Ultragenyx Announces Positive Top-Line Results from Phase 3 Study of DTX401 Gene Therapy for Glycogen Storage Disease Type Ia (GSDIa)

May 30, 2024 8:00 PM EDT

Treatment with DTX401 resulted in a statistically significant reduction in daily cornstarch intake at Week 48 (p<0.0001) with maintenance of glucose control

Company will host investor call today at 5:00 p.m. ET

NOVATO, Calif., May 30, 2024 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) today announced positive topline results from the Phase 3 *GlucoGene* study (NCT05139316) evaluating DTX401, an investigational gene therapy for the treatment of patients aged eight years and older with glycogen storage disease type Ia (GSDIa).

The study achieved its primary endpoint, demonstrating that treatment with DTX401 resulted in a statistically significant and clinically meaningful reduction in daily cornstarch intake compared with placebo at Week 48. The mean percent reduction was 41.3% in the DTX401 group (n=20) compared with 10.3% in the placebo group (n=24) at Week 48 (p<0.0001). Across patients treated with DTX401, the mean reduction in cornstarch continued to decline over the 48-week period. In the treatment group, all patients achieved a reduction in cornstarch, with 68% achieving ≥30% reduction and 37% achieving ≥50% reduction compared to the placebo group, which achieved the same reductions in 13% and 4% of patients, respectively, at Week 48.

“This is an incredible milestone for the DTX401 program. These clinically important and statistically significant results are consistent with our Phase 1/2 findings, and the continued improvement in these treated patients reflects the acquired ability to break down glycogen as a source of endogenous glucose from their treated livers,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “We want to thank the patients, families and treating community for their ongoing participation in this study and their support of progress for the broader GSDIa community.”

The study also successfully met key secondary endpoints of reduction in the number of cornstarch doses per day and maintenance of glucose control at Week 48. Treatment with DTX401 resulted in a mean reduction of 1.1 cornstarch doses per day in the DTX401 treatment group compared with a mean reduction of 0.2 in the placebo group (p=0.0011). Patients in the DTX401 group also showed significant improvement in both frequency and quantity of nighttime cornstarch dosing compared with the placebo group. This blinded study established non-inferiority (p<0.0001) of glucose control between the study groups while the treatment group significantly reduced daily cornstarch intake.

The Patient Global Impression of Change (PGIC) at Week 48 showed a median score of 2.0 (moderately improved) for the DTX401 treatment group and 1.0 (minimally improved) for the placebo group (p=0.132). Moderately or higher improved PGIC scores correlated with a ≥30% reduction in total daily cornstarch intake indicating that this is a clinically meaningful threshold for patients.

“With these Phase 3 results, the significant reduction in cornstarch intake with continued management of glucose control has the potential to offer meaningful benefit to patients while improving their quality of life on a daily basis,” stated Rebecca Riba-Wolman, M.D., director of the Glycogen Storage Disease Program & Disorders of Hypoglycemia at Connecticut Children’s Medical Center/University of Connecticut Medical School and study investigator. “GSDIa is a disease that never takes a break, where you must constantly think about your own, or your child's, safety and risk of severe low blood sugar and acidosis throughout the day and especially at night. A treatment that can improve these daily concerns for people with GSDIa without significant risks is essential.”

The study demonstrated an acceptable and expected safety profile for DTX401 consistent with Phase 1/2 study results. Anticipated vector-induced hepatic effects were all non-serious and manageable with a prophylactic corticosteroid regimen. No AAV8 class effects of dorsal root ganglion toxicity or thrombotic microangiopathy were observed in the study through Week 48.

Full 48 Week data from the Phase 3 study will be presented at a scientific conference later this year. These results will be discussed with regulatory authorities to support a marketing application in 2025.

Phase 1/2 Data Presented at American Society of Gene and Cell Therapy 2024
Ultragenyx recently presented long-term DTX401 Phase 1/2 data demonstrating durable response, with sustained, clinically meaningful reductions in cornstarch lasting up to 5 years in patients treated with open-label DTX401 as of the data cut-off. All 12 patients in the study have been followed for an average of 4 years and continue to demonstrate improved glucose control, with a mean total daily reduction of cornstarch intake of 72% (p<0.0001) from baseline to their last available timepoint.

Conference Call and Webcast Information
Ultragenyx will host a conference call at 5:00 p.m. ET today to discuss the topline data from the DTX401 Phase 3 *GlucoGene* study. The live and replayed webcast of the call will be available through the company’s website at https://ir.ultragenyx.com/events-presentations.

About the Phase 3 *GlucoGene* study
The 48-week randomized, double-blind, placebo-controlled study treated 46 patients aged eight years and older with DTX401 (1.0 x 10^13 GC/kg dose measured by ddPCR) or placebo. There were 44 patients in the modified intention-to-treat (mITT) population with efficacy data within the Week 48 analysis period following treatment with DTX401 (n=20) or placebo (n=24). At Week 48, eligible patients crossed over and received the alternate treatment. After crossover, patients will be followed for an additional 96 weeks. After study completion, patients will be offered enrollment into a Disease Monitoring Program (DMP) where they will be followed for at least 10 years post-DTX401 infusion.

About Glycogen Storage Disease Type Ia (GSDIa)
GSDIa is a serious 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.

About DTX401
DTX401 is an investigational AAV8 gene therapy designed to deliver stable expression and activity of G6Pase-α under control of the native promoter to allow the treated liver cells to respond to normal hormonal signals intended to manage glucose, including insulin, glucagon and cortisol. 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, 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 Ultragenyx Pharmaceutical Inc.
Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultrarare 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, 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 May 3, 2024, 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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