Efficacy and safety of amlitelimab (an anti-OX40 ligand antibody) in patients with moderate-to-severe atopic dermatitis: 24-week results from a Phase 2b trial (STREAM-AD)

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Introduction/Background: Targeting and binding OX40 ligand (OX40L) expressed on antigen-presenting cells may inhibit the persistent immune response that drives atopic dermatitis (AD) pathophysiology. Amlitelimab (SAR445229; KY1005) is a potential first-in-class, fully human, non-depleting anti-OX40L monoclonal antibody that blocks OX40L-OX40 interactions and has shown efficacy and an acceptable safety profile in a Phase 2a trial in adults with moderate-to-severe AD. Here, we present 24-week efficacy and safety results (Part 1) from an ongoing dose-ranging Phase 2b trial. The study remains blinded to individual patient data (Part 2 ongoing).

Objectives: To evaluate the efficacy and safety of amlitelimab in adults with moderate-to-severe AD.
**Methods:** STREAM-AD (NCT05131477) is a 52-week, randomised, double-blinded, placebo-controlled Phase 2b monotherapy trial. This study is designed with 2 parts (double-blind throughout): a 24-week treatment period (Part 1, completed and presented here) and a 36-week maintenance/withdrawal period (Part 2, ongoing). Adults (18 to <75 years; n=390) with moderate-to-severe AD were randomised 1:1:1:1:1 to receive subcutaneous amlitelimab Q4W (250 mg with 500 mg loading dose [LD], n=77; 250 mg without LD, n=78; 125 mg without LD, n=77; or 62.5 mg without LD, n=79) or placebo Q4W (n=79). The primary endpoint was percentage change in Eczema Area and Severity Index (EASI) from baseline at Week 16. Key secondary endpoints included percentage change in EASI at Week 24 and percentage of patients with at least 75% reduction from baseline in EASI (EASI-75), percentage of patients with Investigator Global Assessment response of 0 (clear) or 1 (almost clear) and a reduction from baseline of ≥2 points (IGA 0/1), and proportion of patients with a weekly average reduction of Peak Pruritus Numerical Rating Scale (PP-NRS) ≥4 points from baseline. The primary efficacy analysis included all randomised patients who completed Week 24 or discontinued treatment or study prior to Week 24 visit (n=390), whereas the safety analysis included all treated patients (n=388).

**Results:** Treatment with amlitelimab resulted in statistically significant improvements in percentage change in EASI from baseline to Week 16 compared to placebo for all four doses studied. The 250 mg with LD group had the numerically highest response versus placebo at Week 16, with a least-squares mean change from baseline of −32.1% (95% CI: −43.9, −20.3; P<0.0001); the remaining groups without LD had the following responses versus placebo: 250 mg, −27.3 (95% CI: −39.1, −15.6; P<0.0001); 125 mg, −22.2 (95% CI: −34.0, −10.4; P=0.0002); and 62.5 mg, −30.2 (95% CI: −41.9, −18.5; P<0.0001). There were also clinically meaningful improvements in all key secondary efficacy outcome measures, with all amlitelimab dose groups demonstrating nominally significant (P<0.05) efficacy versus placebo for EASI-75, IGA 0/1, and PP-NRS ≥4, except 250 mg (no LD) in IGA 0/1 at Week 16 (P=0.0562). Continued
improvements were generally observed through Week 24 in primary and key secondary efficacy outcomes. Amlitelimab was well tolerated across all dose groups, with no safety concerns identified.

**Conclusions:** In this dose-ranging Phase 2b trial of amlitelimab in adults with moderate-to-severe AD, amlitelimab demonstrated clinically meaningful efficacy over 24 weeks with an acceptable safety profile across all four dose groups.

**Keywords:** Monoclonal antibody, anti-OX40L, Phase 2b, biologic therapy, dose-ranging

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