TRPH-222, a Novel Anti-CD22 Antibody Drug Conjugate (ADC), Has Significant Anti-Tumor Activity in NHL Xenografts and Reduces B-Cells in Monkeys

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INTRODUCTION

- CD22 is a B-cell specific transmembrane protein with expression restricted to mature B-cells. It is overexpressed on a wide range of B-cell malignancies including NHL (non-Hodgkin lymphoma), FL (follicular lymphoma), DLBCL (diffuse large B-cell lymphoma), MCL (mantle cell lymphoma) and MZL (marginal zone lymphoma)
- The restricted lineage of CD22 and rapid internalization upon antibody binding make CD22 an appealing target for an antibody-drug conjugate (ADC) therapeutic for B-cell malignancies
- SMARTAg™ site specific non-cleavable conjugation enforces a maximum drug to antibody ratio (DAR) of 2 with high stability, enabling improved therapeutic index

TRPH-222 SMARTag™ ADC

- TRPH-222 is an anti-CD22 antibody site-specifically modified at one site in each heavy chain to express formylglycine (FG), allowing site-specific conjugation of a maytansinoid payload, a protease-insensitive spacer, and a functional group for coupling to an aldehyde on the antibody FG residues

RESULTS

- TRPH-222 Has Significant Anti-Tumor Activity in B-Cell Lymphoma Xenografts
- TRPH-222 was well tolerated with no body weight loss
- Dose- and schedule-dependent TRPH-222 anti-tumor activity, with tumor regression observed in large, more established xenografts

CONCLUSIONS

- TRPH-222 has significant anti-tumor activity in a range of NHL xenograft models and reduced normal B-cells in vivo in monkeys
- Very high doses of TRPH-222 were well tolerated in both monkeys and rats supporting an improved therapeutic index. Doses described herein correspond to human equivalent doses significantly higher than for most ADCs approved or currently in development

Study Aims

- Characterize the anti-tumor activity of TRPH-222 in human NHL xenograft models
- Evaluate the B cell depletion and tolerability of TRPH-222 in cynomolgus monkeys

To our knowledge, this represents the highest well-tolerated dose of a maytansinoid-containing ADC in primates, suggesting potential for best-in-class therapy in NHL

A Phase 1 study evaluating TRPH-222 in relapsed/refractory NHL is planned for Q3 2018