Ultragenyx Announces Positive Longer-term Data from Phase 3 Study of DTX401 AAV Gene Therapy for the Treatment of Glycogen Storage Disease Type Ia (GSDIa)

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At Week 96 participants experienced even greater reductions in daily cornstarch intake while maintaining low levels of hypoglycemia, improved levels of euglycemia and improved fasting tolerance

Phase 3 results are further supported by early data from open-label Japanese cohort (n=3) where all participants were able to eliminate daily cornstarch while maintaining or improving glycemic control

DTX401 was well tolerated with an acceptable safety profile

NOVATO, Calif., Sept. 08, 2025 (GLOBE NEWSWIRE) -- Today, Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) announced positive longer-term results from its Phase 3 study of DTX401 AAV gene therapy for the treatment of glycogen storage disease type Ia (GSDIa). Previously reported 48 Week data show that patients treated with DTX401 (n=20) experienced statistically significant and clinically meaningful reductions in daily cornstarch intake compared to placebo, while maintaining glycemic control. At Week 96, even greater reductions in cornstarch were observed with maintained low levels of hypoglycemia, improved levels of euglycemia, and improved fasting tolerance. The data were presented at the International Congress of Inborn Errors of Metabolism (ICIEM) 2025 in Kyoto, Japan.

“In the second year of treatment, patients were able to further reduce cornstarch intake while continuing to maintain good glucose control. These results are consistent with the positive data observed in the Phase 1/2 study and underscore the robustness and progressive improvement of treatment effect that can potentially be achieved with this gene therapy,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “The ability to reduce dependence on cornstarch reflects the establishment of the liver’s ability to break down glycogen to produce glucose during times of fasting or metabolic stress. This ability to regulate glucose levels has reduced the burden of disease and potential threat of severe or fatal hypoglycemia for these patients.”

Participants achieved statistically significant and clinically meaningful reductions in cornstarch while maintaining glycemic control
As previously reported, the study met its primary endpoint with patients treated with DTX401 (n=20) experiencing a mean reduction in cornstarch of 41% at Week 48 compared to 10% reduction in the placebo group (n=24) ($p < 0.0001$). Data at Week 96 showed even greater improvements, with both the DTX401 group (n=20) and the crossover group (n=19) achieving a mean reduction in daily cornstarch intake of 61% from baseline. Participants in both groups also experienced statistically significant improvements in other cornstarch-related endpoints.

At Week 96, the DTX401 group saw an increased mean reduction in nighttime cornstarch of 70% and the crossover group saw a mean reduction of 75%. Two-thirds of participants across both groups eliminated at least one nighttime cornstarch dose following treatment with DTX401. Importantly, participants maintained low levels of hypoglycemia and improved levels in euglycemic range (70-120 mg/dL) throughout the second year of the study despite substantial reductions in daily cornstarch intake. Participants dosed with DTX401 also experienced improved fasting tolerance in a controlled fasting challenge (CFC) through year 2 of the study, demonstrating protection from severe hypoglycemia (< 54 mg/dL).

Dr. John Mitchell, scientist in the Child Health and Human Development Program at the Research Institute of the McGill University Health Centre, pediatric endocrinologist at the Montreal Children’s Hospital, and an investigator on the study said: “The current treatment for GSDIa with multiple doses of uncooked cornstarch provides a heavy burden for individuals with this disease and requires continuous vigilance to prevent hypoglycemia. At present, there is no treatment that addresses the underlying cause and there is a clear unmet need for patients for a disease modifying therapy. Treatment with DTX401 resulted in an impressive reduction of both cornstarch quantity and dosing frequency while maintaining glucose levels in the target range. Treated individuals had less reliance on cornstarch with normalization of mealtimes. However, for me, the most significant result from the study is the reduction in the number of cornstarch doses overnight. Uninterrupted sleep leads to improvement in quality of life and less fatigue for patients and their families. This has important implications for the GSD population at large.”

Clinical benefits translated to improvements in patient-reported quality of life
At Week 96, 83% of the DTX401 group and 95% of the crossover group reported improvements in disease burden (+1 to +3 change) as measured by the Patient Global Impression of Change (PGIC), a single item questionnaire that asked participants how their condition changed since the start of the study.

Improvements in quality of life were further demonstrated through interviews with Phase 3 study participants. During Week 48 and Week 96 interviews, DTX401-treated participants most frequently reported reductions in cornstarch intake that, at the group level, exceeded the baseline-identified threshold for meaningful change; as well as less hypoglycemia and less tiredness—all of which were reported as treatment priorities in baseline interviews. The most frequently reported functional improvements at Week 48 and Week 96 included improvements in physical, social and diet/daily regimen impacts.

DTX401 well tolerated with an acceptable safety profile
The study demonstrated an acceptable and expected safety profile for DTX401 consistent with Phase 1/2 study results. Anticipated hepatic reactions were manageable with a prophylactic corticosteroid regimen. No AAV8 class effects of dorsal root ganglion toxicity, malignancy or thrombotic microangiopathy were observed in the study through Week 96. Hypertriglyceridemia was observed in all study groups but more frequently following DTX401.

Results further supported by data from three participants treated in open-label arm in Japan
The Phase 3 data is further supported by early results from all participants (n=3, all were pediatric ages 8-17 yo) treated with DTX401 in an open-label cohort that demonstrated a mean reduction in daily cornstarch intake of 95% at Week 24 compared to baseline. Ultimately, all three participants were able to discontinue daily cornstarch entirely as of Week 24 (n=2) and Week 36 (n=1). Glycemic control was maintained or improved with lower levels of hypoglycemia and improved euglycemia across the group with no serious adverse events reported.

About the Phase 3 GlucoGene study

The 48-week randomized, double-blind, placebo-controlled study treated 46 participants aged eight years and older with DTX401 (1.0 x 10^13 GC/kg dose measured by ddPCR) or placebo. There were 44 participants in the modified intention-to-treat (mITT) population providing efficacy data within the Week 48 analysis period following treatment with DTX401 (n=20) or placebo (n=24). At Week 48, eligible participants crossed over and received the alternate treatment. After crossover, participants will be followed for an additional 96 weeks. After study completion, participants will be offered enrollment into the GSDIa Disease Monitoring Program (DMP) where they will be followed for at least 10 years post-DTX401 infusion.

About DTX401
DTX401 is an investigational AAV8 gene therapy designed to deliver stable expression and activity of G6Pase under control of the native promoter to allow the treated liver cells to respond to normal hormonal signals intended to manage glucose, including insulin and cortisol. DTX401 is administered as a single intravenous infusion and has been shown in preclinical studies to improve G6Pase activity and reduce hepatic glycogen levels, a well-described biomarker of disease progression. DTX401 has been granted orphan drug designation, regenerative medicine advanced therapy (RMAT) designation and Fast Track designation from the U.S. FDA, as well as PRIority MEdicines (PRIME) and orphan drug designation from the European Medicines Agency.

About Glycogen Storage Disease Type Ia (GSDIa)
GSDIa is a rare, serious, and life-threatening disease due to an inborn error of carbohydrate metabolism caused by pathogenic variants of the G6PC gene which encodes the enzyme G6Pase, an enzyme that is critical for the release of glucose from glycogen and other metabolic sources. Deficiency of G6Pase results in severe hypoglycemia during periods of fasting between meals and during the night along with excess hepatic glycogen storage, metabolic derangements and other disease related complications. Cornstarch is critical in the management of GSDIa throughout the day and night in providing an exogenous source of glucose to avoid sudden and severe drops in plasma glucose levels however current management strategies carry a significant burden to patients and families. There are no approved pharmacologic therapies. GSDIa is estimated to affect approximately 6,000 people in commercially accessible geographies.

About Ultragenyx Pharmaceutical Inc.
Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx's strategy is predicated upon time- and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at: www.ultragenyx.com.

Ultragenyx Forward-Looking Statements and Use of Digital Media
Except for the historical information contained herein, the matters set forth in this press release, including statements related to Ultragenyx's expectations and projections regarding its future operating results and financial performance, business plans and objectives for DTX401, expectations regarding the tolerability and safety of DTX401, expectations regarding the adequacy of clinical data to support the marketing application and approval of DTX401, our intent to file, and potential timing and success of, the marketing application and other regulatory approvals for DTX401, expectations regarding timing of receiving potential approval of DTX401, expectations regarding the prevalence of patients of DTX401, future regulatory interactions, and the value to be generated by DTX401, and future clinical and regulatory developments for DTX401 are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, collaboration with third parties, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals, the ability of the company to successfully develop DTX401, the company's ability to achieve its projected development goals in its expected timeframes, the risk that results from earlier studies may not be predictive of future study results, risks related to adverse side effects, risks related to reliance on third party partners to conduct certain activities on the company's behalf, smaller than anticipated market opportunities for the company's products and product candidates, manufacturing risks, competition from other therapies or products, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's products and drug candidates. Ultragenyx undertakes no obligation to update or revise any forward-looking statements.

For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 6, 2025, and its subsequent periodic reports filed with the SEC.

In addition to its SEC filings, press releases and public conference calls, Ultragenyx uses its investor relations website and social media outlets to publish important information about the company, including information that may be deemed material to investors, and to comply with its disclosure obligations under Regulation FD. Financial and other information about Ultragenyx is routinely posted and is accessible on Ultragenyx's Investor Relations website (https://ir.ultragenyx.com/) and LinkedIn website (https://www.linkedin.com/company/ultragenyx-pharmaceutical-inc-/).

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