



## Ultragenyx Announces Positive Topline Results from First Cohort of Phase 1/2 Clinical Study of DTX401 Gene Therapy in Glycogen Storage Disease Type Ia

January 4, 2019

*DTX401 Response Observed in All Three Patients, with Two Patients Demonstrating Clinically Meaningful Improvement in Time to Hypoglycemia  
Study to Advance to Cohort 2 at a Higher Dose*

NOVATO, Calif., Jan. 04, 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 topline 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). A biologic response, reflected by improved glucose control and increased time to hypoglycemia during fasting, was observed in all three patients, with two patients demonstrating a clinically meaningful improvement in time to hypoglycemia during a controlled fasting challenge.

"Two of three patients in this first dose cohort experienced a sufficient increase in time to hypoglycemia such that they may be able to sleep through the night without taking supplemental cornstarch," said Eric Crombez, M.D., Chief Medical Officer of the Ultragenyx Gene Therapy development unit. "In addition to the promising results observed with the controlled fasting challenge, all three patients have demonstrated improvement in glucose control throughout the day, and all three patients have been able to decrease their daily cornstarch intake by approximately half. We are extremely encouraged by these results and look forward to beginning enrollment in the second cohort this month, with results expected in mid-2019."

"We are very pleased with what we are seeing in this first cohort of patients. After 20 years of research in preparation for this study, it is extremely rewarding to see such positive results on the low dose. We are excited about the potential as the dose is increased," said David Weinstein, M.D., M.M.Sc., Professor and Director, Glycogen Storage Disease Program at Connecticut Children's Medical Center and UConn Health.

### **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  $2.0 \times 10^{12}$  GC/kg dose of DTX401, an AAV8 expressing the glucose-6-phosphatase gene (G6Pase- $\alpha$ ) 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.

### **DTX401 Cohort 1 Data Summary**

#### *Efficacy Summary*

The first patient in Cohort 1 had a clinically meaningful improvement in time to hypoglycemia from 3.8 hours at baseline to 7.7 hours at Week 12 (103 percent increase). This patient received a tapering course of steroids, beginning on day 59, to manage a mild asymptomatic elevation in alanine aminotransferase (ALT) levels, which returned to normal levels following the start of the steroid taper.

Patient 2 had a clinically meaningful improvement in time to hypoglycemia from 4.1 hours at baseline to 9.0 hours at Week 12 (120 percent increase). In this instance, the fasting challenge was terminated based on possible hypoglycemia symptoms, and at the time the test was terminated, the patient's glucose level remained well above 60 mg/dL. This patient received a tapering course of steroids beginning at Week 12 to address a slightly elevated ALT.

Patient 3 showed a biologic response, reflected by an improvement in time to hypoglycemia from 5.4 hours at baseline to 6.5 hours at Week 12 (20 percent increase).

Additional data from future fasting test assessments are needed to determine whether the results from all three patients are sustained or improved over time.

#### *Safety Summary*

As of the primary cutoff date of November 28, 2018, 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. These two patients successfully completed their tapering steroid regimens. The initial highest dose of steroids in the steroid taper regimen was prospectively reduced to 40 mg/kg to help reduce any risk for hypoglycemia in this particular null genotype population based on the advice of GSDIa experts.

### **DTX401 Cohort 2 Initiation**

The independent Data Monitoring Committee (DMC) has completed its review of Week 12 data from Cohort 1 and has concluded that it is safe to proceed to the second dose cohort of the study. Ultragenyx believes a higher dose may be more optimal in achieving the best clinical response and has elected to proceed to the next higher dose given the safety profile observed in the first cohort. In Cohort 2, three patients will be enrolled and will each receive a single dose of  $6.0 \times 10^{12}$  GC/kg. The first patient in the second dose cohort is expected to be dosed in January 2019, and Cohort 2 data are expected in mid-2019.

### **About GSDIa**

GSDIa is the most common genetically inherited glycogen storage disease. It is caused by a defective gene for the enzyme G6Pase- $\alpha$ , 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 adeno-associated virus vector (AAV) type 8 gene therapy designed to deliver stable expression and activity of G6Pase- $\alpha$  under control of the native promoter. DTX401 is administered as a single intravenous infusion and has been shown in preclinical studies to improve G6Pase- $\alpha$  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 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](http://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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 6, 2018, and its subsequent periodic reports filed with the Securities and Exchange Commission.

#### **Contact Ultragenyx Pharmaceutical Inc.**

Investors & Media  
Danielle Keatley  
415-475-6876



Source: Ultragenyx Pharmaceutical Inc.