SUMMARY OF CHANGES
FOR RADEMIKIBART
INVESTIGATOR'S BROCHURE

Sponsors:	Connect Biopharm LLC (dba, Connect Biopharma) Simcere Pharmaceutical Group Limited (Simcere)	
Investigational Product:	Rademikibart (CBP-201, SIM0718)	
Edition Number:	9.0	Dated: 24 August 2026
Replaces Edition:	8.0	Dated: 28 February 2025

SUMMARY OF CHANGES

The rademikibart Investigator's Brochure (IB) has been updated to incorporate information from new nonclinical studies as well as completed and ongoing clinical trials. No new risks have been identified, and the risk-benefit profile remains unchanged.

Changes from IB Edition 8.0 to Edition 9.0 are summarized below.

Section No.	Section Title	Revision
1	Summary	Updated the summary to reflect changes made throughout the IB.
2	Introduction	Updated the background sections on the indications under development for rademikibart (AD, asthma, and COPD). Revisions include updates to disease pathophysiology, prevalence, current treatment guidelines, and approved therapies.
3	Physical, Chemical, and Pharmaceutical Properties and Formulation	Updated the packaging information for the investigational product.

4	Nonclinical Studies	• Added results from 2 in vitro pharmacology studies on receptor trafficking, internalization, and cell fate effects.
		• Added results from an ex vivo human precision cut lung slice and airway smooth muscle study.
		• Updated the PK summary as follows:
		  ○ Added information on a transgenic mouse EFD study and a transgenic mouse pre/postnatal development study.
		  ○ Rounded PK results to present a consistent number of significant figures.
		  ○ Revised the units for AUC_{inf} to μg·h/mL in order to calculate safety margins with clinical values.
		• Added results from 3 GLP developmental and reproductive toxicology studies.
		• Added a section on safety margins for human dosing.

5	Effects in Humans	• Updated the list of clinical trials, trial status, and number of participants exposed in the rademikibart clinical development program. • Added results from 2 completed trials: a Phase 1 trial in healthy participants (Trial SIM0718-101) and a Phase 3 trial in participants with AD (Trial SIM0718-302). • Added preliminary safety, PK, and PD results from completed parts of an ongoing Phase 1 trial in healthy participants and participants with stable asthma and COPD (Trial CBP-201-105 Parts A and B).

Section No.	Section Title	Revision
		• Rounded PK results to present a consistent number of significant figures. • Reduced the summary of efficacy for earlier phase trials. • Condensed and integrated the summary of safety for the healthy participants. • Added a section on injection site reactions. • Updated the overall summaries of clinical pharmacology, efficacy, and safety.
6	Summary of Data and Guidance for the Investigator	• Updated the warnings and precautions section to include stapokibart as an approved product in the same class as rademikibart; however, no new warnings or precautions were added. • Updated the most common TEAEs, SAEs, and AESIs, to align with updated clinical trial information. • Updated the risk/benefit section to address the unmet need for AD and pulmonary disease and to add the efficacy of rademikibart in clinical trials. Stapokibart was also added as an approved product in the same class as rademikibart; however, no new identified risks were added. • Updated the number of adolescent participants treated with rademikibart and the safety and PK analyses. There was no change to the conclusion – no dose adjustment is required for adolescents. • Updated the number of geriatric participants treated with rademikibart and the safety and PK analyses. There was no change to the conclusion – no dose adjustment is required for participants ≥65 years of age. • Updated the pregnancy and lactation section based on the 3 completed developmental and reproductive toxicology studies. As a precaution, women who are pregnant or breastfeeding are excluded from participating in clinical trials of rademikibart and women of childbearing potential are required to use contraception.
7	References	Reformatted and updated the list of references.
Global		Made editorial and formatting changes for clarity and consistency.

Abbreviations: AD, atopic dermatitis, AESI, adverse event of special interest; AUC_{inf}; area under the concentration-time curve from Time 0 to the last quantifiable concentration; COPD, chronic obstructive pulmonary disease; EFD, embryo-fetal development; GLP, Good Laboratory Practice; IB, Investigator's Brochure; PD, pharmacodynamics; PK, pharmacokinetics; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

REVISIONS

IB Edition 9.0, with changes from Edition 8.0 tracked, is presented on the following pages. New text is presented as underlined and deleted text as ~~strikethrough~~.

INVESTIGATOR'S BROCHURE
FOR
RADEMIKIBART

SPONSORS:	Connect Biopharm LLC (dba, Connect Biopharma) Simcere Pharmaceutical Group Limited (Simcere)
INVESTIGATIONAL ~~DRUG~~PRODUCT:	Rademikibart (CBP-201, SIM0718)
EDITION NUMBER:	~~9~~8.0 (supersedes edition ~~8~~7.0 of 28 February 2025~~19 August 2024~~)
DATE:	24 August 2026~~28 February 2025~~

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ACQ	Asthma Control Questionnaire
AD	Atopic dermatitis
ADA	Anti-drug antibody
ADCC	Antibody-dependent cell-mediated cytotoxicity
AE	Adverse event
AESI	Adverse event of special interest
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATS	American Thoracic Society
AUC	Area under curve ~~the plasma concentration-time curve~~
AUC_{0-Xh}	Area under the concentration-time curve from Time 0 to X hours postdose
AUC_{0-inf} (also referred to as $AUC_{0-\infty}$ and AUC_{inf})	Area under the concentration-time curve from time 0 extrapolated to infinity
AUC_{0-last} (also referred to as AUC_{last} and AUC_{0-t})	Area under the concentration-time curve from time 0 to the last measurable concentration~~recorded timepoint~~
~~AUC_{0-t}~~	~~Area under the curve from time 0 to a designated timepoint~~
~~AUC_{inf}~~	~~Area under the curve at the infimum~~
~~AUC_{last}~~	~~Area under the concentration-time curve at the last recorded timepoint~~
BD	Bronchodilator
BLQ	Below the limit of quantification
~~BMI~~	~~Body mass index~~
BSA	Body surface area
CDC	Complement-dependent cytotoxicity
~~CFB~~	~~Change from baseline~~
~~CFR~~	~~Code of Federal Regulations~~
~~CHO~~	~~Chinese hamster ovary~~
CI	Confidence interval
CL	Clearance
CL/F	Apparent oral clearance uncorrected for bioavailability
C_{max}	Maximum observed concentration
COPD	Chronic obstructive pulmonary disease

Abbreviation	Definition
~~CPK~~	~~Creatine phosphokinase~~
CRSwNP	Chronic rhinosinusitis with nasal polyps
CTCAE	Common Terminology Criteria for Adverse Event
C_{trough}	Trough concentration
~~CV~~	~~Coefficient of variance~~
DART	Developmental and reproductive toxicology
~~DCSI~~	~~Development Core Safety Information~~
DDI	Drug-drug interaction
DILI	Drug-induced liver injury
DLQI	Dermatology Life Quality Index
~~DS~~	~~Drug substance~~
EASI	Eczema Area and Severity Index
ECG	Electrocardiogram
EFD	Embryo-fetal development
ELISA	Enzyme-linked immunosorbent assay
~~EOS~~	~~End of Study~~
~~EOT~~	~~End of Treatment~~
~~ER~~	~~Exposure-response~~
~~ERS~~	~~European Respiratory Society~~
FACS	Fluorescence-activated cell sorting
~~FAS~~	~~Full analysis set~~
~~FDA~~	~~Food and Drug Administration~~
FEED	Fertility and early embryonic developmental
FeNO	Fractional exhaled nitric oxide
FEV_1	Forced expiratory volume in 1 second
FIH	First-in-human
FVC	Forced vital capacity
GD	Gestation day
GINA	Global Initiative for Asthma
GLP	Good Laboratory Practice
~~GMP~~	~~Good Manufacturing Practice~~
GMR	Geometric mean ratio
~~GOF~~	~~Goodness-of-fit~~
HASM	Human airway smooth muscle
HEK	Human embryonic kidney
~~IB~~	~~Investigator's Brochure~~

Abbreviation	Definition
IC_{50}	Half-maximal inhibitory concentration
ICS	Inhaled corticosteroid
Ig	Immunoglobulin
IGA	Investigator Global Assessment
~~ICS~~	~~Inhaled corticosteroid~~
~~ICF~~	~~Informed consent form~~
IL-4Rα	Interleukin-4-receptor alpha
IL~~-4, -13~~	Interleukin~~-4, -13~~
~~INCS~~	~~Intranasal corticosteroid~~
IP	Investigational product
~~IRT~~	~~Interactive Response Technology~~
ISR	Injection site reaction~~s~~
~~ITT~~	~~Intention-to-Treat~~
IV	Intravenous(ly)
JAK	Janus kinase
KD	Dissociation constant
LABA	Long-acting β-agonist
LAMA	Long-acting muscarinic agent
LD	Lactation day~~Loading dose~~
LDH	Lactate dehydrogenase
~~LLOQ~~	~~Lower limit of quantification~~
~~LOCF~~	~~Last observation carried forward~~
~~LSM~~	~~Least squares mean~~
mAb	Monoclonal antibody
MAD	Multiple ascending dose
MRTiv	Mean residence time following IV dose
~~MSD~~	~~Meso Scale Discovery~~
MTD	Maximum tolerated dose
~~N~~nAb	Neutralizing antibod~~y~~ies
~~NAEPP~~	~~National Asthma Education and Prevention Program~~
~~NCA~~	~~Noncompartmental modeling analysis~~
NCS	Nasal Congestion Score
~~NMPA China~~	~~National Medical Products Administration (China)~~
NOAEL	No-observed-adverse-effect level
NPS	Nasal Polyp Score
~~NPIF~~	~~Nasal Peak Inspiratory Flow~~

Abbreviation	Definition
PBMC	Peripheral blood mononuclear cell
PBST	Phosphate buffered saline containing Tween 20
PCLS	Precision-cut lung slice
PD	Pharmacodynamic(s)
PEF	Peak expiratory flow
PFS	Prefilled syringe
~~PD~~	~~Pharmacodynamic(s)~~
PK	Pharmacokinetic(s)
POEM	Patient-Oriented Eczema Measure
PND	Postnatal day
PPND	Pre/postnatal development
PP-NRS	Peak Pruritus Numerical Rating Scale
PNHS	Pooled normal human serum
P-NRS	Pruritus Numerical Rating Scale
~~POEM~~	~~Patient-Oriented Eczema Measure~~
PRO	Patient-reported outcomes
PT	Preferred Term
QW	Once a week
Q2W	Every 2 weeks
Q4W	Every 4 weeks
~~RSI~~	~~Reference Safety Information~~
SAD	Single ascending dose
SAE	Serious adverse event
SAR	Serious adverse reaction
SC	Subcutaneous(ly)
~~SCORAD~~	~~SCORing Atopic Dermatitis~~
SD	Standard deviation
SE	Standard error
~~SEAP~~	~~Secreted alkaline phosphatase~~
SOC	System Organ Class
STAT	Signal transducer and activator of transcription ~~(protein)~~
$t_{1/2}$	Terminal h~~H~~alf-life
TARC	Thymus and activation regulated chemokine
~~TCS~~	~~Topical corticosteroid~~
TEAE	Treatment-emergent adverse event
TF-1	Unique human cell line that proliferates dependently on GM-CF, IL-3, or erythropoietin

Abbreviation	Definition
TK	Toxicokinetic(s)
T_{max}	Time to maximum concentration
~~V_z/F~~	~~Apparent volume of distribution uncorrected for bioavailability~~
ULN	Upper limit of normal
US	United States
VC	Vehicle control
V_z	Apparent volume of distribution
V_z/F	Apparent volume of distribution uncorrected for bioavailability
WBC	White blood cell

1. SUMMARY

Rademikibart (also known as CBP-201, SIM0718) is a novel human monoclonal antibody (mAb) of the IgG4 subclass that binds to the cell surface protein interleukin-4-receptor α (IL-4Rα) and inhibits IL-4 and IL-13 signaling. Connect Biopharm LLC (dba, Connect Biopharma) and its partner in China, Simcere Pharmaceutical Group Limited, are developing rademikibart for the treatment of atopic dermatitis (AD) and respiratory diseases with Ttype-2 inflammation, including asthma and chronic obstructive pulmonary disease (COPD). In vitro and in vivo nonclinical studies have been conducted to characterize the pharmacologic properties of rademikibart, confirming the mechanism of action, providing proof-of-concept efficacy evidence, and determining potential toxicities of rademikibart in human participants. The rademikibart clinical development strategy has been informed by clinical experience with the marketed products, DUPIXENT (dupilumab) and KANGYUEDA (stapokibart), which is are also an IL-4Rα antagonists. Dupilumab was initially approved in March 2017 in the United States (US) and is available in many markets globally. Stapokibart has been approved for AD but is only available in China.

Extensive in vitro, ex vivo and in vivo studies have been conducted to characterize the pharmacological properties of rademikibart. Rademikibart binds to recombinant soluble monomeric human IL-4Rα with a dissociation constant (KD) of approximately 20.7 pM. It does not bind to mouse or monkey IL-4Rα. Rademikibart inhibits proliferation of TF-1 cells stimulated with IL-4 and IL-13 with a half-maximal inhibitory concentration (IC_{50}) of 8.00 and 9.68 ng/mL, respectively. It also inhibits IL-4- and IL-13-mediated STAT6 activation in human embryonic kidney (HEK) Blue IL-4/IL-13 secreted alkaline phosphatase cells; with an IC_{50} of 7.04 and 6.56 ng/mL, respectively. In ex vivo assays, rademikibart inhibited IL-4-induced production of thymus and activation regulated chemokine (TARC) in human peripheral blood mononuclear cells (PBMCs), and the IC_{50} was 101.7 ng/mL. These studies show that rademikibart is a highly potent antibody against the IL-4Rα. Additional mechanistic studies further characterized the biological activity of rademikibart. In vitro evaluation of IL-4Rα receptor trafficking demonstrated greater antibody internalization with rademikibart compared with dupilumab in EOL-1 cells using complementary internalization assays. In apoptosis assays conducted in EOL-1 cells and primary human eosinophils, rademikibart induced higher levels of apoptosis signaling than dupilumab. In primary human airway smooth muscle (HASM) cells, rademikibart inhibited IL-4/IL-13-driven signaling responses and increased β_2-agonist-induced HSP20 phosphorylation, supporting enhanced cyclic AMP-dependent relaxation signaling. In human precision-cut lung slice (PCLS) models, rademikibart partially reversed IL-13-induced β_2-adrenergic hyporesponsiveness and restored bronchodilator responsiveness, whereas dupilumab showed a modest dose-dependent partial rescue, substantially lower than rademikibart at equivalent doses. Collectively, these findings provide additional mechanistic evidence that rademikibart inhibits IL-4Rα-mediated signaling and may mitigate type 2 cytokine-driven alterations in airway smooth muscle function and bronchodilator responsiveness. No rademikibart-related adverse effects or changes on the central nervous, cardiovascular, respiratory, and lymphoid systems were found following subcutaneous (SC) administration of up to 200 mg/kg/week of rademikibart in cynomolgus monkeys.

Rademikibart does not bind to native mouse or cynomolgus monkey IL-4Rα.cross-react with IL-4Rα of the preclinical species. Therefore, full assessment of the potential toxicity of rademikibart

based on conventional laboratory animal data was not possible and the nonclinical safety assessment relied on a combination of studies in cynomolgus monkeys (non-pharmacologically responsive) and transgenic mice expressing human IL-4Rα (pharmacologically responsive). The off-target toxicity of rademikibart was evaluated in a 4-week Good Laboratory Practice (GLP) study in cynomolgus monkeys (Li 2017). Rademikibart (6, 40, and 200 mg/kg) was administered once a week (QW) by SC injection and was very well tolerated at all dose levels. No abnormal clinical observations or abnormalities in hematology, blood chemistry, or pathology were noted. No abnormalities in cardiac and lung function were observed. Based on this study, the no-observed-adverse-effect level (NOAEL) was 200 mg/kg, the highest dose tested, which corresponds to a C_{max} of approximately 6279 µg/mL and an area under the concentration-time curve at through the last measured time-point (AUC_{last}) of approximately 837.4 µmg·× h/mL. With the availability of the B-hIL-4/hIL-4RA (transgenic) mice that express human IL-4 and IL-4Rα, a GLP 26-week toxicity study of rademikibart with a 4-week recovery period in transgenic mice by SC injection was conducted. No abnormal clinical observations or abnormalities in pathology were found. Non-adverse Ffindings in hematology and clinical chemistry occurred at 200 mg/kg on Day 184 that were consistent with the intended pharmacology of rademikibart, considered to likely be test-article-related due to its pharmacological effect as a mAb includinged decreases in absolute count of lymphocytes and white blood cell counts in males and an increase in serum globulin and a decrease in albumin/globulin ratio in females and males. Under the conditions of the study, the NOAEL was considered to be the highest tested dose tested of 200 mg/kg.

Reproductive toxicology studies in B-hIL-4/hIL-4RA transgenic mice did not show any rademikibart-related effects on male or female fertility at doses up to approximately 22 times the highest anticipated human AUC exposure, or on embryo-fetal or pre-/postnatal development, including behavior and reproductive function of F1 offspring, at doses up to 13- to 18-fold the highest anticipated human AUC exposure.

A total of 2892 participants have been dosed across 15 rademikibart clinical trials (11 completed and 4 ongoing). Trials include healthy participants, participants with AD, and participants with respiratory diseases (asthma, COPD, and chronic rhinosinusitis with nasal polyps [CRSwNP]). An estimated 2316 participants have received at least 1 dose of rademikibart: 2272 via SC injection and 44 via intravenous (IV) infusion. Rademikibart doses administered SC ranged from 75 to 600 mg, and a single 300 mg dose was administered IV.

Clinical trials have been conducted for rademikibart in healthy participants and in participants with asthma and Type 2 inflammation, AD, and chronic rhinosinusitis with nasal polyps (CRSwNP). A total of 9 clinical trials of rademikibart have been completed, of which 1 trial in CRSwNP was terminated early by the Sponsor due to slow enrollment during the COVID-19 pandemic (Table 2). A total of 1498 participants have received at least one dose of rademikibart in completed trials, including 384 healthy participants, 874 participants with moderate-to-severe AD, 214 participants with moderate-to-severe persistent asthma with T2 inflammation and 26 participants with CRSwNP.

Rademikibart pharmacokinetics (PK) have been evaluated in healthy participants and in participants following single doses up to 600 mg SC, following multiple doses up to 300 mg SC QW, and following 300 mg IV dose administered over 30 minutes. Rademikibart has demonstrated consistent PK properties across various trials involving healthy participants and

patient populations, and between adults and adolescents (≥12 to <18 years of age)participants with conditions such as moderate-to-severe asthma and AD. As all rademikibart dosing regimens have been generally well -tolerated, the maximum- tolerated dose (MTD) has not been established.

Following a 300 mg IV dose, rademikibart concentrations decreased monoexponentially with an approximately 6-day $t_{1/2}$. The rate of infusion did not impact the mean C_{max}; therefore, in current trials utilizing IV dosing, rademikibart is administered via a short 2-minute infusion (push).

Rademikibart administered via the SC route exhibits relatively dose-proportional absorption (ie, dose-proportional increases in C_{max})exhibits relatively dose-proportional absorption (ie, dose-proportional increases in C_{max}). Overall exposure (AUC) increases slightly disproportionately with dose, manifesting and nonlinear elimination with increasing dose. The nonlinearity in clearance following SC dosing (CL/F) results in slower post-peak decline in concentrations, longer $t_{1/2}$, and lower apparent extravascular clearance (CL/F) greater-than-dose-proportional increases in overall drug exposure (AUC) with increasing dose. Theis decrease in CL/F with dose suggests also indicates that rademikibart is eliminated via 2 elimination pathways, one of which is concentration-dependent and saturable, thus likely target-mediated, with the second pathway likely proteolytic catabolism followed by nonspecific elimination via the reticuloendothelial system, which is common to all mAbs. Initial population PK modeling estimates that the saturable CL pathway is 50% saturated inhibited at concentrations far below C_{trough} reported on any multiple-dose trial; thus, saturable CL is unlikely to influence the multiple-dose concentration profile of rademikibart in clinical practice.

Despite the dose dependency in CL, there is no evidence of time-dependency in rademikibart CL/F following multiple dosing. Once steady state is reached, concentrations generally remain stable through the duration of treatment, consistent with time-invariant PK. For a given dose level, mean $t_{1/2}$ appears to be similar following a single dose and following the last dose in multiple-dose studies; thus, accumulation is predictable and varies only with dose and with dosing frequency. The 300 mg Q2W SC multiple-dose regimen most commonly used in clinical trials results in approximately 2-fold accumulation.

Given that C_{max} following a 600 mg loading dose of rademikibart administered SC is similar to steady-state C_{max} following 300 mg administered SC Q2W, in current trials utilizing SC dosing a 600 mg loading dose is administered first, followed by 300 mg Q2W maintenance dose. In a dosing regimen consisting of a 600 mg loading dose (LD) followed by 300 mg Q2W maintenance dose, the LD achievedThe C_{trough} concentrations by the end of the 2-week dosing interval following the loading dose are similar that were close to the steady-state concentrations which were subsequently maintained with the 300 mg Q2W maintenance dose through duration of treatment.

The immunogenicity incidence has been generally low and nonpersistent, with low anti-drug antibody (ADA) titers, and late onset, and appears to be inversely proportional to the rademikibart dose. Overall, the onset of immunogenicity appears to present minimal safety risk and is unlikely to lead to loss of efficacy with continued exposure.

Exploratory pharmacodynamic (PD) analysis across AD trials indicates that rademikibart dosing results in a steady decline of serum TARC and lactate dehydrogenase (LDH) levels, which are biomarkers associated with improvement in AD. In participants with asthma, decreases in mean

fractional exhaled nitric oxide (FeNO) and IgE were noted with onset in Week 1 and continuing up to the end of the trialstudy (EOS). Preliminary exposure-response modeling in participants with asthma has shown that the greatest change from baseline (CFB) in both pre-bronchodilator forced expiratory volume in 1 second (FEV_1) and the Asthma Control Questionnaire (ACQ) score occurred after the 600 mg loading doseLD.

Rademikibart has shown efficacy across clinical trials involving participants with moderate-to-severe asthma, COPD, and and with AD. Activity consistent with the mechanism of action was also observed in the early terminated trial in CRSwNP.

In the a Phase 2 asthma trial, participants with persistent moderate-to-severe asthma treated with rademikibart 150 and 300 mg SC Q2W preceded by a 600 mg loading dose LD showed significant improvements in lung function, as measured by pre-bronchodilator FEV_1, compared to placebo. These improvements were observed as early as Week 1 and sustained through Week 24. Additionally, there was a trend towards a positive effect on asthma exacerbation, with a reduction in the risk of having ≥1 asthma exacerbation during the 24-week treatment period. Preliminary results from an ongoing Phase 1 clinical trial in asthma and COPD have demonstrated improvements in lung function following a single IV dose of rademikibart 300 mg.

Four Five clinical trials (Phases 1b through 32) of repeated doses of rademikibart in AD participants have been completed. Rademikibart has demonstrated robust and consistent efficacy in completed clinical trials, across a variety of clinical outcomes, reflecting clinically meaningful and statistically significant improvement in AD signs, symptoms, and quality of life. Higher doses (150 mg and 300 mg) showed greater improvements in skin-related clearance endpoints compared to lower doses and placebo. Patient-reported outcomes (PROs) were improved with all doses compared to placebo. Phase 2 trials demonstrated the efficacy of rademikibart, with significant improvements in Eczema Area and Severity Index (EASI)-75, EASI-90, and Investigator Global Assessment (IGA) response rates at Week 16. The Additionally, long-term efficacy results in a completed Phase 2 trial showed that the disease status of participants with moderate-to-severe AD treated continued treatment with rademikibart 300 mg either Q2W orand Q4W could be sustainably controlled, and in many instances improved, the disease status of participants with moderate-to-severe ADas treatment continued. In a Phase 3, randomized, placebo-controlled trial in participants with moderate-to-severe AD, rademikibart was superior to placebo in improving skin lesions, reducing lesion area, relieving pruritus, improving the quality of life, and improving subjective symptoms of AD.

In the nasal polyps trial, although the trial was terminated early, the available data indicated a numeric reduction in endoscopic nasal polyp score (NPS) and average daily nasal congestion score (NCS) for participants treated with rademikibart1.

Rademikibart demonstrated a favorable safety profile in healthy participants and participants across indications. Most treatment-emergent adverse events (TEAEs) were mild-to-moderate in severity.

Of the 1964 rademikibart-treated participants in 11 completed clinical trial and the completed parts of 1 ongoing trial, 2.5% of rademikibart-treated participants experienced serious adverse events (SAEs), of which 3 events were considered by Investigators to be related to rademikibart (vestibular neuronitis [participant with AD], alanine aminotransferase (ALT) increased [healthy participant], and syncope [participant with AD]). One additional SAE in the ongoing blinded

trials was classified as related to investigational product (IP) (periorbital haemorrhage in a participant with asthma). Two deaths have been reported to date. One participant with AD experienced a fatal cardiac arrest. The second death occurred due to pneumonia in a participant with asthma in an ongoing blinded trial. Both deaths were considered not related to rademikibart/blinded IP.~~A total of 48 serious adverse events (SAEs), including 1 death, was reported for 34 participants who received rademikibart in in the 9 completed clinical trials, of which none were considered possibly related to rademikibart.~~

In 5 completed AD trials, the most common TEAEs reported for rademikibart (>5% of participants and higher than placebo) were upper respiratory tract infection (15.6%), COVID-19 (6.3%), and hyperuricaemia (5.3%). In a completed Phase 2 trial in asthma, the most common TEAEs for rademikibart (>5% and higher than placebo) were COVID-19 (12.1%), injection site erythema (6.5%), and nasopharyngitis (5.6%). In a second trial in asthma and COPD, no TEAE occurred in more than 1 participant.

Injection site reactions (ISRs) are an identified risk with SC administration of rademikibart. In completed trials of rademikibart SC in participants with asthma, AD, and CRSwNP, 7.2% of rademikibart-treated participants experienced TEAEs associated with ISRs. All events were mild-to-moderate in severity.

In the clinical development program, adverse events of special interest (AESIs) are defined as conjunctivitis, keratitis, anaphylactic reaction, ISRs ≥Grade 3 lasting more than 24 hours, and parasitic and opportunistic infections. Of the 1386 rademikibart-treated participants in 7 completed clinical trials and the completed parts of 1 ongoing trial in participants with asthma, AD, COPD, and CRSwNP, the most common AESIs were conjunctivitis (3.8% of participants) and keratitis (0.4%). AESIs of parasitic/opportunistic infection and anaphylactic reaction were reported in 1 participant each (0.07%). There were no reports of ISRs ≥Grade 3 lasting >24 hours.

The trial on CRSwNP was terminated early, but the available data showed that no participant experienced an SAE~~ and TEAEs were mostly mild-to-moderate in severity~~.

~~The most frequently reported AESIs in the 1,114 participants in the completed clinical studies in participants with asthma, AD, and CRSwNP were injection site reactions (ISRs) lasting more than 24 hours (5.5%) and conjunctivitis (3.3%). AESIs of keratitis were infrequent (0.36%) and only occurred in participants with AD. AESIs of AST/ALT increased to >5 × ULN were reported in only 3 participants (0.27%). One participant each (0.09%) experienced an AESI of parasitic/opportunistic infection and anaphylactic reaction. There were no reports of symptomatic overdose.~~

~~Rademikibart was generally safe and well-tolerated across various trials involving healthy participants and participants with conditions including moderate-to-severe asthma, AD, and CRSwNP. In healthy participant trials, most treatment-emergent adverse events (TEAEs) were mild-to-moderate in severity. In clinical trials of AD and asthma, the incidences of the treatment-related TEAEs during the treatment period were all below 10% among participants receiving rademikibart; most were mild or moderate in severity, with the vast majority resolving before the end of the study. The incidence of these TEAEs leading to treatment interruption or discontinuation was low, and no rademikibart-related SAEs or deaths were reported in the AD~~

~~study population. In participants with moderate-to-severe asthma, 67.4% reported at least 1 TEAE, with no deaths and no rademikibart-related SAEs in the asthma study.~~

~~The trial on CRSwNP was terminated early, but the available data showed that no participant experienced an SAE and TEAEs were mostly mild-to-moderate in severity.~~

~~Overall, rademikibart as a single 600 mg dose followed by chronic dosing (300 mg Q2W) in the treatment of participants with AD and asthma has been well-tolerated. The safety profile was comparable to those of the approved similar products.~~

In summary, rademikibart was generally safe and well tolerated across clinical trials involving healthy participants and participants with AD or respiratory diseases (asthma, COPD, and CRSwNP). ~~Across clinical trials, r~~Rademikibart has demonstrated consistent PK properties, efficacy, and a favorable safety profile with manageable risks.

2. INTRODUCTION

2.1. Respiratory Diseases With Type 2 Inflammation

2.1.1. Asthma

Asthma is a common chronic inflammatory lung disease caused by genetic and environmental factors. It is characterized by widespread, variable, and reversible airflow obstruction, airway inflammation, excessive mucus production, and airway hyperresponsiveness that lead to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. Asthma represents a substantial global health burden, affecting approximately 260 million individuals worldwide (GBD 2025) ~~affects more than 300 million people worldwide~~. Ten to 15% of this population has moderate-to-severe asthma, which remains difficult to control despite recommended maintenance therapy ~~refractory to currently available treatments~~. These patients experience a greater risk of disease exacerbation, hospital admission, and death, as well as a consistently lower quality of life (Bateman 2015; Chung 2014). Patients with severe persistent uncontrolled asthma are those whose symptoms, exacerbations, and limited airflow continue in spite of treatment with medium-to-high-dose inhaled corticosteroids and a second added controller drug or systemic corticosteroids (GINA 2026 Report). Many patients experience adverse effects of systemic and inhaled corticosteroids on adrenal function, bone metabolism, and growth in children. Phenotyping has recently contributed to the understanding of underlying disease and treatment response to pharmacological agents (Chung 2018; Fitzpatrick 2017).

Management of severe and treatment-resistant asthma usually includes optimization of inhaled therapy including high-dose inhaled corticosteroids and long-acting β-agonist (LABA), as well as a maintenance dose of oral corticosteroids (Chung 2018). However, repeated or chronic use of systemic corticosteroids is associated with clinically significant adverse effects, including impacts on adrenal function, bone metabolism, and growth in children (Chung 2014). The joint European Respiratory Society (ERS)/American Thoracic Society (ATS) Task Force on severe asthma recently recommended use of medications targeting interleukin-5 (IL-5) and anti-IL-5Rα for severe uncontrolled adult eosinophilic asthma phenotypes (Holguin 2020). The Task Force also suggests a trial of chronic macrolide treatment to reduce asthma exacerbations (based on Global Initiative for Asthma [GINA] Step 5 or National Asthma Education and Prevention Program [NAEPP] Step 5 therapies, irrespective of asthma phenotype) and use of medications targeting IL-4/IL-13 for adult patients with severe corticosteroid-dependent and severe eosinophilic asthma irrespective of blood eosinophil levels (Holguin 2020). The GINA 2026 Report provides updated recommendations for the management of severe asthma, including guidance on selection of biologic therapies based on clinical features and biomarkers associated with type 2 inflammation (GINA 2026 Report). Recent updates include recognition of emerging long-acting biologic therapies targeting IL-5 pathways (eg, depemokimab) as additional treatment options for severe eosinophilic asthma (GINA 2026 Report). The CHEST 2026 companion guidance (Oberle 2026) complements this, recommending anti-IL-5/5Rα therapy or DUPIXENT (dupilumab) for moderate-to-severe asthma not responding to omalizumab after 4 to 6 months, and dupilumab or tezepelumab for severe asthma not responding to other agents. Clinical trials evaluating fixed-dose triple therapy (eg, budesonide–glycopyrronium–formoterol) in patients with inadequately controlled asthma have also recently demonstrated improvements in lung function and reductions in severe exacerbations compared with dual inhaled

corticosteroids (ICS)-LABA therapy (Papi 2026). Guidelines now recommend the option of adding a triple therapy combination ICS-LABA- long acting muscarinic agents (LAMA) (eg, budenoside-formoterol-glycopyrronium) to Step 5 when asthma is not well controlled despite medium- or high-dose ICS-LABA (GINA 2026 Report), but notes that the reduction in severe exacerbations when comparing ICS-LABA to ICS-LABA-LAMA is far smaller than what biologics achieve.

2.1.2. Chronic Obstructive Pulmonary Disease (COPD)

COPD is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms, such as breathlessness (or dyspnea), cough, sputum production, and progressive airflow limitation. This is typically caused by airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases (GOLD 2026 Report). Cigarette smoking is the primary cause of COPD and is responsible for approximately 70% of COPD cases (Barnes 2019; GOLD 2026 Report). Additional Other risk factors for COPD are air pollution including nanoparticles, occupational exposure, respiratory infections, childhood asthma, and rare genetic conditions such as α-1 antitrypsin deficiency (GOLD 2026 Report). COPD is a major cause of disability, morbidity, and mortality, resulting in millions of deaths annually worldwide and contributing significantly to health care costs. It is a major global health issue driven by an aging main global epidemic increasing as populations age, due to longer life expectancy and is the fourth-ranked cause of death worldwide, affecting approximately 10% of subjects people ≥45 years (Celli 2021; GOLD 2026 Report). In the US, COPD is the sixth leading cause of death (American Lung Association 2021).

COPD, once thought to be a self-inflicted condition caused by tobacco smoking, is a heterogeneous and complex disease with various endo-phenotypes and clinical presentations. The pathological hallmarks of COPD are inflammation of the small airways (bronchiolitis) and destruction of lung parenchyma (emphysema) (Cosio Piqueras 2001). It is a complex condition that involves the activation of multiple inflammatory cells, such as lymphocytes, neutrophils, macrophages, and eosinophils, which contribute to the inflammatory response (Agustí 2019; Barnes 2018). A subgroup of COPD patients (~20 to 40%) have been identified who are characterized by a concomitant elevation in blood eosinophils, suggesting a tType 2 inflammatory component of the disease (Vanetti 2025).

Type 2 inflammation is a specific pattern of immune response that exists across a spectrum of atopic diseases. IL-4 and IL-13 are key drivers of Ttype 2 inflammation and signal through the shared receptor IL-4Rα, expressed by airway epithelial cells as well as innate and adaptive immune cells. IL-4 and IL-13 promote activation and trafficking of Ttype 2 inflammatory cells, including eosinophils, to the lungs via the release of chemoattractants, in particular eotaxin-3 (also known as eosinophil chemotactic protein), from airway epithelial cells (George 2020; Ghebre 2018). Eosinophils play a crucial role in Ttype 2 inflammation, contributing to airway damage and heightened immune responses. In COPD, their presence reflects a mixed inflammatory pattern distinct from the neutrophilic inflammation traditionally associated with the disease (Brightling 2019). This eosinophilic involvement has been linked to a greater predisposition to exacerbations, likely due to increased airway reactivity and susceptibility to environmental triggers (Bafadhel 2018). By targeting this pathway with inhaled corticosteroids (ICS), the frequency and severity of exacerbations can be significantly reduced, highlighting the importance of peripheral eosinophil counts as both a diagnostic tool and a guide for personalized

treatment strategies in COPD. ~~Peripheral eosinophilia (≥300 cells/μL), a marker of Type 2 inflammation, defines a clinically significant subgroup of COPD patients characterized by a higher risk of exacerbations (Yun 2018) and this eosinophilic phenotype is gaining recognition as an important treatable trait. Elevated eosinophil levels not only signal a distinct inflammatory pathway but also serve as a predictive biomarker for identifying patients who are more likely to benefit from ICS therapy in association with inhaled bronchodilators, LABAs and long-acting muscarinic antagonists (LAMAs) (GOLD 2024 Report) or the biologic medication dupilumab (Bhatt 2025).~~ Recent updates to the GOLD strategy have introduced biologic therapies into the COPD treatment paradigm, beginning with the inclusion of dupilumab in the 2025 report as an add-on option for patients with persistent exacerbations despite optimized inhaled triple therapy (ICS/LABA/LAMA), particularly in those with blood eosinophil counts ≥300 cells/μL (GOLD 2025 Report). GOLD 2026 further expands the evidence base for biologic therapies, with dupilumab or mepolizumab as add-on maintenance treatment in patients on ICS+LABA+LAMA triple therapy with blood eosinophils ≥300 cells/μL who remain inadequately controlled or continue to exacerbate despite optimized inhaled therapy (GOLD 2026 Report).

2.2. Atopic Dermatitis

AD is a chronic, pruritic inflammatory skin disease that predominantly affects children but also occurs in adults. Clinical manifestations include erythematous papules and plaques with oozing, scaling, crusts, excoriations, and lichenification. AD tends to affect certain areas chronically such as the face, neck, and the flexural folds of the extremities. Pruritus is the primary symptom. This condition is associated with multiple comorbidities and impairs the quality of life for both the affected individual and their family. Approximately 20% of children in developed countries are affected by AD, which continues to increase in prevalence, particularly in low-income countries (Flohr 2014). The global prevalence of AD is high, affecting up to approximately 15% to 20% of children and 5% to 10% of adults in developed countries (Langan 2020; Nutten 2015).

Treatment for AD begins with nonpharmacologic measures such as bathing practices and moisturizers, then proceeds to adoption of topical drug products such as corticosteroids or calcineurin inhibitors. For patients who do not respond to optimized topical therapy, phototherapy or systemic drug treatment may be adopted. Systemic treatments include corticosteroids and immunosuppressant drugs such as cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil (Garritsen 2018). These therapies are associated with significant safety limitations, including risk of infections, malignancies, organ toxicity (eg, hepatic and renal), and hematologic abnormalities.~~systemic drug products have an array of serious adverse reactions (SARs) including infections, malignancies, solid organ (liver, kidney, intestine) toxicities, impairment of vaccine responses, and reduction in blood counts.~~

Significant advancements in the treatment of AD have been achieved with the approval of various Janus kinase (JAK) inhibitors and biologic therapies. Biologic therapies target key immune components involved in AD pathogenesis. Dupilumab, an IL-4Rα blocker, was the first biologic approved for moderate-to-severe AD and has demonstrated consistent long-term efficacy and safety (DUPIXENT China PI Jul 2025; DUPIXENT SmPC Apr 2025; DUPIXENT USPI Apr 2026). A second IL-4Rα antagonist, KANGYUEDA (stapokibart), has been approved for AD but is only available in China (KANGYUEDA China PI Nov 2025). Tralokinumab has also demonstrated efficacy in clinical trials (ADBRY USPI Dec 2025; ADTRALZA EU SmPC

2025) and provides an alternative by selectively blocking IL-13, a cytokine central to AD inflammation.

JAK inhibitors, which regulate immune signaling pathways, include approved medications baricitinib (OLUMIANT EU SmPC 2025), upadacitinib (RINVOQ China PI Jun 2023; RINVOQ EU SmPC 2025; RINVOQ USPI Oct 2025), ruxolitinib, a JAK1/2 inhibitor available as a topical cream for mild-to-moderate AD (OPZELURA USPI Sep 2025), and abrocitinib (CIBINQO China PI May 2025; CIBINQO EU SmPC 2025; CIBINQO USPI Dec 2023). Both upadacitinib and abrocitinib are JAK1-selective inhibitors approved for moderate-to-severe AD. More recently approved medications include lebrikizumab (another antibody targeting the IL-13 pathway) (EBGLYSS EU SmPC 2026; EBGLYSS USPI Oct 2025), and nemolizumab (NEMLUVIO USPI Jun 2026), targeting IL-31, which plays a key role in pruritus associated with AD; these medications were approved for moderate-to-severe AD in individuals aged 12 and above. These therapies have transformed the treatment landscape for AD, providing targeted options that address the disease's underlying immunological mechanisms and improve patient outcomes.

2.3. Rademikibart Mechanism of Action: Targeting the IL-4/13 Receptor Complex

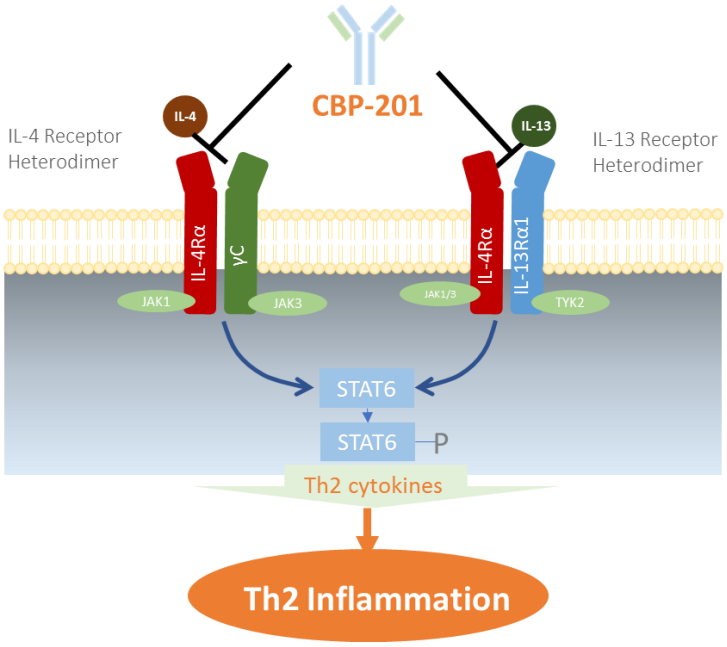
IL-4 is a cytokine secreted by various white blood cells, —including activated T cells, mononuclear cells, macrophages, basophils, and eosinophils, —that plays a key role in T and B-cell activation, proliferation, and the differentiation of $CD4^+$ T cells into Th2 type cells, thereby mediating allergic inflammation (Paul 2015). In contrast, IL-13, produced by activated T cells and mononuclear cells, promotes B-cell differentiation, IgE biosynthesis, and mucus production (Corren 2013). IL-4's biological activity is mediated through activation of both the Type 1 receptor (a heterodimer of IL-4Rα and IL-2Rγ, expressed exclusively on hematopoietic cells) and the Type 2 receptor (composed of IL-4Rα and IL-13α1, the sole signaling receptor for IL-13, expressed on both hematopoietic and nonhematopoietic cells) (Chomarat 1997; Ingram 2012; White 2010).

IL-4Rα is expressed on both immune and nonimmune cells, with higher protein and transcript levels found in tonsillar unstimulated B cells compared to T cells, and lower levels on resting human lymphocytes as well as on monocytes and macrophages (Gandhi 2014; Gordon 2010). PreNonclinical studies have demonstrated that inhibition of IL-4Rα is effective in ameliorating allergic inflammation in animal models, suggesting that blocking this receptor may have the potential to treat a broad range of allergic inflammatory diseases (Beckmann 1990). This approach is further supported by the regulatory approval of dupilumab for conditions such as moderate-to-severe AD, asthma, and COPD (DUPIXENT China PI Jul 2025; DUPIXENT SmPC Apr 2025; DUPIXENT USPI Apr 2026).

Rademikibart, another antibody directed against the IL-4Rα subunit, inhibits IL-4 signaling via the Type 1 receptor (IL-4Rα/γc), and both IL-4 and IL-13 signaling through the Type 2 receptor (IL-4Rα/IL-13Rα) (Figure 1). PreNonclinical characterization of rademikibart has shown that the antibody is highly potent in blocking STAT6 signaling and cell proliferation stimulated by IL-4 and IL-13. Blockade of IL-4Rα has been validated as a useful target in treatment of multiple chronic allergic conditions and rademikibart has been well-tolerated in clinical trials with

favorable PK properties. Rademikibart is under development for the treatment of moderate-to-severe asthma and COPD as well as other inflammatory conditions such as AD.

Figure 1: Mechanism of Action of Rademikibart



The mAb rademikibart blocks IL-4 and IL-13 in the mediation of inflammation. Rademikibart binds to the common IL4R$_\alpha$ subunit and blocks the formation of both the IL-4 and IL-13 receptor complexes. IL-4 and IL13 normally bind these receptor complexes, stimulating the release of T-helper (Th)2 proinflammatory cytokines through a JAK (Janus kinase)-STAT mediated intracellular mechanism.

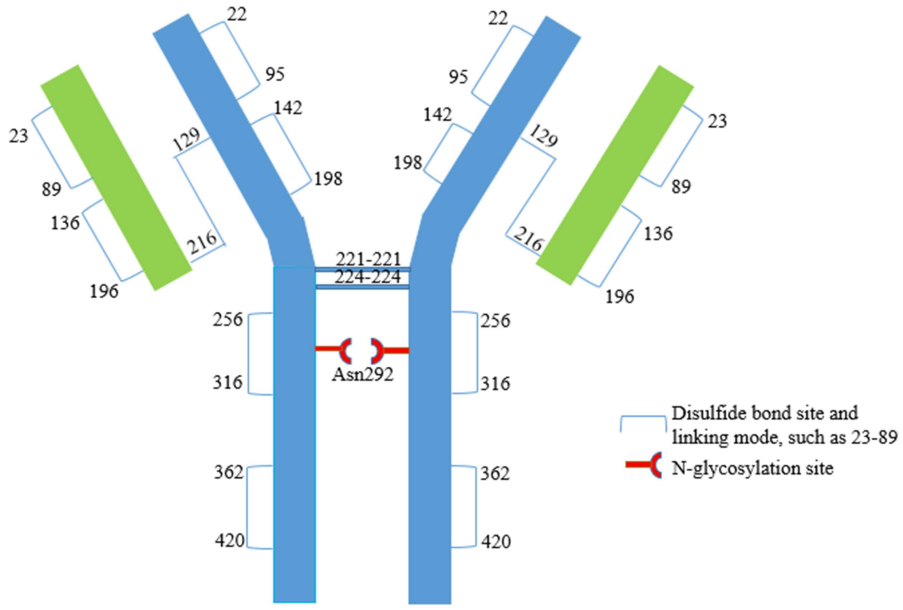
3. PHYSICAL, CHEMICAL, AND PHARMACEUTICAL PROPERTIES AND FORMULATION

3.1. Investigational Product Substance

Nomenclature

Common Name:	Rademikibart
Nonproprietary Name:	Rademikibart
Proprietary Name:	Not applicable
CAS Registry Number:	2648260-80-2
Other Name:	Human anti-interleukin-4 receptor subunit α (IL-4Rα) antibody

Structure



Physical Properties

Appearance:	Colorless to pale yellow liquid
pH:	5.9-6.5
Molecular formula:	$C_{6364}H_{9830}N_{1708}O_{1995}S_{42}$ (glycosylated form): $C_{6364}H_{9804}N_{1708}O_{1998}S_{42}$ (deglycosylated form
Molecular weight:	146.45 kDa (glycosylated form) 143.55 kDa (deglycosylated form)~~:~~
Molecular weight of heavy chain:	48.23 kDa
Molecular weight of light chain:	23.56 kDa

Rademikibart is a novel mAb (IgG4) targeting human IL-4 receptor α (IL-4Rα) subunit. It shares structural similarity with dupilumab, a mAb that also targets IL-4Rα as both are human mAbs with an IgG4 structure and a kappa (κ) light chain, classified as an IgG4 κ antibody. However, rademikibart binds to distinct human IL-4Rα epitopes with higher affinity as compared with dupilumab (Zhang 2023).

3.2. Investigational Product Formulation

The rademikibart investigational product is formulated as a liquid sterile solution at 150 mg/mL in 10 mM L-histidine, 60 mM trehalose, and 100 mM NaCl with 0.02% polysorbate 80 at pH 6.2. The matching placebo solution contains the same excipients without rademikibart.

Rademikibart is supplied in 1 of 3 presentations: a 150 mg in a 1 mL deliverable volume single-dose glass vial, 150 mg in a 1 mL single-dose prefilled syringe (PFS), or 300 mg in a 2 mL single-dose PFS. The PFS is equipped with a needle and needle safety device.

The placebo is supplied in identical formats to match the active investigational product in any given trial.

Rademikibart is intended for SC or IV administration.

The vials and PFSs are packaged in cardboard carton ~~(2 per carton)~~ with supportive custom inserts. Placebo syringes are similarly packaged to maintain blinding.

The rademikibart drug and matching placebo investigational products are to be stored between 2°C to 8°C. The drug product is stable for at least 1 month at 30ºC. The expiry date is provided on the investigational product labeling. Handling and disposal instructions are provided for each trial in the clinical protocol or pharmacy manual.

4. NONCLINICAL STUDIES

An overview of the nonclinical studies conducted with rademikibart is provided in Table 1.

Table 1: Summary of Nonclinical Studies Conducted for Rademikibart

Name/Type of Study	Duration	Species / Test System	Dose; Route of Administration	Study Number
Pharmacology				
Evaluation of rademikibart binding activity to human IL-4Rα	NA	Human sIL-4Rα-His ELISA	In vitro	CBP- 201-NC1006
Affinity detection of rademikibart binding with sIL-4Rαa	NA	Human sIL-4Rα Biacore	In vitro	KNDS-2008-012
Evaluation of rademikibart binding activity to IL-4Rα of different species	NA	Human, monkey, and mouse sIL-4Rα-His ELISA	In vitro	CBP- 201-NC1003
Evaluation of rademikibart inhibition of IL-4 and IL-13-induced STAT6 signaling in HEK Blue IL-4/IL-13 cells	NA	HEK Blue IL- 4/ IL-13 cells	In vitro; dupilumab as a positive control	CBP- 201-NC1001
Evaluation of rademikibart inhibition of IL-4 and IL-13-induced TF-1 cell proliferation	NA	TF-1 cells	In vitro; dupilumab as a positive control	CBP- 201-NC1002
Evaluation of rademikibart inhibition of IL-4 induced TARC production in human PBMCs	NA	Human PBMC cells	In vitro	CBP- 201-NC1007
Evaluation of rademikibart inhibition of IL-4-induced B-cell activation	NA	Double-humanized IL-4/IL-4Rα (transgenic mice) / Splenocytes	In vitro; dupilumab as a positive control	Biocytogen-21P013001
Evaluation of rademikibart inhibition of IL-13-induced B-Cell activation	NA	Double-humanized IL-4/IL-4Rα (transgenic mice) / Splenocytes	In vitro; dupilumab as a positive control	Biocytogen-21P059601
Evaluation of effect of rademikibart on OVA-induced asthma	4 weeks	Double-humanized IL-4/IL-4Rα (transgenic mice)	10, 25 and 50 mg/kg, SC on OVA-induced asthma, dupilumab positive control	Biocytogen-21P0107

Table 1: Summary of Nonclinical Studies Conducted for Rademikibart

Name/Type of Study	Duration	Species / Test System	Dose; Route of Administration	Study Number
Detection of ADCC	NA	Effector cells: human PBMC cells; Target cells: SK-BR-3 human breast cancer cells	In vitro;- Herceptin positive control	CBP- 201- NC1005
Evaluation of CDC activity in vitro	NA	Target cells: Daudi cells	In vitro; Rituxan positive control	CBP- 201- NC1008
In vitro characterization of rademikibart and dupilumab via antibody internalization and apoptosis assays	NA	Target cells: Raji, EOL-1, partially purified eosinophils	In vitro; dupilumab as comparator	CBP-201-NC1015
Anti-IL-4Ra antibody effects on HASM excitation-contraction coupling and PCLS β2AR hyporesponsiveness	NA	Primary HASM cells and human PCLS	In vitro (primary cells); dupilumab as comparator	CBP-201-NC1018
Effect of rademikibart and dupilumab pre-treatment on IL-13-induced airway hyporesponsiveness in PCLS	NA	Human PCLS	Ex vivo; dupilumab as comparator	CBP-201-NC1019
Safety pharmacology assessments in a 4-week SC injection toxicity study of rademikibart in cynomolgus monkeys[a]	4 weeks with a 4-week recovery	Cynomolgus monkey (5 males and 5 females/group)	0, 6, 40, 200 mg/kg; SC; ~~once weekly~~QW for a total of 5 doses	P17- S169-RD
Pharmacokinetics				
Pharmacokinetic study of rademikibart after single SC injection and IV injection to cynomolgus monkeys	Single dose followed by a 56-day period of blood collection	Cynomolgus monkey (3 males and 3 females/group)	2, 6, or 20 mg/kg; SC, single dose; 6 mg/kg; IV, single dose	P17- S169-PK
4-week SC injection toxicity study of rademikibart with a 4-week recovery period in cynomolgus monkeys[a]	4 weeks with a 4-week recovery	Cynomolgus monkey (5 males and 5 females/group)	0, 6, 40, 200 mg/kg; SC, ~~once weekly~~QW for a total of 5 doses	P17- S169-RD

Table 1: Summary of Nonclinical Studies Conducted for Rademikibart

Name/Type of Study	Duration	Species / Test System	Dose; Route of Administration	Study Number
Toxicology				
4-week SC injection toxicity study of rademikibart with a 4-week recovery period in cynomolgus monkeys[a]	4 weeks with a 4-week recovery	Cynomolgus monkey (5 males and 5 females/group)	0 (saline), 6, 40, 200 mg/kg; SC; ~~once weekly~~QW for a total of 5 doses	P17-S169-RD
4-week dose range finding study of rademikibart in transgenic mice[b]	4 weeks	Transgenic BhIL-4/hIL-4Rα mice (80 animals with 10 per sex across 4 groups)	0 (placebo), 50, 200 mg/kg; SC (plus 200 mg/kg TK group); ~~once weekly~~QW for a total of 5 doses	M21-S199-DR
26-week toxicity study of rademikibart with a 4-week recovery period in transgenic mice[a]	26 weeks with a 4-week recovery	Transgenic BhIL-4 /hIL-4Rα mice (400 animals with 40 per sex across 6 groups)	0 (placebo for 50), 50, 0 (placebo for 200), 200 mg/kg; SC (plus 50 and 200 mg/kg TK groups); ~~once weekly~~QW for a total of 27 doses	M21-S199-RD
Tissue cross-reactivity study of rademikibart in frozen normal human tissues[a]	NA	Human tissues (3 donors/tissue)	2 and 10 µg/mL; In vitro	O17-175-1ZJ
In vitro hemolysis test of rademikibart with human red blood cells[a]	NA	Human red blood cells (1 donor)	140.4 mg/mL; In vitro	O17-S169-HE
Reproductive Toxicology				
Fertility and early embryonic developmental toxicity study of rademikibart administered by SC injection	Males: dosed from 10 weeks before mating through 2-week mating period. Females: dosed from 2 weeks before mating through GD 7; C-section on GD 15	B-hIL-4/hIL-4RA mice (320 animals; 40 per sex across 4 groups)	0 (vehicle control), 50, 100, and 200 mg/kg; SC; QW Male mice: 13 doses Female mice: 5-6 doses	CBP-201-NC1023

Table 1: Summary of Nonclinical Studies Conducted for Rademikibart

Name/Type of Study	Duration	Species / Test System	Dose; Route of Administration	Study Number
Embryo and fetal developmental toxicity study of rademikibart administered by SC injection	Dosed on GD 6 and GD 13; C-section on GD 18	B-hIL-4/hIL-4RA mated female mice (176 animals; 32/group main study, 12/group TK study)	0 (vehicle control), 100, 300, 500 mg/kg; SC; QW for a total of 2 doses (main study); 1 dose on GD 17 (TK study)	CBP-201-NC1022
Prenatal and postnatal developmental toxicity study of rademikibart administered by SC injection	F0: dosed from GD 6 through LD 21 F1 (untreated): evaluated through adulthood	B-hIL-4/hIL-4RA mated female mice (176 animals; 32/group main study, 12/group TK study)	F0: 0 (saline), 100, 300, 500 mg/kg; SC; QW from GD 6 through LD 21for a total of 7 doses	CBP-201-NC1024

Abbreviations: ADCC, antibody-dependent cell-mediated cytotoxicity; β2AR, beta 2 agonist receptor; CDC, complement-dependent cytotoxicity; ELISA, enzyme-linked immunosorbent assay; F0, maternal mice; F1, offspring mice; GD, gestation day; GLP, Good Laboratory Practice; HASM, human airway smooth muscle; HEK, human embryonic kidney; IL-4rα, interleukin-4-receptor alpha; IL-4, -13, interleukin-4, -13; IV, intravenous; LD, lactation day; NA, not applicable; OVA, ovalbumin; PBMC, peripheral blood mononuclear cell; PCLS, precision-cut lung slice; QW, once a week; SC, subcutaneous; STAT, signal transducer and activator of transcription (protein); TARC, thymus and activation regulated chemokine; TK, toxicokinetics.
[a.] Study conducted in compliance with ~~Good Laboratory Practice~~ GLP regulations.
[b.] Non-GLP dose-range-finding study not summarized in Section 4.3.1.

4.1. Nonclinical Pharmacology

4.1.1. Primary Pharmacology

4.1.1.1. In Vitro

In vitro and ex vivo studies conducted to characterize the pharmacological properties of rademikibart have confirmed that rademikibart is a highly potent antibody against IL-4Rα (Zhang 2023).

4.1.1.1.1. Binding and Receptor Selectivity

The binding of rademikibart to the soluble IL-4Rα was detected by enzyme-linked immunosorbent assay (ELISA) (Study CBP-201-NC1006) and Biacore technology (Study KNDS-2008-012). The KD was calculated to be 106 pM via an ELISA and to be 20.7 pM using the Biacore technology.

The specificity of rademikibart's binding to human IL-4Rα was investigated (Study CBP-201-NC1003). To determine the cross-reactivity of rademikibart, the extracellular domain of monkey and mouse IL-4Rα gene were cloned (Genebank, XM005591515.2 and M29854.1, for the mouse and monkey genes, respectively). Soluble IL-4Rα protein was then produced in ~~human embryonic kidney (~~HEK~~)~~ cells and purified. The ability of rademikibart to bind monkey and mouse soluble IL-4Rα was tested by ELISA. The data showed that rademikibart could bind human soluble IL-4Rα and did not bind either monkey or mouse soluble IL-4Rα.

4.1.1.1.2. Inhibition of IL-4 and IL-13 Signaling

Rademikibart was evaluated in assays of inhibition of IL-4- and IL-13-mediated activation of transcription factor STAT6 in HEK Blue IL-4/IL-13 cells, which express the Type 2 IL-4 receptor (Study CBP-201-NC1001). In this assay, rademikibart displayed a mean IC_{50} of 7.04 ± 2.46 and 6.56 ± 1.47 ng/mL for inhibition of the activation of STAT6 induced by IL-4 and IL-13, respectively. Furthermore, in vitro cell-based assays showed that rademikibart inhibited proliferation of TF-1 cells stimulated with IL-4 and IL-13 with an IC_{50} of 8.00 ± 1.61 ng/mL and 9.68 ± 0.75 ng/mL, respectively (Study CBP201NC1002).

Human PBMCs express both Type 1 and Type 2 IL-4 receptors. They produce various cytokines, including chemokine CCL17 (also known as TARC) in response to IL-4. Rademikibart inhibited IL-4-induced TARC production in human PBMCs. TARC binds to chemokine receptors CCR4 and CCR8 (Study CBP-201-NC1007). The estimated IC_{50} of rademikibart in inhibiting TARC production in human PBMCs was 101.7 ng/mL (or 0.7 nM).

Isolated splenocytes from double-humanized IL-4/IL-4Rα transgenic mice were incubated with different concentrations of rademikibart, dupilumab or human IgG4, κ isotype control (hIgG4) in the presence of 50 pM human IL-4. After 72 hours, B-cell activation was analyzed by fluorescence-activated cell sorting (FACS). Rademikibart 0.1 μg/mL ~~rademikibart~~ significantly reduced the activation marker CD23 on B cells. Rademikibart 1 and 10 μg/mL ~~rademikibart~~ completely block~~ad~~ed human IL-4 induced B-cell activation ~~using~~ in transgenic mice. Rademikibart blocked IL-4 induced B cell~~s~~ activation in a dose-dependent manner (Study Biocytogen-21P013001).

Isolated splenocytes from transgenic mice were incubated with different concentrations of rademikibart, dupilumab or human IgG4, or κ isotype control (hIgG4) in the presence of 50 nM human IL-13 or murine IL-13. After 72 hours, B-~~-~~cell~~s~~ activation was analyzed by FACS. In both human IL-13- and mouse IL-13-~~-~~activated transgenic mice B cell~~s~~ in vitro model~~s~~, rademikibart 1 and 10 μg/mL ~~rademikibart~~ substantially reduced the activation marker CD23 and major histocompatibility complex (MHC) II on B cells. Rademikibart blocked human IL-13 and mouse IL-13-induced B-cell activation in a dose-dependent manner (Study Biocytogen-21P059601).

Rademikibart is an IgG4 designed to act as a functional inhibitor of IL-4 and IL-13 by binding to IL-4Rα without inducing Fc-mediated effector functions ~~in order to avoid~~ and resultant cytotoxicity. An in vitro cell-based assay was conducted to confirm the lack of antibody-dependent cell-mediated cytotoxicity (ADCC). In the study, PBMCs were isolated from 4 healthy participants, and the SK-BR-3 cell line was used as the target cell (Study CBP-201-NC1005). The study showed that while Herceptin (trastuzumab; used as a positive control) demonstrated some positive ADCC activity as expected, rademikibart was negative for ADCC activity in all donors, confirming the lack of ADCC for rademikibart.

4.1.1.1.3. Complement-Dependent Cytotoxicity (CDC)

~~Complement-dependent cytotoxicity (~~CDC~~)~~ is mediated by an antibody-mediated cell-killing process. The cell surface antigen and the corresponding antibody specifically bind to form an immune complex, which leads to perforation of the cell membrane and lysis death. An in vitro cell-based assay was conducted to confirm the lack of CDC for rademikibart. In the study, Daudi

cells were used as the target cell, and pooled normal human serum (PNHS) was used as the source of complement (Study CBP-201-NC1008). The study showed that, while Rituxan (rituximab; used as a positive control) demonstrated positive CDC activity as expected, rademikibart was negative, confirming the lack of CDC for rademikibart.

4.1.1.1.4. Receptor Trafficking, Internalization, and Cell Fate Effects

Rademikibart was evaluated in mechanistic in vitro studies to characterize its effects on IL-4Rα receptor trafficking and downstream cellular fate, including receptor internalization and apoptosis, in comparison with dupilumab (Study CBP-201-NC1015).

Antibody internalization was assessed using live-cell imaging (Incucyte) and pHrodo-based assays in EOL-1 cells. In this controlled cell system, rademikibart demonstrated robust, time-dependent internalization, with increasing intracellular signal intensity observed over prolonged incubation. Rademikibart exhibited greater internalization compared with dupilumab across tested concentrations and timepoints, including at lower concentrations following extended incubation. Consistent findings were observed using orthogonal pHrodo assays, in which rademikibart showed stronger internalization activity relative to dupilumab and isotype controls at higher concentrations.

To evaluate downstream cellular consequences, apoptosis assays were conducted in both EOL-1 cells and primary human eosinophils using complementary assay platforms. In EOL-1 cells, rademikibart induced higher levels of caspase-3/7–associated apoptosis signaling compared with dupilumab and isotype controls following 48 hours of incubation, with effects observed across the full range of tested concentrations. These findings were confirmed in primary human eosinophils, a disease-relevant effector cell population in type 2 inflammation. In live-cell imaging assays, rademikibart induced greater apoptosis signaling relative to dupilumab and control antibodies, with consistent effects observed across concentrations and donor-derived samples.

Across these complementary mechanistic and translational systems, rademikibart demonstrated a differentiated pharmacologic profile relative to dupilumab characterized by enhanced receptor internalization and increased downstream apoptosis signaling in IL-4/IL-13–responsive cells. Greater internalization activity observed in the controlled EOL-1 cell system was evident both at higher concentrations at early timepoints and at lower concentrations following extended incubation, and was directionally consistent with increased apoptosis signaling in both EOL-1 cells and primary human eosinophils. Collectively, these findings support a mechanism in which rademikibart promotes efficient, time-dependent receptor internalization that is associated with sustained modulation of IL-4Rα-mediated signaling and downstream cellular effects. These effects occur independently of Fc-mediated cytotoxic mechanisms, as supported by the absence of ADCC (CBP-201-NC1005) and CDC (CBP-201-NC1008) activity.

4.1.1.1.5. Human Precision Cut Lung Slice and Airway Smooth Muscle Studies

Ex vivo studies (CBP-201-NC1019) were conducted in human PCLS to evaluate the effects of rademikibart on β_2-agonist–mediated bronchodilation under type 2 inflammatory conditions.

Cryopreserved PCLS from four healthy human donors were rapidly thawed in pre-warmed media to remove cryoprotectant, then incubated at 37°C for 30 minutes in fresh media. Slices were transferred to Transwell inserts in 24-well plates and allowed to equilibrate for a further

60 minutes before baseline imaging and viability assessment. Initial assay optimization demonstrated that extended pre-treatment (18 hours) resulted in a marked reduction in bronchodilatory responsiveness, consistent with induction of β2-adrenergic receptor hyporesponsiveness. Under IL-13–induced hyporesponsive conditions, rademikibart treatment (0.3, 3.0, and 30.0 μg/mL) partially restored formoterol responsiveness, whereas dupilumab showed a modest dose-dependent partial rescue, substantially lower than rademikibart at equivalent doses. Consistent findings were replicated in an independent laboratory (CBP-201-NC1018) using a similar hPCLS model, in which IL-13+IL-4 treatment induced β2-adrenergic hyporesponsiveness, and rademikibart partially reversed this effect, while the reference antibody (dupilumab comparator) had little effect.

Mechanistically, this effect is consistent with inhibition of IL-4/IL-13–driven STAT6 signaling in airway smooth muscle (ASM), which has been implicated in alterations in cAMP-dependent relaxation pathways and downstream contractile machinery contributing to β2-agonist hyporesponsiveness. In primary HASM cells, type 2 cytokine exposure (IL-13+IL-4) did not reduce formoterol-induced phosphorylation of HSP20, a downstream effector of cAMP/PKA-mediated relaxation signaling; however, treatment with rademikibart increased β2-agonist–induced HSP20 phosphorylation relative to vehicle, whereas the reference antibody (dupilumab) showed no effect (CBP-201-NC1018).

Collectively, these findings demonstrate that rademikibart can partially mitigate IL-13–mediated β2-adrenergic hyporesponsiveness in human lung tissue and provide convergent mechanistic evidence in ASM that IL-4Rα blockade may enhance β2-agonist–induced relaxation signaling. Ex vivo PCLS data establish a functional restoration of bronchodilator responsiveness under type 2 inflammatory conditions, while complementary HASM studies support a downstream effect on cyclic AMP–dependent relaxation pathways, including modulation of HSP20 phosphorylation. Together, these nonclinical findings support the potential of rademikibart to restore β2-agonist responsiveness in acute inflammatory settings, such as exacerbations, where bronchodilator efficacy is impaired and rapid restoration is clinically important.

4.1.1.2. In Vivo

An in vivo study in transgenic mice was conducted to provide proof-of-concept evidence, which indicates that rademikibart would be effective in treating respiratory diseases associated with type ~~T~~2 inflammation (Zhang 2023).

Using B-hIL-4/hIL-4RA double-humanized mice, this study was to establish an animal model of asthma, and to study the effect of rademikibart in this model (Study Biocytogen-21P0107). A total of 48 B-hIL-4/hIL-4RA mice were randomly divided into 6 groups with 8 animals in each group and labeled. The model mice had OVA-induced asthma. OVA was intraperitoneally injected on Day 0, Day 7, and Day 14 for sensitization, and then atomized OVA was inhaled by mice daily on D21-D25 for 30 min each day. Negative control mice were injected with IgG4-Isotype and positive control group was injected with dupilumab. Mice in rademikibart treatment groups were injected with rademikibart at 10, 25, or 50 mg/kg on Day 20 and Day 23, SC. Animal serum, alveolar lavage fluid (BALF), and lung tissue were collected at the end of study ~~EOS~~ on Day 26 for follow-up tests.

At the end of the in vivo experiment, treatment with different doses of rademikibart reduced the total number of increased leukocytes and eosinophils observed in the BALF of the asthma

model. Similarly, treatment with different doses of rademikibart substantially reduced the serum concentration of OVA-specific IgE which has also been observed to increase in this animal model. According to pathological examination results of the lungs, treatment with different doses of rademikibart decreased obvious eosinophil infiltration and mucus secretion in the lungs of the model animals. Compared with the model group, the degree of pulmonary bronchial mucus secretion and the degree of eosinophil infiltration in the rademikibart treatment groups were reduced.

Thus, in this OVA-induced asthma model, treatment with rademikibart could attenuate the infiltration of white blood cells and eosinophils into the lung, and inhibit the production of OVA-specific IgE, and reduce the secretion of mucus in the lung trachea. Therefore, rademikibart was effective in this experimental asthma model, while there was no obvious difference in pharmacodynamic effect between different concentrations of rademikibart and between rademikibart and dupilumab.

4.1.2. Safety Pharmacology

The safety pharmacology of rademikibart was evaluated as part of the GLP-compliant 4-week repeat-dose SC toxicity study in cynomolgus monkeys (JOINN Study P17-S169-RD). Off-target toxicity and effects on the central nervous, cardiovascular, respiratory, and lymphoid systems were monitored during the dosing period and at the end of a 4-week treatment-free recovery period.

A total of 40 monkeys (5/sex/group) were randomly assigned to 4 groups that received rademikibart SC at doses of 0 (saline), 6, 40, or 200 mg/kg/dose weekly for 4 weeks (5 total doses) with administration occurring on Days 1, 8, 15, 22, and 29. Dose was adjusted in the rademikibart groups by altering the dosage volume of the supplied rademikibart formulation (formulation concentration: 140.8 mg/mL).

Following SC administration of up to 200 mg/kg/week of rademikibart in cynomolgus monkeys, no rademikibart-related adverse events (AEs) or changes on the central nervous, cardiovascular, respiratory, and lymphoid systems were recorded.

4.1.3. Immunogenicity

4.1.3.1. Immunogenicity in Monkeys

Immunogenicity of rademikibart in monkeys was assessed in the 4-week repeat dose toxicity study in cynomolgus monkeys (JOINN Study P17-S169-RD). A total of 40 animals were assigned to 4 groups with 10 (5/sex) each, and were given saline, 6, 40, or 200 mg/kg rademikibart. The animals were given saline or rademikibart by SC injection ~~once weekly~~QW for 4 consecutive weeks with a 4-week recovery period. Anti-rademikibart antibody levels in serum were determined with a validated Meso Scale Discovery method (JOINN Study P17-175-XV).

No monkey treated with saline, 6 mg/kg of rademikibart, or 200 mg/kg of rademikibart developed anti-rademikibart antibodies during the dosing and the recovery periods of the study. In the rademikibart 40 mg/kg treatment group, 2 animals (2/4) tested positive for ADAs on Day 57, one of which had an antibody titer <1, the other had a titer of 128. Overall, 1 out of 12 monkeys assessed on Day 57 (1/12) had a specific ADA with titer >1.

In conclusion, cynomolgus monkeys had little immunogenic reaction to repeated rademikibart treatment for 4 weeks with a 4-week recovery period.

4.1.3.2. Human Tissue Cross-Reactivity

Tissue cross-reactivity of rademikibart with normal human tissues was evaluated using a streptavidin-biotin immunohistochemistry method (JOINN Study O17-175-1ZJ). A total of 36 different kinds of tissue (derived from 3 different donors) were used in the study. Biotinylated rademikibart was used as the primary antibody, and a biotinylated human IgG4 myeloma was used as the isotype control antibody.

This study was designed with the following test arms:

- 2 test article groups with different concentrations of the test article (rademikibart-biotin, 2.0 μg/mL and 10.0 μg/mL).;
- 1 isotype control group (human IgG4, Myeloma-Biotin, 10.0 μg/mL).;
- 1 negative control group (phosphate buffered saline containing Tween 20 [PBST]).

Positive staining was detected in the cytomembrane of normal human tonsil lymphocytes at 2.0 μg/mL or 10.0 μg/mL Rademikibart-Biotin, but no positive staining was found in normal human skeletal muscle (negative control). No positive staining was detected in either positive or negative control tissues when using the isotype (IgG4) control or the negative (PBST) control.

In test article groups which examined 36 different types of human tissue, positive staining was found in the cytomembrane of normal human lymphocytes from the cortex and medulla of lymph node, thymus and tonsil, and red and white pulp of the spleen using 2.0 μg/mL or 10.0 μg/mL concentrations of Rademikibart-Biotin. No positive staining was detected in the normal human tissues above mentioned when using either the isotype or negative control group. In addition, positive staining was observed in the round cell of the colon and ileum mucoderm at both the 2.0 μg/mL and 10.0 μg/mL concentrations of Rademikibart-Biotin, and the isotype and negative control group. Therefore, these results were considered to represent nonspecific binding. No positive staining was observed in the other human tissues.

In conclusion, rademikibart was demonstrated to specifically bind to normal human lymphocytes located in the spleen, lymph node, thymus, and tonsil.

4.2. Pharmacokinetics and Product Metabolism in Animals

The PK properties of rademikibart were characterized in mice, monkeys, and transgenic mice (nonpregnant and pregnant). In Balb/c mice at 5 mg/kg dosing, the $t_{1/2}$ of rademikibart was approximately 185 hours, the C_{max} was approximately 40 μg/mL, and the AUC_{last} was approximately 819088.8 μg·h/mL. In the single-dose PK study in monkeys (JOINN Study P17-S169-PK), the maximal drug concentrations were reached approximately 24 to 48 hours after dosing. The mean terminal $t_{1/2}$ was approximately 280, 183, and 221 hours following a single SC administration of 2, 6, and 20 mg/kg, respectively; and approximately 249 hours following a single IV administration of 6 mg/kg. The mean C_{max} was 17.989 μg/mL, 78.21 μg/mL, and 25049.59 μg/mL for the 2, 6, and 20 mg/kg SC doses, respectively; the mean AUC_{last} was 7.75 × 10^3 μg × h/mL, 27.656 × 10^3 μg × h/mL, and 98.436 × 10^3 μg· × h/mL, respectively. The bioavailability was approximately 79.3%.

In a single-dose PK study in normal mice and transgenic mice, after a SC injection of 5 mg/kg of rademikibart to C57BL/6 normal mice, plasma rademikibart concentrations reached peak at 24 hours, with a C_{max} of 29.4 μg/mL. Terminal $t_{1/2}$ was 231 hours, and exposure AUC_{last} and AUC_{0-120h} were 8530 ~~h·μg/mL~~ and 2980 h·μg/mL, respectively. After a single SC injection of 5 mg/kg of rademikibart to transgenic mice, the plasma rademikibart concentrations reached peak at 24 hours, with a C_{max} of 23.6 μg/mL. Terminal $t_{1/2}$ was 59.8 hours, and the exposure AUC_{last} (AUC_{0-120h}) was 2020 h·μg/mL.

In the repeat-dose, toxicology and toxicokinetic (TK) study in cynomolgus monkeys (JOINN Study P17-S169-RD), following the fourth SC administration (Day 22) of 6, 40, and 200 mg/kg of rademikibart, the mean C_{max} values were 174~~.28~~, 125~~01.55~~, and 628~~079.41~~ μg/mL, respectively; the mean AUC_{last} values were 24.3~~28~~ × 10^3, 169.~~76~~ × 10^3, and 837.~~40~~ × 10^3 μg·h/mL~~mg × h/mL~~2, respectively; and the accumulation factors ($AUC_{last(4th)}$/$AUC_{last(1st)}$) were 2.64, 2.56, and 2.14, respectively.

The distribution of rademikibart was not evaluated in cynomolgus monkeys because rademikibart does not bind IL-4Rα target in these animals. Thus, distribution in monkeys is not considered relevant for distribution in humans who express the rademikibart target. As a monoclonal IgG4 antibody, rademikibart is expected ~~thought~~ to be degraded into amino acids and excreted through the same catabolic pathway as endogenous IgG.

In the repeat-dose, toxicology and TK study in transgenic mice (JOINN Study M21-S199-RD), the mean C_{max}, AUC_{0-168h}, and estimated AUC_{inf} of rademikibart in males at 200 mg/kg after dosing on Day 176 ~~was~~ were 5000 μg/mL, 586 × 10^3 μg·h/mL~~h·mg/mL~~, and 1940 × 10^3 μg·h/mL~~h·mg/mL~~, respectively; the mean C_{max}, AUC_{0-168h}, and estimated AUC_{inf} of rademikibart in females at 200 mg/kg after dosing on Day 176 were~~was~~ 4250 μg/mL, 509 × 10^3 μg·h/mL~~·mg/mL~~, and 900 μg·h/mL~~·mg/mL~~, respectively. The peak concentration and drug exposure of rademikibart in plasma were positively correlated with dosing. After the 26th dose of ~~At 50 and 200 mg/kg dose levels following~~ once a week SC injection of rademikibart in transgenic mice~~, after the 26th dose~~, the accumulation factor, calculated as (~~AUC$_{0-168h}$ h~~, Day 176/AUC_{0-168h}, Day 1~~)~~, was 3.31 in females and ~~to~~ 4.29 in males for the 50 mg/kg dose level and~~,~~ 2.75 in females and ~~to~~ 3.22 in males for the 200 mg/kg dose level~~, respectively~~. There was no significant sex difference in mean C_{max}~~, and mean~~ AUC_{0-168h}, or AUC_{inf} between male and female animals in each dose group~~,~~; except for a slight sex difference in mean AUC_{inf} after 26th dose in the high-dose group ~~after 26th dose, there was no significant sex difference in other mean AUC_{inf}~~.

~~As a monoclonal IgG4 antibody, rademikibart is thought to be degraded into amino acids and excreted through the same catabolic pathway as endogenous IgG.~~

In the transgenic mouse embryo-fetal development (EFD) study (Study CBP-201-NC1022), rademikibart was administered by SC injection at doses of 100, 300, or 500 mg/kg on gestation day (GD) 6 and GD 13 and GD 17 (TK mice only). On GD 6, C_{max} was 797, 2340, and 3500 μg/mL, respectively, and AUC_{0-168h} was 77.8, 219, and 321 × 10^3 μg·h/mL, respectively. On GD 17, C_{max} was 635, 1700, and 2380 μg/mL, respectively, and AUC_{0-96h} was 31.7, 81, and 128 × 10^3 μg·h/mL, respectively.

In the transgenic mouse pre/postnatal development (PPND) study (Study CBP-201-NC1024), rademikibart was administered by SC injection at doses of 100, 300, or 500 mg/kg weekly from

GD 6 through postnatal day (PND) 21. On GD 6, C_{max} was 803, 2380, and 3790 µg/mL, respectively, and $AUC_{0\text{-}144h}$ was 73.3, 215, and 324 × 10^3 µg·h/mL, respectively. On PND 21, C_{max} was 1480, 2750, and 4640 µg/mL, respectively, and $AUC_{0\text{-}144h}$ was 95.2, 272, and 450 × 10^3 µg·h/mL, respectively.

4.3. Toxicology

4.3.1. Repeated-Dose Toxicity Studies

4.3.1.1. GLP 4-Week Toxicology in Monkeys (JOINN Study P17-S169-RD)

A total of 40 monkeys (20/sex) were randomly assigned to 4 groups with 5/sex/group in JOINN Study P17-S169-RD. Monkeys were given saline injection as a negative control for Group 1 and rademikibart at doses of 6, 40, or 200 mg/kg for Group 2, 3, or 4, respectively. The animals were administered rademikibart or saline via SC injection once weeklyQW for 4 weeks.

The results of the 4-week GLP toxicology study in cynomolgus monkeys support a NOAEL of 200 mg/kg rademikibart administered once weeklyQW. There were no mortalities or euthanasia in extremis in any treated group. There were no treatment-related abnormal clinical observations or statistically significant changes in body weight, food consumption, body temperature, electrocardiogram (ECG) parameters, blood pressure, hematology, or urinalysis. There were also no treatment-related changes observed post-euthanasia in organ weights, gross pathology, or histology following the 4 weeks of treatment. Hematology and lymphocyte subset analyses were also conducted, and no test -article-related changes in hematology were observed in animals of any group throughout the study (such as red blood cells, white blood cells, neutrophils, lymphocytes, monocytes, eosinophils, or basophils). There were also no changes in $CD4^+$, $CD8^+$, or $CD4^+/CD8^+$ lymphocyte cells.

Serum complement C3 and C4 concentrations were measured in animals at Days 1, 16, 30, and 57 but no significant changes due to drug treatment or dose were noted throughout the study.

Serum immunoglobulins were analyzed. Both IgM and IgA showed no changes between the different dose levels. The IgG level did increase after rademikibart administration, but this was expected because rademikibart is an IgG protein. The increased IgG value correlated with the administered drug dose level.

Serum cytokines were also measured in samples from animals treated with rademikibart. No test -article-related changes in cytokines were noted in animals of any group throughout the study.

In conclusion, SC injection of rademikibart to cynomolgus monkeys once weeklyQW for 4 weeks resulted in a NOAEL of 200 mg/kg (highest dose), which corresponds to a C_{max} of approximately 628079.4 µg/mL and an AUC_{last} of approximately 837.4 × 10^3 µg·h/mL at the last highest dose. There were no clinically meaningful changes in clinical observations, macroscopic observations, coagulation, clinical chemistry, hematology, lymphocytes, serum complement, or cytokine levels in the study.

4.3.1.2. GLP 26-Week Toxicity Study of Rademikibart in Transgenic Mice (JOINN Study M21-S199-RD)

A total of 400 transgenic mice (200/sex) were randomly assigned to 6 groups with 40 animals/sex/group in Groups 1, 2, and 3 designated for toxicology evaluation and, 10/sex in Group 4, and 35/sex/group in Groups 5 and 6 for TK assessment ~~in JOINN Study M21-S199-RD~~. Mice in Groups 1 and 4 received a placebo (1 mL/bottle) as an excipient control, those in Groups 2 and 5 received rademikibart at a dose of 50 mg/kg, and those in Groups 3 and 6 received 200 mg/kg. The animals were dosed via SC injection ~~once weekly~~QW for 26 weeks (27 times in total) to Day 184.

Changes considered to be likely related to the pharmacological effect of the test article included decreases in absolute lymphocyte count and white blood cells (WBCs) in males at 200 mg/kg (Day 184), an increase in globulin and a decrease in A/G ratio in females and males at 200 mg/kg (Day 184) and decreases in count of CD3-CD49b+ cells (NK cells) in males at 50 mg/kg and 200 mg/kg (Day 184), and a decrease in CD3-CD45R+ cell counts (B cells) in males at 200 mg/kg (Day 184).

During the study, no abnormal clinical signs were observed in animals at any dose level. No test-article-related changes in body weight or body weight gain, food consumption, body temperature, coagulation, cytokines and bone marrow smears were observed in animals at any dose levels.

Anti-drug antibody testing was inconclusive in transgenic mice, possibly due to nonspecific interference in the matrix.

No test-article-related organ weights changes were observed during the terminal or recovery necropsy. There were no test-article-related macroscopic findings or microscopic lesions were identified in all designated organs (including injection site) in animals euthanized at the terminal or recovery necropsy.

In summary, SC injection of rademikibart to transgenic mice ~~once weekly~~QW for 26 weeks (totally 27 times) at 50 and 200 mg/kg resulted in non-adverse decreases in CD3-CD49b+ cell counts at ≥50 mg/kg, decreases in CD3-CD45R+ cell counts at 200 mg/kg, and a decrease in lymphocyte count at 200 mg/kg in males on Day 184, and these changes were considered to be ~~probably~~ related to the pharmacological effect of test article. There were no abnormalities at the injection site, no test-article related changes in body wight, and no macroscopic or microscopic changes identified. Under the conditions of the study, the NOAEL was considered to be 200 mg/kg.

4.3.2. Reproductive Performance and Developmental Toxicity Studies

Three GLP developmental and reproductive toxicology (DART) studies have been conducted with rademikibart.~~Nonclinical reproductive or developmental toxicology studies have not been conducted with rademikibart~~.

4.3.2.1. GLP Fertility and Early Embryonic Developmental (FEED) Toxicity Study in B-hIL-4/hIL-4RA Mice (Study CBP-201-NC1023)

The purpose of this study was to evaluate male and female fertility and early embryonic development in B-hIL-4/hIL-4RA mice after weekly SC administration of rademikibart to groups

of 40 male and 40 female mice at 0 (vehicle control [VC]), 50, 100 or 200 mg/kg. In male mice, test article was administered QW from 10 weeks before mating to necropsy (a total of 13 doses). In female mice, test article was administered QW from 2 weeks before mating until GD 7 (a total of 5 to 6 doses). Male mice were euthanized after successful mating and female mice were euthanized on GD 15.

The following parameters were evaluated: body weight, food consumption, clinical signs, and male and female mating indices. In male mice, sperm assessments, male organ weights (testes, epididymides, prostate gland, seminal vesicles), and histopathology of male reproductive organs (200 mg/kg only) were evaluated. In female mice, estrous cycle, embryo-fetal survival indices, and histopathology of reproductive organs (uterus, cervix, ovaries [VC and 200 mg/kg only]) were evaluated.

There were no treatment-related mortality, clinical signs, or effects on body weight or food consumption.

In male mice, there were no effects on sperm parameters, number of days of mating, mating rate, fertility parameters or organ weights; there were also no treatment-related histopathological changes in the testes, epididymides, prostate gland, or seminal vesicles in the 200 mg/kg group.

In female mice, there were no effects on number of days of mating, mating rate, estrous cyclicity, fertility parameters, embryogenesis, or organ weights. There were also no treatment-related histopathological changes in female reproductive organs in the 200 mg/kg group.

In summary, rademikibart was well tolerated when administered weekly to male and female B-hIL-4/hIL4-RA mice. All animals survived to scheduled necropsy and there were no test article-related effects on male or female fertility or early embryonic development. Therefore, the NOAEL in this FEED study was 200 mg/kg.

4.3.2.2. GLP Embryo and Fetal Developmental Toxicity Study in B-hIL-4/hIL-4RA Mice (Study CBP-201-NC1022)

The purpose of this study was to evaluate the effects of rademikibart on embryo-fetal development in B-hIL-4/hIL-4RA mice after SC administration on GD 6 and GD 13 (and GD 17 [TK study only]) at doses of 0 (VC), 100, 300, or 500 mg/kg. A total of 44 presumed pregnant females per group were included (32/group main study; 12/group TK), yielding actual groups sizes of 27, 28, 22, and 26 pregnant females per group, respectively, in the main study and 8, 9, 8, and 9 pregnant females per group, respectively, in the TK study.

The following parameters were evaluated: clinical signs, body weight, food consumption, gross necropsy (GD 18), Cesarean section parameters (implantation sites, fetal viability, corpora lutea), and fetal morphometrics (body weight, body length, tail length), sex, external morphology, and visceral and skeletal morphology (VC and 500 mg/kg only). Toxicokinetic evaluation and ADA production were also evaluated (TK study).

No moribundity or death was observed in any group and there were no rademikibart-related clinical signs, effects on body weight or food consumption, or necropsy observations.

Rademikibart treatment did not affect embryo-fetal survival or growth, and there were no treatment-related fetal external abnormalities at any dose or visceral or skeletal abnormalities (500 mg/kg group only).

The TK analysis revealed that the mean rademikibart $AUC_{0\text{-}96h}$ and $AUC_{0\text{-}168h}$ increased in an approximately dose-proportional manner with increase in dose on GD 6 and GD 13. $AUC_{0\text{-}96h}$ exposures on GD 13 were lower than those on GD 6 with GD 13/6 ratios 0.6, 0.5, and 0.5 at 100, 300, and 500 mg/kg, respectively.

Rademikibart was able to cross the placenta and on GD 18, the rademikibart concentration ratios in maternal serum compared to fetal tissues were 9.8 ± 1.8, 18.4 ± 2.1, and 35.8 ± 15.9 at 100, 300, and 500 mg/kg, respectively.

Anti-rademikibart antibodies were not detected in the VC group or the rademikibart 300 or 500 mg/kg groups. Anti-rademikibart antibodies were detected in some animals in the 100 mg/kg group.

In summary, rademikibart was well tolerated after SC administration to pregnant B-hIL-4/hIL-4RA mice on GD 6 and GD 13 at doses of 100, 300, or 500 mg/kg. There were no effects on maternal health parameters and no effects on embryo-fetal survival, growth, or morphology. Therefore, the NOAEL was 500 mg/kg for maternal and embryo-fetal developmental toxicity. At this dose, the C_{max} was 3500 µg/mL and the $AUC_{0\text{-}168h}$ was 321 × 10^3 µg·h/mL on GD 6; the C_{max} was 2380 µg/mL and the $AUC_{0\text{-}96h}$ was 128 × 10^3 µg·h/mL on GD 13. ADAs were detected in the 100 mg/kg group. Rademikibart can cross the placental barrier and was found in the fetus at lower concentrations than in the mother.

4.3.2.3. GLP Prenatal and Postnatal Developmental Toxicity Study in B-hIL-4/hIL-4RA Mice (Study CBP-201-NC1024)

The purpose of this study was to evaluate the effects of rademikibart on pregnancy, parturition, and lactation in the maternal (F0) generation, and on pre/postnatal development of the offspring (F1 generation) after SC administration at doses of 0 (VC), 100, 300, or 500 mg/kg to pregnant an lactating B-hIL-4/hIL-4RA mice on GD 6, 12, and 18 and on post-delivery/PND 3, 9, 15, and 21. A total of 176 presumed pregnant females were included (32/group main study; 12/group TK), yielding a total number of 28, 30, 29, and 27 pregnant mice per group, respectively, in the main study and 10, 8, 11, and 8, respectively, in the TK study. Parental (F0) mice were euthanized and necropsied on PND 22. F1 offspring were weaned on PND 22 and retained on study until adulthood.

The following parameters were evaluated in the study:

- Maternal (F0): clinical signs, body weight, food consumption, gestation length, parturition, nursing, lactation, TK on GD 6 and PND 21 (serum), and LD 15 (serum and milk), ADA production.
- Offspring (F1): external appearance, survival rate, pre- and post-weaning body weight, physiological development, reflex and motor function, learning behavior (Morris water maze test for mice), spontaneous activity (open-field test), organ weights, gross necropsy observations, reproductive performance. Successfully mated F1 females were evaluated on GD 15 for effects on embryo-fetal development of their fetuses (F2 generation).

In the F0 generation, there was no treatment-related mortality, clinical signs, or effects on body weight or food consumption, and there were no effects on any reproductive parameters (eg, maintenance of pregnancy, gestation length, parturition, lactation, or maternal behavior).

In F1 offspring, there were no abnormal changes in total litter size, live litter size, male-to-female ratio, external appearance, postnatal survival, pre and postnatal growth, physiological development, reflex function, learning behavior, or spontaneous activity. There were also no treatment-related necropsy findings. F1 males and females showed normal reproductive function, and there were no effects on embryogenesis of the F2 generation that could be attributed to F0 treatment with rademikibart.

During the post-weaning period (PND 50 to 69), 1 F1 offspring died in each of the VC, 100, and 300 mg/kg groups. Clinical signs before death and microscopic findings suggested that dilation of ventricles in the brain and thinning of the brain parenchyma due to compression were the main causes of death. These deaths occurred at a low incidence and were not dose related. Therefore, the causes of death were likely to be spontaneous lesions in this strain of mice and not related to rademikibart treatment.

The mean exposure ($AUC_{0\text{-}144h}$) to rademikibart in serum from F0 mice increased in an approximately dose-proportional manner on GD 6 and LD 21, with a T_{max} of 24 to 48 hours. There was no significant accumulation of rademikibart from GD 6 to LD 21. At 24 hours after administration on LD 15, rademikibart was detected in serum and milk from parous female mice, with milk:serum ratios of 0.2, 0.2, and 0.3 at 100, 300, and 500 mg/kg, respectively, suggesting that rademikibart is able to cross the blood-milk barrier to enter milk, but at relatively low levels.

Anti-rademikibart antibodies were detected in some parous animals in the 100 and 300 mg/kg groups.

In summary, rademikibart was well tolerated after administration to pregnant and lactating F0 B-hIL-4/hIL-4RA mice. There were no effects on the F0 generation health or reproductive function, and no effects on the F1 generation survival, growth, postnatal development, behavior, or reproductive function. Therefore, the NOAEL was 500 mg/kg for F0 female mice and for pre/postnatal development of F1 offspring. At this dose the C_{max} was 3790 µg/mL and the $AUC_{0\text{-}144h}$ was 324×10^3 µg·h/mL on GD 6, and the C_{max} was 4640 µg/mL and the $AUC_{0\text{-}144h}$ was 450×10^3 µg·h/mL on PND 21. Rademikibart can cross into milk and ADA was detected in the F0 generation in the 100 and 300 mg/kg dose groups.

4.3.3. Genotoxicity and Carcinogenicity Studies

Nonclinical studies have not been conducted to evaluate the carcinogenic or mutagenic potential of rademikibart. Due to its large molecular size (146 kDa), it is mostly confined to extracellular space and has no genotoxic potential. It is highly specific for human IL-4Rα with the mechanism of action of blocking IL-4 and IL-13 signaling; therefore, has low potential for off- target effects that could potentially impact tumor initiation and progression. In addition, no lesions related to tumor proliferation or tumorigenesis were observed in the GLP nonclinical toxicology studies in monkeys (4 weeks) or transgenic mice (26 weeks) described in Section 4.3.1.

4.3.4. Other Toxicity Studies

4.3.4.1. Human Red Blood Cell Hemolysis Test (JOINN Study O17-S169-HE)

Rademikibart at 140.4 mg/mL had no hemolytic or aggregation effect on isolated human red blood cells in a standard 3-hour exposure assay in which saline was used as a negative control and sterile water for injection was used as a positive control.

4.3.5. Safety Margins for Human Dosing

Exposure margins were calculated using C_{max} and $AUC_{0\text{-}168h}$ exposures at NOAEL doses in the 26-week transgenic mouse study and the 4-week monkey study (Table 2). For the comparison to human overall systemic exposure following a single dose ($AUC_{0\text{-}inf}$), AUC during the dosing interval at the NOAEL dose was used as a practical surrogate for animal $AUC_{0\text{-}inf}$, since rademikibart exhibits time-invariant PK.

Table 2: Rademikibart Exposure Margins Based on General Toxicity Studies

Human			26-Week Mouse[a] (M21-S199-DR)		4-Week Monkey[b] (P17-S169-RD)	
Clinical Trial	C_{max} (µg/mL)	AUC (µg.h/mL)	C_{max} Margin	AUC Margin	C_{max} Margin	AUC Margin
300 mg IV, single dose, healthy participants[c]	104	15,051	46	36	60	56
600 mg SC, single dose, healthy participants[d]	46	25,202	103	22	137	33
600 mg LD SC, then 300 mg Q2W SC, atopic dermatitis[e]	31	10,692	154	51	203	78

Abbreviations: AUC, area under the curve; $AUC_{0\text{-}inf}$, area under the concentration-time curve from Time 0 to the last quantifiable concentration; $AUC_{0\text{-}tau}$, area under the concentration-time curve from Time 0 to the last time period with measurable drug; $AUC_{0\text{-}Xh}$, area under the concentration-time curve from Time 0 to X hours postdose; C_{max}, maximum observed concentration; IV, intravenous; LD, loading dose; NOAEL, no-observed-adverse-effect level; Q2W, every 2 weeks; SC, subcutaneous.

[a] NOAEL dose of 200 mg/kg/week; mean C_{max} = 4760 µg/mL; $AUC_{0\text{-}168h}$ = 547.5 × 10^3 µg·h/mL after last dose.

[b] NOAEL dose of 200 mg/kg/week; mean C_{max} = 6279 µg/mL; $AUC_{0\text{-}144h}$ = 837.4 × 10^3 µg·h/mL after last dose.

[c] Mean from Trials CBP-201-105 Part A and CBP-201AU001, single-dose C_{max} and $AUC_{0\text{-}inf}$.

[d] Mean from Trials CBP-201AU001 and CBP-201CN001, single-dose C_{max} and $AUC_{0\text{-}inf}$.

[e] Steady-state C_{max} and $AUC_{0\text{-}tau}$ estimated using population PK modeling from sparse sampling in participants with atopic dermatitis enrolled in Trial CBP-201-WW001.

Exposure margins at the NOAEL doses in transgenic mouse EFD and PPND studies are shown in Table 3. For the EFD study, the GD 6 $AUC_{0\text{-}168h}$ was used and for the PPND study, the GD 6 and PND 21 $AUC_{0\text{-}144h}$ values were used as comparators to the observed human $AUC_{0\text{-}inf}$ or projected $AUC_{0\text{-}tau}$ values.

Table 3: **Rademikibart Exposure Margins From Developmental and Reproductive Toxicity Studies at NOAEL Doses**

	Human		Tg Mouse EFD[a] (CBP-201-NC1022)			Tg Mouse PPND[b] (CBP-201-NC1024)		
	C_{max} (µg/mL)	AUC (µg.h/mL)	Day	C_{max} Margin	AUC Margin	Day	C_{max} Margin	AUC Margin
300 mg IV, single dose, healthy participants[c]	104	15,051	GD 6	34	21	GD 6	36	22
						PND 21	45	30
600 mg SC, single dose, healthy participants[d]	46	25,202	GD 6	76	13	GD 6	82	13
						PND 21	101	18
600 mg LD SC, then 300 mg Q2W SC, atopic dermatitis[e]	31	10,692	GD 6	113	30	GD 6	122	30
						PND 21	150	42

Abbreviations: AUC, area under the curve; $AUC_{0\text{-inf}}$, area under the concentration-time curve from Time 0 to the last quantifiable concentration; $AUC_{0\text{-Xh}}$, area under the concentration-time curve from Time 0 to X hours postdose; C_{max}, maximum observed concentration; EFD, embryo-fetal development study; GD, gestation day; IV, intravenous; LD, loading dose; NOAEL, no-observed-adverse-effect level; PND, postnatal development; PPND, pre/postnatal development; Q2W, once every 2 weeks; SC, subcutaneous; SD, single dose; Tg transgenic.

[a] NOAEL dose of 500 mg/kg; on GD6, C_{max} = 3500 µg/mL and $AUC_{0\text{-168h}}$ = 321 × 10^3 µg·h/mL.

[b] NOAEL dose of 500 mg/kg; on GD 6, C_{max} = 3790 µg/mL and $AUC_{0\text{-144h}}$ = 324 × 10^3 µg·h/mL; on PND 21, C_{max} = 4640 µg/mL and $AUC_{0\text{-144h}}$ = 450 × 10^3 µg·h/mL.

[c] Mean from Trials CBP-201-105 Part A and CBP-201AU001, single-dose C_{max} and $AUC_{0\text{-inf}}$.

[d] Mean from Trials CBP-201AU001 and CBP-201CN001, single-dose C_{max} and $AUC_{0\text{-inf}}$.

[e] Steady-state C_{max} and $AUC_{0\text{-tau}}$ estimated using population PK modeling from sparse sampling in participants with atopic dermatitis enrolled in Trial CBP-201-WW001.

5. EFFECTS IN HUMANS

As of 08 June 2026, the date of data cutoff for the IB, a total of 2892 participants have been dosed across 15 rademikibart clinical trials (11 completed and 4 ongoing). The trials included 600 healthy participants, 1206 participants with AD, and 1086 participants with respiratory diseases (asthma, COPD, and CRSwNP). An estimated 2316 participants have received at least 1 dose of rademikibart: 2272 via SC injection and 44 via IV infusion. Rademikibart doses administered SC ranged from 75 to 600 mg, and a single 300 mg dose was administered IV. Table 4 presents a summary of IP (rademikibart or placebo) exposure by trial. A summary of results for the 11 completed trials is presented in this section. In addition, preliminary results are presented for the completed parts of ongoing Trial CBP-201-105 (Parts A and B – listed as separate entries in Table 4).

~~A total of 9 clinical trials of rademikibart have been completed, of which 1 trial in CRSwNP was terminated early by the Sponsor due to slow enrollment during the COVID-19 pandemic (Table 2). As of the date of this Investigator's Brochure, a total of 1498 participants have received at least one dose of rademikibart in completed trials, including 384 healthy participants, 874 participants with moderate-to-severe AD, 214 participants with moderate-to-severe persistent asthma with T2 inflammation and 26 participants with CRSwNP.~~

Table 4: Overview of Clinical Trials With Rademikibart

Trial (Locations)	Design	Population	Investigational Product and Estimated Number of Participants Dosed (n)	Status
Trials in Healthy Adult Participants				
CBP-201-AU001 (Australia)	Phase 1, randomized, double-blind, placebo-controlled, single ascending dose safety, tolerability, PK, and PD trial	Healthy adult participants	75 mg SC: 6 150 mg SC: 6 300 mg SC: 6 300 mg IV: 6 600 mg SC: 6 Placebo SC/IV: 10 N=40 (rademikibart=30)	Complete
CBP-201-CN001 (China)	Phase 1, randomized, double-blind, placebo-controlled, single-ascending dose safety, tolerability, PK, and PD trial	Healthy adult participants	150 mg SC: 10 300 mg SC: 10 600 mg SC: 10 Placebo SC: 6 N=36 (rademikibart=30)	Complete
CBP-201-CN004 (China)	Phase 1, randomized, open-label, parallel-designed trial to evaluate the PK similarity of single-dose injection with different dosage forms and strengths	Healthy adult participants	150 mg SC × 2 prefilled syringes: 108 300 mg SC × 1 prefilled syringe: 108 150 mg SC × 2 vials: 108 N=324 (rademikibart=324)	Complete
SIM0718-101 (China)	Phase 1, randomized, open-label, single-dose, parallel-group PK trial	Healthy adult participants	300 mg SC × 1 prefilled syringe: 88 150 mg SC × 2 vials: 88 N=176 (rademikibart=176)	Complete
CBP-201-105 (US)[a]	Phase 1, randomized, double-blind, and placebo-controlled trial to evaluate a single IV dose at varying infusion rates (Part A)	Healthy adult participants (Part A)	300 mg IV: 18 Placebo IV: 6 Part A: N=24 (rademikibart=18)	Part A complete
Trials in Participants With Respiratory Diseases				
CBP-201-WW002 (US, China, Poland, Hungary, South Korea)	Phase 2, multicenter, randomized, double-blind, parallel-group, placebo-controlled, 24-week efficacy and safety trial	Adult participants with moderate-to-severe persistent asthma with type ~~T~~2 inflammation	600 mg loading dose+150 mg SC Q2W: 106 600 mg loading dose+300 mg SC Q2W: 108 Placebo SC: 108 N=322 (rademikibart=214)	Complete

Table 4: Overview of Clinical Trials With Rademikibart

Trial (Locations)	Design	Population	Investigational Product and Estimated Number of Participants Dosed (n)	Status
CBP-201-WW003[a] (US, China, Poland)	Phase 2 multicenter, randomized, double-blind, placebo-controlled, 24-week efficacy and safety trial	Adult participants with chronic rhinosinusitis with nasal polyps	600 mg loading dose+300 mg SC Q2W: 13 600 mg loading dose+300 mg SC Q4W: 13 Placebo SC: 14 N=40 (rademikibart=26) ~~(terminated early)~~	Complete (terminated early)[b]
CBP-201-105[a] (US)	Phase 1, randomized, double-blind, and placebo-controlled safety and efficacy trial	Adult participants Part B: stable asthma or COPD Part C: acute asthma or COPD exacerbation	Part B1 (Asthma) Rademikibart 300 mg IV: 10 Placebo IV: 2 Part B2 (COPD) Rademikibart 300 mg IV: 8 Placebo IV: 2 Part C (Asthma or COPD) Rademikibart 300 mg IV or placebo IV: 3 (blinded) N=25 (rademikibart=20 [estimated])	Part B (complete) Part C (enrollment ongoing)
SIM0718-301 (China)	Phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled safety and efficacy trial	Adult and adolescent participants with asthma	Rademikibart 600 mg loading dose+300 mg SC Q2W, or placebo (blinded) N=418 (rademikibart=209 [estimated])	Ongoing (enrollment complete)
CBP-201-206 (US, UK, Argentina, Australia, Georgia, Serbia)	Phase 2, multicenter, randomized, double-blind, parallel-group, placebo-controlled trial as an add-on treatment for acute asthma exacerbations	Adult and adolescent participants with asthma	Rademikibart 600 mg SC or placebo SC (blinded) N=139 (rademikibart=70 [estimated])	Ongoing (enrollment ongoing)
CBP-201-207 (US, UK, Argentina, Australia, Georgia, Serbia)	Phase 2, multicenter, randomized, double-blind, parallel-group, placebo-controlled trial as an add-on treatment for acute COPD exacerbations	Adult participants with COPD	Rademikibart 600 mg SC or placebo SC (blinded) N=142 (rademikibart=71 [estimated])	Ongoing (enrollment ongoing)

Table 4: Overview of Clinical Trials With Rademikibart

Trial (Locations)	Design	Population	Investigational Product and Estimated Number of Participants Dosed (n)	Status
Trials in Atopic Dermatitis				
CBP-201-AU002 (Australia, New Zealand)	Phase 1b, randomized, double-blind, placebo-controlled, 11-week, multiple ascending dose safety, PK, and preliminary efficacy trial	Adult participants with moderate-to-severe AD	150 mg SC QW: 8 300 mg SC QW: 7 Placebo SC: 8 75 mg SC QW: 8 N=31 (rademikibart=23)	Complete
CBP-201-WW001 (US, Australia, New Zealand, China)	Phase 2, randomized, double-blind, placebo-controlled multicentered, 16-week efficacy, safety, PK, and PD trial	Adult participants with moderate-to-severe AD	600 mg loading dose+150 mg SC Q2W: 57 600 mg loading dose+300 mg SC Q2W: 57 600 mg loading dose+300 mg SC Q4W: 56 Placebo SC: 56 N=226 (rademikibart=170)	Complete
CBP-201-CN002[bc] (China)	Phase 2, randomized, double-blind, placebo-controlled, 52-week efficacy and safety trial	Chinese adult and adolescent participants with moderate-to-severe AD	Stage 1: 600 mg loading dose+300 mg SC Q2W (14 weeks of treatment): 219 Placebo SC Q2W: 111 Stage 2: *Participants achieved EASI-50 at Week 16: 225* 300 mg SC Q2W-300 mg SC Q2W: 91 (double-blind) 300 mg SC Q2W-300 mg SC Q4W: 91 (double-blind) Placebo-300 mg SC Q2W: 22 (double-blind) Placebo-300 mg SC Q4W: 21 (double-blind) *Participants did not achieve EASI-50 at Week 16: 86* 300 mg SC Q2W-300 mg SC Q2W: 27 (open-label) Placebo-300 mg SC Q2W: 59 (open-label) ~~*Total participants exposed to*~~ N=330 (rademikibart: =321)	Complete

Table 4: Overview of Clinical Trials With Rademikibart

Trial (Locations)	Design	Population	Investigational Product and Estimated Number of Participants Dosed (n)	Status
CBP-201-CN003 (China)	Phase 2, multicenter, single-arm, open-label, 12-week safety and efficacy trial	Chinese participants with moderate-to-severe AD	600 mg loading dose+300 mg SC Q2W: 360 N=360 (rademikibart=360)	Complete
SIM0718-302 (China)	Phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled safety and efficacy trial	Adult and adolescent patients with moderate-to-severe AD	Stage 1 (blinded) Rademikibart 600 mg loading dose+300 mg SC Q2W, or placebo SC: 259 Stage 2 (open label) Rademikibart 300 mg SC Q2W (250)[d] N=259 (rademikibart=254)	Complete
Total Number of Participants Exposed ~~to Rademikibart in Completed Trials~~			**~~1498~~N=2892 (rademikibart=2316 [estimated])**	

Abbreviations: AD, atopic dermatitis; COPD, chronic obstructive pulmonary disease; ~~US, United States; SC, subcutaneous; T2, Type 2;~~ EASI, Eczema Area and Severity Index; IV, intravenous; PD, pharmacodynamics; PK, pharmacokinetics; ~~PD, pharmacodynamics;~~ Q2W, every 2 weeks; Q4W, every 4 weeks; QW, every week; SC, subcutaneous; UK, United Kingdom; US, United States.

[a] This trial is listed twice in the table because it includes healthy volunteers (Part A) and participants with respiratory diseases (Parts B and C).

[b~~a~~] This trial was terminated early by the Sponsor.

[c~~b~~] All subjects who completed the Stage 1 treatment entered the Stage 2 treatment and received rademikibart.

[d] In Trial SIM0718-302, all participants who completed blinded Stage 1 entered open-label Stage 2 and received rademikibart. Five participants in Stage 1 only received placebo and did not enter Stage 2.

5.1. Clinical Pharmacology

5.1.1. Overall Summary of Pharmacokinetics in Humans

Rademikibart PK have been evaluated in healthy participants administered either a single SC dose up to 600 mg or a single 300 mg IV dose; in participants with respiratory diseases administered either a single 300 mg IV dose, a single 600 mg SC dose, or a 600 mg SC loading dose followed by 150 mg SC Q2W or 300 mg SC Q2W or Q4W; and in participants with AD administered either multiple SC doses up to 300 mg QW or a 600 mg SC loading dose followed by up to 300 mg SC Q2W or Q4W.~~Rademikibart PK have been evaluated in healthy participantsand in participants following a single dose up to 600 mg SC, following multiple dose up to 300 mg SC QW, and following 300 mg IV dose administered over 30 minutes.~~
Rademikibart has demonstrated consistent PK properties across various trials involving healthy participants and patient populations, and between adults and adolescents (12 to 17 years of age, inclusive)~~participants with conditions such as moderate-to-severe asthma and AD~~. As all rademikibart dosing regimens have been generally well ~~-~~tolerated, the MTD has not been established.

Rademikibart PK following a 300 mg IV dose decline monoexponentially with an approximately 6-day $t_{1/2}$. Increasing the rate of infusion from 300 mg/30 minutes to 300 mg/2 minutes does not impact the mean C_{max}; therefore, in current trials utilizing IV dosing, rademikibart is administered via a short 2-minute infusion.

Rademikibart administered via the SC route reaches T_{max} within 2 to 11 days and exhibits relatively dose-proportional absorption (ie, dose-proportional increases in C_{max}). Overall exposure (AUC) increases slightly disproportionately with dose, manifesting ~~and nonlinear elimination with increasing dose. The nonlinearity in clearance following single-dose administration (CL/F) results~~ in slower post-peak decline in concentrations, longer $t_{1/2}$, and lower CL/F ~~greater than dose-proportional increases in overall drug exposure (AUC)~~with increasing dose. The~~is~~ decrease in CL/F with dose ~~also indicates~~suggests that rademikibart is eliminated via 2 elimination pathways, one of which is concentration-dependent and saturable, thus likely target-mediated, with the second pathway likely proteolytic catabolism followed by nonspecific elimination via the reticuloendothelial system, which is common to all mAbs. Initial population PK modeling estimates that the saturable CL pathway is 50% saturated ~~inhibited~~ at concentrations far below C_{trough} reported on any multiple-dose trial; thus saturable CL is unlikely to influence the multiple-dose concentration profile of rademikibart in clinical practice.

Despite the dose dependency in CL, there is no evidence of time-dependency in rademikibart CL/F following multiple dosing. Once steady state is reached, concentrations generally remain stable through the duration of treatment, consistent with time-invariant PK. For a given dose level, mean $t_{1/2}$ appears to be similar following a single dose and following the last dose on multiple-dose studies; thus, accumulation is predictable and varies only with dose and ~~with~~ dosing frequency. The 300 mg Q2W SC multiple-dose dosing regimen most commonly used in clinical trials results in approximately 2-fold accumulation.

Given the dose-proportionality in C_{max} and the 2-fold accumulation, a single 600 mg dose of rademikibart administered SC results in similar C_{max} to the steady-state C_{max} following 300 mg administered SC Q2W, and therefore in the current trials utilizing SC dosing, a 600 mg loading

dose is administered first, followed by 300 mg Q2W maintenance dose. In a dosing regimen consisting of a 600 mg LD followed by 300 mg Q2W maintenance dose, the LD achieved The C_{trough} concentrations by the end of the 2-week dosing interval following the loading dose are similar that were close to the steady-state concentrations, which were subsequently maintained with the 300 mg Q2W maintenance dose through the duration of treatment.

5.1.2. Overall Summary of Immunogenicity in Humans

The immunogenicity incidence has been generally low and nonpersistent (ie, transient or indeterminate), with mostly low ADA titers, and appears to be inversely proportional to rademikibart dose. Onset is generally late and often after rademikibart concentrations are no longer detectable. No clinically relevant differences in the incidence of TEAEs between ADA-positive and ADA-negative participants have been observed. While some trials reported higher CL in ADA-positive compared to ADA-negative participants, the late onset of ADA in participants categorized as ADA-positive suggests that emergence of ADA is unlikely to be the cause of higher rademikibart CL in these participants, but rather that higher CL results in lower concentrations that may precipitate emergence of ADA. CL/F appears to be lower in ADA-positive than in ADA-negative participants, but causality is unknown (ie, whether ADA onset increases CL, or if higher CL results in lower concentration that precipitate ADA onset). Overall, the onset of immunogenicity appears to present minimal safety risk and is unlikely to lead to loss of efficacy with continued exposure.

5.1.3. Overall Summary of Pharmacodynamics in Humans

Exploratory PD analysis across AD trials indicates that rademikibart dosing results in a steady decline of serum TARC and LDH levels, which are biomarkers associated with improvement in AD.

In a Phase 2 clinical trial in participants with asthma, decreases in mean FeNO and IgE were noted with onset in Week 1 and continuing up to the end of the trialEOS. Preliminary exposure-response modeling in participants with asthma has shown that the greatest change from baseline CFB in both pre-bronchodilator FEV_1 and the ACQ score occurred early in treatment after the 600 mg loading doseLD.

Preliminary results from a second clinical trial in asthma demonstrated that improvements in lung function and airway inflammation, as measured by FEV_1, % predicted FEV_1, forced vital capacity (FVC), and FeNO, were observed following a single IV dose of rademikibart 300 mg. Preliminary results from the COPD cohort in this trial also demonstrated clinically meaningful improvements in FEV_1.

5.1.4. Pharmacokinetics, Immunogenicity, and Pharmacodynamics Evaluated in Clinical Trials

5.1.4.1. Healthy Participant Trials

Trial CBP-201AU001: Single Ascending Dose Trial in Adult Participants

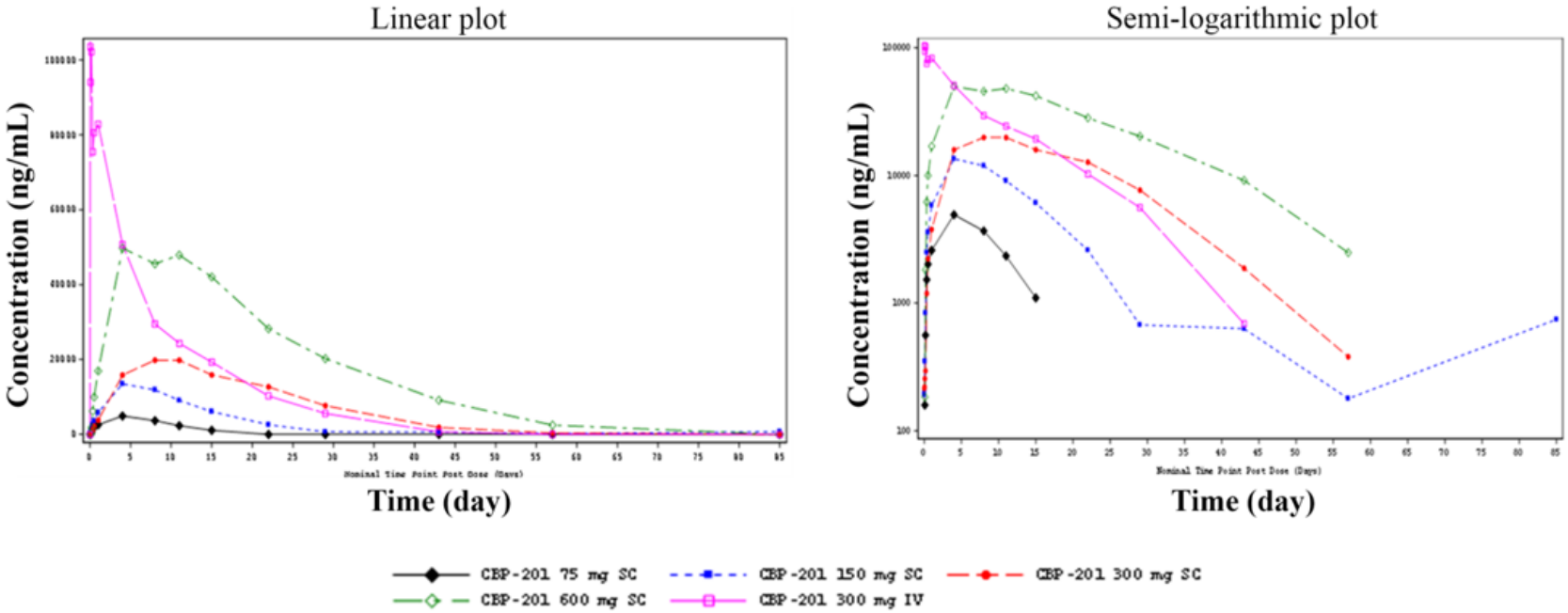
Trial CBP-201-AU001 – Single Ascending Dose was a first-in-human (FIH) placebo-controlled Phase 1a trial to assess the safety, tolerability, PK, and PD profile of rademikibart in 40 healthy

adult participants. Participants were enrolled into 1 of 5 cohorts, with the first 4 cohorts dosed SC (75, 150, 300, and 600 mg) and the last cohort dosed IV 300 mg as a 30-minute infusion.

Pharmacokinetic Results

The mean plasma concentrations and PK parameter of rademikibart are summarized in Figure 2 and Table 5.

Figure 2: Mean Plasma Rademikibart Concentration Profiles Over Time by Treatment Group (CBP-201-AU001)



~~Data source: CBP-201AU001 Clinical Study Report V1.0 Figure 3 and Figure 4~~

Table 5: Plasma Rademikibart Pharmacokinetic Parameters (CBP-201-AU001)

PK Parameter (unit)	Statistics	75 mg SC N=6	150 mg SC N=6	300 mg SC N=5	600 mg SC N=6	300 mg IV N=6
$AUC_{0\text{-last}}$ (ng·h/mL)	Mean±SD	98900008658.755 ± 558000386.0496	492000019735.855 ± 28800007533.8568	1110000006168.137 ± 5460000585 43.3516	29900000 23455.295 ± 8060000 57430.8118	17100000081215.377 ± 3910000 07683.4969
$AUC_{0\text{-inf}}$ (ng·h/mL)	Mean±SD	17700002552.530 ± 448000 7919.5171	38800000368.500 ± 665000226.9826	11400000 42779.230 ± 5380000 75093.3650	31400000 38621.492 ± 8190000 3029.8808	17600000 551979.103 ± 384000 01952.6411
C_{max} (ng/mL)	Mean±SD	49201.769 ± 26806.4560	135 0023.826 ± 46109.3118	206 00565.288 ± 6980.5580	557 0044.035 ± 105 0010.0199	107 000037.125 ± 189 0013.2762
T_{max} (h)	Median	74.7767	73.5108	240.050	203.5217	2.1767
	Min, Max	71.80, 78.28	70.93, 191.47	169.03, 244.48	72.02, 245.23	1.00, 4.00
$t_{1/2}$ (h)	Mean±SD	83.8755 ± 3.3335	1310.715 ± 6.21086	175.104 ± 35.04.9553	2487.902 ± 51.7129	144.001 ± 25.0241
T_{last} (h)	Median	3387.917	5098.633	101007.667	13404.808	8387.858
	Min, Max	239.37, 342.08	505.03, 209 01.33	6732.73, 13904.90	101008.28, 135046.20	669.42, 10004.58
CL/F (mL/h)	Mean±SD	43.7074 ± 11.04474	39.5124 ± 6.676903	34.43638 ± 24.10488	20.43779 ± 6.165865	17.7074 ± 3.41087
V_z/F (L)	Mean±SD	5.31078 ± 1.54476	7.44363 ± 1.176647	8.55480 ± 5.87292	7.2110 ± 2.298854	3.65483 ± 0.80704

Abbreviations: $AUC_{0\text{-inf}}$, area under the concentration-time curve from Time 0 extrapolated to infinity; $AUC_{0\text{-last}}$, area under the concentration-time curve from Time 0 to the last quantifiable concentration; CL/F, apparent oral clearance uncorrected for bioavailability; C_{max}, maximum observed concentration; h, hour; Max, maximum; Min, minimum; PK, pharmacokinetics; SC, subcutaneous; SD, standard deviation; $t_{½}$, apparent elimination half-life; T_{max}, time to maximum observed concentration; T_{last}, time of last detectable concentration; V_z/F, apparent volume of distribution uncorrected for bioavailability. Data source: CBP-201-AU001 Clinical Study Report V1.0 Table 12.

The overall exposures (AUCs) to rademikibart following SC dosing increased in a greater-than-dose-proportional manner, suggesting a nonlinear component to clearance. Mean CL/F decreased with dose while. Mmean V_z/F was low and independent of dose. The mean post-peak decline in concentrations exhibited some nonlinearity and a trend of longer $t_{1/2}$ at higher doses.

Median T_{max} was longer at higher doses (75 hours following 75 mg and 150 mg versus 240 hours following 300 mg), but mean C_{max} values were relatively dose-proportional, indicating dose-proportional absorption.

The absolute bioavailability of rademikibart following a 300 mg SC dose was estimated at 58%.

Immunogenicity Results

ADA incidence was evaluated through Day 85 postdose. Across all dose levels, 28% (8/29) of participants were treatment-induced ADA-positive (3/6 at 75 mg SC, 1/6 at 150 mg SC, 3/5 at 300 mg, 0/6 at 600 mg SC and 1/6 at 300 mg IV). Titers were generally low. The time of onset was ≥ Day 75 and thus long after rademikibart concentrations became undetectable. There were no apparent or clinically relevant differences in the incidence of TEAEs between ADA-positive and ADA-negative participants. Neutralizing activity was not assessed.

Pharmacodynamic Results

Serum TARC was assessed through 12 weeks postdose. A single dose administration of rademikibart significantly ($p<0.05$) reduced serum TARC levels through Day 21, with comparable reductions for all 4 SC doses and the IV dose. After Day 42, the mean values for each dose converged and were similar to that of the placebo ($p>0.05$).

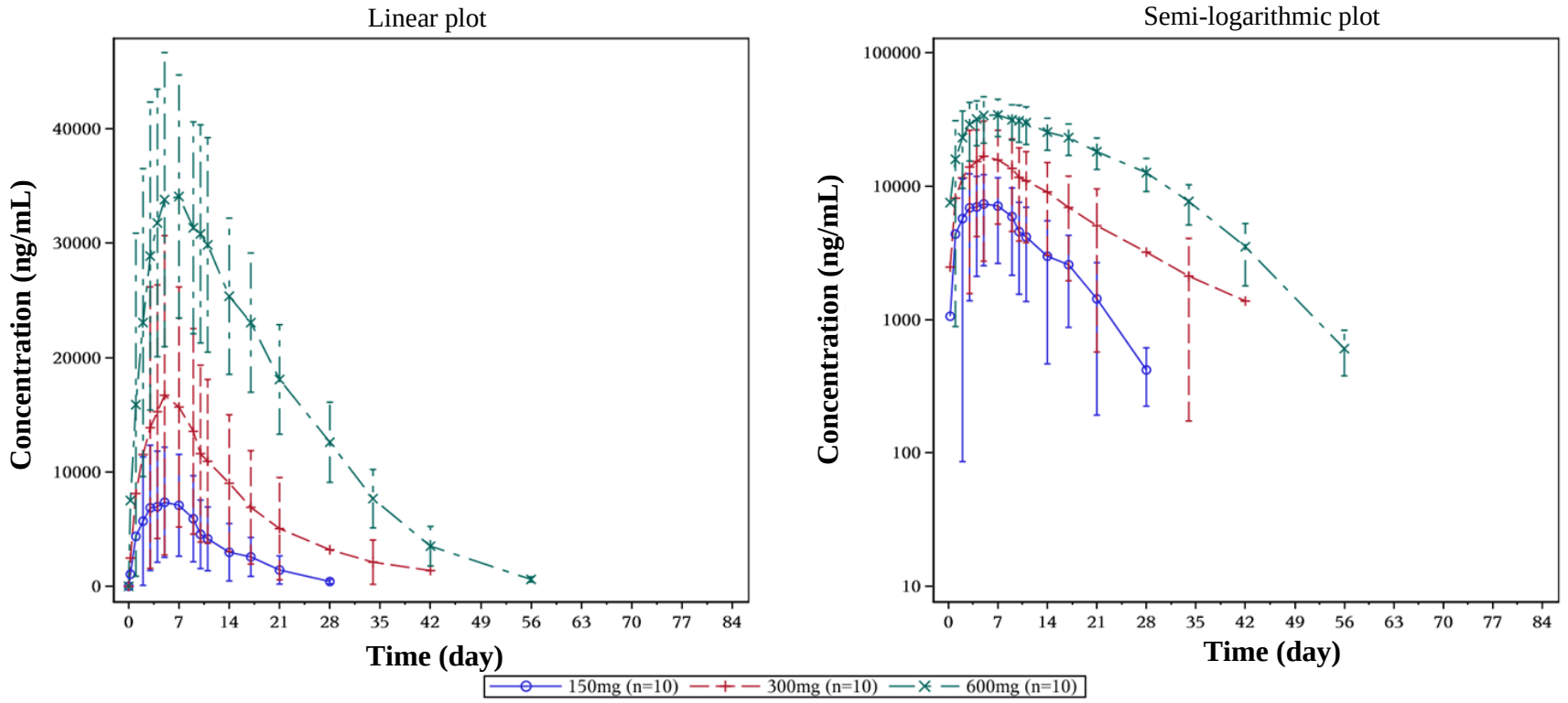
Trial CBP-201-CN001: –Single Ascending Dose (SAD) Trial ~~in a Chinese Population~~

Trial CBP-201-CN001 was a Phase 1 randomized, double-blind, placebo-controlled SAD trial to assess the safety, tolerability, PK, and PD of rademikibart in 36 healthy Chinese adult participants following rademikibart 150, 300, or 600 mg administered SC.

Pharmacokinetic Results

The mean plasma concentrations of rademikibart are presented in Figure 3 and the PK parameters are summarized in Table 6.

Figure 3: Mean Plasma Rademikibart Concentration Profiles Over Time by Treatment Group (CBP-201-CN001)



~~Data source: CBP-201CN001 Clinical Study Report V1.0 Figure 3~~

Table 6: Summary of Plasma Rademikibart PK Parameters by Dose Group (CBP-201-CN001)

PK Parameters (unit)	Statistics	Rademikibart 150 mg (N=10)	Rademikibart 300 mg (N=10)	Rademikibart 600 mg (N=10)
T_{max} (h)	Median	119.99 (23.99, 167.99)	119.98 (71.98, 215.98)	144.00 (23.99, 240.00)
	Min, Max	23.99, 167.99	71.98, 215.98	23.99, 240.00
T_{last} (h)	Median	5043.99 (336, 672)	6721.98 (504, 1010)	101008.00 (1010, 1340)
	Min, Max	335.99, 671.99	503.98, 1007.98	1007.98, 1343.97
C_{max} (ng/mL)	Mean±SD	781003.02 ± 547067.912	1780009.85 ± 1380007762.419	3580043.62 ± 12600584.605
AUC_{0-t} (ng·h/mL)	Mean±SD	213000025767.047± 164000000245.8011	607000001619.887 ± 503000001341.8899	183000004897.553 ± 617000003379.1726
$AUC_{0-\infty}$ (ng·h/mL)	Mean±SD	218000001019.943 ± 168000003964.8467	625000003510.509 ± 511000009329.0478	190000008964416.052 ± 611000008454.1826
CL/F (L/h)	Mean±SD	0.12044 ± 0.0877	0.0770 ± 0.0445	0.0347 ± 0.0110
V_z/F (L)	Mean±SD	9.742 ± 5.74360	11.148 ± 5.8930	8.093 ± 2.79877
$t_{1/2}$ (h)	Mean±SD	64.73 ± 18.655	114.08 ± 40.985	162.00 ± 34.107

Abbreviations: $AUC_{0-\infty}$, area under the concentration-time curve from Time 0 extrapolated to infinity; AUC_{0-t}, area under the concentration-time curve from Time 0 to the last quantifiable concentration; CL/F, apparent oral clearance uncorrected for bioavailability; C_{max}, maximum observed concentration; h, hour; PK, pharmacokinetics; SD, standard deviation; $t_{½}$, apparent elimination half-life; T_{max}, time to maximum observed concentration; T_{last}, time of last detectable concentration; V_z/F, apparent volume of distribution uncorrected for bioavailability.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} and T_{last} which are presented as median (minimum, maximum).
Data source: CBP-201CN001 Clinical Study Report V1.0 Table 14.

In the dose range of 150 to 600 mg administered SC, the mean peak concentrations of rademikibart increased relatively proportionately to increases with dose, while post-peak decline in concentrations exhibited slower decline at higher doses with evidence of nonlinearity. C_{max} was reached in 5 to 6 days. The mean V_z/F ranged from 8.0913-11.15 L and was not dose dependent. The mean CL/F was low and decreased with increasing dose, suggesting a nonlinear component to CL/F. The estimated $t_{1/2}$ increased with increasing dose.

Dose proportionality analysis indicated that C_{max} increased relatively proportionately to dose, while increases in AUC_{0-t} and $AUC_{0-\infty}$ were greater than the dose-proportional, indicating that rademikibart exhibits dose-proportional absorption and nonlinear elimination.

Immunogenicity Results

Samples for ADA analysis were collected through Day 85 post-dose. Overall, treatment-induced ADA incidence was 36.7% (11/30) [5/10 (50.0%), 3/10 (30.0%) and 3/10 (30.0%) in the 150 mg, 300 mg and 600 mg SC dose groups, respectively]. All titers were low and time of onset was ≥Day 29. ADA-positive participants in the 300 mg and 600 mg dose groups had lower mean concentrations than ADA-negative participants, but variability was high. No apparent difference in PK by ADA status was observed for the 150 mg dose. Neutralizing activity was not assessed.

Pharmacodynamic Results

PD samples for serum TARC analysis were collected through Day 85 postdose. Serum TARC levels decreased from Baseline in the rademikibart and placebo dose groups; however, before Day 42 the decrease was greater in all rademikibart dose groups compared to placebo. Exploratory PK/PD analysis did not show any apparent trend with increasing plasma rademikibart concentration.

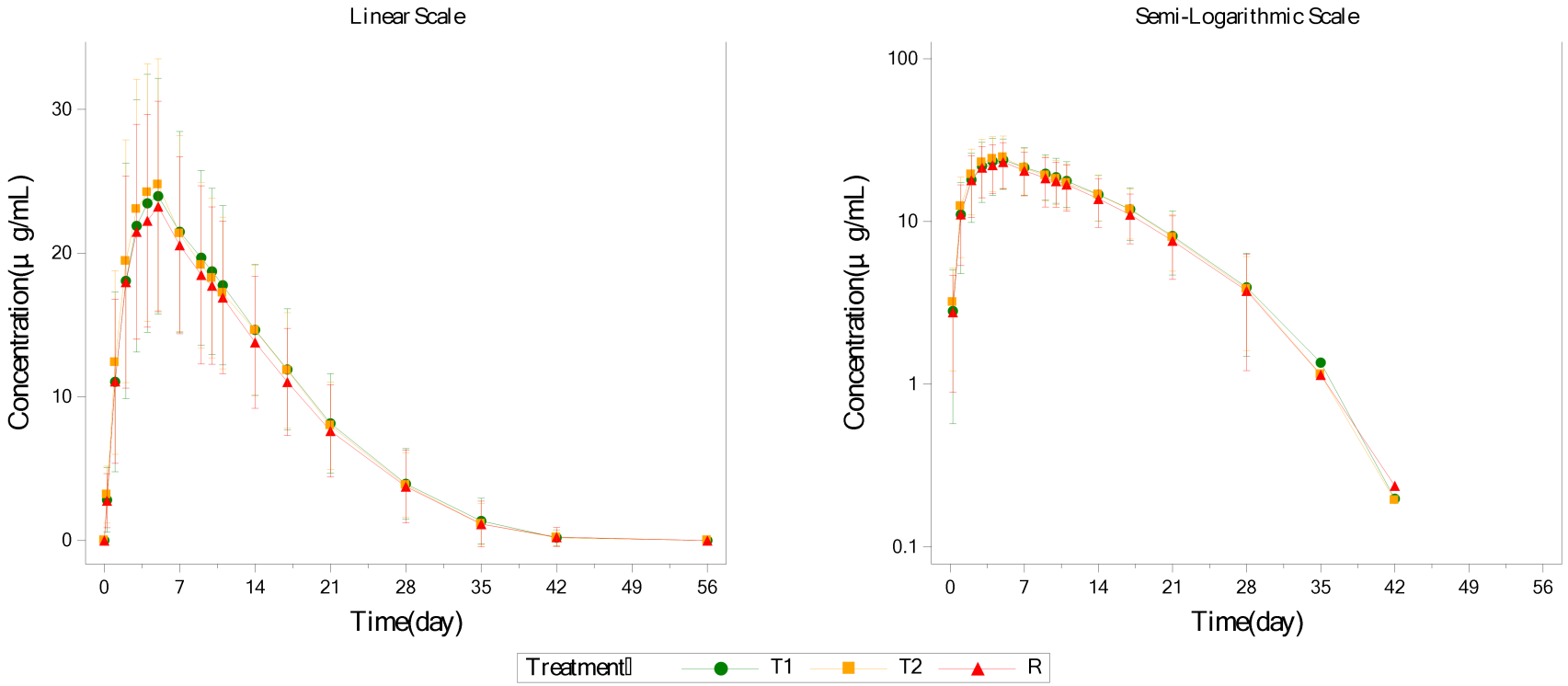
Trial CBP-201-CN004: –Single Dose Relative Bioavailability Trial

CBP-201-CN004 was a randomized, open-label, parallel-design single-dose relative bioavailability trial in 324 healthy participants. It compared two PFS product presentations of rademikibart (1 mL syringe containing 150 mg/1 mL [T1] and 2 mL syringe containing 300 mg/2 mL [T2]) with rademikibart in a vial format (R).

Pharmacokinetic Results

The mean plasma concentrations of rademikibart are presented in Figure 4 and the PK parameters are summarized in Table 7.

Figure 4: Mean Plasma Rademikibart Concentrations by Treatment Groups (CBP-201-CN004)



~~Data source: CBP-201-CN004 Clinical Study Report-V1.0-Figure 12-1.~~

Table 7: Summary of Rademikibart PK Parameters, (CBP-201-CN004)

PK parameters (unit)	Statistics	Rademikibart T1 (N=107)	Rademikibart T2 (N=108)	Rademikibart R (N=108)
$t_{1/2}$ (day)	Mean±SD	5.58 ± 1.65	5.51 ± 1.40	5.57 ± 1.68
T_{max} (day)	Median	5.00 (3.00, 11.00)	5.00 (2.00, 10.97)	5.00 (2.00, 10.99)
	Min, Max	3.00, 11.00	2.00, 10.97	2.00, 10.99
C_{max} (μg/mL)	Mean±SD	25.3 ± 8.55	26.1 ± 8.94	24.3 ± 7.45
AUC_{0-t} (day·*μg/mL)	Mean±SD	396 ± 141	395 ± 137	376 ± 131
AUC_{0-inf} (day·*μg/mL)	Mean±SD	409 ± 143	407 ± 139	388 ± 135
CL/F (L/day)	Mean±SD	0.883 ± 0.591	0.852 ± 0.401	0.891 ± 0.409
V_z/F (L)	Mean ±SD	6.61 ± 3.09	6.56 ± 3.30	6.81 ± 3.10

Abbreviations: AUC_{0-inf}, area under the concentration-time curve from Time 0 extrapolated to infinity; AUC_{0-t}, area under the concentration-time curve from Time 0 to the last quantifiable concentration; CL/F, Apparent oral clearance uncorrected for bioavailability; C_{max}, maximum observed concentration; PK, pharmacokinetics; SD, standard deviation; $t_{½}$, apparent elimination half-life; T_{max}, time to maximum observed concentration; V_z/F, apparent volume of distribution uncorrected for bioavailability.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} which is presented as median (minimum, maximum).
Data source: CPB-201-CN004 Clinical Study Report V1.0 Table 12-1.

There was no difference in plasma rademikibart concentration-time profiles from the 3 formulations; the mean plots were superimposable, with similar mean peak concentrations, similar time to mean peak, and similar post-peak decline. Median T_{max} was 5.0 days for all 3 treatments and mean $t_{1/2}$ ranged from 5.5 to 5.6 days. CL/F, Vz/F, C_{max}, and AUCs were all similar.

Immunogenicity Results

Samples for ADA analysis were collected through Day 57 post-dose. The overall treatment-induced ADA incidence was 14.2% (46/324) with 11.11% (12/108) for T1 and 15.74% (17/108) each for T2 and R dose groups. Time of onset was ≥ Day 28 post-dose and titers were generally low. Mean plasma concentrations of rademikibart in ADA-positive participants were generally lower than in ADA-negative participants across all 3 dose groups (T1, T2, and R).

Time of onset for treatment-emergent NnAb results was ≥ Day 43 in the T1 group and ≥Day 29 in the T2 and R groups. All ADA-positive participants eventually became NanAb-positive by Day 57.

Pharmacodynamic Results

No pharmacodynamic endpoints were assessed oin this trial.

Trial SIM0718-101: Single SC Dose Comparing 2 Formulations

SIM0718-101 was a Phase 1, randomized, open-label, single-dose, parallel group trial in healthy adult participants in China to compare the PK of a single SC dose of rademikibart 300 mg (2 mL) in 1 PFS (Group T) to 2 SC doses of rademikibart 150 mg (1 mL) vials (Group R).

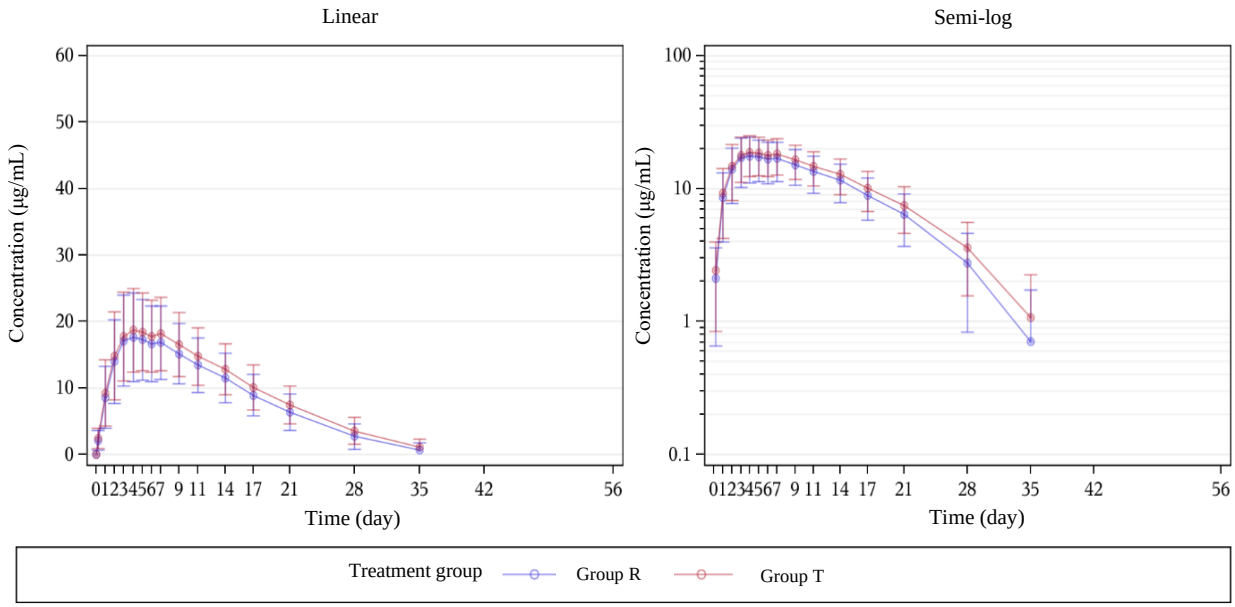
Participants were randomized in a 1:1 ratio to Group T and Group R. All participants received rademikibart on Day 1 and were followed for 8 weeks.

A total of 176 participants received rademikibart, 88 in Group T and 88 in Group R. One participant was excluded from PK concentration summaries and PK parameter analyses due to incomplete drug administration and another participant was excluded from PK parameter analyses due to early termination on Day 4 (Hour 72), while rademikibart was still in its absorption phase.

Pharmacokinetic Results

Mean plasma concentrations of rademikibart are presented in Figure 5 and PK parameters are summarized in Table 8.

Figure 5: Mean (± SD) Rademikibart Plasma Concentration-Time Curves in Each Treatment Group (SIM0718-101)



Abbreviation: SD, standard deviation.
Note: Group T refers to rademikibart 300 mg (2 mL) in 1 prefilled syringe and Group R refers to 2 subcutaneous doses of rademikibart 150 mg (1 mL) vials.

Table 8: Summary of Plasma Rademikibart PK Parameters by Treatment Group (Trial SIM0718-101)

Parameter	Group T 300 mg/2 mL PFS (N=87)	Group R 150 mg/mL vial × 2 vials (N=87)
C_{max} (μg/mL)	20.2±6.43	19.0±6.74
AUC_{0-t} (day·μg/mL)	334±113	298±109
AUC_{0-inf} (day·μg/mL)	343±115	311±110
T_{max} (day)	4.00 (2.00, 11.00)	4.00 (2.00, 11.00)
$t_{1/2}$ (day)	5.06±1.36	5.14±1.39
CL/F (L/day)	1.02±0.540	1.12±0.498
V_z/F (L)	7.14±3.29	8.02±4.36

Abbreviations: AUC_{0-inf}, area under the concentration-time curve from Time 0 extrapolated to infinity; AUC_{0-t}, area under the concentration-time curve from Time 0 to the last quantifiable concentration; CL/F, apparent oral clearance uncorrected for bioavailability; C_{max}, maximum observed concentration; PK, pharmacokinetic; SD, standard deviation; $t_{½}$, apparent elimination half-life; PFS, prefilled syringe; T_{max}, time to maximum observed concentration; V_z/F, apparent volume of distribution uncorrected for bioavailability.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} which is presented as median (minimum, maximum).

The geometric mean ratios (GMRs) and their 90% CIs for the comparison of rademikibart exposures (C_{max}, AUC_{0-t}, and AUC_{0-inf}) following SC administration from 300 mg/2 mL PFS relative to two 150 mg/mL vials were 108.16% (98.79%-118.42%), 112.82% (102.50%-124.17%), and 110.31% (101.88%-120.62%), respectively. Since the 90% CIs of all 3 GMRs fell within the 80.00%-125.00% bioequivalence range, exposures to rademikibart dosed SC from the 30 mg/2 mL PFS can be considered similar to those dosed from two 150 mg/mL vials.

Immunogenicity Results

Treatment-emergent ADA and neutralizing antibody (nAb) incidences were 27.3% (24/88) and 23.9% (21/88), respectively, following administration from PFS in Group T and 39.1% (34/87) and 33.3% (29/87), respectively, following administration from 2 vials in Group R. In majority of participants, the onset of ADA and nAb positivity was late (Day 43 or Day 57) and median ADA titers were low, ranging from 20 to 748.8.

There were no apparent differences in plasma concentrations of ADA-positive relative to ADA-negative participants.

Trial CBP-201-105 (Part A): Single IV Dose at Different Infusion Rates

Trial CBP-201-105 is a Phase 1, 3-part, randomized, double-blind, and placebo-controlled trial to evaluate a single IV dose of rademikibart 300 mg in healthy adults (Part A), adults with stable asthma or COPD (Part B), and adults experiencing an acute asthma or COPD exacerbation (Part C). Parts A and B are complete; Part C is ongoing.

In Part A, 24 participants were administered rademikibart or placebo at different infusion rates: 30 minutes (Cohort A1), 15 minutes (Cohort A2), or 2 minutes (Cohort A3). Within each cohort,

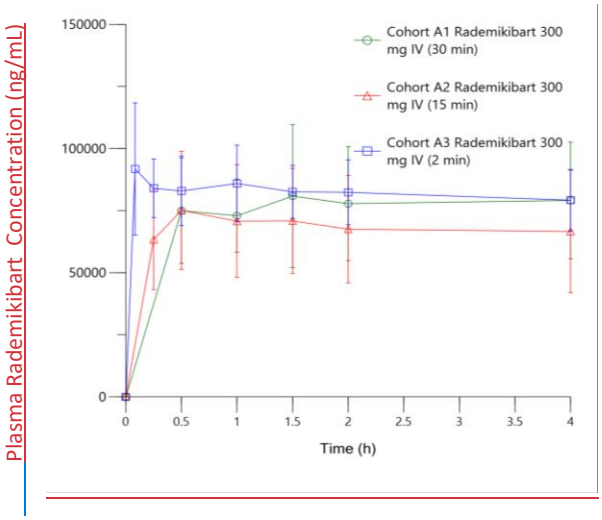
6 participants received rademikibart and 2 received placebo. All participants were followed for 8 weeks.

Pharmacokinetic Results

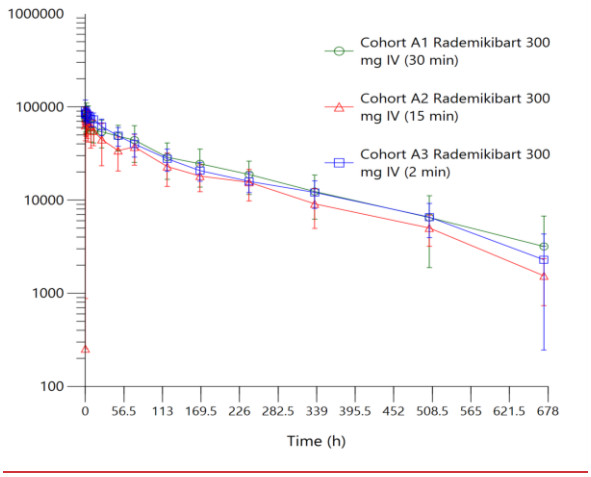
Preliminary PK analysis was performed on QC'd plasma rademikibart PK data available from all participants who completed Part A of the study. The mean concentrations in each of the 3 IV infusion cohorts are presented in Figure 6 (through 4 hours postdose in Figure 6A [linear scale] and through Day 29 [672 hours] postdose in Figure 6B [semi-log scale]). PK parameters are summarized in Table 9.

Figure 6: Mean (± SD) Rademikibart Plasma Concentrations in Each IV Infusion Cohort (CBP-201-105, Part A)

A) 0-4 hours Postdose (Linear Scale)



B) 0-672 hours Postdose (Semi-log Scale)



Abbreviations: h, hour; IV, intravenous; min, minutes; SD, standard deviation.

Table 9: Summary of Plasma Rademikibart PK Parameters in Each IV Infusion Cohort (CBP-201-105, Part A)

Parameter	Rademikibart 300 mg		
	Cohort A1 30 min IV (N=6)	Cohort A2 15 min IV (N=6)	Cohort A3 2 min IV (N=6)
C_{max} (µg/mL)	85.7 (25.5)	76.2 (23.2)	101.7 (22.9)
T_{max} (h)	1.00 (0.50-2.00)	0.75 (0.50-1.00)	0.38 (0.08-1.00)
AUC_{0-24} (h·µg/mL)	1560 (508)	1340 (428)	1740 (290)
AUC_{0-last} (h·µg/mL)	12100 (6000)	9080 (3170)	11700 (3040)
AUC_{0-inf} (h·µg/mL)	12500 (6240)	9740 (3450)	12300 (3650)
$t_{½}$ (h)	138 (39.7)	133 (41.7)	143 (36.2)
CL (mL/h)	28.6 (12.1)	35.7 (17.4)	26.2 (7.56)
V_z (L)	5.27 (1.60)	6.29 (1.74)	5.14 (0.63)
MRTiv (h)	197 (47.7)	193 (52.1)	202 (36.0)

Abbreviations: AUC_{0-24}, area under the concentration-time curve from Time 0 to 24 hours postdose; AUC_{0-inf}, area under the concentration-time curve from Time 0 extrapolated to infinity; AUC_{0-last}, area under the concentration-time curve from Time 0 to the last quantifiable concentration; CL, total body clearance; C_{max}, maximum observed concentration; h, hour; IV, intravenous; PK, pharmacokinetic; min, minute; MRTiv, mean residence time following IV dose; SD, standard deviation; $t_{½}$, apparent elimination half-life; T_{max}, time to maximum observed concentration; V_z, volume of distribution during the terminal phase.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} which is presented as median (minimum, maximum).

The mean concentration versus time profiles were similar between the 3 cohorts, with similar magnitude of mean peak and essentially monoexponential post-peak decline. Mean C_{max} was comparable across the 3 cohorts, indicating that increasing the rate of infusion from 300 mg/30 minutes to 300 mg/2 minutes had no discernible impact on maximum exposures to rademikibart. Mean overall exposure metrics (AUCs) and mean $t_{½}$, CL, V_z, and MRTiv values were all similar among the 3 cohorts, as expected from the same dose of rademikibart with the only difference among the cohorts being the infusion rate.

Immunogenicity Results

Treatment-emergent ADA incidence among the 18 participants who received active rademikibart was 11.1% (2/18): 1/6 in Cohort A1, 0/6 in Cohort A2, and 1/6 in Cohort A3. ADA-positive responses were first detected in both participants at the Day 43 Visit and were persistent in duration, with slightly higher titers detected on Day 57/End of Trial Visit. All ADA-positive samples were also nAb-positive. Both participants' plasma rademikibart concentrations were below the limit of quantification (BLQ) at the time of onset of their immunogenic response.

5.1.4.2. Respiratory ~~Asthma~~ Trials

5.1.4.2.1. Asthma Trials

Trial CBP-201-WW002: ~~–~~24-Week Efficacy and Safety in Adults With Asthma

Trial CBP-201-WW002 was a multicenter, randomized, double-blind, placebo-controlled, efficacy and safety trial of rademikibart in 322 participants with moderate-to-severe persistent asthma with ~~T~~type 2 inflammation conducted in the US, China, South Korea, Poland, and Hungary. Participants were randomized to receive 300 mg (high dose) or 150 mg (low dose) Q2W SC for 24 weeks with an 8-week post-treatment follow ~~-~~up. Participants received a 600 mg loading dose~~LD~~ of rademikibart or placebo on Day 1, followed by the start of their randomized treatment 2 weeks later. The rademikibart 150 mg Q2W dosing arm was considered a conservative preliminary surrogate for a rademikibart 300 mg Q4W dosing regimen.

Pharmacokinetic Results

Mean (SD) rademikibart plasma concentrations are summarized in Table 10. Week 1 mean concentrations correspond to the C_{max} following the 600 mg loading dose~~LD~~ in both treatment groups and were slightly higher in participants in the 150 mg dose group. By Week 12, mean predose concentrations were at steady state in the 300 mg group and were maintained through end of treatment ~~(EOT)~~ (Week 24). In the 150 mg dose group, mean predose concentrations at Week 12 were approximately half the value of those at Week 4, and the decreasing trend continued through the 24 weeks of treatment. Concentrations decreased rapidly after treatment was stopped in both groups.

Table 10: Summary of PK Concentrations by Timepoints and Treatment Groups for Rademikibart (CBP-201-WW002)

Week	Mean (SD) (n) Rademikibart Concentrations (ng/mL)	
	600 mg LD + 300 mg Q2W N=105	600 mg LD + 150 mg Q2W N=105
Week 1	27800 (16500) (98)	31200 (18000) (96)
Week 4	20200 (14000) (89)	15700 (11600) (91)
Week 12	24700 (18300) (83)	8050 (9080) (84)
Week 16	24000 (19800) (81)	7020 (8460) (90)
Week 24 (EOT)	23500 (21000) (80)	5190 (5930) (85)
Week 28	11100 (13700) (82)	1140 (3170) (84)
Week 32 (EOS)	2130 (5870) (75)	17.9 (141) (82)

Abbreviations: EOS, end of study; EOT, end of treatment; LD, loading dose; PK, pharmacokinetics; Q2W, every 2 weeks; SD, standard deviation.
Note: BLQ imputed as 0.
~~Data source: CPB-201-WW002 PK Analysis Report Table 1~~

Immunogenicity Results

While the overall treatment-emergent ADA incidence in all participants was 10.7% (33/309), the incidence was higher in the 150 mg group (22.3% [23/103]) relative to the 300 mg group (5.0% [5/100]), with the incidence in the 300 mg group similar to that of placebo (4.7% [5/106]). There was also a higher incidence of persistent ADA response (12 participants) in the 150 mg group relative to the 300 mg or placebo groups (1 participant in each). Majority of titers were low~~, with 3 participants with incidences of moderate titers and 1 with high. NAb incidence was low; 13.6% (14/103) in the 150 mg dose group and 4.0% (4/100) in the 300 mg dose group~~.

Pharmacodynamic Results

A decrease in the mean levels of FeNO and IgE were noted in both the rademikibart 150 mg and 300 mg groups, starting as early as Week 1 and continuing up to the Week 32 Visit/end of the trial~~EOS~~. A decrease in mean blood levels of TARC was noted in both active dose groups, with onset in Week 1 and continuing up to Week 24. By the Week 32 Visit/end of the trial ~~EOS~~, the TARC levels had increased compared to Baseline in the 150 mg dose group but remained decreased compared to Baseline in the 300 mg dose group.

There were no remarkable changes noted in periostin, C-reactive protein, eotaxin-3, or Eosinophil Cationic Protein throughout the trial, however each of these biomarkers had a highly variable Baseline which limited the ability to detect any relationship.

Preliminary exposure-response modeling in participants from this trial showed that the greatest ~~CFB~~ change from baseline in both pre-bronchodilator FEV1 and the ACQ score occurred after the 600 mg loading dose~~LD~~.

Trial CBP-201-105 (Part B1): Single IV Dose in Adults With Stable Asthma

Trial CBP-201-105 is a Phase 1, multipart, randomized, double-blind, and placebo-controlled trial to evaluate a single IV dose of rademikibart 300 mg in healthy adults (Part A), adults with stable asthma or COPD (Parts B1 and B2, respectively), and adults experiencing an acute asthma or COPD exacerbation (Parts C1 and C2, respectively). Parts A and B are complete; Part C is ongoing.

In Part B1, 12 adult participants with stable asthma were administered a single dose of rademikibart 300 mg (N=10) or placebo (N=2) via a 2-minute IV infusion. All participants were followed for 6 weeks. PK results through Day 4 and spirometry results are available and are summarized below. Biomarker and immunogenicity results are not yet available.

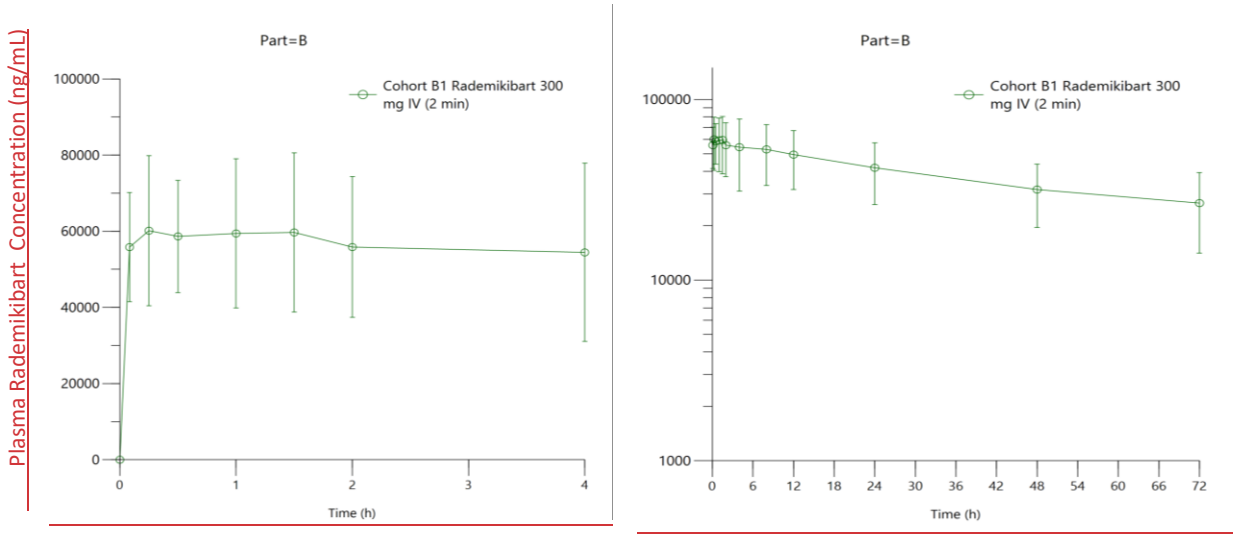
Pharmacokinetic Results

Preliminary PK analysis was performed on partial (from predose through 72 hours posdose) QC'd plasma rademikibart PK data available from all participants who completed Part B1. The mean plasma rademikibart concentrations for participants who received rademikibart are presented in Figure 7 (through 4 hours postdose in Figure 7A [linear scale] and through Day 4 [72 hours] postdose in Figure 7B [semi-log scale]). Peak mean rademikibart concentration was reached within 15 minutes of the start of the 2-minute infusion and remained relatively unchanged in the first 4 hours postdose, decreasing in a monoexponential manner to approximately half the peak value by 72 hours postdose. PK parameters C_{max}, T_{max}, and AUC_{0-24} are summarized in Table 11. The mean maximum (C_{max}) and overall Day 1 (AUC_{0-24})

rademikibart exposures in this sub-population of participants with asthma were generally comparable to those reported in healthy participants enrolled in Cohort A of this study (Table 9).

Figure 7: Mean (±SD) Rademikibart Plasma Concentrations in Participants With Stable Asthma (CBP-201-105, Part B1)

A) 0-4 hours Postdose (Linear Scale) **B) 0-72 hours Postdose (Semi-log Scale)**



Abbreviations: h, hour; IV, intravenous; min, minutes; SD, standard deviation.

Table 11: Summary of Plasma Rademikibart PK Parameters in Participants With Stable Asthma (CBP-201-105, Part B1)

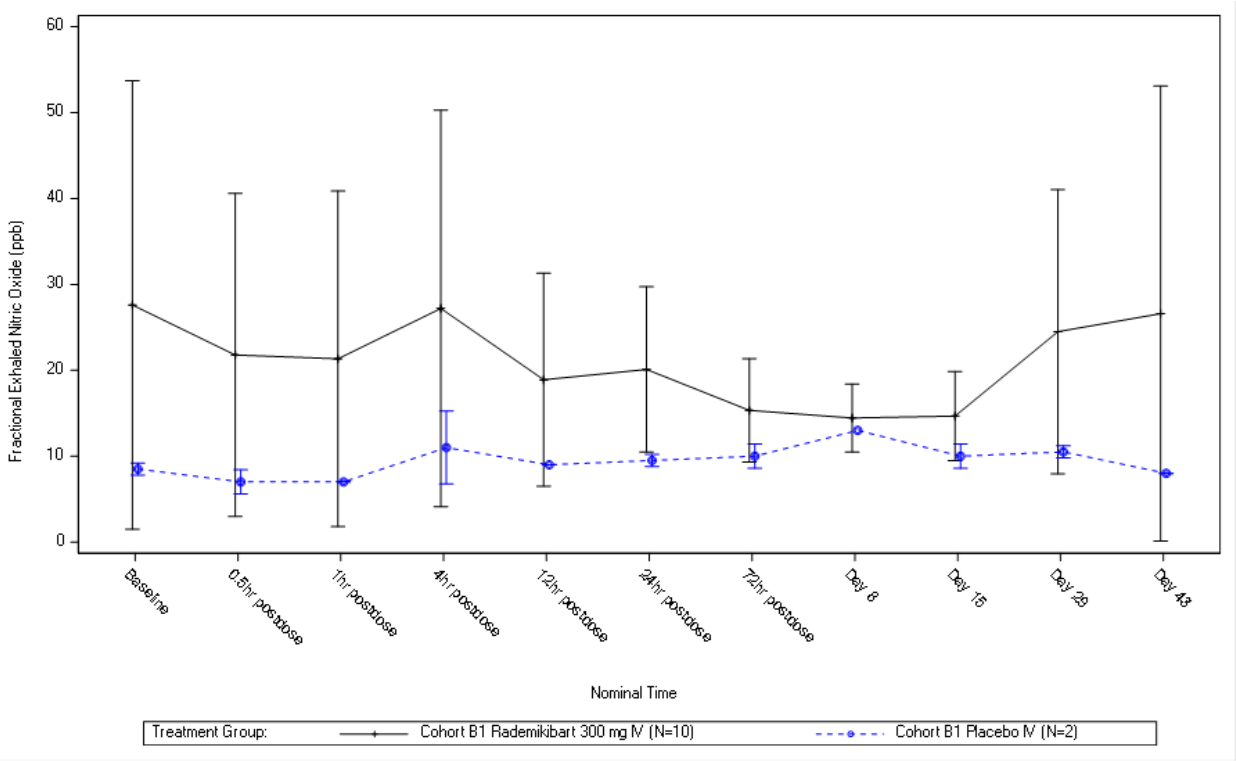
Parameter	Rademikibart 300 mg IV (N=10)
C_{max} (µg/mL)	65.8 (20.4)
T_{max} (h)	0.25 (0.08 - 4.00)
AUC_{0-24} (h·µg/mL)	1190 (433)

Abbreviations: AUC_{0-24}, area under the concentration-time curve from Time 0 to 24 hours postdose; C_{max}, maximum observed concentration; h, hour; IV, intravenous; PK, pharmacokinetic; SD, standard deviation; T_{max}, time to maximum observed concentration.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} which is presented as median (minimum, maximum).

Pharmacodynamic Results

In the rademikibart group, a clinically meaningful decrease from baseline in mean FeNO values, defined as >10 ppb, was observed as early as Day 4 with a nadir at Day 8 followed by a gradual return to baseline by Day 43 (End of Trial Visit) (Figure 8). The placebo group had a lower baseline mean FeNO value than the rademikibart group, which remained relatively unchanged over time.

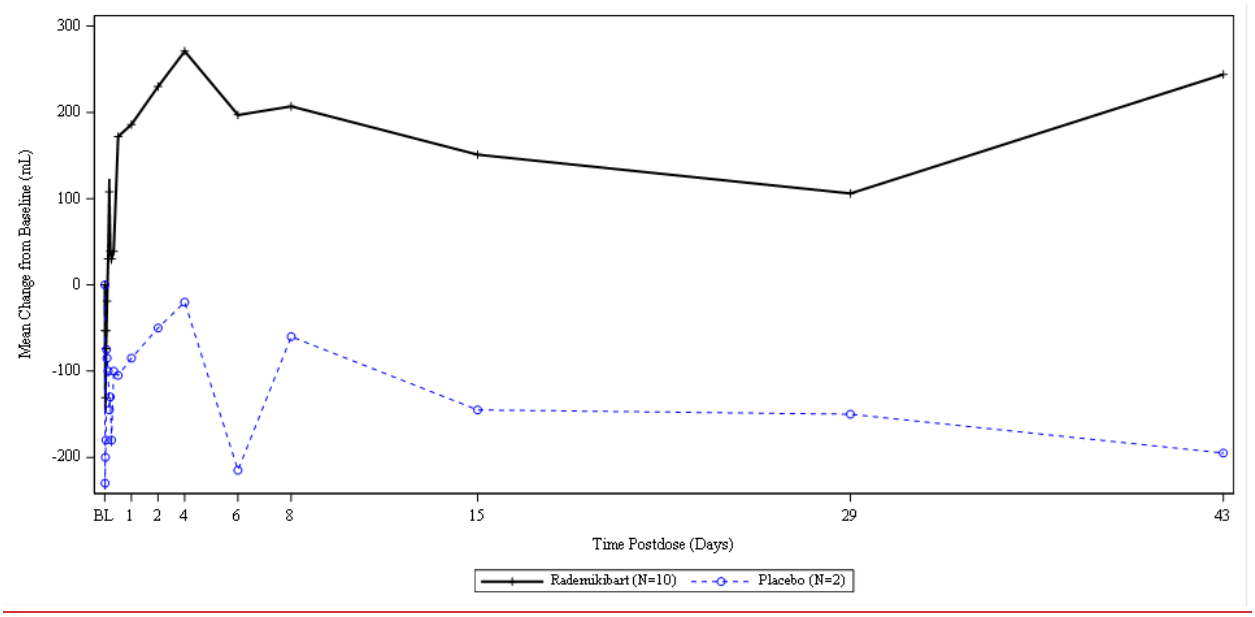
Figure 8: Mean (±SD) FeNO Values Over Time (CBP-201-105, Part B1)



Abbreviations: FeNO, fractional exhaled nitric oxide; h, hour; IV, intravenous; SD, standard deviation.
Note: FeNO values obtained on Day 1 postdose for Participant 1103-054 were excluded through Day 1, 3 hours postdose due to an adverse event (infusion related reaction) that resolved prior to Day 1, 4 hours postdose.

Figure 9 show the change from baseline in mean pre-bronchodilator (BD) FEV_1 values over the trial. There was an initial decline in pre-BD FEV_1 in the rademikibart group over the first 30 minutes, which then steadily increased over the next 12 hours. From 12 hours through Day 43 (End of Trial Visit), clinically meaningful increases from baseline in FEV_1, defined as >100 mL, were observed at all timepoints in the rademikibart group (ranging from 106 to 271 mL). An initial decline was also observed for the placebo group, which was more pronounced than the rademikibart group and showed little to no improvement over time.

Figure 9: Mean Change From Baseline in Pre-BD Spirometry Value for FEV_1 (CBP-201-105, Part B1)



Abbreviations: BD, bronchodilator; BL, baseline; FEV_1, forced expiratory volume in 1 second.

Differences between the pre-BD and post BD (pre-post-BD) mean FEV_1 measurements were calculated at baseline, Day 2, and Day 15 (Table 12). Small but clinically meaningful improvements in pre-BD % predicted FEV_1 were observed at Day 2 and Day 15 for the rademikibart group while decreases in pre-BD % predicted FEV_1 were observed for the placebo group. No additional improvements from baseline in post-BD % predicted FEV_1 were observed for the rademikibart group, while a decrease was observed in the placebo group.

Table 12: Comparison of Pre- and Post-BD Changes in Mean FEV_1 and Mean Percent Predicted FEV_1 (CBP-201-105, Part B1)

	Baseline			Day 2			Day 15		
	Pre-BD	Post-BD	Difference	Pre-BD	Post-BD	Difference	Pre-BD	Post-BD	Difference
Mean FEV_1 (mL)									
Rademikibart	1940	2510	570 (29.4%)	2126	2474	348 (16.4%)	2091	2387	296 (14.2%)
Placebo	1810	2105	295 (16.3%)	1725	1950	225 (13.0%)	1665	1725	60 (3.6%)
Mean % Predicted FEV_1									
Rademikibart	71.59	92.59	21.00	78.65	90.95	12.30	76.98	87.88	10.90
Placebo	79.15	92.10	12.95	75.45	85.20	9.75	72.95	75.55	2.60

Abbreviations: BD, bronchodilator; FEV_1, forced expiratory volume in 1 second.

5.1.4.2.2. COPD Trials

Trial CBP-201-105 (Part B2): Single IV Dose in Adults With Stable COPD

Trial CBP-201-105 is a Phase 1, multipart, randomized, double-blind, and placebo-controlled trial to evaluate a single IV dose of rademikibart 300 mg in healthy adults (Part A), adults with stable asthma or COPD (Parts B1 and B2, respectively), and adults experiencing an acute asthma or COPD exacerbation (Parts C1 and C2, respectively). Parts A and B are complete; Part C is ongoing.

In Part B2, 10 adult participants with stable COPD were administered a single dose of rademikibart 300 mg (N=8) or placebo (N=2) via a 2-minute IV infusion. All participants were followed for 6 weeks. PK results through Day 4 and spirometry results are available and are summarized below. Biomarker and immunogenicity results are not yet available.

Pharmacokinetic Results

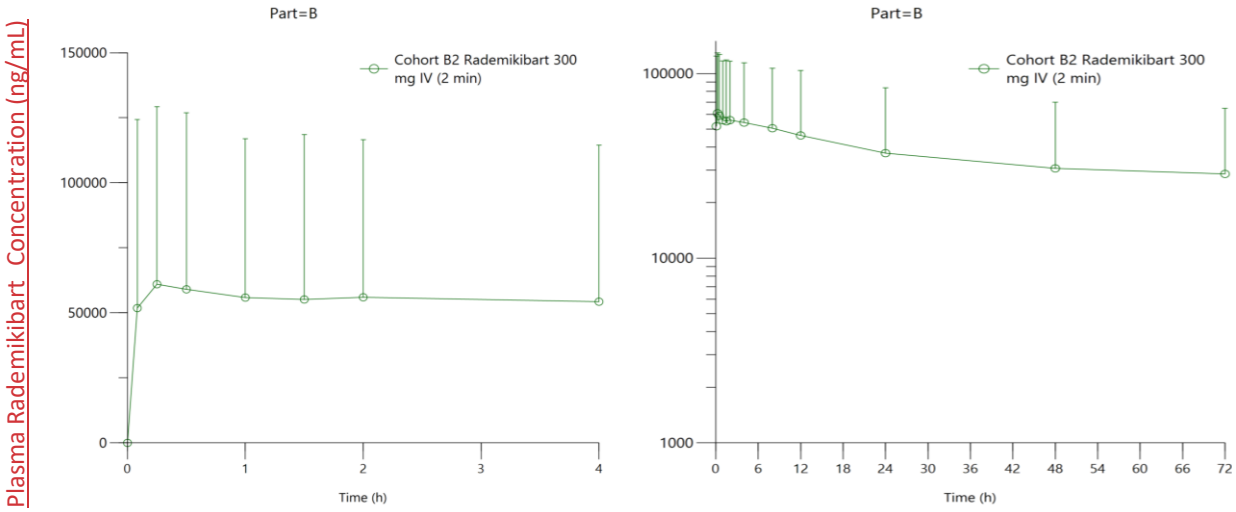
Preliminary PK analysis was performed on partial (from predose through 72 hours posdose) QC'd plasma rademikibart PK data available from all participants who completed Part B2 of the trial.

The mean plasma rademikibart concentrations in Cohort B2 participants who received 300 mg rademikibart as a 2-minute IV infusion are presented in Figure 10 (through 4 hours postdose in Figure 8A [linear scale] and through Day 4 (72 hours) postdose in Figure 8B [semi-log scale]). There was a notably high variability in individual rademikibart concentration-time profiles among the 8 participants with stable COPD. Peak mean concentration was reached within 15 minutes of the start of the 2-minute infusion and remained relatively unchanged in the first 4 hours postdose, decreasing to approximately half the peak value by 72 hours postdose.

Preliminary PK parameters C_{max}, T_{max}, and AUC_{0-24} are summarized in Table 13. Despite the high variability, the mean maximum and overall Day 1 rademikibart exposures in this subpopulation of participants with COPD were generally comparable to those observed in healthy participants and participants with asthma enrolled in Cohort A (Table 9) and Cohort B1 (Table 11) of this trial, respectively.

Figure 10: Mean (± SD) Rademikibart Plasma Concentrations in Participants With Stable COPD (CBP-201-105, Part B2)

A) 0-4 hours Postdose (Linear Scale) **B) 0-72 hours Postdose (Semi-log Scale)**



Abbreviations: COPD, chronic obstructive pulmonary disease; h, hour; IV, intravenous; min, minutes; SD, standard deviation.

Table 13: Summary of Plasma Rademikibart PK Parameters in Participants With Stable COPD (CBP-201-105, Part B2)

Parameter	Rademikibart 300 mg IV (N=8)
C_{max} (µg/mL)	65.4 (70.5)
T_{max} (h)	0.38 (0.08 – 8.00)
AUC_{0-24} (h·µg/mL)	1120 (1330)

Abbreviations: AUC_{0-24}, area under the concentration-time curve from Time 0 to 24 hours postdose; C_{max}, maximum observed concentration; h, hour; IV, intravenous; PK, pharmacokinetics; SD, standard deviation; T_{max}, time to maximum observed concentration.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} which is presented as median (minimum – maximum).

Immunogenicity Results

Immunogenicity analysis is ongoing.

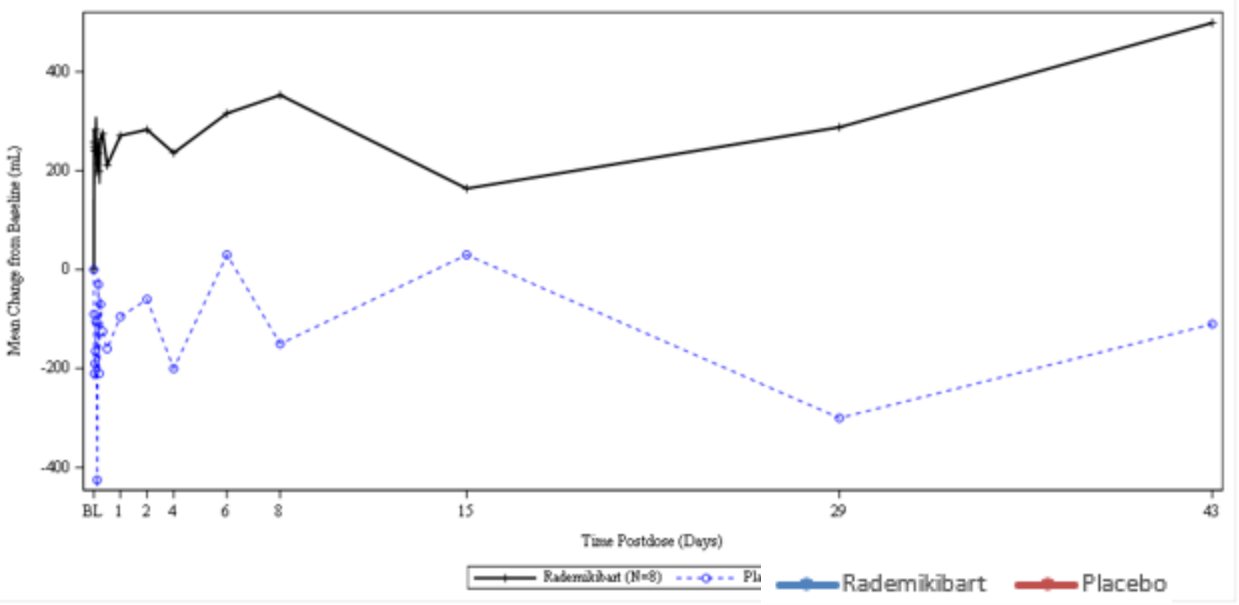
Pharmacodynamic Results

Pre-BD FEV_1 and FVC were measured at multiple timepoints through Day 43 (End of Trial Visit). Figure 11 shows the change from baseline in mean pre-BD FEV_1 values over time. Clinically meaningful increases from baseline in FEV_1, defined as >100 mL (Donohue 2005), were observed in the rademikibart group at all timepoints from 15 minutes postdose through Day 43 (End of Trial Visit) with increases ranging from 164 to 499 mL. In the placebo group,

mean FEV_1 values decreased from baseline at all but 2 timepoints with changes ranging from a 30 mL increase to a 425 mL decrease.

Small changes were observed over time in the rademikibart group for other PD parameters (FeNO, pre-BD FVC, post-BD FEV_1, post-BD FVC).

Figure 11: Mean Change From Baseline in Pre-BD Spirometry Values for FEV_1 Over Time (CBP-201-105, Part B2)



Abbreviations: BD, bronchodilator; FEV_1, forced expiratory volume in 1 second.

5.1.4.3. Atopic Dermatitis Trials

Trial CBP-201-AU002: ~~–~~Multiple Ascending Dose Trial in ~~AD~~ Participants With AD

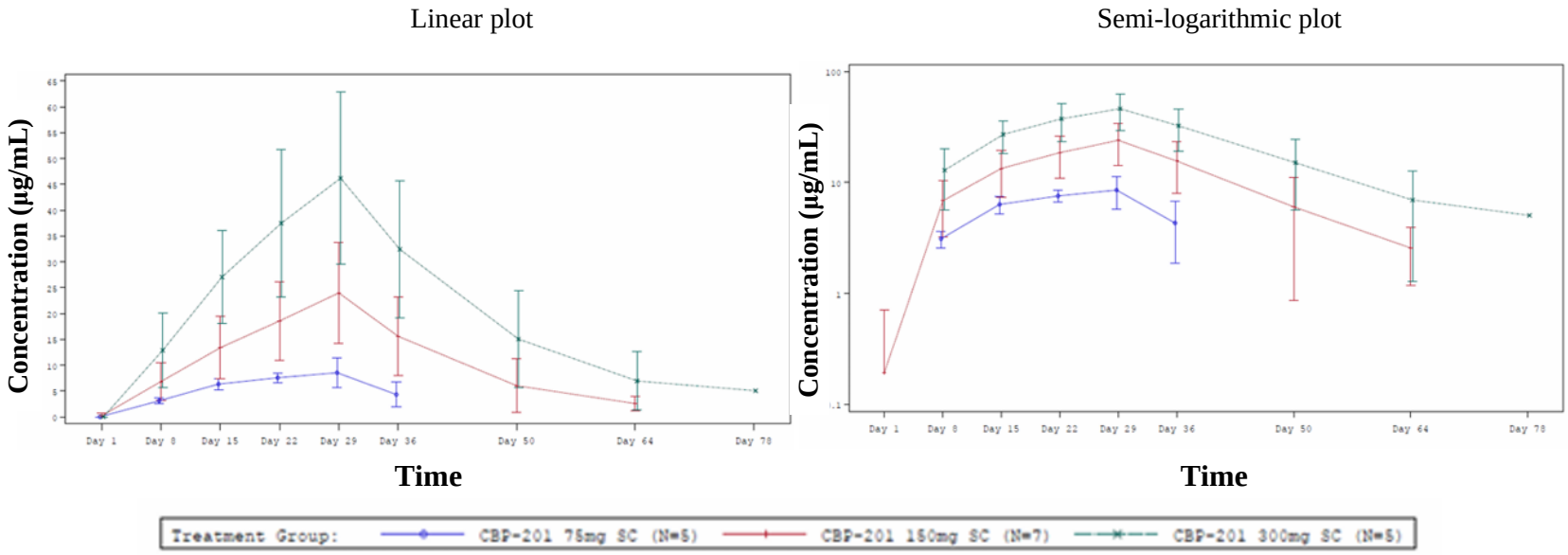
CBP-201AU002 was a Phase 1b 11-week, double-blind, randomized, placebo-controlled, multicenter, multi-ethnic, multiple ascending dose (MAD) trial of the safety, tolerability, PK and preliminary efficacy of rademikibart in 32 participants with moderate-to-severe AD.

Pharmacokinetic Results

PK were determined from 17 participants: 5, 7, and 5 participants each in the rademikibart 75, 150, and 300 mg SC QW groups, respectively. Multiple-dose PK parameters were calculated from semi-sparse sampling (1 predose and 5 postdose samples) following the last (Day 22) dose.

The mean rademikibart concentration-time profiles are presented in Figure 12, and PK parameters are summarized in Table 14.

Figure 12: Mean (±SD) Plasma Rademikibart Concentrations (µg/mL) Over Time in Multiple Ascending Dose Trial (CBP-201AU002)



Abbreviations: SC, subcutaneous; SD, standard deviation.
~~Data source: CBP-201AU002 Clinical Study Report V1.0 In-text Figure 1 and Figure 2~~

None of the 3 QW dosing regimens reached steady state by the 4th dose (Day 22, last dosing day). The highest mean ~~concentrations (~~C_{max}~~)~~ values were observed on Day 29, approximately 1 week after the fourth rademikibart administration on Day 22. Comparison of Day 29 and Day 36 concentrations suggested a more than dose-proportional difference between the 75 mg and 150 mg dose groups and a proportional difference between the 150 mg and 300 mg dose groups.

Statistical analysis indicated that C_{max} increased relatively proportionately to dose across the 75 to 300 mg range and AUC (overall exposure) increased relatively dose-proportionately between the 150 mg and 300 mg dose levels. Comparison of AUCs between 75 mg and 150 mg doses indicated less than proportional increase in exposure with dose.

Table 14: Plasma Rademikibart Pharmacokinetic Parameters in Multiple Ascending Dose Trial (CBP201-AU002)

Treatment Group	Parameter (Unit)	Statistics		
		n	Mean	SD
Rademikibart 75 mg SC (N=5)	AUC_{0-t} (day·*µg/mL)	4	1921.6	36.05.99
	AUC_{0-inf} (day*µg/mL)	NC		
	C_{max} (µg/mL)	3	9.9219	0.53105
	$t_{1/2}$ (day)	NC		
	CL/F (L/day)	NC		
	V_z/F (L)	NC		
Rademikibart 150 mg SC (N=7)	AUC_{0-t} (day·*µg/mL)	7	66059.6	346.31
	AUC_{0-inf} (day·*µg/mL)	4	938.0	23029.80
	C_{max} (µg/mL)	7	24.03.982	9.8035
	$t_{1/2}$ (day)	4	9.033	1.9040
	CL/F (L/day)	4	0.688	0.16879
	V_z/F (L)	4	8.753	2.122158
Rademikibart 300 mg SC (N=5)	AUC_{0-t} (day·*µg/mL)	5	1460.0	650.06
	AUC_{0-inf} (day·*µg/mL)	4	178078.5	3710.73
	C_{max} (µg/mL)	5	46.2193	16.6419
	$t_{1/2}$ (day)	4	9.840	1.403974
	CL/F (L/day)	4	0.714	0.1381
	V_z/F (L)	4	10.031	1.79857

Abbreviations: AUC_{0-t}, area under the concentration-time curve from Time 0 to the last quantifiable concentration; AUC_{0-inf}, area under the concentration-time curve from Time 0 extrapolated to infinity; CL/F, apparent oral clearance uncorrected for bioavailability; C_{max}, maximum observed concentration; N, number of participants in the PK set; n, number of participants with the PK parameter; NC, not calculatable; PK, pharmacokinetic; SC, subcutaneous; SD, standard deviation; $t_{½}$, apparent elimination half-life; V_z/F, Apparent volume of distribution uncorrected for bioavailability.

~~Data source: CBP-201AU002 Clinical Study Report V1.0 In-text Table 4~~

Immunogenicity Results

Samples for ADA analysis were collected up to Day 78. Overall treatment-induced ADA incidence was 22% (5/23), with 4/8 (50%) participants in the 75 mg dose group, 1/8 (12.5%) in the 150 mg dose group, and none (0%) in the 300 mg dose and placebo groups; thus, the incidence decreased with increasing dose. All titers were low and had late onset (Day 78). There was no clinically relevant difference in the incidence of TEAEs between ADA-positive and ADA-negative participants. Neutralizing activity was not assessed.

Pharmacodynamic Results

PD parameters of interest included serum IL-4, IL-13, IgE, TARC, LDH levels and peripheral eosinophil count. Timing of PD assessments coincided with PK. Results showed a decline in TARC levels in the rademikibart cohorts compared to the placebo, and this decline was consistently associated with improvement in AD. There was also a trend of lower mean LDH values across all rademikibart doses compared to placebo. There were no apparent or consistent trends in levels of IL-4, IL-13, IgE, or absolute or relative (percent change from baseline~~CFB~~) eosinophil counts with increasing rademikibart dose levels.

Trial CBP-201-WW001: ~~–~~16-Week Efficacy and Safety Trial in Adults With AD

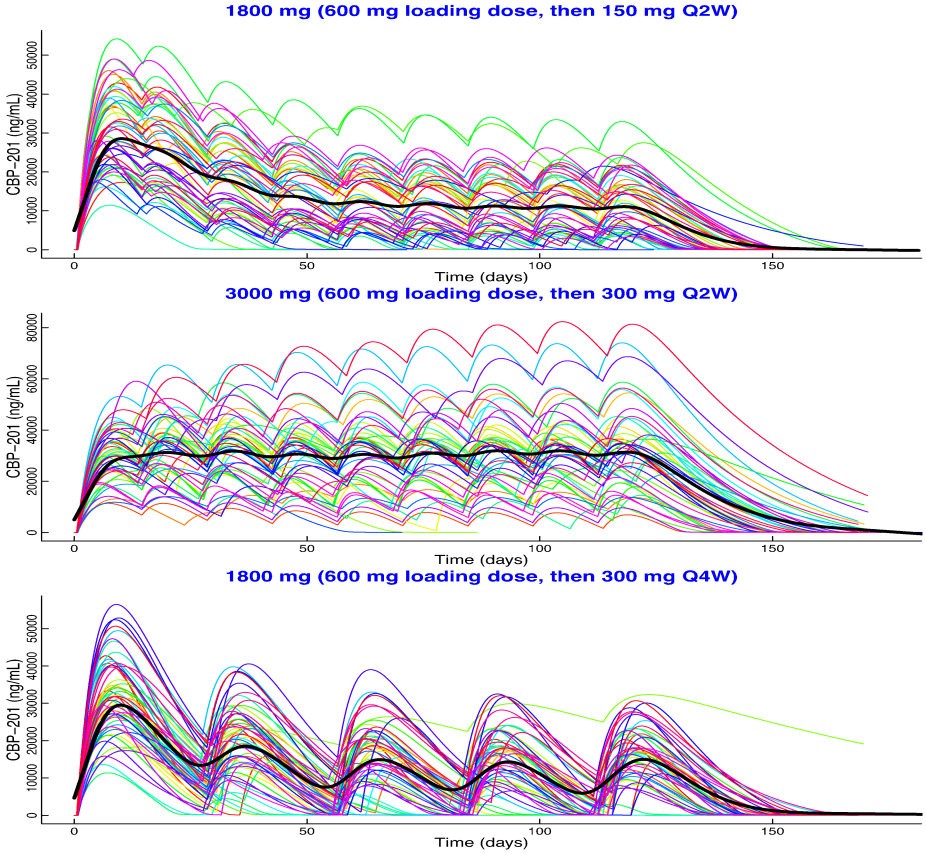
CBP-201-WW001 was a Phase 2b, randomized, double-blind, placebo-controlled multicentered trial of the efficacy, safety, PK, and PD of rademikibart in 226 participants with moderate-to-severe AD conducted in the US, Australia, New Zealand and China. Participants were randomized (1:1:1:1) to receive either 1 of 3 active rademikibart treatments or matched placebo. Active treatments consisted of rademikibart 600 mg SC loading dose ~~LD~~ followed by 16 weeks of maintenance dose of either 150 or 300 mg SC Q2W, or 300 mg SC Q4W.

Pharmacokinetic Results

Due to sparse sampling, a population PK model was derived to estimate PK parameters. The model that best described the data was a 2-compartment model with first-order absorption from a depot and 2 clearance pathways, one of which was saturable. Simulations of rademikibart concentrations for the 3 dosing regimens are presented in Figure 13 and model-estimated exposure parameter values are in Table 15. As concentration at which the saturable CL pathway was 50% inhibited (164 to 184 ng/mL) was far below C_{trough} concentrations seen on this trial, saturable CL is unlikely to influence the concentration profile of rademikibart in clinical practice.

Covariate analysis indicated that Chinese participants had 23% lower bioavailability and 20% lower non-saturable CL than non-Chinese participants, that participants with higher Baseline neutrophil counts had higher saturable and non-saturable CL, and that the ADA-positive participants had approximately 15% higher non-saturable CL.

Figure 13: Simulated Rademikibart Concentration vs Time (CBP-201-WW001)



Abbreviations: Q2W, every 2 weeks; Q4W, every 4 weeks.
~~Data source: CBP-201-WW001 Clinical Study Report V1.0 In-text Figure 9~~

Table 15: Plasma Rademikibart Pharmacokinetic Parameters (CBP-201-WW001)

	First Dose			Last Dose		
	C_{max} (ng/mL)	C_{trough} (ng/mL)	C_{avg} (ng/mL)	C_{max} (ng/mL)	C_{trough} (ng/mL)	C_{avg} (ng/mL)
Summary of Exposure – 1800 mg (600 mg Loading Dose, then 150 mg Q2W)						
Mean	31100~~084~~	246003~~4~~	249001~~1~~	1370066~~8~~	8570~~4~~	11700~~9~~
Standard Deviation	100002	9940~~36~~	8220	7790~~2~~	6630~~28~~	7380~~76~~
Minimum	114004~~8~~	79302~~7~~	90908~~6~~	3350~~1~~	120	1740~~39~~
Maximum	5420019~~9~~	4790088~~3~~	441002	3740039~~4~~	254007	3350045~~4~~
Summary of Exposure – 3000 mg (600 mg Loading Dose, then 300 mg Q2W)						
Mean	3100009~~96~~	24402~~0~~	2440039~~0~~	3520019~~2~~	2630027~~9~~	3180022
Standard Deviation	9670~~1~~	1040039~~5~~	786057	1590047	14600553	1540035
Minimum	114001~~7~~	2990~~87~~	8890~~1~~	6920	2040	5100098

Table 15: Plasma Rademikibart Pharmacokinetic Parameters (CBP-201-WW001)

	First Dose			Last Dose		
	C_{max} (ng/mL)	C_{trough} (ng/mL)	C_{avg} (ng/mL)	C_{max} (ng/mL)	C_{trough} (ng/mL)	C_{avg} (ng/mL)
Maximum	532003	491008 4	426005 80	814003 53	703004 8	773002 67
Summary of Exposure – 1800 mg (600 mg Loading Dose, then 300 mg Q4W)						
Mean	322001 67	84807 7	210003 1	181000 50	34109 8	115004 93
Standard Deviation	10400 4	5770 1	7730 2	7240 3	4580	5990 86
Minimum	114003 80	99	5580	30100 8	54	911
Maximum	565004 86	217002 9	387001 5	330008	276005 74	303002 0

Abbreviations: C_{avg}, average concentration; C_{max}, maximum observed concentration; C_{trough}, trough concentration; Q2W, once every 2 weeks; Q4W, once every 4 weeks.
Data source: CBP-201-WW001 Clinical Study Report V1.0 In-text Tables 44, 45 and 46.

Immunogenicity Results

The overall incidence of treatment-emergent ADA and NnAb was low (9.9% [16/162] for ADA and 7.4% [12/162] for NnAb), with low ADA titers, and not persistent in duration (either transient or indeterminate), suggesting minimal safety risk of anaphylaxis and/or loss of efficacy with continued exposure. ADA incidences were higher in the lower dose/dose frequency groups (14.3% [8/56] in the 150 mg Q2W and 12.5% [7/56] in the 300 mg Q4W]) relative to the 2.0% (1/50) incidence in the 300 mg Q2W group.

Pharmacodynamic Results

TARC was the most predictive PD marker of response to the treatment and also as a biomarker for improvement in clinical scoring with active treatment. However, all PD biomarkers evaluated in this trial (TARC, serum IL-4, IL-13, IgE, and peripheral eosinophil count) failed to yield a consistent exposure-response relationship. For each of these biomarkers, the presence of outlier values at Baseline and later time-points may have limited the ability to detect an exposure-response relationship.

Trial CBP-201-CN002: –52-Week Efficacy and Safety Trial in Adults With AD in China

CBP-201-CN002 was a randomized, double-blind, 2-stage placebo-controlled dose-optimization trial evaluating the efficacy and safety of rademikibart in 330 Chinese participants with moderate-to-severe AD. In Stage 1, participants were randomized 2:1 to rademikibart or placebo. Rademikibart was administered as a 600 mg SC loading dose LD followed by 300 mg SC Q2W maintenance dose (n = 219; Group A) or as placebo (n = 111; Group B). Assignment to Stage 2 was based on the following criteria:

- Participants who reached EASI-50 at Week 16 entered Stage 2 (Weeks 16 to 52) with 1:1 randomization to either Group C (rademikibart 300 mg Q2W) or Group D (rademikibart 300 mg Q4W).
- Participants who failed to maintain EASI-50 for 2 consecutive visits during Stage 2 in Groups C or D were transferred to Group E (rademikibart 300 mg Q2W).

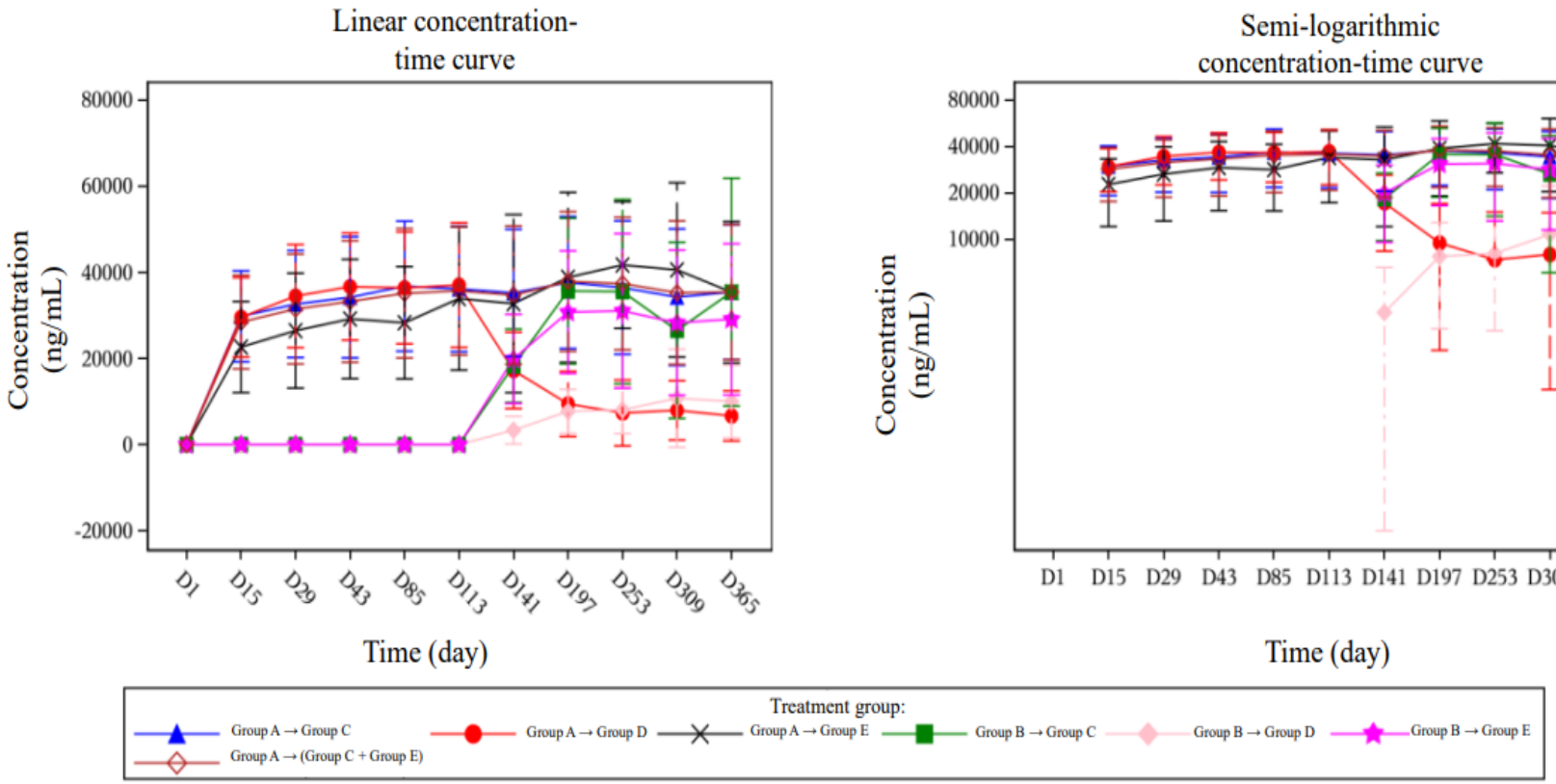
- Participants who did not achieve EASI-50 by Week 16 proceeded to Group E.

At Week 52, all participants moved to an 8-week follow-up period.

Pharmacokinetic Results

Predose PK samples were collected at select timepoints through Stage 1 and Stage 2. Mean rademikibart concentrations are presented in Figure 14.

Figure 14: Mean (±SD) Rademikibart Concentration vs Time by Treatment Groups, (Stage 1 + Stage 2 Combined; CBP-201-CN002)



Abbreviations: D, Day; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SD, standard deviation.
Treatment Groups: A = rademikibart 600 mg SC loading dose~~LD~~ + 300 mg SC Q2W maintenance dose; B = Placebo; C = rademikibart 300 mg Q2W; D = rademikibart 300 mg Q4W; E = 300 mg Q2W.
~~Data source: CBP-201-CN002 Clinical Study Report V1.0 In-text Figure 11-29.~~

Participants assigned to the 600 mg rademikibart loading dose ~~LD~~ followed by 300 mg SC Q2W maintenance dose in Group A reached close to steady-state C_{trough} concentrations by 2nd dose and were at steady state by the 4th dose. By Day 197, all participants who received 300 mg Q2W in Groups C, E, and C+E of Stage 2 had similar steady-state concentrations, regardless of their Stage 1 randomization (active or placebo). The mean steady-state concentrations in these groups were approximately 4 times higher than those in Group D (300 mg Q4W), which also reached steady state by Day 197.

Immunogenicity Results

The overall incidence of ADA/~~N~~nAb was low, and responses were generally transient. In participants receiving rademikibart, the ADA incidence during the 16-week Stage 1 was 0.6% (1/170).

Among the 241 participants who received rademikibart over the 52-week duration of Stage 1 + Stage 2, the overall ADA incidence was 5.8%, and the overall ~~N~~nAb incidence was 5.0%. ADA-positive participants generally exhibited substantially lower plasma rademikibart concentrations, even prior to ADA onset, compared to ADA-negative participants.

Pharmacodynamic Results

In Stage 1, TARC was significantly decreased in the rademikibart group compared with the placebo group. Across both stages, change from baseline ~~CFB~~ in TARC showed a downward trend with increasing rademikibart concentrations, suggesting a possible exposure-response relationship. Change from baseline ~~CFB~~ in serum IL-4 also showed a similar, though less pronounced, downward trend with the increase of rademikibart concentrations. The percentage changes in IL-3, IgE and eosinophil count failed to yield a consistent exposure-response relationship.

Trial CBP-201-CN003: ~~—~~12-Week Safety and Efficacy Trial in ~~Chinese AD~~ Participants With AD

CBP-201-CN003 was a Phase 2, multicentered, single-arm, open-label trial to evaluate the safety and efficacy of 600 mg loading dose ~~LD~~ followed by 300 Q2W SC maintenance dose of rademikibart for 12 weeks in 360 Chinese participants with moderate-to-severe AD.

Pharmacokinetic Results

No PK samples were collected in this trial.

Immunogenicity Results

While 4/360 (1.11%) of participants had pre-existing ADA, none (0%) developed immunogenicity while on treatment (Weeks 2 – 12/end of treatment~~EOT~~). Onset of treatment-induced ADA occurred on the last follow-up visit (Week 20/end of trial~~EOS~~), with low overall incidence (4.4% ([16/360]) and predominantly low titers.

Pharmacodynamic Results

No PD samples were collected in this trial.

Trial SIM0718-302: 52-Week Efficacy and Safety Trial in Adolescents and Adults With AD

SIM0718-302 was a Phase 3, randomized, double-blind, parallel-group, placebo-controlled clinical trial evaluating the efficacy and safety of rademikibart in adults (18 to 75 years old) and adolescents (12 to <18 years old) with moderate-to-severe AD. The trial included a 16-week double-blind treatment period (Stage 1), a 36-week open-label maintenance treatment period (Stage 2), and an 8-week follow-up period. In Stage 1, participants were randomized in a 1:1 ratio to receive rademikibart or placebo by SC injection. A loading dose of rademikibart 600 mg or placebo (given as two 2 mL injections) was administered on Day 1 followed by rademikibart 300 mg or placebo (given as one 2 mL injection) Q2W until Week 16. In Stage 2, at the Week 16 Visit, participants randomized to placebo switched to a treatment regimen of rademikibart 300 mg Q2W after completing the safety and efficacy assessments, while participants originally receiving rademikibart 300 mg Q2W continued with the same treatment regimen until Week 50.

A total of 259 participants were dosed, of which 254 received rademikibart, including 55 adolescents. In Stage 1, 128 participants received rademikibart, including 27 adolescents, and 131 received placebo, including 28 adolescents. In Stage 2, 126 of the 131 participants from the Stage 1 placebo group switched to rademikibart.

Pharmacokinetic Results

Mean predose/trough rademikibart concentrations in Stage 1 and Stage 2 participants receiving rademikibart are presented in Table 16.

Steady-state rademikibart concentrations were achieved by Week 8 of 300 mg Q2W dosing, with trough concentrations at 2 weeks following the 600 mg loading dose only slightly below those at steady-state. Overall, the trough concentrations were similar between adults and adolescents, with mean differences less than 20%.

Additionally, 13 adolescent participants underwent intensive sampling after the 600 mg loading dose in Stage 1 and their PK parameters are summarized in Table 17.

Table 16: Mean (±SD) Plasma Rademikibart Concentrations (µg/mL) in Adolescent and Adult Participants With AD (SIM0718-302, Stages 1 and 2)

Timepoint	Adults	Adolescents	Adults + Adolescents
Stage 1			
	N=101	N=27	N=128
Day 1 predose	BLQ (n=99)	BLQ (n=27)	BLQ (n=126)
Week 2 predose	31.9 ± 11.6 (n=98)	35.0 ± 15.8 (n=27)	32.5 ± 12.6 (n=125)
Week 8 predose	35.6 ± 15.0 (n=97)	39.1 ± 20.0 (n=27)	36.4 ± 16.2 (n=124)
Week 16 predose	36.6 ± 16.4 (n=95)	43.8 ± 19.5 (n=27)	38.2 ± 17.3 (n=122)
Stage 2			
	N=204	N=55	N=259
Week 36 predose	36.5 ± 16.4 (n=190)	40.7 ± 17.3 (n=52)	37.4 ± 16.6 (n=242)
Week 52	34.1 ± 16.2 (n=161)	36.8 ± 18.0 (n=48)	34.7 ± 16.6 (n=209)

Abbreviations: AD, atopic dermatitis; BLQ, below the limit of quantification; SD, standard deviation.
Note: At Day 1 predose, rademikibart concentrations were BLQ for all participants.

Table 17: Summary of Rademikibart PK Parameters in Adolescent Participants Following 600 mg Loading Dose (SIM0718-302, Stage 1)

Parameter	Adolescents (N=13)
C_{max} (μg/mL)	54.6 ± 21.4
T_{max} (h)	135.47 (70.75 - 166.48)
AUC_{last} (h·μg/mL)	14000 ± 5860

Abbreviations: AUClast, area under the concentration-time curve from Time 0 to the last quantifiable concentration; C_{max}, maximum observed concentration; h, hour; PK, pharmacokinetic; SD, standard deviation; T_{max}, time to maximum observed concentration.
Note: Parameter values are presented as arithmetic mean (SD), except for T_{max} which is presented as median (minimum – maximum).

Immunogenicity Results

The incidence of treatment-emergent ADA (ie, baseline ADA-negative or baseline ADA-positive with ≥4-fold increase in titer postdose) was low: 3.9% (5/128) in the participants administered rademikibart in both Stages 1 and 2, and 6.1% (8/131) in participants administered placebo in Stage 1 and rademikibart in Stage 2. Both groups had generally low titers (<1000). An additional 6 participants were ADA-baseline positive but not boosted and thus categorized as ADA-negative. The proportion of participants who were nAb positive at least once during the trial was 3.1% (4/128) in the rademikibart continuation group and 1.5% (2/131) in the placebo crossover group, with 1 participant in the rademikibart continuation group nAb-positive at baseline only.

Pharmacodynamic Results

During Stage 1, serum IL-4 levels increased in a subset of participants (approximately 59%) administered rademikibart, peaking at 430% ±935% from baseline. Levels gradually decreased at the subsequent timepoints. A transient increase in IL-4 was also observed at Weeks 36 and 52 of Stage 2 in participants in the placebo crossover group. In both groups, IL-4 levels returned to baseline at follow-up Week 60.

Serum IgE, TARC, and LDH levels all showed more substantial decline relative to baseline in rademikibart participants relative to placebo participants during Stage 1, with similar magnitude of decline in both groups by the end of Stage 2.

There were no apparent or consistent trends in IL-13 or eosinophil counts over time in the 2 groups of participants.

5.2. Clinical Efficacy

~~In clinical trials, r~~Rademikibart has shown efficacy across various clinical trials involving participants with moderate-to-severe asthma, COPD, AD, and CRSwNP.

In ~~the~~ an asthma Phase 2 trial (CBP-201-WW002), participants treated with rademikibart 150 mg and 300 mg SC Q2W showed significant improvements in lung function, as measured by

pre-bronchodilator FEV_1, compared to placebo. These improvements were observed as early as Week 1 and sustained through Week 24. Additionally, though not powered to detect a change, there was a trend towards a positive effect on asthma exacerbations, with a reduction in the risk of having ≥1 asthma exacerbation during the 24-week treatment period.

Pre- and post-bronchodilator FEV_1 and FVC were also evaluated as PD assessments in an ongoing Phase 1 trial in participants with stable asthma or COPD administered a single IV dose of rademikibart 300 mg (Part B of Trial CBP-201-105). Preliminary results demonstrated clinically meaningful improvements in lung function; see Section 5.1.4.2 for a summary of the results.

For AD, multiple trials demonstrated that rademikibart significantly improved EASI, IGA, ~~and~~ Peak Pruritus Numerical Rating Scale (PP-NRS) scores, and other measures of efficacy. Higher doses (150 mg and 300 mg SC Q2W) showed greater improvements compared to lower doses and placebo. Phase 2 and Phase 3 trials confirmed the efficacy of rademikibart, with significant improvements in EASI-75, EASI-90, and IGA response rates at Week 16. The long-term (Week 52) efficacy results in ~~one of the~~ 2 completed ~~Phase 2~~ trials (CBP-201-CN002 [Phase 2] and SIM0718-302 [Phase 3]) showed that the disease status of participants treated with rademikibart 300 mg Q2W and Q4W could be sustainably controlled and improved as treatment continued.

In the nasal polyps trial (CBP-201-WW003), although the trial was terminated early, the available data indicated a numeric reduction in endoscopic NPS and average daily NCS for participants treated with rademikibart.

Overall, rademikibart demonstrated efficacy in improving clinical outcomes for participants with moderate-to-severe asthma, COPD, AD, and chronic rhinosinusitis with nasal polyp.

5.2.1. Respiratory Diseases

5.2.1.1. Asthma Trials

Trial CBP-201-WW002: ~~-~~ 24-Week Efficacy and Safety in Adults With Asthma

Participants with moderate-to-severe persistent asthma were randomized (1:1:1) to receive rademikibart 300 mg or 150 mg rademikibart SC Q2W or placebo administered SC for 24 weeks and followed with an 8-week post-treatment follow-up. Participants received a 600 mg loading dose ~~LD~~ of rademikibart or placebo followed by the start of their randomized treatment 2 weeks later.

The primary objective of the trial was to assess the efficacy of rademikibart versus placebo in participants with moderate-to-severe persistent asthma with type ~~T~~2 inflammation as measured by lung function improvements. Key secondary objectives were to evaluate the effect of rademikibart on the incidence of asthma exacerbations and time to first exacerbation and to evaluate the safety and tolerability of rademikibart.

The trial included 322 participants (106 participants in the rademikibart 150 mg group, 108 participants in the rademikibart 300 mg group, and 108 participants in the placebo group) aged 18 to 75 years with persistent moderate-to-severe asthma not adequately controlled with a medium-to-high-dose ICS/LABA therapy. In the original protocol, participants were also

required to have a blood eosinophil count of ≥150 cells/μL at Screening, which was amended in protocol version 4 ~~participant~~ to require a blood eosinophil count ≥300 cells/μL at Screening. Participants were also required to have experienced at least 1 asthma exacerbation in the past 12 months. Of the 322 participants, 87.9% completed trial intervention and completed the trial.

The demographic and baseline disease characteristics were well balanced across the 3 treatment groups. The mean (SD) pre-bronchodilator FEV_1 at Baseline was 1.9083 (0.6468) L in the rademikibart 150 mg group, 1.9019 (0.5895) L in the rademikibart 300 mg group, and 1.8363 (0.5778) L in the placebo group. A total of 168 participants (52.2%) had a central laboratory blood eosinophil ≥300 cells/μL at Screening. The mean (SD) FeNO at Baseline was 35.8 (35.12) ppb in the rademikibart 150 mg group, 33.8 (32.65) ppb in the rademikibart 300 mg group, and 31.6 (31.47) ppb in the placebo group. The mean (SD) ACQ at Baseline was 2.71 (0.723) in the rademikibart 150 mg group, 2.68 (0.705) in the rademikibart 300 mg group, and 2.72 (0.642) in the placebo group. Most participants had only 1 asthma exacerbation over the previous 12 months with 20 participants experiencing ≥1 asthma exacerbation in the previous 12 months.

Treatment with rademikibart 150 mg and rademikibart 300 mg demonstrated a clinically and statistically significant LS mean improvement in pre-bronchodilator (trough) FEV_1 at Week 12 (0.235 and 0.284 L, respectively) that was a statistically significant improvement over placebo at Week 12 (0.095 L) (Table 18). Improvements in lung function were observed very soon after the start of treatment. For both rademikibart 150 mg and rademikibart 300 mg, a significant improvement in FEV_1 was observed as early as Week 1 ($p<0.001$ for both comparisons) and it was sustained through Week 24.

Table 18: Summary of Absolute Change From Baseline in Pre-bronchodilator (Trough) FEV_1 (L) at Week 12 (CBP-201-WW002; Full Analysis Set)

	Placebo N=108 n (%)	Rademikibart 150 mg N=106 n (%)	Rademikibart 300 mg N=108 n (%)
Baseline			
N	108	106	108
Mean (SD)	1.8363 (0.5778)	1.9083 (0.6468)	1.9019 (0.5895)
Median	1.7520	1.7715	1.7875
Min, Max	0.838, 3.812	0.904, 3.787	0.862, 3.876
Week 12			
N	96	89	86
Mean (SD)	1.9336 (0.6825)	2.1559 (0.7235)	2.1474 (0.6139)
Median	1.8285	1.9920	2.1090
Min, Max	0.647, 4.103	0.817, 4.242	0.935, 3.577
Change from Baseline to Week 12			
N	96	89	86
Mean (SD)	0.0929 (0.3325)	0.2381 (0.3052)	0.2871 (0.3553)

Median	0.0055	0.2250	0.2090
Min, Max	-0.615, 1.457	-0.424, 0.960	-0.570, 1.210
LS Means (95% CI)[a]	0.095 (0.027, 0.162)	0.235 (0.166, 0.304)	0.284 (0.214, 0.354)
Difference in LS Means (95% CI)[b]		0.140 (0.044, 0.236)	0.189 (0.092, 0.286)
p-value[a]		0.005	<0.001

Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in one second; LS, least squares; Max, maximum; Min, minimum; RTSM, Randomization and Trial Supply Management; SD, standard deviation.

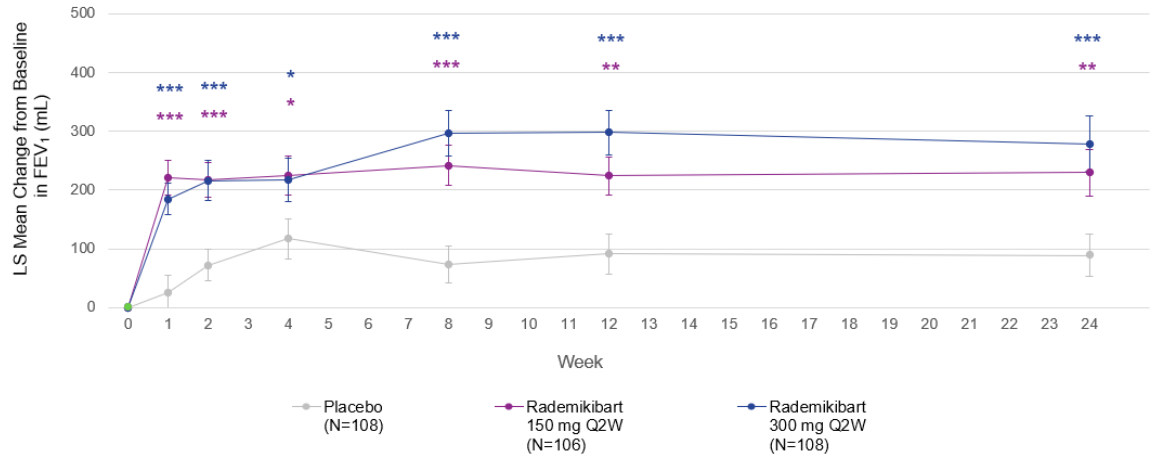
Note: Baseline is defined as the last non-missing value prior to the first dose of study drug.

[a] LS Means and p-values are obtained from ANCOVA model which is adjusted by treatment, blood eosinophil stratification factor from RTSM (≥300 cells/μL or <300 cells/μL), baseline weight, baseline height, baseline FeNO, and baseline measure of FEV1.

[b] Difference is calculated as rademikibart-placebo.

Similarly, a significant improvement in the percent change from baseline ~~CFB~~ in mean pre-bronchodilator (trough) FEV_1 was observed as early as Week 1 ($p<0.001$ for both comparisons) and it was sustained through Week 24 (Figure 15).

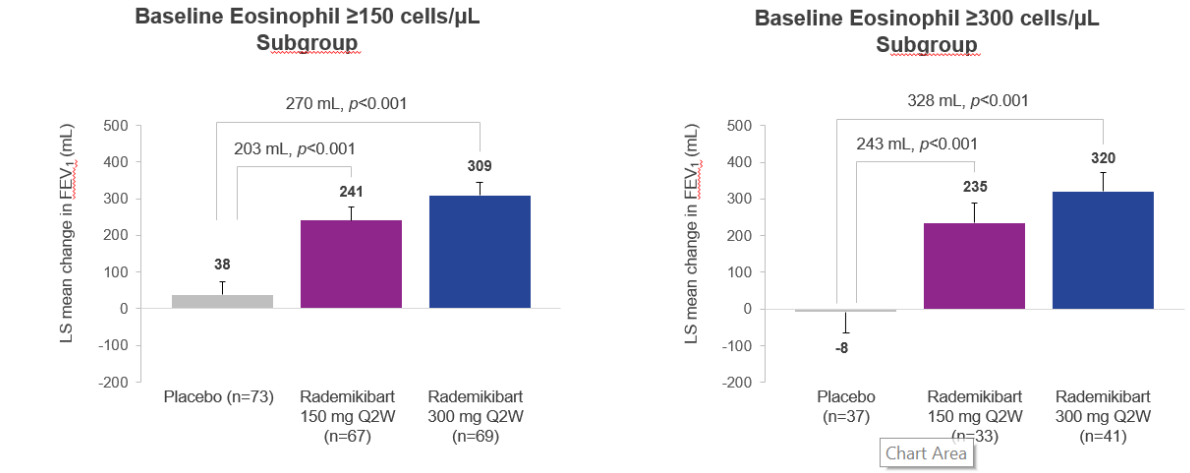
Figure 15: Absolute Change from Baseline in Mean Pre-bronchodilator (Trough) FEV_1 With Rademikibart Compared With Placebo (CBP-201-WW002)



‡Data not shown. ***p<0.001, **p<0.01, *p<0.05.
Full Analysis Set. LS Means and p-values are obtained from MMRM model adjusted by treatment, blood eosinophil stratification factor from RTSM (>= 300 cells/uL or < 300 cells/uL), baseline weight, baseline height, baseline FeNO, and baseline measure of FEV1. Std Error bars. FEV_1 - Forced expiratory volume in one second.

Subgroup analyses showed that substantial improvements were observed with rademikibart 150 mg and rademikibart 300 mg compared to placebo in subgroups of participants with baseline eosinophils ≥150 cells/μL and ≥300 cells/μL (Figure 16). Likewise, subgroup analyses showed that further improvement was observed with rademikibart 150 mg and rademikibart 300 mg compared to placebo in participants with FeNO ≥25 ppb ($p<0.001$ for both comparisons). A post hoc subgroup analysis of "COPD-like" participants (eg, participants with age of onset asthma >40 years and post-BD FEV_1/ FVC 0.7) showed similar treatment effects compared to the overall population.

Figure 16: Absolute Change from Baseline in Mean Pre-bronchodilator (Trough) FEV_1 by Eosinophil Subgroup With Rademikibart Compared With Placebo (CBP-201-WW002)



Error bars = standard error.

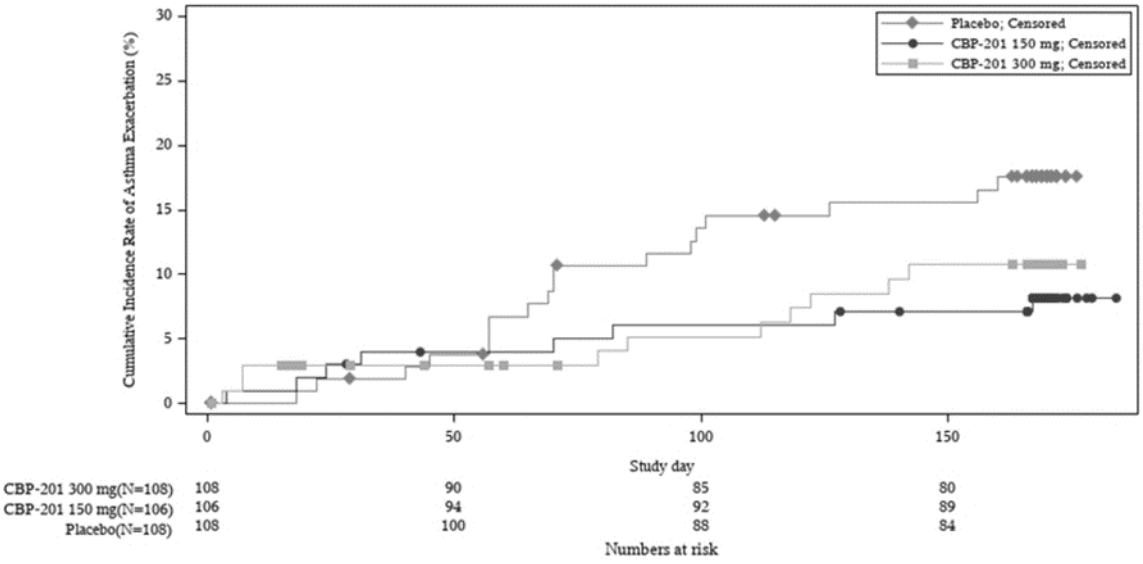
n, number of patients with data at Week 12. FEV_1 = Forced expiratory volume in one second. Q2W, every other week. Data were analyzed with ANCOVA

In an exploratory post hoc analysis of this trial, the absolute in pre-BD FEV_1, derived from self-administered at-home spirometry on Days 1 through 7, was analyzed in participants with baseline eosinophil counts ≥300 cells/μL. In this subpopulation, 77% of the Week 1 improvement in pre-BD FEV_1 was achieved within 24 hours post-dose (FEV_1 change from baseline~~CFB~~: 93 mL improvement vs -101 mL for placebo), with 84% of the total improvement realized by Day 2.

Asthma exacerbation was considered an exploratory endpoint, and the trial was not powered to detect differences in incidence of exacerbation. The majority of participants had no asthma exacerbation during the 24-week treatment period (Figure 17). Despite this power limitation, there were trends to support a positive effect of rademikibart treatment on asthma exacerbation. Compared with placebo, the risk of having ≥1 asthma exacerbation during the 24-week treatment period decreased by 58% in the rademikibart 150 mg group and by 42% in the rademikibart 300 mg group. A numerical reduction in the total number of asthma exacerbations was observed in the rademikibart 150 mg and rademikibart 300 mg groups compared with placebo as evidenced by more than half of the asthma exacerbations reported during the 24-week treatment period occurring in the placebo group (26 for the placebo group vs 11 and 13, for rademikibart 150 mg and 300 mg, respectively).

In participants reporting asthma exacerbation during the 24-week treatment period, there was a trend towards prolonging the time to first asthma exacerbation in the rademikibart 300 mg group. The mean time to first asthma exacerbation was 65.4 days in the rademikibart 150 mg group, 81.3 days in the rademikibart 300 mg group, and 77.7 days in the placebo group.

Figure 17: Time to Asthma Exacerbation With Rademikibart Compared With Placebo (CBP-2012-WW002)



Both rademikibart 150 mg and rademikibart 300 mg resulted in a numerical improvement in the weekly mean asthma symptom score, the number of nights (per week) with awakening due to asthma, the weekly mean number of nighttime awakenings due to asthma, and the weekly mean score of daily activities affected by asthma during the 24-week treatment period.

For both rademikibart 150 mg and rademikibart 300 mg, a numeric improvement in asthma control was also observed. At Week 24, the mean ACQ-6 score (Q1-5 + 7) decreased by 1.17 in the rademikibart 150 mg group and by 1.09 in the rademikibart 300 mg compared to 0.76 in the placebo group. The numeric improvement was evident as early as Week 1. Using the shortened ACQ-5 score that focuses only on participant-reported symptoms, well controlled asthma at Week 24 was reported in a numerically higher percentage of participants in the rademikibart 150 mg (28.7%) and rademikibart 300 mg (20.2%) groups compared with the placebo group (12.1%).

Except for a significant improvement compared to placebo in the absolute change from baseline ~~CFB~~ in weekly mean evening peak expiratory flow (PEF) at Week 1 observed for both rademikibart 150 mg and rademikibart 300 mg, positive trends were observed in morning PEF and evening PEF.

Overall, in this Phase 2 trial, participants treated with rademikibart demonstrated significant improvements in lung function by Week 1 and was sustained through Week 24, as measured by in-clinic spirometry. Additionally, the post hoc analysis demonstrates that rademikibart delivers rapid and significant lung function improvement, with notable gains within 24 hours of a single 600 mg loading dose~~LD~~. These findings highlight rademikibart's potential as a fast-acting, effective therapy for type ~~T~~2 inflammation-driven airway disease and suggest its possible utility in early treatment following acute exacerbations of asthma or COPD.

5.2.2. Atopic Dermatitis Trials

Four Five trials have been completed in adult participants with moderate-to-severe AD including aone Phase 1b trial, and 3three Phase 2 clinical trials, and one Phase 3 trial. In all4 completed trials, rademikibart has demonstrated robust and consistent efficacy, across a variety of clinical outcomes, reflecting clinically meaningful and statistically significant improvement in AD signs, symptoms, and quality of life.

5.2.2.1. Trial CBP-201-AU002: –Multiple Ascending Dose Trial in Adults With AD Participants

CBP-201-AU002 was a randomized, double-blind, placebo-controlled, MAD Phase 1b trial. This trial was conducted at 13 trial sites in Australia and New Zealand.

Twenty-four (24) participants were randomized to receive rademikibart (8 participants each for 75 mg, 150 mg, and 300 mg SC once a weekQW for 4 consecutive weeks) and 8 to receive placebo. Thirty-one (31; 96.9%) of 32 participants completed the trial, with 1 participant in the 300 mg rademikibart group prematurely withdrawn from the trial prior to dosing.

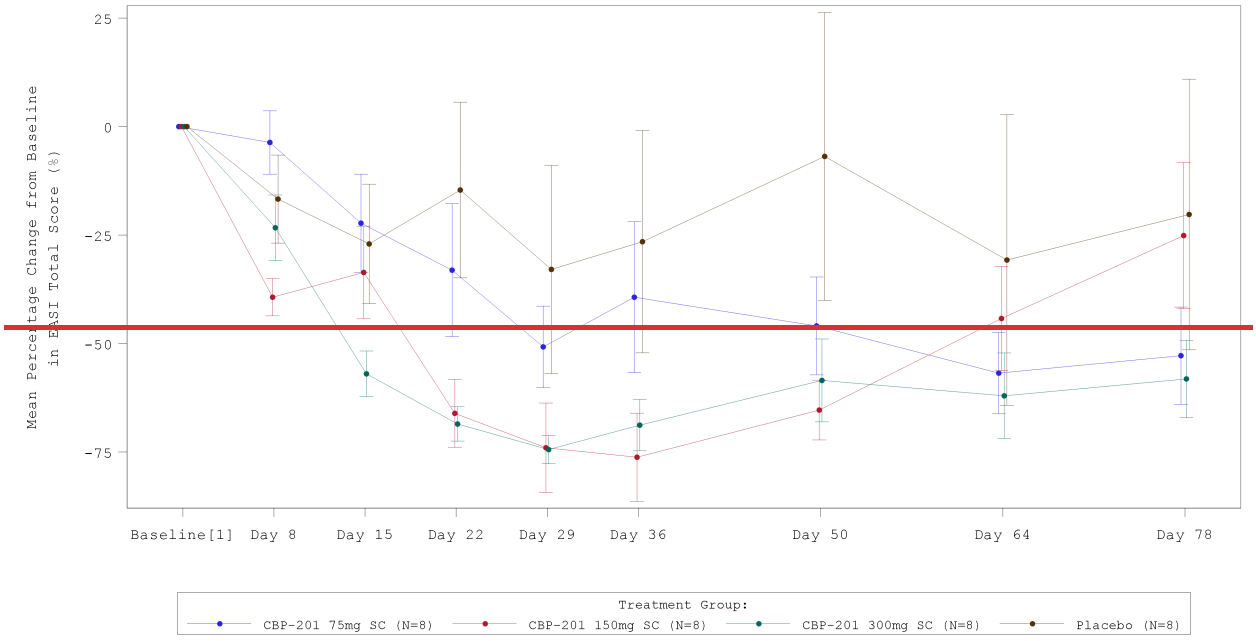
The mean age, height, and body weight of participants were similar between pooled rademikibart and placebo groups. The median age of all participants was 35.0 years. Overall, there were equal numbers of males (51.6%) and females (48.4%) in the trial, although numbers of males and females within cohorts varied. All participants in the placebo group were White, and most participants in the rademikibart cohorts were White. The mean baseline EASI total score was 24.493 (SD=11.2842) for participants in the pooled rademikibart group and 33.363 (SD=15.2713) in the placebo group. The IGA scores were similar in the pooled rademikibart group and placebo group.

This Phase 1b trial preliminarily showed the efficacy of rademikibart in the treatment of participants with moderate-to-severe AD. Overall, AD participants who received 150 mg and 300 mg of rademikibart achieved improvements in EASI score, IGA score, body surface area (BSA) affected by AD, and severity and frequency of pruritus (determined by P-NRS), and quality of life assessed by DLQI.

Rademikibart at 150 mg and 300 mg rademikibart improved participant EASI total scores, with the greatest improvement occurring between Day 22 and Day 36. As shown in Figure 18, based on the mean percentage change in the EASI total score from Baseline, participants in the 150 mg rademikibart showed improvement (lower total EASI score) from Day 22 (-66.086%) to Day 50 (-65.33%) and participants in the 300 mg rademikibart group showed improvement from Day 15 (-56.977%) to Day 36 (-68.802%). In comparison, the mean percentage change of the placebo group was as follows: Day 15: -27.041%; Day 22: -14.617; Day 36: -26.528%; and Day 50: -6.875%. The mean percentage change of EASI total score from Baseline in the 75 mg rademikibart and placebo groups were comparable throughout the trial assessment period.

Overall, the improvement in EASI scores was greater in participants who received 150 mg and 300 mg rademikibart; in contrast, the improvement in EASI scores was much less in participants who received 75 mg rademikibart and placebo (Figure 18).

Figure 18: Mean Percentage Change from Baseline in EASI Total Score (ITT Set) in Multiple Ascending Dose Trial (CBP-201-AU002)



The plot shows the mean CFB values as well as the standard error of the mean. Baseline is defined as the last available valid, non-missing observation prior to first investigational product (IP): rademikibart administration on Day 1. Results that were reported after the start of rescue therapy are not included.
Participant 101-303 was randomized to the rademikibart 300 mg but withdrew from the trial prior to being treated. The participant is included in the ITT Set but was excluded from the figures.

IGA of AD results were consistent with the findings in EASI total score, showing improvement in the 150 mg and 300 mg rademikibart cohorts on Day 22 through to Day 36. Overall, improvement of IGA response scores was greatest for participants receiving 150 mg or 300 mg rademikibart compared to the participants receiving 75 mg rademikibart or placebo, where a much smaller percentage of participants showed improvement over the 78 days of the trial.

By Day 29, 50% of participants in the 150 mg and 57.1% of participants in the 300 mg rademikibart groups showed a >2-point IGA response improvement compared to no participants in the 75 mg rademikibart group and 25% of participants in the placebo group.

The change in BSA affected by AD was consistent with improvements in EASI total score and IGA, which were observed in the 150 mg and 300 mg rademikibart cohorts on Day 22 through to Day 64. In the 300 mg rademikibart cohort, the percentage improvement continued to be observed through to the end of trial EOS visit.

The results of P-NRS indicated improvement in both severity and frequency of pruritus across all rademikibart cohorts with continued improvement in the 150 mg and 300 mg cohorts. The data presented for P-NRS are consistent with data obtained for EASI total score, IGA score, and BSA affected by AD. The P-NRS improvement in severity and frequency of pruritus was first observed on Day 8, while improvements in EASI total score, IGA score, and percentage BSA affected by AD were first observed on Day 15.

~~The mean CFB in DLQI total scores in the 150 mg and 300 mg rademikibart groups were lower than placebo scores from Day 8 through to Day 50, with the lowest score being reported on Day 36 in the 150 mg rademikibart cohort. The absolute values of DLQI scores in the 150 mg and 300 mg rademikibart cohorts on Day 36 were 4.63 (SD=3.378) and 4.71 (SD=3.638), respectively, compared to 6.17 (SD=2.994) in the 75 mg rademikibart cohort and 13.33 (SD=8.335) in the placebo group.~~

~~See Table 19 for efficacy results related to this trial.~~

Table 19: Efficacy Results in CBP-201AU002 Trial

	Efficacy Evaluation Parameter	75 mg Rademikibart (N=8) n (%)	150 mg Rademikibart (N=8) n (%)	300 mg Rademikibart (N=8) n (%)	Placebo (N=8) n (%)
D8 After the 1st dose	≥75% improvement in EASI from baseline	0	0	0	0
	IGA score of 0 1	0	0	0	0
	≥3 point improvement in P NRS from baseline	1 (12.5%)	1 (12.5%)	1 (14.3%)	0
D15 After the 2nd dose	≥75% improvement in EASI from baseline	1 (12.5%)	0	1 (14.3%)	1 (12.5%)
	IGA score of 0 1	0	0	0	0
	≥3 point improvement in P NRS from baseline	1 (12.5%)	1 (12.5%)	3 (42.9%)	0
D22 After the 3rd dose	≥75% improvement in EASI from baseline	1 (12.5%)	4 (50.0%)	2 (28.6%)	1 (12.5%)
	IGA score of 0 1	1 (12.5%)	0	0	1 (12.5%)
	≥3 point improvement in P NRS from baseline	1 (12.5%)	3 (37.5%)	4 (57.1%)	1 (12.5%)
D29	≥75% improvement in EASI	1 (12.5%)	6 (75.0%)	3 (42.9%)	3 (37.5%)

Table 19: Efficacy Results in CBP-201AU002 Trial

	Efficacy Evaluation Parameter	75 mg Rademikibart (N=8) n (%)	150 mg Rademikibart (N=8) n (%)	300 mg Rademikibart (N=8) n (%)	Placebo (N=8) n (%)
1 week after discontinuation	from baseline				
	IGA score of 0 1	0	4 (50.0%)	3 (42.9%)	1 (12.5%)
	≥3 point improvement in P-NRS from baseline	1 (12.5%)	4 (50.0%)	4 (57.1%)	2 (25.0%)
D36 2 weeks after discontinuation	≥75% improvement in EASI from baseline	1 (12.5%)	6 (75.0%)	2 (28.6%)	2 (25.0%)
	IGA score of 0 1	0	4 (50.0%)	2 (28.6%)	1 (12.5%)
	≥3 point improvement in P-NRS from baseline	1 (12.5%)	4 (50.0%)	6 (85.7%)	4 (50.0%)
D50 4 weeks after discontinuation	≥75% improvement in EASI from baseline	1 (12.5%)	2 (25.0%)	2 (28.6%)	2 (25.0%)
	IGA score of 0 1	0	1 (12.5%)	2 (28.6%)	0
	≥3 point improvement in P-NRS from baseline	0	2 (25.0%)	5 (71.4%)	2 (25.0%)

Table 19: Efficacy Results in CBP-201AU002 Trial

	Efficacy Evaluation Parameter	75 mg Rademikibart (N=8) n (%)	150 mg Rademikibart (N=8) n (%)	300 mg Rademikibart (N=8) n (%)	Placebo (N=8) n (%)
D64 6 weeks after discontinuation	≥75% improvement in EASI from baseline	1 (12.5%)	2 (25.0%)	1 (14.3%)	2 (25.0%)
	IGA score of 0 1	0	1 (12.5%)	2 (28.6%)	1 (12.5%)
	≥3 point improvement in P NRS from baseline	1 (12.5%)	0	4 (57.1%)	2 (25.0%)

~~This Phase 1b trial preliminarily showed the efficacy of rademikibart in the treatment of participants with moderate-to-severe AD. Overall, AD participants who received 150 mg and 300 mg of rademikibart achieved improvements in EASI score, IGA score, BSA affected by AD, severity and frequency of pruritus (determined by P-NRS), and quality of life assessed by DLQI.~~

5.2.2.2. Trial CBP-201-WW001: –16-Week Efficacy and Safety Trial in Adults With AD

CBP-201-WW001 was a Phase 2, randomized, double-blind, placebo-controlled, efficacy and safety trial in adult participants (~~n~~N=226) with moderate-to-severe AD in Australia, New Zealand, US, and China. Participants were randomized (1:1:1:1) to receive rademikibart ~~(~~600 mg loading dose ~~LD~~ followed by 150 mg Q2W~~)~~, rademikibart ~~(~~600 mg loading dose ~~LD~~ followed by 300 mg Q4W~~)~~, rademikibart ~~(~~600 mg loading dose ~~LD~~ followed by 300 mg Q2W~~)~~, or matching placebo administered SC for 16 weeks and followed with an 8-week post-treatment follow-up.

~~The median age of the overall population was 38.5 years (range18-73 years), and the median body mass index (BMI) of the overall population was 28.40 kg/m^2 (range 14.8-66.4 kg/m^2). The trial enrolled 54% females and 46% males. Participants were primarily White (58%) or Asian (23%) and most were based in the US (76%).~~ Baseline disease characteristics (including duration of AD history, Baseline IGA score, total EASI score, and BSA involvement) were generally balanced between the all rademikibart group and the placebo group. The median duration of AD history was 13.0 years (range: 1 to 58 years) with a median total EASI rating of 21.15 (range 16.0-68.4) and median BSA involvement 35.10% (range 11.0%-94.0%). Approximately 70% of the participants had a Baseline IGA score of 3 (moderate) and the remaining participants had a Baseline IGA score of 4 (severe).

Administration of rademikibart resulted in rapid improvements in EASI, IGA, and PP-NRS at 16 weeks. All doses of rademikibart met the primary endpoint (LS mean percent change from baseline ~~CFB~~ in EASI at Week 16 versus placebo), with greater reductions observed in EASI in the rademikibart 300 mg Q2W and rademikibart 300 mg Q4W groups. Significant improvements with rademikibart were also seen for a range of secondary efficacy endpoints, including proportions of EASI and IGA 0/1 responders and change in PP-NRS. The efficacy responses of 300 mg rademikibart Q2W and Q4W were consistently greater than 150 mg Q2W when compared to placebo across most outcomes. The primary and secondary efficacy results are summarized in Table 19.

~~The primary efficacy endpoint of percentage reduction in EASI scores from Baseline to Week 16 were analyzed by last observation carried forward (LOCF) and are summarized in Table 20.~~

~~In the overall population at Week 16, a percent reduction (ie, improvement) in EASI scores was observed across the rademikibart treatment groups which was greater than that in the placebo group. Mean (SD) percent reductions from Baseline were 57.57% (33.061), 63.62% (36.412), and 62.96% (33.574) for the rademikibart 150 mg Q2W, 300 mg Q2W, and 300 mg Q4W groups, respectively, compared with a mean percent reduction of 39.67% (34.486) for the placebo group.~~

~~By ANCOVA model, the least squares mean (LSM) (standard error [SE]) difference vs placebo was 17.89 (6.537), 23.36 (6.794), and 23.83 (6.575) for the rademikibart 150 mg Q2W, 300 mg Q2W, and 300 mg Q4W groups, respectively. The difference was statistically significant for all~~

3 rademikibart treatment groups: p=0.0067 (150 mg Q2W), p=0.0007 (300 mg Q2W), and p=0.0004 (300 mg Q4W), indicating that rademikibart was significantly better than placebo in improving EASI. The main endpoint of the trial was reached (Table 20).

By rademikibart dose, the LSM (SE) percentage reduction in EASI was greater in the rademikibart 300 mg Q2W and Q4W groups (63.03% [4.961] and 63.50% [4.661], respectively) compared with the rademikibart 150 mg Q2W group (57.56% [4.610]).

A line graph with error bars depicting mean percent reduction in EASI from Baseline is presented by treatment over time in Figure 19.

Table 20: Percent Reduction in EASI Score from Baseline to Week 16 (CBP-201-WW001; Full Analysis Set, LOCF)

	Rademikibart (150 mg Q2W) (N=57)	Rademikibart (300 mg Q2W) (N=57)	Rademikibart (300 mg Q4W) (N=56)	Placebo (N=56)
Percent Reduction from Baseline to Week 16				
N	56	49	55	55
Mean (SD)	57.57 (33.061)	63.62 (36.412)	62.96 (33.574)	39.67 (34.486)
Median	64.70	79.30	70.00	41.00
Min, Max	-18.7, 100.0	-29.0, 100.0	-25.8, 100.0	-39.9, 100.0
Analysis of Covariance (ANCOVA)[a]				
LSM (SE)	57.56 (4.610)	63.03 (4.961)	63.50 (4.661)	39.67 (4.638)
LSM, 95% CI	48.470, 66.645	53.252, 72.811	54.310, 72.686	30.525, 48.811
LSM difference (SE), Rademikibart vs placebo	17.89 (6.537)	23.36 (6.794)	23.83 (6.575)	
95% CI	5.003, 30.777	9.971, 36.756	10.868, 36.792	
p-value	0.0067	0.0007	0.0004	

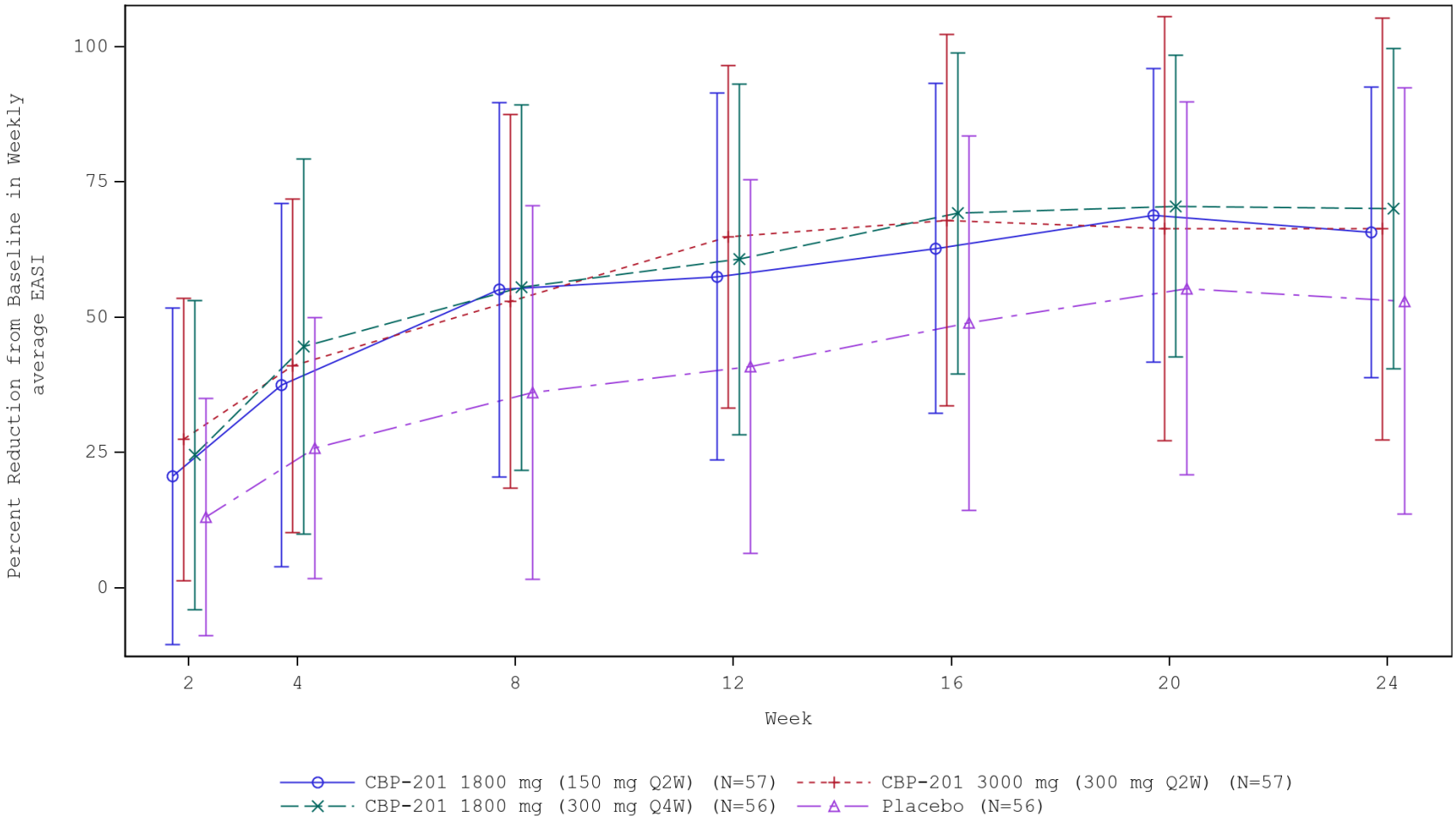
Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; EASI, Eczema Area and Severity Index; LOCF, last observation carried forward; LSM, least squares mean; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SD, standard deviation; SE, standard error.

[a] ANCOVA model includes treatment, baseline EASI score, and baseline Investigator Global Assessment (moderate, severe).

Note: The last observed postbaseline value was assumed for any missing value at Week 16, with assessments after the first use of rescue medication (either permitted or prohibited) set to missing.

Note: The analysis consisted of 3 hypotheses, which were tested in the following regimens in descending order: (1) after a 600 mg LD, 300 mg dose Q2W; (2) after a 600 mg LD, 150 mg dose Q2W; (3) after a 600 mg LD, 300 mg dose Q4W. This was to adjust for multiplicity using gatekeeping procedure at the 5% level of significance as long as the previous hypothesis was rejected.

Figure 19: Mean Percent Reduction (± SD) from Baseline for EASI (CBP-201-WW001; Full Analysis Set, OC)



Abbreviations: EASI, Eczema Area and Severity Index; OC, observed cases; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SD, standard deviation.

IGA response rates at 16 weeks for each of the 3 rademikibart groups were higher than that of placebo. There were 9 (15.8%) IGA responders in the 150 mg Q2W group, 16 (28.1%) in the 300 mg Q2W group, and 11 (19.6%) in the 300 mg Q4W group, compared with 5 (8.9%) responders in the placebo group. The differences in IGA response rates for rademikibart vs placebo were 6.9%, 19.1%, and 10.7% for the rademikibart 150 mg Q2W, 300 mg Q2W, and 300 mg Q4W groups, respectively. A statistically significant difference was detected for the rademikibart 300 mg Q2W group vs placebo (p=0.0089) but not for the rademikibart 150 mg Q2W or 300 mg Q4W groups (p=0.2684 and p=0.1052, respectively).

A statistically significant ≥90% reduction from Baseline in EASI score (EASI-90) was achieved at Week 16 for participants in the rademikibart 300 mg Q2W and rademikibart 300 mg Q4W groups compared with the placebo group. The difference was not statistically significant for the rademikibart 150 mg Q2W group (p=0.3950).

At Week 16, a reduction (ie, improvement) in weekly average PP-NRS scores was observed across the rademikibart treatment groups which was greater than that in the placebo group. Mean (SD) CFB was -2.61 (2.610), -3.70 (2.504), and -2.91 (2.883) for the 150 mg Q2W, 300 mg Q2W, and 300 mg Q4W rademikibart groups, respectively, compared with a mean change of -2.42 (2.459) for the placebo group.By ANCOVA model, the LSM (SE) difference vs placebo was -0.39 (0.466), -1.30 (0.474), and -0.91 (0.462) for the rademikibart 150 mg Q2W, 300 mg Q2W, and 300 mg Q4W groups, respectively. These reductions were statistically significantly greater than placebo for the rademikibart 300 mg Q2W group (p=0.0064), narrowly missed significance for the 300 mg Q4W group (p=0.0506) and was not significant for the rademikibart 150 mg Q2W group (p=0.4004).

Based on full analysis set (FAS), primary, secondary, and other efficacy endpoints were summarized, and additional exploratory subgroup analyses were conducted on enrolled Chinese participants. Efficacy results for the China subgroup were generally consistent with those of the overall population. The China subgroup also generally showed greater improvements for rademikibart compared with placebo, and no deviation from the overall trend of efficacy compared with the overall population, despite the small sample size.

Main trial results are shown in Table 21.

In this Phase 2 trial, all 3 dose groups successfully achieved the primary efficacy endpoint, and the 300 mg Q2W group achieved all the predefined secondary efficacy endpoints. Overall, in participants with moderate-to-severe AD, treatment with rademikibart by various treatment regimens demonstrated clinically meaningful and statistically significant superiority vs placebo on the primary and all secondary endpoints, as well as a clear consistency in response across all primary, secondary, and other efficacy endpoints.

Table 19: Primary and Secondary Efficacy Results in the CBP-201-WW001 Trial (Full Analysis Set)

	150 mg Q2W		300 mg Q2W		300 mg Q4W		Placebo	
	FAS N=57	China Subgroup	FAS N=57	China Subgroup	FAS N=56	China Subgroup	FAS N=56	China Subgroup
Primary Endpoint: Percent Reduction in EASI Score from Baseline to Week 16 (FAS, LOCF)								
Number of Participants	56	11	49	4	55	9	55	6
Mean (SD)	57.57 (33.061)	59.37 (41.060)	63.62 (36.412)	83.73 (16.285)	62.96 (33.574)	75.11 (30.249)	39.67 (34.486)	32.48 (35.378)
Median (minimum, maximum)	64.70 (-18.7, 100.0)	75.50 (-14.9, 99.4)	79.30 (-29.0, 100.0)	87.80 (60.6, 98.7)	70.00 (-25.8, 100.0)	86.40 (0.0, 100.0)	41.00 (-39.9, 100.0)	30.50 (-7.1, 70.9)
Analysis of Covariance (ANCOVA)								
LSM (SE)	57.56 (4.610)	59.31 (10.818)	63.03 (4.961)	81.88 (18.195)	63.50 (4.661)	75.05 (11.987)	39.67 (4.638)	33.92 (15.058)
LSM, 95% CI	48.470, 66.645	36.983, 81.638	53.252, 72.811	44.322, 119.429	54.310, 72.686	50.314, 99.792	30.525, 48.811	2.840, 64.996
LSM difference (SE), Rademikibart vs Placebo	17.89 (6.537)	25.39 (18.637)	23.36 (6.794)	47.96 (23.945)	23.83 (6.575)	41.14 (19.397)		
95% CI	5.003, 30.777	-13.072, 63.857	9.971, 36.756	-1.463, 97.379	10.868, 36.792	1.101, 81.169		
P-value	0.0067	0.1857	0.0007	0.0566	0.0004	0.0445		
Secondary Efficacy Endpoint: IGA Response Rate at Week 16								
n/N	9/57	2/11	16/57	2/6	11/56	2/9	5/56	0/6
%	15.8	18.2	28.1	33.3	19.6	22.2	8.9	0.0
95% CI	7.48, 27.87	2.28, 51.78	16.97, 41.54	4.33, 77.72	10.23, 32.43	2.81, 60.01	2.96, 19.62	0.00, 45.93
Difference in response rate Rademikibart vs Placebo	6.9	18.2	19.1	33.3	10.7	22.2		
95% CI	-5.20, 18.92	-4.61, 40.97	5.29, 32.99	-4.39, 71.05	-2.09, 23.52	-4.94, 49.38		

Table 19: Primary and Secondary Efficacy Results in the CBP-201-WW001 Trial (Full Analysis Set)

		150 mg Q2W		300 mg Q2W		300 mg Q4W		Placebo	
		~~FAS~~ N=57	~~China Subgroup~~	~~FAS~~ N=57	~~China Subgroup~~	~~FAS~~ N=56	~~China Subgroup~~	~~FAS~~ N=56	~~China Subgroup~~
P-value		0.2684	~~0.2662~~	0.0089	~~0.1213~~	0.1052	~~0.2148~~		
Secondary efficacy endpoint: EASI-50/EASI-75/EASI-90 response rate at Week 16									
EASI-50	n/N	29/57	~~8/11~~	31/57	~~3/6~~	34/56	~~6/9~~	18/56	~~2/6~~
	%,	50.9	~~72.7~~	54.4	~~50.0~~	60.7	~~66.7~~	32.1	~~33.3~~
	95% CI	37.29, 64.37	~~39.03, 93.98~~	40.66, 67.64	~~11.81, 88.19~~	46.75, 73.50	~~29.93, 92.51~~	20.29, 45.96	~~4.33, 77.72~~
	Difference in response rate	18.7	~~39.4~~	22.2	~~16.7~~	28.6	~~33.3~~		
	95% CI	0.90, 36.57	~~-6.60, 85.39~~	4.44, 40.04	~~-38.32, 71.65~~	10.87, 46.27	~~-15.36, 82.03~~		
	P-value	0.0434	~~0.1148~~	0.0171	~~0.5582~~	0.0024	~~0.2049~~		
EASI-75	n/N	23/57	~~6/11~~	27/57	~~3/6~~	22/56	~~5/9~~	7/56	~~0/6~~
	%	40.4	~~54.5~~	47.4	~~50.0~~	39.3	~~55.6~~	12.5	~~0.0~~
	95% CI	27.56, 54.18	~~23.38, 83.25~~	33.98, 61.03	~~11.81, 88.19~~	26.50, 53.25	~~21.20, 86.30~~	5.18, 24.07	~~0.00, 45.93~~
	Difference in response rate	27.9	~~54.5~~	34.9	~~50.0~~	26.8	~~55.6~~		
	95% CI	12.45, 43.25	~~25.12, 83.97~~	19.28, 50.46	~~9.99, 90.01~~	11.34, 42.23	~~23.09, 88.02~~		
	P-value	0.0008	~~0.0245~~	<0.0001	~~0.0455~~	0.0012	~~0.0253~~		
EASI-90	n/N	8/57	~~2/11~~	14/57	~~1/6~~	13/56	~~3/9~~	5/56	~~0/6~~
	%	14.0	~~18.2~~	24.6	~~16.7~~	23.2	~~33.3~~	8.9	~~0.0~~
	95% CI	6.26, 25.79	~~2.28, 51.78~~	14.13, 37.76	~~0.42, 64.12~~	12.98, 36.42	~~7.49, 70.07~~	2.96, 19.62	~~0.00, 45.93~~
	Difference in response rate	5.1	~~18.2~~	15.6	~~16.7~~	14.3	~~33.3~~		

Table 19: Primary and Secondary Efficacy Results in the CBP-201-WW001 Trial (Full Analysis Set)

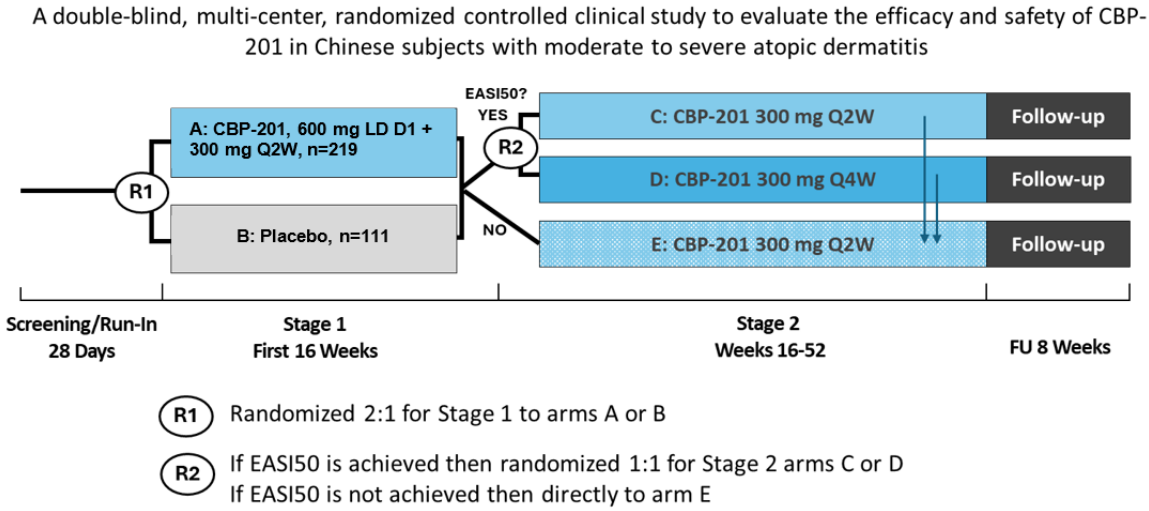
		150 mg Q2W		300 mg Q2W		300 mg Q4W		Placebo	
		~~FAS~~ N=57	~~China Subgroup~~	~~FAS~~ N=57	~~China Subgroup~~	~~FAS~~ N=56	~~China Subgroup~~	~~FAS~~ N=56	~~China Subgroup~~
	95% CI	-6.60, 16.82	~~-4.61, 40.97~~	2.19, 29.07	~~-13.15, 46.49~~	0.94, 27.63	~~2.54, 64.13~~		
	P-value	0.3950	~~0.2662~~	0.0263	~~0.2963~~	0.0396	~~0.1138~~		
Secondary Efficacy Endpoint: Change From Baseline in Weekly Average PP-NRS at Week 16 (~~FAS,~~ LOCF)									
Number of Participants		52	~~11~~	49	~~6~~	55	~~9~~	51	~~6~~
Mean (SD)		-2.61 (2.610)	~~-2.24 (3.209)~~	-3.70 (2.504)	~~-2.63 (2.511)~~	-2.91 (2.883)	~~-3.19 (2.512)~~	-2.42 (2.459)	~~-1.32 (1.622)~~
Median (minimum, maximum)		-2.70 (-7.5, 2.8)	~~-0.80 (-6.0, 2.5)~~	-4.10 (-8.0, 1.1)	~~-2.55 (-5.4, 0.6)~~	-2.70 (-10.0, 1.9)	~~-3.60 (-6.4, 0.6)~~	-1.70 (-8.0, 3.0)	~~-1.20 (-4.1, 0.4)~~
Analysis of Covariance (ANCOVA)									
LSM (SE)		-2.64 (0.327)	~~-2.12 (0.768)~~	-3.56 (0.339)	~~-2.75 (1.030)~~	-3.16 (0.320)	~~-3.61 (0.889)~~	-2.25 (0.331)	~~-0.78 (1.067)~~
LSM, 95% CI		-3.290, -1.999	~~-3.701, -0.543~~	-4.224, -2.888	~~-4.862, -0.628~~	-3.792, -2.531	~~-5.440, -1.783~~	-2.905, -1.599	~~-2.974, 1.414~~
LSM difference (SE), Rademikibart vs Placebo		-0.39 (0.466)	~~-1.34 (1.294)~~	-1.30 (0.474)	~~-1.96 (1.492)~~	-0.91 (0.462)	~~-2.83 (1.446)~~		
95% CI		-1.310, 0.526	~~-4.001, 1.318~~	-2.238, -0.370	~~-5.031, 1.102~~	-1.821, 0.002	~~-5.803, 0.140~~		
P-value		0.4005	~~0.3093~~	0.0064	~~0.1993~~	0.0506	~~0.0610~~		

Abbreviations: ANCOVA, analysis of covariance; CI, confidence interval; EASI, Eczema Area and Severity Index; ~~FAS, full analysis set;~~ LOCF, last observation carried forward; LSM, least squares mean; PP-NRS, Peak Pruritus Numerical Rating Scale; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SD, standard deviation; SE, standard error.

5.2.2.3. Trial CBP-201-CN002: –52-Week Efficacy and Safety Trial in Adolescents and Adults With AD ~~in China~~

CBP-201-CN002 was a Phase 2, 52-week, double-blind, multicenter, randomized, placebo-controlled, efficacy and safety trial in Chinese participants with moderate-to-severe AD. The trial was designed with 2 stages, Stage 1 (16-week treatment period), and Stage 2 (36-week treatment and 8-week follow-up periods). In Stage 1, participants were randomized (2:1) double-blind to receive rademikibart ~~(~~600 mg~~)~~ SC or matching placebo SC on Day 1 and rademikibart ~~(~~300 mg Q2W~~,~~ (Group A) or placebo (Group B) from Week 2– to Week 14. At the Week 16 visit, all participants ~~subjects~~ were assessed for efficacy, and the treatment assignment for Stage 2 maintenance treatment was based on whether a participant ~~subject~~ achieved a 50% or greater reduction from Baseline in EASI score (ie, EASI-50) prior to the administration of study treatment. Week 16 EASI-50 responders were rerandomized (1:1) double-blind to receive rademikibart 300 mg Q2W (Stage 2 Group C) or Q4W (Stage 2 Group D), with final doses administered at Weeks 50 and 48, respectively. Participants who did not achieve EASI-50 at Week 16 (non-responders) were assigned to receive rademikibart 300 mg Q2W (Stage 2 Group E), with the final dose administration at Week 50. At Week 52, all participants were followed up for 8 weeks (Figure 18). A total of 321 participants received rademikibart in the study across Stage 1 and Stage 2.

Figure 18: Study Schema for Trial CBP-201-CN002



In the original protocol, 255 participants were planned to be enrolled. Due to the sample size adjustments in protocol amendment 2.0, a total of 330 eligible participants were randomized in a 2:1 ratio to receive rademikibart (219 participants, Group A) or placebo (111 participants, Group B). The demographics and AD baseline characteristics were evenly distributed between the rademikibart group and the placebo group in Stage 1. In the rademikibart group and the placebo group, 99 (45.2%) and 50 (45.0%) participants had moderate AD (IGA=3), and 120 (54.8%) and 61 (55.0%) had severe AD (IGA=4) at baseline, respectively. The Baseline mean (SD) EASI was 29.27 (11.658) and 28.62 (12.092), the Baseline mean (SD) PP-NRS was 7.19 (1.680) and 7.17 (1.459), respectively.

A total of 311 participants completed Stage 1 and entered the Stage 2 Maintenance Phase. Among them, 225 participants achieved EASI-50 at Week 16 (responders) and 86 participants who did not achieve EASI-50 (non-responders) at Week 16:

- 113 responders were randomized to Group C, including 91 participants who received rademikibart in Stage 1 (Group A-C) and 22 participants who received placebo in Stage 1 (Group B-C), while 112 responders were randomized to Group D including 91 participants who received rademikibart in Stage 1 (Group A-D) and 21 participants who received placebo in Stage 1 (group B-D). In these 4 groups, 86 (94.5%), 21 (95.5%), 85 (93.4%), and 16 (76.2%) participants completed the Stage 2 treatment, respectively.
- 86 non-responders at Week 16 entered Group E in Stage 2, including 27 participants who received rademikibart in Stage 1 (Group A-E) and 59 participants who received placebo in Stage 1 (Group B-E). In these 2 groups, 21 (77.8%) and 56 (94.9%) participants completed the Stage 2 treatment, respectively.

~~The primary endpoint of this trial was the proportion of participants whose IGA score was 0-1 and decreased by ≥2 points from Baseline at Week 16. The proportion (95% CI) of responders in the rademikibart group and the placebo group was 29.0% (23.0%, 35.0%) and 5.9% (1.4%, 10.4%), respectively, and the difference (95% CI) between groups was 23.1% (15.7%, 30.4%) (p<0.0010).~~

~~The proportion (95% CI) of participants achieving EASI-75 and EASI-90 at Week 16 in the rademikibart group was 58.6% (51.9%, 65.3%) and 33.4% (27.0%, 39.8%), respectively. In the placebo group, the corresponding proportions were 22.6% (14.5%, 30.7%) and 6.4% (1.4%, 11.4%), respectively. The difference (95% CI) between groups was 36.0% (25.5%, 46.5%) for EASI-75 and 27.0% (18.9%, 35.0%) for EASI-90, respectively (both p<0.0010).~~

~~The absolute decrease and percentage decrease in the EASI score from Baseline at Week 16 in the rademikibart group were both significantly higher than those in the placebo group.~~

~~In the rademikibart group, the proportion (95% CI) of participants achieving an improvement (reduction) in weekly average PP-NRS ≥4 and ≥3 from Baseline at Week 16 was 36.3% (29.7%, 42.8%) and 50.0% (43.2%, 56.9%), respectively. In the placebo group, the corresponding proportions were 10.5% (4.5%, 16.5%) and 20.3% (12.7%, 28.0%), respectively. The difference (95% CI) between groups was 25.7% (16.9%, 34.6%) for the PP-NRS reduction ≥4 and 29.7% (19.5%, 40.0%) for the PP-NRS reduction ≥3, respectively (both p<0.0010). The decrease and percentage decrease in the weekly average PP-NRS from Baseline at W16 in the rademikibart group were significantly higher than those in the placebo group.~~

Rademikibart 300mg Q2W induced rapid improvements in eczematous lesions and pruritus during the initial 16 weeks, and these findings are compatible with those from CBP-201-WW001 trial of rademikibart. Detailed results of primary and key secondary efficacy endpoints are shown in Table 20. All the sensitivity analysis results of primary and key secondary efficacy endpoints were consistent with the primary analysis results.

Table 20: Primary and Secondary Efficacy Results in Stage 1 of CBP-201-CN002 Trial

		300 mg Q2W N=219	Placebo N=111
Primary efficacy endpoint of CBP-201-CN002: IGA response rate at Week 16			
n/N		64/219	7/111
%		29.0	5.9
95% CI		23.0, 35.0	1.4, 10.4
Difference in response rate (%) Rademikibart vs Placebo		23.1	
95% CI		15.7, 30.4	
P-value		<0.0010	
Key secondary efficacy endpoint: EASI-75 response rate at Week 16			
n/N		128/219	25/111
%		58.6	22.6
95% CI		51.9, 65.3	14.5, 30.7
Difference in response rate (%) Rademikibart vs Placebo		36.0	
95% CI		25.5, 46.5	
P-value		<0.0010	
Key secondary efficacy endpoint: EASI-90 response rate at Week 16			
EASI-90	n/N	73/219	7/111
	%	33.4	6.4
	95% CI	27.0, 39.8	1.4, 11.4
	Difference in response rate (%)	27.0	
	95% CI	18.9, 35.0	
	P-value	<0.0010	
Key secondary efficacy endpoint: proportion of participants achieving an improvement (reduction) in weekly average PP-NRS ≥4 and ≥3 from Baseline at Week 16			
PP-NRS reduction ≥3	n/N	109/218	23/111
	%,	50.0	20.3
	95% CI	43.2, 56.9	12.7, 28.0
	Difference in response rate (%)	29.7	
	95% CI	19.5, 40.0	
	P-value	<0.0010	

Table 20: Primary and Secondary Efficacy Results in Stage 1 of CBP-201-CN002 Trial

		300 mg Q2W N=219	Placebo N=111
PP-NRS reduction ≥4	n/N	78/216	12/110
	%,	36.3	10.5
	95% CI	29.7, 42.8	4.5, 16.5
	Difference in response rate (%)	25.7	
	95% CI	16.9, 34.6	
	P-value	<0.0010	
Key secondary efficacy endpoint: change/percentage change in the weekly average PP-NRS score from Baseline at Week 16			
Change	Mean at baseline	7.19	7.17
	Mean at visit	4.24	6.18
	Least square mean (SE)	-2.95 (0.170)	-0.99 (0.236)
	95% CI	-3.28, -2.62	-1.46, -0.53
	Difference, Rademikibart vs Placebo (SE)	-1.96 (0.290)	
	95% CI	-2.53, -1.39	
	P-value	0.0010	
Percentage change	Least square mean (SE)	-40.0 (2.448)	-13.50 (3.412)
	95% CI	-44.80, -35.20	-20.19, -6.82
	Difference, Rademikibart vs Placebo (SE)	-26.50 (4.183)	
	95% CI	-34.70, -18.30	
	P-value	<0.0010	

Abbreviations: CI, confidence interval; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; SE, standard error; Q2W, every 2 weeks.

In Stage 2, Week 16 responders who were re-randomized to either Group C (Rademikibart 300 mg Q2W) or Group D (Rademikibart 300 mg Q4W) showed a steady decrease in EASI scores from Baseline in both groups from Week 16 to Week 52, followed by a gradual rebound from Week 53 to Week 60 compared to Week 52. The proportion of participants who achieved EASI-90 at Week 52 in the Q2W-Q2W (A-C), Q2W-Q4W (A-D), placebo-Q2W (B-C), and placebo-Q4W (B-D) groups was 70.5%, 72.3%, 72.1%, and 61.9%, respectively. The proportion of participants whose IGA score was 0-1 and decreased by ≥2 points from Baseline at Week 52 in the rademikibart 300 mg Q2W-Q2W (A-C), Q2W-Q4W (A-D), placebo-Q2W (B-C), and placebo-Q4W (B-D) groups was 59.1%, 62.6%, 63.0%, and 49.1%, respectively.

The weekly average PP-NRS in the Q2W-Q2W (A-C), Q2W-Q4W (A-D), placebo-Q2W (B-C), and placebo-Q4W (B-D) groups decreased steadily compared with Baseline from Week 16 to Week 52.

The proportion of participants who maintained EASI-75 response from Baseline at Week 52 among those participants who had already achieved EASI-75 at Week 16 in the Q2W-Q2W (A-C), Q2W-Q4W (A-D), placebo-Q2W (B-C), and placebo-Q4W (B-D) groups was 90.1%, 92.3%, 98.4%, and 89.8%, respectively.

The proportion of participants who maintained an IGA score of 0-1 and decreased ≥2 points from Baseline at Week 52 among those participants who had already achieved an IGA score of 0-1 and decreased ≥2 points from Baseline at Week 16 participants in the Q2W-Q2W (A-C), Q2W-Q4W (A-D), placebo-Q2W (B-C), and placebo-Q4W (B-D) groups was 78.0%, 87.1%, 66.7%, and 90.5%, respectively.

In Stage 2, among Week 16 non-responders who entered Group E (Rademikibart 300 mg Q2W), the proportion of participants whose IGA score was 0-1 and decreased by ≥2 points from Baseline at Week 52 was 27.0% in the Q2W-Q2W (A-E) group and 44.9% in the placebo-Q2W (B-E) group. EASI scores steadily decreased from Baseline in both groups from Week 16 to Week 52. The proportion of participants who achieved EASI-75 at Week 52 in the Q2W-Q2W (A-E) and placebo-Q2W (B-E) groups was 51.4% and 80.7%, respectively. The proportion of participants achieving EASI-90 at Week 52 in the Q2W-Q2W (A-E) and placebo-Q2W (B-E) groups was 36.3% and 62.7%, respectively.

In general, the long-term efficacy results in Stage 2 of this trial showed that the disease status of participants with moderate-to-severe AD treated with rademikibart 300 mg Q2W and Q4W could be sustainably controlled and improved as treatment continued.

5.2.2.4. Trial CBP-201-CN003: 12-Week Safety and Efficacy Trial in Adults With Chinese AD Participants

CBP-201-CN003 was a Phase 2, safety and efficacy, single-arm, open-label trial in Chinese participants with AD. All enrolled participants received a 600 mg loading dose LD followed by 300 mg Q2W SC maintenance dose of rademikibart for 12 weeks. The primary outcome measures were safety related, including TEAEs and TEAEs related to study treatment.

A total of 360 participants were enrolled and received at least one 1 dose of rademikibart study treatment. Table 21 presents a summary of efficacy results. Based on FAS, under With the rademikibart 300 mg Q2W dosing regimen, the efficacy parameters (EASI, IGA, BSA, and PP-NRS, and DLQI) all improved somewhat from Baseline at the assessment time-points of each visit from Baseline to Week 20,; and most parameters achieved with the best responses were observed around at Week 12. All the sensitivity analysis results were basically consistent with the main analysis results.

Table 21: Proportion of Participants Achieving Efficacy Endpoints by Visit (CBP-201-CN003)

	Wk2	Wk4	Wk8	Wk12	Wk16	Wk20
EASI-50	22.6%	65.0%	84.2%	95.3%	93.9%	88.6%
EASI-75	5.0%	25.6%	57.7%	74.7%	76.5%	72.5%
EASI-90	1.4%	8.4%	26.1%	46.4%	49.6%	47.0%
EASI-100	0%	1.2%	5.3%	12.9%	15.8%	17.1%

IGA score 0-1 and decreased by ≥2 pts from Baseline	0.8%	9.2%,	31.7%,	50.7%,	52.9%,	47.1%,
IGA score decreased by ≥2 pts from Baseline	1.9%	17.2%	43.2%	62.5%	63.4%	56.2%
IGA score <2 pts	20.9%	53.6%	77.2%	86.8%	87.2%	81.2%
>3 decrease in weekly average PP-NRS score	16.4%	36.1%	57.2%	67.6%	67.1%	60.9%

Abbreviations: EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale in the past 24 hours; pts, points; Wk, Week.

~~Based on FAS, the proportions of participants achieving EASI-50, EASI-75, EASI-90, and EASI-100 at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 gradually increased from Baseline to Week 12; from the end of treatment at Week 12 to Week 20, the response rates following end of treatment did not show a significant trend towards decreasing, and remained at relatively high levels.~~

~~The proportions of participants achieving EASI-100 with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 0%, 1.2%, 5.3%, 12.9%, 15.8%, and 17.1%, respectively; The proportions of participants achieving EASI-90 with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 1.4%, 8.4%, 26.1%, 46.4%, 49.6%, and 47.0%, respectively; The proportions of participants achieving EASI-75 with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 5.0%, 25.6%, 57.7%, 74.7%, 76.5%, and 72.5%, respectively. All the sensitivity analysis results were basically consistent with the main analysis results.~~

~~Based on FAS, the proportions of participants whose IGA score was 0-1 and decreased by ≥2 points from Baseline, the proportion of participants whose IGA score was decreased by ≥2 points from Baseline, and the proportion of participants with IGA score ≤2 all presented a trend towards gradually increasing from Week 2 to Week 12 as treatment prolonged. The proportions (95% CI) of participants whose IGA score was 0-1 and decreased by ≥2 points from Baseline with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 0.8%, 9.2%, 31.7%, 50.7%, 52.9%, and 47.1%, respectively. The proportions of participants whose IGA score was decreased by ≥2 points from Baseline with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 1.9%, 17.2%, 43.2%, 62.5%, 63.4%, and 56.2%, respectively. The proportions (95% CI) of participants with IGA score ≤2 with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 20.9%, 53.6%, 77.2%, 86.8%, 87.2%, and 81.2%, respectively. All the sensitivity analysis results were basically consistent with the main analysis results.~~

~~Based on FAS, the proportion of participants with a ≥3-point decrease in weekly average PP-NRS score from Baseline and the proportion of participants with a ≥4 point decrease in weekly average PP-NRS score from Baseline presented trends towards gradually increasing from Week 1 to Week 12, and showed a trend towards decreasing slowly from the end of treatment at Week 12 to Week 20, yet remained at relatively high levels. The proportions of participants with a ≥3-point decrease in weekly average PP-NRS score from Baseline with rademikibart 300 mg Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 16.4%, 36.1%, 57.2%, 67.6%, 67.1%, and 60.9%, respectively. The proportions (95% CI) of participants with a ≥4-point decrease in weekly average PP-NRS score from Baseline with rademikibart 300 mg~~

~~Q2W at Week 2, Week 4, Week 8, Week 12, Week 16, and Week 20 were 6.4%, 22.6%, 44.9%, 59.0%, 59.3%, and 52.5%, respectively. All the sensitivity analysis results were basically consistent with the main analysis results.~~

~~Based on FAS, under the rademikibart 300 mg Q2W dosing regimen, the efficacy parameters (EASI, BSA, PP-NRS, and DLQI) all improved somewhat from Baseline at the assessment time points of each visit from Baseline to Week 20; with the best responses were observed around Week 12.~~

~~Based on FAS, the proportion of participants receiving concomitant medications for the treatment of the study disease (AD) was 45.8% (165/360) during Day 1 to Week 12; specifically, it was 42.8% (154/360), 33.3% (120/360), and 31.1% (112/360) during Day 1 to Week 4, Week 5 to Week 8, and Week 9 to Week 12, respectively. The proportion of participants receiving topical corticosteroids (TCSs) for the treatment of the study disease (AD) was 22.5% (81/360) during Day 1 to Week 12; specifically, it was 18.3% (66/360), 17.2% (62/360), and 16.9% (61/360) during Day 1 to Week 4, Week 5 to Week 8, and Week 9 to Week 12, respectively. The proportion of participants receiving concomitant medications for the treatment of the study disease (AD), and the proportion of participants receiving TCSs for the treatment of the study disease (AD) presented trends towards gradually decreasing during treatment. Overall, favorable efficacy of rademikibart was observed in all efficacy endpoints in participants with moderate-to-severe AD during treatment with rademikibart 300 mg Q2W for 12W, and the efficacy was sustained for 8 weeks following drug withdrawal.~~

~~In 4 completed trials, rademikibart has demonstrated robust and consistent efficacy, across a variety of clinical outcomes, reflecting clinically meaningful and statistically significant improvement in AD signs, symptoms and quality of life.~~

5.2.2.5. Trial SIM0718-302: 52-Week Efficacy and Safety Trial in Adolescents and Adults With AD

SIM0718-302 was a Phase 3, randomized, double-blind, parallel-group, placebo-controlled clinical trial evaluating the efficacy and safety of rademikibart in adults and adolescents with moderate-to-severe AD. The trial included a 16-week double-blind treatment period (Stage 1), a 36-week open-label maintenance treatment period (Stage 2), and an 8-week follow-up period. In Stage 1, participants were randomized in a 1:1 ratio to receive rademikibart or placebo by SC injection. A loading dose of rademikibart 600 mg or placebo (given as two 2 mL injections) was administered on Day 1 followed by rademikibart 300 mg or placebo (given as one 2 mL injection) Q2W until Week 16. In Stage 2, at the Week 16 Visit, participants in the placebo group switched to a treatment regimen of rademikibart 300 mg Q2W after completing the safety and efficacy assessments, while participants originally receiving rademikibart 300 mg Q2W continued with the same treatment regimen until Week 50.

Efficacy was evaluated using PRO assessments (PP-NRS, Dermatology Life Quality Index [DLQI], and Patient-Oriented Eczema Measure [POEM]) and Investigator efficacy assessments (IGA, EASI, and percent BSA of AD involvement).

A total of 259 participants were dosed, of which 254 received rademikibart. In Stage 1, 128 participants received rademikibart and 131 received placebo. In Stage 2, 126 of the 131 participants in the placebo group switched to rademikibart.

During the 16-week induction treatment period (Stage 1), rademikibart was superior to placebo in improving skin lesions, reducing lesion area, relieving pruritus, improving the quality of life of participants with AD, and improving the subjective symptoms of AD.

The trial met the predefined co-primary endpoints:

- The proportion of participants whose IGA score was 0-1 and decreased by ≥2 points from baseline at Week 16 was 47.7% in the rademikibart group vs 17.6% in the placebo group, with an inter-group difference of 30.0% (p<0.0001).
- The proportion of participants who achieved an EASI-75 at Week 16 was 74.2% in the rademikibart group vs 34.4% in the placebo group, with an inter-group difference of 39.9% (p<0.0001).

The results of sensitivity and supplementary analyses conducted for the primary estimands were consistent with those of the primary analysis, demonstrating its robustness. The trial also met all the predefined secondary and other efficacy endpoints as summarized in Table 22.

Table 22: Efficacy Measures at Week 16 (SIM0718-302)

Secondary Efficacy Measures at Week 16	Rademikibart 300 mg Q2W (N=128)	Placebo Q2W (N=131)
EASI-50 response rate, %	89.8%	47.3%
EASI-90 response rate, %	43.0%	14.5%
Mean % change from baseline in EASI	-81.53%	-48.67%,
Proportion of participants with reduction in IGA score by ≥2 points, %	62.5%	25.2%
Mean % change from baseline in the BSA of AD involvement	-76.08	-41.87
Response rate for PP-NRS improvement ≥3 points, %	54.7%	27.5%
Response rate for PP-NRS improvement ≥4 points, %	37.5%	19.1%
Mean % change from baseline in PP-NRS	-50.19%	-23.12%
Proportion of participants with PP-NRS score of 0 or between 1 and 3, %	47.7%	22.1%
Mean % change from baseline in DLQI/cDLQI	-60.30%	-25.73%,
Mean % change from baseline in POEM	-55.48%	-15.93%
Proportion of participants with POEM sleep score of >0 at baseline and 0 postdose, %	40.2%	13.5%

Abbreviations: AD, atopic dermatitis; BSA, body surface area; cDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; POEM, Patient-Oriented Eczema Measure; PP-NRS, Peak Pruritus Numerical Rating Scale; Q2W, every 2 weeks.

During the maintenance treatment period (Stage 2), all participants received rademikibart 300 mg Q2W. The efficacy endpoints of EASI-75 response rate and IGA 0/1 response rate in the rademikibart 300 mg Q2W/rademikibart 300 mg Q2W group further improved after Week 16 and were maintained until Week 52. In the placebo group, after switching to rademikibart at Week 16, the efficacy endpoints of EASI-75 response rate and IGA 0/1 response rate rapidly improved to a level comparable to that in the rademikibart group and were also maintained until Week 52. Efficacy results at Week 52 are summarized in Table 23.

Table 23: Efficacy Measures at Week 52 (SIM0718-302)

	Rademikibart 300 mg Q2W/ Rademikibart 300 mg Q2W (N=128)	Placebo/ Rademikibart 300 mg Q2W (N=131)
IGA 0/1 response rate, %	87.1%	75.6%
EASI-75 response rate, %	96.6%	95.9%
EASI-90 response rate, %	85.3%	78.9%
Mean % change from baseline in EASI	-95.1%	-93.0%
Response rate for pruritus NRS improvement ≥3 points, %	92.0%	88.3%
Response rate for pruritus NRS improvement ≥4 points, %	75.9%	76.6%
Mean % change from baseline in DLQI	-77.05%	-69.77%
Mean % change from baseline in POEM	-66.13%	-57.12%
Proportion of participants with a POEM sleep score of >0 at baseline and 0 postdose, %	72.3%	58.0%

Abbreviations: DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; NRS, Numerical Rating Scale; POEM, Patient-Oriented Eczema Measure; Q2W, every 2 weeks.

Overall vs adult vs adolescent subgroup analyses suggested that the results of the co-primary endpoints and each of the secondary efficacy endpoints in both the adult and adolescent subgroups were consistent with the efficacy trend in the overall participants.

5.2.3. Other Trials

5.2.3.1. Nasal Polyps

CBP-201-WW003 was a multicenter, randomized, double-blind, placebo-controlled, Phase 2 trial designed to evaluate the efficacy and safety of rademikibart in adult participants with CRSwNP whose disease remained inadequately controlled despite daily treatment with intranasal corticosteroid ~~(INCS)~~ therapy. The co-primary endpoints for the assessment of efficacy were the change from baseline ~~CFB~~ in endoscopic NPS at Week 24 and the change from baseline ~~CFB~~ in average daily NCS at Week 24. The trial design included follow-up safety visits at Weeks 28 and 32. The trial originally planned to enroll 147 participants but was prematurely discontinued due to recruitment issues resulting from the COVID-19 pandemic and operational issues related to the ongoing war between Ukraine and Russia.

A total of 40 participants of 147 planned were randomized in the trial in a 1:1:1 ratio and received treatment with rademikibart 300 mg Q2W (n=13) or rademikibart 300 mg Q4W (n=13) or placebo Q2W (n=14) via SC injection administered at every 2-week visit to the trial site for the 24-week treatment period or for the duration of participation prior to trial termination.

~~There were 28/40 (70.0%) males and 12/40 (30.0%) females in the trial. The majority of participants in the rademikibart 300 mg Q2W group were Asian (7/13 [53.8%]), and the majority of participants in the rademikibart 300 mg Q4W group (9/13 [69.2%]) and placebo group (10/14 [71.4%]) were White.~~

~~Mean age was similar between the 3 treatment groups. In the rademikibart 300 mg Q2W group, mean (SD) age was 53.0 years (14.80), in the rademikibart 300 mg Q4W group, mean (SD) age was 47.3 years (11.35), and in the placebo group, mean (SD) age was 47.9 years (17.96). Height and weight were similar between the 3 treatment groups.~~

At Week 24, the mean endoscopic NPS was 6.0 in the rademikibart 300 mg Q2W group (n=1) and 5.0 in the rademikibart 300 mg Q4W group (n=1). The reduction in the mean endoscopic NPS from Baseline to Week 24 could not be assessed as it was represented by only 2 participants in the rademikibart group. There were no participants in the placebo group with data on endoscopic NPS at Week 24.

For the change from baseline ~~CFB~~ in average daily NCS at Week 24, a numeric reduction was observed for the rademikibart groups. At Week 24, the mean (SD) average daily NCS was 1.6429 (0.7071) in the rademikibart 300 mg Q2W group (n=2) and 1.2000 (NA) in the rademikibart 300 mg Q4W group (n=1). The mean (SD) reduction in average daily NCS from Baseline to Week 24 was -0.8571 (1.4142) in the rademikibart 300 mg Q2W group and -1.8000 (NA) in the rademikibart 300 mg Q4W group. There were no participants in the placebo group with data on NCS at Week 24.

For the change from baseline ~~CFB~~ in average daily NCS at Week 16, a numeric mean reduction was observed for the rademikibart groups, but it was a small sample size and could not be compared with placebo. The mean (SD) reduction in average daily NCS from Baseline to Week 16 was -0.5357 (0.9785) in the rademikibart 300 mg Q2W group (n=4), -0.4643 (0.7857) in the rademikibart 300 mg Q4W group (n=4), and -1.0833 (1.2964) in the placebo group (n=2).

5.3. Clinical Safety

Rademikibart was generally safe and well tolerated and demonstrated ~~had~~ a favorable safety profile across 15 clinical trials in different indications (healthy participants, ~~and~~ participants with AD, and participants with respiratory diseases) (Table 4).~~across indications. A total of 48 SAEs were reported for rademikibart in the 9 trials, of which none were considered possibly related to rademikibart.~~

~~Rademikibart was generally safe and well-tolerated across completed trials involving healthy participants and participants with moderate-to-severe asthma and AD.~~ Rademikibart has been evaluated as ~~I~~in healthy participants in 5 single-dose clinical trials. Doses evaluated ranged from 75 to 600 mg SC or 300 mg IV. Rademikibart was well tolerated. M~~m~~ost TEAEs were mild-to-moderate in severity. No dose-related trends were seen and there was no meaningful difference in TEAEs by route of administration (SC vs IV).~~,~~ ~~with no treatment-related SAEs reported.~~

In 2 trials in participants with moderate-to-severe asthma, 70.1% of participants administered rademikibart ~~67.4%~~ reported at least 1 TEAE. Most TEAEs were mild-to-moderate in severity.~~, with n~~ No deaths~~,~~ and no treatment-related SAEs were reported~~, and most TEAEs being mild-to-moderate in severity~~. In the first trial, the most common AEs in rademikibart-treated participants (>5% and higher than placebo) were COVID-19 (12.1%), injection site erythema (6.5%), and nasopharyngitis (5.6%). In the second trial, no Preferred Term (PT) occurred in more than 1 participant.

In 1 trial in participants with moderate-to-severe COPD, no PT occurred in more than 1 participant.

A trial in participants with CRSwNP was terminated early, but the available data showed that 47.5% of participants reported TEAEs, mostly mild-to-moderate in severity.

In 5 trials in ~~For~~ participants with moderate-to-severe AD, the incidence of TEAEs was similar between rademikibart and placebo groups, ~~with~~ and most TEAEs ~~being~~ were mild-to-moderate. The most common TEAEs reported for rademikibart (>5% and higher than placebo) were upper respiratory tract infection (15.6%), COVID-19 (6.3%), and hyperuricaemia (5.3%).

~~A trial in participants with CRSwNP was terminated early, but the available data showed that 47.5% of participants reported TEAEs, mostly mild-to-moderate in severity.~~

Across the 11 completed trials and the completed parts of 1 ongoing trial, 2.5% of rademikibart-treated participants experienced SAEs, of which 3 were considered by Investigators to be related to rademikibart (vestibular neuronitis [participant with AD], ALT increased [healthy participant], and syncope [participants with AD]). One additional SAE in the ongoing blinded trials was classified as related to IP (periorbital haemorrhage in a participant with asthma).

Two deaths have been reported to date. One participant with AD experienced a fatal cardiac arrest. The second death occurred due to pneumonia in a participant with asthma in an ongoing blinded trial. Both deaths were considered not related to rademikibart/blinded IP.

~~Across completed clinical trials, AESIs for evaluation included conjunctivitis, keratitis, anaphylactic reaction, ISRs lasting more than 24 hours, AST/ALT increased to >5 × ULN, parasitic and opportunistic infections, and symptomatic drug overdose. While the majority of AESIs and injection site TEAEs were related to rademikibart, the overall incidence was not high. With the exception of 1 event of rademikibart-related AESI (keratitis in a participant with AD) of Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 reported in the 300 mg Q2W group, the remaining rademikibart-related AESIs and injection site TEAEs were all of CTCAE Grade 1 or Grade 2.~~

In the clinical development program, AESIs include conjunctivitis, keratitis, anaphylactic reaction, ISRs ≥Grade 3 lasting more than 24 hours, and parasitic and opportunistic infections. Across 8 clinical trials in participants with asthma, AD, COPD, and CRSwNP, the most common AESIs were conjunctivitis (3.8%) and keratitis (0.4%). AESIs of parasitic/opportunistic infection and anaphylactic reaction were each experienced by 1 participant (0.07%). All except 1 AESI were mild-to-moderate in severity.

ISRs are an identified risk with SC administration of rademikibart. In 7 trials of rademikibart SC in participants with asthma, AD, and CRSwNP, 7.2% of rademikibart-treated participants experienced TEAEs associated with ISRs. All events were mild-to-moderate in severity.

Overall, rademikibart demonstrated a favorable safety profile with manageable risks across different participant populations. An overview of key safety data ~~across~~ for each trial~~s~~ is provided in the following sections.

5.3.1. Healthy Participant Trials

Four completed trials and 2 completed parts of an ongoing trial have evaluated single doses of rademikibart ranging from 75 to 600 mg SC or 300 mg IV in healthy participants.

- Trial CBP-201AU001: A Phase 1, single ascending dose trial in healthy adult participants to evaluate a single dose of rademikibart 75, 150, 300, 600 mg via SC injection; rademikibart 300 mg via a 30-minute IV infusion; or placebo SC/IV. (N=40)
- Trial CBP-201CN001: A Phase 1, single ascending dose trial in healthy adult participants to evaluate a single SC dose of rademikibart 150, 300, 600 mg or placebo. (N=36)
- Trial CBP-201-CN004: A Phase 1, single dose relative bioavailability trial in healthy adult participants to evaluate a single 300 mg SC dose of rademikibart administered as either two 150 mg PFSs, one 300 mg PFS, or 2 vials of 150 mg. (N=324)
- Trial SIM0718-101: A Phase 1, single dose relative bioavailability trial in healthy adult participants to evaluate a single 300 mg SC dose of rademikibart administered as either two 150 mg PFSs or one 300 mg PFS. (N=176)
- Trial CBP-201-105 (Part A): A Phase 1, single IV dose trial in healthy adult participants to evaluate a single 300 mg IV dose of rademikibart or placebo administered at different infusion rates: 30, 15, or 2 minutes. (N=24)

Rademikibart was well tolerated. No dose-related trends were seen and there was no meaningful difference in TEAEs by route of administration (SC vs IV).

A summary of TEAEs by trial is presented in Table 24. There was a higher overall incidence of TEAEs with rademikibart compared with placebo (75.3% vs 54.5%, respectively). Most TEAEs were Grade 1 or 2 in severity. There was a low incidence of TEAEs ≥Grade 3 for rademikibart (1.4%).

A summary of TEAEs by PT that occurred in ≥5% of total rademikibart-dosed participants is presented in Table 25. Of these, TEAEs that occurred at a higher incidence than placebo included protein urine present (14.9% vs 0, respectively), blood triglycerides increased (10.9% vs 0), blood uric acid increased (10.7% vs 0), injection site erythema (9.5% vs 0), and white blood cells urine positive (5.2% vs 4.5%).

Two SAEs were reported, both in rademikibart-dosed participants.

- One SAE was reported in Trial CBP-201-CN004. A 22-year-old male participant who was involved in a road traffic accident 36 days after he was administered a single dose of rademikibart 300 mg SC. The event was considered by the Investigator to be "definitely unrelated" to rademikibart.
- One SAE was reported in Trial SIM0718-101. A 22-year-old male participant was hospitalized for a Grade 1 event of ALT increased 56 days after he was administered a single dose of rademikibart 300 mg SC. The Investigator considered the event to be related to rademikibart. The Sponsor considered the event to be unlikely related to rademikibart based on the weak temporal relationship due to the time to onset. This product class is not associated with hepatotoxicity, and rademikibart does not undergo significant hepatic elimination. The participant continued on the trial, and the event resolved.

No deaths, TEAEs leading to trial withdrawal, or drug-induced liver injury (DILI) events were reported. There was a higher incidence of ISR TEAEs with rademikibart compared with placebo (11.4% vs 0, respectively).

5.3.1.1. Trial CBP-201-AU001

In the FIH SAD trial, CBP-201-AU001, a single dose of rademikibart (75, 150, 300, 600 mg), or placebo were administered by SC injection and an additional cohort received a 30-minute IV infusion of 300 mg of rademikibart or placebo. Single doses of rademikibart administered by SC or IV injection were safe and well-tolerated through 12 weeks of post-injection follow-up. All TEAEs were mild-to-moderate in severity; there were no severe TEAEs. In addition, there were no serious TEAEs, deaths, or events that led to withdrawal from trial participation. There were no AEs related to abnormal laboratory values or ECGs.

The frequency of TEAEs did not increase with increasing rademikibart dose. The most common TEAEs were headache (53.3% of pooled rademikibart groups; 30.0% of placebo participants) and upper respiratory tract infections (33.3% of pooled rademikibart groups; 40.0% of placebo participants). ISRs were uncommon, with single episodes of injection site pain (rademikibart 75 mg SC) and injection site paresthesia (rademikibart 300 mg SC).

The overall incidence of TEAEs was the same for the 300 mg IV cohort and the comparable 600 mg SC cohort, however, there were more than twice the number of events reported in the 600 mg SC cohort compared to the 300 mg IV cohort. There were no treatment-related TEAEs reported for the CBP201 300 mg IV cohort.

Table 24: Overall Summary of TEAEs in Healthy Participants by Trial

	CBP-201AU001			CBP-201CN001		CBP-201-CN004	SIM0718-101	CBP-201-105 (Part A)		Total (N=600)	
	75-600 mg SC (N=24)	300 mg IV (N=6)	PBO (N=10)	150-600 mg SC (N=30)	PBO (N=6)	300 mg SC (N=324)	300 mg SC (N=176)	300 mg IV (N=18)	PBO (N=6)	Rademikibart (N=578)	PBO (N=22)
Any TEAE	20 (83.3%)	4 (66.7%)	7 (70.0%)	19 (63.3%)	4 (66.7%)	239 (73.8%)	151 (85.8)	2 (11.1%)	1 (16.7%)	435 (75.3)	12 (54.5%)
TEAEs ≥Grade 3	0	0	0	1 (3.3%)	0	7 (2.2%)	0	0	1 (16.7%)	8 (1.4%)	1 (4.5%)
SAEs	0	0	0	0	0	1 (0.3%)	1 (0.6%)	0	0	2 (0.3%)	0
Deaths	0	0	0	0	0	0	0	0	0	0	0
TEAEs that led to trial withdrawal	0	0	0	0	0	0	0	0	0	0	0
ISR TEAEs	2 (8.3%)	NA	0	0	0	24 (7.4%)	37 (21.0%)	NA	NA	63 (11.4%)[a]	0

Abbreviations: ISR, injection site reaction; IV, intravenous; NA, not applicable; PBO, placebo; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.
[a] The denominator only includes participants who received rademikibart via SC injection (N=554).

Table 25: Summary of TEAEs by PT in ≥5% of Total Rademikibart-Dosed Participants by Trials of Healthy Participants

	CBP-201AU001			CBP-201CN001		CBP-201-CN004	SIM0718-101	CBP-201-105 (Part A)		Total	
	75-600 mg SC (N=24)	300 mg IV (N=6)	PBO (N=10)	150-600 mg SC (N=30)	PBO (N=6)	300 mg SC (N=324)	300 mg SC (N=176)	300 mg IV (N=18)	PBO (N=6)	Rademikibart (N=578)	PBO (N=22)
Upper respiratory tract infection	9 (37.5)	1 (16.7)	4 (40.0)	0	0	48 (14.8)	42 (23.9)	0	0	100 (17.3)	4 (18.2)
Protein urine present	0	0	0	0	0	85 (26.2)	1 (0.6)	0	0	86 (14.9)	0
Blood triglycerides increased	0	0	0	0	0	39 (12.0)	24 (13.6)	0	0	63 (10.9)	0

Table 25: Summary of TEAEs by PT in ≥5% of Total Rademikibart-Dosed Participants by Trials of Healthy Participants

	CBP-201AU001			CBP-201CN001		CBP-201-CN004	SIM0718-101	CBP-201-105 (Part A)		Total	
	75-600 mg SC (N=24)	300 mg IV (N=6)	PBO (N=10)	150-600 mg SC (N=30)	PBO (N=6)	300 mg SC (N=324)	300 mg SC (N=176)	300 mg IV (N=18)	PBO (N=6)	Rademikibart (N=578)	PBO (N=22)
Blood uric acid increased	0	0	0	3 (10.0)	0	57 (17.6)	2 (1.1)	0	0	62 (10.7)	0
Injection site erythema	0	0	0	0	0	24 (7.4)	31 (17.6)	0	0	55 (9.5)	0
Red blood cells urine positive	0	0	0	4 (13.3)	3 (50.0)	11 (3.4)	24 (13.6)	0	0	39 (6.7)	3 (13.6)
White blood cells urine positive	0	0	0	1 (3.3)	1 (16.7)	0	29 (16.5)	0	0	30 (5.2)	1 (4.5)

Abbreviations: IV, intravenous; PBO, placebo; PT, Preferred Term; SC, subcutaneous; TEAE, treatment-emergent adverse event.

5.3.1.2. Trial CBP-201-CN001

In trial CBP-201-CN001, rademikibart was evaluated in a SAD trial in 36 healthy adult participants in China. Single dose of rademikibart (150, 300, and 600 mg) or placebo were administered by SC and followed for 85 days. A total of 36 healthy participants were enrolled in 3 dose groups (150, 300, and 600 mg), and each dose group received rademikibart injection or placebo in a 10:2 ratio. No participant withdrew from the trial. Rademikibart was well-tolerated with no SAEs, or TEAEs leading to premature withdrawal in this trial. No ISRs were reported.

The most common TEAEs in the rademikibart dose groups were blood creatine phosphokinase increased (16.7% for pooled rademikibart participants; 33.3% for placebo participants), red blood cells urine positive (13.3% for pooled rademikibart participants; 50% for placebo participants), and blood glucose increased (13.3% for pooled rademikibart participants; none was reported in placebo participants). One rademikibart participant experienced a severe (Grade 4) TEAE of blood creatine phosphokinase increased that resolved without treatment. All other TEAEs were mild (Grade 1) in severity. There were no significant changes from Baseline for vital signs and no abnormal clinically significant physical examination findings. One participant in the 600 mg dose group had 1 case of abnormal, clinically significant, 12-lead ECG result, reported as AE (mild [Grade 1] ventricular extrasystoles) that resolved without intervention.

5.3.1.3. Trial CBP-201-CN004

In the single-dose open-label Phase 1b trial, CBP-201-CN004, a 300 mg SC dose of rademikibart was administered via 2 PFS product presentations of rademikibart (1.2 mL containing 150 mg/mL and 2.25 mL containing 300 mg/2mL) was compared to rademikibart in a vial format. A total of 324 participants were randomized and exposed to study treatment in this trial. No TEAEs leading to premature withdrawal occurred.

The most common TEAEs by PT were protein urine present (26.2%), followed by blood uric acid increased (17.6%). Most TEAEs were mild or moderate in severity. The TEAEs by PTs with an incidence of >5% were protein urine present (26.2%), blood uric acid increased (17.6%), upper respiratory tract infection (14.8%), blood triglycerides increased (12.0%), injection site erythema (7.4%), and sinus bradycardia (5.9%).

No TEAEs led to early withdrawal. No TEAEs leading to death occurred.

A total of 24 (7.4%) participants experienced 32 ISR-related AEs, all of which were ISR-related AEs lasting more than 24 hours, 7 of which occurred in 6 (5.6%) participants in the rademikibart T1 group, 17 of which occurred in 11 (10.2%) participants in the rademikibart T2 group, and 8 of which occurred in 7 (6.5%) participants in the rademikibart R group. The most common ISR-related AEs were injection site erythema (7.4%); followed by injection site pain and injection site pruritus (each 0.6%). The maximum severity observed was Grade 2, with the relationship to the study treatment assessed as "possibly related", and the outcome was "recovered/resolved". No ISR-related AEs of Grade 3 or higher were reported.

5.3.2. Respiratory Diseases ~~Asthma~~ Trials

5.3.2.1. Asthma Trials

Trial CBP-201-WW002: ~~–~~24-Week Efficacy and Safety in Adults With Asthma

In trial CBP-201-WW002, participants with moderate-to-severe asthma were randomized (1:1:1) to receive 300 mg or 150 mg rademikibart Q2W or placebo administered SC for 24 weeks and followed with an 8-week post-treatment follow-up. Participants received a 600 mg loading dose ~~LD~~ of rademikibart or placebo followed by the start of their randomized treatment 2 weeks later.

An overall safety summary is shown in Table 26. The percentage ~~r~~of participants who reported at least 1 TEAE was 72.6% in the rademikibart 150 mg group, 70.4% in the rademikibart 300 mg group, and 59.3% in the placebo group.

There were no deaths reported during the trial.

A total of 11 serious TEAEs were reported by 8 participants: 2 participants (1.9%) in the rademikibart 150 mg group, 3 participants (2.8%) in the rademikibart 300 mg group, and 3 participants (2.8%) in the placebo group. Asthma was reported as an SAE in 4 participants (1.2%) overall: 1 participant (0.9%) in the rademikibart 150 mg group, 1 participant (0.9%) in the rademikibart 300 mg group, and 2 participants (1.9%) in the placebo group. All other SAEs were reported by 1 participant each. No participants reported treatment-related SAEs in either rademikibart group~~s~~.

At the PT level, COVID-19 and cough were the most frequently reported TEAEs: 9.4% and 6.6%, respectively, in the rademikibart 150 mg group; 14.8% and 13.0%, respectively, in the rademikibart 300 mg group; and 10.2% and 16.7%, respectively, in the placebo group.

Treatment-emergent AESIs were conjunctivitis reported in 1 participant in the rademikibart 150 mg group and 1 participant in the rademikibart 300 mg group; and ISRs lasting longer than 24 hours reported in 14 participants in the rademikibart 150 mg group and 8 participants in the rademikibart 300 mg group.

Table 26: Summary of Adverse Events ~~Reported in the~~ (CBP-201-WW002) ~~Phase 2 Trial~~

	Placebo N=108 n (%)	Rademikibart 150 mg N=106 n (%)	Rademikibart 300 mg N=108 n (%)	Overall N=322 n (%)
Number Of Participants With At Least One				
TEAE	64 (59.3)	77 (72.6)	76 (70.4)	217 (67.4)
Grade 1	17 (15.7)	36 (34.0)	24 (22.2)	77 (23.9)
Grade 2	43 (39.8)	38 (35.8)	49 (45.4)	130 (40.4)
Grade 3	4 (3.7)	2 (1.9)	2 (1.9)	8 (2.5)
Grade 4	0	1 (0.9)	1 (0.9)	2 (0.6)
Grade 5	0	0	0	0

Table 26: Summary of Adverse Events Reported in the (CBP-201-WW002) Phase 2 Trial

	Placebo N=108 n (%)	Rademikibart 150 mg N=106 n (%)	Rademikibart 300 mg N=108 n (%)	Overall N=322 n (%)
TEAE related to study drug	10 (9.3)	25 (23.6)	19 (17.6)	54 (16.8)
TEAE related to study procedure	0	14 (13.2)	7 (6.5)	21 (6.5)
TEAE occurring in more than 5% participants	37 (34.3)	33 (31.1)	36 (33.3)	106 (32.9)
Serious TEAE	3 (2.8)	2 (1.9)	3 (2.8)	8 (2.5)
TEAE leading to death	0	0	0	0
TEAE leading to drug discontinuation	2 (1.9)	4 (3.8)	3 (2.8)	9 (2.8)
TEAE leading to drug interruption	2 (1.9)	3 (2.8)	2 (1.9)	7 (2.2)
Adverse Event of Special Interest				
Conjunctivitis	0	1 (0.9)	1 (0.9)	2 (0.6)
Keratitis	0	0	0	0
Anaphylaxis	0	0	0	0
Parasitic and opportunistic infections	0	0	0	0
Pregnancy	0	0	0	0
Symptomatic overdose	0	0	0	0
Injection site reactions longer than 24 hours	0	14 (13.2)	8 (7.4)	22 (6.8)
AST/ALT elevated >5× ULN	0	0	0	0

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event; ULN, upper limit of normal.

Note: TEAEs are defined as any AEs that occurred or worsened during the treatment period and follow-up period, whether or not considered related to the treatment.

Note: Any missing severity is deemed Grade 3. Any missing causality is deemed as related.

There were no major clinically significant abnormalities in safety laboratory values (hematology, serum chemistry, and urinalysis), vital signs, ECG values, or physical examination. Specifically, no significant changes in eosinophil numbers were noted in any of the treatment groups during the trial. One participant in the rademikibart 300 mg group reported a related TEAE of eosinophil percentage increased (from 5% at Baseline to 11% on trial Day 142) and a TEAE of eosinophil count increased (from 0.25×10^9/L at Baseline to 0.89×10^9/L on trial Day 226). One participant in the rademikibart 300 mg group reported an unrelated TEAE of eosinophil count increased (from 0.27×10^9/L at Baseline to 1.19×10^9/L on trial Day 141).

Both rademikibart 150 mg and 300 mg were generally well -tolerated in the population of participants with persistent moderate-to-severe asthma not adequately controlled with a stable ICS/LABA therapy as an add-on therapy.

Trial CBP-201-105 (Part B1): Single IV Dose in Adults With Stable Asthma

Trial CBP-201-105 is a Phase 1, multipart, randomized, double-blind, and placebo-controlled trial to evaluate a single IV dose of rademikibart 300 mg in healthy adults (Part A), adults with stable asthma or COPD (Parts B1 and B2, respectively), and adults experiencing an acute asthma or COPD exacerbation (Parts C1 and C2, respectively). Parts A and B are complete; Part C is ongoing.

In Part B1, 12 adult participants with stable asthma were administered a single dose of rademikibart 300 mg (N=10) or placebo (N=2) via a 2-minute IV infusion. All participants were followed for 6 weeks.

Rademikibart 300 mg IV was well tolerated. Four of the 10 participants in the rademikibart group and 1 of the 2 participants in the placebo group experienced TEAEs. No TEAE PT occurred in more than 1 participant. All TEAEs were Grade 1 or 2 in severity. Two participants, both in the rademikibart group, had TEAEs considered related to IP. One participant experienced a Grade 1 TEAE of infusion related reaction 3 minutes after the end of the IP infusion. The event resolved without treatment approximately 3.5 hours later. A second participant experienced 2 TEAEs of thrombocytopenia (Grade 1 and Grade 2); both events resolved without treatment.

No AESIs, TEAEs of DILI, hypersensitivity reactions, infusion site reactions, SAEs, or TEAEs that led to trial withdrawal were reported.

There were no clinically significant abnormal findings or clinically meaningful differences between rademikibart and placebo for vital signs or ECG parameters. Additionally, there were no clinically meaningful changes in safety laboratory results (hematology, chemistry, or urinalysis).

5.3.2.2. COPD Trials

Trial CBP-201-105 (Part B2): Single IV Dose in Adults With Stable COPD

Trial CBP-201-105 is a Phase 1, multipart, randomized, double-blind, and placebo-controlled trial to evaluate a single IV dose of rademikibart 300 mg in healthy adults (Part A), adults with stable asthma or COPD (Parts B1 and B2, respectively), and adults experiencing an acute asthma or COPD exacerbation (Parts C1 and C2, respectively). Parts A and B are complete; Part C is ongoing.

In Part B2, 10 adult participants with stable COPD and a blood eosinophil count ≥200 cells/μL were administered rademikibart 300 mg (N=8) or placebo (N=2) via a 2-minute IV infusion. Participants were followed for 6 weeks.

Rademikibart 300 mg IV was well tolerated. Two participants in the rademikibart group and 0 in the placebo group experienced TEAEs. TEAEs included anaemia (in a participant with an ongoing medical history of anemia) and COPD exacerbation (in a participant who had very low plasma rademikibart concentrations). Both events were Grade 2 and were considered unlikely related to rademikibart.

No AESIs, TEAEs of DILI, hypersensitivity reactions, infusion site reactions, SAEs, or TEAEs that led to trial withdrawal were reported.

There were no clinically significant abnormal findings or clinically meaningful differences between rademikibart and placebo for vital signs or ECG parameters. Additionally, there were no clinically meaningful changes in safety laboratory results (hematology, chemistry, or urinalysis).

5.3.3. Atopic Dermatitis Trials

5.3.3.1. Trial CBP-201-AU-002: –Multiple Ascending Dose Trial in Adults With AD Participants

Overall, rademikibart was safe and well -tolerated at doses of up to 300 mg administered via SC injection for 4 weeks in a Phase 1b trial CBP-201-AU002. The percentage of participants experiencing at least 1 TEAE was similar across the rademikibart treatment dose groups: 87.5% in the 75 mg group, 87.5% in the 150 mg group, and 85.7% in the 300 mg group.

The most common TEAEs during the trial were exacerbation of AD (26.1% in the pooled rademikibart group and 37.5% in the placebo group), headache (17.4% in the pooled rademikibart group), and upper respiratory tract infection (8.7% in the pooled rademikibart group).

There were no SAEs or deaths reported.

For other significant AEs, there were 3 AEs or TEAEs that led to withdrawal of study treatment (rademikibart or placebo): 1 participant (75 mg rademikibart) withdrew from the study treatment on Day 8 due to an AE of eczema flare. Another participant (75 mg rademikibart) withdrew from the study treatment on Day 15 due to a TEAE of moderate flare of AD. The third participant (placebo group) withdrew from the study treatment on Day 8 due to a TEAE of exacerbation of AD.

Hematology, chemistry, and urinalysis parameters in some participants were outside the normal reference ranges, but there were only 2 clinically significant laboratory abnormalities across the trial, both in the placebo group.

There were no clinically significant abnormalities in vital signs or ECG parameters for any participants across the trial. All clinically significant physical examination findings were related to skin abnormalities due to AD, with the exception of right index fingernail erythema in a participant in the placebo group.

There were no safety concerns found and rademikibart was well -tolerated when administered to male and female adult participants with moderate-to-severe AD at doses of 75, 150, and 300 mg administered SC.

5.3.3.2. Trial CBP-201-WW001: –16-Week Efficacy and Safety Trial in Adults With AD

In Phase 2 trial CBP-201-WW001, the safety profile of rademikibart ~~in this trial~~ was generally comparable to that of placebo, with no clinically relevant differences observed between treatment groups. Rademikibart and placebo had similar incidence of TEAEs (48~~.~~2% and 5~~43.6~~%), serious TEAEs (2~~1.8~~% and ~~43.6~~%), and TEAEs leading to discontinuation (1~~.~~2% and 2~~1.8~~%), respectively (Table 27).

The most common TEAEs in the rademikibart dose groups were AD (15%) and headache (5%); all other TEAEs were reported for <5% of rademikibart-treated participants. The most common TEAEs in the placebo group were AD (14%), COVID-19 (7%), nasopharyngitis (7%), and skin infections (5%). TEAEs reported in >2% of participants in the all rademikibart group and at twice the rate of the placebo group were headache (5% rademikibart, 0% placebo), nausea (4% rademikibart, 0% placebo), and conjunctivitis (3% rademikibart, 0% placebo).

Most reported TEAEs were mild-to-moderate in severity. The proportion of participants with Grade ≥3 TEAEs (ie, severe, life-threatening, or fatal) was higher in the rademikibart 300 mg Q4W group (7%) than the rademikibart 150 mg Q2W group (2%), rademikibart 300 mg Q2W group (2%), or placebo group (2%). One participant in the rademikibart 300 mg Q4W group experienced a fatal (Grade 5) TEAE of cardiac arrest 57 days after the last dose of study drug with the relationship assessed as unrelated to study drug. The Investigator considered the participant's medical history of hypertension, hypercholesterolemia, and obesity as alternative explanations for the event.

The incidence of SAEs was low and similar in the rademikibart 300 mg Q4W group (2 participants, 4%), rademikibart 150 mg Q2W group (1 participant, 2%), rademikibart 300 mg Q2W group (0 participants, 0%), and placebo group (2 participants, 4%). SAEs in the rademikibart 150 mg Q2W group were nausea, vomiting, and headache. SAEs in the rademikibart 300 mg Q4W group were angina, cardiac arrest, and rib fractures. SAEs in the placebo group were cholelithiasis and pneumonia. None of the SAEs were considered related to study drug.

TEAEs leading to study drug discontinuation were uncommon and consisted of uterine leiomyoma (1 participant in the rademikibart 150 mg Q2W group), gamma-glutamyltransferase increased (1 participant in the rademikibart 300 mg Q4W group), and dermatitis atopic (1 participant in the placebo group); no TEAEs leading to study drug discontinuation were reported at the 300 mg Q2W dose.

Treatment-emergent AESIs (defined at the time of this study as conjunctivitis, keratitis, or other ophthalmic events) were reported for 8 participants receiving rademikibart and 1 placebo participant. In the rademikibart-treated participants, conjunctivitis was reported for 5 (3%) participants and other ophthalmic events (eye pruritus and photopsia) were reported for 3 (2%) participants. There were no participants with keratitis. TEAEs related to injection site reactions were also infrequent, reported for 3 (2%) subjects in the All rademikibart group (1 in each dose group) and 1 (2%) subject in the placebo group.

There were no clinically relevant trends in clinical safety laboratory (hematology, blood chemistry, and urinalysis) values, vital sign values, ECG findings, or physical examination findings across doses or over time for up to 16 weeks of treatment.

Table 27: Summary of Adverse Events ~~Reported in the Rademikibart (CBP-201-WW001) Phase 2 Trial~~

n (%) Participants with…	Rademikibart 300 mg Q2W N=57	Rademikibart 150 mg Q2W N=57	Rademikibart 300 mg Q4W N=56	All Rademikibart N=170	Placebo N=56
Any TEAE	26 (46%)	24 (42%)	32 (57%)	82 (48%)	30 (54%)
Serious TEAE	0	1 (2%)	2 (4%)	3 (2%)	2 (4%)
Grade ≥3 TEAE	1 (2%)	1 (2%)	4 (7%)	6 (4%)	1 (2%)
Discontinuation due to TEAE	0	1 (2%)	1 (2%)	2 (1%)	1 (2%)
Treatment-related TEAE	6 (11%)	6 (11%)	8 (14%)	20 (12%)	5 (9%)
AESIs	2 (4%)	3 (5%)	3 (5%)	8 (5%)	1 (2%)
Injection site reaction	1 (2%)	1 (2%)	1 (2%)	3 (2%)	1 (2%)

Abbreviations: AESI, adverse event of special interest; Q2W, every 2 weeks; Q4W, every 4 weeks; TEAE, treatment-emergent adverse event.

5.3.3.3. Trial CBP-201-CN002: ~~–~~52-Week Efficacy and Safety Trial in Adults and Adolescents With AD ~~in China~~

In the CBP-201-CN002 trial, rademikibart was well-tolerated in Chinese participants with moderate-to-severe AD. In Stage 1, the incidence of TEAEs was comparable in the rademikibart and placebo groups. The incidence of TEAEs related to the study drug, AESIs, and ISRs were slightly higher in the rademikibart group than in the placebo group, and the incidence of SAEs and severe AEs was lower in the rademikibart group than in the placebo group. In Stage 2, the incidence of TEAEs in ~~g~~Groups C, D, and E was essentially comparable, the overall incidence of TEAEs was slightly higher than that in Stage 1, and the overall incidence of AESIs and ISRs was essentially comparable to that in Stage 1.

In Stage 1, 71.8% of 330 participants experienced TEAEs. In Stage 2, 83.5% of 310 participants experienced TEAEs (Table 28).

Table 28: ~~Safety~~ Summary~~: Incidence~~ of Adverse Events ~~in Trial~~ (CBP-201-CN002)

	Stage 1		Stage 2		
	Rademikibart 300 mg Q2W	Placebo	Rademikibart 300 mg Q2W	Rademikibart 300 mg Q4W	Rademikibart 300 mg Q2W
Group	**A**	**B**	**C**	**D**	**E**
Any TEAE (%)	73.1	69.4	82.3	84.8	83.5
TEAE considered related to study drug (%)	30.6	22.5	24.8	25.0	29.4

SAE (%)	0.5	2.7	0.9	2.7	7.1
SAE considered related to study drug (%)	0.0	0.0	0.0	0.0	0.0
AE resulting in death (%)	0.0	0.0	0.0	0.0	0.0
AESI (%)	11.9	3.6	10.6	10.7	11.8
AEs resulting in drug discontinuation (%)	0.9	0.9	0.0	0.0	1.2
AEs resulting in drug interruption (%)	2.3	1.8	2.7	5.4	14.1
Injection site reaction (%)	9.1	2.7	5.3	7.1	7.1
Severe AE (%)[a]	1.8	4.5	2.7	4.5	7.1

Abbreviations: AE, adverse event; AESI, adverse event of special interest; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[a] Common Terminology Criteria for Adverse Events (CTCAE) Grade ≥3.

The TEAEs in Stage 1 with an incidence >5.0% in either the rademikibart or placebo group (ranked by incidence from highest to lowest in the rademikibart group) were dermatitis atopic (rademikibart group vs placebo group: 10.5% vs 17.1%, respectively), hyperlipidemia (10.5% vs 5.4%), hyperuricemia (9.6% vs 4.5%), upper respiratory tract infection (6.4% vs 6.3%), and injection site erythema (5.0% vs 0.9%).

The TEAEs in Stage 2 with an incidence >5.0% in the 241 participants who received rademikibart in Groups C, D, and E combined included COVID-19 (29.0%), dermatitis atopic (17.4%), upper respiratory tract infection (12.4%), pyrexia (6.6%), and urinary tract infection (5.4%). These incidence rates should be interpreted with caution due to the lack of a control group.

The TEAEs that occurred in Stage 1 and Stage 2 were generally mild-to-moderate in severity. No participants reported TEAEs that were Common Terminology Criteria for Adverse Events (CTCAE) Grade 4 or 5 in severity.

Across Stage 1 and Stage 2, 5 (3.1%) participants in the Q2W group experienced 8 SAEs, (1 case each of COVID-19 pneumonia, cataract, abortion induced incomplete, joint tuberculosis, joint effusion, arteriosclerosis coronary artery, pelvic abscess, and iliac artery occlusion), 2 (2.8%) participants in the Q2W-Q4W group experienced 4 SAEs (1 case each of meniscus injury, osteoarthropathy, tendonitis, and psoriasis) and 1 (6.3%) participant in the Q4W group experienced 1 SAE (rhabdomyolysis). No participant reported a treatment-related SAE.

Across Stage 1 and Stage 2, the overall incidence of AESIs was 13.7%, including conjunctivitis (7.2%), ISRs lasting more than 24 hours (6.8%), keratitis (1.2%), anaphylactic reaction (0.4%), aspartate aminotransferase (AST)/ALT increased >5 × upper limit of normal (ULN) (0.4%), parasitic and opportunistic infections (0.4%), and pregnancy (0.4%)

The long-term safety profile observed in this trial was generally consistent with the safety results of other AD trials of this product, and no new safety signals were identified.

5.3.3.4. Trial CBP-201-CN003: –12-Week Safety and Efficacy Trial in Adults With Chinese AD Participants

In trial CBP-201-CN003, 66.9% of the 360 participants experienced TEAEs, for which the severity was mostly CTCAE Grade 1 or Grade 2. As classified by PT, the TEAEs with >5.0% incidence (in descending order of incidence) included: upper respiratory tract infection (19.7%), hyperlipidaemia (6.1%), and hyperuricaemia (5.3%). A total of 13 (3.6%) participants experienced 13 TEAEs of CTCAE Grade ≥3, and none were considered related to treatment.

No TEAEs leading to death occurred during the trial. A total of 12 participants (3.3%) experienced 13 SAEs including erysipelas, pneumonia haemophilus, complicated appendicitis, peritonitis, breast cancer, lymphoma, gastric cancer, hypokalaemia, anaphylactic shock, cerebral infarction, acute myocardial infarction, cholecystitis acute, and ureterolithiasis. No treatment-emergent SAEs were considered related to the study drug.

As classified by PT, the top 3 injection site TEAEs (in descending order of incidence) in terms of incidences included: injection site erythema (4.2%), injection site induration (3.9%), and injection site oedema (2.5%). Most injection site TEAEs were considered related to the treatment. All injection site TEAEs had recovered/resolved before the end of the trial. One (0.3%) participant experienced a TEAE leading to treatment discontinuation (breast cancer), which was assessed as not related to treatment.

The post-treatment changes in laboratory tests were without clinical significance for the majority of participants in this trial; except that the hematology parameter eosinophil percentage decreased somewhat from Baseline at Week 20, the blood chemistry parameter creatine phosphokinase increased somewhat from Baseline at Week 20, and the blood chemistry parameter lactate dehydrogenase decreased somewhat from Baseline at Week 20, the overall trends of most laboratory values did not change significantly. The 12-lead ECG, vital signs, physical examinations, or eye examinations of the vast majority of participants before and after administration showed no significant changes.

In summary, rademikibart demonstrated a consistent and favorable safety profile in these participants with moderate-to-severe AD.

5.3.3.5. Trial SIM0718-302: 52-Week Efficacy and Safety Trial in Adolescents and Adults With AD

SIM0718-302 was a Phase 3, randomized, double-blind, parallel-group, placebo-controlled clinical trial evaluating the efficacy and safety of rademikibart in adults and adolescents with moderate-to-severe AD. The trial included a 16-week double-blind treatment period (Stage 1), a 36-week open-label maintenance treatment period (Stage 2), and an 8-week follow-up period. In Stage 1, participants were randomized in a 1:1 ratio to receive rademikibart or placebo by SC injection. A loading dose of rademikibart 600 mg or placebo (given as two 2 mL injections) was administered on Day 1 followed by rademikibart 300 mg or placebo (given as one 2 mL injection) Q2W until Week 16. In Stage 2, at the Week 16 Visit, participants in the placebo group switched to a treatment regimen of rademikibart 300 mg Q2W after completing the safety and efficacy assessments, while participants originally receiving rademikibart 300 mg Q2W continued with the same treatment regimen until Week 50.

A total of 259 participants were dosed, of which 254 received rademikibart. In Stage 1, 128 participants received rademikibart and 131 received placebo. In Stage 2, 126 of the 131 participants in the placebo group switched to rademikibart.

Safety Results for Stage 1

In Stage 1, the incidence of TEAEs was comparable between the rademikibart and placebo groups (60.9% and 64.9%, respectively). There was no significant imbalance between the treatment groups with regard to the TEAE profile. In the rademikibart group, the most common (≥5% of participants) TEAE was upper respiratory tract infection (18.0%). In the placebo group, the most common TEAEs were upper respiratory tract infection (13.7%) and ALT increased (6.1%).

The majority of TEAEs were Grade 1 or 2 in severity. Three participants (2.3%) in the rademikibart group had TEAEs ≥Grade 3: meniscus injury (1 participant), pneumonitis (1 participant), and pulmonary mass and lung adenocarcinoma (1 participant). All TEAEs ≥Grade 3 were assessed by the Investigator as unrelated to IP. No TEAEs ≥Grade 3 occurred in the placebo group.

There was a lower incidence of TEAEs considered related to IP in the rademikibart group compared with the placebo group (18.8% vs 26.7%, respectively). In the rademikibart group, the most common (≥1% of participants) related TEAEs were upper respiratory tract infection (5.5%) and conjunctivitis (3.9%). No related TEAEs were ≥Grade 3.

There were numerically higher incidences of AESIs and TEAEs of injection site reaction in the rademikibart group compared with the placebo group (3.9% vs 3.1% and 1.6% vs 0%, respectively). Eight AESIs were reported in 5 participants in the rademikibart group and 4 AESIs were reported in 4 participants in the placebo group. AESIs included conjunctivitis (3.9% vs 2.3%), conjunctivitis allergic (0% vs 0.8%), and keratitis (0.8% vs. 0%). All AESIs and TEAEs of injection site reaction were Grade 1 or 2, and all resolved.

One participant withdrew from the trial due to TEAEs: lung adenocarcinoma and pulmonary mass. Both events met the SAE criteria. The events were considered by the Investigator to be unrelated to IP.

Three (2.3%) participants in the rademikibart group reported 4 SAEs: meniscus injury, pneumonitis, pulmonary mass, and lung adenocarcinoma (1 event each), all of which were Grade 3 in severity. All SAEs were considered by the Investigator to be unrelated to IP, and all resolved. No SAEs were reported for the placebo group.

Safety Results for the Entire Rademikibart Treatment Period (Stages 1 and 2):

No significant changes in the incidence and distribution of TEAEs and related TEAEs were observed with continued rademikibart treatment. During the entire treatment period, the incidences of TEAEs in the rademikibart continuation group and the placebo crossover group were 82.8% and 74.6%, respectively, and the incidences of related TEAEs were 32.0% and 25.4%, respectively.

To better compare the safety of continuous rademikibart administration (Weeks 0 to 60) versus placebo (Weeks 0 to 16), after adjustment for exposure duration, the incidence of TEAEs in the rademikibart continuation group was numerically lower than that in the placebo group. The

incidence of TEAEs in the 2 groups was 300.8 and 485.0 per 100 person-years, respectively, and the incidences of related TEAEs were 70.3 and 155.7 per 100 person-years, respectively.

The majority of TEAEs during the study were Grade 1 or 2, and most TEAEs resolved. Sixteen participants (6.3%) had TEAEs ≥Grade 3. Only 1 participant (0.4%) had a Grade 4 TEAE. A participant in the placebo crossover group had a Grade 4 platelet count decreased after starting rademikibart in Stage 2 that was considered unrelated to rademikibart. No Grade 5 TEAEs were reported.

A total of 14 participants (5.5%) reported 17 SAEs during the entire rademikibart treatment period: 9 SAEs in 7 participants in the rademikibart continuation group and 8 SAEs in 7 participants in the placebo crossover group. No SAE PT occurred in more than 1 participant, and most SAEs were assessed by Investigators as unrelated to IP. Two SAEs were considered by the Investigator to be related to IP. Vestibular neuronitis occurred in the rademikibart continuation group 30 days after starting rademikibart in Stage 2. The last dose of rademikibart was administered 19 days prior to the SAE onset. The Sponsor did not consider the event to be related to rademikibart because vestibular neuronitis is also not a known adverse reaction of rademikibart or other drugs of this product class. Syncope occurred in the placebo crossover group 39 days after starting rademikibart in Stage 2. The last dose of drug was administered 14 days prior to the SAE onset. Both SAEs resolved and both participants continued on the trial and no action was taken with rademikibart dosing. The Sponsor did not consider the event to be related to rademikibart but instead related to the participant's medical history.

Twenty-two AESIs were reported for 15 participants: 13 events in 8 participants in the rademikibart continuation group and 9 events in 7 participants in the placebo crossover group. AESIs for the 2 groups combined were conjunctivitis (19 events in 15 participants) and keratitis (3 events in 2 participants). All except 2 events (conjunctivitis and keratitis in 1 participant in the rademikibart group during Stage 1) were considered to be related to IP.

No participant withdrew from the trial in Stage 2 due to TEAEs.

There were no clinically significant changes in laboratory test parameters, ECGs, or vital signs during the trial.

5.3.4. Other Trials

5.3.4.1. Nasal Polyps Trial

The early terminated Phase 2 nasal polyps trial (CBP-201-WW003) randomized 40 participants: 13 participants received rademikibart SC 300 mg Q2W, 13 participants received rademikibart SC 300 mg Q4W, and 14 participants received SC placebo. Out of the 40 participants randomized, 2 participants (5.0%) completed study treatment;; 1 participant in the rademikibart 300 mg Q2W group and 1 participant in the rademikibart 300 mg Q4W group. A total of 36 (94.7%) participants discontinued from the trial due to trial early termination and 2 (5.0%) participants discontinued due to trial withdrawal by participant. The overall mean (SD) duration of study drug was 49.0 days (51.18) in the trial. The median number of injections administered was 8 across treatment groups.

Out of 40 participants randomized, 19 participants (47.5%) reported TEAEs: 6 participants (46.2%) in the rademikibart 300 mg Q2W group, 6 participants (46.2%) in the rademikibart

300 mg Q4W group, and 7 participants (50.0%) in the placebo group. Most TEAEs reported across treatment groups were of maximum severity of Grade 1 or Grade 2. The AESI of ISRs lasting longer than 24 hours occurred in 1 participant (7.7%) in the rademikibart 300 mg Q2W group and 2 participants (15.4%) in the rademikibart 300 mg Q4W group.

No SAEs, deaths or TEAEs leading to study drug discontinuation were reported in the trial. There were no clinically significant abnormalities and or changes from baseline observed in ECG parameters or physical examination findings.

5.3.5. Overall Safety

5.3.5.1. Common Adverse Events

Atopic Dermatitis

A pooled safety analysis of the 54 completed clinical trials of participants with AD was conducted (CBP-201AU002, CBP-201-WW001, CBP-201-CN002, CBP-201-CN003, and SIM0718-302)through September 22, 2023 was conducted. A total of 971 participants received rademikibart 300 mg Q2W only and 306 participants received placebo. The most common PTs in the rademikibart group (>5% of participants and higher than placebo) were upper respiratory tract infection (15.6% vs 7.1%), COVID-19 (6.3% vs 1.9%), and hyperuricaemia (5.3% vs 2.2%).that included a total of 772 participants, of whom 699 received rademikibart at any dose and 73 received placebo. (Trial CBP-201-CN003 was ongoing at the time of the analysis and 185 of the 360 participants were included in the pooled analysis.) The most common TEAEs in participants receiving rademikibart (>5% and higher than placebo), included COVID-19 (14.3%), upper respiratory tract infection (9.0%), and hyperlipidaemia (5.4%).

Respiratory Diseases

In the 1 completed clinical trial of participants with asthma (CBP-201-WW002) that included a total of 322 participants, of whom 214 received rademikibart SC at any dose and 108 received placebo, the most common TEAEs in participants receiving rademikibart (>5% and higher than placebo), included COVID-19 (12.1% vs 10.2%), injection site erythema (6.5% vs 0%), and nasopharyngitis (5.6% vs 4.6%). In a second trial in asthma (CBP-201-105 Part B1), 10 participants received a single dose of rademikibart 300 mg via IV infusion. No TEAE occurred in more than 1 participant.

In a trial in COPD (CBP-201-105 Part B2), 8 participants received a single dose of rademikibart 300 mg via IV infusion. No TEAE occurred in more than 1 participant.

5.3.5.2. Injection Site Reactions (ISRs)

ISRs are an identified risk with SC administration of rademikibart. In 7 completed trials of rademikibart SC in participants with asthma, AD, and CRSwNP, 98 of the 1368 (7.2%) rademikibart-treated participants experienced TEAEs associated with ISRs (Table 29). ISR TEAEs lasting >24 hours occurred in 66 (4.8%) rademikibart-treated participants. All ISR TEAEs were Grade 1 or 2 in severity. Most ISR TEAEs were considered to be at least possibly related to rademikibart.

Table 29: Incidence of Injection Site Reaction TEAEs in Participants Administered Rademikibart SC in 7 Completed Trials of Asthma, AD, and CRSwNP

	Asthma	AD					CRSwNP	
	CBP-201-WW002 (n=214)	CBP-201AU002 (n=23)	CBP-201-WW001 (n=170)	CBP-201-CN002 (n=321)	CBP-201-CN003 (n=360)	SIM0718-302 (n=254)	CBP-201-WW003 (n=26)	Total (N=1368)
ISR TEAEs	31 (14.5%)	0	3 (1.8%)	32 (10.0%)	27 (7.5%)	2 (0.8%)	3 (11.5%)	98 (7.2%)
ISRs lasting >24 hours	23 (10.7%)	0	0	21 (6.5%)	19[a] (5.3%)	0	3 (11.5%)	66 (4.8%)
ISR TEAEs >Grade 3	0	0	0	0	0	0	0	0
ISRs >Grade 3 lasting >24 hours (AESI)	0	0	0	0	0	0	0	0

Abbreviations: AD, atopic dermatitis; AESI, adverse event of special interest; CRSwNP, chronic rhinosinusitis with nasal polyps; ISR, injection site reaction; SC, subcutaneous; TEAE, treatment-emergent adverse event.

[a] Four additional participants had ISR TEAEs that resolved the day after the start date of the event but were missing a resolution time in order to determine if the event duration was >24 hours.

~~5.3.5.2.~~5.3.5.3. Serious Adverse Events (SAEs)

Of the 1964 participants treated with rademikibart in 11 completed trials and the 2 completed parts of Trial CBP-201-105, 49 participants (2.5%) experienced a total of 66 SAEs. The most common SAEs by System Organ Class (SOC) were as follows:

- Infections and Infestations (11 events in 9 participants)
- Injury, Poisoning and Procedural Complications (8 events in 8 participants)
- Respiratory, Thoracic and Mediastinal Disorders (6 events in 5 participants)
- Cardiac Disorders (7 events in 5 participants)
- Gastrointestinal Disorders (6 events in 5 participants).

Individual SAE PTs that were reported more than once in rademikibart-treated participants included acute myocardial infarction (3 events) and arteriosclerosis coronary artery, bile duct stone, COVID-19 pneumonia, meniscus injury, and asthma (2 events each).

Three SAEs were considered by Investigators to be related to rademikibart (serious adverse reactions [SARs]): vestibular neuronitis, ALT increased, and syncope. ~~A total of 48 SAEs were reported by 34 of the 1498 (2.3%) participants who received rademikibart in the 9 completed clinical trials of rademikibart, of which none were considered possibly related to rademikibart.~~

The cumulative count of SAEs across these trials does not indicate a trend of significant untoward risk. ~~A summary of these SAEs is displayed in Table 23.~~

In addition, of the 702 participants administered rademikibart or placebo in 4 ongoing blinded trials, 51 SAEs have been reported to date, of which 1 was considered related to blinded IP (periorbital haemorrhage).

Two deaths have been reported in the clinical development program. Both deaths were considered not related to rademikibart/blinded IP. One participant with AD experienced a fatal cardiac arrest. The Investigator considered the participant's medical history of hypertension, hypercholesterolemia, and obesity as alternative explanations for the event. The second death occurred due to pneumonia in a participant with asthma in an ongoing trial. The event was considered secondary to an acute exacerbation of bronchial asthma that was inadequately treated and led to the other complications along with the severe pneumonia.

Table 23: Cumulative Summary Tabulation of SAEs by SOC and PT in Participants Exposed to Rademikibart

System Organ Class Preferred Term	Number of Events
Cardiac Disorders	6
Acute Myocardial Infarction	2
Angina Pectoris	1
Arteriosclerosis Coronary Artery	2
Cardiac Arrest	1
Endocrine Disorders	1
Thyroid Mass	1
Eye Disorders	1
Cataract	1
Gastrointestinal Disorders	4
Gastric Ulcer	0
Nausea	1
Pancreatic Mass	1
Vomiting	1
Splenic Artery Aneurysm	1
Hepatobiliary Disorders	4
Bile Duct Stone	2
Cholelithiasis	0
Cholecystitis Acute	1
Drug Induced Liver Injury	1*
Immune System Disorders	1
Anaphylactic Shock	1
Infections and Infestations	9

Table 23: Cumulative Summary Tabulation of SAEs by SOC and PT in Participants Exposed to Rademikibart

System Organ Class Preferred Term	Number of Events
Complicated Appendicitis	1
COVID-19 Pneumonia	2
Erysipelas	1
Hepatic Infectious Mononucleosis	1*
Joint Tuberculosis	1
Otitis Media Acute	0
Pelvic Abscess	1
Peritonitis	1
Pneumonia	0
Pneumonia Haemophilus	1
Injury, Poisoning and Procedural Complications	4
Abortion Induced Incomplete	1
Avulsion Fracture	0
Humerus Fracture	0
Meniscus Injury	1
Rib Fracture	1
Road Traffic Accident	1
Metabolism and Nutrition Disorders	1
Type 2 Diabetes Mellitus	0
Hypokalaemia	1
Musculoskeletal and Connective Tissue Disorders	4
Joint Effusion	1
Osteoarthritis	0
Osteoarthropathy	1
Rhabdomyolysis	1
Tendonitis	1
Neoplasms Benign, Malignant, and Unspecified (incl. cysts and polyps)	4
Breast Cancer	1
Gastric Cancer	1
Lymphoma	1
Testis Cancer	1*

Table 23: Cumulative Summary Tabulation of SAEs by SOC and PT in Participants Exposed to Rademikibart

System Organ Class Preferred Term	Number of Events
Nervous System Disorders	2
Cerebral Infarction	1
Headache	1
Psychiatric Disorders	1
Anxiety Disorder	1
Renal and Urinary Disorders	1
Ureterolithiasis	1
Respiratory, Thoracic, and Mediastinal Disorders	3
Acute Respiratory Failure	1
Asthma	2
Skin and Subcutaneous Disorders	1
Dermatitis Atopic	0
Psoriasis	1
Vascular Disorders	1
Iliac Artery Occlusion	1
Total	**48**

[a] The subject had ended the study at the time of the SAE.

5.3.5.3.5.3.5.4. Adverse Events of Special Interest (AESIs)

AESIs were initially defined as conjunctivitis, keratitis, anaphylactic reaction, ISRs lasting more than 24 hours, AST/ALT increased to >5 × ULN, parasitic and opportunistic infections, and symptomatic drug overdose. The definition was subsequently revised to limit ISRs lasting more than 24 hours to a severity of ≥Grade 3. Trials with rademikibart administered via IV infusion do not include ISRs because an AESI as ISRs are associated with SC administration. In addition, "AST/ALT increase >5 × ULN" was removed as an AESI; however, the protocols for ongoing trials require that any cases of DILI be closely monitored. "Symptomatic drug overdose" was also removed as an AESI as no cases have been reported across all trials in the clinical development program to date.

A summary of the number of participants with an AESIs across the completed clinical trials in participants with asthma, AD, COPD, and CRSwNP that included a total 1,114 participants is presented in Table 30. Of the 1386 rademikibart-treated participants, Tthe most common frequently reported AESIs were ISRs lasting more than 24 hours (5.5%) and conjunctivitis (3.83%) and . AEs of keratitis were infrequent (0.436%) and only occurred in participants with AD. AESIs of AST/ALT increased to >5 × ULN was reported in 3 participants (0.27%). One participant each (0.079%) experienced an AESI of parasitic/opportunistic infection (otitis externa fungal) and anaphylactic reaction. There were no reports of symptomatic overdose. All except

1 AESI were Grade 1 or 2 in severity. One Grade 3 AESI of keratitis was reported in a participant with AD in the 300 mg Q2W group of Trial CBP-201-CN002.

Table 30: Number of Rademikibart-Treated Participants With AESIsAdverse Events of Special Interest in Completed TrialsStudies of Asthma, COPD, AD, and CRSwNP

AESI	Clinical TrialsStudies in Asthma, COPD, AD, and CRSwNP									Totals (N=13861114) n (%)
	Asthma		COPD	AD					CRSwNP	
	CBP-201-WW002 (n=214)	CBP-201-105 (Part B1)[a] (n=10)	CBP-201-105 (Part B2)[a] (n=8)	CBP-201-AU002 (n=23)	CBP-201-WW001 (n=170)	CBP-201-CN002 (n=321)	CBP-201-CN003 (n=360)	SIM0718-302 (n=254)	CBP-201-WW003 (n=26)	
Conjunctivitis	2[ab]	0	0	0	5[bc]	18	12	15	0	52 (3.8%)37 (3.3%)
Keratitis	0	0	0	0	0	3	1	2	0	6 (0.4%)4 (0.36%)
Anaphylactic reaction	0	0	0	0	0	1	0	0	0	1 (0.079%)
ISRs ≥Grade 3 lasting >24 hours	022[e]	N/A	N/A	0	0	017	019	0	03[d]	061 (5.5%)
AST/ALT increased to >5 × ULN	0			0	1	1	0		0	3 (0.27%)
Parasitic and opportunistic infections	0	0	0	0	0	1	0	0	0	1 (0.079%)
Symptomatic drug overdose	0			0	0	0	0		0	0

Abbreviations: AD, atopic dermatitis; AESI, adverse event of special interest; COPD, chronic obstructive pulmonary disease; CRSwNP, chronic rhinosinusitis with nasal polyps; ISR, injection site reaction; N/A, not applicable.

Notes: Rademikibart was administered via subcutaneous injection in all trials except CBP-201-105 where it was administered via intravenous (IV) infusion. Participants received rademikibart 300 mg every 2 weeks (Q2W) except unless when noted.

[a] Participants in CBP-201-105 received a single dose of rademikibart 300 mg via IV infusion. Part B of the trial is complete; Part C remains ongoing.

[ba] Includes 1 participant receiving 150 mg Q2W and 1 participant receiving 300 mg Q2W.

[cb] Includes 2 participants receiving 150 mg Q2W, 1 participant receiving 300 mg Q2W, and 2 participants receiving 300 mg every 4 weeks (Q4W).

[e] Includes 14 participants receiving 150 mg Q2W and 8 participants receiving 300 mg Q2W.

[d] Includes 1 receiving rademikibart 300 mg Q2W and 2 participants receiving 300 mg Q4W.

6. SUMMARY OF DATA AND GUIDANCE FOR THE INVESTIGATOR

This section of the IB also serves as the Development Core Safety Information (DCSI) for rademikibart.

6.1. Product Description

Rademikibart is an investigational novel human mAb of the IgG4 subclass that binds to the cell surface protein IL-4Rα and inhibits IL-4 and IL-13 signaling. It is being developed for the treatment of allergic inflammatory diseases including AD, asthma, and COPD.

The rademikibart IP is formulated as a liquid sterile solution at 150 mg/mL which also contains L-histidine, trehalose, and NaCl with polysorbate 80. Rademikibart drug product is supplied in 3 presentations: a single-dose glass vial that delivers 150 mg rademikibart in 1 mL, a single-dose PFS that delivers 150 mg rademikibart in 1 mL and a single-dose PFS that delivers 300 mg rademikibart in 2 mL. The placebo products are supplied in matching product presentations.

6.2. Therapeutic Indications Under Development

The indications under development for rademikibart include AD and respiratory system diseases including asthma and COPD.

6.3. Posology and Method of Administration

Rademikibart is intended for SC or IV administration. The dose, frequency, and duration of administration is described in each clinical trial protocol.

6.4. Contraindications

Rademikibart should not be used in participants with known hypersensitivity to rademikibart or any of its excipients.

6.5. Warnings and Precautions for Use

No special warnings or precautions for the use of rademikibart have been established. Warnings for dupilumab and stapokibart, ~~a~~ marketed ~~similar~~ products in the same class, inform the potential risks for rademikibart (DUPIXENT China PI Jul 2025; DUPIXENT EU SmPC 2025; DUPIXENT USPI Apr 2026; KANGYUEDA China PI Nov 2025). Although not observed with rademikibart, the clinician should be aware of the theoretical potential for parasitic (helminth) infection with rademikibart treatment due to the ability of the study drug to suppress the immune system, particularly with chronic dosing, as reported for dupilumab. Similarly, live vaccines should be avoided while using rademikibart due to the theoretical potential for poor response. Serious ~~E~~eosinophilic conditions (including vasculitic rash, worsening pulmonary symptoms, neuropathy) due to increased eosinophils that have been reported for dupilumab in participants with asthma have not been observed with rademikibart, but should be monitored. Other warnings for the marketed products ~~dupilumab~~ include the risk of hypersensitivity reactions (dupilumab

and stapokibarteg, generalized urticaria, serum sickness), conjunctivitis and keratitis (dupilumab and stapokibart), and arthralgia (dupilumab).

6.6. Undesirable Effects

6.6.1. Common Adverse Events

Rademikibart has been well -tolerated and has exhibited an acceptable and clinically manageable safety profile.

In clinical trials in healthy participants, the most common TEAEs for rademikibart (>5% of participants and higher than placebo) protein urine present (14.9% vs 0, respectively), blood triglycerides increased (10.9% vs 0), blood uric acid increased (10.7% vs 0), injection site erythema (9.5% vs 0), and white blood cells urine positive (5.2% vs 4.5%).

In clinical trials in AD, tThe most common TEAEs reported for rademikibart in participants in clinical trials of AD (>5% of participants and higher than placebo) were upper respiratory tract infection (15.6%), COVID-19 (6.3%14.3%), and hyperuricaemia (5.3%)upper respiratory tract infection (9.0%), and hyperlipidaemia (5.4%).

In a completed Phase 2 clinical trial in asthma, Tthe most common TEAEs for rademikibart reported in participants in the clinical trial of asthma (>5% and higher than placebo) were COVID-19 (12.1%), injection site erythema (6.5%), and nasopharyngitis (5.6%). In a Phase 1 trial in asthma, no TEAE occurred in more than 1 participant.

In a Phase 1trial in COPD, no TEAE occurred in more than 1 participant.

Across all trials, most TEAEs were mild or moderate (Grade 1 or 2) in severity.

6.6.2. Serious Adverse Events

A total of 6648 SAEs have been reported by 4934 of the 19641498 (2.53%) participants who received rademikibart in the 9 11 completed clinical trials and 2 completed parts of an ongoing trial.; of which none were considered possibly related to rademikibart. The most frequent SAE by SOC was infection and infestation (N=9). Individual SAE PTs that were reported more than once in rademikibart-treated participants included acute myocardial infarction (3 events) and arteriosclerosis coronary artery, bile duct stone, COVID-19 pneumonia, meniscus injury, and asthma (2 events each).

Three SAEs were considered by Investigators to be related to rademikibart (SARs): vestibular neuronitis, ALT increased, and syncope. One additional SAE in the ongoing blinded trials was classified as related to IP (periorbital haemorrhage).

6.6.3. Adverse Events of Special Interest

Of The most frequently reported AESIs in the 1114 the 1386 rademikibart-treated participants in the completed clinical trials in participants with asthma, AD, COPD, and CRSwNP, the most common AESIs were ISRs lasting more than 24 hours (5.5%) and conjunctivitis (3.83%) and - AEs of keratitis were infrequent (0.436%) and only occurred in participants with AD. AESIs of AST/ALT increased to >5 × ULN was reported in 3 participants (0.27%). One participant each (0.09%) experienced an AESI of parasitic/opportunistic infection and anaphylactic reaction were

reported in 1 participant each (0.07%). There were no reports of ISRs ≥Grade 3 lasting >24 hours ~~symptomatic overdose~~.

6.6.4. Reference Safety Information for Assessment of Expectedness of Serious Adverse Reactions

The Reference Safety Information (RSI) is used for the assessment of expectedness for regulatory reporting of serious adverse reactions that are reported in clinical trials. The RSI does not represent a comprehensive overview of the safety profile, which is presented in Section 5.3. No SARs are considered expected by the Sponsor for regulatory reporting purposes.

6.7. Risk/Benefit

Despite advances in chronic pulmonary care and AD therapy, there remains a significant unmet medical need for safe, rapid, and effective therapies that can more directly target the underlying inflammatory drivers of these diseases.

~~Market experience with dupilumab to date and rademikibart Phase 1 and Phase 2 clinical data demonstrate that the blocking of IL-4Rα is safe and well-tolerated~~In clinical trials, rademikibart has shown efficacy in participants with moderate-to-severe asthma, COPD, AD, and CRSwNP with a favorable~~, and the good clinical~~ safety profile that is consistent with ~~pre~~nonclinical toxicology trials ~~using surrogate antibodies~~. Based on the safety results from the SAD trial with rademikibart at doses up to 600 mg SC~~,~~ and rademikibart exposure up to 52 weeks in other Phase 2 and Phase 3 trials, there are no important identified or potential risks for rademikibart.

~~Risks based on warnings and precautions from the dupilumab marketing experience include eye-related side-effects (eg, conjunctivitis and keratitis) and hypersensitivity reactions (eg, generalized urticaria, serum sickness).~~

Based on ~~Combined with the~~ rademikibart's mechanism of action and~~,~~ nonclinical ~~data,~~ and clinical data along with ~~of rademikibart and~~ data ~~of~~ from dupilumab and stapokibart, 2 approved IL-4Rα antagonists, ~~it is considered that~~ there ~~is~~ are no important identified/potential risks ~~of~~ for rademikibart.

Potential r~~R~~isks for rademikibart are based on warnings and precautions from the dupilumab and stapokibart marketing experience and include eye-related side-effects (eg, conjunctivitis and keratitis) and hypersensitivity reactions (eg, generalized urticaria, serum sickness).

While the majority of AESIs ~~and injection site TEAEs~~ in trials in AD, asthma, and CRSwNP were related to rademikibart, the ~~overall~~ incidences of each AESI ~~was~~ were not high. With the exception of 1 ~~event of rademikibart-related AESI (~~Grade 3 keratitis in a participant with AD~~) of CTCAE Grade 3 reported in the 300 mg Q2W group~~, the remaining ~~rademikibart-related~~ AESIs ~~and injection site TEAEs~~ were ~~all of CTCAE~~ Grade 1 or Grade 2.

Rademikibart was well ~~-~~tolerated and exhibited an acceptable and controllable safety profile. The cumulative SAEs did not indicate a trend of significant untoward risks. The i~~I~~ncidence of ISRs has been higher in the rademikibart group compared with the placebo group, however, ~~the majority~~ all were Grade 1 or 2 in severity and none were considered to be SAEs~~resolved spontaneously, and there was no SAR report associated with ISRs~~. Therefore, the ISRs were comprehensively assessed as an identified risk for rademikibart based on the risk mechanism, the clinical data for this product, and the data for a product with the same target.

Conjunctivitis-associated AEs were all Grade 1 or 2 which did not lead to study drug ~~interruption or~~ discontinuation. Therefore, conjunctivitis remains as a potential risk for rademikibart and requires further monitoring due to insufficient available data and unclear mechanism of action.

Ophthalmic adverse events of conjunctivitis and keratitis, and ≥Grade 3 ISRs lasting longer than 24 hours were categorized as AESIs in rademikibart clinical trials for close monitoring. ISRs are assessed as identified risk, and conjunctivitis is assessed as potential risk. The above risks can be reasonably controlled by regular injection site assessment and eye examination as part of physical examinations during the trial, and drug interruption/discontinuation and symptomatic treatment as appropriate.

The review of safety data collected do not alter the anticipated ~~favorable~~ benefit-risk profile for rademikibart. In conclusion, previous clinical experience with rademikibart shows no major safety or tolerability concerns. The clinical benefits outweigh the identified and potential risks therefore, t~~T~~he current risk/benefit ratio is favorable.

6.8. Pediatric Use

No dedicated clinical trial has been conducted to evaluate the effects of rademikibart on pediatric participants. ~~There is limited data on the effects in adolescent participants ≥12 years of age. A total of 12 adolescent participants in a Phase 2 study of AD received rademikibart for up to 52 weeks.~~ A total of 65 adolescent participants (≥12 to <18 years of age) were administered at least 1 dose of rademikibart across 2 clinical trials in AD (Phase 2 Trial CBP-201-CN002 and Phase 3 Trial SIM0718-302). Of these, all 65 participants received 300 mg SC Q2W or Q4W and 35 participants received a 600 mg SC loading dose. Adolescent participants did not experience any treatment-related SAEs or TEAEs leading to rademikibart discontinuation or trial withdrawal.

Direct comparison of rademikibart concentrations between adolescents (N=27) and adults (≥18 years of age, N=101) who received rademikibart in Stage 1 of Trial SIM0718-302 showed similar concentrations between the 2 age groups. Additionally, in population PK analysis, age (≥18 years and <18 years) had no significant effect on PK parameters. Thus, ~~Based on results from population PK analysis that included data from adolescent participants,~~ no dose adjustment is required for adolescents. ~~These participants did not experience any treatment-related SAEs or AEs leading to discontinuation.~~

Based on data from clinical trials of dupilumab in pediatric participants with AD and asthma, the safety profile in adolescents is anticipated to be similar to adults for this drug class (DUPIXENT China PI Jul 2025; DUPIXENT EU SmPC 2025; DUPIXENT USPI Apr 2026).

6.9. Geriatric Use

No dedicated clinical trial has been conducted to evaluate the effects of rademikibart on elderly participants aged ~~>~~≥65 years. A total of 74~~75~~ elderly participants with AD or asthma have received ~~dupilumab~~ rademikibart for up to 52 weeks. Overall, the safety profile observed in the elderly population (≥65 years of age) was similar to that in the overall AD and asthma trial populations.

Based on results from population PK analysis that included data from elderly AD participants, age is not a significant covariate on rademikibart clearance, and thus no dose adjustment is

required for participants ~~>~~ ≥65 years of age. ~~Of these participants, none experienced a treatment-related SAEs.~~

6.10. Pregnancy and Lactation

~~No preclinical reproductive toxicology studies have been conducted, and the risk for use of rademikibart in pregnancy and lactation is unknown.~~Nonclinical reproductive toxicology studies have been conducted in transgenic B-hIL-4/hIL-4RA mice to evaluate FEED, EFD, and PPND. No rademikibart-related effects were noted in male or female fertility, embryo-fetal development, or postnatal development, including behavioral assessments and reproductive capability in F1 offspring at large exposure margins; therefore, concern for developmental toxicity effects in humans is low.

There are no clinical data on the use of rademikibart in pregnant women to inform a drug-associated risk of adverse developmental outcomes. To date, a total of 5 pregnancies have been reported in rademikibart-dosed participants. Pregnancy outcomes were as follows: elective abortion (3 participants), elective abortion incomplete followed by hysteroscopic electrosuction (1 participant), and therapeutic termination of pregnancy due to ectopic pregnancy (1 participant). As a precaution, pregnant women are excluded from participating in clinical trials of rademikibart, and women of childbearing potential are required to use contraception. Refer to the specific clinical trial protocol for more information on contraception requirements.

Rademikibart was detected in milk of transgenic mice at low levels (milk:serum ratios of 0.2-0.3). Systemic exposure to infants is expected to be low due to low oral bioavailability of antibodies. As a precaution, w~~W~~omen who are ~~pregnant or~~ breastfeeding are excluded from participating in clinical trials of rademikibart.

6.11. Renal and Hepatic Impairment

Rademikibart, as a mAb, is not expected to undergo significant renal or hepatic elimination. No clinical trials or formal analyses have been conducted to evaluate the effect of renal impairment or hepatic impairment on the pharmacokinetics of rademikibart.

6.12. Interaction With Other Medicinal Products and Forms of Interaction

No dedicated drug-drug interaction (DDI) studies in animals or humans have been conducted.

Therapeutic proteins which are cytokines or have cytokine modulatory properties may have potential to differentially affect CYP activities, however this interaction is generally less than 2-fold (Lenoir 2021). Theoretically, mAbs of the IgG4 subclass, like rademikibart, may have the potential to affect CYP enzyme activities.

A retrospective DDI analysis was performed with data from a Phase 2 AD trial (Connect trial CBP-201-WW001) and consisted of a review of the concomitant medication dataset which identified 130 drugs that are inducers or inhibitors of CYP pathways and were taken before or during administration of rademikibart. For each of the 8 CYP pathways examined (2E1, 1A2, 2B6, 2C19, 2C8, 2C9, 2D6, 3A4), there was no evidence that administration of drugs known to inhibit or induce that pathway were associated with a systematic change in clearance of rademikibart. No effects potentially related to DDIs were identified in data from any of the

170 participants who received active rademikibart treatment for up to 16 weeks. These results support that rademikibart is neither a victim nor a potential perpetrator of CYP-mediated DDIs.

6.13. Overdose

The effects of an overdose with rademikibart are unknown.

6.14. Pharmacokinetics

The MTD of rademikibart has not been established: all dosing regimens evaluated in a clinical setting (300 mg IV, up to 300 mg QW SC, and up to 600 mg loading dose LD followed by 300 mg Q2W SC) have been generally well tolerated.

Rademikibart exhibits dose-proportional absorption but not dose-proportional elimination; therefore, there are greater-than-dose-proportional increases in overall drug exposure (AUC) with increasing dose. However, there is no time-dependency in rademikibart CL or CL/F following multiple dosing; accumulation with multiple doses is predictable (ie, 2-fold with 300 mg Q2W SC regimen) and, once steady state is reached, concentrations remain relatively stable through the duration of treatment.

6.15. Immunogenicity

The immunogenicity (ADA and NnAb) incidence following rademikibart has been generally low and non-persistent, with low ADA titers, and appears to be inversely proportional to the rademikibart dose. Overall, the onset of immunogenicity appears to present minimal safety risk and is unlikely to lead to loss of efficacy with continued exposure.

6.16. Nonclinical Toxicology

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of rademikibart. Due to its large molecular size, it is mostly confined to extra cellular space and has no genotoxic potential. It is highly specific for human IL-4Rα with the mechanism of action of blocking IL-4 and IL-13 signaling; therefore, has low potential for off-target effects that could potentially impact tumor initiation and progression.

7. REFERENCES

7.1. Publications

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