Ultragenyx Announces Positive 36-Week Data from Phase 3 Study of DTX301 AAV8 Gene Therapy for the Treatment of Ornithine Transcarbamylase (OTC) Deficiency

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Statistically significant improvements in primary endpoint of ammonia control compared with placebo at 36 weeks

Clinically important changes observed in patient global impression scale for overall OTC symptoms, OTC deficiency symptoms, and OTC impact on daily living

DTX301 was well tolerated with an acceptable safety profile

NOVATO, Calif., March 12, 2026 (GLOBE NEWSWIRE) -- Today Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) announced positive results from its Phase 3 *Enh3ance* study of DTX301, an investigational AAV8 gene therapy for the treatment of ornithine transcarbamylase (OTC) deficiency. At Week 36 in the randomized, double-blind placebo-controlled period of the trial, DTX301-treated patients (n=18) demonstrated a statistically significant and clinically meaningful 18% (p=0.018) reduction in 24-hour plasma ammonia (AUC_{0-24}) compared to placebo (n=19) and maintained average ammonia AUC_{0-24} in the normal range through Week 36. Eight of nine patients with abnormal ammonia AUC_{0-24} at baseline, despite optimal current drug treatment and diet restriction, reached normal ammonia levels rapidly, which were generally maintained during this treatment period.

“Given the importance of and effort made to keep ammonia levels under control in patients with OTC deficiency, the further reduction in ammonia levels in patients treated with DTX301 demonstrates the benefit of this gene therapy and of directly addressing the underlying cause of this disease,” said Eric Crombez, M.D. chief medical officer of Ultragenyx. “Importantly, the improvement in ammonia control was maintained as some patients began reducing use of alternate pathway medications and liberalizing their protein restricted diet. We are extremely encouraged by these findings given the significant medical needs faced by patients with OTC deficiency, who remain at risk for unpredictable and potentially life threatening hyperammonemic crises.”

Baseline 24-hour ammonia AUC levels were normal in 50% of DTX301-treated patients and 68% of placebo patients, who were all on current care of scavenger medications and strict dietary control of protein intake. Patients treated with DTX301 (n=18) experienced reductions in 24-hour ammonia rapidly by Week 6 and were decreased by 18% (p=0.018) compared to placebo (n=19) at Week 36. Ammonia was generally maintained in normal range in treated patients despite their mean 27% reduction in ammonia scavenger medications at Week 36 (n=18) and an approximately 13% increase in protein intake relative to no change in placebo (n=19).

Assessed at Week 24, patient global impression scale (PGIC) for OTC symptoms (total n=15 reporting) overall showed 71% of treated patients were much improved (equivalent to +3) versus 0% of placebo. For Week 24, PGIC evaluations of OTC deficiency symptoms and OTC impact on daily living (total n=30 reporting), both showed 64% were either much improved (43%) or moderately improved (21%) and on placebo only 19% were moderately improved (none were much improved).

DTX301 was well tolerated with an acceptable safety profile, consistent with prior Phase 1/2 safety data. The most common treatment-emergent adverse events were mild to moderate transient hepatic reactions managed with steroids. One serious adverse event (SAE) of acute hepatitis was assessed as treatment-related and resolved with steroids. No SAEs or AEs related to thrombotic microangiopathy, dorsal root ganglion toxicity, malignancies, or other complex immune reactions. Hyperammonemic crises requiring hospitalization occurred five times in the placebo group with one death, and only one such event in the treated group and no deaths. Two patients in the placebo arm discontinued, including one death due to hyperammonemia crisis and one patient who became AAV8 antibody positive prior to crossover. One patient in the DTX301 arm discontinued after Week 36 for non-clinical reasons.

As planned, the study is continuing to its second primary endpoint which evaluates reduction in treatment burden, including use of ammonia scavengers and dietary management, across both the treatment and placebo-crossover groups following treatment with DTX301 through 64 weeks of follow-up. Data are expected in the first half of 2027. The conduct of the program is reflected in the company’s February 2026 guidance on 2026 spend and will be managed within the company goals of 2027 profitability.

About DTX301 (avalotcagene ontaparvovec)
DTX301 (avalotcagene ontaparvovec) 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 the United States and EU and Fast Track Designation in the United States.

About the *Enh3ance* Study
The Phase 3 *Enh3ance* study enrolled 37 patients across 10 countries and 16 sites. Participants were randomized 1:1 between DTX301 and placebo during the 36-week Randomized Control Period (RCP), at which time study data are unblinded, and placebo patients will cross over to treatment. The primary endpoints of the study are plasma ammonia as measured by 24-hour ammonia (AUC_{0-24}) at Week 36 and Complete Responder rate at the final study visit after DTX301 exposure, with patients from both the crossover and treatment groups followed through 64 Weeks. The Phase 3 dose for DTX301 is 1.7 x 10^13 GC/kg, as determined by the droplet digital PCR (ddPCR) test method.

About OTC Deficiency
OTC deficiency, the most common urea cycle disorder, is caused by a genetic defect in a liver enzyme responsible for detoxification of ammonia. OTC deficiency is defined by acute hyperammonemic episodes, caused by excessive amounts of ammonia in the blood, that have a profound impact on patients’ health and quality of life, and can lead to hospitalization, cognitive and neurologic impairments, and death. Current management includes a strict diet that limits protein, and ammonia scavenger medications, which provide an alternate pathway for ammonia elimination. Current treatment may improve hyperammonemia but does not completely eliminate the risk of serious hyperammonemic crises as well as the risk of catastrophic outcomes. Many patients still have elevated excursions of their ammonia levels when evaluated over a 24 hour cycle period. It is estimated that more than 10,000 people are affected by OTC deficiency in commercially accessible geographies, of whom approximately 80% 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. 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.

About Ultragenyx
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 and Use of Digital Media
Except for the historical information contained herein, the matters set forth in this press release, including statements related to the development, timing and progress of DTX301, the timing, scope and outcome of future data results from the Phase 3 study of DTX301, including data expected in the first half of 2027, future regulatory interactions related to DTX301, the safety and tolerability profile of DTX301, the potential clinical benefit of DTX301 for patients with OTC deficiency, business plans and objectives for DTX301, future clinical and regulatory developments for DTX301 and the management of development activities within the Company's previously issued guidance on 2026 spend and its goal of achieving profitability in 2027 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, 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 risk that interim or topline clinical results may not be predictive of final study results or longer-term outcomes, the ability of the company to successfully develop DTX301, complexities related to the development of gene therapy product candidates such as DTX301, 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 and supply risks, the ability of the company and its third party manufacturers to comply with regulatory requirements, 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 18, 2026, 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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