MEDICAL THERAPIES AND PHARMACOLOGY

KY1005 AN ANTI-OX40L MAB WITH POTENTIAL IN ATOPIC DERMATITIS (AD) RESULTS OF A PHASE 1 STUDY ASSESSING THE SAFETY, PHARMACOKINETICS, AND T-CELL-DEPENDENT ANTIBODY RESPONSE (TDAR) IN HEALTHY VOLUNTEERS

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Introduction: KY1005 is a human non-depleting monoclonal antibody blocking OX40L interaction with OX40 expressed on activated T cells. OX40L is a co?stimulatory molecule, inducibly expressed on antigen?presenting cells. This pathway stimulates Teff and suppresses Treg with enhancement of the Th2 response, prolonging the inflammatory response. OX40/OX40L expression is upregulated in AD skin.

Objectives: The primary objective of this Phase I dose escalation study was to evaluate the safety/ tolerability of KY1005 in healthy subjects. Additional objectives included characterisation of the primary TDAR to keyhole limpet hemocyanin (KLH) neoantigen, the recall response to tetanus toxoid (TT), and PK of KY1005.

Materials and Methods: 64 subjects, recruited across 3 Single-Ascending-Dose cohorts and 5 Multiple-Ascending-Dose (MAD) cohorts (6:2 active vs. placebo ratio). MAD cohorts received a loading dose and 2 additional doses (50% of the loading dose). Subjects were followed for up to 16 weeks. In the MAD cohorts the primary (KLH) and recall (TT) TDAR was analysed by serum IgG and IgM three weeks after the challenge. KY1005 concentrations were assessed throughout.

Results: No deaths, SAEs, severe hypersensitivity or severe injection site reactions occurred. One hypersensitivity reaction localised to the throat/mouth occurred during the

first infusion at the top dose, 12mg/kg. This resolved without intervention. KY1005 showed inhibition of the primary IgG and IgM at doses 0.45mg/kg and above. Changes in recall titres were also observed. Half-life ranged between 17 and 28 days, with no dose?related trend.

Conclusions: KY1005 demonstrated an acceptable safety/tolerability profile. Suppression of primary and recall TDAR demonstrates KY1005 is pharmacologically active at doses ≥0.45mg/kg. The PK of KY1005 was predictable supporting the use of once monthly dosing. These results support the continued development of KY1005 in immune mediated diseases such as AD. A phase 2a study of KY1005 in AD is ongoing.