CBP-201, a Next-Generation IL-4Rα Antibody, Achieved All Primary and Secondary Efficacy Endpoints in the Treatment of Adults with Moderate-to-Severe Atopic Dermatitis (AD): A Randomized, Double-blind, Pivotal Trial in China (CBP-201-CN002)

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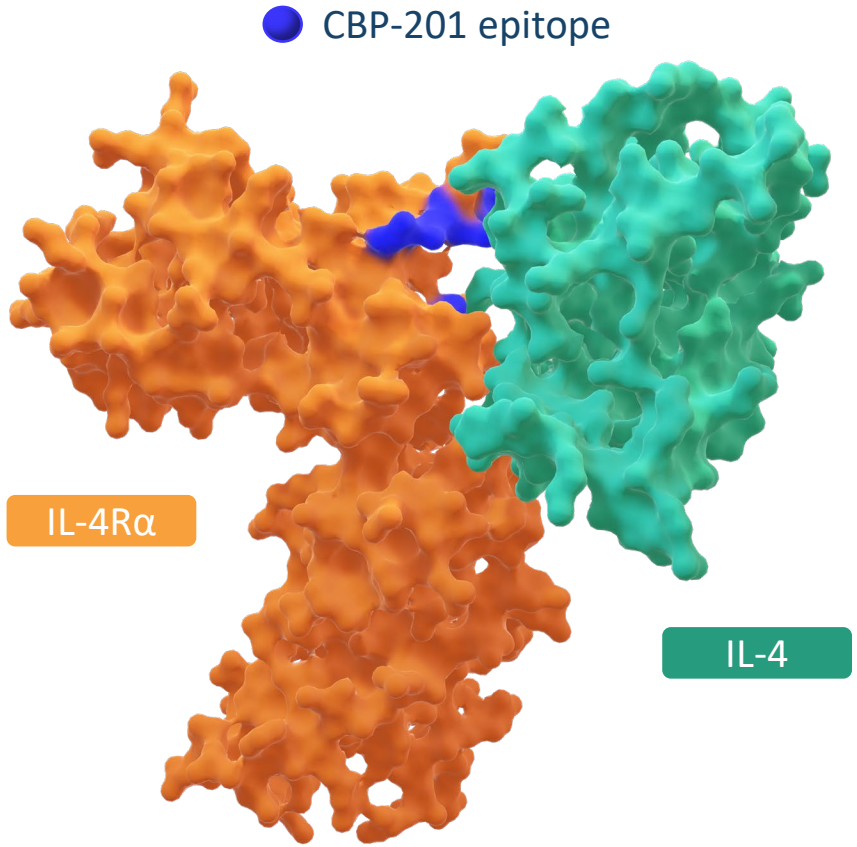
Background and Objective

Background

- CBP-201 is a next-generation mAb that binds to a distinct IL-4Rα epitope with higher affinity than dupilumab, inhibiting the actions of IL-4 and IL-13
  - CBP-201 has been shown to downregulate intracellular signaling *in vitro* and cytokine gene expression in human skin *ex vivo* with greater potency than dupilumab[1,2]
- In clinical trials of CBP-201 in adults with moderate-to-severe AD, including the global Phase 2 study:[3–6]
  - AD signs and symptoms decreased rapidly
  - AD improvements were gained with Q2W and Q4W dosing, generally without plateauing across 16 weeks of treatment
  - CBP-201 and placebo had similar, low incidence of TEAEs
- CBP-201 is being evaluated in CN002, a pivotal trial of patients with moderate-to-severe AD in China

Objective

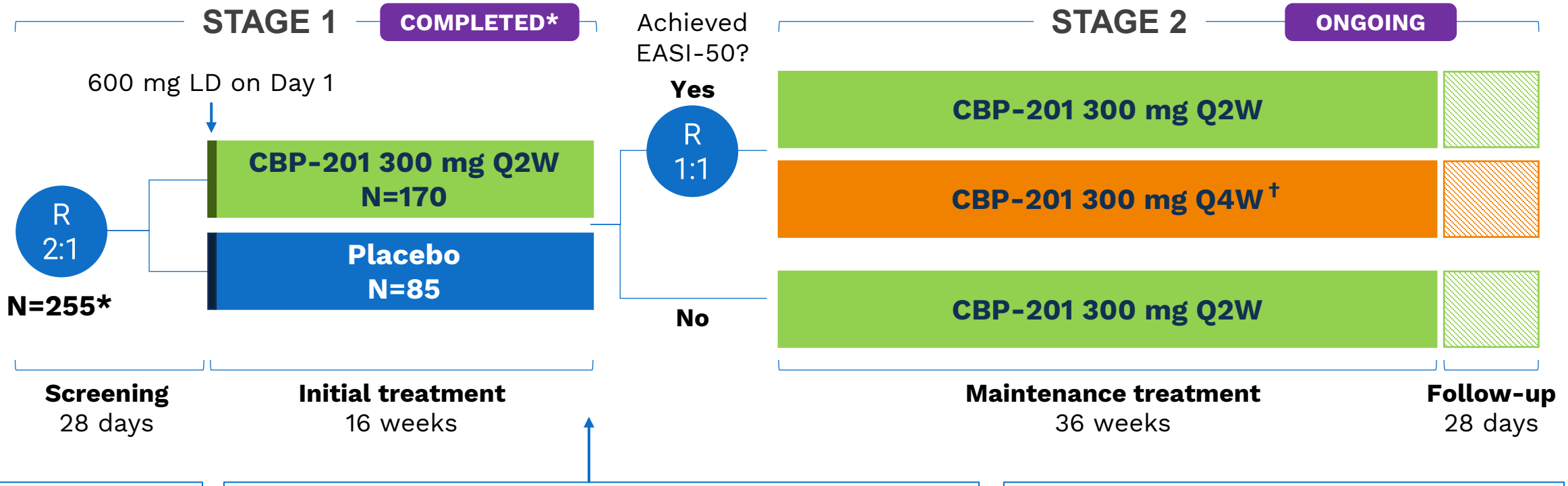
Here we report the primary and secondary efficacy outcomes and safety results at Week 16 from the primary analysis in CN002



References: 1. Yang et al. SID 2022, Portland, OR (Poster LB945). 2. Manuscript submitted. 3. Strober et al. Maui Derm 2022, Maui, HI. 4. Silverberg et al. Poster P0214 (Abstract 469), EADV 2022, Milan, Italy. 5. Strober et al. Poster P0215 (Abstract 470), EADV 2022, Milan, Italy. 6. Wang et al. Poster P0269 (Abstract 2647), EADV 2020, Vienna, Austria. ClinicalTrials.gov identifiers: NCT04444752 (WW001 trial), NCT05017480 (CN002 trial).
Abbreviations: AD, atopic dermatitis; mAb, monoclonal antibody; TEAE, treatment-emergent adverse events; Q2/4W, every 2/4 weeks.

Study Design of CN002

The primary and secondary endpoints, in patients with moderate-to-severe AD, occurred in Stage 1



Key inclusion criteria

- Age 18–75 years old*
- AD for ≥1 year
- IGA ≥3
- EASI ≥16
- BSA ≥10%
- PP-NRS ≥4

Primary efficacy endpoint at Week 16

- % of patients with IGA 0-1, and ≥2-point decrease from baseline

Secondary efficacy endpoints at Week 16

- % of patients achieving EASI-50/75/90
- % of patients achieving PP-NRS reduction ≥4 or ≥3
- % change in EASI, PP-NRS, and BSA
- Change in SCORAD, DLQI, and POEM

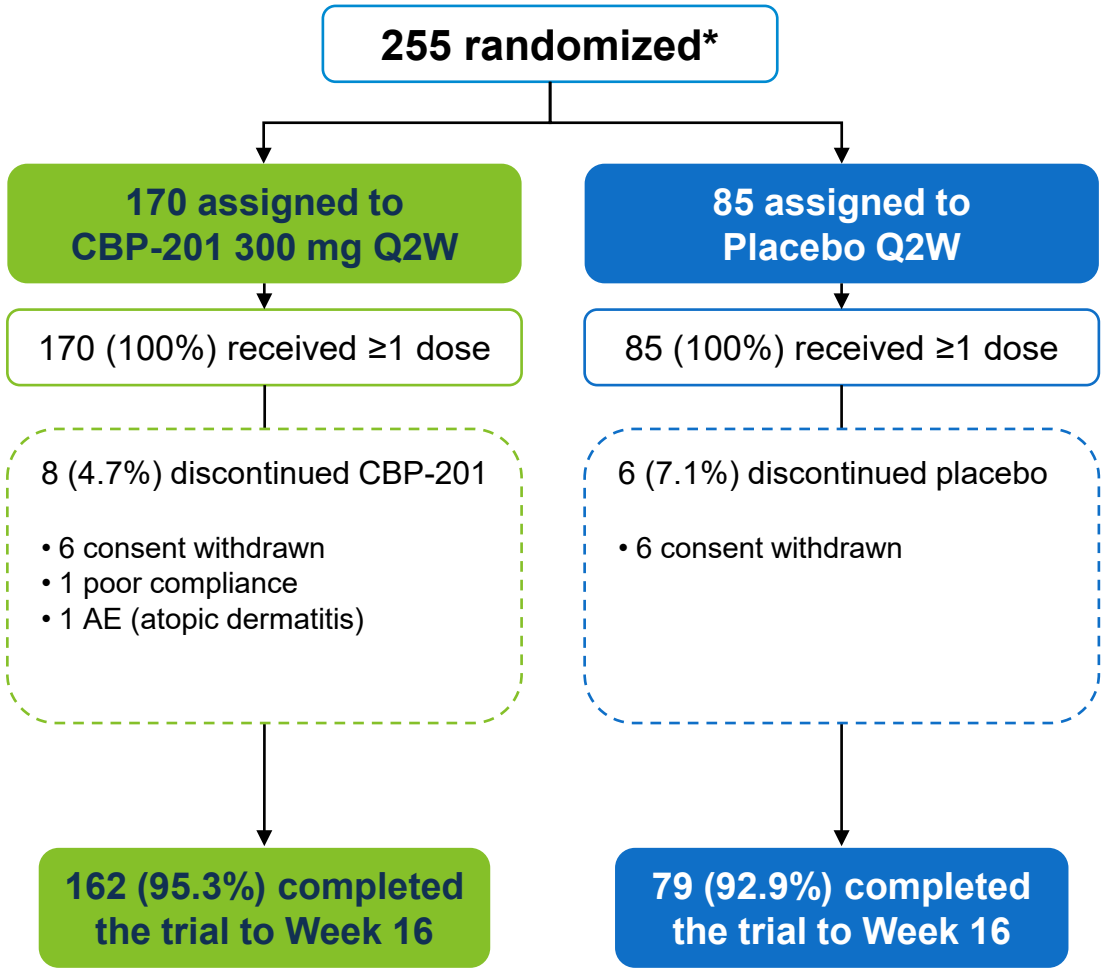
Statistics

- Binary endpoints were analyzed by Cochran-Mantel-Haenszel test, with missing data in the CBP-201 group imputed by jump to reference after applying the rule of intercurrent event; multiple imputation was used for placebo
- Continuous score changes were analyzed using Mixed-Effect Model for Repeated Measures

In the CBP-201 arms, each 2 mL subcutaneous injection contains 300 mg of CBP-201. *The primary analysis population (adults only). †To maintain blinding, all patients receive placebo between Q4W doses.
Abbreviations: AD, atopic dermatitis; BSA, Body Surface Area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-50/75/90, at least 50%/75%/90% decreases from baseline; IGA, Investigator Global Assessment; LD, Loading Dose; PP-NRS, Peak Pruritus Numeric Rating Scale; POEM, Patient Oriented Eczema Measure; Q2/4W, every 2/4 weeks; SCORAD, Scoring Atopic Dermatitis.

Patient Disposition in Stage 1

There was a high completion rate for Stage 1 of the CN002 trial



*The primary analysis population (adults only).

Abbreviations: AE, adverse event; Q2W, every 2 weeks.

Baseline Demographic and Disease Characteristics

All patients had moderate-to-severe AD and the treatment arms were well balanced

Characteristics*	CBP-201 N=170	Placebo N=85	Total N=255
Age (years) Mean (SD) Median (min, max)	 39.3 (16.1) 36.0 (18, 74)	 40.7 (17.5) 36.0 (18, 74)	 39.7 (16.5) 36.0 (18, 74)
Female, n (%)	57 (34%)	33 (39%)	90 (35%)
BMI (kg/m^2), Mean (SD) Median (min, max)	 23.9 (4.1) 23.6 (14.8, 47.1)	 25.0 (4.7) 24.6 (18.1, 46.9)	 24.3 (4.3) 23.9 (14.8, 47.1)
IGA, n (%) 3 (moderate) 4 (severe)	 78 (45.9%) 92 (54.1%)	 38 (44.7%) 47 (55.3%)	 116 (45.5%) 139 (54.5%)
EASI score, Mean (SD) Median (min, max)	 29.6 (11.9) 27.3 (16.0, 72.0)	 29.3 (12.0) 26.3 (16.0, 66.9)	 29.5 (11.9) 26.9 (16.0, 72.0)
BSA Percentage involvement Mean (SD) Median (min, max)	 48.7 (20.8) 44.3 (13.5, 100.0)	 48.4 (21.4) 45.0 (18.0, 100.0)	 48.6 (20.9) 44.5 (13.5, 100.0)
PP-NRS score Mean (SD) Median (min, max)	 7.2 (1.8) 7.0 (2, 10)	 7.0 (1.7) 7.0 (2, 10)	 7.1 (1.8) 7.0 (2, 10)
DLQI score Mean (SD) Median (min, max)	 15.9 (7.3) 16.0 (1, 30)	 15.6 (6.0) 14.0 (5, 30)	 15.8 (6.9) 15.0 (1, 30)

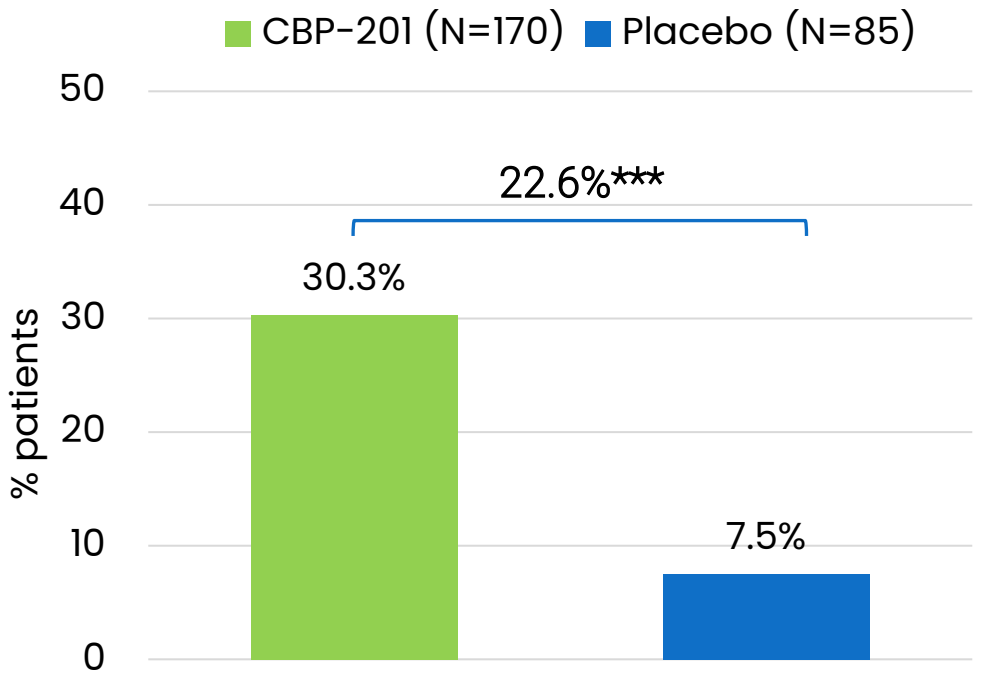
*The primary analysis population (adults only).

Abbreviations: AD, atopic dermatitis; BMI, body mass index; BSA, Body Surface Area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; PP-NRS, Peak Pruritus Numeric Rating Scale.

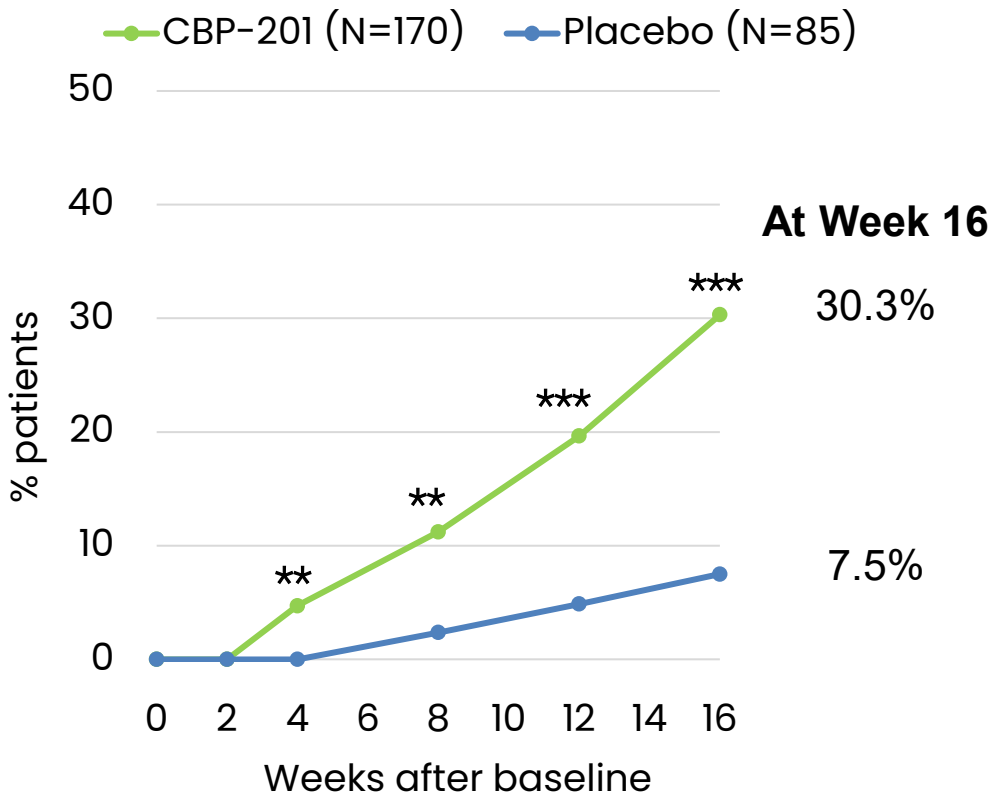
Primary Endpoint: IGA 0/1 and ≥2-Point Reduction at Week 16

IGA response was highly significant and continued to separate from placebo at Week 16

Primary Endpoint: IGA 0/1 and ≥2-point reduction at Week 16



Patients achieving IGA 0/1 with ≥2-point reduction by visit



Efficacy outcomes in the FAS

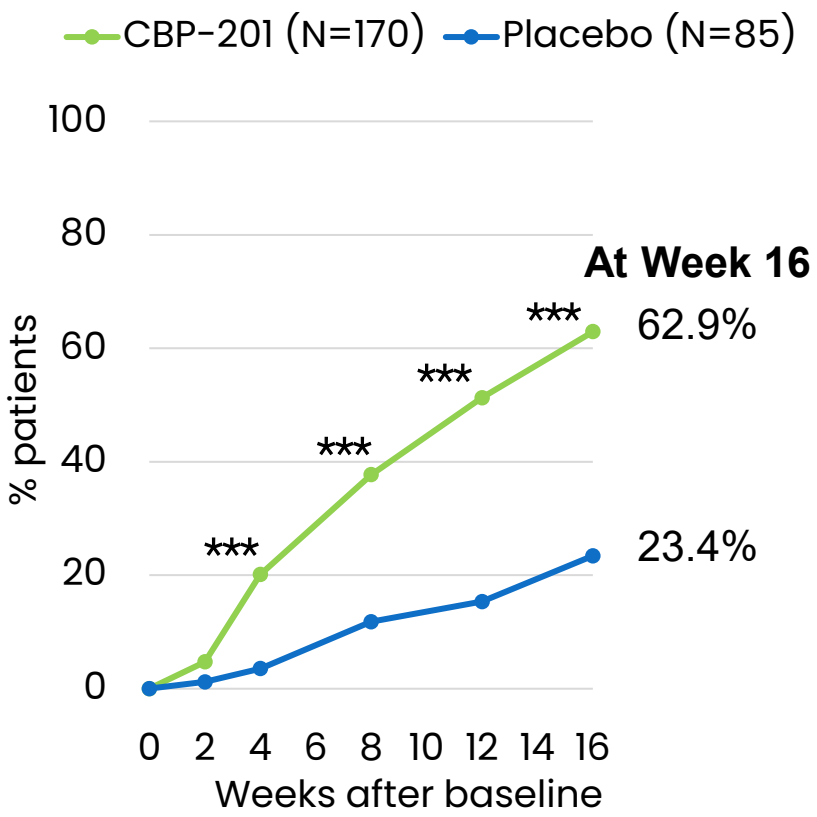
***P<0.001, **P<0.01 vs placebo. Binary endpoints were analyzed by Cochran-Mantel-Haenszel test. For binary analyses, missing data in the CBP-201 group was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm.

Abbreviations: FAS, Full Analysis Set; IGA, Investigator Global Assessment.

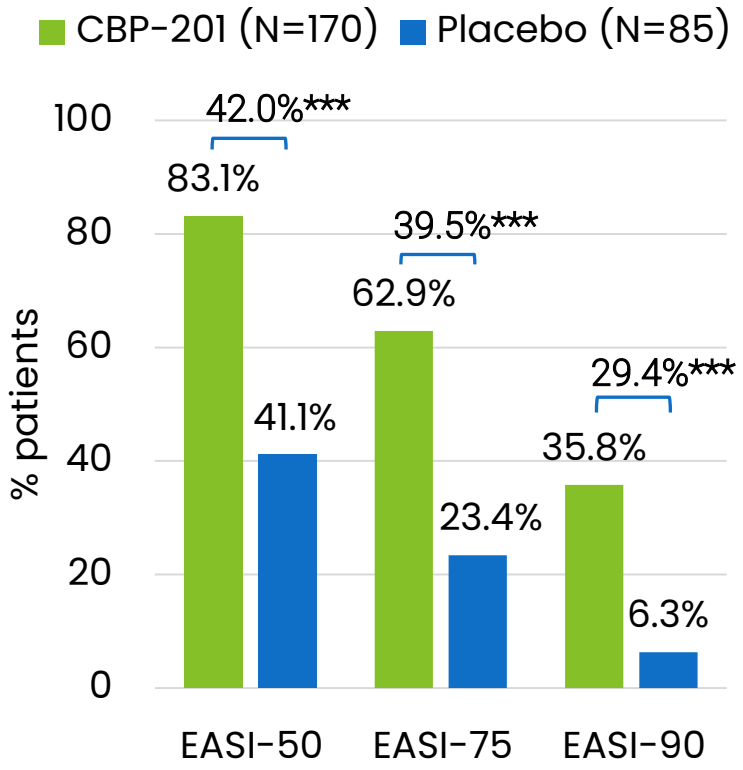
Secondary Endpoints: EASI Responses at Week 16

Significant improvements in EASI occurred at Week 2 and across all response categories at Week 16

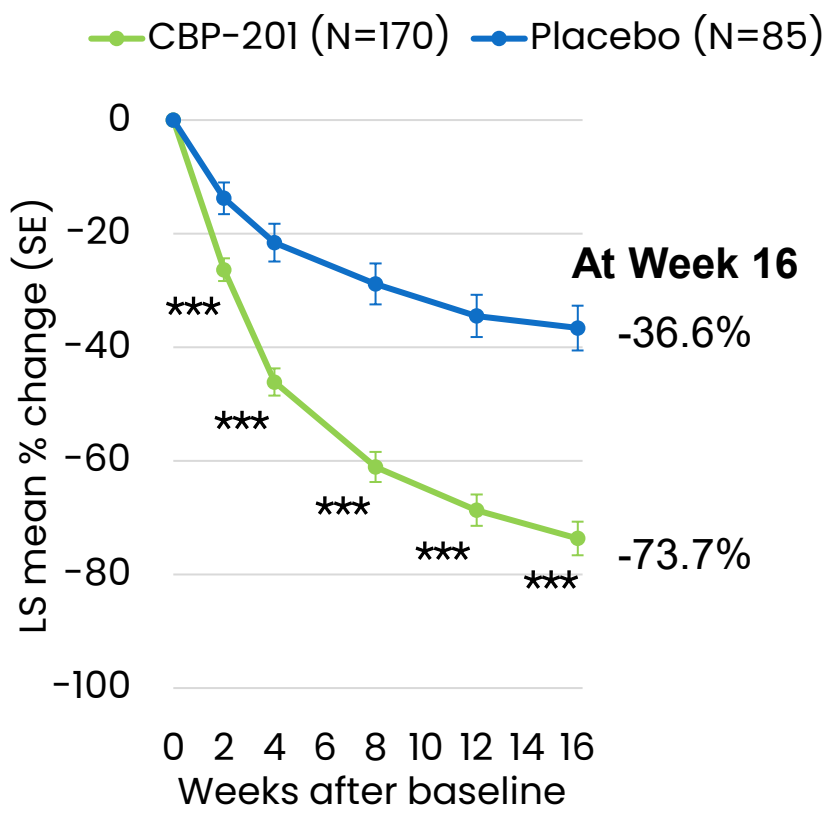
EASI-75 by visit



EASI-50, -75, -90 at Week 16



Change in EASI by visit



Efficacy outcomes in the FAS

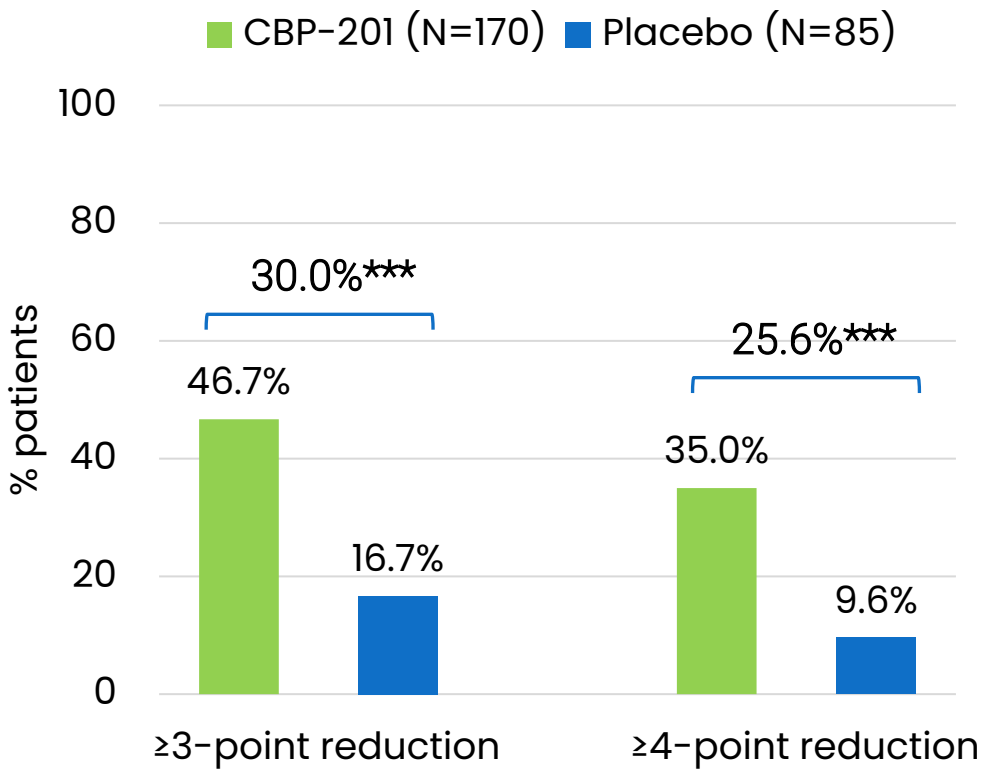
***P<0.001 vs placebo. Binary endpoints were analyzed by Cochran-Mantel-Haenszel test. For binary analyses, missing data in the CBP-201 group was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm. Continuous score changes were analyzed using Mixed-Effect Model for Repeated Measures.

Abbreviations: EASI, Eczema Area and Severity Index; EASI-50/75/90, at least 50%/75%/90% decrease from baseline in Eczema Area and Severity Index score; FAS, Full Analysis Set; LS, least squares; SE, standard error.

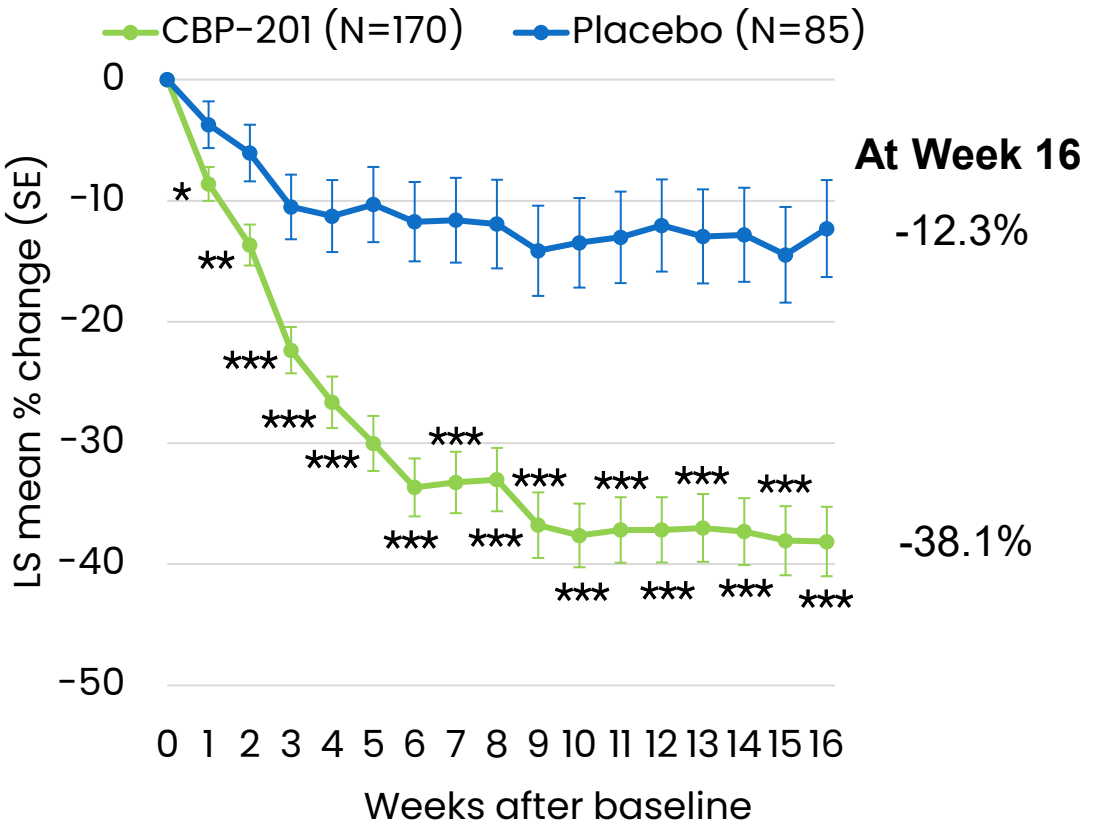
Secondary Endpoints: PP-NRS Responses at Week 16

CBP-201 demonstrated significant improvement in pruritus as early as Week 1

PP-NRS ≥3 or ≥4-point reduction at Week 16



Change in PP-NRS by visit



Efficacy outcomes in the FAS

***P<0.001, **P<0.01, *P<0.05 vs placebo. Binary endpoints were analyzed by Cochran-Mantel-Haenszel test. For binary analyses, missing data in the CBP-201 group was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm. Continuous score changes were analyzed using Mixed-Effect Model for Repeated Measures.

Abbreviations: FAS, Full Analysis Set; PP-NRS, Peak Pruritus Numerical Rating Scale; LS, least squares; SE, standard error.

Safety Results from Stage 1

CBP-201 was generally well tolerated with no new safety signals

Overview of TEAEs

n (%) Patients	CBP-201 N=170	Placebo N=85
Any TEAEs	125 (73.5%)	62 (72.9%)
TEAE related to study drug	54 (31.8%)	20 (23.5%)
Serious TEAEs (none were related to study drug)	1 (0.6%)	3 (3.5%)
Severe TEAEs (grade 3)	4 (2.4%)	5 (5.9%)
TEAEs leading to study drug discontinuation	1 (0.6%)	0
Herpes virus infection*	1 (0.6%)	1 (1.2%)

Serious TEAEs: meniscus injury, osteoarthropathy, and tendonitis in a patient receiving CBP-201; avulsion facture, humerus facture, gastric ulcer in 3 patients receiving placebo

Prespecified TEAEs of special interest

n (%) Patients	CBP-201 N=170	Placebo N=85
Conjunctivitis	8 (4.7%)	3 (3.5%)
Keratitis	2 (1.2%)	0
Anaphylaxis (mild, not related to study drug)†	1 (0.6%)	0
Injection site reactions lasting longer than 24 hours (all mild)	11 (6.5%)	0

Injection site reactions: mainly comprised of erythema, induration, and edema, and none led to discontinuation

None of the following TEAEs of special interest were observed: 'AST/ALT elevated >5×ULN', 'parasitic and opportunistic infections', 'pregnancy', 'symptomatic overdose'

*Other herpes TEAEs were: 'herpes simplex' (n=1 per treatment arm); 'herpes simplex reactivation' and 'oral herpes' (both n=1 in the CBP-201 arm); 'herpes zoster' (n=1 in the placebo arm). †The patient with anaphylaxis remained in the study and received study drug.

Abbreviations: TEAE, treatment-emergent adverse event.

Summary of CN002 Stage 1

- CN002 achieved all primary and secondary endpoints at Week 16 for the primary analysis population of adults with moderate-to-severe AD
- Clinical improvements in AD severity and extent as measured by IGA and EASI were observed without plateauing at Week 16 in patients receiving CBP-201
- Efficacy responses were rapid and sustained through to Week 16
- CBP-201 was well tolerated
  - Most TEAEs were mild to moderate in severity, and did not lead to study drug discontinuation
  - Safety and tolerability results were consistent with targeting the IL-4Rα pathway

Abbreviations: AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment.