**IMG-007, a nondepleting OX40 monoclonal antibody with an extended half-life, improves skin lesions in adults with moderate-to-severe atopic dermatitis: interim results from a phase 2a trial**

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**Introduction/Background:** OX40 is a costimulatory receptor primarily expressed by activated T cells and plays an important role in amplifying immunopathogenic responses in atopic dermatitis (AD). IMG-007 is a novel non-depleting anti-OX40 monoclonal antibody (mAb) bioengineered to abolish the antibody-dependent cellular cytotoxicity (ADCC) function while retaining potent inhibition of OX40/OX40L signaling. A single dose of IMG-007 at up to 600 mg was well tolerated in healthy adults with no reports of pyrexia or chills. IMG-007 also demonstrated a slow antibody clearance and an extended half-life with a potential to be dosed every 12 weeks (Q12W) in AD patients.

**Objectives:** This Phase 2a study is the first to evaluate safety and efficacy of a non-depleting OX40 mAb in moderate-to-severe AD patients. The objective is to demonstrate that blocking OX40 without depleting T cells results in good clinical safety and efficacy.

**Methods:** This open-label study enrolled adult patients with moderate-to-severe AD, defined as body surface area (BSA) ≥10%, investigator global assessment (IGA) ≥3, and eczema area and severity index (EASI) ≥16. Patients were to receive three intravenous infusions of 300 mg IMG-007 at baseline, Week 2, and 4 and be followed up for up to 24 weeks. Topical or systemic AD medications were prohibited during the study. Key endpoints included safety and efficacy as measured by EASI, IGA, BSA, and SCORing atopic dermatitis (SCORAD) index.

**Results:** A total of 13 patients were enrolled from 6 centers in the U.S. and Canada, which included 4 (30.8%) women, 9 (69.2%) men; mean age 49.8 years (standard deviation [SD] 15.0]). Mean disease duration was 29.6 years (SD 19.8) and 8 (61.5%) patients had IGA score of 3 at baseline. Mean baseline EASI score was 29.5 (SD 13.7), affected BSA was 52.0 (SD 25.5), SCORAD score was 71.7 (SD 10.6). Three (23.1%) patients received prior biologics or Janus kinase inhibitors. As of an interim data cutoff of April 1, 2024, all patients in the study had completed at least the Week 16 visit. Overall, IMG-007 was well-tolerated. A total of 9 (69.2%) patients reported treatment-emergent adverse events (TEAEs). All AEs were of mild or moderate intensity, except for one patient with erythrodermic AD who experienced a
severe AE of AD flare. There were no serious adverse events (SAEs), treatment-related AEs, and no pyrexia or chills. After treatment with IMG-007, there was a rapid improvement in the extent (per BSA) and severity (per EASI and SCORAD) of skin lesions with continued improvement sustained through Week 24. The mean percent reduction from baseline in BSA involved was 56%, 56%, and 66% at Week 12, 16, and 20, respectively. For the SCORAD index, the mean percent reduction from baseline was 34%, 30%, and 42% at Week 12, 16, and 20, respectively. Similar trend was noted based on mean percent reduction from baseline in EASI score (68%, 77%, and 87% at Week 12, 16, and 20, respectively).

**Conclusions:** IMG-007 was safe and well tolerated without any reports of pyrexia or chills in patients with moderate-to-severe AD. Treatment with IMG-007 for a short duration of 4 weeks resulted in a rapid and sustained improvement in the extent and severity of AD suggesting that blocking OX40 without depleting T cells could optimize potential benefit/risk profile in the long-term disease management in AD patients.

**Keywords:** OX40, IMG-007, efficacy, safety, atopic dermatitis, biologics