Ultragenyx Announces Completion of Dosing Across Stage 1 Cohorts in Pivotal Phase 1/2/3 Cyprus2+ Study Evaluating UX701 Gene Therapy for the Treatment of Wilson Disease

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Safety and initial efficacy data from Stage 1 expected in the first half of 2024

Dose selection and initiation of Stage 2 to follow in the second half of 2024

NOVATO, Calif., Jan. 25, 2024 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) today announced that all patients have been dosed with UX701 across the three dose-escalation cohorts in Stage 1 of its pivotal Phase 1/2/3 *Cyprus*$^{2+}$ 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 normalizing copper metabolism in patients with Wilson disease.

"With the support of patients, physicians and the Wilson disease community, we've completed Stage 1 enrollment in the *Cyprus*$^{2+}$ program, which moves us one step closer to beginning Stage 2, the pivotal, randomized placebo-controlled stage of the study," said Eric Crombez, M.D., chief medical officer at Ultragenyx. "Beyond the seamless nature of this study, another important differentiator of this program is that it leverages our Pinnacle PCL™ platform, which enabled a single run to support Stage 1, demonstrating that the productivity improvements generated by our platform are able to support larger-scale clinical programs."

Data presented in October 2023 at a Company Analyst Day demonstrated that UX701 has been well tolerated in the first dose cohort, with no unexpected related treatment emergent adverse events observed as of the data cut-off date. Four of five patients enrolled in Cohort 1 had started tapering standard-of-care treatment, including two that came completely off of chelators and/or zinc therapy. Additional interim data from all three Stage 1 dose cohorts are expected in the first half of 2024, which will be followed by dose selection and initiation of Stage 2 in the second half of 2024.

U.S. residents can learn more by visiting www.ultraclinicaltrials.com.

Phase 1/2/3 *Cyprus*$^{2+}$ study design
This study evaluating UX701 for the potential treatment of Wilson disease is designed with three 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, 15 patients were enrolled into three sequential dosing cohorts to evaluate doses of 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 medication by Week 52. After the initial 52-week study period, all patients will have long-term follow up 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 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 AAV9 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) granted Orphan Drug Designation to UX701.

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 UX701, expectations regarding the tolerability and safety of UX701, and future clinical and regulatory 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 uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals, the ability of the company to successfully develop UX701, 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 November 3, 2023, 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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