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Ultragenyx Announces Positive Interim Data From Phase 2 Study of UX007 in Long-Chain Fatty Acid Oxidation Disorder Patients

Improvements observed in both exercise tolerance assessments

Phase 3 planning to be initiated

NOVATO, Calif., Oct. 13, 2015 (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 interim data on the acute effects of the investigational treatment UX007 (triheptanoin) at the end of the initial 24-week treatment period of the Phase 2 study in long-chain fatty acid oxidation disorder (LC-FAOD) patients.

"We are encouraged by these positive exercise tolerance and safety interim results, which add to the growing body of data that support the continued development of UX007 in LC-FAOD," said Sunil Agarwal, M.D., Chief Medical Officer of Ultragenyx. "We look forward to discussing the data with regulatory authorities to define appropriate next steps."

Phase 2 Study Design and Baseline Characteristics

The single-arm, open-label Phase 2 study evaluated 29 pediatric and adult patients across three main symptom groups (musculoskeletal, liver/hypoglycemia, and cardiac). Patients needed to have moderate to severe FAOD with significant disease in at least one of these domains or a frequent medical events history in order to enroll. The study began with a four-week run-in period to assess baseline data while on the standard of care therapy including medium-chain triglyceride (MCT) oil, if applicable. The patients were then followed to evaluate the effects of UX007 treatment over 24 weeks on several endpoints, including cycle ergometer performance, 12-minute walk test (12MWT), liver disease/hypoglycemia, cardiac disease, and quality of life.

The 24-week analysis mainly evaluated the acute effects of UX007 on the musculoskeletal aspects of the disease. The last assessment in this analysis occurred at 18 weeks for the 12MWT and at 24 weeks for the cycle ergometry assessment. The administration of these tests was staggered in order to avoid patient exhaustion during a single visit. Patients who opt to continue will be treated for a total of 78 weeks, and rates of major medical events, such as rhabdomyolysis, hypoglycemia and cardiac events, will be monitored and compared to rates for the two years prior to treatment with UX007. The goal of the study is to evaluate the safety and tolerability of UX007 and to determine both the appropriate patient population as well as endpoints for evaluation in a Phase 3 study. These Phase 2 interim results are based on open-label uncontrolled treatment referenced to baseline run-in period for each patient, which limits definitive conclusions about efficacy and safety.

The majority of patients enrolled presented with musculoskeletal disease compared to a limited number presented with liver and cardiac symptoms. Patients spanned a wide age range from ten months to 58 years old. Patients with four LC-FAOD genotypes were enrolled: twelve (41%) with VLCAD, ten (35%) with LCHAD, four (14%) with CPT-II, and three (10%) with TFP. Prior to initiating treatment with UX007, 27 of the 29 patients were on the standard of care MCT oil therapy. UX007 was then titrated to a target dose of 25-35% of total daily caloric intake. The average dose of UX007 through 24 weeks was 30% of total daily caloric intake.

Four of the 29 enrolled patients discontinued prior to 24 weeks, one of which was attributed to an adverse event (diarrhea) from treatment with UX007. Patients performed only the assessments that were appropriate and valid for their age when they entered the study; therefore not all patients performed all assessments included in the study design. Of the 25 patients who continued on UX007 for all 24 weeks, 7 and 8 patients met the age (over six years old) and other eligibility requirements for the cycle ergometry test and 12MWT and completed tests for 24 week analyses, respectively. All but one patient performed both tests. 17 out of the 25 patients were either too young to complete the exercise testing (14/17) or unable to complete the testing due to other physical constraints (3/17). These patients will be reported on at the 78 week analysis.

Summary of Efficacy Results

Improvements were observed in both measures of exercise tolerance in patients who performed the tests. Improvements in

adult patient-reported quality of life scores were also observed in those patients, but no difference was seen in parent-reported scores for pediatric patients.

Overall major medical events appeared to decrease in the 25 patients who completed the 24 weeks of treatment when compared to the reported event rate in these patients in the 18-24 months prior to treatment with UX007. These data are preliminary and require significantly more time for proper evaluation at the 78 week time-point. The major medical event rate aggregates events related to hypoglycemia, rhabdomyolysis, and cardiomyopathy.

Musculoskeletal Patients

Cycle Ergometry

Seven qualified patients of the appropriate age performed the test at baseline and week 24. The three areas of evaluation with cycle ergometry included workload (measured in watts produced at a fixed heart rate), respiratory exchange ratio (RER), a measure of energy supply, and duration of cycling. Patients showed improvements in both workload and duration and no change in RER.

At week 24, the seven patients produced a 60% increase in watts over baseline representing a mean increase of +446.8 watts (median: +127.5; min, max: -388, +2438) from baseline of 744.6 watts. These results suggest an increase in muscle performance at a steady level of cardiac exertion as measured by heart rate.

Of the patients who completed all 40 minutes of the cycle ergometry test at baseline and at week 24, no patients had a reduced duration between baseline and week 24. For the patients (n=3) who were not able to complete all 40 minutes at baseline, mean duration increased 11.1 minutes at week 24 from 11.5 minutes at baseline, representing an increase of 97%.

12 Minute Walk Test (12MWT)

Eight qualified patients performed the test at baseline and at week 18 and showed a mean increase of +188 meters (median: 93.5; min, max: -80, 880) from a baseline mean of 673.4 meters, representing an increase of 28%. An improvement in the mean energy expenditure index (EEI), the ratio of heart rate per meter walked, was also observed that suggests an increase in exercise efficiency during the walk test.

The data on the 12MWT and cycle ergometry together support an improvement in muscle function and exercise efficiency in a small number of patients that would need to be confirmed in larger controlled studies.

Liver/Hypoglycemia and Cardiac Patients

Patients with liver/hypoglycemia and cardiac disease make up a limited number of patients who completed week 24 of the study; 3 and 2 patients, respectively. There were limited data on glucose or liver enzymes to evaluate ongoing disease in these younger patients but these patients qualified for entry due to frequent history of events and will contribute to the event rate measurement over 78 weeks. Hypoglycemia events/interventions in patients with liver disease will continue to be monitored over time. None of the patients were observed to have decompensated heart failure through the 24 weeks, but cardiomyopathy and related events will also be monitored over the complete 78 weeks of the study.

Other Efficacy Results

Quality of life was assessed via two separate surveys in the Phase 2 study. In the SF-12 patient-reported survey completed by adult patients (n=6) who participated in the cycle ergometry and 12MWT, significant improvements were reported in both the physical health and mental health composite scores as well as all subscores after 24 weeks of treatment with UX007.

While impairment in the physical health summary of the SF-10 parent-reported survey for pediatric patients (n=8) was reported, there was no change at week 24. There was no impairment and change reported in the psychosocial summary of the SF-10 survey at baseline and at week 24, respectively. The Peabody Developmental Motor Score (PDMS-2), an assessment of gross motor skills in patients under six years old, and the Pediatric Disability Inventory (PEDI-CAT), a care-giver score of functional disability, also showed no impairment in the overall patient population at baseline and no change after 24 weeks.

Safety/Tolerability Results

Four of the 29 enrolled patients discontinued prior to 24 weeks. One patient discontinued due to diarrhea in week 1, which resolved within a few days of discontinuation, and three patients withdrew consent (weeks 1, 8, 8) for reasons not attributed

to treatment with UX007. All other patients opted to continue treatment in the extension phase of the study.

There have been no deaths. One serious related adverse event for moderate gastroenteritis with vomiting was considered treatment-related. A viral infection was suspected, but the investigator could not rule out cause by UX007 given the proximity to dosing. That patient continues to be treated in the study and maintained dosing throughout the event, which has now resolved.

Overall, 18 patients (62%) had treatment-related adverse events, most of which were mild-to-moderate in nature. The most common treatment-related adverse events were diarrhea, abdominal/gastrointestinal pain, and vomiting. Some gastrointestinal events were managed by adjusting dosing or dosing with food. The most common adverse events, including those not deemed treatment-related, were viral infections, gastrointestinal disorders, rhabdomyolysis, fever, and headache.

Additional Phase 2 Results and Phase 3 Planning

All 25 patients opted to continue to be treated for a total of 78 weeks. Data after 78 weeks, including rates of major medical events before and after treatment with UX007, are expected to be released in the second half of 2016.

Based on these interim Phase 2 data, Ultragenyx intends to begin planning for a Phase 3 study of UX007 in LC-FAOD. An update on the design and timing of the Phase 3 study will be provided after discussions with regulatory authorities in the first half of 2016.

About LC-FAOD and UX007

LC-FAOD are a group of autosomal recessive genetic disorders characterized by metabolic deficiencies in which the body is unable to convert long-chain fatty acids into energy. The inability to produce energy from fat can lead to severe depletion of glucose in the body, and serious liver, muscle, and heart disease, which can lead to hospitalizations or early death. LC-FAOD are included in newborn screening panels across the U.S. and in certain European countries. LC-FAOD patients are currently treated with the avoidance of fasting, low-fat/high carbohydrate diets, carnitine, and medium-chain triglyceride (MCT) oil, a medical food product. Despite current therapy, many patients have significant metabolic events including hospitalizations and mortality due to LC-FAOD.

UX007 is a purified, pharmaceutical-grade form of triheptanoin, a specially designed synthetic triglyceride compound, 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 expected timing of release of additional data, and expected timing of discussion of Phase 3 design with regulatory authorities and initiation of a Phase 3 study 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, including 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 14, 2015, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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