CLINICAL INVESTIGATION PROTOCOL

A randomised, double-blind, placebo-controlled, parallel-group Phase IIa study to evaluate the efficacy, safety and pharmacokinetics of two subcutaneous dose regimens of CVB-0217 in adults with moderate-to-severe chronic plaque psoriasis

Protocol number	CVB-0217-201
Short title	PSO-ADVANCE 2a
EU CT number	2026-501842-37-00
Investigational medicinal product	CVB-0217 solution for injection, 150 mg/mL, prefilled syringe
Development phase	Phase IIa
Sponsor	Corvane Biologics AG, Industriezone Rottenmatte 8, 3930 Visp, Switzerland
Coordinating investigator	Prof. Dr. med. Claudia Rüegg, Department of Dermatology, Hôpital de Montvallier
Protocol version and date	Version 3.0 (Amendment 2, draft for review), 20 October 2026
Supersedes	Version 2.0 (Amendment 1), 5 June 2026

Draft for internal review. Amendment 2 has not been approved by the competent authorities or ethics committees and must not be implemented at investigational sites. Version 2.0 remains in force.

Confidentiality statement. This document contains confidential information belonging to Corvane Biologics AG. It is provided to investigators, members of ethics committees, regulatory authorities and study staff solely for the conduct of the study described. Its contents may not be disclosed to third parties without the prior written authorisation of the sponsor, except as necessary to obtain the informed consent of participants.

The study will be conducted in accordance with the protocol, the principles of the Declaration of Helsinki, the ICH guideline for Good Clinical Practice E6(R3), Regulation (EU) No 536/2014 and applicable national requirements.

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PROTOCOL APPROVAL

The undersigned have reviewed and approved this protocol, including all appendices, and confirm that it contains the information required to conduct the study in compliance with Good Clinical Practice.

Name	Role	Signature	Date
Dr. Andrea Zurbriggen	Head of Clinical Development, Corvane Biologics AG		
Dr. Helena Marti	Medical Monitor, Corvane Biologics AG		
Lukas Imboden	Lead Biostatistician, Corvane Biologics AG		
Dr. Rafael Ott	Head of Quality Assurance, Corvane Biologics AG		

COORDINATING INVESTIGATOR'S SIGNATURE

I have read this protocol and agree to conduct the study as described, in compliance with Good Clinical Practice and applicable regulatory requirements. I will ensure that all persons assisting me are informed about their obligations.

Name	Role	Signature	Date
Prof. Dr. med. Claudia Rüegg	Coordinating Investigator, Hôpital de Montvallier		

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DOCUMENT HISTORY

Table 1. Version history of the protocol

Version	Date	Type	Summary of changes
1.0	12 March 2026	Original protocol	First version submitted with the initial application in Switzerland, Germany, Poland and Czechia.
2.0	5 June 2026	Substantial amendment 1	Added Week 2 safety visit; clarified washout periods for systemic therapies; updated reference safety information to Investigator's Brochure edition 4.
3.0 (draft)	20 October 2026	Substantial amendment 2	Revised dropout assumption (Section 9.2); IGRA-based tuberculosis screening; PK and ADA sampling at Week 2; temperature excursion limits for the IMP; DMC charter reference; editorial corrections.

Changes proposed in this draft are shown as tracked revisions with the reviewer's name and date. Comments by the medical monitor and the lead biostatistician are shown in the margin and will be resolved before the amendment is finalised.

Reviewers of this draft

Reviewer	Function	Review period
Dr. Helena Marti	Medical Monitor, Clinical Development	14–19 October 2026
Lukas Imboden	Lead Biostatistician, Biometrics	16–20 October 2026

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PROTOCOL SYNOPSIS

Item	Description
Title	A randomised, double-blind, placebo-controlled, parallel-group Phase IIa study to evaluate the efficacy, safety and pharmacokinetics of two subcutaneous dose regimens of CVB-0217 in adults with moderate-to-severe chronic plaque psoriasis (PSO-ADVANCE 2a).
Protocol number / phase	CVB-0217-201 / Phase IIa
Sponsor	Corvane Biologics AG, Visp, Switzerland
Investigational product	CVB-0217, a humanised IgG1κ monoclonal antibody that binds the p19 subunit of interleukin-23 (IL-23), supplied as a 150 mg/mL solution in a 1 mL prefilled syringe for subcutaneous (SC) injection.
Rationale	IL-23 drives the differentiation and survival of pathogenic Th17 cells, which are central to the pathogenesis of psoriasis. In the first-in-human study CVB-0217-101, single and repeated SC doses up to 600 mg were well tolerated and reduced the Psoriasis Area and Severity Index (PASI) in a dose-dependent manner. This study will establish proof of concept and select the dose regimen for Phase IIb.
Objectives	**Primary:** to evaluate the efficacy of CVB-0217 150 mg and 300 mg SC every 4 weeks (Q4W) compared with placebo at Week 16. **Secondary:** to evaluate further efficacy measures, safety and tolerability, pharmacokinetics (PK) and immunogenicity of CVB-0217. **Exploratory:** to explore the effect of CVB-0217 on serum and skin biomarkers of the IL-23/IL-17 pathway.
Primary endpoint	Proportion of participants achieving at least 75% improvement from baseline in PASI (PASI 75) at Week 16. Participants with missing data at Week 16 will be counted as non-responders.
Secondary endpoints	PASI 90 and PASI 100 at Week 16; static Physician's Global Assessment (sPGA) of 0 or 1 with at least a 2-grade improvement at Week 16; change from baseline in Dermatology Life Quality Index (DLQI) and itch numeric rating scale; incidence of treatment-emergent adverse events (TEAEs); serum CVB-0217 trough concentrations; incidence of anti-drug antibodies (ADA).
Study design	Multicentre, randomised (1:1:1), double-blind, placebo-controlled study with a screening period of up to 4 weeks, a 16-week placebo-controlled treatment period, a blinded extension to Week 24 in which participants on placebo switch to CVB-0217 300 mg, and a safety follow-up until Week 32 (Figure 2).
Population	Adults aged 18 to 75 years with chronic plaque psoriasis for at least 6 months, PASI ≥ 12, sPGA ≥ 3 and body surface area (BSA) involvement ≥ 10% at screening and baseline, who are candidates for systemic therapy or phototherapy.
Number of participants	120 participants randomised (40 per arm) at approximately 14 sites in Switzerland, Germany, Poland and Czechia, assuming a dropout rate of 12% by Week 16.
Treatment	Arm A: CVB-0217 150 mg SC (one injection) plus one placebo injection, Q4W. Arm B: CVB-0217 300 mg SC (two injections), Q4W. Arm C: placebo SC (two injections), Q4W; switch to CVB-0217 300 mg at Week 16. Doses are given at Day 1 and Weeks 4, 8, 12, 16 and 20.
Key inclusion criteria	Age 18–75 years; chronic plaque psoriasis ≥ 6 months; PASI ≥ 12, sPGA ≥ 3 and BSA ≥ 10%; candidate for systemic therapy or phototherapy; negative pregnancy test and use of highly effective contraception in women of childbearing potential.
Key exclusion criteria	Non-plaque psoriasis; prior exposure to agents targeting IL-23 or IL-12/23 p40; active or untreated latent tuberculosis; active or recurrent infections; positive HBV, HCV or HIV test; malignancy within 5 years; live vaccination within 12 weeks; pregnancy or breastfeeding.

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Item	Description
Assessments	Efficacy: PASI, sPGA, BSA, DLQI, itch NRS, standardised photography. Safety: AEs, physical examination, vital signs, ECG, clinical laboratory tests, injection-site assessments. PK: pre-dose serum concentrations at every visit. Immunogenicity: ADA and neutralising antibodies. Biomarkers: serum cytokines, hsCRP and optional skin biopsies.
Planned study period	First participant first visit: December 2026 (planned). Last participant last visit: April 2028. Clinical study report: Q4 2028.
Duration	Up to 36 weeks per participant (screening 4 weeks, treatment 24 weeks, follow-up 8 weeks after the last dose).
Statistical methods	The primary endpoint will be analysed in the full analysis set using a Cochran–Mantel–Haenszel test stratified by baseline PASI (< 20 vs ≥ 20) and prior biologic exposure. Each CVB-0217 arm will be compared with placebo at a two-sided significance level of 0.025 (Bonferroni). With 40 participants per arm, the study has at least 90% power to detect a difference in PASI 75 response of 45% versus 8%.
Interim analysis	No efficacy interim analysis is planned. An independent Data Monitoring Committee (DMC) will review unblinded safety data every 3 months.

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TABLE OF CONTENTS

1 INTRODUCTION 9
1.1 Background 9
1.2 CVB-0217 9
1.2.1 Nonclinical data 9
1.2.2 Clinical data 9
1.3 Rationale for dose selection 9
1.4 Benefit–risk assessment 10
2 OBJECTIVES AND ENDPOINTS 10
3 STUDY DESIGN 11
3.1 Overall design 11
3.2 Scientific rationale for the design 12
3.3 End of study definition 12
4 STUDY POPULATION 12
4.1 Inclusion criteria 12
4.2 Exclusion criteria 13
4.3 Lifestyle considerations 13
4.4 Screen failures 13
5 STUDY INTERVENTION 14
5.1 Investigational medicinal product 14
5.2 Preparation, handling and storage 14
5.3 Randomisation and blinding 14
5.4 Concomitant therapy 14
6 DISCONTINUATION AND WITHDRAWAL 15
7 STUDY ASSESSMENTS AND PROCEDURES 16
7.1 Schedule of assessments 16
7.2 Efficacy assessments 19
7.3 Safety assessments 19
7.4 Pharmacokinetics 19
7.5 Immunogenicity 19
7.6 Biomarkers 20
7.7 Study procedures by visit 20
7.7.1 Screening (Day −28 to Day −1) 20
7.7.2 Day 1 (randomisation) 20
7.7.3 Weeks 2 to 12 20
7.7.4 Week 16 (primary endpoint) and blinded extension 20
7.7.5 Follow-up and end of study 20
8 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS 20
8.1 Follow-up of adverse events 21
8.2 Pregnancy 21
9 STATISTICAL CONSIDERATIONS 21
9.1 Statistical hypotheses 21
9.2 Sample size determination 21
9.3 Estimands 21
9.4 Analysis sets 22
9.5 Statistical analyses 22
9.5.1 Primary endpoint 22
9.5.2 Secondary and exploratory endpoints 22
9.5.3 Pharmacokinetic and pharmacodynamic analyses 22
9.5.4 Safety analyses 22
9.6 Data Monitoring Committee 23

CONFIDENTIAL – DRAFT

10 REGULATORY, ETHICAL AND STUDY OVERSIGHT 23
10.1 Ethics and informed consent 23
10.2 Data protection 23
10.3 Monitoring and quality assurance 23
10.4 Data handling and record keeping 23
10.5 Insurance and compensation 23
10.6 Publication policy 23
10.7 Risk-based quality management 24
11 REFERENCES 25
APPENDIX 1 – CLINICAL LABORATORY PARAMETERS 26
APPENDIX 2 – PSORIASIS AREA AND SEVERITY INDEX 26
APPENDIX 3 – SUMMARY OF CHANGES IN AMENDMENT 2 27
APPENDIX 4 – CONTRACEPTION GUIDANCE 28
APPENDIX 5 – LIVER SAFETY: ACTIONS AND FOLLOW-UP ASSESSMENTS 28

List of tables

Table 1. Version history of the protocol 3
Table 2. Abbreviations and definitions of terms 8
Table 3. Identified and potential risks and their mitigation 10
Table 4. Objectives and endpoints 11
Table 5. Study treatment by arm and dosing visit 14
Table 6. Schedule of assessments 16
Table 7. Blood volume collected per visit 17
Table 8. Adverse events of special interest 21
Table 9. Attributes of the primary estimand 22
Table 10. Analysis sets 22
Table 11. Clinical laboratory parameters 26
Table 12. PASI area score 26
Table 13. Summary of changes in Amendment 2 27
Table 14. Highly effective methods of contraception 28
Table 15. Liver safety algorithm 28

List of figures

Figure 1. Simulated serum CVB-0217 concentrations after 150 mg and 300 mg SC Q4W (median and 90% prediction interval, 400 virtual participants per regimen; arrows indicate dosing visits) 10
Figure 2. Study design. IRT, interactive response technology; Q4W, every 4 weeks; SC, subcutaneous. 12

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LIST OF ABBREVIATIONS

Table 2. Abbreviations and definitions of terms

Abbreviation	Definition	Abbreviation	Definition
ADA	Anti-drug antibodies	**IL**	Interleukin
AE	Adverse event	**IMP**	Investigational medicinal product
ALT	Alanine aminotransferase	**IRT**	Interactive response technology
AST	Aspartate aminotransferase	**k_a**	First-order absorption rate constant
AUC	Area under the concentration–time curve	**MedDRA**	Medical Dictionary for Regulatory Activities
BMI	Body mass index	**NRI**	Non-responder imputation
BSA	Body surface area	**NRS**	Numeric rating scale
CI	Confidence interval	**PASI**	Psoriasis Area and Severity Index
CL/F	Apparent clearance	**PK**	Pharmacokinetic(s)
CMH	Cochran–Mantel–Haenszel	**PPS**	Per-protocol set
C_{trough}	Trough (pre-dose) serum concentration	**Q4W**	Every 4 weeks
CTCAE	Common Terminology Criteria for Adverse Events	**SAE**	Serious adverse event
DLQI	Dermatology Life Quality Index	**SC**	Subcutaneous
DMC	Data Monitoring Committee	**sPGA**	Static Physician's Global Assessment
eCRF	Electronic case report form	**SUSAR**	Suspected unexpected serious adverse reaction
ET	Early termination	**TB**	Tuberculosis
FAS	Full analysis set	**TEAE**	Treatment-emergent adverse event
GCP	Good Clinical Practice	**$t_{1/2}$**	Terminal elimination half-life
hsCRP	High-sensitivity C-reactive protein	**ULN**	Upper limit of normal
IGRA	Interferon-gamma release assay	**V/F**	Apparent volume of distribution

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1 INTRODUCTION

1.1 Background

Psoriasis is a chronic, immune-mediated inflammatory disease affecting approximately 2 to 3% of the population in Europe. Plaque psoriasis, the most common form, is characterised by sharply demarcated, erythematous and scaly plaques that typically involve the elbows, knees, scalp and lower back. About one quarter of patients have moderate-to-severe disease, defined by the extent and severity of skin involvement or by its impact on quality of life.[1] The disease is associated with psoriatic arthritis, cardiovascular and metabolic comorbidities and depression.

Advances in the understanding of the IL-23/Th17 axis have transformed the treatment of psoriasis. IL-23, a heterodimeric cytokine composed of the p19 and p40 subunits, promotes the expansion and maintenance of Th17 cells that produce IL-17A, IL-17F and IL-22. Monoclonal antibodies that selectively neutralise IL-23 through its p19 subunit have achieved high and durable response rates with infrequent dosing. Nevertheless, a proportion of patients do not respond adequately, lose response over time or prefer fewer injections, so that there remains a need for agents with improved potency or longer dosing intervals.

1.2 CVB-0217

CVB-0217 is a humanised IgG1κ monoclonal antibody that binds the p19 subunit of human IL-23 with a dissociation constant of 18 pM and does not bind IL-12. Its Fc region carries the M252Y/S254T/T256E substitutions, which increase affinity for the neonatal Fc receptor and extend the elimination half-life. The drug product is manufactured at Corvane's site in Visp and filled into 1 mL glass prefilled syringes on the aseptic filling line FL-5.

1.2.1 Nonclinical data

In cynomolgus monkeys, weekly SC doses of up to 100 mg/kg for 26 weeks were well tolerated without adverse findings; the no-observed-adverse-effect level corresponds to an exposure more than 40-fold above that expected at the 300 mg dose in humans. In an imiquimod-induced psoriasis-like dermatitis model, a murine surrogate antibody reduced ear thickness and IL-17A expression by more than 70%. Full details are given in the Investigator's Brochure.[2]

1.2.2 Clinical data

In the first-in-human study CVB-0217-101, 48 healthy volunteers received single SC doses of 30 to 600 mg, and 24 participants with psoriasis received three doses of 150 or 300 mg every 4 weeks. CVB-0217 was well tolerated. The most frequent adverse events were nasopharyngitis (14%), headache (9%) and mild injection-site erythema (7%); no serious adverse events were considered related. Exposure increased approximately dose-proportionally, and the mean terminal half-life was 23 days. At Week 12, 58% of participants with psoriasis in the 300 mg group achieved PASI 75.

1.3 Rationale for dose selection

Doses of 150 mg and 300 mg Q4W were selected on the basis of the population PK and exposure–response model developed from study CVB-0217-101 (Section 7.4). The model predicts median steady-state trough concentrations of approximately 15 µg/mL and 30 µg/mL, respectively, both above the concentration associated with 80% of the maximal PASI response (EC_{80}, 6.5 µg/mL), as shown in Figure 1. With 150 mg, fewer than 5% of simulated participants have a steady-state trough below the EC_{80}, compared with fewer than 1% with 300 mg. The two regimens therefore allow the

[1] Severity definitions follow the European consensus: PASI > 10 or BSA > 10% or DLQI > 10 ("rule of tens").
[2] Corvane Biologics AG. CVB-0217 Investigator's Brochure, edition 4, 28 April 2026.

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dose–response relationship to be characterised at the plateau of the expected exposure–response curve, which is the information required to select the Phase IIb dose.

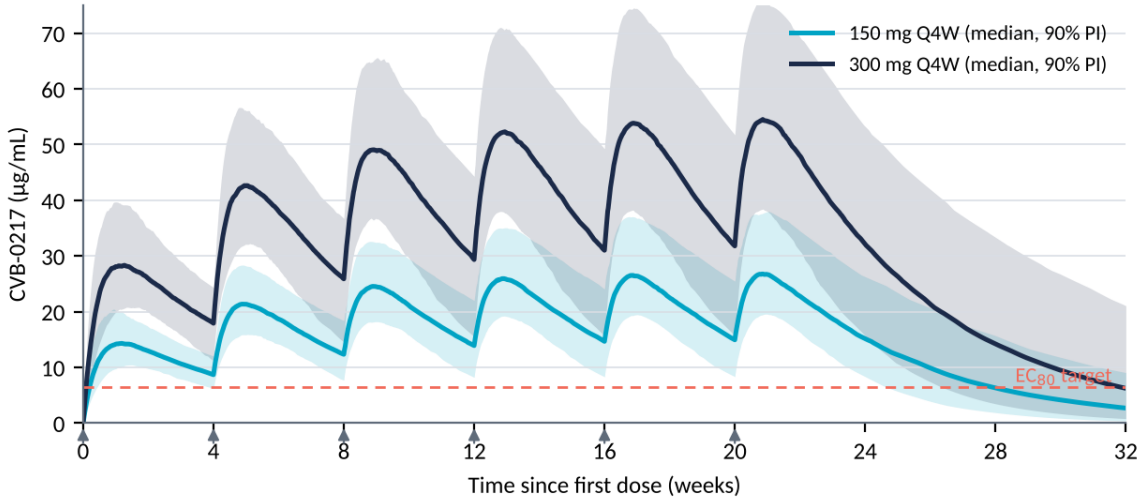


Figure 1. Simulated serum CVB-0217 concentrations after 150 mg and 300 mg SC Q4W (median and 90% prediction interval, 400 virtual participants per regimen; arrows indicate dosing visits).

1.4 Benefit–risk assessment

Participants may benefit from improvement in their psoriasis. Potential risks include infections, in particular reactivation of latent tuberculosis, hypersensitivity reactions and injection-site reactions, as observed with other agents targeting the IL-23 pathway. These risks are minimised by the eligibility criteria, tuberculosis screening, observation after the first injections, regular safety assessments and review by an independent DMC. Participants randomised to placebo are exposed to the burden of the study without active treatment for 16 weeks; rescue treatment is not permitted, but participants may withdraw at any time. The sponsor considers the benefit–risk balance favourable.

Table 3. Identified and potential risks and their mitigation

Risk	Basis	Mitigation in this study
Serious infections	Mechanism of action; class effect of IL-23 inhibitors	Exclusion of active or recurrent infections; AE monitoring; treatment interruption rules
Tuberculosis reactivation	Class effect; IL-23/Th17 axis involved in granuloma maintenance	IGRA screening; exclusion or treatment of latent TB; vigilance for symptoms
Hypersensitivity reactions	Therapeutic protein; one mild urticaria case in CVB-0217-101	60-minute observation after first two dosing visits; emergency equipment on site
Injection-site reactions	Observed in 7% of participants in CVB-0217-101	Rotation of injection sites; standardised grading
Immunogenicity	Therapeutic protein	ADA sampling at regular intervals; analysis of impact on PK and efficacy
Embryo-fetal toxicity	No data in humans; no findings in enhanced pre- and postnatal studies	Pregnancy testing; highly effective contraception

2 OBJECTIVES AND ENDPOINTS

The objectives and corresponding endpoints are summarised in Table 4. Endpoint definitions and analysis methods are described in Section 9.

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Table 4. Objectives and endpoints

Objective	Endpoint(s)
Primary	
To evaluate the efficacy of CVB-0217 150 mg and 300 mg Q4W compared with placebo	Proportion of participants achieving PASI 75 at Week 16
Secondary	
To evaluate further measures of efficacy	PASI 90 and PASI 100 at Week 16; sPGA 0/1 with ≥ 2-grade improvement at Week 16; PASI 75 at Weeks 4, 8, 12 and 24
To evaluate the effect on quality of life and symptoms	Change from baseline in DLQI and itch NRS at Week 16
To evaluate safety and tolerability	Incidence and severity of TEAEs, SAEs and injection-site reactions; laboratory abnormalities
To characterise the PK of CVB-0217	Serum trough concentrations; CL/F, V/F and k_a estimated by population PK
To assess immunogenicity	Incidence and titre of ADA and neutralising antibodies
Exploratory	
To explore pharmacodynamic effects	Change from baseline in serum IL-17A, IL-17F, IL-22 and hsCRP; skin transcriptome (optional biopsy)

3 STUDY DESIGN

3.1 Overall design

This is a multicentre, randomised, double-blind, placebo-controlled, parallel-group study (Figure 2). After a screening period of up to 28 days, eligible participants will be randomised in a 1:1:1 ratio to CVB-0217 150 mg, CVB-0217 300 mg or placebo. Randomisation will be stratified by baseline PASI (< 20 vs ≥ 20) and prior exposure to a biologic therapy for psoriasis (yes vs no) using interactive response technology (IRT).

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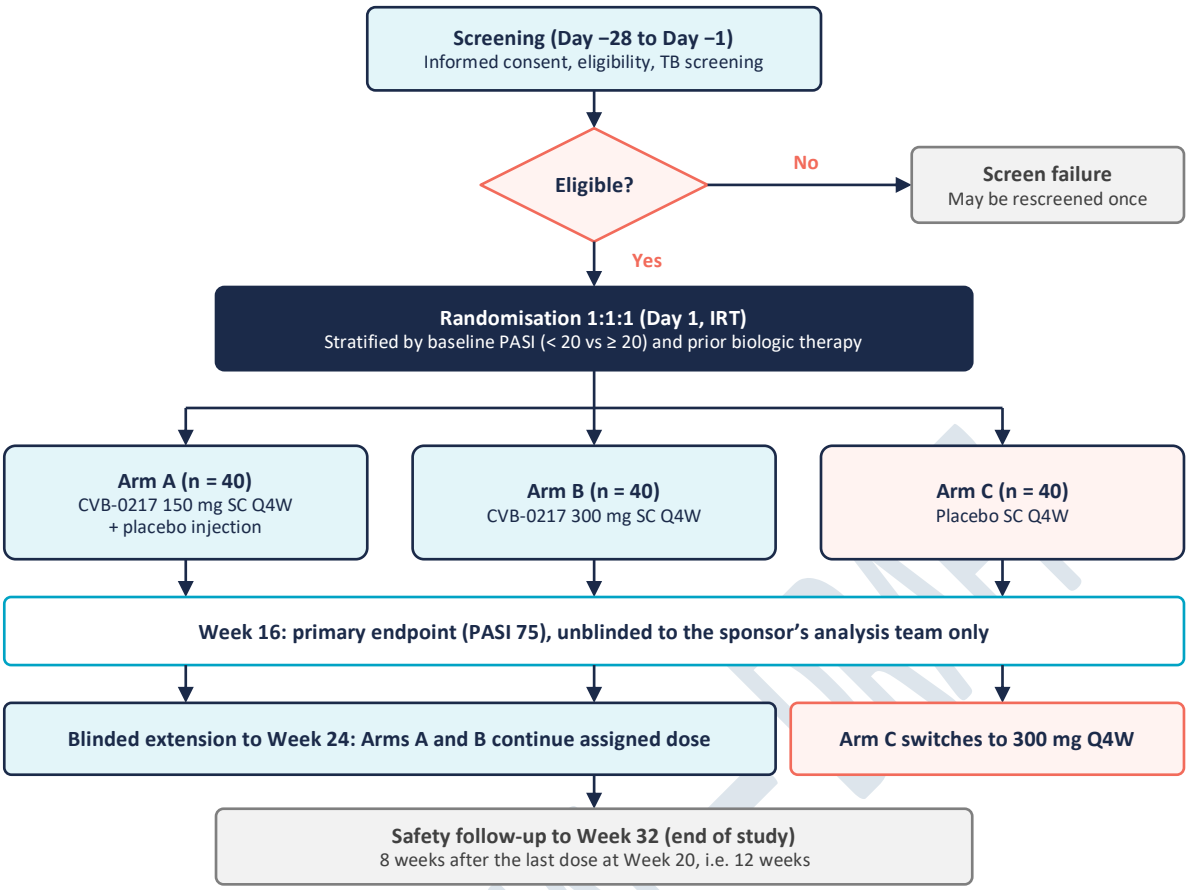


Figure 2. Study design. IRT, interactive response technology; Q4W, every 4 weeks; SC, subcutaneous.

3.2 Scientific rationale for the design

A placebo control is necessary to assess efficacy reliably in a disease with spontaneous fluctuations and to characterise the safety profile of CVB-0217. The 16-week placebo-controlled period is consistent with regulatory guidance and allows the primary endpoint to be assessed after four doses, when steady state is approached. The switch of placebo participants to CVB-0217 at Week 16 limits the time without active treatment and provides additional safety and PK data. To maintain the blind, all participants receive two injections at each dosing visit.

3.3 End of study definition

A participant has completed the study when he or she has completed the Week 32 visit. The end of the study is defined as the date of the last visit of the last participant. The sponsor will notify the competent authorities and ethics committees within 15 days of the end of the study in each member state.

4 STUDY POPULATION

Prospective approval of protocol deviations from the eligibility criteria (waivers) is not permitted.

4.1 Inclusion criteria

Participants are eligible only if all of the following criteria apply:

1. Signed and dated informed consent obtained before any study-specific procedure.
2. Men or women aged 18 to 75 years at the time of signing the informed consent.
3. Diagnosis of chronic plaque psoriasis for at least 6 months before randomisation.

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4. Moderate-to-severe psoriasis at screening and on Day 1, defined as PASI ≥ 12, sPGA ≥ 3 and BSA ≥ 10%.
5. Candidate for systemic therapy or phototherapy in the opinion of the investigator.
6. Women of childbearing potential must:
   a) have a negative serum pregnancy test at screening and a negative urine test on Day 1;
   b) agree to use a highly effective method of contraception until 20 weeks after the last dose.

4.2 Exclusion criteria

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

1. Non-plaque forms of psoriasis (erythrodermic, generalised pustular or guttate) or drug-induced psoriasis.
2. Previous exposure to CVB-0217 or to any agent targeting IL-23 or the p40 subunit of IL-12/IL-23.
3. Use of systemic non-biologic therapy within 4 weeks, of biologic therapy within 12 weeks (or 5 half-lives, whichever is longer), or of phototherapy within 4 weeks before Day 1.
4. Active tuberculosis, or latent tuberculosis defined by a positive interferon-gamma release assay (IGRA) performed within 4 weeks before Day 1, unless adequately treated according to local guidelines.
5. Active infection requiring systemic treatment within 2 weeks before Day 1, or a history of recurrent or chronic infections.
6. Positive test for hepatitis B surface antigen, hepatitis B core antibody with detectable HBV DNA, hepatitis C RNA or HIV.
7. ALT or AST > 2 × ULN, total bilirubin > 1.5 × ULN, haemoglobin < 100 g/L or neutrophils < 1.5 × 10^9/L at screening.
8. History of malignancy within 5 years, except adequately treated basal-cell or squamous-cell carcinoma of the skin.
9. Live vaccination within 12 weeks before Day 1 or planned during the study.
10. Pregnancy or breastfeeding, or planned pregnancy during the study.

4.3 Lifestyle considerations

Participants should avoid prolonged exposure to sunlight and must not use tanning beds or other ultraviolet light sources during the study. Topical treatment is restricted to bland emollients without active ingredients, which must not be applied within 12 hours before a study visit.

4.4 Screen failures

Participants who consent but are not randomised are screen failures. A minimal set of data (demography, reason for screen failure, eligibility criteria and serious adverse events) will be recorded. Participants may be rescreened once, with a new participant number, if the reason for screen failure was temporary.

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5 STUDY INTERVENTION

5.1 Investigational medicinal product



CVB-0217 is supplied as a sterile, preservative-free, clear to slightly opalescent solution containing 150 mg/mL CVB-0217 in 20 mM histidine buffer with sucrose and polysorbate 80, pH 6.0. Each 1 mL glass prefilled syringe has a staked 27G needle and a passive needle guard. Placebo is identical in appearance and composition except for the active substance. Both are filled on line FL-5 at the sponsor's site in Visp and labelled in accordance with Annex VI of Regulation (EU) No 536/2014.

At each dosing visit two syringes are administered SC into the abdomen or thigh, at least 3 cm apart, by trained site staff. Injections into psoriatic plaques, bruises or scars must be avoided.

Table 5. Study treatment by arm and dosing visit

Arm	Syringe 1	Syringe 2	Dose per visit	Dosing visits
A	CVB-0217 150 mg	Placebo	150 mg	Day 1, Weeks 4, 8, 12, 16, 20
B	CVB-0217 150 mg	CVB-0217 150 mg	300 mg	Day 1, Weeks 4, 8, 12, 16, 20
C	Placebo → CVB-0217 150 mg	Placebo → CVB-0217 150 mg	0 mg → 300 mg	Switch at Week 16

5.2 Preparation, handling and storage

The IMP must be stored at 2 to 8 °C in the original carton to protect it from light and must **not** be frozen or shaken. Before injection, the syringes are allowed to reach room temperature for 30 minutes. A single temperature excursion of up to 72 hours at or below 25 °C is acceptable; any other excursion must be reported to the sponsor, and the affected material quarantined until released. Temperature logs are reviewed by the monitor at each visit.

5.3 Randomisation and blinding

Participants will be assigned to treatment through the IRT according to a computer-generated randomisation schedule with a block size known only to the unblinded statistician. Investigators, participants, site staff and sponsor personnel involved in the conduct of the study remain blinded until the final database lock, except for the analysis team responsible for the Week 16 analysis. In a medical emergency, the investigator can unblind an individual participant through the IRT; whenever possible the medical monitor should be contacted beforehand.

Participants must remain under observation for at least 60 minutes after the first two dosing visits and for 30 minutes after subsequent visits. Site staff will document the time of injection, the injection sites and any immediate reactions in the eCRF.

5.4 Concomitant therapy

All medications taken within 12 weeks before screening and during the study must be recorded. The following are prohibited until Week 32: systemic treatments for psoriasis, phototherapy, topical corticosteroids, vitamin D analogues and calcineurin inhibitors (except low-potency corticosteroids on the face and intertriginous areas), live vaccines, and any investigational product. Inactivated vaccines are permitted.

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6 DISCONTINUATION AND WITHDRAWAL

Participants may withdraw consent at any time without giving a reason and without affecting their further care. The investigator must permanently discontinue study treatment in case of:

- pregnancy;
- a serious hypersensitivity reaction or anaphylaxis related to the IMP;
- active tuberculosis or a serious opportunistic infection;
- malignancy other than non-melanoma skin cancer;
- ALT or AST > 5 × ULN, or > 3 × ULN with total bilirubin > 2 × ULN (potential drug-induced liver injury).

Participants who discontinue treatment should remain in the study and attend all scheduled visits, or at least the Week 16 and Week 32 visits. Participants who withdraw from the study should complete an early termination (ET) visit. A participant is considered lost to follow-up after three documented, unsuccessful contact attempts.

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7 STUDY ASSESSMENTS AND PROCEDURES

7.1 Schedule of assessments

Table 6. Schedule of assessments

Procedure	Screening	Day 1	Week 2	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32 / EoS	ET
Study period	Scr.	Double-blind, placebo-controlled						Extension		Follow-up		
Visit window	D–28 to –1	–	±3 d	±3 d	±3 d	±3 d	±3 d	±5 d	±5 d	±7 d	±7 d	–
Informed consent[a]	✓											
Eligibility criteria	✓	✓										
Demography and medical history	✓											
Prior and concomitant medication	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Physical examination[b]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Height, weight, BMI	✓						✓				✓	✓
Vital signs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12-lead ECG	✓	✓					✓				✓	✓
IGRA (tuberculosis)[c]	✓											
HBV, HCV, HIV serology	✓											
Pregnancy test[d]	✓	✓		✓	✓	✓	✓	✓			✓	✓
Haematology and biochemistry	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Urinalysis	✓	✓				✓	✓				✓	✓
hsCRP		✓		✓		✓	✓		✓		✓	✓
PASI, sPGA, BSA	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
DLQI and itch NRS		✓		✓		✓	✓		✓		✓	✓
Standardised photography[e]		✓					✓				✓	

Procedure	Screening	Day 1	Week 2	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32 / EoS	ET
Study period	**Scr.**	**Double-blind, placebo-controlled**						**Extension**		**Follow-up**		
Visit window	**D–28 to –1**	**–**	**±3 d**	**±3 d**	**±3 d**	**±3 d**	**±3 d**	**±5 d**	**±5 d**	**±7 d**	**±7 d**	**–**
Randomisation (IRT)		✓										
IMP administration[f]		✓		✓	✓	✓	✓	✓				
Post-dose observation[g]		✓		✓	✓	✓	✓	✓				
Injection-site assessment		✓	✓	✓	✓	✓	✓	✓	✓			
PK sample (pre-dose)[h]		✓	✓[h]	✓	✓	✓	✓	✓	✓	✓	✓	✓
ADA sample (pre-dose)[h]		✓	✓[h]	✓		✓	✓		✓		✓	✓
Serum biomarkers		✓		✓		✓	✓		✓		✓	
Skin biopsy (optional)[i]		✓					✓					
Adverse events	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[a] Written informed consent must be obtained before any study-specific procedure, including washout of prohibited medication.
[b] Full examination at screening, Week 16 and Week 32/EoS; symptom-directed examination at other visits.
[c] IGRA within 4 weeks before Day 1; chest X-ray only if the IGRA result is positive or indeterminate.
[d] Serum test at screening; urine test before each dose and at EoS in women of childbearing potential.
[e] At selected sites with standardised photography equipment; target plaque and global views.
[f] Two SC injections per visit to maintain the blind (Table 5).
[g] 60 minutes after the first two dosing visits, 30 minutes thereafter (Section 5.3).
[h] Collected before dosing. Week 2 samples added in Amendment 2 for population PK.
[i] Lesional and non-lesional 4 mm punch biopsies on Day 1 and Week 16 in consenting participants (approximately 30).
EoS, end of study; ET, early termination visit. Shading: blue, placebo-controlled period; light blue, blinded extension; grey, follow-up.

Table 7. Blood volume collected per visit

Sample type (mL)	Screening	Day 1	Week 2	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32/EoS	ET
Safety laboratory (haematology, biochemistry)	12	12	12	12	12	12	12	12	12	12	12	12
Serology and IGRA	14	–	–	–	–	–	–	–	–	–	–	–
Pharmacokinetics	–	4	4	4	4	4	4	4	4	4	4	4
Anti-drug antibodies	–	6	6	6	–	6	6	–	6	–	6	6
Serum biomarkers	–	10	–	10	–	10	10	–	10	–	10	–

CONFIDENTIAL

Sample type (mL)	Screening	Day 1	Week 2	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32/EoS	ET
Total per visit	**26**	**32**	**22**	**32**	**16**	**32**	**32**	**16**	**32**	**16**	**32**	**22**

The total blood volume over the study, excluding unscheduled and early termination visits, is 288 mL, well below the volume of a single blood donation. Additional samples for repeat laboratory tests are not expected to exceed 30 mL per participant.

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7.2 Efficacy assessments

Efficacy assessments are performed by an investigator trained and certified in the scoring instruments, preferably the same assessor for a given participant throughout the study. The PASI combines the extent of involvement and the severity of erythema, induration and desquamation in four body regions (Appendix 2 – Psoriasis Area and Severity Index). The sPGA rates the overall severity of psoriasis on a 5-point scale from 0 (clear) to 4 (severe).

7.3 Safety assessments

Safety is assessed through adverse events, physical examinations, vital signs, 12-lead ECGs and clinical laboratory tests (Appendix 1). Laboratory samples are analysed by a central laboratory. Injection-site reactions are graded according to CTCAE version 5.0. Suicidal ideation and behaviour are assessed with a structured questionnaire at screening, Week 16 and Week 32.

7.4 Pharmacokinetics

Serum concentrations of CVB-0217 will be measured with a validated electrochemiluminescence assay with a lower limit of quantification of 0.05 µg/mL. Sparse samples collected before dosing (Table 6) will be analysed together with the data from study CVB-0217-101 using a population PK model. The structural model is a one-compartment model with first-order absorption and elimination; after a single SC dose D the concentration at time t is given by

$$C(t) = \frac{F \cdot D \cdot k_a}{V(k_a - k_e)} \left(e^{-k_e t} - e^{-k_a t} \right) \tag{1}$$

where F is the absolute bioavailability, V the volume of distribution and k_a and k_e the first-order absorption and elimination rate constants ($k_e = \mathrm{CL}/V$). For repeated dosing at a dosing interval τ, the concentration after the nth dose follows from the superposition principle:

$$C_n(t) = \sum_{i=0}^{n-1} \frac{F D k_a}{V(k_a - k_e)} \left(e^{-k_e (t - i\tau)} - e^{-k_a (t - i\tau)} \right) \tag{2}$$

The accumulation ratio at steady state and the terminal half-life are

$$R_{\mathrm{ac}} = \frac{1}{1 - e^{-k_e \tau}}, \qquad t_{1/2} = \frac{\ln 2}{k_e} \tag{3}$$

With the parameter estimates from study CVB-0217-101 (CL/F = 0.24 L/day, V/F = 7.9 L, k_a = 0.31 day^{-1}), (3) gives a half-life of 22.8 days and an accumulation ratio of 1.75 for dosing every 28 days. Inter-individual variability of clearance is described by an exponential model with body weight as covariate:

$$CL_i = \theta_{\mathrm{CL}} \cdot \left(\frac{\mathrm{WT}_i}{70\ \mathrm{kg}} \right)^{\theta_{\mathrm{WT}}} \cdot e^{\eta_{\mathrm{CL},i}} \tag{4}$$

where $\eta_{\mathrm{CL},i}$ is normally distributed with mean 0 and variance ω^2. Exposure over a dosing interval at steady state is derived from the individual apparent clearance:

$$\mathrm{AUC}_{\tau,\mathrm{ss}} = \int_0^{\tau} C_{\mathrm{ss}}(t)\, \mathrm{d}t = \frac{D}{CL/F} \tag{5}$$

7.5 Immunogenicity

Anti-drug antibodies will be detected with a three-tiered approach (screening, confirmatory and titration assays); confirmed positive samples will be tested for neutralising activity in a cell-based assay. The impact of ADA on PK, efficacy and safety will be explored descriptively.

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7.6 Biomarkers

Serum concentrations of IL-17A, IL-17F, IL-22 and hsCRP will be measured at the time points shown in Table 6. In consenting participants, lesional and non-lesional skin biopsies will be collected on Day 1 and at Week 16 for transcriptomic analysis. Remaining samples may be stored for up to 15 years for research related to psoriasis and CVB-0217, subject to the participant's separate consent.

7.7 Study procedures by visit

7.7.1 Screening (Day –28 to Day –1)

After written informed consent, the investigator reviews the eligibility criteria and records demography, medical history, psoriasis history and prior treatments. Screening laboratory tests, IGRA and viral serology are performed. Participants who require a washout of prohibited medication may start it only after signing the informed consent; the screening period is then extended accordingly, up to a maximum of 12 weeks in total.

7.7.2 Day 1 (randomisation)

Eligibility is confirmed on the basis of the screening results and the Day 1 PASI, sPGA and BSA assessments. Baseline photographs, questionnaires, blood and urine samples and, in consenting participants, skin biopsies are obtained before randomisation. The participant is then randomised in the IRT and receives the first two injections. Vital signs are measured before dosing and 30 and 60 minutes after the injections.

7.7.3 Weeks 2 to 12

At each visit the investigator records adverse events and concomitant medication, measures vital signs and collects pre-dose blood samples. Efficacy assessments are performed from Week 4. At Weeks 4, 8 and 12 the IMP is administered after all other procedures have been completed. Participants who miss a dosing visit should be dosed within the visit window; doses that cannot be given within the window are skipped and recorded as missed.

7.7.4 Week 16 (primary endpoint) and blinded extension

The Week 16 visit includes the full set of efficacy, safety, PK and biomarker assessments. Participants in Arm C begin CVB-0217 300 mg at this visit; the switch is performed by the IRT without unblinding site staff or participants. During the extension, visits at Weeks 20 and 24 follow the same pattern as those of the placebo-controlled period.

7.7.5 Follow-up and end of study

After the last dose at Week 20, participants attend follow-up visits at Weeks 28 and 32. At the Week 32 visit the investigator discusses further treatment options with the participant. Participants who discontinue early attend an early termination visit and, if possible, the Week 32 visit.

8 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

An adverse event (AE) is any untoward medical occurrence in a participant administered the IMP, whether or not considered related to it. AEs are collected from the signing of the informed consent until the Week 32 visit and coded using MedDRA. The investigator assesses the severity (mild, moderate, severe) and the causal relationship (related or not related) of each AE.

A serious adverse event (SAE) is any AE that results in death, is life-threatening, requires hospitalisation or prolongation of hospitalisation, results in persistent or significant disability, is a congenital anomaly, or is considered medically important. SAEs must be reported to the sponsor

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within 24 hours of the investigator becoming aware of them. The sponsor reports SUSARs to the competent authorities and ethics committees within the timelines of Regulation (EU) No 536/2014.

Table 8. Adverse events of special interest

Event	Definition	Reporting
Serious infections	Infections meeting SAE criteria or requiring intravenous anti-infectives	Within 24 hours
Tuberculosis	Active TB or new latent TB (IGRA conversion)	Within 24 hours
Hypersensitivity	Anaphylaxis, serum sickness or angioedema	Within 24 hours
Malignancy	Any malignancy except non-melanoma skin cancer	Within 24 hours
Hepatic events	Potential drug-induced liver injury (Hy's law criteria)	Within 24 hours

8.1 Follow-up of adverse events

All AEs are followed until resolution, stabilisation or the end of the study, whichever occurs first. SAEs and adverse events of special interest that are ongoing at the end of the study are followed until resolution or until the investigator considers them chronic or stable. The investigator provides follow-up information on SAEs within 24 hours of receipt.

8.2 Pregnancy

Pregnancies in female participants or in partners of male participants that occur from the first dose until 20 weeks after the last dose must be reported to the sponsor within 24 hours, using the pregnancy form. Female participants who become pregnant discontinue treatment immediately. The pregnancy is followed until its outcome is known, and the infant until the age of 12 months.

9 STATISTICAL CONSIDERATIONS

9.1 Statistical hypotheses

For each CVB-0217 dose the null hypothesis is that the proportion of participants achieving PASI 75 at Week 16 is equal to that of placebo, against the two-sided alternative that the proportions differ. The family-wise type I error rate is controlled at 5% by testing each comparison at a two-sided level of 2.5% (Bonferroni).

9.2 Sample size determination

The sample size is based on the comparison of CVB-0217 150 mg with placebo, the comparison with the smaller expected difference. For two proportions p_1 and p_2, the number of participants per arm is

$$n = \frac{\left(z_{1-\alpha/2}\sqrt{2\bar{p}(1-\bar{p})} + z_{1-\beta}\sqrt{p_1(1-p_1)+p_2(1-p_2)}\right)^2}{(p_1-p_2)^2} \qquad (6)$$

where $\bar{p} = (p_1 + p_2)/2$. Assuming PASI 75 response rates of 45% for CVB-0217 150 mg and 8% for placebo, $\alpha = 0.025$ (two-sided) and a power of 90% ($z_{0.9875} = 2.241$, $z_{0.90} = 1.282$), (6) gives $n = 33$ evaluable participants per arm. Allowing for a dropout rate of 12%, 38 participants per arm are required; 40 per arm (120 in total) will be randomised. For the 300 mg dose, with an assumed response rate of 55%, the power exceeds 99%.

9.3 Estimands

The primary estimand, defined according to ICH E9(R1), is described by the following attributes:

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Table 9. Attributes of the primary estimand

Attribute	Definition for the primary estimand
Treatment condition	CVB-0217 150 mg or 300 mg SC Q4W versus placebo, each in addition to bland emollients
Population	Adults with moderate-to-severe chronic plaque psoriasis as defined by the eligibility criteria
Variable	PASI 75 response at Week 16 (yes/no)
Intercurrent events	Discontinuation of treatment for lack of efficacy or use of prohibited psoriasis therapy: composite strategy (counted as non-response). Discontinuation for other reasons: treatment-policy strategy
Population-level summary	Difference in response proportions between each CVB-0217 arm and placebo

9.4 Analysis sets

Table 10. Analysis sets

Analysis set	Definition	Use
Full analysis set (FAS)	All randomised participants, analysed according to the randomised treatment	Primary efficacy analysis
Per-protocol set (PPS)	FAS participants without major protocol deviations affecting the primary endpoint	Sensitivity analysis
Safety set	All participants who received at least one dose of IMP, analysed according to treatment received	Safety analyses
PK set	Participants with at least one quantifiable CVB-0217 concentration	PK analyses

9.5 Statistical analyses

9.5.1 Primary endpoint

The proportion of PASI 75 responders at Week 16 will be compared between each CVB-0217 arm and placebo using a CMH test stratified by the randomisation strata. Differences in proportions will be presented with 97.5% confidence intervals. Participants with missing data at Week 16, or who discontinue treatment because of lack of efficacy, will be considered non-responders (non-responder imputation, NRI). Sensitivity analyses will use multiple imputation and the PPS.

9.5.2 Secondary and exploratory endpoints

Binary secondary endpoints will be analysed like the primary endpoint. Continuous endpoints will be analysed with a mixed model for repeated measures including treatment, visit, treatment-by-visit interaction, stratum and baseline value. No adjustment for multiplicity is made for secondary endpoints. Safety data will be summarised descriptively by treatment received.

9.5.3 Pharmacokinetic and pharmacodynamic analyses

Serum trough concentrations will be summarised by treatment, visit and ADA status. Individual exposure measures (steady-state trough concentration and AUC over a dosing interval, (5)) will be derived from the population PK model and related to PASI response at Week 16 using a logistic E_{max} model. Changes in serum biomarkers will be summarised descriptively and explored as a function of exposure.

9.5.4 Safety analyses

TEAEs will be summarised by system organ class and preferred term, severity and relationship to the IMP, separately for the placebo-controlled period and for the entire treatment period. Exposure-

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adjusted incidence rates per 100 participant-years will be presented for adverse events of special interest. Laboratory values will be summarised as shifts from baseline using CTCAE grades.

9.6 Data Monitoring Committee

An independent DMC consisting of two dermatologists and one statistician will review unblinded safety data every 3 months and may recommend modification or termination of the study. Its responsibilities and procedures are described in the DMC charter (version 1.0, 2 June 2026). The DMC has no role in efficacy decisions.

10 REGULATORY, ETHICAL AND STUDY OVERSIGHT

10.1 Ethics and informed consent

The protocol, the informed consent form and any other written information for participants will be submitted to the competent authorities and ethics committees through the EU clinical trials portal and, in Switzerland, to the competent cantonal ethics committee and the national regulatory authority. The investigator will obtain written informed consent from each participant before any study procedure, after explaining the aims, methods, anticipated benefits and potential risks of the study.

10.2 Data protection

Participants are identified only by a participant number in all study documents transmitted to the sponsor. Personal data are processed in accordance with Regulation (EU) 2016/679 and the Swiss Federal Act on Data Protection. Participants have the right to access and correct their data.

10.3 Monitoring and quality assurance

The sponsor applies a risk-based monitoring approach combining centralised statistical monitoring with on-site visits. Source data verification is performed for informed consent, eligibility, the primary endpoint and SAEs in all participants. The sponsor’s quality assurance department or regulatory authorities may audit or inspect the study at any time.

10.4 Data handling and record keeping

Data are entered by site staff into a validated electronic data capture system compliant with 21 CFR Part 11 and EU GMP Annex 11. Source documents are retained at the site. The investigator file and the sponsor’s trial master file are archived for at least 25 years after the end of the study, as required by Regulation (EU) No 536/2014.

10.5 Insurance and compensation

The sponsor has taken out liability insurance covering damage to health suffered by participants as a result of their participation in the study, in accordance with the legal requirements of each participating country. Participants receive compensation for travel expenses and time spent at study visits as approved by the ethics committees.

10.6 Publication policy

The results of the study will be published irrespective of their outcome. A summary of results will be posted in the EU clinical trials portal within 12 months of the end of the study, together with a lay summary. The coordinating investigator and the sponsor will prepare a manuscript for a peer-reviewed journal; authorship follows internationally accepted criteria.

CONFIDENTIAL - DRAFT

10.7 Risk-based quality management

Critical-to-quality factors identified during protocol development include the eligibility assessment of disease severity, the blinded and correct administration of the IMP, the timing of the Week 16 assessments and the reporting of SAEs. Quality tolerance limits are defined for the proportion of participants with major eligibility deviations (5%) and with a missing primary endpoint (12%); breaches are reported in the clinical study report together with the actions taken.

CONFIDENTIAL – DRAFT

11 REFERENCES

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CONFIDENTIAL – DRAFT

APPENDIX 1 – CLINICAL LABORATORY PARAMETERS

Samples are analysed by the central laboratory (Labor Rottenmatte AG, Visp). Reference ranges are provided in the laboratory manual; values outside the ranges below are flagged in the laboratory report.

Table 11. Clinical laboratory parameters

Panel	Parameter	Unit	Reference range (adults)
Haematology	Haemoglobin	g/L	120–160 (F); 135–175 (M)
	Leucocytes	10^9/L	4.0–10.0
	Neutrophils	10^9/L	1.8–7.5
	Lymphocytes	10^9/L	1.0–4.0
	Platelets	10^9/L	150–400
Biochemistry	ALT / AST	U/L	≤ 45 / ≤ 35
	Alkaline phosphatase	U/L	40–130
	Total bilirubin	µmol/L	≤ 21
	Creatinine	µmol/L	45–90 (F); 60–110 (M)
	eGFR (CKD-EPI)	mL/min/1.73 m²	≥ 90
	Glucose (fasting)	mmol/L	3.9–5.6
	Total cholesterol / triglycerides	mmol/L	< 5.2 / < 1.7
	hsCRP	mg/L	< 3.0
Urinalysis	Protein, glucose, blood, leucocytes (dipstick)	–	Negative
	Microscopy (if dipstick abnormal)	/HPF	Erythrocytes < 3
Serology	HBsAg, anti-HBc, anti-HCV, HIV-1/2 Ag/Ab	–	Negative
	Interferon-gamma release assay	IU/mL	< 0.35 (negative)
Pregnancy	Serum β-hCG (screening)	IU/L	< 5
	Urine hCG (before each dose)	–	Negative

APPENDIX 2 – PSORIASIS AREA AND SEVERITY INDEX

The PASI is calculated from the severity of erythema (E), induration (I) and desquamation (D), each scored from 0 to 4, and the area score (A, 0 to 6) in each of four body regions r (head, upper limbs, trunk, lower limbs), weighted by the proportion of body surface area w_r of the region:

$$\mathrm{PASI} = \sum_{r=1}^{4} w_r \cdot A_r \cdot (E_r + I_r + D_r)\,, \quad w = (0.1, 0.2, 0.3, 0.4) \tag{7}$$

The PASI ranges from 0 (no psoriasis) to 72. PASI 75, PASI 90 and PASI 100 denote improvements of at least 75%, 90% and 100% from the baseline score.

Table 12. PASI area score

Area score	0	1	2	3	4	5	6
Involvement of region	0%	< 10%	10–29%	30–49%	50–69%	70–89%	90–100%

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APPENDIX 3 – SUMMARY OF CHANGES IN AMENDMENT 2

The following table lists the substantial changes proposed in protocol version 3.0 compared with version 2.0, with the rationale for each change. Editorial changes that do not affect the conduct of the study are not listed.

Table 13. Summary of changes in Amendment 2

Section	Change	Rationale
Synopsis; 9.2	Dropout assumption increased from 10% to 12%; sample size unchanged (120)	Updated estimate from the Phase I extension and comparable Phase II studies
Synopsis; 9.5.1	Non-responder imputation specified as the primary approach for missing data	Request from the lead biostatistician; alignment with the estimand framework
4.2	Tuberculosis screening by IGRA within 4 weeks before Day 1	Alignment with current national screening recommendations
5.3	Observation period moved to the randomisation and blinding section; wording clarified	Editorial consistency
5.2	Permitted temperature excursion extended to 72 hours at ≤ 25 °C	Supported by stability data from line FL-5
7.1	PK and ADA samples added at Week 2	Estimation of the absorption rate constant in the population PK model
9.6	DMC charter version referenced	Traceability of DMC procedures

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APPENDIX 4 – CONTRACEPTION GUIDANCE

Women of childbearing potential must use one of the following highly effective methods of contraception (failure rate below 1% per year) from screening until 20 weeks after the last dose. Male participants with partners of childbearing potential must use a condom during the same period.

Table 14. Highly effective methods of contraception

Category	Methods
Hormonal, associated with inhibition of ovulation	Combined oral, intravaginal or transdermal contraception; progestogen-only oral, injectable or implantable contraception
Intrauterine	Intrauterine device; intrauterine hormone-releasing system
Surgical	Bilateral tubal occlusion; vasectomised partner (provided he is the sole partner and azoospermia has been confirmed)
Behavioural	Sexual abstinence, if in line with the preferred and usual lifestyle of the participant

APPENDIX 5 – LIVER SAFETY: ACTIONS AND FOLLOW-UP ASSESSMENTS

Participants with abnormal liver tests are managed according to the following algorithm. Repeat tests should be performed within 48 to 72 hours, and alternative causes such as viral hepatitis, alcohol, concomitant medication or biliary obstruction should be investigated.

Table 15. Liver safety algorithm

Laboratory finding	Action with the IMP	Follow-up
ALT or AST > 3 × ULN and ≤ 5 × ULN, bilirubin normal	Continue; repeat tests within 72 hours	Weekly until < 2 × ULN
ALT or AST > 5 × ULN	Interrupt; discontinue permanently if confirmed	Twice weekly until resolution; hepatology referral
ALT or AST > 3 × ULN and total bilirubin > 2 × ULN or INR > 1.5	Discontinue permanently; report as SAE within 24 hours	Full liver work-up; follow until resolution
ALT or AST > 3 × ULN with symptoms (fatigue, nausea, right upper quadrant pain, rash, eosinophilia)	Discontinue permanently	As above

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