukinumab) will be analyzed with the log-rank statistic.

In general, data will be summarized by visit through Week 48. However, for PASI responder variables (PASI75, PASI90, PASI100) and IGA responder variables (IGA 0/1, IGA 0), as well as selected other efficacy variables, summaries will be prepared for time points between Weeks 16 and 48 among those subjects who were responders at Week 16. Further details will be provided in the SAP.

Has been changed to:

Other efficacy variables will be summarized by treatment and visit and will generally be summarized based on imputed data (NRI and multiple imputation [MI] for binary and continuous variables, respectively, unless otherwise stated in the SAP). In some cases, variables may also be summarized based on observed case data (ie, subjects with missing data or who have prematurely discontinued IMP are treated as missing). There may be cases where the multiple imputation model fails to converge. In such situations, the last observation carried forward (LOCF) approach will instead be used to impute the missing data. If LOCF is used instead of multiple imputation for this reason, this will be clearly specified in the corresponding table summary. Should there be no missing data for a study variable, then only observed case data will be presented. Note that for LOCF imputation, any missing data or data collected following discontinuation of IMP will be imputed with the most recent previous value. See Section 14.7 for further details.

~~**Time to PASI75/90/100 response will be estimated and presented using the Kaplan-Meier product-limit method for each treatment. Time to a given response will be defined as the length in days from the first dose of IMP until the first date when the response is achieved. Subjects who discontinue IMP prior to achieving a response will be censored at the date of IMP discontinuation. Subjects who reach the Week 48 Visit without achieving the given PASI response will be censored at the date of the Week 48 Visit. The median time to response, including the 2-sided 95% CI, will be calculated for each treatment. Between group differences (bimekizumab vs secukinumab) will be analyzed with the log-rank statistic.**~~

~~**In general, data will be summarized by visit through Week 48. However, for PASI responder variables (PASI75, PASI90, PASI100) and IGA responder variables (IGA 0/1, IGA 0), as well as selected other efficacy variables, summaries will be prepared for time points between Weeks 16 and 48 among those subjects who were responders at Week 16. Further details will be provided in the SAP.**~~

Time to PASI75/90/100 response will be estimated and presented using the Kaplan-Meier product-limit method based on the RS by initially randomized treatment groups (Bimekizumab vs secukinumab). This could make the interpretation of the data challenging given that there are two different bimekizumab dosing regimens starting at Week 16, but it is anticipated that most responses will be observed by Week 16 when all bimekizumab subjects are on the same regimen. Time to a given response will be defined as the length in days from the first dose of IMP until the first date when the response is achieved. Subjects who discontinue IMP prior to achieving a response will be censored at the date of IMP discontinuation. Subjects who reach the Week 48 Visit without achieving the given PASI response will be censored at the date of the Week 48 Visit. The median time to response, including the 2-sided 95% CI, will be calculated for each treatment. Between group differences (bimekizumab vs secukinumab) will be analyzed with the log-rank statistic.

In general, data will be summarized by visit through Week 48. All summaries of data up to Week 16 will be based on the RS for the 2 randomized treatment groups (bimekizumab and secukinumab). For visits after Week 16, by-visit summaries will be prepared for the following 3 groups of subjects:

1. **Subjects in the MS summarized by the 3 maintenance treatment groups (bimekizumab 320mg Q4W, bimekizumab 320mg Q8W, and secukinumab). Note that while the MS is primarily defined for the evaluation of data after Week 16, these summary tables will include data at all visits (Baseline to Week 48) to provide a comprehensive summary of subjects by maintenance treatment group for the MS.**
2. **A subset of Group 1 above. Specifically, this will include only those subjects who are responders at Week 16 for the variable being summarized. This will provide an assessment of how efficacy is maintained among Week 16 responders.**
3. **Subjects in the RS summarized by the 2 randomized treatment groups (bimekizumab and secukinumab). Data from Baseline to Week 48 will be included in these tables. This provides an intent-to-treat analysis among all randomized subjects in the study through Week 48.**

All efficacy variables will be summarized in the manner described for Group 1 above. Summaries for Groups 2 and 3 will be done only for a subset of efficacy variables, namely, PASI75/90/100, IGA Clear or Almost Clear, Scalp IGA Clear or Almost Clear, pp-IGA Clear or Almost Clear, mNAPSI75/90/100, and DLQI 0/1. Further details on these analyses will be provided in the SAP.

Change #45

Section 14.7 Handling of dropouts or missing data

Missing data for the secondary efficacy variables (which are all binary) will be imputed using NRI. Additionally, the 2 additional approaches described above for the primary efficacy variable will be used for the secondary efficacy variables.

Has been changed to:

Missing data for the secondary efficacy variables (which are all binary) will be imputed using NRI. Additionally, the 2 ~~**additional**~~**missing data-handling** approaches described above for the primary efficacy variable will be used for the secondary efficacy variables.

Change #46

Section 14.9 Determination of sample size

A total of 700 subjects will be randomly assigned in a 1:1 ratio to one of the following treatment groups:

- Bimekizumab 320mg (350 subjects)
- Secukinumab (350 subjects)

Has been changed to:

A total of 700 subjects will be randomly assigned in a 1:1 ratio **at Baseline** to one of the following treatment groups:

- Bimekizumab 320mg (350 subjects)

- Secukinumab (350 subjects)

18.2 Protocol Amendment 1.1

Rationale for the amendment

The primary rationale for this local amendment was to incorporate the use of photographs of skin and nails during Schedule of study assessments only for sites in the US, Australia, Belgium, Poland, and Germany and only for patients who consent (see Table 5–1).

Modifications and changes

Specific changes

Change #1

Section 5 Study Design, Table 5–1.

The specific assessment requiring the taking of photographs of skin and nails during Baseline, Weeks 1, 2, 4, 8, 12, 16, 32, and 48/EOT was added as stated below (table header used for clarification and was not changed):

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Photographs of skin and nails (subset of sites)		X	X	X		X	X	X	X				X				X	

Change #2

Section 8.1

Added the following text: "In case subjects agree to participate in the photography sub-study (see Section 9.12) they will need to sign a separate informed consent form."

Change #3

Section 8.2 Treatment Period

Added text referring to the assessment requiring photographs of skin and nails during the following time points:

- Baseline
- Week 1
- Week 2
- Week 4
- Week 8
- Week 12
- Week 16

- Week 32
- Week 48/EOT

Change #4

Section 9.12 Photographs

The following text was added as subsection 9.14

At certain clinical sites, representative photographs of the changes in skin and nail appearance will be captured. Subjects who consent to the procedure will have full body (anterior and posterior views) photographs taken. Only those subjects with nail disease at Baseline will have nail photographs taken. Only those subjects with palmoplantar disease at Baseline will have photographs of their palms or soles of their feet taken. Only those subjects with scalp disease at Baseline will have scalp photographs taken. Photographs will be anonymized and will be used for publication purposes.

Study sites selected for photography will be trained and receive standardized photographic equipment by a centralized photographic vendor. Photographs will be electronically transferred from the site to the vendor.

At the end of the study, the site will receive an electronic file of all subject photographs for archiving.

The central photography vendor will tabulate and transfer all subject photos to the Sponsor at the end of the study.

18.3 Protocol Amendment 2

No subjects were enrolled under this amendment.

Rationale for the amendment

The protocol has been amended for the following reasons:

- Extended the study duration for an additional 96 weeks in an Open-Label Extension Period. Changes include addition of a new schedule of assessments for the additional 96 weeks, additional other objectives and endpoints, and updates to Section 8, Study procedures by visit.
- Added planned re-randomization by treatment regimens and PASI response at Week 48 in the OLE Period.
- Clarified secondary efficacy variable for IGA response at Week 16, and added other efficacy variables for IGAxBSA and PASE score suggestive of PsA.
- Modified the text in Section 7 to include guidance for allowing subjects the option to self-inject IMP at home after Week 48.
- Updated Section 12.2.1 (Evaluation of PDILI) for improved clarity and consistency with other Phase 3 studies of bimekizumab in subjects with PSO.
- Added statistical analyses for the OLE Period.

Modifications and changes

Global changes:

The following changes were made throughout the protocol:

- The maximum duration of the study has been changed from 69 weeks to 165 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 term "Treatment Period" has been changed to "double-blind Treatment Period" throughout the document to clearly distinguish it from the OLE Period.
- The list of abbreviations was updated accordingly.
- Minor spelling, editorial, and formatting changes were made throughout the document.

Change #1

Section 1 Summary, third and fourth paragraphs:

Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. For each subject, the study will last a maximum of 69 weeks and will consist of 3 periods, a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at 44 weeks), and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]).

During the first 16 weeks of the Treatment Period, eligible subjects will be randomized 1:1 to receive one of the following blinded IMP regimens:

Has been changed to:

Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. For each subject, the study will last a maximum of ~~69~~**165** weeks and will consist of ~~3~~**4** periods, a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at ~~44 weeks),~~**Week 44), an Open-Label Extension (OLE) Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W);** and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP]).

During the first 16 weeks of the **double-blind** Treatment Period, eligible subjects will be randomized 1:1 to receive one of the following blinded IMP regimens:

Change #2

Section 1 Summary, 8th through 11th paragraphs:

At Week 48, all subjects will undergo the Week 48 study assessments and will enter the SFU Period.

Has been changed to:

At **the completion of the** Week 48~~, all~~**visit assessments,** subjects **may receive open-label bimekizumab treatment for an additional 96 weeks. All subjects enrolling in the OLE Period will** ~~undergo~~**, after signing a new ICF, be evaluated for eligibility, be randomized, and receive their first dose of bimekizumab in the OLE Period.**

During the OLE Period eligible subjects will receive the following IMP regimens as determined by the subject's treatment regimen and PASI response in the double-blind Treatment Period.

At Week 48, subjects receiving:

- **Bimekizumab 320mg Q4W who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**
- **Bimekizumab 320mg Q4W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Bimekizumab 320mg Q8W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Bimekizumab 320mg Q8W who achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q8W.**
- **Secukinumab who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Secukinumab who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**

At Week 96, 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 judgment, the Investigator decides differently.

During the OLE Period, subjects will attend study visits at Weeks 52, 56, 64, and 72, and then every 12 weeks.

All subjects not enrolling in the OLE Period will have the Week 48 study assessments and will enter the SFU Period.

Change #3

Section 3.3 Other objectives:

The following text was added:

- **Assess the maintenance of efficacy of bimekizumab dosing Q4W versus Q8W**
- **Assess the safety and efficacy of initiating bimekizumab therapy in subjects who received secukinumab in the double-blind Treatment Period**

Change #4

Section 4.2.1 Secondary efficacy variables:

- IGA response (0/1) (defined as Clear or Almost Clear with at least a 2-category improvement relative to Baseline) at Week 16

Has been changed to:

- IGA response (0/1) ~~at Week 16~~**(defined as Clear or Almost Clear with at least a 2-category improvement relative to Baseline) at Week 16**

Change #5

Section 4.3.1 Other efficacy variables:

The following text has been added:

- **Absolute and percent change from Baseline in the product of IGA and BSA (IGAxBSA)**
- **Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47)**

Change #6

Section 5.2 Study periods:

This study will include 3 periods, a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at 44 weeks), and a SFU Period (20 weeks after the final dose of IMP). The end of the study is defined as the date of the last visit of the last subject in the study.

Has been changed to:

This study will include ~~3~~**4** periods, a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at **Week** 44**), an optional OLE Period (96** weeks~~),~~**; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W** and **at Week 140 for subjects receiving bimekizumab 320mg Q4W), and an** SFU Period (20 weeks after the final dose of IMP). The end of the study is defined as the date of the last visit of the last subject in the study.

Change #7

The following section has been added:

5.2.3 OLE Period

After completion of the Week 48 visit assessments, subjects will be allowed to enroll in the OLE Period. All subjects enrolling in the OLE Period will sign a new ICF, and then receive the following IMP regimens as determined by the subject's treatment regimen and PASI response in the double-blind Treatment Period.

At Week 48, subjects receiving:

- **Bimekizumab 320mg Q4W who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**
- **Bimekizumab 320mg Q4W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Bimekizumab 320mg Q8W who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Bimekizumab 320mg Q8W who achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q8W.**

- **Secukinumab who do not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Secukinumab who achieve PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**

At Week 96, 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 judgment, the Investigator decides differently.

During the OLE Period, subjects will attend study visits at Weeks 52, 56, 64, and 72, and then every 12 weeks. At study visits, IMP will be administered in the clinic by sc injection as applicable. In between study visits, subjects will self-inject IMP at home.

All subjects not enrolling in the open-label study will have the Week 48 study assessments and will enter the SFU Period.

The assessments to be performed at each OLE Period visit are presented in Table 5-2.

Change #8

Section 5.3 Study duration per subject:

For each subject, the study will last a maximum of up to 69 weeks, as follows:

- Screening Period: 2 to 5 weeks
- Double-blind Treatment Period: 48 weeks (final dose at Week 44)
- Safety Follow-Up Period: a SFU Visit is planned 20 weeks after the final dose of IMP

Has been changed to:

For each subject, the study will last a maximum of up to ~~**69**~~**165** weeks, as follows:

- Screening Period: 2 to 5 weeks
- Double-blind Treatment Period: 48 weeks (final dose at Week 44)
- **OLE Period: 96 weeks (final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W)**
- Safety Follow-Up Period: a SFU Visit is planned 20 weeks after the final dose of IMP **visit**

Change #9

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.

Table 5-1: Schedule of study assessments

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Informed consent	X																	
Inclusion/exclusion	X	X[c]																
Urine drug screen	X																	
Demographic data	X																	
Psoriasis history	X																	
eC-SSRS	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Significant past medical history and concomitant diseases	X	X[d]																
Physical exam[c, e]	X							X			X			X			X	X
Height		X																
Body weight		X							X		X			X			X	
Vital signs[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology and biochemistry	X	X	X	X		X	X	X	X		X		X		X		X	X
Urinalysis	X	X							X		X		X		X		X	X
ECG	X								X				X				X	
Pregnancy testing[g]	X	X				X	X	X	X	X	X	X	X	X	X	X	X	X
Hepatitis B and C testing[h]	X																	

Table 5-1: Schedule of study assessments

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
HIV testing[i]	X																	
Chest x-ray[j]	X																	
IGRA tuberculosis test	X															X		
Tuberculosis questionnaire	X	X						X			X			X			X	X
PASI	X	X	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	X	X	
Blood sample for bimekizumab/secukinumab plasma concentrations[k]		X	X	X		X	X	X	X	X	X			X			X	X
Blood sample for anti-bimekizumab antibodies[k]		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	X	X	
DLQI		X				X	X	X	X				X				X	
Patient Symptoms (itch, pain, and scaling)		X				X	X	X	X				X				X	
PHQ-9	X	X				X	X	X	X	X	X	X	X	X	X	X	X	
scalp IGA[l]		X	X[l]	X[l]		X[l]	X[l]	X[l]	X[l]				X[l]				X[l]	
mNAPSI[m]		X							X[m]				X[m]				X[m]	
pp-IGA[n]		X							X[n]				X[n]				X[n]	

Table 5-1: Schedule of study assessments

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Patient Global Assessment of psoriasis		X				X	X	X	X				X				X	
PASE		X															X	
PGADA		X							X[o]				X[o]				X[o]	
WPAI-SHP V2.0		X							X				X				X	
EQ-5D-3L		X				X			X				X				X	
Concomitant medication	X	X	X	X	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	X	X	X	X
Randomization		X							X									
IRT[p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IMP administration[q]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic Case Report Form; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=European Quality-of-Life 5-Dimensions 3-Level; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=Modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; 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; PsA=psoriatic arthritis; scalp IGA=scalp-specific Investigator's Global Assessment; SFU=Safety Follow-Up; TB=tuberculosis; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Table 5-1: Schedule of study assessments

Protocol activity / Visit[a]/ Week	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	

[a] Visit windows of ±3 days from the first dose from the Week 1 visit to the Week 24 visit. Visit windows of ±7 days from Week 28 through Week 48/PEOT. The SFU Visit window is ±7 days relative to the scheduled visit date.
[b] 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] Ensure no significant changes in medical history.
[e] The physical examination will be performed as per Section 12.3.5.
[f] Vital signs (blood pressures, 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 the Screening. Urine pregnancy testing will be performed at all other visits.
[h] Subjects who have evidence of or test positive for hepatitis B by any of the following criteria: 1) positive for hepatitis B surface antigen; 2) positive for anti-hepatitis B core antibody are excluded. A positive test for HCV is defined as: 1) positive for hepatitis C antibody, and 2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction) are also excluded. Subjects will also be tested for anti-hepatitis B surface antibody.
[i] The HIV test results will not be recorded in the eCRF.
[j] Screening chest x-ray must occur within 3 months prior to Screening Visit.
[k] All blood samples taken prior to dosing.
[l] The scalp IGA will be assessed only for those subjects with scalp involvement (scalp IGA score >0) at Baseline.
[m] The mNAPSI will be assessed only in subjects with nail involvement (mNAPSI score >0) at Baseline.
[n] The pp-IGA will be assessed only in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline.
[o] The PGADA is assessed for all subjects at Baseline. At all subsequent visits, the PGADA is only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).
[p] IMP administration is based on randomization.
[q] The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the end of the study, the dosing window is ±7 days relative to the scheduled dosing visit.

Has been changed to:

The schedule of study assessments is presented in Table 5-1 **for the Screening and double-blind Treatment Periods, and in Table 5-2 for the OLE Period**. At each visit, all study assessments should be performed prior to administration of IMP.

Table 5-1: Schedule of study assessments, Screening and double-blind Treatment Periods

Protocol activity \ Visit[a]/ Week	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Informed consent	X																	
Inclusion/exclusion	X	X[c]																
Urine drug screen	X																	
Demographic data	X																	
Psoriasis history	X																	
eC-SSRS	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Significant past medical history and concomitant diseases	X	X[d]																
Physical exam[c, e]	X							X			X			X			X	X
Height		X																
Body weight		X							X		X			X			X	
Vital signs[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology and biochemistry	X	X	X	X		X	X	X	X		X		X		X		X	X
Urinalysis	X	X							X		X		X		X		X	X
ECG	X								X				X				X	
Pregnancy testing[g]	X	X				X	X	X	X	X	X	X	X	X	X	X	X	X
Hepatitis B and C testing[h]	X																	
HIV testing[i]	X																	
Chest x-ray[j]	X																	
IGRA tuberculosis test	X															X		

Table 5-1: Schedule of study assessments, Screening and double-blind Treatment Periods

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
Tuberculosis questionnaire	X	X						X			X			X			X	X
PASI	X	X	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	X	X	
Blood sample for bimekizumab/secukinumab plasma concentrations[k]		X	X	X		X	X	X	X	X	X			X			X	X
Blood sample for anti-bimekizumab antibodies[k]		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	X	X	
DLQI		X				X	X	X	X				X				X	
Patient Symptoms (itch, pain, and scaling)		X				X	X	X	X				X				X	
PHQ-9	X	X				X	X	X	X	X	X	X	X	X	X	X	X	
scalp IGA[l]		X	X[l]	X[l]		X[l]	X[l]	X[l]	X[l]				X[l]				X[l]	
mNAPSI[m]		X							X[m]				X[m]				X[m]	
pp-IGA[n]		X							X[n]				X[n]				X[n]	
Patient Global Assessment of psoriasis		X				X	X	X	X				X				X	
PASE		X															X	
PGADA		X							X[o]				X[o]				X[o]	
WPAI-SHP V2.0		X							X				X				X	

Table 5-1: Schedule of study assessments, Screening and double-blind Treatment Periods

Visit[a]/ Week / Protocol activity	Screening	Treatment Period																SFU[b]
		Baseline (first	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	
EQ-5D-3L		X				X			X				X				X	
Concomitant medication	X	X	X	X	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	X	X	X	X
Randomization		X							X									
IRT[p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IMP administration[q]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic Case Report Form; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=European Quality-of-Life 5-Dimensions 3-Level; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=Modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; 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; PsA=psoriatic arthritis; scalp IGA=scalp-specific Investigator's Global Assessment; SFU=Safety Follow-Up; TB=tuberculosis; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Table 5-1: Schedule of study assessments, Screening and double-blind Treatment Periods

Protocol activity \ Visit[a]/ Week	Screening	Treatment Period																SFU[b]
		Baseline (first dose)	1	2	3	4	8	12	16	20	24	28	32	36	40	44	48/ PEOT	

[a] Visit windows of ±3 days from the first dose from the Week 1 visit to the Week 24 visit. Visit windows of ±7 days from Week 28 through Week 48/PEOT. The SFU Visit window is ±7 days relative to the scheduled visit date.
[b] The SFU Visit will occur 20 weeks after the final **dose if subject does not enroll in the OLE Period**.
[c] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.
[d] Ensure no significant changes in medical history.
[e] The physical examination will be performed as per Section 12.3.5.
[f] Vital signs (blood pressures, 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 the Screening. Urine pregnancy testing will be performed at all other visits.
[h] Subjects who have evidence of or test positive for hepatitis B by any of the following criteria: 1) positive for hepatitis B surface antigen; 2) positive for anti-hepatitis B core antibody are excluded. A positive test for HCV is defined as: 1) positive for hepatitis C antibody, and 2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction) are also excluded. Subjects will also be tested for anti-hepatitis B surface antibody.
[i] The HIV test results will not be recorded in the eCRF.
[j] Screening chest x-ray must occur within 3 months prior to Screening Visit.
[k] All blood samples taken prior to dosing.
[l] The scalp IGA will be assessed only for those subjects with scalp involvement (scalp IGA score >0) at Baseline.
[m] The mNAPSI will be assessed only in subjects with nail involvement (mNAPSI score >0) at Baseline.
[n] The pp-IGA will be assessed only in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline.
[o] The PGADA is assessed for all subjects at Baseline. At all subsequent visits, the PGADA is only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).
[p] IMP administration is based on randomization.
[q] The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through ~~**the end of the study**~~**Week 48**, the dosing window is ±7 days relative to the scheduled dosing visit.

Table 5-2: Schedule of study assessments, OLE Period

Visit[a]/ Week / Protocol activity	48 (1st OLE dose)	Year 2												Year 3												SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT	
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C
Informed consent	X																									
Eligibility[c]	X																									
eC-SSRS		X	X		X		X			X			X			X			X			X			X	X
Physical exam[d,e]					X		X			X			X			X			X			X			X	X
Body weight													X												X	
Vital signs[f]		X	X		X		X			X			X			X			X			X			X	X
Hematology and biochemistry		X	X		X		X			X			X			X			X			X			X	X
Urinalysis					X		X			X			X			X			X			X			X	X
ECG													X												X	
Pregnancy testing (urine)[h]		X	X		X		X			X			X			X			X			X			X	X
IGRA tuberculosis test													X												X	
Tuberculosis questionnaire			X		X		X			X			X			X			X			X			X	X
PASI		X	X		X		X			X			X			X			X			X			X	
Percentage of BSA		X	X		X		X			X			X			X			X			X			X	
Blood sample for bimekizumab plasma concentrations[h]							X						X						X						X	X
Blood sample for anti-bimekizumab antibodies[h]							X						X						X						X	X
IGA		X	X		X		X			X			X			X			X			X			X	
DLQI							X						X						X						X	
Patient Symptoms (itch, pain, and scaling)			X		X		X			X			X			X			X			X			X	
PHQ-9		X	X		X		X			X			X			X			X			X			X	
scalp IGA[i]							X						X						X						X	
mNAPSI[j]							X						X						X						X	

Table 5-2: Schedule of study assessments, OLE Period

Protocol activity \ Visit[a]/ Week	48 (1st OLE dose)	Year 2												Year 3												SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT	
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C
pp-IGA[k]							X						X						X						X	
EQ-5D-3L							X						X						X						X	
Patient Global Assessment of PSO																										
PASE													X												X	
PGADA[l]													X												X	
WPAI-SHP V2.0													X												X	
Concomitant medication		X	X		X		X			X			X			X			X			X			X	X
Adverse events		X	X		X		X			X			X			X			X			X			X	X
Randomization	X																									
IRT[m]	X	X	X		X		X			X			X			X			X			X			X	X
IMP administration – Q4W [n, o]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
IMP administration – Q8W [n, o]	X		X		X		X		X		X		X		X		X		X		X		X			

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic Case Report Form; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=European Quality-of-Life 5-Dimensions 3-Level; H=home; HCV=hepatitis C virus; HIV=human immunodeficiency virus; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=Modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; 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; PsA=psoriatic arthritis; scalp IGA=scalp-specific Investigator's Global Assessment; SFU=Safety Follow-Up; TB=tuberculosis; WPAI SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from Week 48 through Week 72. Visit windows of ±14 days from Week 76 through Week 144. The SFU Visit window is ±7 days relative to the scheduled visit date.

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

[c] Criteria for OLE Period, Section 6.3.

[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 12.3.5.

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

Table 5-2: Schedule of study assessments, OLE Period

Visit[a]/ Week / Protocol activity	48 (1st OLE dose)	Year 2												Year 3												SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT	
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C

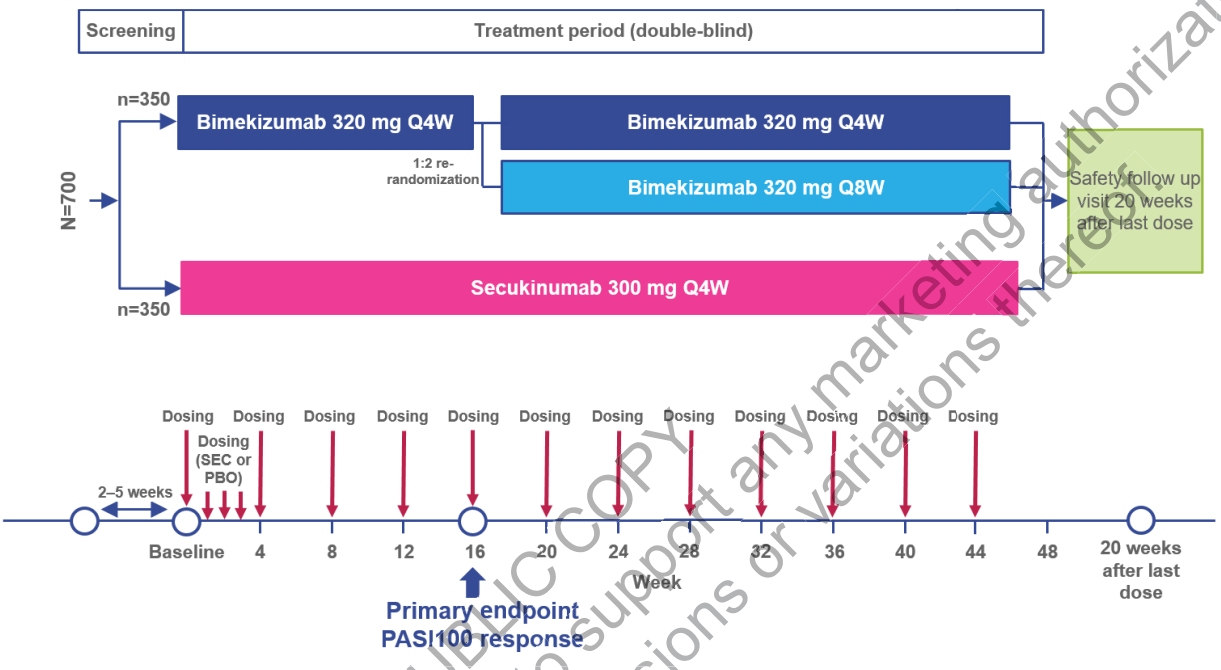
[g] Pregnancy testing will consist of urine pregnancy testing at all visits.
[h] All blood samples taken prior to dosing.
[i] The scalp IGA will be assessed only for those subjects with scalp involvement (scalp IGA score >0) at Baseline.
[j] The mNAPSI will be assessed only in subjects with nail involvement (mNAPSI score >0) at Baseline.
[k] The pp-IGA will be assessed only in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline.
[l] The PGADA is assessed only for subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47).
[m] IMP administration is based on randomization.
[n] From Week 48 through Week 72, the dosing window is ±7 days relative to the scheduled dosing visit. From Week 76 through the Week 144/PEOT visit, the dosing window is ±14 days relative to the scheduled dosing visit.
[o] 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 #10

Section 5.7 Schematic diagram:

The study schematic diagram for PS0015 is presented in Figure 5-1.

Figure 5-1: Schematic diagram

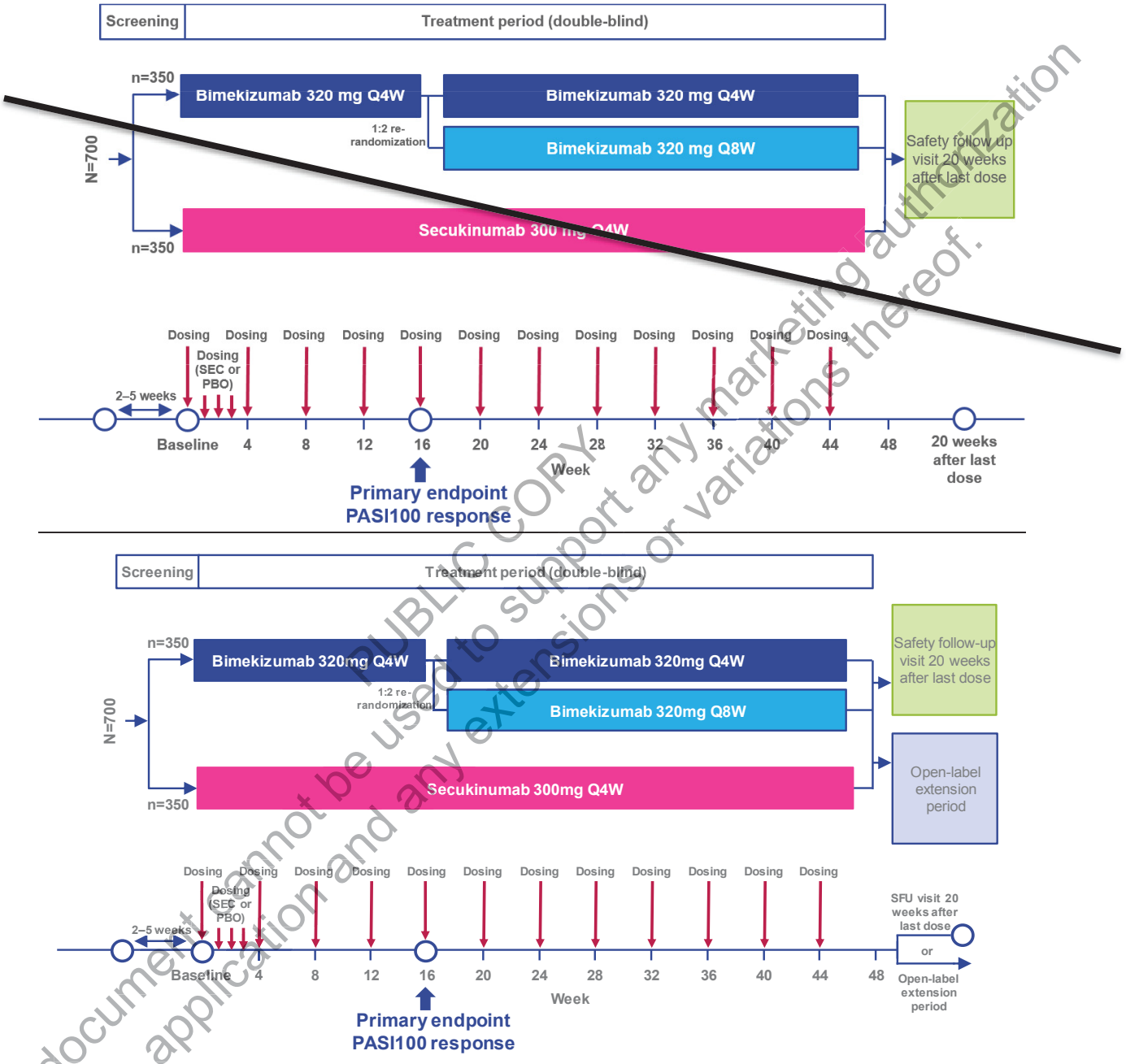


IGA=Investigator's Global Assessment; IMP=investigational medicinal product; PASI100=Psoriasis Area Severity Index complete response; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks; SEC=secukinumab
Note: At Week 28 and all following visits, subjects on continuous treatment for at least 12 weeks with a persistent IGA score ≥3 over at least a 4-week period are defined as nonresponders and should discontinue IMP.

Has been changed to:

The study schematic diagram for PS0015 **from Screening through Week 48** is presented in Figure 5-1**, and from Week 48 through Week 144 is presented in Figure 5-2.**

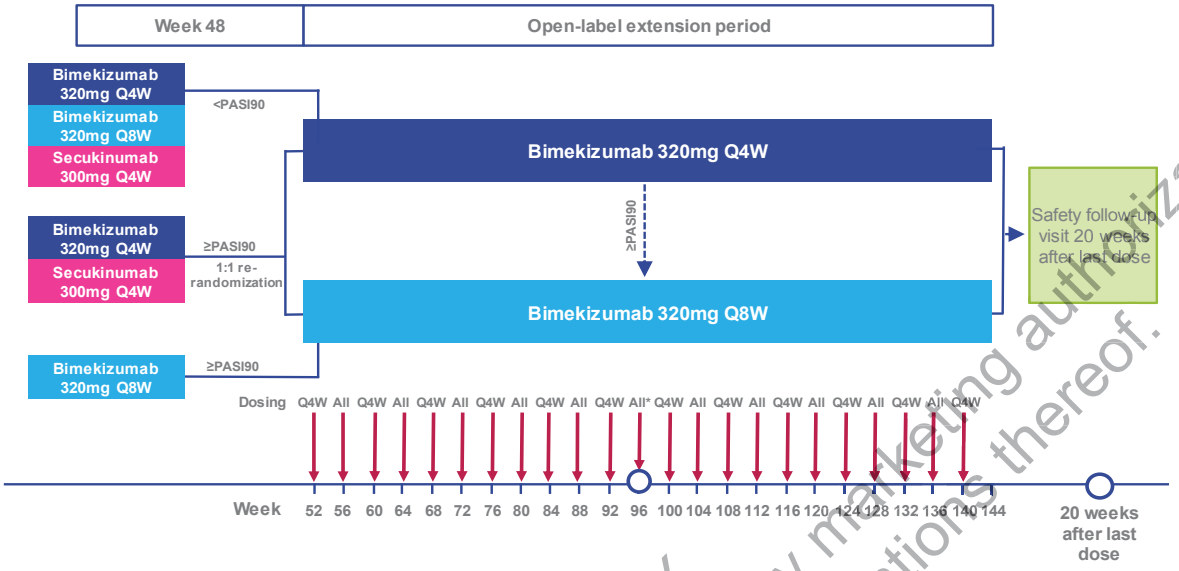
Figure 5-1: Schematic diagram, Screening and double-blind Treatment Period (through Week 48)



IGA=Investigator's Global Assessment; IMP=investigational medicinal product; PASI100=Psoriasis Area Severity Index complete response; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks; SEC=secukinumab

Note: At Week 28 and all following visits, subjects on continuous treatment 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.

Figure 5-2: Schematic diagram, OLE Period (Week 48 through Week 144)



Q4W=every 4 weeks; Q8W=every 8 weeks; PASI=Psoriasis Area Severity Index; PASI90=90% improvement in the PASI score

***At Week 96, 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 judgment, the Investigator decides differently.**

Change #11

Section 5.8.1 Study design:

The following text was added:

The addition of the OLE Period will allow collection of long-term efficacy and safety data from eligible subjects on open-label bimekizumab for an additional 96 weeks.

Change #12

The following section was added:

Section 6.3 Eligibility for the OLE Period:

Prior to entering the OLE Period, subjects on double-blind study treatment must complete all of the Week 48 visit assessments. Prior to initiating the OLE Period assessments, all subjects will be asked to read and sign a separate ICF. To be eligible to participate in the OLE Period of this study, the subject must have completed the double-blind Treatment Period without meeting any withdrawal criteria and have been compliant with the ongoing clinical study requirements.

Change #13

Section 6.4 Withdrawal criteria:

8. At Week 28 and all following visits, subjects on continuous treatment 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.

Has been changed to:

8a. At Week 28 and all following visits **up to Week 48,** subjects on continuous treatment 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.

Change #14

Section 7.2 Treatments to be administered, from 4th paragraph to end:

The dosing scheme is depicted in Table 7-1.

Table 7-1: Dosing scheme, double-blind Treatment Period

Week Dose Assignment	Baseline (first dose)	1	2	3	4	8	12	16[a]	20	24	28	32	36	40	44
Bimekizumab 320mg	●●	○○	○○	○○	●●	●●	●●	Q4W ●●	●●	●●	●●	●●	●●	●●	●●
								Q8W ●●	○○	●●	○○	●●	○○	●●	○○
Secukinumab 300mg	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲

Q4W=every 4 weeks; Q8W=every 8 weeks

Notes: A bimekizumab 160mg injection is depicted by a black circle (●). A placebo injection is depicted by a white circle (○). A secukinumab 150mg injection is depicted by a black triangle (▲).

[a] Subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

Has been changed to:

The dosing scheme **for Baseline through Week 44** is depicted in Table 7-1. **The dosing scheme from Week 48 through Week 140 is depicted in Table 7-2.**

Table 7-1: Dosing scheme, double-blind Treatment Period

Week Dose Assignment	Baseline (first dose)	1	2	3	4	8	12	16[a]	20	24	28	32	36	40	44
Bimekizumab 320mg	●●	○○	○○	○○	●●	●●	●●	Q4W ●●	●●	●●	●●	●●	●●	●●	●●
								Q8W ●●	○○	●●	○○	●●	○○	●●	○○
Secukinumab 300mg	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲	▲▲

Q4W=every 4 weeks; Q8W=every 8 weeks
Notes: A bimekizumab 160mg injection is depicted by a black circle (●). A placebo injection is depicted by a white circle (○). A secukinumab 150mg injection is depicted by a black triangle (▲).
[a] Subjects in the bimekizumab 320mg treatment arm will be re-randomized 1:2 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.

Table 7-2: Dosing scheme, OLE Period

Week	48 (1st OLE)	Year 2												Year 3										
Dose Assignment		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140
Bimekizumab 320mg Q4W	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Bimekizumab 320mg Q8W	●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●	

Q4W=every 4 weeks; OLE=Open-Label Extension; Q8W=every 8 weeks
Notes: A bimekizumab 160mg injection is depicted by a black circle (●).

During the OLE Period, IMP administration on weeks with no scheduled clinic visit should primarily be performed by subjects at home. Self-injection training will be provided to the subject/caregiver by qualified site personnel at Week 40 and Week 44. At Week 48 and subsequent clinic visits, the subject/caregiver will perform self-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 # 15

Section 7.5 Handling and storage requirements:

The following text has been added:

In addition, the Investigator (or designee) will instruct the subject on how to handle the IMP during 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 supplied. All efforts should be made to follow the treatment scheme as per protocol.

Change #16

Section 7.7 Procedures for monitoring subject compliance:

Investigational medicinal product 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:

~~**Investigational**~~**During the double-blind Treatment Period (up to Week 44), investigational** medicinal product 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 60, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. Dates, body 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 with the subject. 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.

Change #17

Section 7.8.1.1 Topical medications, 2nd paragraph:

Mild and low potency topical steroids will be permitted for use limited to the face, axilla, and/or genitalia, as needed. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.

Has been changed to:

~~**Mild**~~**In the double-blind Treatment Period, mild** and low potency topical steroids will be permitted for use limited to the face, axilla, and/or genitalia, as needed. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.

In the OLE Period, the medications listed as permitted for the double-blind Treatment Period will be allowed. In addition, topical steroids and vitamin D analog ointment will be permitted for use, as needed.

Change #18

Section 7.9 Blinding, first paragraph, 3rd paragraph, and last paragraph:

Due to differences in presentation between the bimekizumab and secukinumab, special precautions will be taken to ensure study blinding and study sites will have blinded and unblinded personnel.

During the study the Sponsor will provide blinded and unblinded site monitors for the purposes of verifying safety, efficacy, and drug administration and documentation records. Unblinded study site personnel need to be available in order to resolve queries. Study monitors and study site personnel, blinded to treatment assignment, will not discuss or have access to any drug related information.

Has been changed to:

Due to differences in presentation between the bimekizumab and secukinumab, special precautions will be taken to ensure study blinding **during the double-blind Treatment Period** and study sites will have blinded and unblinded personnel.

During the **double-blind Treatment Period of the** study**,** the Sponsor will provide blinded and unblinded site monitors for the purposes of verifying safety, efficacy, and drug administration and documentation records. Unblinded study site personnel need to be available in order to

resolve queries. Study monitors and study site personnel, blinded to treatment assignment, will not discuss or have access to any drug related information.

For subjects participating in the OLE Period, there will be no blinding and the blinding procedures described above will no longer apply.

Change #19

Section 7.10 Randomization and numbering of subjects, last paragraph:

Subject numbers and kit numbers will be tracked via the IRT.

Has been changed to:

In the OLE Period, subjects:

- **Who received bimekizumab 320mg Q4W and achieved PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**
- **Who received bimekizumab 320mg Q4W and who did not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Who received bimekizumab 320mg Q8W and who did not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Who received bimekizumab 320mg Q8W and who achieved PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q8W.**
- **Who received secukinumab and who did not achieve PASI90 at Week 48 of the double-blind Treatment Period will receive bimekizumab 320mg Q4W.**
- **Who received secukinumab and who achieved PASI90 at Week 48 of the double-blind Treatment Period will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.**

At Week 96, 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 judgment, the Investigator decides differently.

Subject numbers and kit numbers will be tracked via the IRT **during the double-blind Treatment Period and the OLE Period**.

Change #20

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.

- Visit windows of ±3 days on either side of the scheduled dosing are permitted up to and including Week 24; however, the Investigator should try to keep the subjects on the original dosing schedule. From the Week 28 Visit through the Week 48/PEOT Visit, 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 visit window is relative

to Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside the visit window must be discussed with the Medical Monitor.

- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the end of the study the dosing window is ±7 days relative to the scheduled dosing visit.

Has been changed to:

Table 5-~~1 (Schedule of study assessments) provides~~**and Table 5-2 provide** a general overview of study assessments **during the double-blind Treatment Period and the OLE Period, respectively.** A list of procedures to be completed at each visit is described below.

- Visit windows of ±3 days on either side of the scheduled dosing are permitted up to and including Week 24; however, the Investigator should try to keep the subjects on the original dosing schedule. From the Week 28 Visit through the Week ~~48/PEOT~~72 Visit, 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. **From the Week 76 Visit through the Week 144/PEOT Visit, 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 visit window is relative to Baseline and applicable for all subsequent visits. Changes to the dosing schedule outside the visit window must be discussed with the Medical Monitor.
- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the ~~end of~~**through** the ~~study~~**Week 72 Visit,** the dosing window is ±7 days relative to the scheduled dosing visit. **From Week 76 Visit through the Week 144/PEOT, the dosing window is ±14 days relative to the scheduled dosing visit.**

Change #21

The following sections have been added:

Section 8.3 OLE Period

Section 8.3.1 Week 48 Visit (±7 days relative to Baseline)

The following procedures/assessments will be performed/recorded after completion of assessments listed for Week 48 (Section 8.2.13) and prior to administration of IMP:

- **Sign a separate ICF for the OLE Period**
- **Inclusion/exclusion: Confirm that subject completed the double-blind Treatment Period without meeting any withdrawal criteria and has been compliant with the ongoing clinical study requirements**
- **Upon confirmation of subject's eligibility, randomization will occur**
- **Contact IRT**

After completion of the above-mentioned procedures, IMP administration will occur, preferably by self-injection under supervision of the site personnel.

Section 8.3.2 Week 52 Visit (±7 days relative to Baseline)

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

- **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 prior to dosing:**
  - **Hematology and biochemistry**
  - **Urine pregnancy test**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **PHQ-9**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

After completion of the above-mentioned procedures, administration of IMP will occur for subjects on bimekizumab 320mg Q4W dosing only, preferably by self-injection under supervision of the site personnel.

Section 8.3.3 Week 56 Visit (±7 days relative to Baseline)

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

- **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 prior to dosing:**
  - **Hematology and biochemistry**
  - **Urine pregnancy test**
- **Tuberculosis questionnaire**
- **PASI**
- **Percentage of BSA**

- **IGA**
- **Patient symptoms (itch, pain, and scaling)**
- **PHQ-9**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

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.

Section 8.3.4 Self-injection at home (Weeks 60, 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 on the following weeks: Weeks 60, 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 on the following weeks: Weeks 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 8.3.5 Week 64, Week 84, Week 108, Week 132 Visits (±14 days relative to Baseline)

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

- **Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB**
- **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 prior to dosing:**
  - **Hematology and biochemistry**
  - **Urinalysis**

  - **Urine pregnancy test**
- **Tuberculosis questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **Patient symptoms (itch, pain, and scaling)**
- **PHQ-9**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

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

- **at each of these visits for subjects on bimekizumab 320mg Q4W dosing, preferably by self-injection under supervision of the site personnel**
- **at Week 64 for subjects on bimekizumab 320mg Q8W dosing, 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.

Section 8.3.6 Week 72 and Week 120 Visits (±14 days relative to Baseline)

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

- **Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB**
- **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 prior to dosing:**
  - **Hematology and biochemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**
- **Tuberculosis questionnaire**
- **PASI**

- **Percentage of BSA**
- **IGA**
- **DLQI**
- **Patient symptoms (itch, pain, and scaling)**
- **PHQ-9**
- **scalp IGA for subjects with scalp involvement at Baseline**
- **mNAPSI for subjects with nail involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **EQ-5D-3L**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**
- **Contact IRT**
- **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.**

Section 8.3.7 Week 96 Visit (±14 days relative to Baseline)

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

- **Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB**
- **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 tests should be obtained prior to dosing:**
  - **Hematology and biochemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **IGRA tuberculosis test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**

- **Record 12-lead ECG**
- **Tuberculosis questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **DLQI**
- **Patient symptoms (itch, pain, and scaling)**
- **PHQ-9**
- **scalp IGA for subjects with scalp involvement at Baseline**
- **mNAPSI for subjects with nail involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **PASE**
- **PGADA (only for subjects with PsA)**
- **WPAI-SHP V2.0**
- **EQ-5D-3L**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**
- **Contact IRT**

At week 96, 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.

Section 8.3.8 Week 144 Visit (±14 days relative to Baseline)

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

- **Physical exam including evaluation of signs and symptoms of active TB and risk for exposure to TB**
- **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 tests should be obtained prior to dosing:**

  - **Hematology and biochemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **IGRA tuberculosis test**
  - **Bimekizumab plasma concentrations**
  - **Anti-bimekizumab antibodies**
- **Record 12-lead ECG**
- **Tuberculosis questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **DLQI**
- **Patient symptoms (itch, pain, and scaling)**
- **PHQ-9**
- **scalp IGA for subjects with scalp involvement at Baseline**
- **mNAPSI for subjects with nail involvement at Baseline**
- **pp-IGA for subjects with palmoplantar involvement at Baseline**
- **PASE**
- **PGADA (only for subjects with PsA)**
- **WPAI-SHP V2.0**
- **EQ-5D-3L**
- **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 8.4 Premature End of Treatment Visit:

The following bullet has been added:

- **If the subject will be withdrawn from IMP prior to the Week 144 visit of the OLE Period, the subject will undergo the same assessments as the Week 144 visit (see Section 8.3.8), and will enter the SFU Period.**

Change #22

Section 8.5 Safety Follow-Up Visit (20 weeks after final dose, ±7 days)

- Bimekizumab/ secukinumab plasma concentrations

Has been changed to:

- Bimekizumab~~/~~ **(**secukinumab **for subjects not entering the OLE Period)** plasma concentrations

Change #23

Section 8.6 Unscheduled visit, 2nd paragraph:

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.

Has been changed to:

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.

Change #24

Section 12.2 Laboratory measurements, Table 12-2

Table 18–6: 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	Urine dipstick for pregnancy testing[b]

Table 18–6: Laboratory measurements

Hematology	Chemistry	Urinalysis dipstick[a]
MCH	Creatinine	
MCHC	ALP	
MCV	AST	
Platelet count	ALT	
RBC count	GGT	
WBC count	Total bilirubin	
	LDH	
	CRP	
	Lipid panel	
	NT-proBNP	
	Serum pregnancy testing[b]	

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BUN=blood urea nitrogen; CRP=C-reactive protein; GGT=gamma glutamyltransferase; LDH=lactate dehydrogenase; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; MCV=mean corpuscular volume; NT-proBNP=N-terminal pro B-type natriuretic peptide; 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] Pregnancy testing will consist of serum testing at the Screening. Urine pregnancy testing will be performed at all other visits.

Has been changed to:

Table 18–7: 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	Urine dipstick for pregnancy testing[b]
MCH	Creatinine	**Urine drug screen**
MCHC	ALP	
MCV	AST	
Platelet count	ALT	
RBC count	GGT	
WBC count	Total bilirubin	
	LDH	
	CRP[b]	
	Lipid panel	
	NT-proBNP[b]	
	Serum pregnancy testing[c]	

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BUN=blood urea nitrogen; CRP=C-reactive protein; GGT=gamma glutamyltransferase; LDH=lactate dehydrogenase; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; MCV=mean corpuscular volume; NT-proBNP=N-terminal pro B-type natriuretic peptide; 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] **Assessments of NT-proBNP and CRP will not be performed during the OLE Period.**

[c] Pregnancy testing will consist of serum testing at the Screening. Urine pregnancy testing will be performed at all other visits.

Change #25

Section 12.2.1 Evaluation of PDILI, Table 12-3:

Table 12-3: 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 12.2.1.3); recommended to occur at the site with HCP.	Monitoring of liver chemistry values at least twice per week until values normalize, stabilize, or return to within baseline values. [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 12.2.1.2). IMP discontinuation required if any of the following occur: Subject cannot comply with monitoring schedule.	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 12.2.1.3).	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

Table 12-3: 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**
				Liver chemistry values continue to increase Liver chemistry values remain ≥5xULN (and ≥2x baseline) after 4 weeks of monitoring without evidence of resolution		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. 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 12.2.1.1. 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 12-3: 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 12.2.1.3); recommended to occur at the site with HCP.	Monitoring of liver chemistry values at least twice per week until values normalize, stabilize, or return to within baseline values. [d]
≥3xULN	NA	Yes				
≥8xULN	NA	NA	~~**Need for hepatology consult to be discussed (required if ALT or AST ≥8xULN).**~~ **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 ≥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 12.2.1.2). IMP discontinuation required if any of the following occur: Subject cannot comply with monitoring schedule.	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 12.2.1.3).	Monitoring of liver chemistry values at least twice per week for 2 weeks.[d] • Immediate IMP discontinuation required if liver

Table 12-3: 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**
				Liver chemistry values continue to increase Liver chemistry values remain ≥5xULN ~~**(and ≥2x baseline)**~~ after 4 weeks of monitoring without evidence of resolution		chemistry values continue to increase. After 2 weeks of monitoring liver chemistry values: • ALT or AST remains ≥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**~~**Baseline** values. If ALT or AST remains ≥5xULN after second re-test, immediate, permanent IMP discontinuation required. Continue to monitor until values normalize, stabilize, or return to within baseline values.[d]

Table 12-3: 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**

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 12.2.1.1. 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 12.2.1.2.1**

Change #26

Section 12.2.1.2.1 IMP restart/rechallenge:

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

- The results of additional testing and monitoring described in Section 12.2.1.3 and Section 12.2.1.1 confirm a nondrug-related cause for the abnormal hepatic laboratory parameters and any associated symptoms (ie, a subsequent alternative diagnosis fully explains the hepatic findings).
- 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, DMC, and a hepatologist.
- 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 6.4.1 and Table 12-3), 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 in Section 12.2.1.3 and Section 12.2.1.4 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~~**During the double-blind Treatment Period, the** rechallenge is approved by the UCB responsible physician, DMC, and a hepatologist.
- **During the OLE Period, the rechallenge is approved by the UCB responsible physician.**
- Subject agrees to the Investigator-recommended monitoring plan.

Change #27

Section 12.4.4 Data Monitoring and Adjudication Committees

The DMC membership includes experienced clinicians and a statistician, all of whom have expertise in clinical trials. Cardiovascular and Neuropsychiatric Adjudication Committees will

also periodically review data from this trial. Both Data Monitoring and Adjudication Committee members may not participate in the study as principal or co-Investigators, or as study subject care physicians. The duration of membership for the committees will be inclusive of planned analyses for PS0015. Detailed role, scope, responsibilities, and complete procedures, as well as the identity of members, are described in the separate committee charters.

Has been changed to:

The DMC membership includes experienced clinicians and a statistician, all of whom have expertise in clinical trials. Cardiovascular and Neuropsychiatric Adjudication Committees will also periodically review data from this trial. Both Data Monitoring and Adjudication Committee members may not participate in the study as principal or co-Investigators, or as study subject care physicians. The duration of membership for the committees will be inclusive of **~~planned analyses~~data through the last subject completing the Week 48 Visit** for PS0015. Detailed role, scope, responsibilities, and complete procedures, as well as the identity of members, are described in the separate committee charters.

Change #28

Section 14.1 Definition of analysis sets:

The following text has been added:

The Open-label Set (OLS) will consist of all subjects that receive at least 1 dose of IMP at Week 48 or later in the OLE Period (including the Week 48 dose).

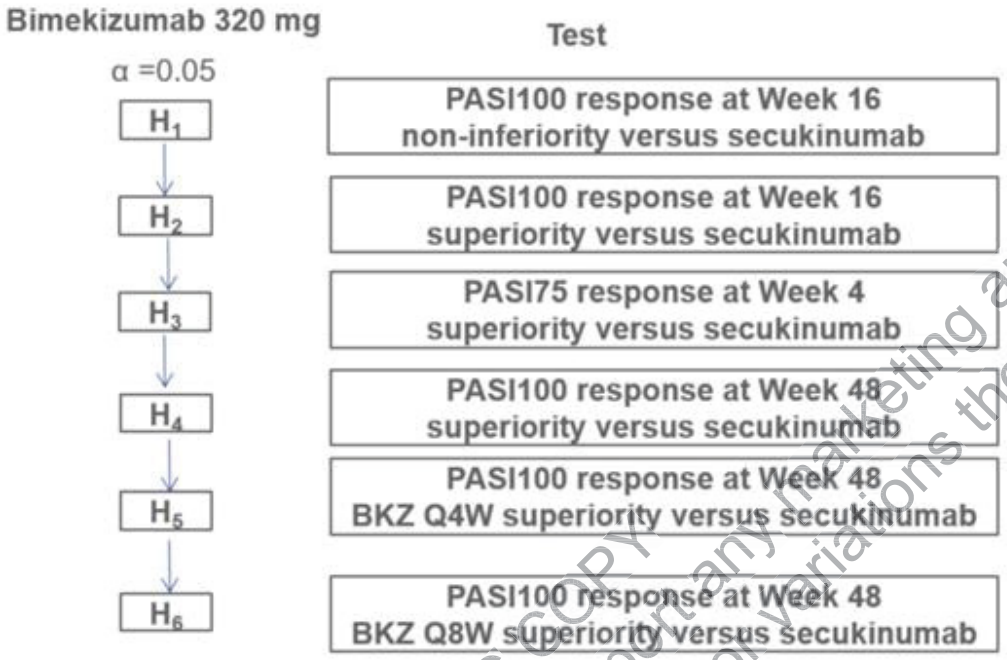
Change #29

Section 14.2 General statistical considerations, second and fifth paragraphs and title of figure 14-1:

The statistical analysis of the primary efficacy variable and secondary efficacy variables will account for multiplicity and control the familywise Type I error rate at a 2-sided alpha level of 0.05 by using a fixed sequence testing procedure.

The hypotheses associated with the subsequent tests are for secondary efficacy endpoints and are based on testing for superiority relative to secukinumab. Figure 14-1 presents the details on this procedure.

Figure 14 1: Hypotheses testing of secondary efficacy endpoints



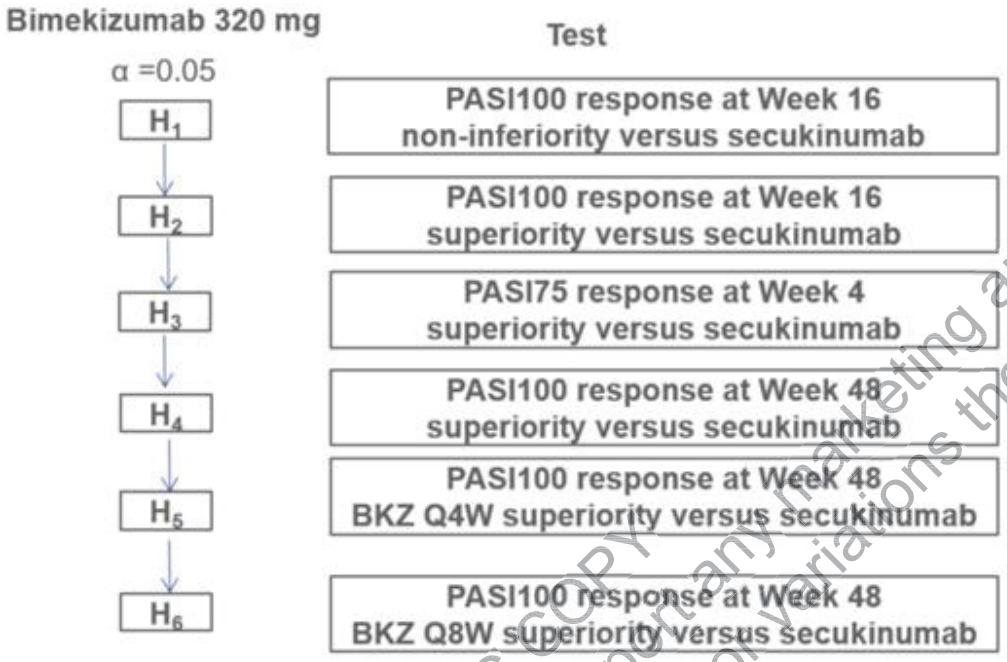
BKZ=bimekizumab; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Tests for H_1, H_2, H_3, and H_4 are based on all subjects initially randomized to bimekizumab compared to secukinumab. For H_5 and H_6, testing is based on the subjects re-randomized at Week 16 to bimekizumab 320mg Q4W, and bimekizumab 320mg Q8W, respectively, compared to secukinumab.

Has been changed to:

The statistical analysis of the primary efficacy variable and **selected** secondary efficacy variables will account for multiplicity and control the familywise Type I error rate at a 2-sided alpha level of 0.05 by using a fixed sequence testing procedure.

The hypotheses associated with the subsequent tests are for **selected** secondary efficacy endpoints and are based on testing for superiority relative to secukinumab. Figure 14-1 presents the details on this procedure.

~~Figure 14-1: Hypotheses~~Hypothesis testing ~~of secondary efficacy endpoints~~



BKZ=bimekizumab; PASI=Psoriasis Area Severity Index; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: Tests for H_1, H_2, H_3, and H_4 are based on all subjects initially randomized to bimekizumab compared to secukinumab. For H_5 and H_6, testing is based on the subjects re-randomized at Week 16 to bimekizumab 320mg Q4W, and bimekizumab 320mg Q8W, respectively, compared to secukinumab.

Change #30

Section 14.3.2.2 Analysis of the other efficacy variables, third paragraph through end of section:

In general, data will be summarized by visit through Week 48. All summaries of data up to Week 16 will be based on the RS for the 2 randomized treatment groups (bimekizumab and secukinumab). For visits after Week 16, by-visit summaries will be prepared for the following 3 groups of subjects:

4. Subjects in the MS summarized by the 3 maintenance treatment groups (bimekizumab 320mg Q4W, bimekizumab 320mg Q8W, and secukinumab). Note that while the MS is primarily defined for the evaluation of data after Week 16, these summary tables will include data at all visits (Baseline to Week 48) to provide a comprehensive summary of subjects by maintenance treatment group for the MS.
5. A subset of Group 1 above. Specifically, this will include only those subjects who are responders at Week 16 for the variable being summarized. This will provide an assessment of how efficacy is maintained among Week 16 responders.
6. Subjects in the RS summarized by the 2 randomized treatment groups (bimekizumab and secukinumab). Data from Baseline to Week 48 will be included in these tables. This provides an intent-to-treat analysis among all randomized subjects in the study through Week 48.

All efficacy variables will be summarized in the manner described for Group 1 above. Summaries for Groups 2 and 3 will be done only for a subset of efficacy variables, namely, PASI75/90/100, IGA Clear or Almost Clear, Scalp IGA Clear or Almost Clear, pp-IGA Clear or Almost Clear, mNAPSI75/90/100, and DLQI 0/1. Further details on these analyses will be provided in the SAP.

Has been changed to:

In general, data will be summarized by visit through Week 48 **in the double-blind Treatment Period and then by visit in the OLE Period separately.** All summaries of data up to Week 16 will be based on the RS for the 2 randomized treatment groups (bimekizumab and secukinumab). For visits after Week 16 **in the double-blind Treatment Period**, by-visit summaries will be prepared for the following 3 groups of subjects:

7. Subjects in the MS summarized by the 3 maintenance treatment groups (bimekizumab 320mg Q4W, bimekizumab 320mg Q8W, and secukinumab). Note that while the MS is primarily defined for the evaluation of data after Week 16, these summary tables will include data at all visits (Baseline to Week 48) to provide a comprehensive summary of subjects by maintenance treatment group for the MS.
8. A subset of Group 1 above. Specifically, this will include only those subjects who are responders at Week 16 for the variable being summarized. This will provide an assessment of how efficacy is maintained among Week 16 responders.
9. Subjects in the RS summarized by the 2 randomized treatment groups (bimekizumab and secukinumab). Data from Baseline to Week 48 will be included in these tables. This provides an intent-to-treat analysis among all randomized subjects in the study through Week 48.

All efficacy variables **in the double-blind Treatment Period** will be summarized in the manner described for Group 1 **and 3** above. Summaries for Group**s** 2 ~~**and 3**~~ will be done only for a subset of efficacy variables, namely, PASI75/90/100, IGA Clear or Almost Clear, Scalp IGA Clear or Almost Clear, pp-IGA Clear or Almost Clear, mNAPSI75/90/100, and DLQI 0/1.

In the OLE treatment period, efficacy variables of interest generally will be summarized descriptively by the combined treatment regimen in the double-blind treatment period and re-randomized treatment in the OLE,

In general, efficacy variables will be summarized using descriptive statistics by treatment group and scheduled visit during the OLE Period based on Baseline at beginning of the study unless otherwise specified.

Further details on ~~**these**~~**the above** analyses **including analysis in the OLE Period** will be provided in the SAP.

Change #31

Section 14.4 Subgroup analyses:

Subgroup analyses will be performed on the primary and secondary efficacy variables that are part of the fixed sequence testing procedure described in Section 14.2. The following variables for subgroup analyses will be defined: age, gender, disease duration, region, weight, body mass index, prior systemic chemotherapy or phototherapy, prior biologic exposure, prior systemic

therapy of any kind, Baseline disease severity, and antibody positivity. These summaries will be based on imputed data (NRI) and will include descriptive statistics only.

Has been changed to:

Subgroup analyses will be performed on the primary and secondary efficacy variables that are part of the fixed sequence testing procedure described in Section 14.2. The following variables for subgroup analyses will be defined: age, gender, disease duration, region, weight, body mass index, prior systemic chemotherapy or phototherapy, prior biologic exposure, prior **primary failure to biologics, prior** systemic therapy of any kind, Baseline disease severity, and antibody positivity. These summaries will be based on imputed data (NRI) and will include descriptive statistics only.

Change #32

Section 14.5.1 Safety analyses, first paragraph:

Safety variables will be analyzed for all subjects in the SS. This will include all subjects who took at least one dose of study medication. Adverse events will be coded according to the Medical Dictionary for Regulatory Activities. Adverse events will be summarized descriptively by treatment group, primary system organ class, High Level Term (HLT), and PT. Additional tables will summarize AEs by intensity and relationship to IMP, AEs leading to withdrawal from the study, SAEs, and deaths. Safety topics of interest will be summarized and will be described in greater detail in the SAP.

Has been changed to:

Safety variables will be analyzed for all subjects in the SS. This will include all subjects who took at least one dose of study medication. **Selected analyses will also be presented for MS and OLS.** Adverse events will be coded according to the Medical Dictionary for Regulatory Activities. Adverse events will be summarized descriptively by treatment group, primary system organ class, High Level Term (HLT), and PT. Additional tables will summarize AEs by intensity and relationship to IMP, AEs leading to withdrawal from the study, SAEs, and deaths. Safety topics of interest will be summarized and will be described in greater detail in the SAP.

Change #33

Section 14.8 Planned interim analysis:

After the final Week 48 Visit, an interim analysis will be performed based on all data available at that time. Further details related to this interim analysis will be outlined in the SAP. A final analysis and final clinical study report will be prepared once all data (through the SFU Visit) have been collected.

Has been changed to:

~~**After the final Week 48 Visit, an**~~An interim analysis ~~**will be performed based on all data available**~~is planned ~~**at that time. Further**~~**Week 48**, details ~~**related to this interim analysis**~~**of which** will be ~~**outlined**~~**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 ~~**clinical study report**~~**CSR** will be prepared once all data (through the SFU ~~**Visit**~~**visit and including the OLE Period)** have been collected.

18.4 Protocol Amendment 3

This was a global amendment. The changes are detailed below in Amendment 3.1.

18.5 Protocol Amendment 3.1

Rationale for the amendment

The protocol has been amended for the following reasons:

- Moved subject self-injection training into the start of the OLE Period at Week 48.
- Added the description of the Patient Global Assessment of PSO, which was inadvertently deleted in global Protocol Amendment #2, back into Section 9.
- Updated the name and contact information of the Clinical Trial Biostatistician.

Global changes:

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 Corporate Drive, Raleigh, NC 27617, USA
Phone:	[redacted]
Fax:	[redacted]

Has been changed to:

Name:	[redacted]
Address:	UCB 208 Bath Road, Slough, SL1 3WE, UK
Phone:	[redacted]
Fax:	[redacted]

Change #2

Table 5–2: Schedule of study assessments, OLE Period

Table Footnote "n"

n From Week 48 through Week 72, the dosing window is ±7 days relative to the scheduled dosing visit. From Week 76 through the Week 144/PEOT visit, the dosing window is ±14 days relative to the scheduled dosing visit.

Has been changed to:

n From Week 48 through Week 72, the dosing window is ±7 days relative to the scheduled dosing visit. From Week 76 through the Week 140 Visit, the dosing window is ±14 days relative to the scheduled dosing visit.

Change #3

Section 7.2 Treatments to be administered, paragraph 5

During the OLE Period, IMP administration on weeks with no scheduled clinic visit should primarily be performed by subjects at home. Self-injection training will be provided to the subject/caregiver by qualified site personnel at Week 40 and Week 44. At Week 48 and subsequent clinic visits, the subject/caregiver will perform self-administration under the supervision of the site staff to ensure that study medication is being properly and safely injected.

Has been changed to:

During the OLE Period, IMP administration on weeks with no scheduled clinic visit should primarily be performed by subjects at home. Self-injection training will be provided to the subject/caregiver by qualified site personnel at ~~Week 40 and Week 44~~ Week 48. **Additional training may be provided by site staff at subsequent clinic visits as needed.** At Week 48 and subsequent clinic visits, the subject/caregiver will perform self-administration under the supervision of the site staff to ensure that study medication is being properly and safely injected.

Change #4

Section 7.5 Handling and storage requirements; paragraph 6

In addition, the Investigator (or designee) will instruct the subject on how to handle the IMP during 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 supplied. All efforts should be made to follow the treatment scheme as per protocol.

Has been changed to:

In addition, the Investigator (or designee) will instruct the subject/**caregiver** on how to handle the IMP during transport, and how to store the IMP following the instruction guide. Cooler bags with freezer packs will be provided to the subjects/**caregivers**. Specific attention will be put on the transport from site to home using cold bags, and the subject/**caregiver** 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 supplied. All efforts should be made to follow the treatment scheme as per protocol.

Change #5

Section 7.8.1.1 Topical medications; paragraph 3

In the OLE Period, the medications listed as permitted for the double-blind Treatment Period will be allowed. In addition, topical steroids and vitamin D analog ointment will be permitted for use, as needed.

Has been changed to:

In the OLE Period, the medications listed as permitted for the double-blind Treatment Period will be allowed. In addition, **any** topical steroids and vitamin D analog ointment will be permitted for use, as needed. **These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures**.

Change #6

Section 7.9 Blinding; paragraphs 4-7

During the double-blind Treatment Period of the study, the Sponsor will provide blinded and unblinded site monitors for the purposes of verifying safety, efficacy, and drug administration and documentation records. Unblinded study site personnel need to be available in order to resolve queries. Study monitors and study site personnel, blinded to treatment assignment, will not discuss or have access to any drug related information.

Study sites will be required to have a written blinding plan in place, signed by the Principal Investigator, which will detail the site's steps for ensuring that the double-blind nature of the study is maintained. Sites will be instructed to keep study subjects blind to the IMP as detailed in the site blinding plan.

Further details are provided in the study manual and site blinding plan.

For subjects participating in the OLE Period, there will be no blinding and the blinding procedures described above will no longer apply.

Has been changed to:

During the double-blind Treatment Period of the study, the Sponsor will provide blinded and unblinded site monitors for the purposes of verifying safety, efficacy, and drug administration and documentation records. Unblinded study site personnel need to be available in order to resolve queries. Study monitors and study site personnel, blinded to treatment assignment, will not discuss or have access to any drug related information. **This will continue at least until all subjects have completed the double-blind Treatment Period of the study.**

During the double-blind Treatment Period of the study, the Sponsor will provide blinded and unblinded site monitors for the purposes of verifying safety, efficacy, and drug administration and documentation records. Unblinded study site personnel need to be available in order to resolve queries. Study monitors and study site personnel, blinded to treatment assignment, will not discuss or have access to any drug related information.

Study sites will be required to have a written blinding plan in place, signed by the Principal Investigator, which will detail the site's steps for ensuring that the double-blind nature of the study is maintained. Sites will be instructed to keep study subjects blind to the IMP as detailed in the site blinding plan.

Further details are provided in the study manual and site blinding plan.

~~For subjects participating in the OLE Period, there will be no blinding and the blinding procedures described above will no longer apply.~~

Change #7

Section 8 STUDY PROCEDURES BY VISIT; paragraph 1, second bullet

- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the Week 72 Visit, the dosing window is ±7 days relative to the scheduled dosing visit. From the Week 76 Visit through the Week 144/PEOT, the dosing window is ±14 days relative to the scheduled dosing visit.

Has been changed to:

- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the Week 72 Visit, the dosing window is ±7 days relative to the scheduled dosing visit. From the Week 76 Visit through the **Week 140 Visit**~~Week 144/PEOT~~, the dosing window is ±14 days relative to the scheduled dosing visit.

Change #8

Section 8.3.1 Week 48 Visit (±7 days relative to Baseline); paragraph 1

The following procedures/assessments will be performed/recorded after completion of assessments listed for Week 48 (Section 8.2.13) and prior to administration of IMP:

Has been changed to:

The following procedures/assessments will be performed/recorded after completion of assessments listed for Week 48 **of the double-blind Treatment Period** (Section 8.2.13) and prior to administration of IMP:

And the following paragraph regarding subject self-injection was added:

Self-injection training will be provided to the subject/caregiver by qualified site personnel to allow self-injection to be performed at home after Week 48. Additional training may be provided by site staff at subsequent clinic visits as needed (see Section 7.2).

Change #9

Section 8.3.5 Week 64, Week 84, Week 108, Week 132 Visits (±14 days relative to Baseline)

Has been changed to:

Section 8.3.5 Week 64 <u>(±7 days relative to Baseline)</u>, Week 84, Week 108, Week 132 Visits (±14 days relative to Baseline)

Change #10

Section 8.3.6 Week 72 and Week 120 Visits (±14 days relative to Baseline)

Has been changed to:

Section 8.3.6 Week 72 <u>(±7 days relative to Baseline)</u> and Week 120 Visits (±14 days relative to Baseline)

Change #11

The following subsection was inadvertently deleted from global Protocol Amendment #2. The subsection has been added back and subsequent subsections were renumbered.

Section 9.9 Patient Global Assessment of psoriasis

The Patient Global Assessment 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 Patient Global Assessment of psoriasis will be performed at the visits specified Table 5–1.

Change #12

Section 15.1 Informed consent

The following sentence was added:

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

18.6 Protocol Amendment 4

Rationale for the amendment

The protocol has been amended for the following reasons:

- 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".
- Update the name and contact information for the Study Physician.
- Update withdrawal criterion to be valid through the entire study, not just up to Week 48.
- Moved the PHQ-9 variable from an other efficacy variable to an other safety variable
- Moved the PHQ-9 description from the assessment of efficacy section to the assessment of safety section
- Clarify duration of monitoring for the DMC and the Cardiovascular and Neuropsychiatric Adjudication Committee.

Specific changes:

Change #1

Change #1

Sponsor name on the cover page

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

Sponsor name on the title page 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 #3

Study Physician

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

Has been changed to:

Name:	[redacted]
Address:	UCB Biopharma SRL Chemin du Foriest B-1420 Braine-l'Alleud Belgium
Phone:	[redacted]
Fax:	[redacted]

Change #4

Section 4.3.1 Other efficacy variables

The following bullet has been deleted

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

Change #5

Section 4.3.2 Other safety variables

The following bullet has been added:

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

Change #6

Section 6.4 Withdrawal criteria

8a. At Week 28 and all following visits up to Week 48, subjects on continuous treatment 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.

Has been changed to:

8b. At Week 28 and all following visits, subjects on continuous treatment 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.

Change #7

Section 9.4 Patient Health Questionnaire-9

This subsection has been moved to Section 12.3.8

Change #8

Section 12.3.8 – Patient Health Questionnaire-9

A new subsection has been added (moved from Section 9.4):

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression (Kroenke et al, 2001). The PHQ-9 scores for depression range from 0 to 27, with higher scores indicating 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 Section 6.4 for PHQ-9-related withdrawal criteria.

Change #9

Section 12.4.4 Data Monitoring and Adjudication Committees

The DMC membership includes experienced clinicians and a statistician, all of whom have expertise in clinical trials. Cardiovascular and Neuropsychiatric Adjudication Committees will also periodically review data from this trial. Both Data Monitoring and Adjudication Committee members may not participate in the study as principal or co-Investigators, or as study subject care physicians. The duration of membership for the committees will be inclusive of data through the last subject completing the Week 48 Visit for PS0015. Detailed role, scope, responsibilities, and complete procedures, as well as the identity of members, are described in the separate committee charters.

Has been changed to:

The DMC membership includes experienced clinicians and a statistician, all of whom have expertise in clinical trials. Cardiovascular and Neuropsychiatric Adjudication Committees will also periodically review data from this trial. Both Data Monitoring and Adjudication Committee members may not participate in the study as principal or co-Investigators, or as study subject care physicians. **The DMC will monitor the study through the last subject completing the Week 48 and SFU visit (for subjects not participating in the OLE period). The Cardiovascular and Neuropsychiatric Adjudication Committees will monitor the study through the last subject completing the OLE and SFU Periods for PS0015.** Detailed role, scope, responsibilities, and complete procedures, as well as the identity of members, are described in the separate committee charters.

18.7 Protocol Amendment 5

This was a global amendment. The changes are detailed below in Amendment 5.1.

18.8 Protocol Amendment 5.1

Rationale for the amendment

Change the dose regimen at Week 64 (or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 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.

Add pregnancy tests every 4 weeks during the OLE Period.

Corrected the visit window for the Week 24 visit from 7 days to 3 days.

Added provision for collecting a concurrent sample for central laboratory testing if laboratory tests are performed locally.

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

Section 1, Summary; Section 5.2.3, OLE Period; Section 7.10, Randomization and numbering of subjects

At Week 96, 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 judgment, 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 64 or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed Week 64.

Change #2

Section 5.6, Schedule of study assessments

Table 5-2: Schedule of study assessments, OLE Period

Visit[a]/ Week / Protocol activity	48 (1st OLE dose)	Year 2												Year 3													SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT		
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C	
Pregnancy testing (urine)[g]		X	X		X		X			X			X			X			X			X			X	X	
IMP administration – Q4W [n, o]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			
IMP administration – Q8W [n, o]	X		X		X		X		X		X		X		X		X		X		X		X				

[g] Pregnancy testing will consist of urine pregnancy testing at all visits.

Has been changed to:

Table 5-2: Schedule of study assessments, OLE Period

Visit[a]/ Week / Protocol activity	48 (1st OLE dose)	Year 2												Year 3												SFU[b]
		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140	144/PEOT	
	C	C	C	H	C	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	H	H	C	C
Pregnancy testing (urine)[g]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IMP administration – Q4W [n, o, p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
IMP administration – Q8W [n, o]	X		X		X		X		X		X		X		X		X		X		X		X			

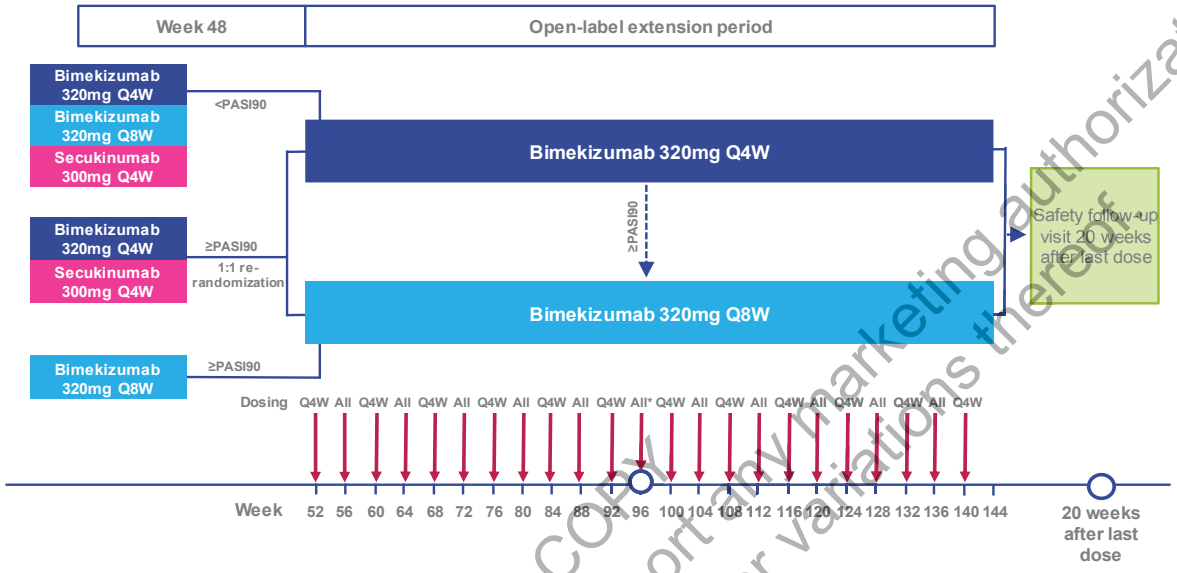
[g] Pregnancy testing will consist of urine pregnancy testing at all visits. **Home pregnancy test kits will be provided to participants for use between clinic visits.**

[p] **Q4W IMP administration only applies to those subjects who have not yet changed to Q8W at Week 64, or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 64 visit after implementation of Protocol Amendment #5.**

Change #3

Section 5.7, Schematic diagram

Figure 5-2: Schematic diagram, OLE Period (Week 48 through Week 144)

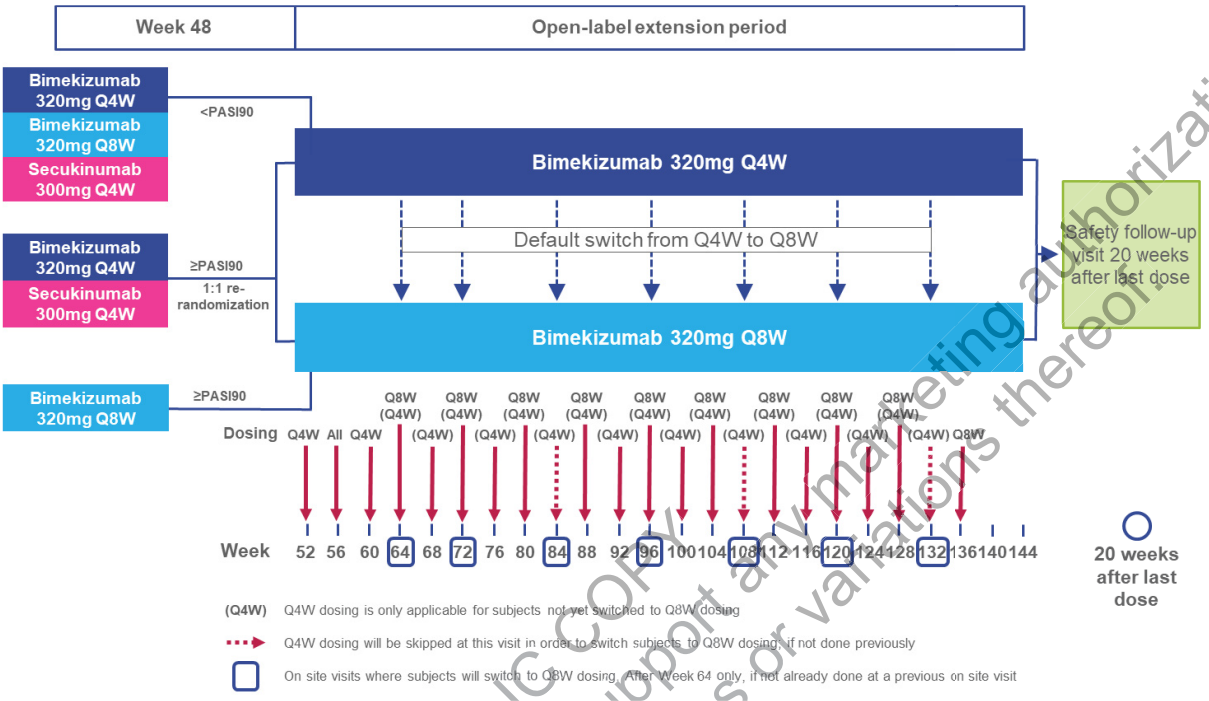


PASI=Psoriasis Area Severity Index; PASI90=90% improvement in the PASI score; Q4W=every 4 weeks; Q8W=every 8 weeks

*At Week 96, 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 judgment, the Investigator decides differently.

Has been changed to:

Figure 5-2: Schematic diagram, OLE Period (Week 48 through Week 144)



PASI=Psoriasis Area Severity Index; PASI90=90% improvement in the PASI score; Q4W=every 4 weeks; Q8W=every 8 weeks

Note: The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64, or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) if the subject has already completed the Week 64 visit prior to implementation of Protocol Amendment #5.1.

Change #4

Section 5.8.2, Dose selection

Therefore, a bimekizumab dose of 320mg Q4W through Week 16 and 320mg Q4W or Q8W thereafter was selected for this study.

Has been changed to:

Therefore, a bimekizumab dose of 320mg Q4W **through Week 16 was selected** for this study.

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 64, 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 64 visit at the time of implementation of Protocol Amendment #5.1 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 #5

Section 7.2, Treatments to be administered

The following text has been added:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64 or at the next scheduled clinic visit after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 visit.

The following table:

Table 7-2: Dosing scheme, OLE Period

Week	48 (1st OLE	Year 2												Year 3										
Dose Assignment		52	56	60	64	68	72	76	80	84	88	92	96	100	104	108	112	116	120	124	128	132	136	140
Bimekizumab 320mg Q4W	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Bimekizumab 320mg Q8W	●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●	

OLE=Open-Label Extension; Q4W=every 4 weeks; Q8W=every 8 weeks
Notes: A bimekizumab 160mg injection is depicted by a black circle (●).

Has been changed to:

Table 7-2: Dosing scheme, OLE Period

Week	48 (1st OLE)	Year 2												Year 3										
		52	56	60	64[a,b]	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**	**C**	**H**	**C**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**	**C**	**H**	**H**
Bimekizumab 320mg Q4W	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●	●●
Bimekizumab 320mg Q8W	●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●		●●	

C=clinic; H=home; OLE=Open-Label Extension; 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 64 or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 visit.**

[b] **Subjects whose dosing interval is changed to bimekizumab 320mg Q8W should be dosed at this visit and will 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 will receive kits for home administration 4 weeks later.**

Change #6

Section 7.9, Blinding

The following text has been added:

After all subjects have completed the double-blind Treatment Period of the study and the interim analysis has occurred, unblinded study site personnel can perform assessments in the OLE Period of the study.

Change #7

Section 8.2.8, Week 24 Visit (±7 days relative to Baseline)

Has been changed to:

Section 8.2.8, Week 24 Visit (±3 days relative to Baseline)

Change #8

Section 8.3.4, Self-injection at home (Weeks 60, 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 on the following weeks: Weeks 60, 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 on the following weeks: Weeks 80, 88, 104, 112, 128, and 136.

Has been changed to:

The subject's dosing interval will change from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at Week 64 or at the next scheduled clinic visit (ie, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #5.1 if the subject has already completed the Week 64 visit.

Subjects receiving bimekizumab 320mg Q4W will be given the opportunity for self-injection of bimekizumab at home on the following weeks: Weeks 60, 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 on the following weeks: Weeks 80, 88, 104, 112, 128, and 136.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. In case of a scheduled home self-injection the pregnancy test needs to be performed immediately prior to self-injecting bimekizumab at home. If the pregnancy test result is positive, IMP should not be administered and the site should be contacted.

Change #9

Section 8.3.5, Week 64 (±7 days relative to Baseline), Week 84, Week 108, Week 132 Visits (±14 days relative to Baseline)

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

Has been changed to:

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

- **At Week 64 if the subject has not completed the Week 64 visit prior to implementation of Protocol Amendment #5.1.**
- **At Week 84 if the subject has already completed the Week 72 visit prior to implementation of Protocol Amendment #5.1.**
- **At Week 108 if the subject has already completed the Week 96 visit prior to implementation of Protocol Amendment #.15.**
- **At Week 132 if the subject has already completed the Week 120 visit prior to implementation of Protocol Amendment #5.1.**

Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W will receive kits for home administration as follows:

- **Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 64 should be dosed at this visit, and will receive kits for home administration 8 weeks later (Table 7-2).**
- **Subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 84, Week 108, or Week 132 should NOT be dosed at that visit, and will receive kits for home administration 4 weeks later (Table 7-2).**

The following procedures/assessments will **be performed/recorded. If IMP is administered on site during this visit, they need to** be performed/recorded prior to administration of IMP:

Change #10

Section 8.3.5, Week 64 (±7 days relative to Baseline), Week 84, Week 108, Week 132 Visits (±14 days relative to Baseline)

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

- at each of these visits for subjects on bimekizumab 320mg Q4W dosing, preferably by self-injection under supervision of the site personnel
- at Week 64 for subjects on bimekizumab 320mg Q8W dosing, 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.

•

Has been changed to:

After completion of the above-mentioned procedures, administration of IMP will occur:

- At each of these visits for subjects on bimekizumab 320mg Q4W dosing, preferably by self-injection under supervision of the site personnel. **This only applies to those subjects who have not yet changed to Q8W after implementation of Protocol Amendment #5**.
- At **Week 64 only** for **those** subjects on bimekizumab 320mg Q8W dosing, 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. **Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2).**

Change #11

Section 8.3.6, Week 72 (±7 days relative to Baseline) and Week 120 Visits (±14 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 as follows:

- **At Week 72 if the subject has already completed the Week 64 visit prior to implementation of Protocol Amendment #5.1.**
- **At Week 120 if the subject has already completed the Week 108 visit prior to implementation of Protocol Amendment #5.1.**

As depicted in Table 7-2, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at one of these visits should be dosed at this visit and will receive kits for home administration 8 weeks later.

Change #12

Section 8.3.6, Week 72 (±7 days relative to Baseline) and Week 120 Visits (±14 days relative to Baseline)

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.

Has been changed to:

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. **Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2).**

Section 8.3.7, Week 96 Visit (±14 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 has already completed the Week 84 visit prior to implementation of Protocol Amendment #5.1. As depicted in Table 7-2, subjects whose dosing interval is being changed to bimekizumab 320mg Q8W at Week 96 should be dosed at this visit, and will receive kits for home administration 8 weeks later.

Change #13

Section 8.3.7, Week 96 Visit (±14 days relative to Baseline)

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.

Has been changed to:

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. **Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2).**

Change #14

Section 12.2, Laboratory measurements

Clinical laboratory assessments consist of serum chemistry, hematology, and urinalysis. A centralized laboratory will be used to supply all laboratory test supplies and analyze all blood and urine samples for hematology, biochemistry, and urinalysis measurements. Any unscheduled laboratory testing should also be collected using the central laboratory.

Has been changed to:

Clinical laboratory assessments consist of serum chemistry, hematology, and urinalysis. A centralized laboratory will be used to supply all laboratory test supplies and analyze all blood and urine samples for hematology, biochemistry, 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.**

Change #15

Section 12.3.2, Pregnancy testing

The following text has been added:

Subjects of child-bearing potential should conduct a home pregnancy test every 4 weeks. Home pregnancy tests will be provided to participants for use at Weeks 60, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. At weeks on which IMP dosing is scheduled

(specified in Table 5-1 and Table 5-2), a negative urine pregnancy test result should be obtained immediately prior to the administration of IMP. In the case of a positive pregnancy test result, IMP should not be administered and the site should be contacted.

Change #16

Section 14.7, Handling of dropouts or missing data

Missing data for the secondary efficacy variables (which are all binary) will be imputed using NRI. Additionally, the 2 missing data-handling approaches described above for the primary efficacy variable will be used for the secondary efficacy variables.

Has been changed to:

Missing data for the secondary efficacy variables (which are all binary) will be imputed using NRI. Additionally, the 2 missing data-handling approaches described above for the primary efficacy variable will be used for the secondary efficacy variables. **Additional missing data handling approaches may be described in the SAP.**

18.9 Protocol Amendment 5.4

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 treatment period for subjects continuing their current treatment or reinitiating treatment at the Week 144/OLE2 Baseline Visit.

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 the subjects in the OLE2 Period, maximum study duration will depend on the time between their participation in the OLE until Week 144 and the start of the OLE2 Period; ie, 209 weeks for subjects still being treated in the OLE Period and who will directly roll over to the OLE2 Period at Week 144; 225 weeks for subjects who have completed Week 144 and the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 Period; Between 209 and 225 weeks for subjects who have completed Week 144 and are participating the in the SFU (for these subjects, the maximum study duration will depend upon when they stop the 20-week SFU period to enter the 4-week OLE2 Screening Period).
- Implementation of a new schedule of assessments (Table 5-3) for the OLE2 Period have been made.

- Schematic diagram (Figure 5-3) for the for the 4-year extension have been made
- A list of inclusion and exclusion criteria has been added for participating in OLE2 Period
- The description of the treatment to be administered has been adapted to take into account the treatment to be administered in OLE2 Period. A new dosing scheme from Week 144/OLE2 Baseline through OLE2 Week 40 has been added (Table 7–3).
- Addition of the study procedures by visit has been made for the OLE2 Period (Section 8.4)

Specific changes

Change #1

Section 1, Summary

Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. For each subject, the study will last a maximum of 165 weeks and will consist of 4 periods, a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at Week 44), an Open-Label Extension (OLE) Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W); and a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP

Has been changed to:

Approximately 935 subjects will be screened in order to have 700 subjects randomized in the study. For each subject, the study will last a maximum of 165 weeks and will consist of **5** periods: a Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at Week 44), an Open-Label Extension (OLE) Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W) **followed by** a Safety Follow-Up (SFU) Period (20 weeks after the final dose of investigational medicinal product [IMP**] depending on subject's participation in the second OLE Period [OLE2 Period]; see paragraph below).**

And the following paragraph was added

Subjects participating in the OLE2 Period (implemented as part of Protocol amendment 5.4) will enter the OLE2 Period after completing the OLE 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 treatment period with final visit at OLE2 Week 48, followed by a 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 #5.4 (addition of a 48-week treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- **OLE2 Group A: Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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 Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit will be treated with bimekizumab Q4W for the first 16 weeks, and then will switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

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

Change #3

2.2.1.2 Ongoing studies

Eight additional studies of bimekizumab in the treatment of PSO are ongoing.

- PS0008 is a Phase 3, multicenter, randomized, double-blind, parallel-group, active-comparator-controlled study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0009 is a Phase 3 randomized, double-blind, placebo- and active comparator-controlled study to evaluate the efficacy and safety of bimekizumab administered sc to adult subjects with moderate to severe plaque PSO.
- 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.

- PS0013 is a Phase 3, multicenter, randomized withdrawal, double-blind, placebo-controlled study to evaluate the efficacy and safety of bimekizumab in adult subjects with moderate to severe chronic plaque PSO.
- PS0014 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.
- 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.

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 #5.4 implementation** are **presented** and **described** in the current version of the IB.

Change #4

Section 5.2 Study periods

Screening Period (2 to 5 weeks), a double-blind Treatment Period (48 weeks; final dose at Week 44), an optional OLE Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W), and an SFU Period (20 weeks after the final dose of IMP).

Was changes to:

This study will include **the following** periods:

- A Screening Period (2 to 5 weeks)
- A double-blind Treatment Period (48 weeks; final dose at Week 44)
- An optional OLE Period (96 weeks; final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W) **followed by a** SFU Period (20 weeks after the final dose of IMP **administered in the OLE Period depending upon subject's participation in the OLE2 Period), and**
- **An optional 48-week OLE2 Period followed by a SFU Period (SFU2, 20 weeks after the final dose of IMP administered in the OLE2 Period).**

The OLE2 Period was added as per Protocol Amendment #5.4 at the time when subjects will still be treated in the OLE (prior to Week 144 Visit) or will have finished treatment in the OLE (after completing Week 144 Visit):

- **Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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).

- **Eligible subjects who have completed the Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit 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 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

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

Change #5

Section 5.2.3 OLE Period

The following sentence was added:

The last dose bimekizumab 320mg Q8W in the OLE Period will be administered at Week 136. The End of Treatment Visit of the OLE Period will be the Week 144 Visit.

Change #6

The following section was added:

Section 5.2.5 OLE2 Period

Subjects enrolled as per Protocol Amendment #5.1 will be treated in the OLE Period until Week 136 (last dose of bimekizumab 320mg Q8W) and will be followed in a SFU Period for 20 weeks after attending the Week 144 Visit (see Section 5.2.3). After the implementation of Protocol Amendment #5.4 (addition of a 48-week treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- **OLE2 Group A: Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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 Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit will be treated with bimekizumab Q4W for the first 16 weeks, and then will switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

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

The assessments to be performed at each visit of the OLE2 Period are presented in Table 5-3.

Change #7

Section 5.2.5 Safety Follow-up

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

The assessments for the SFU are presented in Table 5–1 and Table 5–2.

Was changes to:

Section 5.2.5 Safety Follow-up Period

The assessments for the SFU Visits are presented in Table 5–1, Table 5–2**, and Table 5-3.**

Two SFU Periods are considered since Protocol Amendment #5.4 implementation: a first SFU following the OLE Period and a second SFU (SFU2) following the OLE2 Period (added as per Protocol Amendment #5.4 implementation).

Subjects having completed Week 144 Visit and who are in the SFU or have completed the SFU will be invited to reinitiate their treatment in the OLE2 Period.

Subjects still being treated in the OLE Period (not having attended Week 144 yet) will have the opportunity to directly roll over in the OLE2 Period without participating in the first SFU.

Subjects who decide not to participate in OLE2 Period will undergo the first SFU period for 20 weeks after their last dose in the OLE 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 have a **SFU2** Visit 20 weeks after their final dose of IMP **administered up to OLE2 Week 48.**

Change #8

Section 5.4 Study duration per subject

For each subject, the study will last a maximum of up to 165 weeks, as follows:

- Screening Period: 2 to 5 weeks
- Double-blind Treatment Period: 48 weeks (final dose at Week 44)
- OLE Period: 96 weeks (final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W)

Safety Follow-Up Period a SFU Visit is planned 20weeks after the final dose of IMP visit

Was changed to:

For each subject, the study will last a maximum of up to 165 weeks, as follows:

- Screening Period: 2 to 5 weeks
- Double-blind Treatment Period: 48 weeks (final dose at Week 44)
- OLE Period: 96 weeks (final dose at Week 136 for subjects receiving bimekizumab 320mg Q8W and at Week 140 for subjects receiving bimekizumab 320mg Q4W) **followed by a Safety Follow-Up Period: a SFU Visit is planned 20 weeks after the final dose of IMP visit in the OLE Period (this SFU will not apply to subjects directly rolling over from the OLE to the OLE2 Period [see Section 5.2.5])**

Subjects eligible for the OLE2 Period **(added as part of Protocol Amendment #5.4) will enter the OLE2 Period after completing Week 144 of the OLE Period. The OLE2 Period will include a 48-week treatment period with a final visit at OLE2 Week 48 and** a SFU **Period (SFU2) of** 20 weeks after the final dose of IMP **administered in the OLE2 Period.**

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

- **209 weeks for subjects still being treated in the OLE Period and who will directly roll over to the OLE2 Period at Week 144**
- **225 weeks for subjects who have completed Week 144 and the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 Period. Note: for, these subjects the study duration will not be continuous.**
- **Between 209 and 225 weeks for subjects who have completed Week 144 and are participating the in the SFU. For these subjects, the maximum study duration will**

depend upon when they stop the 20-week SFU period to enter the 4-week OLE2 Screening Period.

Change #9

Section 5.6 Schedule of study assessments

Table 5-3 Schedule of study assessments, OLE2 Period, was added:

Table 5-3 Schedule of study assessments, OLE2 Period

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	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											
Physical exam [e]	Group B	Group A[f] + B			X		X		X		X	X
Body weight		Group A[e] + 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	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

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	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	X
Patient Symptoms (itch, pain, and scaling)		Group A[f] + B			X		X		X		X	
PHQ-9	Group B	Group A[f] + B			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

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
		C	H	H	C	H	C	H	C	H	C	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		

BSA=body surface area; C=clinic; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; IGA=Investigator's Global Assessment; H=home; IMP=investigational medicinal product; IRT=interactive response technology; OLE=open label extension; PASI=Psoriasis Area Severity Index; PHQ-9=Patient Health Questionnaire-9; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU2=Safety Follow-Up #2; TB=tuberculosis; 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 from the first dose at 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 their 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 12.3.5.

[f] These tests are performed as part of Week 144 visit (the Week 144 Visit coincides with the Week 144/OLE2 Baseline Visit for subjects in Group A, ie, direct enroller from OLE 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. Home pregnancy test kits will be provided to participants for use between clinic visits.

[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.

Table 5-3 Schedule of study assessments, OLE2 Period

Visit [a]/ Week	OLE2 Period											
	OLE2 Screening [b]	W144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12	OLE2 W16	OLE2 W24	OLE2 W32	OLE2 W36	OLE2 W40	OLE2W48/ PEOT	SFU2 [c]
	C	C	H	H	C	H	C	H	C	H	C	C
Protocol activity			OLE2 Groups A + B									

[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 W144/OLE2 Screening Visit onwards.

[m] The dosing window is ±14 days relative to the Week 144/OLE2 Baseline Visit.

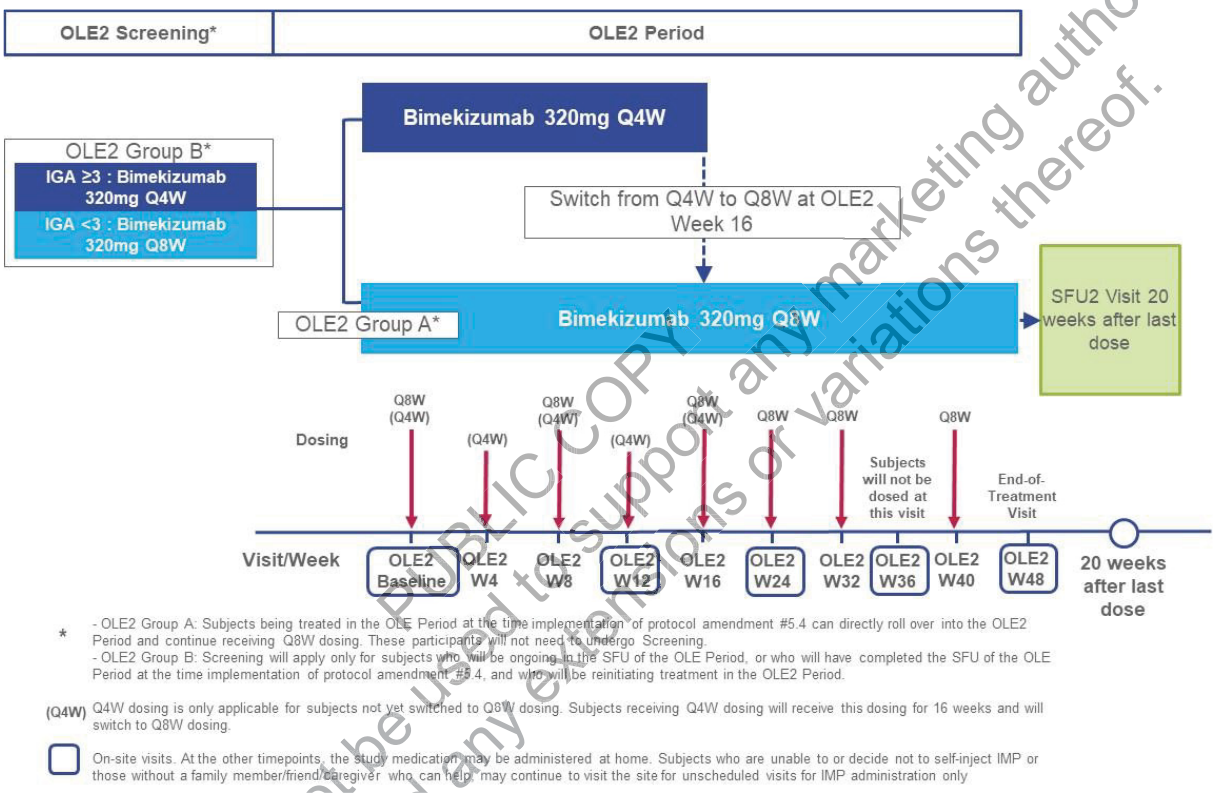
[n] If self-injected at home, the subject/caregiver will document the date, body location, kit number and time point of administration of study medication. All used syringes will be disposed of by subjects/caregivers as determined by the Investigator in an acceptable disposal (sharps) container directly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

Change #10

Section 5.7 Schematic diagram

Figure 5-3 was added:

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 #11

Section

5.8 Rationale for study design and selection of dose

5.8.1 Study design

The following paragraph was added:

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 treatment period for subjects continuing their current treatment or reinitiating treatment at the Week 144/OLE2 Baseline Visit.

Change #12

5.8.2 Dose selection

The following paragraph was added:

Subjects who are participating in the OLE Period can directly roll over to the OLE2 Period and continue receiving bimekizumab 320mg Q8W. Eligible subjects who are in the SFU of the OLE Period or who have completed the SFU at the time of Protocol Amendment #5.4 implementation can reinitiate their treatment in the OLE2 Period based on their 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, in line with the original initial treatment period, followed by 320mg Q8W for the remaining dosing timepoints of the OLE2 Period.

Change #13

The following sections were added:

6.4 Eligibility for the OLE2 Period

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

6.4.1 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:

10. Subject provided informed consent.

11. 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.

12. Subject completes the OLE Period to Week 144 without meeting any withdrawal criteria defined in Section 6.5.

6.4.2 OLE2 Period Group A subjects

To participate in the OLE2 Period, subjects still treated in the OLE Period and who completed the Week 144 Visit by the time of the implementation of Protocol Amendment #5.4 will not need to fulfil other eligibility criteria than those listed in Section 6.4.1 and will continue their treatment from the Week 144/OLE2 Baseline Visit if they do not meet any of the withdrawal criteria defined in Section 6.5.

6.4.3 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 #5.4 implementation:

13. 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.**

14. 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 is met:

15. Female subjects who plan to become pregnant during the OLE2 Period or within 20 weeks following final dose of study medication.

16. 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.

17. 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.

18. **Subject had a positive or indeterminate IGRA in the OLE study to Week 144, unless appropriately evaluated and treated as per Section 12.3.1.**
19. **Subject may not participate in another study of a medicinal product or device under investigation**
20. **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.**
21. **Subjects who have used systemic treatments 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).**
22. **Subject has erythrodermic, guttate, or pustular form of PSO.**
23. **Subject is noncompliant with the study procedures or medications in the opinion of the Investigator.**
24. **Subject has a clinical laboratory value meeting any of the following criteria:**
    h. **≥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)**
    i. **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.
25. **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 (HCV) is defined as: (1) positive for hepatitis C antibody (HCV Ab) and (2) positive via a confirmatory test for HCV (for example, HCV polymerase chain reaction).**
26. **There is confirmation of a pregnancy, as evidenced by a positive pregnancy test (see Section 12.1.4 for more information regarding pregnancies).**

27. 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 eC-SSRS.**
- **Any suicidal behavior since last visit.**

28. 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.

29. 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.

30. Subject has received any live (includes attenuated) vaccination within the 8 weeks prior to the Week 144/OLE2 Baseline Visit.

Change #13

Section 7.2 Treatments to be administered

The following text and Table 7-3 were added:

After the implementation of Protocol Amendment #5.4 (addition of a 48-week treatment period, ie, OLE2 Period), subjects will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- **OLE2 Group A: Subjects in the treatment phase of the OLE Period at the time of Protocol Amendment #5.4 implementation will attend the Week 144 Visit and 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 Week 144 Visit and are in the SFU or have completed the SFU of the OLE Period at the time of Protocol Amendment #5.4 implementation, will reinitiate their 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 and data collected at this visit will be used as baseline data for the OLE2 Period. Subjects in OLE2 Group B with an IGA score ≥3 at the Week 144/OLE2 Baseline Visit will be treated with bimekizumab Q4W for the first 16 weeks, then will switch to bimekizumab 320mg Q8W. Subjects in OLE2 Group B with an IGA score <3 at the Week 144/OLE2 Baseline Visit 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 every 12 weeks. All subjects will be treated until OLE2 Week 40 (last dose of bimekizumab 320mg Q8W).

The dosing scheme from Week 144/OLE2 Baseline through OLE2 Week 40 is depicted in Table 7–3.

Table 7-3 Dosing scheme, OLE2 Period

Visits/Week / Dose Assignment	OLE2 Period								
	Week 144/OLE2 Baseline	OLE2 W4	OLE2 W8	OLE2 W12 [a]	OLE2 W16	OLE2 W24 [b]	OLE2 W32	OLE2 W36 [c]	OLE2 W40
	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; Q4W/Q8W=every 4 weeks for 16 weeks, followed by every 8 weeks; Q8W=every 8 weeks; OLE=Open Label Extension; W=week

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 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.

Change #13

Section 7.6 Dug accountability

The following sentence was added:

The OLE2 Period will be unblinded and blinding precautions will not be applicable.

Change #14

Section 7.7 Procedures for monitoring subject compliance

After Week 48, self-injection at home will be possible at the following weeks: Weeks 60, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. Dates, body 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.

Was changes to:

After Week 48, self-injection at home will be possible at the following weeks: Weeks 60, 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, body 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.

Change #14

Section 7.8.1.1 Topical medications

In the OLE Period, the medications listed as permitted for the double-blind Treatment Period will be allowed. In addition, any topical steroids and vitamin D analog ointment will be permitted for use, as needed. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.

Was changed to:

In the OLE **and OLE2 Periods**, the medications listed as permitted for the double-blind Treatment Period will be allowed. In addition, any topical steroids and vitamin D analog ointment will be permitted for use, as needed. These topical medications should not be used within approximately 24 hours prior to study visits requiring IGA and PASI measures.

Change #15

Section 7.8.2 Prohibited concomitant treatments (medications and therapies)

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 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.

Change #16

Section 7.10 Randomization and numbering of subjects

The following paragraph was added:

Subjects who roll over directly from the OLE 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 OLE Period or who have completed the SFU of the OLE 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 #17

Section 8 STUDY PROCEDURES BY VISIT

Table 5–1 and Table 5–2 provide a general overview of study assessments during the double-blind Treatment Period and the OLE Period, respectively. A list of procedures to be completed at each visit is described below.

- Visit windows of ±3 days on either side of the scheduled dosing are permitted up to and including Week 24; however, the Investigator should try to keep the subjects on the original dosing schedule. From the Week 28 Visit through the Week 72 Visit, 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. From the Week 76 Visit through the Week 144/PEOT Visit, 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 visit window is relative to Baseline and applicable for all subsequent visits Changes to the dosing schedule outside the visit window must be discussed with the Medical Monitor.
- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the

scheduled dosing visit. From Week 28 through the Week 72 Visit, the dosing window is ±7 days relative to the scheduled dosing visit. From the Week 76 Visit through the Week 140 Visit the dosing window is ±14 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.

Was changed to:

Table 5–1, Table 5–2, **Table 5-3 p**rovide a general overview of study assessments during the double-blind Treatment Period, the OLE Period, **and the OLE2 Period,** respectively. A list of procedures to be completed at each visit is described below.

- Visit windows of ±3 days on either side of the scheduled dosing are permitted up to and including Week 24; however, the Investigator should try to keep the subjects on the original dosing schedule. From the Week 28 Visit through the Week 72 Visit, 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. From the Week 76 Visit through the Week 144/PEOT Visit, 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 visit window is relative to Baseline and applicable for all subsequent visits **up to Week 144/OLE2 Baseline Visit. From the Week 144/OLE2 Baseline Visit through the OLE2 Week 48/PEOT Visit, visit windows of ±14 days relative to the Week 144/OLE2 Baseline Visit on either side of the scheduled dosing are permitted; however, the Investigator should try to keep the subjects on the original dosing schedule.** Changes to the dosing schedule outside the visit window must be discussed with the Medical Monitor.
- The dosing window from Baseline through Week 4 is ±2 days relative to the scheduled dosing visit. From Week 8 through Week 24, the dosing window is ±3 days relative to the scheduled dosing visit. From Week 28 through the Week 72 Visit, the dosing window is ±7 days relative to the scheduled dosing visit. From the Week 76 Visit through the **OLE2** Week **40** Visit, the dosing window is ±14 days relative to the scheduled dosing visit.
- For the SFU **and SFU2 Visits** (20 weeks after the final dose), the visit window is ±7 days relative to the scheduled visit date.

Change #18

Section 8.3.8 Week 144 Visit (±14 days relative to Baseline)

The following paragraphs were added:

If Protocol Amendment #5.4 is implemented at the time subjects are treated in the OLE 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 their 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 #5.4 is implemented at the time subjects have completed the Week 144 Visit and are in the SFU Period of the OLE Period or have completed the SFU of the

OLE Period (Group B subjects), these subjects will be invited to enter the OLE2 Period to reinitiate their 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 (Section 8.4.1).

Change #19

The following sections were added

8.4 OLE2 Period

8.4.1 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 OLE Period (OLE2 Group B subjects) will undergo screening. Subjects who have used systemic treatments 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)**
- **AEs (only for subjects in the SFU)**
- **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 biochemistry**
  - **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)**
- **Contact IRT**

8.4.2 OLE2 Baseline Visit

Subjects who will still be treated in the OLE Period at the time of implementing Protocol Amendment #5.4 (OLE2 Group A subjects) will attend Week 144 Visit and directly roll over to the OLE2 Period to continue their 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 OLE or have completed the SFU Period at the time of Protocol Amendment #5.4 implementation (OLE2 Group B subjects) will reinitiate their treatment at the Week 144/OLE2 Baseline Visit, and will be assigned a treatment regimen based on their 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:

- **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 biochemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
- **eC-SSRS**

- **Tuberculosis questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**
- **PHQ-9**
- **DLQI**
- **Patient symptoms (itch, pain, and scaling)**
- **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.

8.4.3 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 dosed at OLE2 Weeks 32 and 40.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. In case of a scheduled home self-injection the pregnancy test needs to be performed immediately prior to self-injecting bimekizumab at home. If the pregnancy test result is positive, IMP should not be administered and the site should be contacted.

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.

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

As depicted in Table 7–3, 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**
- **Patient symptoms (itch, pain, and scaling)**
- **PHQ-9**
- **eC-SSRS**

- **Concomitant medication**
- **AEs**
- **Contact IRT**

The following will be additional assessments will be performed / recorded every 24 weeks (ie, OLE2Weeks 24 and 48) prior to administration of IMP

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

At the OLE2 Week 12 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. Home pregnancy tests will be provided for testing every 4 weeks as appropriate (Table 5–2 and Table 5-3).

8.4.5 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 should be obtained prior to dosing:**
  - **Hematology and chemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
  - **IGRA TB test**
- **Tuberculosis questionnaire**
- **PASI**
- **Percentage of BSA**
- **IGA**

- **DLQI**
- **Patient symptoms (itch, pain, and scaling)**
- **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 #20

Section 8.5 Premature 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 8.4.5) 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 8.7).**

Change #21

The following section was added:

8.7 Safety Follow-Up Visit 2 (20 weeks after final dose in 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 biochemistry**
  - **Urinalysis**
  - **Urine pregnancy test**
- **eC-SSRS**
- **Concomitant medication**
- **AEs**

- **Contact IRT**

Change #22

Section 8.8 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, OLE or OLE2, the participant is in)**, if deemed necessary for the subject's safety and well-being.

Change #23

Section 10.1 Pharmacokinetic variables

The following sentence was added:

Blood samples for the measurement of PK assessments will not be collected in the OLE2 Period.

Change #24

Section 11 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 #25

Section 12.2 Laboratory measurements

Table 12-2 Laboratory measurements

Hematology	Chemistry	Urinalysis dipstick[a]
	Lipid panel	
	NT-proBNP[b]	
	Serum pregnancy testing[c]	

[b] Assessments of NT-proBNP and CRP will not be performed during the OLE Period.
[c] Pregnancy testing will consist of serum testing at the Screening. Urine pregnancy testing will be performed at all other visits.

Was changed to:

Table 12-2 Laboratory measurements

Hematology	Chemistry	Urinalysis dipstick[a]
	Lipid panel[b]	
	NT-proBNP[b]	
	Serum pregnancy testing[c]	

[b] Assessments of NT-proBNP and CRP will not be performed during **any OLE Period; in addition, lipid panel will not be performed during OLE2** Period.
[c] Pregnancy testing will consist of serum testing at the **initial** Screening. Urine pregnancy testing will be performed at all other visits.

Change #26

Section 12.3.2 Pregnancy testing

Pregnancy testing will consist of serum testing at the Screening. The pregnancy test will be urine at other visits.

The Screening Visit serum pregnancy testing results must be negative and received and reviewed prior to randomization.A negative urine pregnancy test result should be obtained immediately prior to each administration of IMP as 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.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. Home pregnancy tests will be provided to participants for use at Weeks 60, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140. At weeks on which IMP dosing is scheduled (specified in Table 5–1 and Table 5–2), a negative urine pregnancy test result should be obtained immediately prior to the administration of IMP. In the case of a positive pregnancy test result, IMP should not be administered and the site should be contacted.

Was changed to:

Pregnancy testing will consist of serum testing at the **initial** Screening. The pregnancy test will be urine at other visits**, including at the OLE2 Screening Visit.**

The Screening Visit serum pregnancy testing results must be negative and received and reviewed prior to randomization.

A negative urine pregnancy test result should 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.

Subjects of childbearing potential should conduct a home pregnancy test every 4 weeks. Home pregnancy tests will be provided to participants for use at Weeks 60, 68, 76, 80, 88, 92, 100, 104, 112, 116, 124, 128, 136, and 140**, and at the OLE2 Weeks 4, 8, 16, 32, and 40**. At weeks on which IMP dosing is scheduled (specified in Table 5–1, Table 5–2**, and Table 5-3**), a negative urine pregnancy test result should be obtained immediately prior to the administration of IMP. In

the case of a positive pregnancy test result, IMP should not be administered and the site should be contacted.

Change #27

Section 12.4.2 Medical history

A complete medical history will be collected as part of the Screening assessment and include all clinically relevant past or coexisting medical conditions and surgeries. Findings will be recorded in the eCRF.

Was changed to:

A complete medical history will be collected as part of the **initial** Screening assessment and include all clinically relevant past or coexisting medical conditions and surgeries. Findings will be recorded in the eCRF.

For OLE2 Group B, only new or modified medical history since completing the SFU will be collected at OLE2 Screening and entered in eCRF.

Change #28

Section 12.4.4 Data Monitoring and Adjudication Committees

The Cardiovascular and Neuropsychiatric Adjudication Committees will monitor the study through the last subject completing the OLE and SFU Periods for PS0015.

Was changed to:

The Cardiovascular and Neuropsychiatric Adjudication Committees will monitor the study through the last subject completing the OLE, SFU, **OLE2,** and **SFU2** Periods for PS0015.

Change #29

Section 14.1 Definition of analysis sets

The following paragraph was added:

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

Change #30

Section 14.3.2.2 Analysis of the other efficacy variables

In general, data will be summarized by visit through Week 48 in the double-blind Treatment Period and then by visit in the OLE Period separately. All summaries of data up to Week 16 will be based on the RS for the 2 randomized treatment groups (bimekizumab and secukinumab). For visits after Week 16 in the double-blind Treatment Period, by-visit summaries will be prepared for the following 3 groups of subjects:

Was changed to:

In general, data will be summarized by visit through Week 48 in the double-blind Treatment Period and then by visit in the OLE Period **and OLE2 Period** separately. All summaries of data

up to Week 16 will be based on the RS for the 2 randomized treatment groups (bimekizumab and secukinumab). For visits after Week 16 in the double-blind Treatment Period, by-visit summaries will be prepared for the following 3 groups of subjects:

And the folloing sentence was added:

In the OLE2 Period, selected efficacy variables of interest will be summarized descriptively by OLE2 Period Treatment Group during the OLE2 Period.

Change #31

Section 14.5.1 Safety analyses

Safety variables will be analyzed for all subjects in the SS. This will include all subjects who took at least one dose of study medication. Selected analyses will also be presented for MS and OLS.

Was changed to

Safety variables will be analyzed for all subjects in the SS. This will include all subjects who took at least one dose of study medication. Selected analyses will also be presented for MS, **OLS,** and **OL2S**.

Change #32

Section 14.8 Planned interim analysis

An interim analysis is planned at Week 48, 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 and including the OLE Period 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 **OLE2** Period **and SFU2 Visit** have been collected.

Change #33

Section 15.1 Informed consent

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

Was changed to

All subjects enrolling in the OLE Period will sign a new ICF. **Similarly, all subjects enrolling in the OLE2 Period will sign a new ICF.**

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 GCP 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 GCP.

Approval Signatures

Name: ps0015-protocol-amend-5.4

Version: 1.0

Document Number: CLIN-000178914

Title: ps0015-protocol-amend-5.4

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Document Approvals	
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