Ultragenyx Announces FDA Clearance of Investigational New Drug (IND) Application for UX701, a New Gene Therapy for the Treatment of Wilson Disease

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Clinical trial will utilize a single-protocol Phase 1/2/3 design

UX701 manufacturing complete at commercial quality and scale using HeLa PCL technology

First patient to be dosed in the first half of 2021

NOVATO, Calif., Jan. 21, 2021 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for serious rare and ultra-rare genetic diseases, today announced that the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application for UX701, an investigational AAV9 gene therapy being evaluated for the treatment of Wilson Disease. Enrollment in a seamless single-protocol Phase 1/2/3 study is expected to begin in the first half of 2021. This will be the company's third in-house clinical gene therapy program and the second program in the clinic with the HeLa producer cell line manufacturing system.

"FDA IND clearance allows for the advancement of this new gene therapy into the clinic and brings forward the hope for a new treatment for patients with Wilson Disease. UX701 has the potential to directly address the underlying basis of disease by restoring the normal transport and excretion of copper," said Eric Crombez, M.D., Chief Medical Officer of the Ultragenyx Gene Therapy development unit. "The seamless Phase 1/2/3 clinical trial design will allow us to efficiently evaluate safety and efficacy of UX701 before studying an optimal dose in a larger number of patients to support registration. We appreciate the agency's support for a novel clinical trial design that could bring this important potentially new treatment to the greatest number of patients as efficiently as possible."

Study Design

UX701 will be studied in a seamless, single-protocol Phase 1/2/3 clinical trial. Manufacture and testing of GMP-grade drug product to supply the clinical study are complete using the company's proprietary HeLa 2.0 producer cell line (PCL) process at the 2,000 liter scale.

Stage 1 (evaluation of initial safety and dose finding)

In the first stage of the study, the safety and efficacy of three dose levels of UX701 will be evaluated in 27 patients (nine per cohort), randomized 2-to-1 (gene therapy versus placebo). The dose cohorts will be enrolled sequentially using ascending doses. The patients will be followed for 52 weeks before transitioning to long-term follow-up and selecting a pivotal dose. The dose will be determined based on the safety profile, changes in biomarkers of copper metabolism (e.g. 24-hr urinary copper, ceruloplasmin concentration, ceruloplasmin activity, non-ceruloplasmin bound copper, and total serum copper), and the reduction in the use of the current standard (SOC), copper chelator and/or zinc.

Stage 2 (optimal dose evaluation for pivotal clinical data generation)

The second and pivotal stage will use the dose selected from Stage 1 and enroll an additional 63 patients, randomized 2-to-1 (gene therapy versus placebo). The co-primary endpoints in Stage 2 will evaluate the effect of UX701 on copper regulation based on 24-hour urinary copper concentration and percent reduction in SOC at Week 52. Key secondary endpoints in Stage 2 include the effect of UX701 on additional biomarkers of copper metabolism and patient- and clinician-reported outcomes from a modified Wilson Disease Functional Rating Scale.

Stage 3 (long-term follow-up)

All patients in Stage 1 and Stage 2 who are randomized to receive placebo may be eligible to receive UX701 at the Stage 2 dose. Patients receiving UX701 will be continued to be monitored for long term safety and durability of response.

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. 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 managed 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 debilitating 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 a truncated version of the ATP7B copper transporter following a single intravenous infusion. It has been shown in preclinical studies to improve copper distribution and excretion from the body and reverse pathological findings of Wilson liver disease. UX701 was granted Orphan Drug Designation in the United States and European Union.

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

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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on October 27, 2020, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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