Pompe disease is caused by mutations in the gene that encodes the lysosomal enzyme α-glucosidase, which is required for the degradation of glycogen, a storage molecule in muscle and other tissues. The loss of this enzyme activity results in accumulation of glycogen and leads to tissue damage.

**Introduction**

Pompe disease is treated with recombinant human α-glucosidase (rhGAA), which is given by intravenous infusion. rhGAA provides symptomatic benefit, improves survival, and decreases the risk of cardiac complications. However, the need for frequent infusions and the associated logistics and costs can be significant for patients and families.

**Objectives**

- To evaluate the safety and efficacy of single ascending oral doses of AT2220 administered 1 hour prior to IV infusion of rhGAA in patients with Pompe disease.
- To evaluate the effect of single ascending oral doses of AT2220 on the plasma pharmacokinetics of rhGAA.
- To evaluate the concentration of AT2220 in skeletal muscle on Day 3 following a single dose of AT2220.
- To evaluate the impact of AT2220 co-administration with rhGAA on the pharmacokinetics of rhGAA and muscle α-glucosidase activity.

**Study Design and Methods**

AT2220-010 is an ongoing, open-label, non-randomized, fixed-sequence, single ascending dose study involving 4 to 6 patients per cohort. Each period is separated by a minimum 14-day rhGAA dosing interval. AT2220-010 is an ongoing, open-label, non-randomized, fixed-sequence, single ascending dose study involving 4 to 6 patients per cohort. Each period is separated by a minimum 14-day rhGAA dosing interval.

**Preliminary Results**

Preliminary results are available for Cohorts 1 and 2 (50 mg and 100 mg). Plasma rhGAA activity AUC increased for all patients for both co-administered doses relative to alglucosidase alfa alone (Figs. 4 and 5). The increases in plasma rhGAA activity AUC suggest an increase in stabilized rhGAA uptake for tissue distribution. From biopsies taken on Day 7, two were increased by 60% and 10%, and one showed no change in rhGAA activity (Fig. 6).

**Safety**

To date, 30 adverse events (AEs) have been reported, none of which was serious. The serious AE was reported in two patients, one with atypical thrombosis and one with aortic dissection.

**Conclusion**

AT2220 was safe and well-tolerated at both 50 mg and 100 mg dose levels evaluated to date. Plasma rhGAA activity AUC increased for all patients for both co-administered doses relative to alglucosidase alfa alone (Figs. 4 and 5). The increases in plasma rhGAA activity AUC suggest an increase in stabilized rhGAA uptake for tissue distribution. From biopsies taken on Day 7, two were increased by 60% and 10%, and one showed no change in rhGAA activity (Fig. 6).