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

Reductions observed in frequency and total duration of major medical events

NOVATO, Calif., Nov. 30, 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 78-week data from the Phase 2 study of UX007 (triheptanoin) in patients with long-chain fatty acid oxidation disorder (LC-FAOD). The frequency and duration of major medical events were reduced significantly during treatment with UX007, and patients demonstrated improved exercise tolerance and quality of life during the study.

"The reduction in frequency and duration of hospitalizations and other major medical events suggests a clinically meaningful improvement for patients and is consistent with the data from the prior retrospective compassionate use study," said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. "These results are encouraging and we continue to further develop the Phase 3 study design and endpoints before meeting with regulators and initiating the study in 2017."

Major Clinical Event Rates

The major clinical event (MCE) rate aggregates events from the 29-patient open-label Phase 2 study related to hypoglycemia, cardiomyopathy and rhabdomyolysis. For this study, events that qualified included those that led to a hospitalization, emergency room visit, or an emergency intervention at home. There was a 48.1 percent reduction (p=0.0208) in the mean annualized rate of MCEs and a 50.3 percent reduction (p=0.0284) in the mean annualized duration of all MCEs after 78 weeks of treatment, compared to the mean annualized number and duration of events in the 18 to 24 months prior to treatment with UX007.

	Annualized Event Rate			Annualized Duration Rate			Total Events		
	Pre	Post	% Change	Pre	Post	% Change	Pre	Post	% Change
All MCEs (total, n=29 patients)									
All events (mean)	1.690	0.877	-48.1%	5.961	2.964	-50.3%	70	39	-44.30%
All events (median)	1.333	0.659	-50.6%	5.332	1.244	-76.7%			
All hospitalization events (mean)	1.391	0.652	-53.1%	5.662	2.739	-51.6%	57	29	-49.10%

Among the event subtypes, rhabdomyolysis was the predominant MCE and there were fewer hypoglycemia events and only a few cardiomyopathy events. There was a reduction in the mean annualized rates and total duration of all events for rhabdomyolysis, cardiomyopathy, and hypoglycemia events after initiation of treatment with UX007. These findings were generally comparable to those observed in the retrospective compassionate use study previously conducted by Ultragenyx with partial reduction in rhabdomyolysis and near complete reduction of hypoglycemia events.

	Annualized Event Rate			Annualized Duration Rate			Total Events		
	Pre	Post	% Change	Pre	Post	% Change	Pre	Post	% Change
Rhabdomyolysis									
All Rhabdomyolysis events (mean)	1.303	0.833	-36.1%	3.949	2.792	-29.3%	55	37	-32.7%
Hospitalization events only (mean)	1.027	0.630	-38.7%	3.674	2.589	-29.5%	43	28	-34.9%
Hypoglycemia									
All Hypoglycemia events (mean)	0.318	0.023	-92.8%	1.414	0.023	-98.4%	12	1	-91.7%
Hospitalization events only (mean)	0.295	0.000	-100.0%	1.391	0.000	-100.0%	11	0	-100.0%
Cardiomyopathy									
All Cardiomyopathy events (mean)	0.069	0.021	-69.6%	0.598	0.149	-75.1%	3	1	-66.7%
Hospitalization events only (mean)	0.069	0.021	-69.6%	0.598	0.149	-75.1%	3	1	-66.7%

Exercise Tolerance

Eight patients performed the twelve minute walk test (12MWT) at baseline and at Week 60, and showed a 29.7 percent improvement (mean increase: +199.8 meters; median: 149.5; min,max: -122, 1000) from a baseline of 673.4 meters. These results demonstrate that the increase in distance walked observed at 18 weeks was maintained through 60 weeks. The cycle ergometry test at 78 weeks was inconclusive and uninterpretable due to missing data as a result of scheduling conflicts, withdrawal of consent, intercurrent illness and other factors.

Quality of Life Assessment

Health Related Quality of life was assessed in the Phase 2 study using age appropriate SF-10™ (5-17 years, n=3) and SF-12v2® (>18 years, n=5) Health Surveys. Significant improvements in the impaired physical summary measures (SF-12v2 Physical Component Summary and SF-10 Physical Health Summary) reported at the start of the study were observed after 78 weeks of treatment with UX007.

Safety/Tolerability Results

Five of the 29 enrolled patients discontinued treatment over the course of the study. One patient discontinued due to diarrhea in week 1, which resolved within a few days of discontinuation, and four patients withdrew consent (weeks 1, 8, 8, 78) for reasons not attributed to treatment with UX007.

There were no deaths. There was one previously reported treatment-related serious adverse event for moderate gastroenteritis with vomiting. This patient completed the study and maintained dosing throughout the event, which has now resolved. Overall, 19 patients (66%) 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 diarrhea, rhabdomyolisis, vomiting, viral infections, gastrointestinal disorders, headache and fever.

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.

Twenty-five patients completed 24 weeks of treatment, at which point the acute effects of UX007 treatment on the muscular aspects of the disease were evaluated. Twenty-four patients opted to continue to be treated for a total of 78 weeks with one who withdrew consent late during this period on turning 18 years old. Safety and quality of life assessments were also measured throughout the study. These Phase 2 results are based on open-label uncontrolled treatment referenced to baseline run-in period using careful medical chart reviews for each patient, but the lack of a randomized parallel control group does limit definitive conclusions about efficacy and safety.

The majority of patients enrolled presented with musculoskeletal disease compared to a limited number who 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.

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. Due to the small number of patients who completed a number of the assessments in this Phase 2 study, the results would need to be confirmed in a larger controlled study.

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 November 8, 2016, and its subsequent periodic reports filed with the Securities and Exchange Commission.

Contact Ultragenyx Pharmaceutical Inc.
Investors & Media
Ryan Martins
844-758-7273