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Ultragenyx Announces Positive Topline Data from Phase 3 Study of Recombinant Human Beta-Glucuronidase in Mucopolysaccharidosis Type 7

Study meets primary endpoint of reduction in urinary GAG excretion and provides evidence of clinical improvement

Company to host conference call today at 5pm ET to discuss results

NOVATO, Calif., July 14, 2016 (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 positive topline data from the pivotal Phase 3 study of recombinant human beta-glucuronidase (rhGUS, UX003), an investigational therapy for the treatment of Mucopolysaccharidosis 7 (MPS 7, Sly syndrome). The study met its primary endpoint of reducing urinary GAG (dermatan sulfate) excretion after 24 weeks of treatment, demonstrating a reduction from baseline of 64.8 percent ($p < 0.0001$). The data are being presented at the 14th International Symposium on MPS and Related Diseases.

"Treatment with rhGUS showed a rapid and sustained reduction in urinary GAG excretion, as well as signs of clinical improvement in this heterogeneous patient population," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "We look forward to working with the FDA and EMA to file these data with the goal of bringing this potential treatment to patients with MPS7 who currently have no other options."

The study provides evidence of clinical improvement with rhGUS treatment. The Multi-domain Responder Index (MDRI) score at 24 weeks of treatment, a secondary endpoint, demonstrated an overall mean improvement (\pm SD) of +0.5 domains (\pm 0.80) ($p = 0.0527$). Six of the 12 patients had an improvement in their MDRI score of +1 or more. Five patients demonstrated no worsening of this progressive disease, or an MDRI score of 0. One patient had an MDRI score of -1. The MDRI is a summation of scores from each of the following domains: the six-minute walk test (6MWT), forced vital capacity (FVC), shoulder flexion, visual acuity, and the Bruininks-Oseretsky Test of Motor Proficiency (BOT-2) fine motor and gross motor function. For each domain, patients received a score of +1 when they demonstrated improvement of a magnitude equal or greater than a pre-defined minimally important difference (MID), -1 for worsening of one MID or greater, and 0 for any change that was less than 1 MID. As expected, many patients were unable to perform one or more tests due to physical or cognitive limitations and were not evaluated on those tests.

For the 6MWT, the improvement (\pm SE) was 20.8 (\pm 16.75) meters at 24 weeks of treatment based on the estimates from 9 patients who had any change from baseline data. Three of these patients demonstrated an improvement of a magnitude equal or greater than the MID with increases of 65 meters, 80 meters and 83 meters at 24 weeks compared to baseline. For the fatigue scores, four patients improved at or above the MID level after 24 weeks of treatment and nine of 12 showed improvement at some point during the study.

All patients experienced treatment emergent adverse events, which were generally mild to moderate in severity. Six of the eight patients with infusion associated reactions (IARs) on rhGUS treatment had events involving the IV catheter. There were two patients that each had a single hypersensitivity-type IAR, including one Grade 3 treatment-related anaphylactoid serious adverse event (SAE) that resulted from an infusion rate error. The second patient had mild fever and diaphoresis that resolved without treatment. No patients demonstrated recurring hypersensitivity reactions to infusions. There was a second SAE that was a Grade 2 unrelated event from an accidental injury. There were no deaths and no treatment discontinuations or missed infusions due to AEs. Seven of the 12 patients developed anti-rhGUS antibodies, which were not associated with immune-mediated AEs.

Based on these data, Ultragenyx plans to meet with the FDA and EMA this year to discuss our plans to submit regulatory filings in the first half of 2017.

Conference Call Details

Ultragenyx will host a conference call on Thursday, July 14, 2016 at 5pm ET, during which Dr. Kakkis will discuss the data presented at the MPS Symposium. The live and replayed webcast of the call will be available through the company's website

at <http://ir.ultragenyx.com/events.cfm>. To participate in the live call by phone, dial 855-797-6910 (USA) or 262-912-6260 (international) and enter the passcode 49849638. The replay of the call will be available for one year.

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 is to determine the efficacy of rhGUS as determined by the percentage reduction in urinary GAG excretion after 24 weeks of treatment. Secondary efficacy objectives 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 was also assessed.

Agreement has been reached with both the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) on the Phase 3 study design. 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 MPS 7

Mucopolysaccharidosis 7 (MPS 7, 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 7 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 1 and MPS 2, MPS 7 is one of the rarest among the MPS disorders. MPS 7 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 7 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 1 (Aldurazyme®, laronidase), MPS 2 (Elaprase®, idursulfase), MPS 4A (Vimizim™, elosulfase alfa), and MPS 6 (Naglazyme®, galsulfase).

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, statements contained 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, may constitute forward-looking statements within the meaning of the "safe harbor"

provisions of the Private Securities Litigation Reform Act of 1995. 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 contained herein. These 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 the endpoints from this study. There can be no assurance that the FDA or EMA will permit Ultragenyx to file for regulatory approval on the basis of the data from this study. Similarly, there can be no assurance that even if we are permitted to file for approval on the basis of these data, that we will receive regulatory approval. 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 March 10, 2016, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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