PRECLINICAL ACTIVITY AND GLP SAFETY TOXICOLOGY DATA AHEAD OF PHASE 1 INITIATION OF IGNX001 IN PEANUT ALLERGY

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Introduction: A significant hurdle to the adoption of current peanut allergy treatments is the long time to achieve effect: 3-4 months for anti-IgE and 6+ months for oral immunotherapy. Consequently, peanut allergic individuals would greatly benefit from an alternative that would provide protection within days, be administered less frequently, and avoid the adverse events and other challenges associated with repeated allergen exposure. Based on the established role of allergen-specific IgG4 as a blocking antibody, we sought to develop an IgG4-based antibody therapeutic with high affinity and specificity to immunodominant epitopes on allergens driving peanut allergy.

Method: We re-engineered high affinity IgE antibodies discovered from peanut allergic individuals using single-cell RNA-sequencing into peanut-specific IgG4 blocking antibodies. After antibody selection and engineering, the final IgG4-based therapeutic candidate, IGNX001, was evaluated in mast cell activation tests and an orally sensitized, orally challenged mouse model of peanut allergy. Additionally, we evaluated IGNX001 in a Good Laboratory Practice (GLP) cynomolgus monkey cardiovascular respiratory safety study and a GLP repeat-dose rat toxicology study.

Results: On average, IGNX001 inhibited over 80% of peanut-mediated mast cell activation after cells were separately sensitized with 19 individual peanut allergic plasmas. In the peanut allergy mouse model, IGNX001 dose-dependently abrogated anaphylaxis and reduced mast cell protease 1 (MCPT-1) release down to levels not statistically different from unsensitized animals at a dose of 5 mg/kg. No effects of IGNX001 on any of the evaluated safety pharmacology parameters were observed in cynomolgus monkeys and IGNX001 was well tolerated with low severity/transient injection site reactions after 5 doses at up to 48X the maximal human dose in the repeat-dose rat toxicology study.

Conclusion: IGNX001 demonstrated potent inhibition of peanut-induced, IgE-mediated mast cell degranulation and abrogated anaphylaxis and mast cell protease release in a peanut allergy mouse model two days after subcutaneous injection. These activity data, coupled with favorable safety toxicology data, warrant further investigation of IGNX001 in humans.