Title Page

Protocol Title:	A Phase 3, Multicenter, Randomized, Double-Blind Study Evaluating the Efficacy and Safety of ABP 654 Compared with Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis
Short Title:	A Study to Investigate ABP 654 for the Treatment of Subjects with Moderate to Severe Plaque Psoriasis
Test Product:	ABP 654
Trade Name:	Not applicable
Indication:	Moderate to Severe Plaque Psoriasis
Study Sponsor:	Amgen, Inc. One Amgen Center Drive Thousand Oaks, CA 91320-1799 USA
Protocol Number:	20190232
Study Phase:	Phase 3
Regulatory Agency Identifying Numbers:	IND: 139331 EudraCT: 2020-003184-25
Approval Date:	Final, 06 August 2020

NCT Number: NCT04607980
This NCT number has been applied to the document
for purposes of posting on Clinicaltrials.gov

Protocol Signature Page - Sponsor:

This protocol has been reviewed and approved by the representative(s) listed below. Any modification of the protocol must be agreed upon by the sponsor and the investigator and must be documented in writing.

Amgen, Inc representative(s):

[redacted] [redacted]

Print Name Title

[redacted] [redacted]

Signature Day (DD MMM YYYY)

Protocol Signature Page – Contract Research Organization (CRO)

This protocol has been reviewed and approved by the representative(s) listed below. Any modification of the protocol must be agreed upon by the sponsor and the investigator and must be documented in writing.

CRO representative(s):

[redacted]	Senior Medical Director
Print Name	Title
[redacted]	10 August 2020
Signature	Date (DD Month YYYY)

Protocol Signature Page - Investigator

I have read this protocol, which has been agreed by Amgen, Inc and given approval/favorable opinion by the Institutional Review Board (IRB)/Independent Ethics Committee (IEC), and I agree that it contains all necessary details for my staff and I to conduct this study as described. I will provide copies of the protocol and any amendments to all study personnel under my supervision and provide access to all information provided by Amgen, Inc or their specified designees. I will discuss the material with the study personnel to ensure that they are fully informed about the study.

I understand that information contained in or pertaining to this protocol is confidential and should not be disclosed, other than to those directly involved in the execution or the ethical review of the study, without written authorization from Amgen, Inc. It is, however, permissible to provide information to a subject in order to obtain consent.

I agree to conduct this study according to this protocol and to comply with its requirements, subject to ethical and safety considerations and guidelines, and to conduct the study in accordance with the general guidelines indicated in the Declaration of Helsinki, International Council for Harmonisation (ICH) guidelines on Good Clinical Practice (GCP), and applicable national or regional regulatory requirements.

I agree to comply with the procedures described for data recording and reporting and to permit monitoring and auditing by Amgen, Inc, and inspection by the appropriate regulatory authorities.

I agree to make my subjects' study records available to Amgen, Inc personnel, their representatives and relevant regulatory authorities in order to verify data that I have entered into the case report forms. I will retain the study-related essential documents until Amgen, Inc indicates that they are no longer needed. I am aware of my responsibilities as an investigator as provided by Amgen, Inc.

I agree to ensure that Financial Disclosure Statements will be completed by me (including, if applicable, my spouse [or legal partner] and dependent children) and my subinvestigators (including, if applicable, their spouses [or legal partners] and dependent children) at the start of the study and for up to 1 year after the study is completed, if there are changes that affect my financial disclosure status.

I understand that Amgen, Inc may decide to suspend or prematurely terminate the study at any time for whatever reason; such a decision will be communicated to me in writing. Conversely, should I decide to withdraw from execution of the study, I will communicate my intention immediately in writing to Amgen, Inc.

Investigator:

Print Name	Title

Institution

Signature	Date (DD Month YYYY)

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1 Protocol Summary

1.1 Synopsis

Protocol Title: A Phase 3, Multicenter, Randomized, Double-Blind Study Evaluating the Efficacy and Safety of ABP 654 Compared with Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis

Sponsor Protocol No.: 20190232

Study Phase: Phase 3

Test product: ABP 654

Regulatory agency identifier numbers: IND number 139331
EudraCT number 2020-003184-25

Sponsor: Amgen, Inc

Rationale:

The current study is designed to investigate the efficacy, safety, and immunogenicity of ABP 654 compared with ustekinumab in subjects with moderate to severe plaque psoriasis.

Objectives and Endpoints:

Objectives	Endpoints
Primary: To compare the efficacy of ABP 654 with ustekinumab in subjects with moderate to severe plaque psoriasis.	**Primary Efficacy Endpoint:** Psoriasis area severity index (PASI) percent improvement from baseline to week 12
Secondary: To assess the safety and immunogenicity of ABP 654 compared with ustekinumab.	**Secondary Efficacy Endpoints:** • PASI percent improvement at other timepoints • PASI 75 response throughout the study • PASI 100 response throughout the study • Static Physician's Global Assessment (sPGA) responses (0/1) at week 12 and week 52 • Body surface area (BSA) change from baseline at week 12 and week 52

Objectives	Endpoints
	Safety Endpoints: • Treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) • Events of interest (EOI) • Incidence of anti-drug antibodies

Overall Design:

Design: This is a randomized, double-blind, active-controlled, multicenter study

Study Population: Adult subjects, including men and women between 18 to 75 years of age, with moderate to severe plaque psoriasis

Parallel: Subjects will be randomized (1:1) to Treatment Group A (ABP 654) or Treatment Group B (ustekinumab)

A Data Monitoring Committee (DMC) will periodically review study data.

Number of Subjects:

Approximately 542 adult subjects will be randomized in a 1:1 ratio to receive ABP 654 or ustekinumab stratified by prior biologic use for psoriasis (yes vs. no), geographic region, and baseline body weight (BW). Subjects with prior biologic use for psoriasis will be capped at 50% of the total randomized subjects. The sample size will provide greater than 95% power to demonstrate equivalence at a significance level of 0.025 on PASI percent improvement from baseline at week 12 with an equivalence margin of (-15, +15), assuming a common standard deviation of 30.0 (Leonardi, 2008; Papp, 2008) and a true mean difference of 0 with 10% drop-out.

Intervention Groups and Duration:

The total duration of study participation for each subject will be 56 weeks, with up to 4 weeks for screening, and for 52 weeks after the first administration of either ABP 654 or ustekinumab.

Dose regimens: ABP 654 (45 mg or 90 mg, subcutaneous [SC] injection) and ustekinumab (45 mg or 90 mg, SC injection).

Test Product, Dose, and Mode of Administration:	ABP 654 administered by SC injection using a blinded pre-filled syringe (PFS) at a dose of 45 mg (baseline BW ≤ 100 kg) or 90 mg (baseline BW > 100 kg) at weeks 0, 4, and 16. Subsequent dosing will be done at the same dose every 12 weeks (Q12W) for subjects not requiring dose intensification (at the Investigator's discretion) or every 8 weeks (Q8W) for subjects requiring dose intensification.
Reference Therapy, Dose, and Mode of Administration:	Ustekinumab administered by SC injection using a blinded PFS at a dose of 45 mg (baseline BW ≤ 100 kg) or 90 mg (baseline BW > 100 kg) at weeks 0, 4, and 16. Subsequent dosing will be done at the same dose. Q12W for subjects not requiring dose intensification or Q8W for subjects requiring dose intensification.

During the approximately 56 weeks of total study participation, each subject will receive a total of either 5 or 6 doses, based on the one group to which they are assigned, as described below. Subjects will receive an initial 3 doses of either ABP 654 or ustekinumab at weeks 0, 4, and 16. From week 28 subjects will receive either ABP 654 or ustekinumab every 8 weeks (Q8W) or every 12 weeks (Q12W).

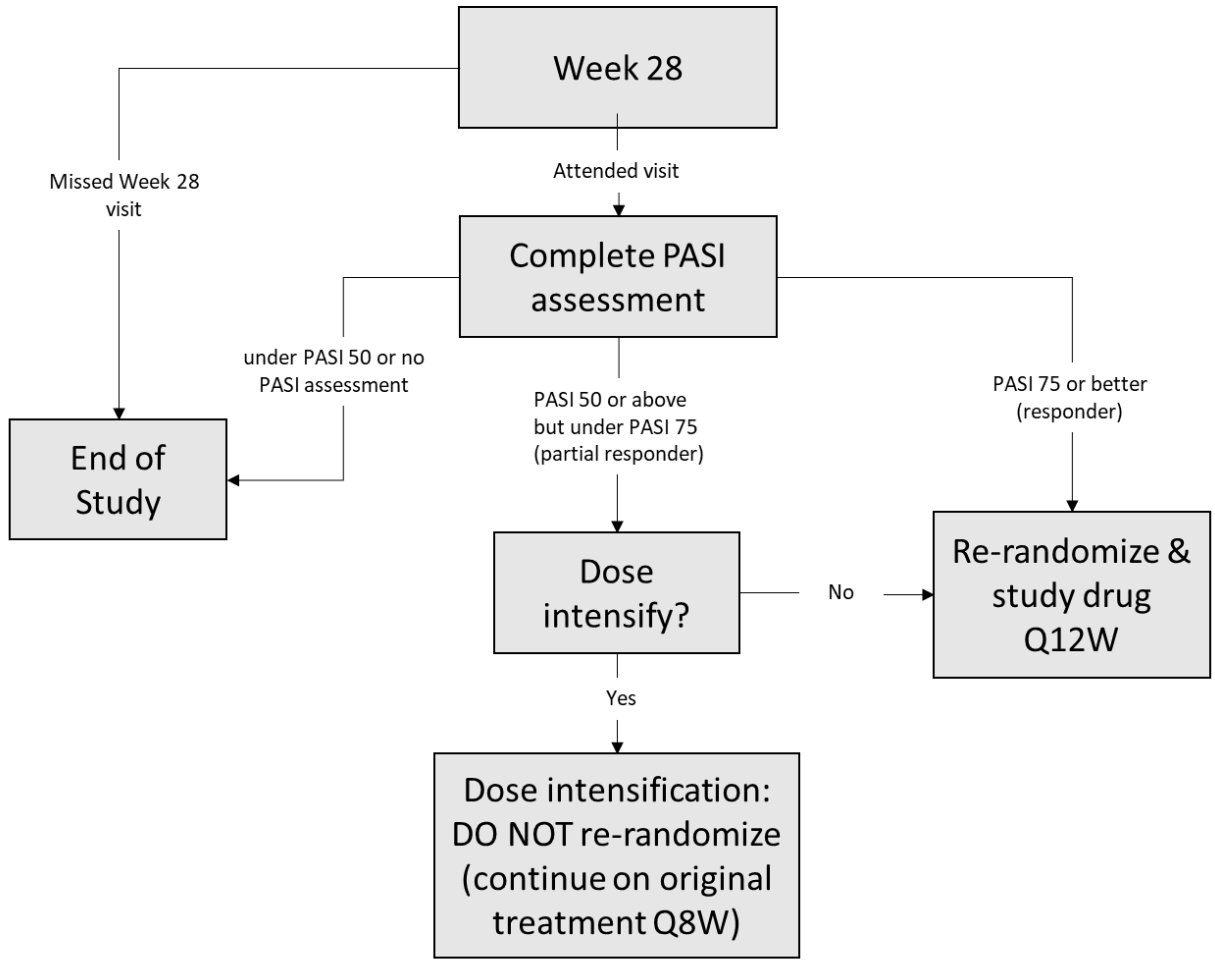
At week 28, disease assessments will be conducted including the evaluation of PASI.

Subjects who do not achieve a PASI 50 response or better improvement at week 28 will be considered to have completed the study and will complete the end of study procedures (ie, week 52 procedures) at week 28. Those unable to complete week 28 visit, or did not have a PASI assessment completed, will be discontinued from the study (see Week 28 Decision Tree Diagram below).

Subjects with a PASI 75 response or better improvement will continue on the study and will be re-randomized in a blinded fashion such that subjects initially randomized to Group A (ABP 654) will continue to receive ABP 654 and those in Group B (ustekinumab) will be re-randomized 1:1 to either continue on ustekinumab (Treatment Group B1) or switch to ABP 654 (Treatment Group B2). Subjects will receive investigational product at week 28 and the last dose of investigational product at week 40.

For subjects with PASI 50 response or better but less than PASI 75 response at week 28, based on the Investigator's discretion, subjects may increase dose frequency to Q8W. Subjects with baseline BW ≤ 100 kg will receive 45 mg Q8W and subjects > 100 kg at baseline will receive 90 mg Q8W at weeks 28, 36, and 44. These subjects will continue on original assigned treatment with dose intensification and will NOT be re-randomized. Subjects not dose intensifying will be re-randomized as described above.

Week 28 Decision Tree Diagram



Abbreviations: PASI = psoriasis area severity index; Q8W = every 8 weeks; Q12W = every 12 weeks

Sites and Regions: This study is planned to be conducted globally at sites in North America and Europe.

Rules, procedures, and stopping rules for dose changes and adjustments: See Sections 6.5 and 7.

Data Monitoring Committee: See Section 9.1.5.

Statistical Analysis

All efficacy analyses will be conducted in the full analysis set, consisting all randomized subjects, according to randomized treatment group. Sensitivity analyses will be performed for the primary and key secondary efficacy endpoints using the per-protocol analysis set.

Clinical equivalence of the primary endpoint will be evaluated by comparing the 2-sided 95% confidence interval (CI) of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 versus ustekinumab with equivalence margin of (-15, +15). Clinical equivalence of the primary endpoint for Japan will be evaluated by comparing the 2-sided 95% CI of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 versus ustekinumab in subjects with baseline BW ≤ 100 kg (and hence are to receive the 45 mg dose) against the (-15, +15) margin.

The 95% CI of the difference will be estimated using analysis of covariance model with the baseline PASI value and stratification factors as covariates. The mean difference of PASI percent improvement between the initial randomized groups (ABP 654 vs ustekinumab) or between the re-randomized groups (ABP 654/ABP 654, ustekinumab/ustekinumab, ustekinumab/ABP 654) at other scheduled visits, the risk difference of PASI 75 and 100 response rate throughout the study, the risk difference of the percent of subjects with sPGA responses (0/1) at week 12 and week 52, and the mean difference in BSA change from baseline at week 12 and week 52 will be summarized descriptively. Separate descriptive summaries by initial randomized groups (ABP 654 vs ustekinumab) will be provided for post week 28 timepoints in subjects with dose intensification.

Safety endpoints will be summarized descriptively in the Safety Analysis Set, consisting of all randomized subjects who received at least 1 dose of investigational product, based on the actual treatment received. In general, summaries will be provided separately from day 1 (first investigational product administration) until week 12, from day 1 until week 28, from week 28 through the end of the study (EOS), and from day 1 through the EOS. The summaries for day 1 through week 12 and day 1 through week 28 will be presented by treatment (ABP 654 vs ustekinumab). The summaries for week 28 through the EOS and day 1 through the EOS will be presented by treatment sequence (ABP 654/ABP 654, ustekinumab/ustekinumab, ustekinumab/ABP 654) for subjects who are re-randomized and treated post re-randomization. Safety data from week 28 through the EOS for subjects with dose intensification will be summarized separately by treatment (ABP 654 vs ustekinumab). All reported adverse events will be assigned the system organ class and preferred term according to the Medical Dictionary

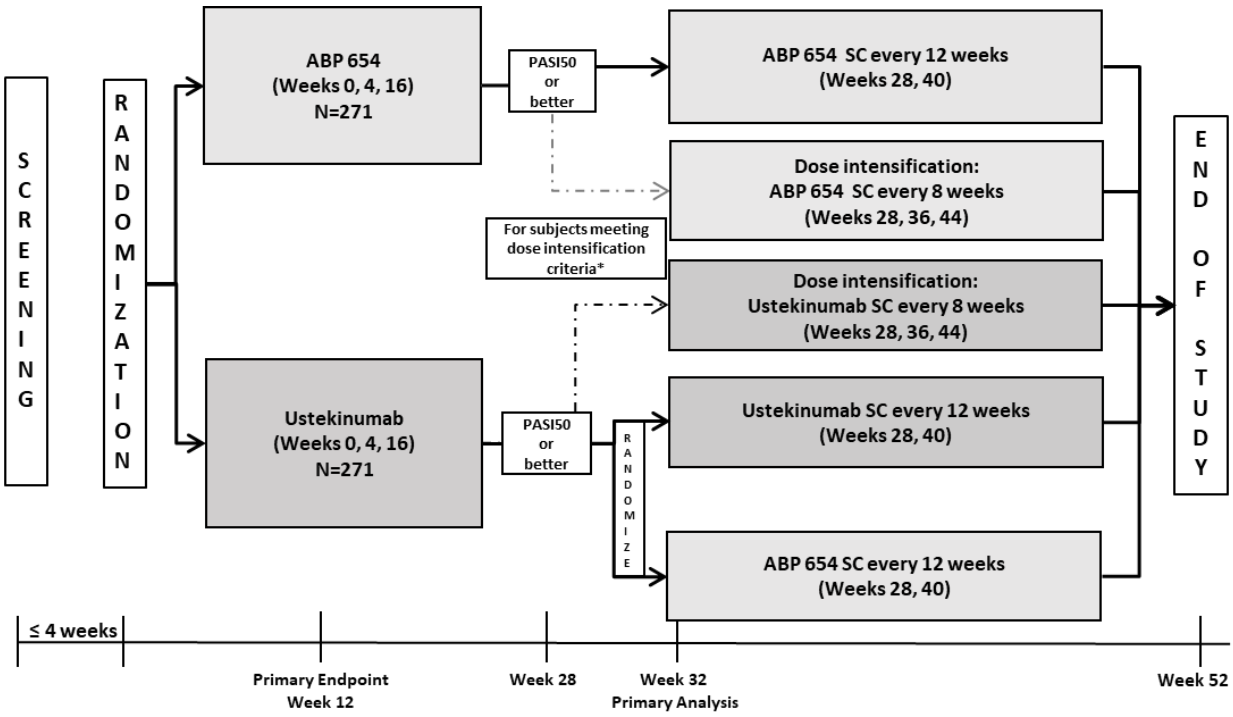
for Regulatory Activities (MedDRA) dictionary and graded by Common Terminology Criteria for Adverse Events (CTCAE; version 4.03). The number and percent of subjects reporting TEAEs, SAEs, and EOIs will be tabulated. The number and percent of subjects developing anti-drug antibodies will be tabulated by visit.

The primary analysis for the study will be performed when all subjects reach week 32 or terminate early. Final analysis will be performed when all subjects reach week 52 or terminate early. An independent DMC will evaluate the safety data throughout the study.

1.2 Study Schema

The study schema is provided in Figure 1-1.

Figure 1-1 Study Schema



- Subjects with body weight at baseline ≤100kg receive 45mg SC; >100kg receive 90 mg SC
- At week 28, non-responders (ie, subjects not achieving PASI 50 response of better) will be considered to have completed the study and will complete the end of study procedures (ie, week 52 procedures) at week 28. Subjects missing the week 28 visit or missing the PASI assessment at week 28, will be discontinued from the study.
- *For subjects with PASI 50 response or better but less than PASI 75 response at week 28, based on investigator's discretion, subjects may increase dose frequency to every 8 weeks (Q8W). Subjects with body weight at baseline ≤ 100kg will receive 45mg Q8W and subjects > 100kg at baseline will receive 90mg Q8W at weeks 28, 36, and 44. These subjects will continue on original treatment and will NOT be re-randomized.

PASI = Psoriasis Area and Severity Index; Q8W = every 8 weeks; Q12W = every 12 weeks; SC = subcutaneous

1.3 Schedule of Assessments

The Schedule of Assessments (SoA) is provided in Table 1-1. The SoA for Dose Intensification Subjects (Q8W) is provided in Table 1-2.

Table 1-1 Schedule of Assessments

	Screening	Baseline	Week (± 3 days)[g]		Week (± 5 days)[g]				End of Study [d] (± 5 days)
Study Visit-Week	≤ 28 days	Day 1/ Week 0	4	12	16	28	32	40	52
Informed consent	X								
Medical / medication history	X								
Physical examination	X	X							X
Height	X	X							
Body weight	X	X	X		X	X			X
Vital signs	X	X	X	X	X	X	X	X	X
Adverse events	X[a]	X	X	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X	X	X
Disease assessments									
PASI / sPGA / BSA	X	X	X	X	X	X		X	X
Laboratory assessments									
Tuberculosis Testing	X								
TB Worksheet	X[b]								
Chest X-ray	X[c]								
Serum pregnancy test	X								
Serology (HBsAg, HCV)	X								
Urine pregnancy test		X	X	X	X	X	X	X	X
Hematology	X	X		X		X	X	X	X
Chemistry	X	X		X		X	X	X	X
Urinalysis	X	X		X		X	X	X	X
Pharmacokinetics		X	X	X		X	X	X	X
Anti-drug antibodies		X	X	X		X	X	X	X

Investigational Product									
Randomization		X				X			
IP Administration [e]		X	X		X	X[f]		X	

Table 1-2 Schedule of Assessments for Dose Intensification Subjects (Q8W)

	Week (± 5 days)[g]				End of Study [d] (± 5 days)
Study Visit-Week	**28**	**32**	**36**	**44**	**52**
Physical examination					X
Body weight	X				X
Vital signs	X	X	X	X	X
Adverse events	X	X	X	X	X
Concomitant medications	X	X	X	X	X
Disease assessments					
PASI / sPGA / BSA	X		X	X	X
Laboratory assessments					
Urine pregnancy test	X	X	X	X	X
Hematology	X	X	X	X	X
Chemistry	X	X	X	X	X
Urinalysis	X	X	X	X	X
Pharmacokinetics	X	X			X
Anti-drug antibodies	X	X			X
Investigational Product					
IP Administration [e]	X		X	X	

BSA = body surface area; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus antibody; IP = investigational product; PASI = Psoriasis Area and Severity Index; PPD = purified protein derivative; sPGA = static Physician's Global Assessment; TB = tuberculosis.
[a]Report SAEs that occur after signing informed consent form. Non-serious AEs are reported as medical history prior to randomization.
[b]Only for subjects with a positive tuberculosis test (ie, positive PPD or positive or indeterminate Quantiferon®/T-spot®)
[c]Prior radiography or formal reports signed off by a radiologist within 3 months of screening is acceptable.
[d]Subjects who missed week 28 visit or terminated early from the study should complete all procedures scheduled for week 52 within 28 days after withdrawal/discontinuation if possible. Subjects not achieving PASI 50 at week 28 will be considered to have completed the study and will complete end of study procedures (ie, week 52 procedures) at week 28.
[e]ABP 654/ ustekinumab will be administered after all other procedures are completed for each dosing visit.
[f]For subjects requiring dose intensification, refer to separate schedule of assessment above for week 28 to week 52 procedures.
[g]Dosing should be delayed if subject has a serious infection (up to 3 days for weeks 4 and 12, and up to 5 days for subsequent visits). Refer to protocol Section 6.5 for details.

2 Introduction

ABP 654 is a biosimilar candidate to Stelara® (ustekinumab) which is an interleukin (IL)-12 and IL-23 antagonist.

The term "investigational product" throughout the protocol, refers to ABP 654 or ustekinumab.

2.1 Study Rationale

Amgen is developing ABP 654 as a biosimilar candidate to Stelara® (ustekinumab). ABP 654 and ustekinumab belong to the pharmacologic class of IL-12 and IL-23 antagonists. The mechanism of action across indications involves the ustekinumab protein molecule binding with specificity to the p40 protein subunit used by both the IL-12 and IL-23 cytokines. This binding disrupts IL-12 and IL-23 mediated signaling and cytokine cascades by disrupting the interaction of these cytokines with a shared cell-surface receptor chain, IL-12 receptor subunit beta 1 (IL-12Rβ).

In the US, ustekinumab is approved for the SC administration in the treatment of moderate to severe plaque psoriasis (Ps) in adults and adolescent subjects (12 years or older), and active psoriatic arthritis (PsA) in adults, as well as maintenance dosing for adult patients with moderate to severe active Crohn's disease and moderate to severe active ulcerative colitis; ustekinumab is also approved for the intravenous (IV) route of administration in the treatment of moderate to severe active Crohn's Disease (CD) in adults and moderate to severe active ulcerative colitis in adults (Stelara® United States Prescribing Information [USPI], March 2020). In the EU, ustekinumab is approved for SC administration in the treatment of moderate to severe Ps in adults and adolescent subjects (6 years or older) and PsA in adults. In the EU, ustekinumab is approved for the treatment of the above indications with the exception that pediatric patients with moderate to severe plaque psoriasis are considered for treatment if 6 years or older (Stelara® Summary of Product Characteristics [SmPC], February 2020).

A biosimilar product, generally, is one that is highly similar to a licensed biologic reference product, and there are no clinically meaningful differences between the biosimilar and reference products in terms of safety, purity, and potency. Biosimilarity is demonstrated by the totality of the evidence, including quality, nonclinical, and clinical evidence. The quality and nonclinical data for ABP 654 and ustekinumab are summarized in the Investigator's Brochure.

2.2 Background

ABP 654 is designed to have an identical primary amino acid sequence, the same primary mechanism of action, and the same biological and functional characteristics as ustekinumab.

ABP 654 has the same dosage forms (solution for injection), product strength, and formulation as ustekinumab (US and EU).

The totality of evidence available from an ongoing analytical program suggests that ABP 654 is analytically similar to ustekinumab with respect to its physicochemical properties and biological activities, except for minor differences expected from cell line changes; these minor differences are not expected to be clinically meaningful. Both ABP 654 and ustekinumab have the same amino acid sequence. ABP 654 and ustekinumab (US and EU) have similar in vitro binding to IL-23, IL-12, and neonatal fragment crystallizable receptor (FcRn), similar inhibition of IL-23 and IL-12, and similar binding kinetics and affinity to IL-23 and IL-12. Effector functions (ADCC and CDC) towards cells expressing IL-12 and/or IL-23 receptors are not expected to occur with ABP 654 and ustekinumab. The lack of ADCC was confirmed when ABP 654 and ustekinumab were tested for effector functions using human IL-12 expressing U937 cells. Lack of CDC activity is currently being investigated.

Refer to the Investigator's Brochure for more information.

As of the date of this protocol, ABP 654 has not been tested in humans. This Study 20190232 is being conducted to demonstrate that there is no clinically meaningful difference between ABP 654 and ustekinumab in terms of efficacy, safety, and immunogenicity in adult subjects with moderate to severe plaque psoriasis. Based on the analytical similarity of ABP 654 and ustekinumab established to date, clinical experience with ustekinumab is deemed relevant to predicting the effects of ABP 654 in humans and is summarized in the following paragraphs. A separate study, Study 20190230, is being conducted to evaluate the single dose pharmacokinetics (PK), safety, tolerability, and immunogenicity of ABP 654 (90 mg SC injection) compared to ustekinumab (US and EU) in healthy subjects.

Ustekinumab has been investigated in a number of clinical trials and for a number of different indications. In healthy subjects, the median time of maximum concentration (T_{max}) value following a single SC administration of 90 mg of ustekinumab was comparable to subjects with psoriasis. The maximum observed concentration (C_{max}) and area under the concentration-time curve (AUC) in healthy subjects was higher than values seen in subjects with psoriasis. This is likely attributed to differing PK sampling schedules between the 2 studies, differences in BW between the 2 populations, or increased IL-12/IL-23 binding target concentrations in subjects with psoriasis. In healthy subjects following a single 90 mg SC dose, the apparent volume of distribution was 90.2 mL/kg and the terminal half-life ($t_{1/2}$) was 22.1 days with an apparent systemic clearance of 3.1 mL/day/kg (BLA 125261 Clinical Pharmacology and Biopharmaceutics Review, 2009).

In subjects with plaque psoriasis, exposure increased in an approximately dose proportional manner after a single SC administration at doses range from 0.27 mg/kg to 2.7 mg/kg. Serum concentrations of ustekinumab were higher in the group receiving the 90 mg dose, as opposed to the 45 mg dose. However, when comparing the difference among the 2 groups dose proportionality was also shown. Assessment of intrinsic factors including BW, age, and sex were performed. When given the same dose of ustekinumab, subjects that weighed > 100 kg had lower median serum ustekinumab concentrations compared with those subjects weighing ≤ 100 kg. Subgroup analysis showed that age, sex, and race had no effects on clinical response (Stelara® USPI, March 2020; BLA 125261 Clinical Pharmacology and Biopharmaceutics Review, 2009).

The clinical efficacy and safety information for ustekinumab as described in the product labeling for Stelara® (Stelara® USPI, March 2020; Stelara® SmPC, February 2020) are considered relevant to predicting the effects of ABP 654 in humans. When ustekinumab was administered to subjects with plaque psoriasis in clinical studies, subjects had a reduction in disease as measured by PASI score (≥ 75% improvement in PASI [PASI 75]) from baseline to week 12 and treatment success (cleared or minimal) on the Physician's Global Assessment (PGA) as compared with the placebo arm. Adverse events reflected in the warnings and precautions section of the product labeling for ustekinumab that may be serious include bacterial, fungal, and viral infections including tuberculosis, malignancies, hypersensitivity reactions, reversible posterior leukoencephalopathy syndrome, and noninfectious pneumonia.

2.3 Benefit/Risk Assessment

ABP 654 is expected to be biosimilar to ustekinumab. The risks and benefits of ABP 654 are therefore expected to be the same as those of ustekinumab, as specified in the product labeling. All subjects in this study will receive an active treatment.

More detailed information about the expected benefits, risks, and reasonably expected adverse events of ABP 654 can be found in the Investigator's Brochure.

Considering the measures taken to minimize risk to subjects participating in this study, the potential risks identified in association with ABP 654 are justified by the anticipated benefits to subjects with moderate to severe plaque psoriasis.

A risk assessment will be performed on an ongoing basis to evaluate the potential impact of coronavirus disease 2019 (COVID-19) on subjects. Risk mitigation measures, including COVID-19 related precautions and procedures (including severe acute respiratory syndrome coronavirus [SARS-CoV-2] testing/screening) will be implemented based on the prevailing

situation during study conduct, at the investigator's discretion and in accordance with local and institutional guidelines as applicable.

3 Objectives and Endpoints

Objects and endpoints are described in Table 3-1.

Table 3-1 Objectives and Endpoints

Objectives	Endpoints
Primary: To compare the efficacy of ABP 654 with ustekinumab in subjects with moderate to severe plaque psoriasis.	**Primary Efficacy Endpoint:** • Psoriasis area severity index (PASI) percent improvement from baseline to week 12
Secondary: To assess the safety and immunogenicity of ABP 654 compared with ustekinumab.	**Secondary Efficacy Endpoint:** • PASI percent improvement at other timepoints • PASI 75 response throughout the study • PASI 100 response throughout the study • Static Physician's Global Assessment (sPGA) responses (0/1) at week 12 and week 52 • Body surface area (BSA) change from baseline at week 12 and week 52 **Safety Endpoints:** • TEAEs and SAEs • EOIs • Incidence of anti-drug antibodies

4 Study Design

4.1 Overall Design

This is a randomized, double-blind, active-controlled phase 3 study in adult subjects with moderate to severe plaque psoriasis. This study is planned to be conducted globally at sites in North America and Europe.

Approximately 542 adult subjects will be randomized (approximately 271 in the ABP 654 group and approximately 271 in the ustekinumab group). See Section 8.3 for sample size determination. Randomization will be stratified based on prior biologic use for psoriasis (yes versus [vs] no (no more than 50% of the total randomized subjects will have prior biologic use

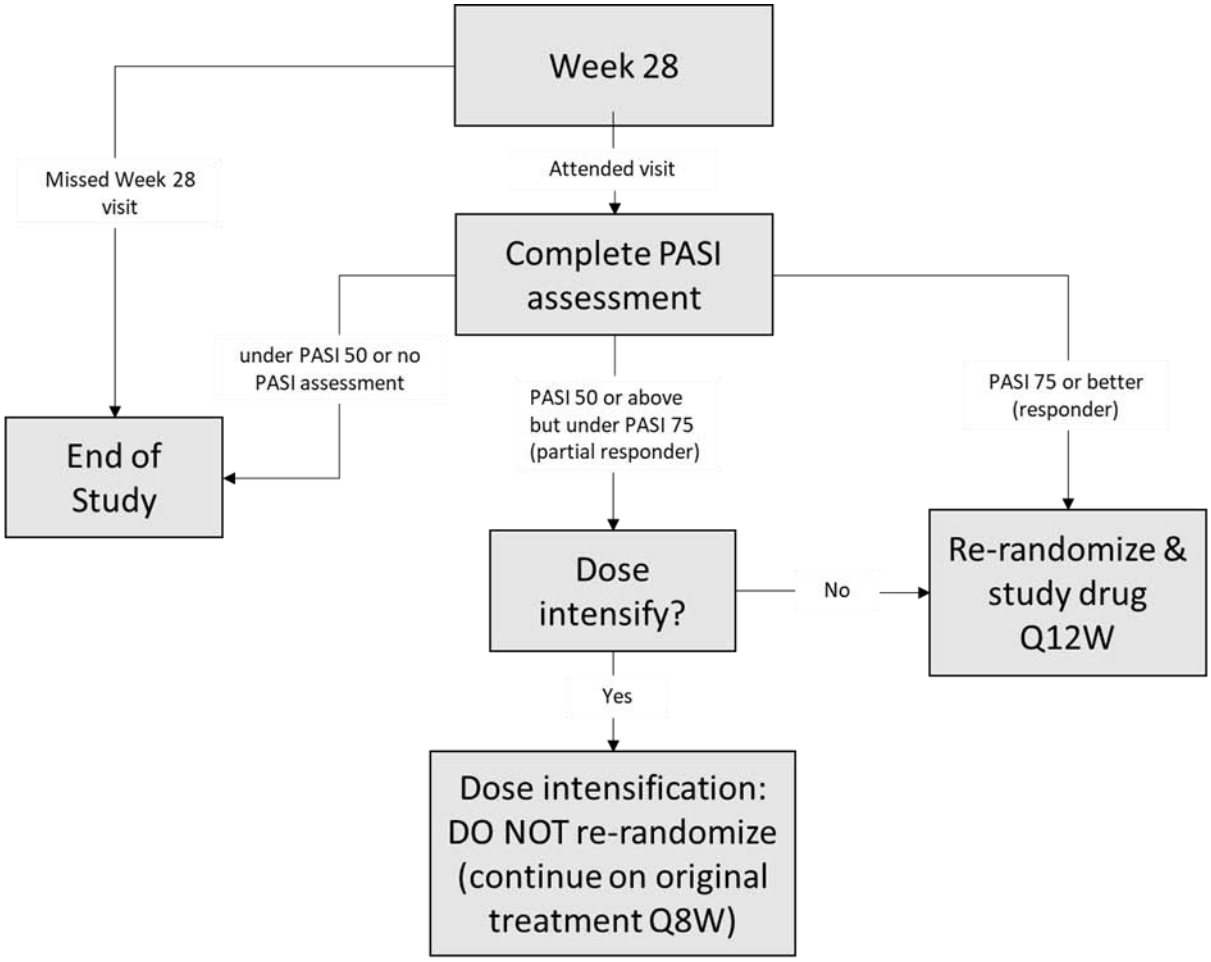
for psoriasis), baseline BW (≤ 100 kg vs > 100 kg), and geographic region. Subjects will be randomized (1:1) to Treatment Group A (ABP 654) or Treatment Group B (ustekinumab). Subjects will receive ABP 654 or ustekinumab at a dose of 45 mg (baseline BW ≤ 100 kg) or 90 mg (baseline BW > 100 kg) administered SC on day 1 (week 0), week 4, and week 16. The primary endpoint (PASI percent improvement from baseline to week 12) will be evaluated at week 12.

At week 28, subjects who do not achieve a PASI 50 response or better improvement will be considered to have completed the study and will complete end of study procedures (ie, week 52 procedures), and those unable to complete the week 28 visit, or did not have a PASI assessment completed, will be discontinued from the study (see Figure 4-1).

Subjects with a PASI 75 response or better improvement will continue on the study and will be re-randomized in a blinded fashion such that subjects initially randomized to Group A (ABP 654) will continue to receive ABP 654 and those in Group B (ustekinumab) will re-randomized, using the same stratification factors as the original randomization, 1:1 to either continue on ustekinumab (Treatment Group B1) or switch to ABP 654 (Treatment Group B2). Subjects will receive investigational product at week 28 and the last dose of investigational product at week 40.

For subjects with PASI 50 response or better but less than PASI 75 response at week 28, based on the Investigator's discretion, the dose frequency may be increased to Q8W. Subjects with baseline BW ≤ 100 kg will receive 45 mg Q8W and subjects > 100 kg at baseline will receive 90 mg Q8W at weeks 28, 36, and 44. These subjects will continue on the originally assigned treatment with dose intensification and will not be re-randomized. Subjects that do not dose intensify will be re-randomized.

Figure 4-1 Week 28 Decision Tree Diagram



Abbreviations: PASI = psoriasis area severity index; Q8W = every 8 weeks; Q12W = every 12 weeks

Efficacy endpoints will include PASI percent improvement from baseline at week 12, PASI percent improvement at other timepoints, PASI 75 and PASI 100 response throughout the study, sPGA response (0/1) at week 12 and week 52, and body surface area (BSA) change from baseline at week 12 and week 52. The sPGA scale is described in Section 9.3 (Appendix 3). Safety endpoints will include treatment-emergent adverse events (TEAEs), SAEs, EOIs, and incidence of anti-drug antibodies. Blinded data will be monitored on an ongoing basis by the clinical study team to ensure subjects' safety.

The study design is presented in Figure 1-1 and the SoA is presented in Section 1.3. The study will consist of a screening period (≤ 4 weeks), a 52-week treatment period, and an EOS visit at week 52.

The planned duration of the clinical study is approximately 56 weeks for screening, randomization, treatment, and completion.

No interim analyses are planned. The primary analysis for the study will be performed when all subjects reach week 32 or terminate early. Final analysis will be performed when all subjects reach week 52 or terminate early.

A DMC will meet to review unblinded data to monitor safety based on the DMC Charter at specified time intervals throughout the study.

This study is double-blinded to minimize bias on the part of the subjects, Investigators, and the sponsor/contract research organization (CRO).

4.2 Scientific Rationale for Study Design

ABP 654 is being developed globally as a biosimilar to the reference product ustekinumab. Accordingly, ustekinumab was chosen as the control group. Analytical similarity has already been demonstrated between ABP 654 and ustekinumab as outlined in Section 2.2.

In the current study, clinical similarity is being evaluated in subjects with moderate to severe plaque psoriasis globally.

4.2.1 Subject Input into Design

Not applicable.

4.3 Justification for Dose

The dose (45 mg or 90 mg, which is based on baseline BW) is the approved psoriasis dosing regimen for ustekinumab (US and EU) for which ABP 654 is being tested for similarity. See Section 6.5 for Dose Modifications.

4.4 End of Study Definition

A subject is considered to have completed the study if he/she has completed all phases of the study including an EOS visit or the last scheduled procedure shown in the SoA.

The EOS is defined as the date of the last visit of the last subject in the study or last scheduled procedure shown in the SoA for the last subject in the trial globally.

5 Study Population

The study population will consist of adult subjects including men and women between 18 to 75 years of age with moderate to severe plaque psoriasis. Subjects must be able to provide written consent and meet all the inclusion criteria and none of the exclusion criteria.

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

5.1 Inclusion Criteria

Subjects cannot be randomized before all inclusion criteria (including test results) are confirmed.

Subjects are eligible to be included in the study only if all of the following criteria apply:

1. Men and women ≥ 18 years and ≤ 75 years of age at the time of randomization
2. Stable moderate to severe plaque psoriasis for at least 6 months (eg, no morphology changes or significant flares of disease activity in the opinion of the Investigator)
3. Baseline score of PASI ≥ 12, involvement of ≥ 10% BSA, and sPGA ≥ 3 at screening and at baseline
4. Candidate for phototherapy or systemic therapy
5. Previous failure, inadequate response, intolerance, or contraindication to at least 1 conventional anti-psoriatic systemic therapy (eg, methotrexate, cyclosporine, psoralen plus ultra-violet light [PUVA])
6. For women (except those at least 2 years postmenopausal or surgically sterile): a negative serum pregnancy test during screening and a negative urine pregnancy test at baseline
7. Signed Institutional Review Board/Ethics Committee (IRB/IEC)-approved informed consent and able to complete study procedures
8. No known history of latent or active TB. Subject must meet any 1 of the following 3 criteria:
    - Subject has a negative test for tuberculosis during screening, defined as either:

- Negative purified protein derivative (PPD; < 5 mm of induration at 48 to 72 hours after test is placed) OR
- Negative Quantiferon®/T-spot test

- Subjects with a positive PPD and a history of Bacillus Calmette-Guérin vaccination are allowed with a negative Quantiferon®/T-spot®
- Subjects with a positive PPD test (without a history of Bacillus Calmette-Guérin [BCG] vaccination) or subjects with a positive or indeterminate Quantiferon®/T-spot test are allowed if they have all of the following:
  - No symptoms per tuberculosis worksheet provided by the sponsor, Amgen
  - Documented history of adequate prophylaxis initiation prior to receiving investigational product in accordance with local recommendations
  - No known exposure to a case of active TB after most recent prophylaxis
  - No evidence of active TB on chest radiograph within 3 months prior to the first dose of investigational product

5.2 Exclusion Criteria

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

Skin disease related conditions

1. Erythrodermic psoriasis (PsO), pustular PsO, guttate PsO, medication induced PsO, or other skin conditions at the time of the screening visit (eg, eczema) that would interfere with evaluations of the effect of investigational product on PsO

Other medical conditions

2. Subject has a planned surgical intervention during the duration of the study
3. Subject has an active infection or history of infections as follows:
   a. Any active infection for which systemic anti-infectives were used within 28 days prior to randomization
   b. A serious infection, defined as requiring hospitalization or intravenous anti-infectives within 8 weeks prior to randomization

c. Recurrent or chronic infections or other active infection that, in the opinion of the Investigator, might cause this study to be detrimental to the subject

4. Known history of human immunodeficiency virus (HIV)
5. Hepatitis B surface antigen (HbsAg) or HCV antibody positivity at screening
6. Uncontrolled, clinically significant systemic disease such as uncontrolled diabetes mellitus, cardiovascular disease, renal disease, liver disease, or hypertension
7. Known malignancy within the previous 5 years (except treated and considered cured cutaneous squamous or basal cell carcinoma, in situ cervical cancer, OR in situ breast ductal carcinoma)
8. Active neurological disease such as multiple sclerosis, Guillain-Barre syndrome, optic neuritis, transverse myelitis or history of neurologic symptoms suggestive of central nervous system demyelinating disease
9. Moderate to severe heart failure (New York Heart Associate [NYHA] class III/IV)
10. Known hypersensitivity to the investigational product or to any of the excipients
11. Any concurrent medical condition that, in the opinion of the Investigator, could cause this study to be detrimental to the subject

Laboratory abnormalities

12. Laboratory abnormalities at screening, including any of the following:
    a. Hemoglobin < 9 g/dL
    b. Platelet count < 100,000/mm^3
    c. White blood cell count (WBC) < 3,000 cells/mm^3
    d. Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) ≥ 2.0 × the upper limit of normal (ULN)
    e. Creatinine clearance < 50 mL/min (Cockcroft-Gault formula)
    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

Washouts and non-permitted drugs

13. Previous treatment with any agent specifically targeting IL-12 or IL-23

14. Received biologic treatment for psoriasis within the previous month or 5 drug half-lives (whichever is the longer) prior to randomization
15. Received any investigational agents within the previous month or 5 drug half-lives (whichever is the longer) prior to randomization
16. Received non-biologic systemic psoriasis therapy within 4 weeks prior to randomization (including but not limited to oral retinoids, methotrexate, cyclosporine, systemically administered calcineurin inhibitors, azathioprine, thioguanine, hydroxyurea, fumarates, mycophenolate mofetil, Janus kinase (JAK) inhibitors, or oral or parenteral corticosteroids including intramuscular or intraarticular administration [exception: ophthalmic, otic, nasal, or inhaled corticosteroids within recommended doses is permitted])
17. Received Ultra-violet A (UVA) phototherapy (with or without psoralen) or excimer laser within 4 weeks prior to randomization, or ultra-violet B (UVB) phototherapy within 2 weeks prior to randomization
18. Received topical psoriasis treatment within 2 weeks prior to randomization (exception: upper mid-strength to least potent [class III to VII] topical steroids permitted on the palms, soles, face, and intertriginous areas; bland emollients [without urea or α– or β–hydroxy acids])
19. Received live viral or live bacterial vaccination within 2 weeks prior to randomization
20. Received BCG vaccination within 1 year prior to randomization
21. Other investigational procedures within 4 weeks prior to randomization and during the study

General

22. Active substance abuse within 24 weeks prior to randomization
23. For women: pregnant or breast feeding, or planning to become pregnant while participating in the study and for at least 15 weeks after the last dose of investigational product
24. Sexually active subjects and their partners who are of childbearing potential (ie, neither surgically nor postmenopausal) and not agreeing to use adequate contraception (eg, true abstinence, sterilization, birth control pills, Depo-Provera injections, or contraceptive implants) while on study and for 5 months after the last dose of investigational product. Male subjects must agree not to donate sperm during the study and for 5 months following the treatment with test article or until the scheduled EOS (whichever is longer)

25. Subject likely not to be available to complete all protocol-required study visits or procedures, and/or to comply with all required study procedures (eg, Clinical Outcome Assessments) to the best of the subject and Investigator's knowledge
26. Any physical or psychiatric disorder that, in the opinion of the Investigator, may compromise the ability of the subject to give informed consent and/or to comply with all required study procedures

5.3 Subject Enrollment

Before subjects begin participation in any study-specific activities/procedures, Amgen requires a copy of the site's written IRB/IEC approval of the protocol, informed consent form (ICF), and all other subject information and/or recruitment material.

The subject must personally sign and date the IRB/IEC and Amgen approved ICF before commencement of study-specific procedures.

A subject is considered enrolled when the Investigator decides that the subject has met all eligibility criteria and has been randomized in the Interactive Web/Voice Response System (IXRS). The Investigator is to document this eligibility decision and date in the subject's medical record.

Each subject will have a unique subject identification number obtained from the IXRS. This will be assigned at the screening visit. The unique 11-digit subject identification will be assigned in sequential order for each site in the format "232XXXXX###," where "232XXXXX" refers to the site number and "###" refers to the sequential subject ordering as each subject at a site is entered into the IXRS (eg, 23212345001). This number will be used to identify the subject throughout the clinical study and must be used on all study documentation related to that subject. The Investigator will keep a record (the subject screening log) that includes limited information (such as date of screening) about the potential candidates for subjects who entered screening.

If a subject withdraws from study participation, his/her unique identification number(s) cannot be re-used for another subject.

The subject identification number must remain constant throughout the entire clinical study; it must not be changed after initial assignment, including if a subject is rescreened. This number will not necessarily be the same as the randomization number assigned for the study.

5.4 Lifestyle Considerations

COVID-19 Considerations

Sites and subjects will follow local and institutional guidelines as applicable for prevention of COVID-19 infection. In the event that a subject experiences any signs/symptoms of COVID-19, the subject should promptly notify the Investigator.

5.4.1 Meals and Dietary Restrictions

Not applicable.

5.4.2 Caffeine, Alcohol, and Tobacco

Not applicable.

5.4.3 Activity

Not applicable.

5.5 Screen Failures

Screen failures are defined as subjects who consent to participate in the clinical study but are not subsequently randomly assigned to study intervention. A minimal set of screen failure information is required to ensure transparent reporting of screen failure subjects to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, reason for screen failure (eg, eligibility requirements failed), and any SAEs.

If a subject has not met all eligibility criteria at the end of the screening period, the subject will be registered as a screen fail. Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened. Rescreened subjects should be assigned the same subject identification number as for the initial screening. Laboratory assessments used to determine subject eligibility may be repeated during the screening period before the subject is considered a screen failure. Screen failed subjects may be rescreened up to 2 times at the Investigator's discretion (ie, a total of 3 screens including initial screening). If screening procedures cannot be completed within 28 days before day 1, the subject will be considered a screen failure but may be eligible for rescreening. These subjects can be rescreened under the same ICF if rescreening and randomization occurs within 30 days of initial consent date. If it is longer than 30 days from the initial consent, the subject will need to be re-consented and all screening procedures need to be repeated.

5.6 Premature Discontinuation

Subjects have the right to withdraw from treatment with investigational product, protocol procedures, or the study completely at any time and for any reason without prejudice to their future medical care by the physician or at the institution.

5.6.1 Premature Discontinuation of Investigational Product or Procedures

Subjects (or a legally acceptable representative) can decline to continue receiving investigational product or procedures at any time during the study but continue participation in the study. If this occurs, the Investigator is to discuss with the subject the appropriate processes for discontinuation from investigational product and must discuss with the subject the possibilities for continuation of the SoA (Section 1.3) including different options of follow-up (eg, in person, by phone/mail, through family/friends, in correspondence/communication with other treating physicians, from the review of medical records) and collection of data, including AEs, and must document this decision in the subject's medical records. Subjects who have discontinued investigational product and/or other protocol-required therapies or procedures should not be automatically removed from the study. Whenever safe and feasible, it is recommended that these subjects remain on study to ensure safety surveillance and/or collection of efficacy data, where possible. Reasons for early removal from protocol-required investigational product(s) or procedural assessments may include:

- Decision by sponsor
- Lost to follow-up
- Death
- Adverse event
- Subject request
- Protocol deviation
- Noncompliance
- Pregnancy

5.6.2 Withdrawal/Discontinuation of Subjects from the Study

Participation in the study is strictly voluntary. Subjects have the right to withdraw from the study by his/her own request at any time and for any reason without any reprisal, and without prejudice to future medical care by the physician or institution.

Subjects who are unable to complete week 28 visit will not be re-randomized, will be discontinued from the study, and will be asked to return to complete an EOS visit within 28 days from determining that the subject will discontinue from the study.

Subjects not achieving PASI 50 at week 28 will be considered to have completed the study and will complete end of study procedures (ie, week 52 procedures) at week 28.

Subjects terminating early from the study should complete all procedures scheduled for week 52 within 28 days after withdrawal/discontinuation if possible.

Withdrawal of consent for a study means that the subject does not wish to receive further protocol-required therapies or procedures, and the subject does not wish to or is unable to continue further study participation. Subject data up to withdrawal of consent will be included in the analysis of the study, and where permitted, publicly available data can be included after withdrawal of consent. The Investigator is to discuss with the subject appropriate procedures for withdrawal from the study, and must document the subject's decision to withdraw in the subject's medical records. If the subject withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent. If a subject withdraws from the study, he/she may request destruction of any samples taken and not tested, and the Investigator must document this in the study center study records and notify the sponsor or designee. Although a subject is not obliged to give his/her reason(s) for withdrawing prematurely from a study, the Investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights. Subjects who are withdrawn will not be replaced. Subjects who prematurely discontinue from the study cannot subsequently rejoin the study.

A subject may be discontinued from the study at any time at the discretion of the Investigator for safety, behavioral, or administrative reasons, including, but not limited to:

- Requirement for alternative therapy or alternative dosing schedule per the Investigator's determination
- The subject develops a malignancy. (Exception: Subjects may be allowed to continue if they develop no more than 2 non-melanoma skin cancers during the study)
- AEs or SAEs
- Any laboratory abnormalities that in the judgment of the Investigator, taking into consideration the subject's overall status, prevents the subject from continuing participation in the study

- Any other reason relating to the subject's safety or integrity of the study data
- Noncompliance with study procedures
- Withdrawal of consent from the study
- Lost to follow-up
- Decision by sponsor/investigator
- Death

Refer to the SoA (Section 1.3) for data to be collected at the time of study discontinuation and evaluations that need to be completed.

If a subject withdraws or is discontinued from the study, the Clinical Research Associate (CRA) will be informed immediately.

5.6.2.1 Premature Discontinuation of the Study

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the Investigators, the IRBs/IECs, the regulatory authorities, and any CRO(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The Investigator shall promptly inform the subjects and should assure appropriate subject therapy and/or follow-up.

5.6.3 Dose Delay

Dose delay may be considered if the subject meets one of the specified conditions in Section 6.5.

5.6.4 Lost to Follow-up

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

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

- The study center must attempt to contact the subject and reschedule the missed visit as soon as possible, counsel the subject on the importance of maintaining the assigned visit schedule, and ascertain whether or not the subject wishes to and/or should continue in the study

- Before a subject is deemed lost to follow-up, the Investigator (or designee) must make every effort to regain contact with the subject (where possible, 3 telephone calls and, if necessary, a certified letter to the subject's last known mailing address or local equivalent methods). These contact attempts should be documented in the subject notes
- Should the subject continue to be unreachable, he/she will be considered to have withdrawn from the study with a primary reason of lost to follow-up

6 Treatments

6.1 Investigational Product(s)

The Investigator must ensure that the investigational product will be used only in accordance with the protocol. Study treatments and investigational products are described below and in Table 6-1.

Subjects will be initially randomly assigned to 1 of 2 treatment groups to receive a dose of either ABP 654 or ustekinumab, as follows:

- Treatment Group A: ABP 654, SC injection, 45 mg (baseline BW ≤ 100 kg) or 90 mg (baseline BW > 100 kg) at weeks 0, 4, and 16
- Treatment Group B: Ustekinumab, SC injection, 45 mg (baseline BW ≤ 100 kg) or 90 mg (baseline BW > 100 kg) at weeks 0, 4, and 16

At week 28, subjects with a PASI 50 response or better may then be subsequently re-randomized to receive either ustekinumab (SC, Q12W) or ABP 654 (SC, Q12W), as follows:

- Treatment Group A (ABP 654): Will continue to receive ABP 654 Q12W at weeks 28 and 40
- Treatment Group B (ustekinumab): Will be re-randomized 1:1 to either continue on ustekinumab Q12W at weeks 28 and 40 (Treatment Group B1) or switch to ABP 654 Q12W at weeks 28 and 40 (Treatment Group B2)

At the Investigator's discretion, subjects from Group A and Group B who achieve PASI 50 response or better, but do not achieve PASI 75 response or better may receive dose intensification Q8W at weeks 28, 36, and 44. These subjects will remain on their original treatment and will not be re-randomized.

In all treatment groups, doses will be administered SC with doses administered based on baseline BW (45 mg for baseline BW ≤ 100 kg or 90 mg for baseline BW > 100 kg).

Investigational product will be administered by authorized, licensed healthcare professionals. The investigation product will be administered using SC injection according to standard practice. It is recommended that each injection be administered at a different anatomic location (such as upper arms, gluteal regions, thighs, or any quadrant of abdomen) than the previous injection, and not into areas where the skin is tender, bruised, erythematous, or indurated.

Table 6-1 Study Investigation(s) Administered

Group Name:	ABP 654	Ustekinumab
Type:	Biologic[a]	Biologic[a]
Dosage Formulation:	Liquid suspension	Liquid suspension
Unit Dose Strength(s):	45 mg/0.5 mL solution in a single dose prefilled syringe for subjects with baseline BW ≤ 100 kg 90 mg/mL solution in a single dose prefilled syringe for subjects with baseline BW > 100 kg	45 mg/0.5 mL solution in a single dose prefilled syringe for subjects with baseline BW ≤ 100 kg 90 mg/mL solution in a single dose prefilled syringe for subjects with baseline BW > 100 kg
Dosage Level(s):	Dose based on baseline BW: • 45 mg (≤ 100 kg) • 90 mg (> 100 kg)	Dose based on baseline BW: • 45 mg (≤ 100 kg) • 90 mg (> 100 kg)
Route of Administration:	SC injection	SC injection
Sourcing:	Provided centrally by the sponsor	Provided centrally by the sponsor
Packaging and Labeling:	Study Intervention will be provided in a PFS. Each PFS will be labeled as required per country requirement.	Study Intervention will be provided in a PFS. Each PFS will be labeled as required per country requirement.

BW = body weight; PFS = pre-filled syringe; Q8W = every 8 weeks; Q12W = every 12 weeks; SC = subcutaneous.

[a] recombinant fully human IgG1κ monoclonal antibody produced by recombinant DNA technology.

6.1.1 ABP 654 Dosage Form

ABP 654 is a recombinant fully human IgGκ monoclonal antibody produced by recombinant DNA technology and is produced in a glyco-engineered Chinese hamster ovary cell line. ABP 654 is purified by processes that include specific viral inactivation and filtration steps. ABP 654 and ustekinumab have the same amino acid sequence.

ABP 654 is supplied as a sterile, single dose, preservative-free solution for SC injection and is supplied in a prefilled syringe (PFS) containing 45 mg/0.5 mL ABP 654 or 90 mg/mL ABP 654. The PFS is a 27-gauge fixed ½ inch needle and is fitted with a passive needle guard and a needle cover that contains dry natural rubber (a derivative of latex).

Each 0.5 mL PFS delivers 45 mg ABP 654, L-histidine and L-histidine monohydrochloride monohydrate, polysorbate 80, and sucrose. Each 1 mL PFS delivers 90 mg ABP 654, L-histidine and L-histidine monohydrochloride monohydrate, polysorbate 80, and sucrose. See the Investigator's Brochure for additional details.

6.1.2 Ustekinumab Dosage Form(s)

Ustekinumab is a recombinant fully human IgGκ monoclonal antibody produced by recombinant DNA technology, and is produced by an Sp2/0 cell line.

Ustekinumab is supplied in 45 mg/0.5 mL and 90 mg/mL single use PFS of Stelara®.

Each single-use PFS delivers 45 mg or 90 mg ustekinumab, L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, and sucrose.

6.1.3 Preparation, Handling, Storage, and Accountability

Study medication should be stored protected from light and according to the storage and expiration information provided on the label (where required) that is affixed to the package containing the investigational product. The PFS should be stored in a secured refrigerator (2° to 8°C) and monitored (manual or automated) in accordance with the labeled storage conditions and country-specific regulations, with access limited to the Investigator and authorized site staff. Study medication should not be frozen. The Investigator or designee must maintain documentation to confirm appropriate temperature conditions have been maintained during transit and storage at site for all study medication received and any discrepancies are reported and resolved before use of the study medication.

The PFS should be checked for cracks or damage that may occur during transport. Damaged product should not be administered and should be returned to Amgen or its designee.

Detailed information regarding the labeling, packaging, storage, preparation, and administration of each investigational product are to be provided separately in the Pharmacy Manual.

All supplies of study medication will be accounted for in accordance with GCP guidelines. There will be an individual investigational product accountability record for each subject and the Investigator, Pharmacist, or designee, should maintain accurate records of the disposition of all study medication supplies received during the study. These records should include the amounts and dates clinical drug supplies were received and returned to Amgen or its designee. If errors or damages in the clinical drug supply shipments occur, the Investigator should contact Amgen or its designee immediately. Copies of the study medication accountability records will be

provided by each Investigator for inclusion in the Trial Master File (TMF). The CRA will periodically check the supplies of study medication held by the Investigator or Pharmacist to verify accountability of all medication used.

The Investigator will administer the medication only to the identified subjects of this study, according to the procedures described in this study protocol. After the EOS, all unused medication and all medication containers should be destroyed on-site (if approved by the sponsor or designee) or returned to Amgen or its designee for destruction. In either instance, complete documentation will be returned to the sponsor or designee. Further guidance and information for the final disposition of unused study medication are provided in the Pharmacy Manual.

The investigational product resupply will be managed by the IXRS.

6.1.4 Product Complaints

A product complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a drug(s) or device(s) after it is released for distribution to market or clinic by either Amgen or by distributors and partners for whom Amgen manufactures the material.

Any product complaint(s) associated with an ABP 654 or ustekinumab supplied by Amgen are to be reported according to the instructions provided in the Pharmacy Manual. Any product complaints associated with an AE are to be reported as per AE reporting guidelines.

6.1.5 Prohibited Treatments

- Nonstudy use of ustekinumab, or therapies that target IL-12 or IL-23, are prohibited (Exclusion Criterion 13)
- Live viral or live bacterial vaccination. The study drug should be withheld for at least 15 weeks before vaccination and only resumed at least 2 weeks after vaccination
- Any biologic treatment for psoriasis, or any experimental (biological or nonbiological) therapy (within or outside of a clinical study), except for the investigational product, for subjects are prohibited (Exclusion Criteria 14 and 15)
- Treatments (Exclusion Criterion 16) which include non-biologic systemic psoriasis therapy (including but not limited to oral retinoids, methotrexate, cyclosporine, systemically administered calcineurin inhibitors, azathioprine, thioguanine, hydroxyurea, fumarates, mycophenolate mofetil, JAK inhibitors, or oral or parenteral corticosteroids

including intramuscular or intraarticular administration [exception: ophthalmic, otic, nasal, or inhaled corticosteroids within recommended doses is permitted])

- Any other nonstudy treatment for psoriasis, including UVA or UVB phototherapy and excimer laser (Exclusion Criterion 17) and topical therapies for psoriasis (except for those specifically allowed, Exclusion Criterion 18) are prohibited

6.2 Measures to Minimize Bias: Blinding and Randomization

6.2.1 Blinding

The study is double-blinded; therefore, the Investigators, study personnel with the exception of the Parexel unblinded biostatistician and unblinded programmers; and the DMC, and the study subjects will remain blinded to treatment allocation.

Randomization data will be kept strictly confidential, accessible only to authorized staff and the DMC until the time of unblinding. Authorized staff includes the randomization statistician, who will store the master randomization list in a secure system, an unblinded statistician, and unblinded programmers, who will provide the DMC with unblinded data for review, as and when required, in accordance with the procedures described in the DMC Charter. All authorized unblinded staff must be documented. Personnel unblinded for the primary analysis will not be subsequently involved in study management.

ABP 654 and ustekinumab will be coded and labeled in a manner that protects blinding.

Unblinding is only allowed in the case of an emergency, when knowledge of the investigational product is essential for the clinical management of the subject. The Investigator must make every effort to contact the sponsor or designee's medical monitor prior to breaking the blind and must contact the sponsor or designee within 1 working day after the event, without revealing to the sponsor (or CRO) the results of the code break, except to the designated global subject safety representative.

Emergency unblinding will be organized through the IXRS. The Investigator must record the date of unblinding and the reason. All unblinding must be adequately documented.

If a SAE is reported, the designated global subject safety representative may unblind the treatment assignment for the individual subject through IXRS in order to meet regulatory reporting requirements. Authorized staff will be provided with a unique Personal Identification Number (PIN) to access the IXRS to obtain blinding information. The PIN is unique to the individual and must not be shared.

6.2.2 Randomization

Upon completion of screening and confirming the subject met all eligibility criteria, the site will contact the IXRS to receive a unique subject randomization number in order to randomize the subject centrally to receive either ABP 654 or ustekinumab in a 1:1 manner. Randomization will be stratified according to the following factors: prior biologic use for psoriasis (yes vs no), baseline BW (≤ 100 kg vs > 100 kg), and geographic region. Subjects with prior biologic use will be capped at 50% of the total randomized subjects.

At week 28, subjects with PASI 50 or better improvement will be re-randomized 1:1 to receive either ustekinumab (SC, Q12W) or ABP 654 (SC, Q12W) (Section 4.1), using the same stratification factors as the original randomization. Each subject will receive a second randomization number when he/she is re-randomized.

In the event of a Quality Assurance audit, the auditor(s) will be allowed access to unblinded study intervention records at the site(s) to verify that randomization/dispensing has been done accurately.

6.3 Study Intervention Compliance

Records of study medication used and intervals between visits will be kept during the study. Drug accountability will be noted by the CRA during site visits and at the completion of the study. The study treatment should be dispensed by the Investigator, or by a qualified individual under the Investigator's supervision. An up-to-date treatment inventory/dispensing record must be maintained.

6.4 Prior and Concomitant Therapy

Prohibited treatments are described in Section 6.1.5.

Any other treatment (not explicitly excluded) which is considered necessary for the subject's welfare may be given at the discretion of the Investigator. Allowed treatments include:

- Bland moisturizers/emollients (without urea or alpha or beta hydroxy acids) are allowed as needed during the study
- Upper mid-strength to least potent (class III to VII) topical steroids are permitted only on the palms, soles, face, and intertriginous areas
- Otic, nasal, ophthalmic, or inhaled CS (eg, to treat asthma) are not considered "systemic immunomodulating treatments" and are allowed during the study

At the screening assessment, prior medication history will be collected.

Any medication or vaccine (including over-the-counter or prescription medicines, vitamins, and/or herbal supplements) that the subject is receiving at the time of randomization or receives during the study must be recorded.

The Medical Monitor should be contacted if there are any questions regarding concomitant or prior therapy.

All subjects who discontinue the study intervention should be offered alternative treatment if applicable. Treatment should be given according to normal clinical practice, after the EOS visit.

6.5 Dose Modification

6.5.1 ABP 654 and Ustekinumab

As of the date of the issuance of this protocol, ABP 654 has not been tested in clinical studies.

There are no dose modifications for investigational product (ABP 654 or ustekinumab) on this study. The ABP 654/ustekinumab dose will be based on the subject's baseline BW and will remain the same throughout the study. Dosing will not be corrected on the basis of BW at current visit.

If the subject presents with a serious infection at the dosing visit(s), the administration of investigational product may be delayed (up to 3 days for weeks 4 and 12 and up to 5 days for doses thereafter); and subjects with serious infections need to be monitored closely and investigational product should not be administered until the infection resolves.

In the case of delayed or missed dose for any reason, subsequent doses should be administered according to the original schedule (ie, at the planned timepoint relative to first dose) investigational product dose(s).

Any toxicities associated or possibly associated with investigational product treatment should be managed according to standard medical practice. A summary of expected adverse drug reactions is provided in the Investigator's Brochure. Ustekinumab has a terminal half-life of approximately 28.1 days, therefore discontinuation results in slow elimination over several months and will have no immediate effect.

If unmanageable toxicity due to investigational product occurs at any time during the study, treatment with the investigational product should be discontinued.

6.6 Intervention After the End of the Study

After completing dosing with investigational product at week 40 and the EOS visit at week 52, subjects will have completed the study. ABP 654 or ustekinumab will not be provided for poststudy use.

6.7 Loss of Subjects to Follow-up

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

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

- The site must attempt to contact the subject and reschedule the missed visit as soon as possible (and within the visit window) and counsel the subject on the importance of maintaining the assigned visit schedule and ascertain whether or not the subject wishes to and/or should continue in the study.
- In cases in which the subject is deemed lost to follow-up, the Investigator or designee must make every effort to regain contact with the subject (where possible, at least 2 telephone calls and, if necessary, 2 certified letters to the subject's last known mailing address or local equivalent methods). These contact attempts should be documented in the subject's medical record and electronic case report form (eCRF).

Should the subject continue to be unreachable, he/she will be considered to be 'lost to follow-up' and to have withdrawn from the study.

7 Study Assessments and Procedures

- Study procedures and their timing are summarized in the SoA (Section 1.3).
- As protocol waivers or exemptions are not allowed with the exception of immediate safety concerns, these should be discussed with the sponsor immediately upon occurrence or awareness to determine if the subject should continue or discontinue study intervention.
- Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.
- All screening evaluations must be completed and reviewed to confirm that potential subjects meet all eligibility criteria. The Investigator will maintain a screening log to record details of all subjects screened and to confirm eligibility or record reasons for screening failure, as applicable.

- Procedures conducted as part of the subject's routine clinical management and obtained before signing of informed ICF may be utilized for screening or baseline purposes provided the procedure met the protocol-specified criteria and were performed within the time frame defined in the SoA (Section 1.3).
- Repeat or unscheduled samples may be taken for safety reasons or for technical issues with the samples.
- Investigational product will be administered after all other procedures are completed for each dosing visit.

7.1 Screening and Eligibility Assessments

Refer to Section 7.1 for assessments to determine subject eligibility for inclusion in the study.

Refer to Section 7.2 for efficacy assessments to determine subject eligibility for the study, including but not limited to, PASI assessments.

Refer to Sections 7.3 and 7.4 for relevant safety assessments to determine subject eligibility for inclusion in the study, including but not limited to laboratory tests and pregnancy testing.

7.1.1 Informed Consent

All subjects or their legally authorized representative must sign and personally date the IRB/IEC approved ICF before any study-specific procedures are performed.

7.1.2 Medical History

Medical history, including any ongoing illnesses, will be collected.

7.1.2.1 Disease-specific Medical History

Moderate to severe plaque psoriasis history will be collected.

7.1.3 Demographics

Demographic data, including (where permitted), date of birth/age, sex, race, and ethnicity will be collected.

7.2 Efficacy Assessments

7.2.1 Psoriasis Area and Severity Index (PASI)

The PASI is a measure of the average redness (erythema), thickness (induration), and scaliness (scaling; each graded on a 0–4 scale of the lesions, weighted by the area of involvement

(Feldman and Krueger, 2005). All assessments for a given subject should be made by the same observer whenever possible.

7.2.2 Static Physician Global Assessment (sPGA)

The sPGA is a 6-point scale (0-5) used to measure the severity of disease (induration, scaling, and erythema) [Section 9.3, Appendix 3]). The sPGA should be completed by the same assessor performing the PASI assessments. All assessments for a given subject should be made by the same observer whenever possible.

7.2.3 Body Surface Area (BSA)

The percent of BSA affected (%BSA) is estimated by assuming that the subject's palm, excluding the fingers and thumb, represents roughly 1% of the body's surface (Chandran, 2009). At any given visit, BSA should be performed by the same assessor performing PASI assessment. Because of interobserver variability in estimated BSA, all assessments for a given subject should be made by the same observer whenever possible.

7.3 Other Study Assessments

7.3.1 Physical Examinations and Weight/Height

Subjects will undergo physical examinations, as indicated in the SoA (Section 1.3). Physical examination findings will be recorded. Physical examinations will be performed by a physician and will include examination of the following: general appearance, head, ears, eyes, nose, throat, neck, skin, cardiovascular system, respiratory system, abdominal system, and nervous system.

Clinically significant abnormal changes from baseline will be reported as AEs.

Baseline BW (kg) and height will be measured with the subject dressed in light clothing, without shoes or jacket. Baseline BW and height will be determined at screening. The baseline BW will be measured at baseline.

Investigators should pay special attention to clinical signs related to previous serious illnesses. Any new abnormalities or worsening of existing abnormalities should be reported as AEs, as appropriate (Section 7.5).

7.3.2 Vital Signs

Vital signs will be measured after the subject has been resting for 5 minutes and will include systolic and diastolic blood pressure, pulse, respiratory rate, and temperature.

Systolic blood pressure and diastolic blood pressure will be measured on the same arm.

Respiratory rate and temperature will also be recorded.

During the study, the measurement of vital signs may be repeated at the discretion of the Investigator for safety reasons. Clinically relevant abnormal findings should be reported as AEs.

7.3.3 Tuberculosis Testing

A TB test will be performed at screening by PPD or Quantiferon®/T-spot® test. PPD tests will be performed locally, and Quantiferon®/T-spot® tests will be performed by the local or central laboratory. Subjects with positive PPD or positive or indeterminate Quantiferon®/T-spot® test may be eligible based on the sponsor's TB risk assessment worksheet and the other criteria listed in Inclusion Criterion 8.

7.3.4 Chest Radiography

Chest radiography will include anterior/posterior or posterior/anterior and lateral views. Historical films or formal reports signed off by a radiologist obtained in the 3 months prior to screening are acceptable.

7.4 Safety Assessments

Planned time points for all safety assessments are provided in the SoA (Section 1.3).

7.4.1 Adverse Events and Serious Adverse Events

Adverse events and SAEs are defined in Section 7.5.1. Adverse events and SAEs will be followed, recorded, and reported in line with the procedures described in Sections 7.5.3 through 7.5.6.

7.4.2 Events of Interest

Events of interest for ABP 654/ustekinumab will be defined in the Statistical Analysis Plan (SAP) and will be reviewed on an ongoing basis as part of this study. There are no additional expedited reporting requirements for EOI, beyond what is defined for any AE report that qualifies to be expedited as part of regulatory reporting rules for investigational products.

7.4.3 Anti-Drug Antibodies

Blood samples for ADA (binding and neutralizing) assessments will be collected at the time points indicated in Section 1.3. Samples should be taken prior to administration of investigational product (pre-dose) on dosing visits. Samples tested positive for binding

antibodies will also be further assessed for neutralizing antibodies. Additional blood samples may be obtained to rule out ADAs during the study.

The detection and characterization of antibodies to ABP 654 will be performed using a validated assay method by the sponsor or under the supervision of the sponsor.

7.4.4 Clinical Safety Laboratory Assessments

Urine pregnancy tests will be performed locally. PPD and Quantiferon®/T-spot® tests will be performed by the local or central laboratory as described in Section 7.3.3. All other laboratory assessments will be performed by a central laboratory. Blood and urine samples will be collected at the times indicated in Section 1.3. At visits when investigational product is administered, clinical laboratory samples will be collected before investigational product administration. Venous blood samples will be taken for hematology and biochemistry testing at visits specified in the SoA (Table 1-1).

Protocol-required safety laboratory assessments are presented in Table 7-1.

Table 7-1 Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters	
Hematology	Absolute neutrophil count Hematocrit Hemoglobin	Platelet count RBC count WBC count (total) WBC count (differential)
Clinical Chemistry	BUN Potassium Total bilirubin Creatinine Sodium Total protein Albumin	Glucose (random) Alkaline phosphatase AST ALT gamma-glutamyltransferase
Routine Urinalysis	pH, specific gravity, creatinine, glucose, bilirubin, blood, and protein	
Other Tests	Follicle-stimulating hormone and estradiol (as needed in women of non-childbearing [WOCBP] potential only) at screening Serum hCG pregnancy test (as needed for WOCBP) at screening Serology (HbsAg, and HCV) at screening TB testing[1] (including a TB worksheet and chest X-ray) at screening Urine pregnancy tests Creatinine clearance Immunology (ADA antibody)	

[1]Quantiferon®/T-spot or purified protein derivative (PPD) testing.

Abbreviations: ADA = anti-drug antibody; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; HbsAG = hepatitis B surface antigen; hCG = human chorionic gonadotropin; HCV = hepatitis C virus; RBC = red blood cell; TB = tuberculosis; WBC = white blood cell; WOCBP = women of childbearing potential.

Refer to the Investigator Laboratory Manual for details regarding the collection, processing, and shipping of the blood and urine samples.

The Investigator must review the laboratory reports as described in Section 7.5.3. Any blood samples (eg, PK, immunogenicity) collected according to the SoA (Section 1.3) can be analyzed for any of the tests outlined in the protocol and for any tests necessary to minimize risks to study subjects. This includes testing to ensure analytical methods produce reliable and valid data throughout the course of the study. This can also include, but is not limited to, investigation of unexpected results, incurred sample reanalysis, and analyses for method transfer and comparability.

Additional and repeat laboratory safety testing may be performed at the discretion of the Investigator.

7.4.4.1 Clinically Significant Changes in Laboratory Values

Clinically significant changes in laboratory values are defined in Section 7.5.1.3.

- All protocol-required laboratory assessments, as defined in Section 1.3 and Table 7-1, must be conducted in accordance with the Laboratory Manual and the SoA (Section 1.3)
- In general, abnormal laboratory findings without clinical significance (based on the Investigator's judgment) are not to be recorded as AEs. However, laboratory value changes that require treatment or adjustment in current therapy are considered AEs. Where applicable, clinical sequelae (not the laboratory abnormality) are to be recorded as the AE

Investigators must document their review of each laboratory safety report.

7.4.5 Pregnancy

Details of all pregnancies and/or lactation in female subjects and female partners of male subjects that occur after the start of study treatment and until 5 months after the last study drug injection will be collected.

If a pregnancy is reported, the Investigator is to inform Amgen within 24 hours of learning of the pregnancy and/or lactation and is to follow the procedures outlined in Section 9.2 (Appendix 2). Amgen or its designee will follow-up with the Investigator regarding additional information that may be requested.

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

Further details regarding pregnancy and lactation are provided in Section 9.2 (Appendix 2). Pregnancy is not an AE unless there is suspicion of investigational product interference with effectiveness of contraceptive measures.

7.5 Adverse Events

7.5.1 Definitions

7.5.1.1 Adverse Events

An AE is any untoward medical occurrence in a clinical trial subject. The event does not necessarily have a causal relationship with the investigational product. An AE can therefore be an unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a treatment, combination product, medical device, or procedure. The Investigator is responsible for ensuring that any AEs observed by the Investigator or reported by the subject are recorded in the subject's medical record as well as the eCRF.

7.5.1.1.1 Events Meeting the Adverse Event Definition

Events that meet the AE definition are as follows:

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, vital signs measurements), including those that worsen from baseline, that are considered clinically significant in the medical and scientific judgment of the Investigator (ie, not related to progression of underlying disease)
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition
- New conditions, including signs and symptoms, detected or diagnosed after study treatment administration even though it may have been present before the start of the study
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction

- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study treatment or a concomitant medication. Overdose associated with any clinical sequelae will be considered an AE and reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses are to be reported regardless of sequelae. In case of overdosage, it is recommended that the subject be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment be instituted immediately
- "Lack of efficacy" or "failure of expected pharmacological action" per se will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfill the definition of an AE or SAE

7.5.1.1.2 Events NOT Meeting the Adverse Event Definition

Events not meeting the AE definition include:

- Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital [inpatient hospitalization for less than 24 hours])
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen
- A pre-existing condition that has not worsened during the study or involves an intervention such as elective cosmetic surgery or a medical procedure while on study is not considered an AE

7.5.1.2 Serious Adverse Events

An SAE is defined as any untoward medical occurrence that meets at least 1 of the following serious criteria:

- Results in death (fatal)
- Life-threatening (places the subject at immediate risk of death)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Congenital anomaly/birth defect

- Other medically important serious event

Definition of Terms

Life-threatening: The term "life-threatening" in the definition of "seriousness" refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe. For example, drug-induced hepatitis that resolved without evidence of hepatic failure would not be considered life-threatening even though drug-induced hepatitis can be fatal. It does not include an AE or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Hospitalization: In general, hospitalization signifies that the subject has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are an AE. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.

Disability/incapacity: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

Other medically important serious event: Medical or scientific judgment is to be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require medical or surgical intervention to prevent 1 of the other outcomes listed in the above definition. These events are typically to be considered serious.

Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

7.5.1.3 Clinical Laboratory Abnormalities and Other Abnormal Assessments

The Investigator is responsible for reviewing all laboratory test results, including review of laboratory test results prior to subject randomization and reviewing subsequent laboratory test

results throughout the study. The Investigator will determine whether an abnormal value in an individual study subject represents a clinically significant change from the subject's baseline values. Laboratory abnormalities without clinical significance (based on the Investigator's judgment) should not be recorded as AEs or SAEs. However, laboratory abnormalities (eg, clinical chemistry, hematology, and urinalysis abnormalities) that require medical or surgical intervention or lead to investigational product interruption, modification, or discontinuation must be recorded as an AE or SAE, as applicable. Where applicable, clinical sequelae (not the laboratory abnormality) are to be recorded as the AE. In addition, laboratory or other abnormal assessments (eg, vital signs) that are associated with signs and/or symptoms must be recorded as an AE or SAE if they meet the definition of an AE or SAE as described in Section 7.5.1. If the laboratory abnormality is part of a syndrome, record the syndrome or diagnosis (eg, anemia), not the laboratory result (eg, decreased hemoglobin).

7.5.2 Assessment of Adverse Events

7.5.2.1 Severity

The Investigator will make an assessment of severity for each AE and SAE reported during the study. The assessment of severity will be based on CTCAE version 4.03: http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm

7.5.2.2 Causality

The Investigator is obligated to assess the relationship between investigational product and each occurrence of each AE or SAE.

Relatedness means that there are facts or reasons to support a relationship between investigational product and the event.

The Investigator will use clinical judgment to determine the relationship.

Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study treatment administration will be considered and investigated.

The Investigator will also consult the IB in his/her assessment.

For each AE or SAE, the Investigator must document in the medical notes that he/she has reviewed the AE or SAE and has provided an assessment of causality.

There may be situations in which a SAE has occurred and the Investigator has minimal information to include in the initial report. However, it is very important that the Investigator always make an assessment of causality for every event before the initial transmission of the SAE data.

The Investigator may change his/her opinion of causality in light of follow-up information and send a SAE follow-up report with the updated causality assessment.

The causality assessment is one of the criteria used when determining regulatory reporting requirements.

7.5.3 Documenting and Reporting Adverse Events

The Investigator is responsible for ensuring that all AEs observed by the Investigator or reported by the subject that occur from the time of randomization through the EOS visit are recorded in subject's medical records as well as the applicable CRF Adverse Event Summary page. The AE grading scale to be used for this study will be CTCAE version 4.03, as described in Section 7.5.2.1.

The Investigator must assign the following AE attributes:

- Adverse event diagnosis or syndrome(s), if known (if not known, signs or symptoms)
- Dates of onset and resolution
- Severity (National Cancer Institute CTCAE version 4.03)
- Assessment of relatedness to investigational product, other protocol-required therapies or devices
- Action taken

The Investigator must assess whether the AE is possibly related to the investigational product. This relationship is indicated by a "yes" or "no" response to the question: "Is there a reasonable possibility that the event may have been caused by the investigational product?" The Investigator is responsible for reviewing laboratory test results and determining whether an abnormal value in an individual study subject represents a clinically significant change from the subject's baseline values. In general, abnormal laboratory findings without clinical significance (based on the Investigator's judgment) are not to be recorded as AEs. However, laboratory value changes that require treatment or adjustment in current therapy are considered AEs. Where applicable, clinical sequelae (not the laboratory abnormality) are to be recorded as the AE.

The Investigator's clinical judgment is used to determine whether a subject is to be removed from treatment due to an AE. A subject, or subject's legal representative, can also voluntarily withdraw from treatment due to an AE. If the subject withdraws consent, the subject is encouraged to undergo, at a minimum, an EOS assessment.

It is the Investigator's responsibility to review all documentation (eg, hospital notes, laboratory reports, and diagnostic reports) related to an AE. Wherever possible, the Investigator's diagnosis, not the individual signs and symptoms, will be documented as the AE.

It is not acceptable for the Investigator to send photocopies of the subject's medical records to sponsor or responsible CRO in lieu of completion of the CRF page.

If specifically requested, the Investigator may need to provide additional follow-up information, such as discharge summaries, medical records, or extracts from the medical records. In this case, all subject identifiers, with the exception of the subject number, will be blinded on the copies of the medical records before submission to the sponsor or responsible CRO.

Investigators are not obligated to actively seek AEs or SAEs after the subject's conclusion of study participation. However, if the Investigator learns of any SAE, including death, at any time after a subject has been discharged from the study, and he/she considers the event to be reasonably related to the investigational product or study participation, the Investigator must promptly notify the sponsor.

7.5.4 Reporting of Serious Adverse Events

The Investigator is responsible for ensuring that all SAEs observed by the Investigator or reported by the subject that occur after signing of the ICF through the EOS visit are reported using the applicable CRF Adverse Event Summary page or via the paper SAE report form for SAEs occurring during screening for subjects not randomized.

All SAEs must be collected, recorded and transmitted to Amgen, or its designee, within 24 hours following the Investigator's knowledge of the event.

The Investigator will submit any updated SAE data to the sponsor or designee within 24 hours of it being available.

The criteria for grade 4 in the CTCAE grading scale differs from the regulatory criteria for SAEs. It is left to the Investigator's judgment to report these grade 4 abnormalities as SAEs.

If the electronic data capture (EDC) system is not functional, the SAE can be reported by faxing a completed paper Serious Adverse Event Form or by direct telephone communication with Parexel at the numbers provided below. The event must be updated electronically in the EDC system by the clinical study center once the EDC function resumes.

Global reporting of SAEs:

Phone (Safety line): +1 (781) 434-5010

NorthAmerica_Medical@parexel.com

After the study is completed at a given center, the EDC system will be taken off-line to prevent the entry of new data or changes to existing data. If a center receives a report of a new SAE from a study subject or receives updated data on a previously reported SAE after the EDC has been taken off-line, then the center can report this information on a paper Serious Adverse Event Form.

7.5.5 Regulatory Reporting Requirements for Serious Adverse Events

If a subject is permanently withdrawn from protocol-required therapies because of a SAE, this information must be submitted to Amgen, or its designee.

Prompt notification by the Investigator to the sponsor (or designee) of SAEs is essential so that legal obligations and ethical responsibilities towards the safety of subjects and the safety of a study treatment under clinical investigation are met.

The sponsor (or designee) has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study treatment under clinical investigation. The sponsor (or designee) will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRBs/IECs, and Investigators.

Individual safety reports must be prepared for suspected unexpected serious adverse reactions according to local regulatory requirements and sponsor (or designee) policy and forwarded to Investigators as necessary.

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

To comply with worldwide reporting regulations for SAEs, the treatment assignment of subjects who develop serious, unexpected, and related AEs may be unblinded by Amgen or designee

before submission to regulatory authorities. Aggregate analyses may also be unblinded by the Safety Assessment Team, as appropriate. Investigators will receive notification of related SAEs reports sent to regulatory authorities in accordance with local requirements.

7.5.6 Reporting of Serious Adverse Event After the Protocol-required Reporting Period

There is no requirement to monitor study subjects for SAEs following the protocol-required reporting period or after the EOS. However, these SAEs can be reported to Amgen. Per local requirements in some countries, Investigators are required to report SAEs that they become aware of after the EOS. If SAEs are reported, the Investigator is to report them to Amgen within 24 hours following the Investigator's knowledge of the event.

Serious adverse events reported outside of the protocol-required reporting period will be captured within the safety database as clinical study cases and handled accordingly based on relationship to investigational product.

7.5.7 Method of Detecting Adverse Events and Serious Adverse Events

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

7.5.8 Adverse Event and Serious Adverse Event Follow-up

During the study the AEs and SAEs should be followed proactively by the Investigator at subsequent visits/contact. All AEs and SAEs will be followed until resolution, stabilization, until the event is otherwise explained, or until the subject is lost to follow-up. At the time the subject's study participation ends, all ongoing AEs and SAEs should be evaluated for resolution. All new or updated information for previously reported SAEs must be sent to Amgen within 24 hours following knowledge of the new information and will be recorded in the originally completed Adverse Event CRF. If specifically requested, the Investigator may need to provide additional follow-up information, such as discharge summaries, medical records, or extracts from the medical records. Information provided about the SAE must be consistent with that recorded on the Adverse Event CRF.

The Investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by Amgen to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional

laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

If a subject is permanently withdrawn from protocol-required therapies because of a SAE, this information must be submitted to Amgen. If a subject dies during participation in the study, the Investigator will provide Amgen with a copy of any post-mortem findings including histopathology if available.

Events of interest are described in Section 7.4.2. Formal pre-specified evaluations for EOIs are not planned at this time.

7.6 Pharmacokinetics

During treatment, a series of serum samples will be taken for measurement of serum concentration of treatments according to the SoA and sent to central laboratory.

Details of the procedures to be followed for sample collection, storage, and shipment will be documented in the Laboratory Manual.

Blood samples will be collected from all subjects. Samples should be taken prior to administration of investigational product (pre-dose) on dosing visits.

The actual date and time (24-hour clock time) of each sample will be recorded.

Samples collected for analyses of serum drug concentration may also be used to evaluate safety or efficacy aspects that address concerns arising during or after the study.

7.7 Pharmacodynamics

Pharmacodynamic parameters are not evaluated in this study.

7.8 Biomarkers

Biomarkers are not evaluated in this study.

8 Statistical Considerations

8.1 General Considerations

All personnel involved with the analysis of the study will remain blinded until database lock for the primary analysis. Personnel unblinded for the primary analysis will not be further involved in the management of the study. Analyses will be performed using SAS® version 9.4 or higher (SAS Institute, Cary, NC, US) by the sponsor or its representatives.

The SAP will be developed and finalized prior to the unblinding for the primary analysis. The SAP will provide a detailed description of the statistical methods and expand on the details provided in the protocol.

All data will be presented by treatment group. Descriptive statistics (number of observations, mean, standard deviation, median, minimum, and maximum) will be provided for continuous variables, and counts and percentages will be presented for categorical variables. Confidence intervals (CIs) and other inferential statistics may also be provided.

In general, baseline will be defined as the last non-missing measurement/procedure before or on the date of first administration of investigational product.

8.2 Statistical Hypotheses

The analysis of the primary efficacy endpoint will test the following hypotheses:

Null Hypothesis (H_0): Mean difference in PASI percent improvement from baseline at week 12 between ABP 654 and ustekinumab is outside an equivalence margin of (-15, 15),

versus

Alternative Hypothesis (H_A): Mean difference in PASI percent improvement from baseline at week 12 between ABP 654 and ustekinumab is within an equivalence margin of (-15, 15).

8.3 Sample Size Determination

Approximately 542 subjects will be randomized in a 1:1 ratio to receive ABP 654 or ustekinumab stratified by prior biologic use for psoriasis, geographic region, and BW. The sample size will provide greater than 95% power to demonstrate equivalence at a significance level of 0.025 on the primary efficacy endpoint of PASI percent improvement from baseline at week 12 with an equivalence margin of (-15, +15), assuming a common standard deviation of 30.0 (Leonardi, 2008; Papp, 2008), a true mean difference of 0 in the primary efficacy endpoint between the 2 groups, and a 10% dropout rate.

8.4 Populations for Analyses

For purposes of analysis, the following analysis sets are defined below and in Table 8-1:

Table 8-1 Populations for Analysis

Population (Analysis Set)	Description
Full Analysis Set (FAS)	The FAS comprises all randomized subjects. This analysis set will be analyzed according to the treatment the subject is randomized to (regardless of actual treatment received) and will be used for analyses/summaries of the primary efficacy endpoint as well as for all secondary efficacy endpoints.
Per Protocol Analysis Set	The Per Protocol Analysis Set consists of all subjects in the FAS who have completed dosing at day 1 and week 4, and have completed PASI assessment at week 12 without experiencing an important protocol deviation that may affect their evaluation for the primary endpoint of the study. This analysis set will be analyzed according to actual treatment received and will be used for sensitivity analyses for the primary and key secondary efficacy endpoints.
Safety Analysis Set	The Safety Analysis Set consists of all randomized subjects who receive at least one dose of investigational product and will be analyzed according to actual treatment received. This analysis set will be used for summaries of safety data, as well as immunogenicity data and PK data.

8.5 Planned Analyses

The primary efficacy analysis of the study will be performed after all subjects randomized reach week 32 or terminate early. The final analysis will be performed when all subjects randomized reach the week 52 visit or terminate early. Below is a description of the planned statistical analyses. Further details are presented in the SAP.

8.5.1 Primary Efficacy Endpoint

The primary analysis of the primary endpoint will be performed in the FAS with missing value imputed using last observation carried forward (LOCF) method. Clinical equivalence of the primary endpoint will be evaluated by comparing the 2-sided 95% CI of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 versus ustekinumab with an equivalence margin of (-15, +15). Clinical equivalence of the primary endpoint for Japan will be evaluated by comparing the 2-sided 95% CI of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 versus ustekinumab in subjects with baseline BW $\leq$ 100 kg (and hence are to receive the 45 mg dose) against the (-15, +15) margin. The least squares (LS) mean difference between the 2 treatment groups and the 95% CI of the difference will be estimated using an analysis of covariance (ANCOVA) model with the baseline PASI value and stratification factors as covariates.

Sensitivity analyses will be performed using observed data for both the FAS and the Per Protocol Analysis Set.

8.5.2 Secondary Efficacy Endpoints

All secondary efficacy endpoints will be analyzed descriptively.

PASI percent change from baseline at other timepoints will be summarized by visit and will be analyzed based on LOCF and as observed in the FAS. PASI percent change from baseline at week 4 and 12 will also be summarized as observed in the Per Protocol Analysis Set. The LS mean differences and 95% CIs of PASI percent improvement between the initial randomized groups (ABP 654 vs ustekinumab) or between the re-randomized groups (ABP 654/ABP 654, ustekinumab/ustekinumab, and ustekinumab/ABP 654) at other scheduled visits will be estimated using ANCOVA models similar to that used for the primary efficacy endpoint. The BSA change from baseline at week 12 and week 52 will be analyzed similarly.

PASI 75 and PASI 100 are defined as at least 75%, or 100%, respectively, improvement from baseline in PASI, respectively. PASI 75 and PASI 100 response rates will be summarized at each scheduled timepoint via non-responder imputation and as observed in the FAS. The response rates for week 4 and 12 will also be summarized as observed in the Per Protocol Analysis Set. Generalized linear models with an identity link will be used to obtain the point estimate and 95% CI for the risk difference of PASI 75 and PASI 100 response rates at each scheduled timepoint.

The sPGA responses (0/1) at week 12 and week 52 (Section 9.3, Appendix 3) will be analyzed similarly as PASI 75 and PASI 100 response rates.

Separate descriptive summaries by initial randomized groups (ABP 654 vs ustekinumab) will be provided for post week 28 timepoints in subjects with dose intensification.

8.5.3 Safety Endpoints

Safety endpoints will be summarized descriptively in the Safety Analysis Set based on the actual treatment received. In general, summaries will be provided separately from day 1 (first investigational product administration) until week 12, from day 1 through week 28, from week 28 through the EOS, and from day 1 through the EOS. The summaries for day 1 through week 12 and from day 1 through week 28 will be presented by treatment (ABP 654 vs ustekinumab). The summaries for week 28 through the EOS and day 1 through the EOS will be presented by treatment sequence (ABP 654/ABP 654, ustekinumab/ustekinumab, and ustekinumab/ABP 654) for subjects who are re-randomized and treated post re-randomization. Safety data from week 28 through the EOS for subjects with dose intensification will be summarized separately by treatment (ABP 654 vs ustekinumab).

All reported AEs will be assigned the SOC and preferred term according to the latest MedDRA dictionary as of the time of the primary analysis and graded by CTCAE. The number and percent of subjects reporting TEAEs, SAEs, and EOIs will be tabulated. Treatment-emergent adverse events (and serious TEAEs) are defined as those that occur on or after the time of first treatment up to EOS visit.

Laboratory data (hematology, serum chemistry, and urinalysis) will be converted to Système International (SI) units for reporting purposes. Absolute values and changes from baseline will be summarized descriptively by visit.

The number and percentage of subjects developing binding ADAs and neutralizing ADAs will be tabulated by visit and by treatment. Only subjects who were re-randomized and treated post re-randomization and had a result post re-randomization will be included in the analyses for week 28 through the EOS visit. Subjects who were not re-randomized or were not treated post re-randomization will be excluded from the analyses for day 1 through the EOS visit.

8.5.4 Pharmacokinetic Analyses

Serum ABP 654 and ustekinumab concentrations from PK sampling will be summarized descriptively for the Safety Analysis Set by treatment for each sampling timepoint.

8.5.5 Demographic and Baseline Characteristics

Demographic characteristics (including age, sex, ethnicity, and race) and baseline characteristics (including height, BW, body mass index, and disease characteristics) will be presented by treatment descriptively for each of the analysis sets defined in Section 8.4.

8.5.6 Exposure to Investigational Product

Exposure to ABP 654/ustekinumab will be summarized descriptively in the Safety Analysis Set for each treatment group for the different reporting periods specified for the safety analyses in Section 8.5.3.

8.5.7 Exposure to Prior and Concomitant Medications

Prior and concomitant medications will be coded using the latest available World Health Organization Drug Dictionary as of the time of the primary analysis and summarized descriptively for the Safety Analysis Set.

8.5.8 Subgroup Analyses and Covariates

The stratification factors will be included as covariates in statistical models for the efficacy analyses. Subgroup analyses will be conducted to evaluate consistency of treatment effect in subgroups defined by the stratification factors and other baseline covariates.

Full details of the subgroup analyses and covariates will be prespecified in the SAP.

8.5.9 Interim Analyses

No interim analysis is planned.

8.5.10 Handling of Missing Data

The handling of missing data for efficacy endpoints are provided in Sections 8.5.1 and 8.5.2.

Missing data for safety endpoints will not be imputed. If dates are missing or incomplete for an AE (including deaths), or concomitant medication, a further algorithm will be provided in the SAP.

9 Supporting Documentation and Operational Considerations

9.1 Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

9.1.1 Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with consensus ethical principles derived from international guidelines including the general principles in the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable ICH GCP guidelines, and applicable laws and regulations. The protocol, protocol amendments, ICF, Investigator's Brochure, and other relevant documents (eg, advertisements) must be submitted to an IRB/IEC by the Investigator and reviewed and approved by the IRB/IEC before the study is initiated. Any amendments to the protocol will require IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study subjects. The Investigator will be responsible for providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC. The Investigator will also be responsible for notifying the IRB/IEC of SAEs or other significant safety findings as required by IRB/IEC procedures, and ensuring that the overall conduct of the study at the site and adherence to requirements of the US Food and Drug Administration (FDA) 21 CFR, ICH GCP guidelines, the IRB/IEC, European regulation 536/2014 for clinical studies (if applicable), and all other applicable local regulations.

9.1.2 Good Clinical Practice

This study will be conducted in accordance with the protocol and with the Note for Guidance on ICH GCP Harmonised Tripartite Guideline E6 (R1)/Integrated Addendum E6 (R2); US FDA CFR (Title 21 Parts 50, 56, 312), requirements for the conduct of clinical studies as provided in the EU Directive 2001/20/EC; the general guidelines indicated in the Declaration of Helsinki; and all applicable laws and regulatory requirements.

9.1.3 Institutional Review Board

Before initiating a study, the Investigator/institution must have written and dated approval/favorable opinion from the IRBs/IECs for the study protocol/amendment(s), written ICF, any ICF updates, subject recruitment procedures (eg, advertisements), and any written information to be provided to subjects and a statement from the IRBs/IECs that these comply with GCP requirements (if applicable). A current copy of the IB should be included as part of the written application to the IRB/IEC.

A copy of the written approval of the protocol and ICF must be received by Amgen or designee before recruitment of subjects into the study and shipment of Amgen investigational product.

Amgen may amend the protocol at any time. The IRB/IEC approval(s) must identify the protocol version as well as the documents reviewed. Any amendments to the protocol will require IRB/IEC approval before the implementation of the changes made to the study, except for changes necessary to eliminate an immediate hazard to the study subjects.

The Investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC
- Notifying the IRB/IEC of SAEs or other significant safety findings, including adverse drug reactions that are both serious and unexpected, as required by IRB/IEC procedures
- Providing oversight of the conduct of the study at the study center and adherence to the requirements of all applicable regulations
- Promptly reporting deviations from, or changes to, the protocol to eliminate immediate hazards to the study subjects

- Obtaining annual IRB/IEC approval/renewal throughout the duration of the study. Copies of the Investigator's reports and the IRB/IEC continuance of approval must be sent to Amgen or designee

9.1.4 Informed Consent

In obtaining and documenting informed consent, the Investigator should comply with the applicable regulatory requirement(s) and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the study, the Investigator should have the IRB/IEC's written approval/favorable opinion of the written ICF and any other written information to be provided to subjects.

- The Investigator or his/her representative will explain the purpose and nature of the study as well as possible adverse effects to the subject or his/her legally acceptable representative and answer all questions regarding the study.
- Subjects must be informed that their participation is voluntary, and consent can be withdrawn at any point.
- Subject data up to withdrawal of consent will be included in the analysis of the study, and where permitted, publicly available data can be included after withdrawal of consent.
- Subjects or their legally acceptable representative will be required to sign a statement of informed consent that meets the requirements of US FDA CFR Title 21 Part 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act (HIPAA) requirements where applicable, and the IRB/IEC or study center.
- Prior to a subject's participation in the study, the written ICF should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.
- The medical record must include a statement that written informed consent was obtained before the subject was randomized to the study and the date the written consent was obtained. Subject withdrawal of consent or discontinuation from study, study treatment, and/or procedures must also be documented in the subject's medical records.
- The original copy of the signed ICF will be retained at the study center.
- A copy of the ICF and any other written information must be provided to the subject or the subject's legally acceptable representative.

- If the ICF is revised, the revised ICF must have received the IRB/IEC's approval/favorable opinion in advance of its use. Subjects must be informed of the changes to the ICF and must re-consent to the most current version during their participation in the study. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the study. The communication of this information should be documented.
- The Investigator is also responsible for asking the subject if the subject has a primary care physician and if the subject agrees to have his/her primary care physician informed of the subject's participation in the clinical study unless it is a local requirement. If the subject agrees to such notification, the Investigator is to inform the subject's primary care physician of the subject's participation in the clinical study. If the subject does not have a primary care physician and the Investigator will be acting in that capacity, the Investigator is to document such in the subject's medical record.

If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. The witness should sign and personally date the ICF after:

- The written ICF and any other written information to be provided to subjects is read and explained to the subject or the subject's legally acceptable representative
- The subject or the subject's legally acceptable representative has orally consented to the subject's participation in the study
- The subject or the subject's legally acceptable representative has signed and personally dated the ICF, if they are capable of doing so

By signing the ICF, the witness attests that the information in the ICF and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

9.1.5 Data Monitoring Committee (DMC)

For details on the DMC, refer to DMC Charter. The DMC will evaluate unblinded safety data throughout the study and convene approximately every 6 months after the first subject is enrolled to review safety data and issue recommendations. The DMC's constitution and the details of their roles and responsibilities are described in the DMC Charter.

A DMC will be formed with members consisting of individuals external to Amgen and the CRO chosen for their expertise in plaque psoriasis. Members of the DMC will include, at a minimum, physicians and statistician(s). The primary role of this independent DMC will be to monitor safety data.

In addition, the DMC will communicate any major safety concerns and recommendations regarding study modification or termination to Amgen senior management at any time during the conduct of the study.

Records of DMC meetings will be maintained by the CRO in a restricted, unblinded location for the duration of the study. Meeting records will be transferred and stored in the study TMF at the conclusion of the study. Selected Amgen, or its designee, staff may serve as liaisons with the DMC, but will not be voting members. Personnel at Amgen or its designee involved in preparation or review of DMC unblinded materials will not be otherwise involved in the study.

9.1.6 Financing and Insurance

9.1.6.1 Contractual and Financial Details

The Investigator (and/or, as appropriate, the hospital administrative representative) and Amgen, or its designee, will sign a clinical study agreement prior to the start of the study, outlining overall Amgen, or its designee, and Investigator responsibilities in relation to the study.

9.1.6.2 Insurance, Indemnity, and Compensation

The sponsor will take out reasonable third-party liability insurance cover in accordance with all legal requirements. The civil liability of the Investigator, the persons instructed by him or her and the hospital, practice, or institute in which they are employed and the liability of the sponsor with respect to financial loss due to personal injury and other damage that may arise as a result of the carrying out of this study are governed by the applicable law.

The sponsor will arrange for subjects participating in this study to be insured against financial loss due to personal injury caused by the pharmaceutical products being tested or by medical steps taken in the course of the study.

9.1.6.3 Financial Disclosure

Investigators and sub Investigators will provide the sponsor or designee with sufficient, accurate financial information as requested to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities.

9.1.7 Data and Records Management

All clinical study information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification. This principle applies to all records referenced in this protocol, irrespective of the type of media used.

A CRF will be used to store and transmit subject information. The CRF must be reviewed and electronically signed and dated by the Investigator on an ongoing basis throughout the study. The Investigator is responsible for verifying that the data entries are accurate and correct by signing the CRF.

Access to the CRF will be strictly password protected and limited to personnel directly participating in the study. Data should be entered into the CRF completely by authorized site personnel (eg, Investigators and the study coordinator). The CRF must be completed as soon as possible after any subject evaluation or communication. If data are to be changed due to erroneous input or other reason, an electronic audit trail will track these changes. The CRFs and computers that store them must be accessible to CRAs and other regulatory auditors.

During each study visit, a physician participating in the study will maintain progress notes in the subject's medical records to document all significant observations. At a minimum, these notes are to contain:

- The date of the visit and the corresponding day or visit in the study schedule
- General condition and status remarks by the subject, including any significant medical findings. The severity, frequency, duration, and resolution of any reported AE, and the Investigator's assessment as to whether or not the reported AE is related to IP
- Changes (including dosages) in concomitant medications/therapies (including over-the-counter medications and vitamins or dietary supplements) or procedures
- A general reference to the procedures completed
- The signature or initials of all physicians making an entry in the medical record (progress notes)

In addition, any contact with the subject by telephone or other means that provides significant clinical information is to also be documented in the medical record (progress notes), as described above.

Information from the medical records (progress notes) and other source documents is to be promptly entered into the appropriate section of the CRF.

Changes to information in the medical record (progress notes) and other source documents are to be initialed and dated on the day the change is made by the Investigator (or designee). If the reason for the change is not apparent, a brief explanation for the change is to be written adjacent to the change. Changes to the CRF will be electronically tracked.

The CRO data management department will write a Data Management Plan, which will be finalized prior to performing any data validation.

9.1.7.1 Source Documentation

Source documents contain the results of original observations and activities of a clinical investigation. They are the original records in which raw data are first recorded. Source documents include, but are not limited to, medical records (progress notes), computer printouts, screening logs, completed scales, and recorded data from automated instruments.

The Investigator/site personnel should maintain adequate and accurate source documents and study records that include all pertinent observations on each of the study center's study subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (eg, through an audit trail).

All source documents from this study are to be maintained by the Investigator and made available for inspection by authorized persons. The Investigator will provide direct access to source documents/data for study-related monitoring, audits, IRB/IEC review, and regulatory inspections. They will be carried out giving due consideration to data protection and medical confidentiality. The sponsor should verify that each subject has consented, in writing, to direct access to his/her original medical records for study-related monitoring, audit, IRB/IEC review, and regulatory inspection.

During the study, a CRA will make site visits to review protocol compliance, compare eCRF entries and individual subject's medical records, assess drug accountability, and ensure that the study is being conducted according to pertinent regulatory requirements. The eCRF entries will be verified with source documentation.

9.1.7.2 Case Report Form

The file structure and format for the CRF will be provided by the sponsor or its representative and should be handled in accordance with the instructions provided.

Data will be entered/loaded into a validated electronic database using a clinical data management system. Computerized data cleaning checks will be used in addition to manual review to check for discrepancies and to ensure consistency of the data.

If corrections are needed, the responsible monitor or data manager will raise a query in the EDC application. The appropriate staff at the study site will answer queries sent to the Investigator. The name of the staff member responding to the query, and time and date stamp will be captured to provide an audit trail. Once all source data verification is complete and all queries are closed, the sponsor or designee will freeze the eCRF page.

The specific procedures to be used for data entry and query resolution using the EDC system/eCRF will be provided to study sites in a training manual. In addition, site personnel will receive training on the EDC system/eCRF.

9.1.7.3 Study Files and Record Retention

All data derived from the study will remain the property of the sponsor. The sponsor assumes accountability for actions delegated to other individuals, eg, the CRO.

Records must be retained in accordance with the current ICH Guidelines on GCP. All essential study documents, including records of subjects, source documents, CRFs, and the IP inventory, must be kept on file.

Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region, or until at least 2 years have elapsed since the formal discontinuation of clinical development of ABP 654. However, essential documents may be retained for a longer period if required by the applicable regulatory requirements or by agreement with the sponsor. The sponsor is responsible for informing the Investigator when these documents need no longer be retained.

If an Investigator moves, withdraws from a study, or retires, the responsibility for maintaining the records may be transferred to another person who will accept responsibility. Notice of transfer must be made to and agreed by the sponsor.

Source documents provide evidence for the existence of the subject and substantiate the integrity of the data collected. Source documents are filed at the Investigator's site.

Data reported on the CRF or entered in the eCRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The

Investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

The study start date is the date on which the first subject is randomized to the study The EOS date is defined as the date when the last subject across all centers is assessed or receives an intervention for evaluation in the study (ie, last subject visit) or has withdrawn prematurely, as applicable.

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

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

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

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

9.1.8 Publication Policy

This study will be registered on ClinicalTrials.gov in accordance with applicable laws and publication policy, and may also be registered on other publicly accessible websites as necessary. The results of the study will be posted for public disclosure within 12 months of study completion.

The sponsor or designee is responsible for preparing and providing the appropriate regulatory authorities with the Clinical Study Report (CSR) according to the applicable regulatory requirements. The sponsor should ensure that the CSR meets the standards of the ICH Guideline for Structure and Content of Clinical Study Reports (ICH E3).

To coordinate dissemination of data from this study, Amgen may facilitate the formation of a publication committee consisting of several Investigators and appropriate Amgen staff. The criteria described below are to be met for every publication.

Authorship of any publications resulting from this study will be determined on the basis of the Uniform Requirement for Manuscripts Submitted to Biomedical Journals International committee of Medical Journal Editors' Recommendations for the Conduct of Reporting, Editing, and Publications of Scholarly Work in Medical Journals, which states: Authorship credit is to be based on: (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Authors need to meet conditions 1, 2, 3, and 4.

When a large, multicenter group has conducted the work, the group is to identify the individuals who accept direct responsibility for the manuscript. These individuals must fully meet the criteria for authorship defined above. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship. All persons designated as authors must qualify for authorship, and all those who qualify are to be listed. Each author must have participated sufficiently in the work to take public responsibility for appropriate portions of the content. All publications (eg, manuscripts, abstracts, oral/slide presentations, book chapters) based on this study must be submitted to Amgen for review. The Clinical Trial Agreement among the institution, Investigator, and Amgen will detail the procedures for, and timing of, Amgen's review of publications.

9.1.9 Auditing and Monitoring

Sponsor-assigned CRAs will conduct regular center visits to the investigational facilities for the purpose of monitoring various aspects of the study, such as assessing subject recruitment, compliance with protocol procedures, completeness and accuracy of data entered into the CRFs, verification of CRF data against original source documents, occurrence of AEs and the safety and rights of subjects are being protected, and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements. The Investigator must agree to sponsor-authorized personnel having direct access to the clinical (or associated) files and clinical study supplies (dispensing and storage areas) to ensure compliance with applicable regulations, and the Investigator will assist with the sponsor's monitoring activities.

Quality control will occur at each stage of data handling to ensure that all data are reliable and have been processed correctly. The sponsor should ensure oversight of any study-related duties and functions carried out on its behalf, including study-related duties and functions that are subcontracted to another party by the sponsor's contracted CRO(s).

The CRFs should be completed in a timely manner and on an ongoing basis to allow regular review by the CRA.

Details describing the strategy, responsibilities, and requirements of the study monitoring are provided in the Study Monitoring Plan.

The purpose of an audit is to assess whether ethics, regulatory, and quality requirements are being fulfilled. The sponsor or its representative may conduct audits at the investigative centers including, but not limited to, drug supply, presence of required documents, the informed consent process, and comparison of CRFs with source documents. Government regulatory authorities may also inspect the Investigator during or after the study. The Investigator (or designee) should contact the sponsor/CRO immediately if this occurs. All medical records (progress notes) must be available for audit. The Investigator must agree to participate with audits conducted at a convenient time in a reasonable manner.

9.1.9.1 Risk and Quality Tolerance Limits

Perceived risks and quality tolerance limits (QTLs) will be identified and documented before the start of the study.

The sponsor and CRO will review risk control measures periodically to ascertain whether the implemented quality management activities remain effective and relevant. The quality management approach and any important deviations from the predefined QTLs (and remedial actions adopted) will be described in the CSR.

9.1.9.2 Protocol Adherence and Deviations

The Investigator and site personnel should conduct the study in compliance with the protocol and should use continuous vigilance to identify and report protocol deviations.

A protocol deviation is any change, divergence, or departure from the study design or procedures defined in the protocol that may be on the part of the Investigator, site personnel, or the subject.

Important protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. For example, important protocol deviations may include randomizing subjects in violation of key eligibility criteria designed to ensure a specific subject population or failing to collect data necessary to interpret primary endpoints, as this may compromise the scientific value of the study.

The Investigator should not implement any deviation from the protocol without agreement from the sponsor and prior review and approval from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard to a study subject.

In the event of an important protocol deviation, the Investigator will discuss the deviation with the sponsor's medical monitor and will come to an agreement as to whether the subject should be withdrawn from the study due to the important protocol deviation.

9.1.10 Data Protection

Subjects will be assigned a unique identifier by the sponsor. Any subject records or datasets that are transferred to the sponsor will contain the identifier only; subject names or any information which would make the subject identifiable will not be transferred.

The subject must be informed that his/her personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the subject.

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

9.1.11 Protocol Approval and Amendment

Protocol modifications, except those intended to reduce immediate risk to study subjects, may be made only by the sponsor.

Any permanent change to the protocol must be handled as a protocol amendment. The written amendment must be submitted to the IRB/IEC, and the Investigator must await approval before implementing the changes. The sponsor or designee will submit protocol amendments to the appropriate regulatory authorities for approval.

The current version of the ICF will require similar modification if the IRB/IEC, Investigator, and/or sponsor, judge the amendment to the protocol to substantially change the study design and/or increase the potential risk to the subject and/or impact the subject's involvement as a study subject. In such cases, the ICF will be renewed for enrolled subjects before their continued participation in the study.

9.2 Appendix 2: Contraceptive Guidance and Collection of Pregnancy Information

Study-specific contraception requirements for males and females of childbearing potential are outlined in Section 5.2.

Male and female subjects of childbearing potential must receive pregnancy prevention counseling and be advised of the risk to the fetus if they become pregnant or father a child during treatment and for 5 months after the last dose of protocol-required therapies.

Additional medications given during the study may alter the contraceptive requirements. These additional medications may require female subjects to use highly effective methods of contraception and/or for an increased length of time. In addition, male subjects may also be required to use contraception. The Investigator must discuss these contraceptive changes with the subject.

Definition of Woman of Childbearing Potential (WOCBP)

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

If fertility is unclear (eg, amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before first dose of study intervention, additional evaluation should be considered.

Women in the following categories are not considered WOCBP:

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

NOTE: Documentation can come from the site personnel's review of the subject's medical records, medical examination, or medical history interview.

3. Post-menopausal female
    - A post-menopausal state is defined as no menses for 12 months without an alternative medical cause.

- A high follicle-stimulating hormone (FSH) level in the post-menopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, a single FSH measurement (> 40 IU/L or mIU/mL) is required.

- Females on HRT and whose menopausal status is in doubt will be required to use one of the non-estrogen hormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of post-menopausal status before study randomization.

Contraception Guidance for Male Subjects:

Male subjects with female partners of childbearing potential are eligible to participate if they agree to ONE of the following and for 5 months following the treatment with test article or until the scheduled EOS (whichever is longer), as described in Section 5.2:

- Sexual abstinence (defined as refraining from heterosexual intercourse during the entire period of risk associated with protocol-required therapies; the reliability of sexual abstinence must be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the subject)
- Use a condom during treatment and for an additional 5 months after the last dose of IP
- The female partner should consider using an acceptable method of effective contraception such as: hormonal, intrauterine device, intrauterine hormonal-releasing system, female barrier method (diaphragm, cap, sponge [a female condom is not an option because there is a risk of tearing when both partners use a condom])
- Note: If the male's sole female partner is of nonchildbearing potential or has had a bilateral tubal ligation/occlusion, he is not required to use additional forms of contraception during the study

Contraceptive Guidance for Female Subjects:

Female subjects of childbearing potential are eligible to participate if they agree to use a highly effective method of contraception consistently and correctly as described in the table below and described in Section 5.2.

Highly Effective Contraceptive Methods That Are User Dependent[1] *Failure rate of < 1% per year when used consistently and correctly.*
Combined (estrogen- and progestin-containing) hormonal contraception associated with inhibition of ovulation[2] • Oral • Intravaginal • Transdermal
Progestogen-only hormonal contraception associated with inhibition of ovulation • Oral • Injectable
Highly Effective Contraceptive Methods That Are User Independent[1]
Implantable progestogen-only hormonal contraception associated with inhibition of ovulation[2] • Intrauterine device (IUD) • Intrauterine hormone-releasing system (IUS) • Bilateral tubal occlusion
Vasectomized Partner A vasectomized partner is a highly effective contraception method provided that the partner is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.
Sexual Abstinence Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the subject.

NOTES:

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

2 Hormonal contraception may be susceptible to interaction with the study intervention, which may reduce the efficacy of the contraceptive method. In this case, two highly effective methods of contraception should be utilized during the intervention period and for at least 5 months following the treatment with test article or until the scheduled EOS (whichever is later).

Pregnancy Testing

- WOCBP should only be included after a confirmed menstrual period and a negative highly sensitive serum pregnancy test.
- Additional pregnancy testing should be performed at intervals during the intervention period per the SoA and at the EOS, and as required locally.
- Pregnancy testing will be performed whenever a menstrual cycle is missed or when pregnancy is otherwise suspected.
- Pregnancy testing, with a sensitivity of 5 mIU/mL will be performed.

Collection of Pregnancy Information:

Male Subjects With Partners Who Become Pregnant

- In the event a male subject fathers a child during treatment, and for an additional 5 months after the last dose of investigational product, the information will be recorded on the Pregnancy Notification Form. The form must be submitted to Amgen or its designee within 24 hours of the center's awareness of the pregnancy. (Note: Sites are not required to provide any information on the Pregnancy Notification Form that violates the country or regions local privacy laws).
- The Investigator will attempt to obtain a signed authorization for release of pregnancy and infant health information directly from the pregnant female partner to obtain additional pregnancy information.
- After obtaining the female partner's signed authorization for release of pregnancy and infant health information, the Investigator will collect pregnancy outcome and infant health information on the pregnant partner and her baby and complete the pregnancy questionnaires. This information will be forwarded to Amgen or its designee.
- Generally, infant follow-up will be conducted up to 12 months after the birth of the child (if applicable).
- Any termination of the pregnancy will be reported to Amgen or its designee regardless of fetal status (presence or absence of anomalies) or indication for procedure.

Female Subjects Who Become Pregnant

- Investigator will collect pregnancy information on any female subject who becomes pregnant while taking protocol-required therapies through 5 months after the last dose of investigational product.
- Information will be recorded on the Pregnancy Notification Form. The form must be submitted to Amgen or its designee within 24 hours of learning of a subject's pregnancy. (Note: Sites are not required to provide any information on the Pregnancy Notification Form that violates the country or regions local privacy laws).
- After obtaining the female subject's signed authorization for release of pregnancy and infant health information, the Investigator will collect pregnancy and infant health information and complete the pregnancy questionnaire for any female subject who becomes pregnant while taking protocol-required therapies through 5 months after the last dose of IP. This information will be forwarded to Amgen or its designee. Generally, infant follow-up will be conducted up to 12 months after the birth of the child (if applicable).
- Any termination of pregnancy will be reported to Amgen or its designee, regardless of fetal status (presence or absence of anomalies) or indication for procedure.
- While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or report of a congenital anomaly or developmental delay, fetal death, or suspected adverse reactions in the neonate will be reported as an AE or SAE. Note that an elective termination with no information on a fetal congenital malformation or maternal complication is generally not considered an AE, but still must be reported to Amgen or its designee as a pregnancy exposure case.
- If the outcome of the pregnancy meets a criterion for immediate classification as a SAE (eg, female subject experiences a spontaneous abortion, stillbirth, or neonatal death or there is a fetal or neonatal congenital anomaly) the Investigator will report the event as a SAE.
- Any SAE occurring as a result of a poststudy pregnancy which is considered reasonably related to the study treatment by the Investigator, will be reported to Amgen or its designee. While the Investigator is not obligated to actively seek this information in former study subjects, he or she may learn of a SAE through spontaneous reporting.
- Any female subject who becomes pregnant while participating will discontinue study treatment.

Collection of Lactation Information

- Investigator will collect lactation information on any female subject who breastfeeds while taking protocol-required therapies through 5 months after the last dose of investigational product.
- Information will be recorded on the Lactation Notification Form and submitted to Amgen or its designee within 24 hours of the Investigator's knowledge of event.
- Study treatment will be discontinued if female subject breastfeeds during the study as described in Exclusion Criterion 23 (Section 5.2).
- With the female subjects signed authorization for release of mother and infant health information, the Investigator will collect mother and infant health information and complete the lactation questionnaire on any female subject who breastfeeds while taking protocol-required therapies through 5 months after discontinuing protocol-required therapies.

9.3 Appendix 3: Static Physician's Global Assessment (sPGA) Scale

Below is the sPGA scale that is being used in this study.

Score	Category	Category Description
0	Clear	• Plaque elevation = 0 (no elevation over normal skin) • Scaling = 0 (no scale) • Erythema = no evidence, hyperpigmentation may be present
1	Almost Clear	• Plaque elevation = ± (possible but difficult to ascertain whether there is a slight elevation above normal skin) • Scaling = ± (surface dryness with some white coloration) • Erythema = light red coloration
2	Mild	• Plaque elevation = slight (slight but definite elevation, typically edges are indistinct or sloped) • Scaling = fine (fine scale partially or mostly covering lesions) • Erythema = light red coloration
3	Moderate	• Plaque elevation = moderate (moderate elevation with rough or sloped edges) • Scaling = coarser (coarse scale covering most or all of the lesions) • Erythema = moderate (definite red coloration)
4	Severe	• Plaque elevation = marked (marked elevation typically with hard or sharp edges) • Scaling = coarse (coarse, non-tenacious scale predominates covering most or all of the lesions) • Erythema = severe (very bright red coloration)
5	Very Severe	• Plaque elevation = very marked (very marked elevation typically with hard sharp edges) • Scaling = very coarse (coarse, thick tenacious scale over most of the lesions, rough surface) • Erythema = very severe (extreme red coloration, dusky to deep red coloration)

9.4 Appendix 4: Abbreviations and Trademarks

ADA	anti-drug antibody
ADCC	anti-dependent cell mediated cytotoxicity
AE	adverse event
ALT	alanine aminotransferase
ANCOVA	analysis of variance
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
BCG	Bacillus Calmette-Guérin
BSA	body surface area
BW	body weight
CD	Crohn's Disease
CDC	complement dependent cytotoxicity
CI	confidence interval
C_{max}	maximum observed concentration
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	coronavirus disease 2019
CRA	Clinical Research Associate
CRF	case report form(s) (paper or electronic as appropriate for this study)
CRO	contract research organization
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DMC	Data Monitoring Committee
DNA	deoxyribonucleic acid
eCRF	electronic case report form
EDC	electronic data capture
EMA	European Medicines Agency
EOI	events of interest
EOS	end of the study
EU	European Union
EudraCT	European Clinical Trials Database
FAS	full analysis set
FcRn	Fc neonatal receptor
FDA	Food and Drug Administration
FSH	follicle-stimulating hormone

GCP	Good Clinical Practice
H_0	null hypothesis
H_A	alternative hypothesis
HBsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HRT	hormone replacement therapy
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IEC	Independent Ethics Committee
IgG	immunoglobulin-gamma
IgGκ	immunoglobulin-kappa
IL-12	interleukin-12
IL-12Rβ	interleukin-12 receptor subunit beta 1
IL-23	interleukin-23
IND	Investigational New Drug
INR	international normalized ratio
IP	investigational product
IRB/IEC	Institutional Review Board/Ethics Committee
IUD	intrauterine device
IUS	intrauterine hormone-releasing system
IV	intravenous
IXRS	Interactive Web/Voice Response System
LOCF	last observation carried forward
LS	least squares
MedDRA	Medical Dictionary for Regulatory Activities
NYHA	New York Heart Associate
PASI	psoriasis area severity index
PASI 50	≥ 50% improvement in psoriasis area severity index
PASI 75	≥ 75% improvement in psoriasis area severity index
PBMC	peripheral blood mononuclear cells
PFS	pre-filled syringe
PGA	Physician's Global Assessment

PIN	Personal Identification Number
PK	pharmacokinetic(s)
PPD	purified protein derivative
Ps	plaque psoriasis
PsA	active plaque psoriasis
PsO	psoriasis
PUVA	psoralen plus ultra-violet light
Q12W	every 12 weeks
Q8W	every 8 weeks
QTL	quality tolerance limit
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV2	severe acute respiratory syndrome coronavirus 2
SC	subcutaneous
SI	Système International
SmPC	Summary of Product Characteristics
SoA	schedule of activities
SOC	system organ class
sPGA	static Physician's Global Assessment
$t_{1/2}$	half-life
TB	tuberculosis
T_{max}	time of maximal concentration
TMF	trial master file
ULN	upper limit of normal
US	United States
USPI	United States Prescribing Information
UVA	ultra-violet A
UVB	ultra-violet B
versus	vs
WBC	white blood cell
WOCBP	woman of childbearing potential

10 References

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