Maze Therapeutics Announces Positive Topline Data from Phase 2 HORIZON Trial of MZE829 Demonstrating the First Clinical Proof-of-Concept in Patients with Broad APOL1-Mediated Kidney Disease

March 25, 2026

– At week 12, treatment with MZE829 resulted in a 35.6% mean uACR reduction in broad AMKD patients, 50% of the patients achieved a greater than 30% reduction in uACR, and treatment was well-tolerated –

– The subgroup of AMKD patients with FSGS that were treated with MZE829 showed a 61.8% mean reduction in uACR –

– Treatment of non-diabetic AMKD patients with MZE829 led to a clinically meaningful mean reduction in uACR from baseline of 48.6% –

– Results provide first clinical proof-of-concept in genetically defined, broad AMKD population, including patients with moderate proteinuria and diabetes –

– Maze plans to advance MZE829 to a pivotal program –

– Maze to host investor conference call and webcast today at 8:00 am EDT –

SOUTH SAN FRANCISCO, Calif., March 25, 2026 (GLOBE NEWSWIRE) -- Maze Therapeutics, Inc. (Nasdaq: MAZE), a clinical-stage biopharmaceutical company developing small molecule precision medicines for patients with kidney and metabolic diseases, today announced positive topline data from the Phase 2 HORIZON trial of MZE829, an oral, small molecule, dual-mechanism APOL1 inhibitor, in patients with broad APOL1-mediated kidney disease (AMKD). The results demonstrated that treatment with MZE829 led to a clinically meaningful mean reduction in proteinuria, as measured by urinary albumin-to-creatinine ratio (uACR), of 35.6% at week 12 in broad AMKD patients, with 50% of patients achieving a greater than 30% reduction in uACR. Maze expects to continue enrollment in the HORIZON trial and to advance MZE829 into a pivotal program in patients with AMKD.

“We are pleased to show initial promising proof-of-concept for MZE829, an oral precision medicine that was designed to treat the underlying cause of AMKD by uniquely inhibiting both pore formation and channel function in the podocyte,” said Harold Bernstein, M.D., Ph.D., president of R&D and chief medical officer of Maze. “Based on the data shown today, as well as genetics data derived through our Compass platform, we believe that MZE829’s dual mechanism approach has the potential to address the unmet need in AMKD patients. We look forward to meeting with regulators and key scientific leaders to align on a pivotal program in patients with AMKD, and anticipate presenting HORIZON data at a future medical conference.”

The HORIZON study is a Phase 2, open-label basket design trial that enrolled patients with broad AMKD carrying the APOL1 high risk genotype, including diabetic and non-diabetic patients and non-diabetic patients with severe focal segmental glomerulosclerosis (FSGS). The primary endpoints of the study are safety and tolerability, and the secondary endpoints are pharmacokinetics and reduction of proteinuria, as measured by urinary albumin-to-creatinine ratio. uACR is a sensitive measure of proteinuria across stages of glomerular kidney disease, particularly in hypertension and diabetes, and has been used to assess the risk of cardiovascular disease. Patients had to be on a stable background therapies for chronic kidney disease (CKD) for at least eight weeks prior to initiating MZE829 treatment. Background therapies included SGLT2 inhibitors and GLP-1 receptor agonists.

For this topline analysis, 15 patients were enrolled in the HORIZON study and all were included in a safety and tolerability analysis. Twelve patients were evaluated for efficacy, i.e., uACR reduction, based on meeting the per protocol compliance threshold. Patients were largely sub-nephrotic at baseline, with 10 patients having a baseline uACR of 300 to 1,000 mg/g. Across all enrolled patients, eight were diagnosed with AMKD without diabetes, of whom five patients had biopsy-confirmed FSGS, and seven were diagnosed with AMKD with diabetes.

Across all evaluated patients, a mean reduction in proteinuria from baseline of 35.6% was observed and 50% of patients achieved at least a 30% reduction in uACR. Reduction in proteinuria was seen throughout the course of the 12-week treatment period. In FSGS patients, treatment with MZE829 led to a mean reduction in uACR of 61.8%. In patients with AMKD without diabetes, treatment with MZE829 resulted in a clinically meaningful mean reduction in uACR of 48.6%. In patients with AMKD with diabetes, five patients were evaluable per protocol for efficacy, with two patients achieving at least a 30% reduction in uACR. MZE829 was well-tolerated across all doses evaluated. No serious adverse events (AEs) or severe treatment-related adverse events (TRAEs) were observed. Within the safety-evaluable population (n=15), the most common TRAEs were headache (n=2)

and diarrhea (n=2). There was one early treatment discontinuation due to mild nausea that occurred just prior to the week 12 visit.

“AMKD is a subset of chronic kidney disease with a large unmet need, potentially affecting over one million patients in the United States alone and millions more globally,” said Kate Bramham, M.B.B.S., Ph.D., consultant nephrologist at King’s College Hospital, senior clinical lecturer at King’s College London, and HORIZON steering committee member. “APOL1 risk variants are linked to earlier disease onset and accelerated disease progression, with patients initiating dialysis an average of 10 years earlier than non-APOL1 CKD patients and progressing rapidly to end-stage kidney disease, despite treatment with available therapies. A 30% uACR reduction is strongly correlated with a 10-year delay in progression to end-stage kidney disease and is widely recognized as a clinically meaningful threshold. MZE829 has the potential to be a truly differentiated treatment option to deliver meaningful, much-needed benefit to patients who currently have no options for targeted therapies.”

Conference Call and Webcast

Maze will host a conference call and webcast with members of the executive team today at 8:00 am EDT to discuss the data and next steps.

To access the call, please dial 1-888-243-4451 (United States or Canada) or 1-412-542-4135 (international) and request to be joined into the Maze Therapeutics, Inc. call.

To access the live webcast and subsequent archived recording of this event and other company presentations, please visit the Investors section of Maze’s website. The archived webcast will remain available for replay and on Maze’s website for 90 days.

About Maze Therapeutics

Maze Therapeutics is a clinical-stage biopharmaceutical company harnessing the power of human genetics to develop novel small molecule precision medicines for patients with kidney and metabolic diseases. Guided by its Compass™ platform, Maze pursues genetically validated targets by integrating variant discovery and functionalization to discover and advance small molecule programs with first- or best-in-class potential. Maze’s pipeline is led by MZE829, a dual-mechanism APOL1 inhibitor in Phase 2 development for APOL1-mediated kidney disease (AMKD), and MZE782, a SLC6A19 inhibitor advancing to Phase 2 with the potential to treat both phenylketonuria (PKU) and chronic kidney disease (CKD). Maze is headquartered in South San Francisco. For more information, please visit mazetx.com, or follow the company on LinkedIn and X.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect the current beliefs and expectations of management. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including, without limitation, statements concerning the company’s future plans and prospects, any expectations regarding the safety or efficacy of MZE829, MZE782 and other candidates under development, the ability of MZE829, MZE782 to treat AMKD or other indications, the planned timing of the company’s clinical trials, data results and further development of MZE829, MZE782 and other therapeutic candidates, the company’s expected cash runway, and the ability to drive financial results and stockholder value. In addition, when or if used in this press release, the words “may,” “could,” “should,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “plan,” “predict” and similar expressions and their variants, as they relate to the company may identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Although the company believes the expectations reflected in such forward-looking statements are reasonable, the company can give no assurance that such expectations will prove to be correct. Readers are cautioned that actual results, levels of activity, safety, performance or events and circumstances could differ materially from those expressed or implied in the company’s forward-looking statements due to a variety of factors, including risks and uncertainties related to the company’s ability to advance MZE829, MZE782 and its other therapeutic candidates, obtain regulatory approval of and ultimately commercialize the company’s therapeutic candidates, the timing and results of preclinical studies and clinical trials, the company’s ability to fund development activities and achieve development goals, its ability to protect its intellectual property, general business and economic conditions, and risks related to the impact on its business of macroeconomic conditions, including inflation, volatile interest rates, tariffs, instability in the global banking sector, and public health crises. Further information on potential risk factors that could affect the company’s business and its financial results are detailed under the heading “Risk Factors” included in the documents the company files from time to time with the U.S. Securities and Exchange Commission, including the company’s Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements speak only as of the date of this press release and the company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

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