



Maze Therapeutics Announces New Clinical Data Supporting MZE001 as a Potential Treatment for Pompe Disease

March 22, 2023

Data Further Supports Proof of Mechanism for MZE001, an Oral Substrate Reduction Therapy, with approximately 60% Reduction in Muscle Glycogen in Healthy Volunteers

Non-invasive Biomarker Developed by Maze to Measure Glycogen Levels Suggests Approximately 1:1 Correlation Between PBMC Blood Test and Muscle Biopsy

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SOUTH SAN FRANCISCO, Calif.-(BUSINESS WIRE)—Maze Therapeutics, a company translating genetic insights into new precision medicines, today announced new data from an exploratory muscle biopsy cohort of its Phase 1 clinical trial of MZE001 in healthy volunteers to evaluate the effects of MZE001 on glycogen synthesis. The data are being presented today, March 22, 2023, from 3:00-3:15 p.m. CT, during a late-breaking clinical session at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in Dallas.

"These data build on the positive results from our Phase 1 study presented earlier this year, demonstrating good tolerability and MZE001's ability to inhibit GYS1, the enzyme that controls glycogen production. We look forward to advancing this program and beginning our Phase 2 trial later this year."

The buildup of glycogen in skeletal, respiratory and cardiac muscle tissues is the primary driver of disease progression in patients with Pompe disease. Enzyme replacement therapy has been partially effective at clearing toxic glycogen accumulation in these tissues. MZE001, a selective inhibitor of glycogen synthase 1 in muscle, is being developed to address this therapeutic gap. Maze has developed a novel biomarker, peripheral blood mononuclear cell (PBMC) glycogen, as a surrogate for glycogen in skeletal muscle.

In the exploratory muscle biopsy cohort, Maze evaluated glycogen synthesis and total glycogen levels in four healthy volunteers following oral administration of twice-daily MZE001 480mg compared to placebo (n=4). Administration of MZE001 led to an approximately 60% reduction in muscle glycogen synthesis and an approximately 50% reduction in total muscle glycogen following ten days of treatment. These data correlated to an approximately 50% reduction in PBMC glycogen at the same dose. Further, there was no impact on blood glucose or insulin levels following twice-daily administration of MZE001 480mg in this cohort, consistent with previously reported Phase 1 data supporting the tolerability of MZE001 with respect to glucose homeostasis.

"We are very excited to see the results from this biopsy evaluation of MZE001 in healthy volunteers, which showed that reduction in muscle glycogen in healthy adults was similar to PBMC glycogen. These findings are a further proof of mechanism for MZE001 and suggest PBMC could be a useful biomarker for response to substrate reduction therapy in patients with Pompe disease, providing further confidence in MZE001's potential as the first oral treatment for this life-threatening disease," said Harold Bernstein, M.D., Ph.D., president, research and development and chief medical officer of Maze. "These data build on the positive results from our Phase 1 study presented earlier this year, demonstrating good tolerability and MZE001's ability to inhibit GYS1, the enzyme that controls glycogen production. We look forward to advancing this program and beginning our Phase 2 trial later this year."

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About Pompe Disease

Pompe disease is a rare, inherited disorder caused by mutations in the gene coding for acid alpha-glucosidase (GAA), which lead to the buildup of glycogen in skeletal muscle, respiratory muscle and cardiac muscle tissues resulting in progressive weakness and respiratory compromise.

About MZE001 and the Phase 1 Clinical Trial

MZE001 is an oral glycogen synthase (GYS1) inhibitor that aims to address Pompe disease by limiting disease-causing glycogen buildup. GYS1 is an enzyme responsible for glycogen production. MZE001 is currently being evaluated as a potential oral treatment for patients with Pompe disease, as well as other glycogen storage disorders. The first-in-human, double-blind, placebo-controlled, single and multiple ascending dose Phase 1 clinical trial was designed to evaluate the safety, tolerability,

pharmacokinetics, pharmacodynamics and food effect of MZE001 in healthy volunteers, and enrolled 112 participants. As previously reported, MZE001 was well tolerated in the trial at doses up to 720mg twice daily. Response to MZE001 was evaluated in patients using a novel biomarker, peripheral blood mononuclear cell (PBMC) glycogen, and demonstrated exposure-dependent reductions in PBMC glycogen across dose levels 10 days after administration, confirming target engagement with GYS1.

About Maze Therapeutics

Maze Therapeutics is a clinical-stage biopharmaceutical company applying advanced data science methods in tandem with a robust suite of research and development capabilities to advance a pipeline of novel precision medicines for patients with genetically defined diseases. Maze has developed the Maze Compass™ platform, a proprietary, purpose-built platform to understand and integrate the critical step of variant functionalization into each stage of genetic drug development. Maze combines human genetic data, functional genomic tools and data science technology to map novel connections between known genes and their influence on susceptibility, timing of onset and rate of disease progression. Using Compass, Maze is building a broad portfolio of wholly owned and partnered programs. Maze is based in South San Francisco. For more information, please visit mazetx.com, or follow us on [LinkedIn](#) and [Twitter](#).

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