Title: Final Results of a Placebo Controlled, Phase 2 Multicenter Study of Ublituximab (UTX), a Novel Glycoengineered Anti-CD20 Monoclonal Antibody (mAb), in Patients with Relapsing Forms of Multiple Sclerosis (RMS)

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OBJECTIVE: To assess the optimal dose and infusion time as well as safety/tolerability of ublituximab (UTX) treatment in RMS.

BACKGROUND: UTX is a novel mAb targeting a unique epitope on the CD20 antigen and glyco-engineered for enhanced B cell targeting through antibody-dependent cellular cytotoxicity (ADCC). The greater ADCC potency of UTX may offer a benefit over currently available anti-CD20s in terms of lower doses and shorter infusion times.

DESIGN/METHODS: TG1101-RMS201 is a Phase 2, placebo-controlled, multicenter study designed to assess the optimal dose and infusion time of UTX in RMS subjects. All subjects, including placebo subjects (post 4-week placebo phase), received 3 UTX infusions on Days 1, 15, and Week 24 and were then followed for 48 weeks. Optimal dose and infusion time was determined by comparing the efficacy of B cell depletion and safety/tolerability between 6 dosing cohorts (450mg or 600mg at infusion times from 1 - 4 hours). MRI and clinical efficacy analyses were also performed.

RESULTS: A total of 48 subjects were enrolled in the study. Median B cell depletion was >99% at the primary analysis point of Week 4, and maintained at Week 24 (n=44) and Week 48 (n=22), with no significant differences in B cell depletion by cohort. Interestingly, T cells showed a significant population shift toward naïve and regulatory phenotypes. T1-Gd enhancing lesions were reduced to zero (100% reduction) at Week 24 (n=44, baseline mean=3.80, p=0.003), and maintained at Week 48 (n=22, baseline mean=2.86, p=0.0004). An 8% decrease in mean T2 lesion volume was observed at Week 24 (n=44, p=0.004), and a 10% decrease was observed at Week 48 (n=22, p=0.016), compared to baseline. An Annualized Relapse Rate (ARR) of 0.07 was observed for all patients. No evaluable subjects demonstrated sustained disability progression. No severe adverse events (AEs) were reported. The most common AEs were infusion related reactions (all grade 1-2), which showed no increase in incidence with faster infusion times.

CONCLUSIONS: In this study, subjects treated with UTX, a novel glycoengineered anti-CD20 antibody showed rapid and robust B cell depletion, a profound reduction in MRI activity, suppression of relapses, and clinical stability. Moreover, UTX can be safely delivered in infusions as fast as 1 hour. Final results from all 48 subjects through Week 48 are anticipated to be available for the final presentation.