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Ultragenyx Announces Topline Data from Phase 2 UX007 Glucose Transporter Type-1 Deficiency Syndrome Seizure Study

Overall seizures not significantly reduced; decrease in absence seizures observed

NOVATO, Calif., March 22, 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 topline data from the Phase 2 study of UX007 in glucose transporter type-1 deficiency syndrome (Glut1 DS) patients with seizures. The study did not meet the primary endpoint of reducing the frequency of total number of observable and absence seizures among patients treated from baseline to Week 8 with UX007 compared to placebo. When evaluating each seizure type independently, treatment with UX007 did show a reduction in absence seizures captured on EEG, but not observable seizures captured by diary.

"These data suggest that UX007 has a clinically meaningful effect in Glut1DS patients with absence seizures," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "We look forward to studying UX007 in our Phase 3 study in Glut1 DS patients with movement disorders, and continue to evaluate our plans in the seizure indication."

Efficacy Results

UX007 did not meet the primary endpoint of the study during the eight-week placebo-controlled treatment period when evaluating observable and absence seizures together. Patients treated with UX007 (n=25) demonstrated a reduction of 13.4% in overall seizure frequency (p=0.41) relative to placebo (n=11).

For the pre-specified secondary analysis of the primary endpoint, patients with absence seizures (n=19) demonstrated a 47.3% reduction (p=0.009) in seizure frequency after eight weeks of treatment with UX007, compared to baseline. While clinically significant, this did not meet the statistical significance threshold of 0.005 using the pre-defined multiplicity adjustment. Patients with observable seizures (n=17) demonstrated a 9.1% reduction (p=0.29) in seizure frequency following treatment.

Among UX007 treated patients with any absence seizures (with or without observable seizures; n=19), 42% were responders (50% or greater reduction in seizure frequency). Of those with absence seizures on EEG at baseline (n=10), 80% were responders. Of the patients who had absence seizures as determined by EEG (without observable seizures; n=8), 88% were responders and no patients were assigned to placebo.

There was no difference in cognitive function as assessed by CANTAB in patients treated with UX007 compared to placebo.

Safety/Tolerability Results

Two of the 36 enrolled patients discontinued treatment during the eight-week placebo-controlled period, and 12 patients have discontinued during the extension period to date. Two patients discontinued due to adverse events, four patients due to tolerability reasons, and eight due to compliance or study burden issues.

There were no deaths, and no treatment-related serious adverse events. During the placebo-controlled period, 18 patients (72%) in the UX007 arm had treatment-related adverse events (AEs) and five patients (45%) in the placebo arm had treatment-related AEs. Most AEs were mild-to-moderate GI events including vomiting, diarrhea, and abdominal pain. Some gastrointestinal events were managed by adjusting dosing or dosing with food.

Phase 2 study design

The randomized, double-blind, placebo controlled Phase 2 study assessed the safety and efficacy of UX007 in patients with Glut1 DS. Thirty-six patients who met a pre-specified seizure count criteria in either observable seizures, such as generalized tonic-clonic or focal seizures, or absence seizures were randomized in a 3:1 ratio to either UX007 or placebo. Dosing was initiated over a 2-week titration period until the patient reached the target dose of 35% of total daily calories

from UX007. A daily seizure diary was used to capture observable seizures and an electroencephalography (EEG) was used at baseline and week 8 to capture absence seizures. Following the double-blind period, patients were given the option of rolling into an open-label extension period during which they were treated with UX007. Frequency reduction percentages provided are estimated based on the pre-specified statistical modeling.

About Glut1 DS and UX007

Glut1 DS is a severely debilitating disease characterized by seizures, developmental delay, and movement disorders. Glut1 DS is caused by a genetic defect in the transport of glucose into the brain. Because glucose is the primary source of energy for the brain, this disorder results in a chronic state of energy deficiency in the brain. Studies suggest a range of 3,000 to 7,000 Glut1 DS patients in the United States. There are currently no FDA approved treatments specific to Glut1 DS, though patients with the seizure phenotype are typically on the ketogenic diet.

UX007 is a highly purified, pharmaceutical-grade synthetic seven carbon fatty acid triglyceride created via a multi-step chemical process. It is an investigational medicine intended to provide patients with medium-length, odd-chain fatty acids that can be metabolized to increase intermediate substrates in the Krebs cycle, a key energy-generating process. Unlike typical even-chain fatty acids, UX007 can be converted to new glucose through the Krebs cycle, potentially providing an important added therapeutic effect, particularly when glucose levels are too low.

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 expectations regarding ongoing or additional studies for its product candidates and timing regarding these studies, 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, the uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of our regulatory filings and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations and the availability or commercial potential of our 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 the company in general, see Ultragenyx's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 17, 2017, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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