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Demonstration of Early Proof-of-Concept for STAR-0310, a Long-Acting OX40 Receptor Antagonist: Initial Safety, PK, and PD Results from a Phase 1a Trial

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Introduction

OX40 (CD134) is a co-stimulatory receptor expressed on activated T cells and implicated in sustaining pathogenic T cell responses in immunologic diseases. Therapeutic blockade of the OX40–OX40L axis has emerged as a promising approach for treating chronic diseases, such as atopic dermatitis, by modulating immune-mediated inflammation and tissue damage. STAR-0310 is a novel, investigational, subcutaneously (SC) administered Fc-engineered monoclonal antibody targeting the OX40 receptor. It incorporates a YTE-modified Fc domain to extend half-life and is designed to reduce antibody-dependent cellular cytotoxicity (ADCC) to minimize adverse immune activation. This is a report of initial results from an ongoing first-in-human, randomized, double-blind, placebo-controlled Phase 1a trial (NCT 06782477) that is evaluating the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of single ascending doses in healthy adult participants.

Materials and Methods

Eligible participants were healthy males and non-pregnant females aged 18–60 years, screened by medical history, physical exam, and laboratory testing. All participants were enrolled at a single clinical site under IRB approval and informed consent. A total of 32 subjects were randomized (3:1) to receive a single SC dose of STAR-0310 or placebo across four dose cohorts: 150, 300, 600, and 1200 mg. Blood samples were collected at predefined time points for STAR-0310 PK and exploratory PD biomarkers.

Results

Initial results show STAR-0310 was well-tolerated at all the dose levels, with no serious treatment-emergent adverse events (TEAEs) or discontinuations. Mild, treatment-related TEAEs were observed in 7/24 (29.2%) participants receiving STAR-0310, with injection site reactions being the most frequently reported (4/24, 16.6%). No fevers or chills were observed, supporting the preclinical observation that STAR-0310 exhibits low ADCC activity. STAR-0310 exhibited dose-proportional increases in serum concentrations, with slow clearance and an extended half-life of up to approximately 68 days (range 60-78 at the 600 mg dose). Receptor occupancy (RO) data showed rapid and sustained peripheral target engagement, with >90% mean RO achieved immediately and maintained through the follow up time points for 300-1200 mg dose levels. Exploratory biomarker data indicated deep (~50-90%) and durable *ex vivo* cytokine inhibition (IL-2, IL-31, IL-4) supporting target modulation and suggesting that STAR-0310 may modulate a broader spectrum of immune

pathways beyond classical Th2-driven responses.

Conclusion

STAR-0310 is a potential best-in-class, T-cell sparing, immunomodulating OX40 antagonist designed to have a long half-life. Based on the initial results from this trial, STAR-0310 was well-tolerated, with no ADCC-related TEAEs. Preliminary PK and PD exhibited sustained target therapeutic effect for at least 3 months following a single dose, demonstrating early proof of concept for a long-acting differentiated OX40 receptor antagonist. These findings support the potential for infrequent maintenance dosing, including the possibility of dosing intervals as long as every 6 months, which may enhance adherence and reduce the treatment burden for patients with chronic inflammatory diseases, including atopic dermatitis and other immune-mediated diseases.