Phase 2 Trial in Progress— Lirentelimab in Adults with Moderate-to-Severe Atopic Dermatitis Inadequately Controlled by Topical Treatments

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BACKGROUND: Atopic dermatitis (AD) is a chronic pruritic inflammatory dermatitis that affects approximately 16.5 million (7.3%) adults in the US, of which around 6.6 million (40%) have moderate-to-severe disease. The current standard of care includes topical treatments supplemented with corticosteroids with and without immunosuppressants. Patients with AD inadequately controlled by topical treatments and immunosuppressants are often treated with biologics and/or JAK inhibitors. Some patients do not have an adequate clinical response or are unable to tolerate these treatments prompting the need for novel therapies.

STUDY RATIONALE: Mast cells (MCs) and eosinophils (eos) are implicated in the pathogenesis of AD. Sialic acid-binding Ig-like lectin (Siglec)-8 is expressed selectively on MCs and eos; engagement with an antibody results in broad inhibition of MC activation and eos depletion. Lirentelimab (AK002) is a humanized, nonfucosylated IgG1 monoclonal antibody that binds specifically to Siglec-8. Preclinical data demonstrates that lirentelimab can broadly inhibit multiple modes of mast cell stimulation that drive AD pathogenesis. Lirentelimab, administered every 4 weeks as an infusion (IV), has been tested in over 600 healthy volunteers and patients with inflammatory and allergic diseases; in those with concomitant AD, improvements in AD were observed. Overall, lirentelimab IV has been well-tolerated; the most common AE being infusion related reactions (IRRs) typically associated with the initial infusions. In a phase 1 study, a subcutaneous (SC) formulation of lirentelimab was well-tolerated with no IRRs. The results of these studies provide a strong rationale for conducting this phase 2 proof-of-concept, randomized, double-blind, placebo-controlled study of lirentelimab SC in adults with moderate–severe atopic dermatitis inadequately controlled by topical treatments (NCT05155085, “ATLAS”).

KEY INCLUSION/Criteria: Adults (18-80 years) are eligible for screening if they have had chronic AD presented for ≥3 years with moderate-to-severe symptoms defined as: Eczema Area and Severity Index (EASI) score ≥16, involvement of ≥10% of the Body Surface Area (BSA), and Investigator Global Assessment (IGA) score ≥3, documented recent history of inadequate response to treatment with medications such as topical corticosteroids, calcineurin inhibitors, JAK inhibitors, or PDE4 inhibitors (crisaborole), and biologic-naïve or biologic-exposed (secondary loss of response, intolerance, or lack of access). The complete list of inclusion/exclusion criteria will be presented.
**STUDY DESIGN:** 130 patients will be randomized 1:1 to receive either 7 SC injections of 300mg lirentelimab or placebo every two weeks and then followed for 12 weeks after the last dose. The primary endpoint is the proportion of patients who achieve EASI-75 at week 14 (2 weeks after last dose) compared with baseline. All patients who receive study medication will be included in the safety analysis. Secondary endpoints include percent change in EASI at week 14 from baseline and proportion of patients with IGA of 0 or 1 and a 2-point improvement at week 14 compared to baseline. Patients who complete the study (day 99 visit of double-blind period) will be given the option to enroll in an open-label extension (OLE) for 7 doses of 300mg lirentelimab SC for 12 weeks. Qualified participants will receive medication, lab tests and medical care related to the study at no cost.

**STUDY SITES:** This study is currently enrolling in the USA and Germany. Please visit clinicaltrials.gov (NCT05155085) or email atlas.info@allakos.com to learn more about this study.

**Figure:** ATLAS, Phase 2 AK002-018, Study Design (Without Open Label Extension)