# Ultragenyx Announces Additional Positive Multi-Year Durability Data from Phase 1/2 AAV Gene Therapy Studies

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NOVATO, Calif., Nov. 29, 2021 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for serious rare and ultra-rare genetic diseases, today announced new long-term durability data from the Phase 1/2 studies of DTX401 for Glycogen Storage Disease Type Ia (GSDIa) and DTX301 for Ornithine Transcarbamylase (OTC) deficiency that were presented at the 14th International Congress of Inborn Errors of Metabolism (ICIEM).

“With initial patients now in year 3 following dosing with DTX401 and DTX301 we are seeing the impact of long-term, durable biological responses and the establishment of normal metabolic pathways to allow for the release of glucose from glycogen during periods of fasting for patients with GSDIa and the breakdown of ammonia for patients with OTC deficiency,” said Eric Crombez, M.D., Chief Medical Officer, Ultragenyx Gene Therapy and Inborn Errors of Metabolism. “By directly correcting the underlying genetic cause of disease these gene therapies have the potential to provide meaningful quality-of-life improvements for patients and enable new flexibility and independence to take part in a more active and less-restrictive lifestyle.”

**DTX401 for Glycogen Storage Disease Type Ia (GSDIa)**
*Additional longer-term Phase 1/2 data presented at ICIEM 2021 demonstrate durability of response, with sustained responses lasting up to 3 years since treatment*

Across all 12 patients in the Phase 1/2 study, the mean reduction in daily cornstarch intake was 69.9% ($p < 0.0001$) ranging from 19-100% when comparing baseline to the most recent visit. The nine patients in Cohorts 1, 2, and 3 continue to demonstrate improved glucose control while tapering or discontinuing oral glucose replacement therapy with cornstarch up to 3 years after receiving DTX401.

The three patients in Cohort 4 have completed a tapering prophylactic steroid regimen. Two of the three patients have reduced the frequency of daily oral glucose replacement therapy from six times per day at baseline to one (Patient 10) and two (Patient 11) times per day as of their last visit.

Across all patients in the Phase 1/2 study, to date there have been no infusion-related adverse events, no treatment-related serious adverse events, and no dose-limiting toxicities reported.

**DTX301 for Ornithine Transcarbamylase (OTC) Deficiency**
*Additional longer-term Phase 1/2 data presented at ICIEM 2021 demonstrate durable metabolic control and sustained responses*

The six patients who previously demonstrated a response remain clinically and metabolically stable, including all three treated at the highest dose (1.7 x 10^13 GC/kg dose), which is the dose that will be used in the Phase 3 study. The longest treated responders have demonstrated a durable response up to 4 years after dosing, and up to 3.5 years after discontinuing ammonia-scavenger medications and liberalizing protein-restricted diets. Two patients were enrolled into Cohort 4 of the DTX301 study and received a tapering prophylactic steroid regimen. Patient 10 is deemed a responder. As of the data cut-off, Patient 11 had completed the prophylactic steroid regimen and is in the process of modifying ammonia-scavenging drugs and or diet.

Across all 11 patients in the Phase 1/2 study, to date there have been no infusion-related adverse events, no treatment-related serious adverse events and no dose-limiting toxicities reported. All treatment-related adverse events have been Grade 1 or 2, with the exception of one episode of grade 3 hyperammonemic crisis related to OTC deficiency.

**About Glycogen Storage Disease Type Ia and DTX401**
GSDIa is the most severe genetically inherited glycogen storage disease. It is caused by a defective gene coding for the enzyme G6Pase-α, resulting in the inability to regulate blood sugar (glucose). Hypoglycemia in patients with GSDIa can be life-threatening, while the accumulation of the complex sugar glycogen in certain organs and tissues can impair the ability of these tissues to function normally. If chronically untreated, patients can develop severe lactic acidosis, progress to renal failure, and potentially die in infancy or childhood. There are no approved pharmacologic therapies. An estimated 6,000 patients worldwide are affected by GSDIa.

DTX401 is an investigational adeno-associated virus (AAV) type 8 gene therapy designed to deliver stable expression and activity of G6Pase-α under control of the native promoter. DTX401 is administered as a single intravenous infusion and has been shown in preclinical studies to improve G6Pase-α activity and reduce hepatic glycogen levels, a well-described biomarker of disease progression. DTX401 has been granted Orphan Drug Designation in both the United States and Europe, and Regenerative Medicine Advanced Therapy (RMAT) designation and Fast Track designation in the United States.

**About Ornithine Transcarbamylase (OTC) Deficiency and DTX301**
OTC deficiency, the most common urea cycle disorder, is caused by a genetic defect in a liver enzyme responsible for detoxification of ammonia. Individuals with OTC deficiency can build up excessive levels of ammonia in their blood, potentially resulting in acute and chronic neurological deficits and other toxicities. It is estimated that more than 10,000 people are affected by OTC deficiency worldwide, of whom approximately 80 percent are classified as late-onset and represent a clinical spectrum of disease severity. In the late-onset form of the disease, elevated ammonia can lead to significant medical issues for patients. Neonatal onset disease occurs only in males, presents as severe disease, and can be fatal at an early age. Approved therapies, which must be taken multiple times a day for the patient's entire life, do not eliminate the risk of future metabolic crises. Currently, the only curative approach is liver transplantation.

DTX301 is an investigational AAV type 8 gene therapy designed to deliver stable expression and activity of OTC following a single intravenous infusion. It has been shown in preclinical studies to normalize levels of urinary orotic acid, a marker of ammonia metabolism. DTX301 was granted Orphan Drug Designation in both the United States and Europe.

**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.

**Forward-Looking Statements**

*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, anticipated cost or expense reductions, the timing, progress and plans for its clinical programs and clinical studies, future regulatory interactions, and the components and timing of regulatory submissions 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 effects from the COVID-19 pandemic on the company's clinical activities, business and operating results, risks related to reliance on third party partners to conduct certain activities on the company's behalf, uncertainty and potential delays related to clinical drug development, including potential delays in identifying, recruiting, enrolling and qualifying patients in our clinical studies or longer than anticipated periods between screening and dosing of patients in our clinical studies, 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 on November 3, 2021, and its subsequent periodic reports filed with the Securities and Exchange Commission.*

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