Ultragenyx Completes Successful End-of-Phase 2 Meeting with FDA and Finalizes Phase 3 Study Design for DTX301 Ornithine Transcarbamylase (OTC) Gene Therapy Program

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Phase 3 Study on Track to Initiate in Second Half 2021

NOVATO, Calif., April 22, 2021 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel therapies for rare and ultra-rare diseases, today announced the successful completion of an End-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA) for the DTX301 ornithine transcarbamylase (OTC) deficiency gene therapy program. The meeting focused on the discussion of the Phase 1/2 data and alignment on Phase 3 design and endpoints.

Based on the outcome of this meeting, Ultragenyx has finalized the Phase 3 study design, which will include a 64-week primary efficacy analysis period and enroll approximately 50 patients 12 years of age and older, randomized 1:1 to DTX301 (1.7 x 10^13 GC/kg dose) or placebo. The co-primary endpoints are change in 24-hour plasma ammonia levels and the percent of patients who achieve a response as measured by discontinuation or reduction in baseline disease management. Ultragenyx previously completed an initial Scientific Advice process with the European Medicines Agency (EMA) and this design incorporates the scientific advice.

The Phase 3 study is expected to begin dosing as planned in the second half of 2021. Following the initial 64-week study period, all patients who received placebo will be eligible to receive DTX301.

“Alignment with the FDA on our Phase 3 plan provides additional clarity on our development pathway for DTX301, and we are rapidly moving ahead toward initiation of the study in the second half of this year,” said Eric Crombez, M.D., Chief Medical Officer of the Ultragenyx Gene Therapy development unit. “We expect that the results from this 64-week Phase 3 study coupled with the longer-term data from the ongoing Phase 1/2 study should provide a robust data package to support the durable effect of DTX301 to establish the normal metabolism of ammonia and improve the lives of patients living with OTC.”

The increase in study duration from 48 to 64 weeks will allow more time for weaning of scavenger medications and dietary protein restrictions which will help assure success in the co-primary endpoint of baseline treatment reduction. Given the strong results in the Phase 1/2 study showing total discontinuation of all scavenger medications and diet in responders, this co-primary endpoint is designed to demonstrate clinically meaningful reduction in baseline disease treatment and is well-powered with the 50-patient, 1:1 randomized design.

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. 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% 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.

About DTX301
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.

In the Phase 1/2 study of DTX301, nine patients were treated in the first three dose finding cohorts and an additional 2 patients were enrolled in a cohort where prophylactic steroids were used. Six of the patients in the dose finding cohorts responded to treatment and have demonstrated durable metabolic control and remain in excellent clinical condition with no significant adverse events, hospitalizations or other events related to OTC deficiency.

The 64-week Phase 3 study will enroll 50 patients 12 years of age and older, randomized 1:1 to DTX301 or placebo. The Phase 3 dose for DTX301 is 1.7 x 10^13 GC/kg, as determined by the droplet digital PCR (ddPCR) test method. The co-primary endpoints are change in 24-hour plasma ammonia levels and the percent of patients who achieve a complete response (complete discontinuation of baseline disease management) or a partial response (decreased baseline ammonia scavenger medication and/or liberalized protein-restricted diet by at least 50%). Secondary endpoints include change in ureagenesis which evaluates the capacity to generate urea from ammonia, change in cognitive function, and safety.

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, 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 12, 2021, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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