Ultragenyx Announces Positive 24-week Data from First Cohort of Phase 1/2 Study of DTX401 Gene Therapy in Glycogen Storage Disease Type Ia

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DTX401 Response in Time to Hypoglycemia and Improved Glucose Control Maintained or Improved in All Three Patients

Data from Higher-dose Cohort 2 Expected Mid-2019

NOVATO, Calif., Feb. 21, 2019 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development of novel products for serious rare and ultra-rare genetic diseases, today announced positive longer-term top-line safety and efficacy data from the first, lowest dose cohort of the ongoing Phase 1/2 study of DTX401, an adeno-associated virus (AAV) based gene therapy for the treatment of glycogen storage disease type Ia (GSDIa). After 24 weeks of treatment, the three patients enrolled in Cohort 1 have either maintained or further increased their time to hypoglycemia during the controlled fasting challenge compared to baseline. All three patients continue to show a clinical response with additional improvements in glucose control reflected by prolonged time to hypoglycemia during a controlled fasting challenge and by reductions in the use of cornstarch to maintain normal glucose levels throughout the day and overnight.

“We are encouraged by this longer-term data showing durable clinical responses in all patients in the first cohort. All three patients have decreased their daily cornstarch by 50 to 75% compared to baseline, reflecting further improvement in glucose metabolism in the liver,” said Eric Crombez, M.D., Chief Medical Officer of the Ultragenyx Gene Therapy development unit. “Importantly, the two patients receiving steroids completed their tapering course weeks before the 24-week fasting challenge and still have demonstrated a sustained clinical response.”

DTX401 Cohort 1 Data Summary
Efficacy Summary
The first patient in Cohort 1 demonstrated sustained improvement in time to hypoglycemia of 6.8 hours at Week 24, from 3.8 hours at baseline and 7.7 hours at Week 12. This patient received a tapering course of steroids, which began during Week 8 and ended at Week 16, to manage a mild asymptomatic elevation in alanine aminotransferase (ALT) levels due to a response to the vector administration.

Patient 2 showed a further improvement in time to hypoglycemia to 13.1 hours at Week 24, from 4.1 hours at baseline and 9.0 hours at Week 12. At Week 24, the fasting challenge was terminated at the patient’s request due to hunger and at the time the test was terminated, the patient’s glucose level remained in the normal range. This patient received a tapering course of steroids, which began at Week 12 and ended at Week 18, to manage a mild asymptomatic elevation in ALT levels due to a response to the vector administration.

Patient 3 continued to show a clinical response, and maintained the improvement in time to hypoglycemia of 6.5 hours at Week 24, from 5.4 hours at baseline and 6.5 hours at Week 12.

Safety Summary
As of February 20, 2019, there have been no infusion-related adverse events and no treatment-related serious adverse events reported. All adverse events have been Grade 1 or 2. Patients 1 and 2 had mild elevations in ALT, similar to what has been observed in other programs using AAV-based gene therapy, and were successfully treated with a tapering course of steroids.

DTX401 Cohort 2 Enrollment Ongoing with Data Expected Mid-2019
Enrollment is ongoing in the higher dose Cohort 2, which includes three patients each receiving a single 6.0 × 10^12 GC/kg dose of DTX401. Data from Cohort 2 are expected in mid-2019.

DTX401 Phase 1/2 Study Design
The open-label, multicenter Phase 1/2 study is evaluating the safety, tolerability and therapeutic response of DTX401 in adults with GSDIa. All patients enrolled in the first cohort had null genotypes, with termination mutations or active site mutations, which should result in no residual enzyme activity. Patients in this first cohort each received a single 2.0 × 10^12 GC/kg dose of DTX401, an AAV8 expressing the glucose-6-phosphatase gene (G6Pase-α) under control of the native promoter. Key efficacy assessments include time to hypoglycemia (defined as glucose <60 mg/dL or onset of clinical symptoms) during a controlled in-hospital fasting challenge, impact on biomarkers such as lipids and uric acid, and measurement of glycogen storage in liver by MRI.

About GSDIa
GSDIa is the most severe genetically inherited glycogen storage disease. It is caused by a defective gene for the enzyme G6Pase-α, resulting in the inability to regulate blood sugar (glucose). Hypoglycemia in patients with GSDIa can be life-threatening, while the accumulation of the complex sugar glycogen in certain organs and tissues can impair the ability of these tissues to function normally. If chronically untreated, patients can develop severe lactic acidosis, progress to renal failure, and potentially die in infancy or childhood. There are no approved pharmacologic therapies. An estimated 6,000 patients worldwide are affected by GSDIa.

About DTX401

DTX401 is an investigational AAV8 gene therapy designed to deliver stable expression and activity of G6Pase-α under control of the native promoter. DTX401 is administered as a single intravenous infusion and has been shown in preclinical studies to improve G6Pase-α activity and reduce hepatic glycogen levels, a well-described biomarker of disease progression. DTX401 has been granted Orphan Drug Designation in both the United States and Europe.

About Ultragenyx Pharmaceutical Inc.
Ultragenyx is a biopharmaceutical company committed to bringing to patients novel products for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

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 related to Ultragenyx's expectations regarding the timing of release of additional data for its product candidates, and enrollment, dosing and other plans for its clinical programs and clinical 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 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 products and 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 Ultragenyx in general, see Ultragenyx's Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 20, 2019, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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