Ultragenyx Initiates Cyprus2+, a Pivotal Clinical Trial Evaluating UX701 Gene Therapy for the Treatment of Wilson Disease

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NOVATO, Calif., Oct. 18, 2021 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for rare and ultra-rare genetic diseases, today announced that it has successfully screened and enrolled multiple patients with Wilson disease into the baseline monitoring period prior to dosing in its pivotal, seamless Phase 1/2/3 study of UX701, the Cyprus2+ study. The company's investigational AAV9 gene therapy is designed to deliver stable expression of the ATP7B copper transporter following a single intravenous infusion, with the goal of establishing normal trafficking of copper in patients with Wilson disease.

“Through collaboration with the FDA and other regulatory agencies we are able to bring forward an innovative and seamless phase 1/2/3 study design, that required agreement on clinical endpoints and manufacturing requirements up-front, allowing us to progress through the phases of development more efficiently,” said Eric Crombez, M.D., Chief Medical Officer of the Ultragenyx Gene Therapy development unit. “We are fortunate to have one of the most experienced and skilled teams in gene therapy and a proprietary and commercial-scale manufacturing platform that enable us to conduct this type of innovative and dynamic clinical program.”

The study will enroll patients receiving ongoing standard of care medication for the treatment of Wilson disease (copper chelators and/or zinc) for at least 12 months, with no medication or dose changes for at least 6 months prior to enrollment. After initial screening that includes testing for pre-existing antibodies to the AAV9 capsid, patients will be evaluated to ensure stable measures of disease during a 4-to 12-week baseline monitoring period (including values for 24-hour urinary copper concentration, complete blood count, and liver function tests).

Seamless Phase 1/2/3 study design
This study evaluating UX701 for the potential treatment of Wilson disease is designed with 3 seamless stages. During the first stage, the safety and efficacy of up to three dose levels of UX701 will be evaluated over the course of 52 weeks and a dose will be selected for further evaluation in stage 2. In this first stage, 27 patients will be randomized into three cohorts in a 2:1 ratio per cohort to receive UX701 at the dose level assigned for the cohort or placebo. The sequential doses to be evaluated are 5.0 x 10^12 GC/kg, 1.0 x 10^13 GC/kg, and 2.0 x 10^13 GC/kg.

In stage 2, a new cohort of patients will be randomized 2:1 to receive the selected dose of UX701 or placebo. The primary safety and efficacy analyses will be conducted at Week 52 of stage 2. The primary efficacy endpoints are change in 24-hour urinary copper concentration and percent reduction in standard of care (SOC) medication by Week 52. After the initial 52-week study period, all patients will have long term follow up in stage 3. Patients randomized to placebo in stages 1 and 2 will be eligible to receive UX701 in stage 3.

About Wilson Disease
Wilson disease is a rare inherited disorder caused by mutations in the ATP7B gene, which results in deficient production of ATP7B, a protein that transports copper. Loss of function of this copper-binding protein results in the accumulation of copper in the liver and other tissues, most notably the central nervous system, and also the failure to properly distribute copper by ceruloplasmin. Patients with Wilson disease experience hepatic, neurologic and/or psychiatric problems. Those with liver disease can experience such symptoms as fatigue, lack of appetite, abdominal pain and jaundice, and can progress to fibrosis, cirrhosis, life-threatening liver failure and death. Wilson disease can be treated by reducing copper absorption or removing excess copper from the body using life-long chelation therapy, but unmet needs exist because some treated patients experience clinical deterioration and severe side effects. Wilson disease affects more than 50,000 individuals in the developed world.

About UX701
UX701 is an investigational AAV type 9 gene therapy designed to deliver stable expression of the ATP7B copper transporter following a single intravenous infusion. It has been shown in preclinical studies to normalize copper trafficking and excretion from the body. The U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to UX701.

About Ultragenyx Pharmaceutical Inc.
Ultragenyx is a biopharmaceutical company committed to bringing novel therapies to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved medicines and treatment candidates aimed at addressing diseases with high unmet medical need and clear biology, 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 business plans and objectives for UX701 and future clinical developments for UX701 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 ability of the company to successfully develop UX701, 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 3, 2021, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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