Title: 6 Month Results of a Phase 2a Multicenter Study of Ublituximab, a Novel Glycoengineered Anti-CD20 Monoclonal Antibody, in Relapsing Multiple Sclerosis

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OBJECTIVE: To assess the safety, B-cell depletion dynamics, and clinical efficacy of UTX in RMS patients. **BACKGROUND:** UTX is a novel glycoengineered mAb targeting a unique epitope on the CD20 antigen to enhance affinity for all variants of FcγRIIIa receptors, demonstrating greater antibody-dependent cellular cytotoxicity activity (ADCC) than rituximab. The enhanced ADCC potency may offer a benefit over currently available anti-CD20s in terms of lower doses and shorter infusion times. **DESIGN:** TG1101-RMS201 is a 52-week, phase 2, placebo-controlled, multicenter study that is designed to assess the optimal dose and infusion time and safety/tolerability of UTX in RMS subjects. Subjects are randomized to UTX or Placebo for 28 days, encompassing the first two infusions on Day 1 and Day 15. Optimal dosing is determined by B-cell depletion, defined as percentage of $CD19^{+}$ B-cells present following UTX administration. Radiological and clinical analyses are also performed. **RESULTS:** To date, B-cell data from 20 subjects have been analyzed up to Week 24 of the 52-week study, encompassing two UTX infusions. At Week 4, median B-cell depletion was 99% from baseline in UTX treated subjects and maintained to Week 24. Zero relapses have been reported during the first 24 weeks. Mean EDSS at baseline was 2.7 (±1.3) and at Week 24 the Mean EDSS was 1.9 (±1.5) with a change of -0.8. Zero Gd lesions were found at Week 24. Most commonly reported AEs were infusion related reactions (Grade ≤2). Faster infusion times, as low as 1-hour for 450mg UTX, did not result in an increased frequency of IRRs. **CONCLUSIONS:** Ublituximab, a novel glycoengineered anti-CD20 antibody, demonstrates rapid and robust B-cell depletion, a profound reduction in Gd enhancing lesions, with clinical stability observed at Week 24. Unlike other IV administered anti-CD20s, UTX is delivered in shorter infusions, providing a potential convenience benefit for future patients.