

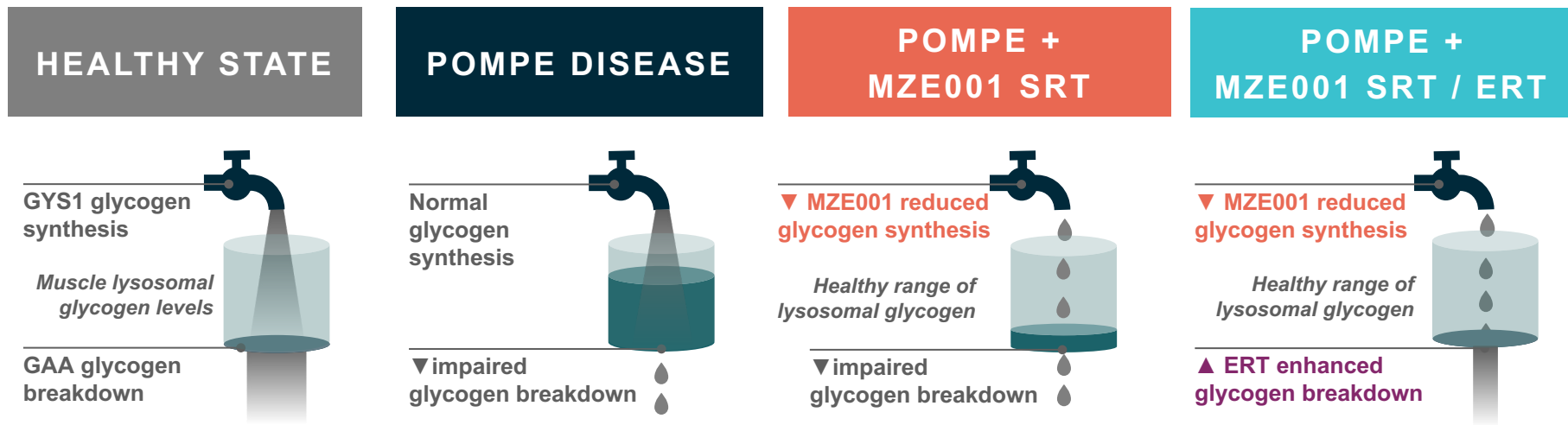
Muscle glycogen reduction in healthy adults treated with MZE001, an oral inhibitor of GYS1 and potential substrate reduction therapy for Pompe Disease



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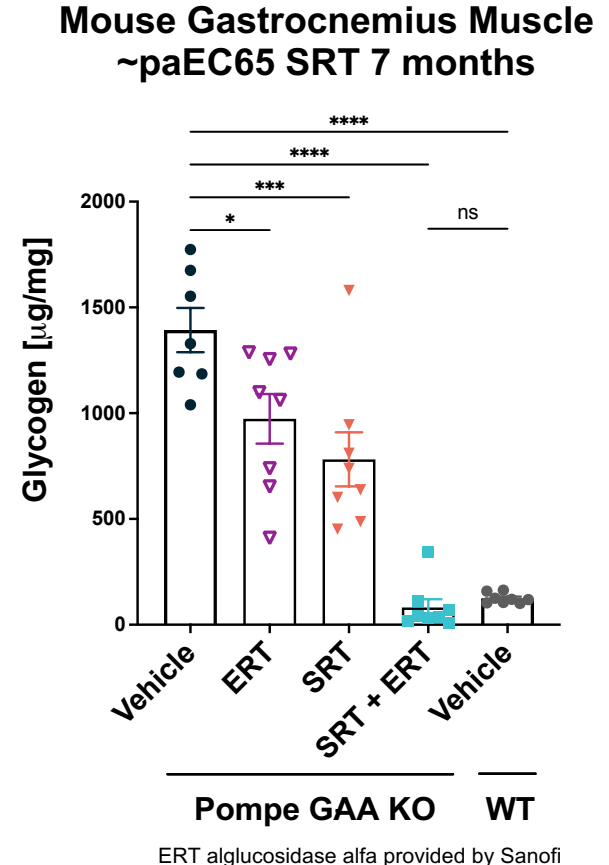
Substrate Reduction Therapy (SRT) to reduce glycogen burden in Pompe disease



MZE001 is an ORAL PILL with a differentiated mechanism of action from SOC ERT and the potential to address current unmet need in patients with late-onset Pompe Disease

MZE001 Preclinical Summary

- UK Biobank phenome analysis shows reduction of human muscle glycogen by ~60-80% from normal is well tolerated (Hamburger WORLD 2022)
- Chronic SRT treatment at ~65% inhibition of GYS1 significantly ameliorates glycogen accumulation in Pompe GAA KO mice (Ullman WORLD 2022, Xi WORLD 2023)
- MZE001 reduction in PBMC glycogen in healthy dogs & Pompe model mice correlates with reduced muscle glycogen, and may be a useful human biomarker for glycogen storage diseases (Satterfield WORLD 2023)

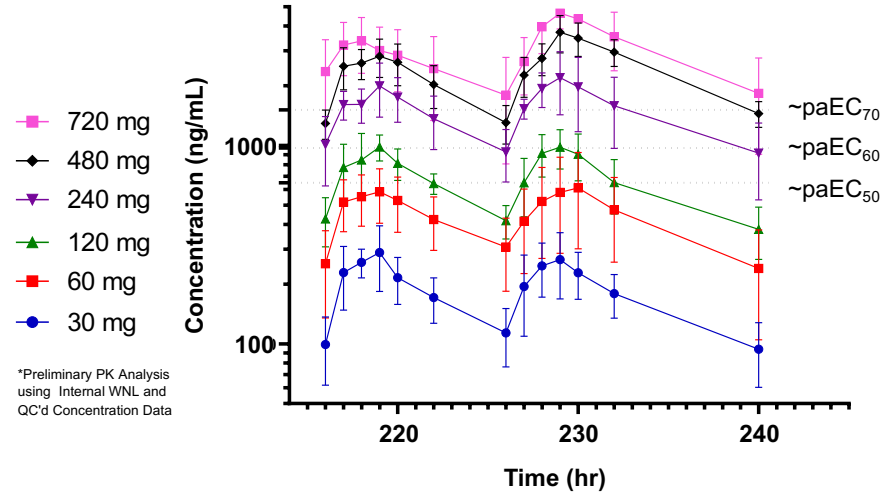


MZE001 was well-tolerated at target efficacious exposures

Safety

- Well-tolerated at multiple doses up to 720mg BID for 10 days
- Few Treatment Emergent Adverse Events observed
- No abnormal laboratory trends
- No clinically relevant ECG abnormalities
- No change in exercise tolerance

Pharmacokinetics

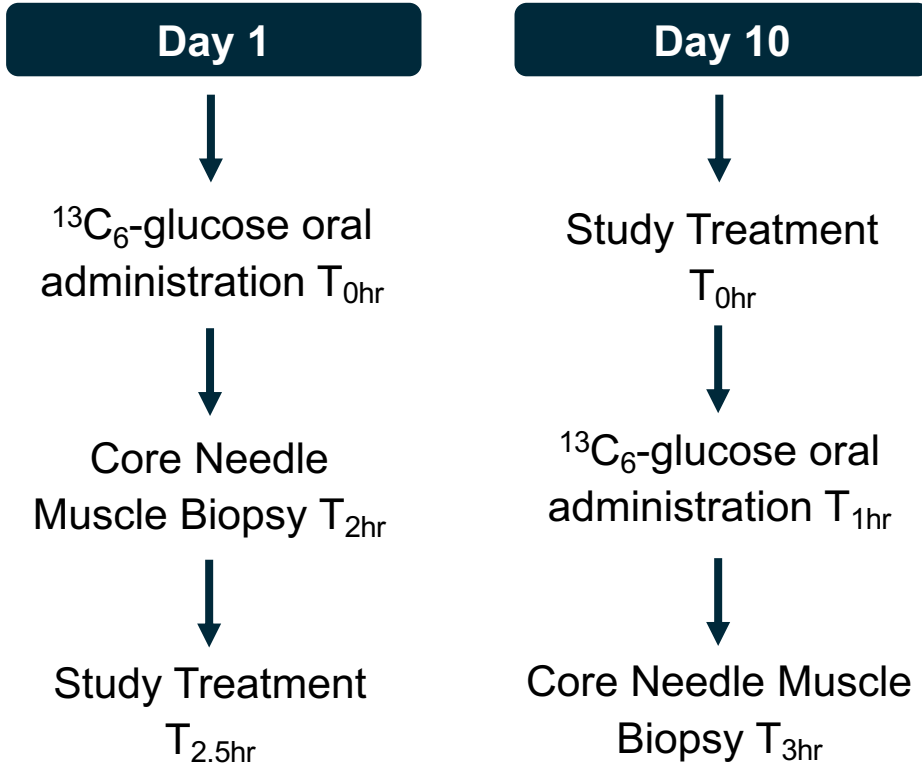


- Approximately dose proportional PK
- Mono-exponential elimination $T_{1/2} \sim 12$ hrs
- Doses 240, 480, 720 mg BID exceed paEC₅₀, paEC₆₀, paEC₇₀ at trough respectively

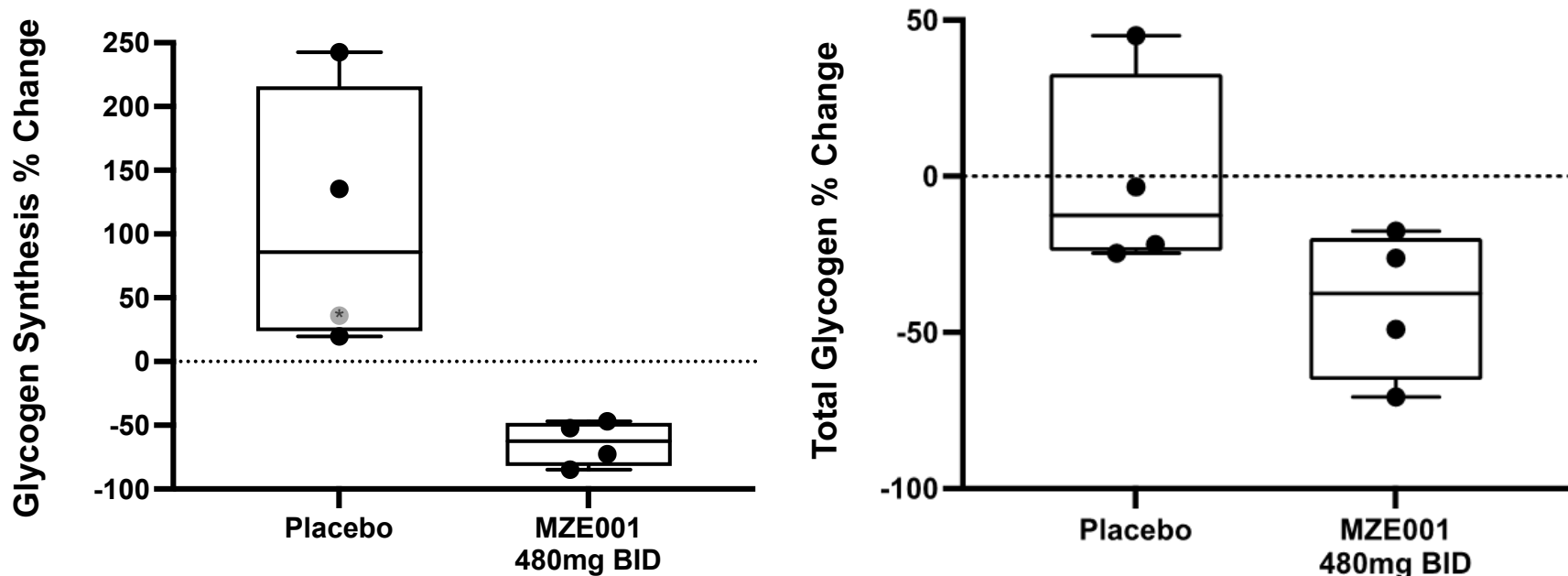
Muscle biopsy study to evaluate effects of MZE001 on glycogen synthesis

Study Objectives:

1. Determine change in muscle glycogen synthesized over 2 hrs at baseline and Day 10
2. Determine change in total muscle glycogen between baseline and Day 10
3. Evaluate glucose handling at baseline and Day 10



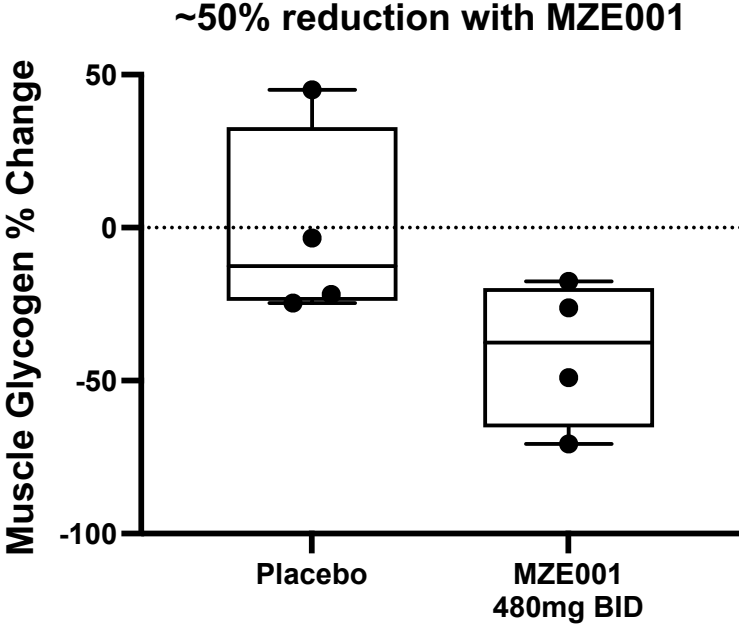
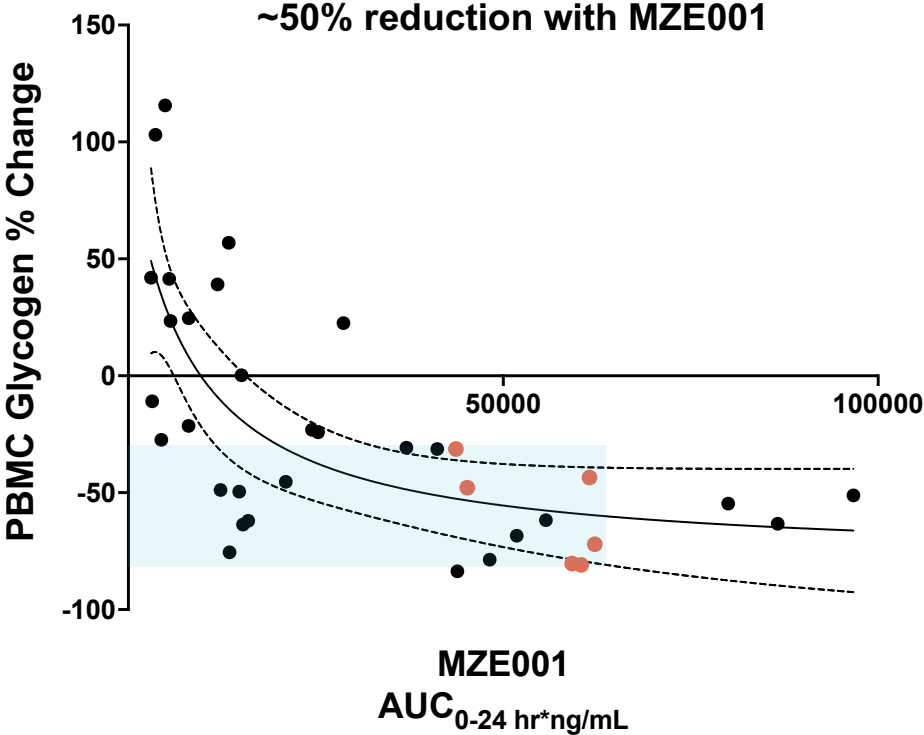
MZE001 reduced acute synthesis & total muscle glycogen in healthy adults



**~60% reduction in muscle glycogen synthesis and
~50% reduction in total muscle glycogen with 10 days MZE001 480 mg BID**

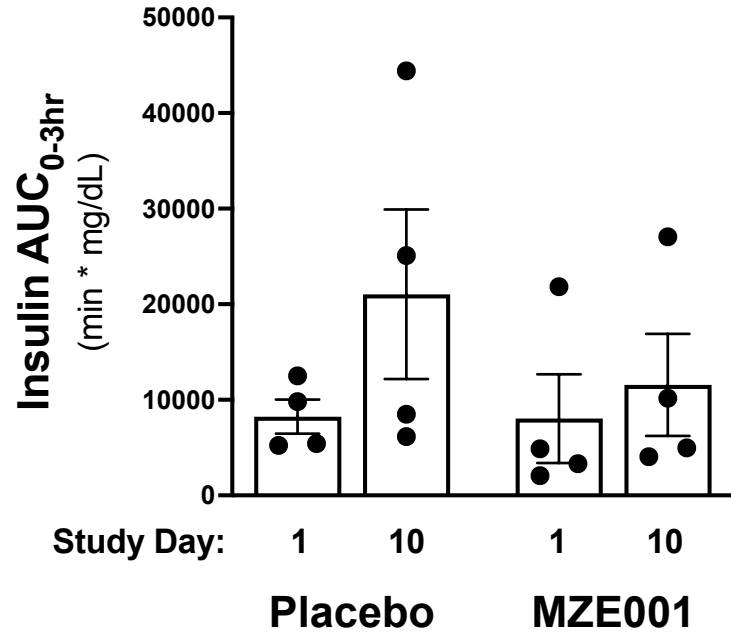
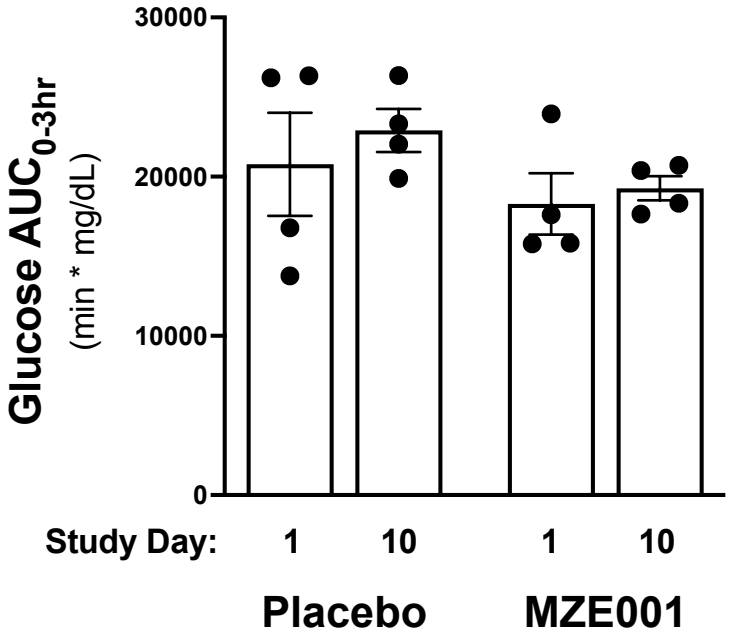
* subject did not receive day 10 labelled $^{13}\text{C}_6$ -glucose

PBMC glycogen may be a useful biomarker for response to SRT (MZE001)



Reduction in PBMC glycogen is similar to reduction in muscle glycogen in healthy adults

Normal oral glucose tolerance tests in healthy adults treated with MZE001



Glucose handling is consistent with Phase 1 data
No effect on blood glucose or insulin with MZE001 480 mg BID x 10 days

Clinical proof-of-mechanism for SRT demonstrated with MZE001

- MZE001 480 mg BID x 10 days safely and substantially reduced acute glycogen synthesis and lowered total muscle glycogen in healthy adults
- PBMC glycogen may be a useful biomarker for response to therapy in patients with Pompe disease
- Clinical proof-of-mechanism for SRT demonstrated with MZE001

Phase 2 clinical PoC study in patients with Pompe Disease to start in 2023