Title: IGNX001 Inhibits Peanut-Mediated Mast Cell Activation in a Translational Spike-In Assay

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Background

Cell-based assays using mast cells or basophils are increasingly employed in allergy diagnosis and the evaluation of potential inhibitors of degranulation. However, these assays are often difficult to perform reproducibly due to blood collection logistics, cell growth rates, receptor expression, or other factors. Murine Hoxb8 mast cells transgenic for the human FcεRIα have shown promise in overcoming these challenges. We sought to use these cells to develop a translational mast cell activation test (MAT) for evaluating IGNX001, a peanut-specific IgG4 antibody-based therapeutic for peanut allergy.

Methods

Plasmas were collected from demographically varied peanut allergic donors from across the United States. Total IgE, peanut specific IgE (psIgE), and Ara h component IgE titers were measured for all plasmas. A translational assay was developed in which Hoxb8 mast cells were first sensitized with peanut allergic plasma spiked with a half-log titration series of IGNX001. Then, without washing, cells were challenged with whole peanut flour protein and degranulation was assessed by flow cytometry.

Results

Seventeen plasmas used in the assay were selected based on high psIgE titer (42 - 517 kUA/L, median 119 kUA/L) with varied Ara h component titers in order to represent a challenging cohort for inhibition. IGNX001 demonstrated concentration-dependent shifts in EC50 and/or suppression of maximal cellular activation. Concentrations at which these effects occurred overlapped with those achievable by reasonable clinical doses administered subcutaneously.

Conclusions

A preclinical translational spike-in MAT was developed to recapitulate the time dependent concentration of an IgG4-based antibody therapeutic in circulation. IGNX001, which competitively inhibits IgE interaction with allergen, demonstrated potent inhibition of cellular activation and provided a case study of how this assay could serve as a valuable pharmacodynamic marker in clinical trials.