May 23, 2017

Ultragenyx Announces Recombinant Human Beta-Glucuronidase Biologics License Application and Marketing Authorization Application Filed and Accepted for Review; FDA Grants Priority Review Status

NOVATO, Calif., May 23, 2017 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ:RARE), a biopharmaceutical company focused on the development of novel products for rare and ultra-rare diseases, today announced that a Biologics License Application (BLA) submitted to the U.S. Food and Drug Administration (FDA) and a Marketing Authorization Application (MAA) submitted to the European Medicines Agency (EMA), for recombinant human beta-glucuronidase (rhGUS, UX003), an investigational therapy for the treatment of Mucopolysaccharidosis VII (MPS VII, Sly syndrome) were accepted for review. The Prescription Drug User Fee Act (PDUFA) goal date for a decision is November 16, 2017 and an opinion from the Committee for Medicinal Products for Human Use (CHMP) is expected in the first half of 2018. rhGUS is an enzyme replacement therapy for the treatment of MPS VII.

The FDA granted rhGUS Priority Review status, which is available for drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists. rhGUS was previously granted Orphan Drug Designation by the FDA.

"We are pleased that the FDA has granted priority review to the rhGUS BLA and are looking forward to working with both the FDA and EMA in the coming months with the goal of bringing this potential treatment to patients with MPS VII who currently have no other options," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx.

About MPS VII

Mucopolysaccharidosis VII (MPS VII, Sly syndrome), originally described in 1973 by William Sly, M.D., is a rare genetic, metabolic disorder and is one of 11 different MPS disorders. MPS VII is caused by the deficiency of beta-glucuronidase, an enzyme required for the breakdown of the glycosaminoglycans (GAGs) dermatan sulfate, chondroitin sulfate and heparan sulfate. These complex GAG carbohydrates are a critical component of many tissues. The inability to properly break down GAGs leads to a progressive accumulation in many tissues and results in a multi-system disease.

While its clinical manifestations are similar to MPS I and MPS II, MPS VII is one of the rarest among the MPS disorders. MPS VII has a wide spectrum of clinical manifestations and can present as early as at birth in a severe form called non-immune hydrops fetalis. There are no approved therapies for MPS VII today. The use of enzyme replacement therapy as a potential treatment is based on 20 years of research work in murine models of the disease. Enzyme replacement as a strategy is well established in the MPS field as there are currently four approved enzyme replacement therapies for other MPS disorders: MPS I (Aldurazyme®, laronidase), MPS II (Elaprase®, idursulfase), MPS IVA (Vimizim™, elosulfase alfa), and MPS VI (Naglazyme®, galsulfase).

About the Phase 3 Study

The Phase 3 randomized, placebo-controlled, blind-start clinical study, conducted at four sites in the U.S., was designed to assess the efficacy and safety of rhGUS in 12 patients between 5 and 35 years of age. Patients were randomized to one of four groups. One cohort began rhGUS therapy immediately, while the other three started on placebo and crossed over to rhGUS at different predefined time points in a blinded manner. This novel trial design generated treatment data from all 12 patients and improved the statistical power relative to a traditional parallel-group design. Patients were dosed with 4 mg/kg of rhGUS every other week for up to a total of 48 weeks, and all groups received a minimum of 24 weeks of treatment with rhGUS.

The primary objective of the study was to determine the efficacy of rhGUS as determined by the percent reduction in urinary GAG excretion after 24 weeks of treatment. Secondary efficacy endpoints include a multi-domain responder index and an individualized clinical response measure, as well as other clinical outcomes including pulmonary function, walking, shoulder flexion, fine and gross motor function, visual acuity, and fatigue. The safety and tolerability of rhGUS were also assessed.

Agreement has been reached with both the U.S. FDA and EMA on the Phase 3 study design. Based on the data from the

Phase 3 study, we met with the FDA and the EMA prior to filing the BLA and MAA. The FDA stated that their evaluation of the pivotal Phase 3 study will be based on the totality of the data on a patient-by-patient basis. FDA advised against the declaration of a primary clinical endpoint in order to allow for more flexibility in the overall efficacy evaluation, appreciating the difficulty of evaluating a single clinical endpoint given the heterogeneity and rarity of the disease. The EMA has agreed that approval under exceptional circumstances could be possible based on the Phase 3 study with urinary GAG levels as a surrogate primary endpoint, provided the data are strongly supportive of a favorable benefit/risk ratio and that some evidence or trend in improvement in clinical endpoints is observed.

About Ultragenyx

Ultragenyx is a clinical-stage biopharmaceutical company committed to bringing to market novel products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases. Founded in 2010, the company has rapidly built a diverse portfolio of product candidates with the potential to address diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are no approved therapies.

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 regarding Ultragenyx's plans or expectations regarding future regulatory interactions and the potential timing and success of filings for regulatory approvals, 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, uncertainties regarding the acceptance by the FDA or EMA of the adequacy of the clinical data in our recently completed Phase 3 rhGUS study, and the clinical validity and relevance of the endpoints from this study. 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 the company in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 5, 2017, and its subsequent periodic reports filed with the Securities and Exchange Commission.

Contact Ultragenyx Pharmaceutical Inc.

Investors & Media

Ryan Martins

844-758-7273