CBP-201, a novel and differentiated IL-4Rα targeting antibody being evaluated in Th2 inflammatory diseases

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CBP-201 is a novel IgG4 targeting IL-4Rα. In a Phase 2b trial (WW001, NCT04444752), all three doses of CBP-201 met the primary endpoint in the treatment of moderate-to-severe atopic dermatitis (AD) with significant reductions in Eczema Area Severity Index scores observed at Week 16. Here, we report the first description of the immunological profile of CBP-201 from our in-house preclinical experiments, including all comparisons to dupilumab.

CBP-201 exhibited higher binding affinity (20.7 pM) to human IL-4Rα than dupilumab (45.8 pM), based on surface plasmon resonance. CBP-201 did not bind to monkey or mouse IL-4Rα. CBP-201 and dupilumab utilized distinct binding epitopes, as shown by amino acid mutation in human IL-4Rα and co-crystallization studies.

CBP-201 potently inhibited signaling of IL-4 and IL-13 in a cell-based STAT6 reporter assay (IC_{50} = 7.0 ± 2.5 and 6.6 ± 1.5 ng/mL, respectively) and significantly reduced IL-4 and IL-13 dependent TF-1 cell proliferation (IC_{50} = 8.0 ± 1.6 and 9.7 ± 0.8, respectively).

TARC/CCL17 is a known biomarker of AD inflammatory activity. CBP-201 inhibited IL-4 and IL-13 induced TARC production in activated human peripheral blood mononuclear cells (IC_{50} = 59.1 ± 1.2 and 13.6 ± 1.1, respectively). CBP-201 and dupilumab were similarly effective at reducing IL-4 and IL-13 mediated activation of primary human B-cells.

The *in vivo* efficacy of CBP-201 was profiled using an allergic inflammation model in transgenic mice expressing human IL-4Rα, and IL-4. CBP-201 reduced eosinophilic tissue infiltration ($p<0.0001$) and antigen-specific IgE ($p<0.0001$).

This is the first description of the immunological profile of CBP-201, demonstrating reductions in clinically validated biomarkers of Th2-driven inflammation. Additionally, we report distinct binding epitopes, higher binding affinity and increased potency demonstrating improved target engagement properties with CBP-201 compared to dupilumab. CBP-201 is under evaluation in AD (NCT04444752 and NCT05017480) and persistent asthma (NCT04773678).