UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 08, 2021

Ultragenyx Pharmaceutical Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-36276**	**27-2546083**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
60 Leveroni Court Novato, California		**94949**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 415 483-8800

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	RARE	NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On January 8, 2021, Ultragenyx Pharmaceutical Inc. (the "Company") issued a press release announcing positive longer-term safety and efficacy data from the first three cohorts of the Company's ongoing Phase 1/2 studies of DTX401 an investigational adeno-associated virus ("AAV") gene therapy for the treatment of Glycogen Storage Disease Type Ia (GSDIa), and DTX301, an AAV gene therapy for the treatment of ornithine transcarbamylase (OTC) deficiency, and other updates related to the Company's gene therapy portfolio.

A copy of the Press Release is filed as Exhibit 99.1 and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	**Description**
99.1	Press Release, dated January 8, 2021.
104	The cover page from the Company's Current Report on Form 8-K dated January 8, 2021 formatted in Inline XBRL.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Ultragenyx Pharmaceutical Inc.

Date: January 08, 2021

By: /s/ Mardi C. Dier

Mardi C. Dier
Executive Vice President & Chief Financial Officer

Exhibit 99.1

Contact Ultragenyx
Investors & Media
Joshua Higa
(415) 475-6370

Ultragenyx Announces Progress Across Broad Gene Therapy Portfolio and Positive Longer-Term Data from Multiple Phase 1/2 Gene Therapy Studies

Durable and Clinically Meaningful Responses Reported from Phase 1/2 Studies of DTX401 for GSDIa and DTX301 for OTC

Phase 3 Studies for DTX401 and DTX301 to Begin in 2021

IND for UX701 for Wilson Disease Submitted; Expect to Enter Clinic in First Half 2021 using AAV Drug Product Made by HeLa PCL Platform

Novato, Calif. — January 8, 2021 —Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for rare and ultra-rare diseases, today announced positive longer-term safety and efficacy data from the first three cohorts of the ongoing Phase 1/2 studies of DTX401, an investigational adeno-associated virus (AAV) gene therapy for Glycogen Storage Disease Type Ia (GSDIa), and DTX301, an AAV gene therapy for ornithine transcarbamylase (OTC) deficiency. In addition, dosing is nearing completion for the prophylactic steroid cohorts in both studies. Discussions with regulatory agencies continue to progress for both programs, and Ultragenyx expects to initiate Phase 3 studies for DTX401 in the first half of 2021 and for DTX301 in the second half of 2021. The company also plans to start a seamless single-protocol Phase 1/2/3 study for UX701, an AAV gene therapy for Wilson disease.

“We continue to see durable and clinically meaningful responses in patients in both the DTX401 and DTX301 programs. GSDIa patients treated with DTX401 demonstrate continually improved glucose metabolism with reduction or elimination of cornstarch dependence over time. OTC patients treated with DTX301 show good metabolic control after tapering or discontinuation of alternate pathway medications and protein restricted diet,” said Eric Crombez, M.D., Chief Medical Officer of the Ultragenyx Gene Therapy development unit. “With the initiation of the UX701 program in Wilson disease and progression of DTX401 and DTX301 to Phase 3 as well as progress in our preclinical stage programs, we are leveraging our proprietary platforms to advance one of the broadest portfolios of gene therapy programs in the industry.”

DTX401 (GSDIa) Program

Phase 1/2 data update: All patients (n=9) responding and demonstrating continued improvement of glucose control while reducing or eliminating cornstarch therapy

All nine patients continue to demonstrate improved glucose control while tapering or discontinuing oral glucose replacement with cornstarch and improvements in energy metabolism pathways over the long term. Patients continue to taper the amount and frequency of cornstarch dosing with progress in eliminating overnight and daytime cornstarch doses. At the primary evaluation timepoint at Week 52, the overall mean reduction in cornstarch was 77% across all three cohorts, including two patients in Cohort 3 showing a reduction of greater than 75%. Longer term follow-up for more than two years for the three patients in Cohort 1 have shown

sustained and continued cornstarch reductions with a mean reduction of 91% through weeks 104 and 120. Two patients (one each from Cohort 1 and 3) are completely off cornstarch therapy at weeks 127 and 60, respectively.

Data collected from continuous glucose monitoring (CGM) implemented in Cohort 3 indicate that glycemic control was maintained and even improved despite the reductions in cornstarch dependence. Through Week 48, these patients had decreased cornstarch use by between 30% and 92%. Even with these substantial cornstarch reductions, the patients had a mean 10% increase in the percent of time spent in euglycemia, defined by blood glucose levels in the normal range of 60 to 120 mg/dL.

Additionally, these reductions in cornstarch dosing have had an impact on energy metabolism and body weight. Seven of nine treated patients had decreases of 5% (5.6 kg) to 21% (10.5 kg) in bodyweight following DTX401 treatment, with a mean decrease of 12% from the mean baseline weight of 82.8 kg in these seven patients. The notable weight loss is attributed to improved glycemic control and potentially increased physical activity reported by patients.

Interviews with patients following their Week 24 and/or Week 52 visits provide support for the study results seen to date. Patients reported improvements in both their physical and mental health. This includes increased energy and strength, supporting normalization of daily activities and weight loss, as well as greater mental acuity and reduced stress, with the latter in part noted as related to diminished fears of missing a cornstarch dose. No negative patient feedback has been received to date on their experiences with DTX401.

The safety profile of DTX401 remains favorable; 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.

All three GSDIa patients dosed in prophylactic steroid cohort doing well with no safety issues

All three patients in a fourth and final Phase 1/2 cohort, which utilizes prophylactic steroids, have been dosed at the same dose as Cohorts 2 and 3. There have been no safety issues through up to 11 weeks post-dosing, and all three patients are doing well and have demonstrated early reduction in daily cornstarch intake.

Phase 3 study of DTX401 in GSDIa expected to initiate in first half 2021

The company has completed Scientific Advice with the European Medicines Agency (EMA) and an End of Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA) to discuss the Phase 2 data, the Phase 3 design, and endpoints. Based in part on this feedback, Ultragenyx plans to conduct a 48-week Phase 3 study in approximately 50 patients, randomized 1:1 to DTX401 or placebo. All patients in the study will cross over to the therapeutic arm and receive therapy at the end of the initial 48-week follow-up period.

Based on the regulatory discussion and pending finalization, Ultragenyx intends to study as primary endpoints glycemic control by assessing the maintenance of glucose control by CGM and the reduction in cornstarch requirements. These primary endpoints will be supported by key secondary endpoints of improvement in percent of time spent in normal glucose control (60-120 mg/dL), time to hypoglycemia in controlled fasting challenge, and the GSDIa functional assessment diary signs and symptom scale. The durability of the treatment will be supported by the longer-term Phase 1/2 data and early treated Phase 3 patients. Based on the results to date, the therapeutic benefit appears to increase over time during the second year after treatment. Ultragenyx expects to initiate the study in the first half of 2021.

DTX301 (OTC) Program

Phase 1/2 data update: All six previous responders demonstrate durable metabolic control, including greater than two-year sustained responses

As previously reported, six out of nine treated patients responded to DTX301 on a dose-dependent basis, including all three treated at the highest dose. The three complete responders have now been stable through 104, 130, and 156 weeks post-treatment with good ammonia control despite discontinuation of their alternative pathway medications and protein-restricted diets. The three other responders also remain stable through Weeks 52 and 130 and are either continuing to taper medications and diet or intend to continue tapering once COVID-19 restrictions are lifted and patients can be more closely followed in clinic. All responders remain in excellent clinical condition with no significant adverse events, hospitalizations, or other events related to OTC deficiency.

There have been no infusion-related adverse events and no treatment-related serious adverse events reported in the study. All treatment-related adverse events have been Grade 1 or 2.

Prophylactic steroid cohort: Two OTC patients dosed with no safety issues; third patient to be dosed this month

Two of three patients have been dosed in the prophylactic steroid cohort, the final cohort in the Phase 1/2 study, at the same dose as in Cohort 3. Through up to 18 weeks post-dosing, both patients are doing well clinically with good metabolic control and without any safety issues. The third patient in the cohort, who has not yet been dosed due to delays related to COVID-19, is expected to be dosed this month.

Phase 3 study of DTX301 in OTC expected to initiate in second half 2021

Ultragenyx completed the initial Scientific Advice process with the EMA regarding the Phase 3 development plan and continues to have discussions with the FDA regarding the Phase 3 study of DTX301. The EOP2 meeting with the FDA had been delayed and is now scheduled to occur late in the first quarter of 2021.

Based on regulatory feedback to date, the proposed Phase 3 study design will include approximately 50 patients, randomized 1:1 to DTX301 or placebo and followed for 48 weeks initially. The change in 24-hour ammonia levels is expected as the primary endpoint. The entry criteria will allow patients with higher baseline ammonia levels than in the Phase 1/2 study to allow sufficient power to assess the change in ammonia. The primary endpoint will be supported by the change in the rate of ureagenesis as a key secondary endpoint that evaluates the capacity to generate urea from ammonia. Additional secondary endpoints include reduction or discontinuation of scavenger medications and normalization of protein-restricted diet.

The Phase 3 study is expected to begin dosing in the second half of 2021. Placebo patients participating in the study will receive DTX301 at the end of the initial 48-week follow-up period. The company will continue to follow patients in the ongoing Phase 1/2 study during the Phase 3 in order to augment the overall long-term data package supporting the durability of DTX301.

Update on Dose Level Determination Method for DTX301 and DTX401

A new droplet digital PCR (ddPCR) test method has been implemented to determine the level of genome copy (GC) titers for Ultragenyx's gene therapy candidates. This new process improves the accuracy, precision, and specificity compared to the prior quantitative PCR (qPCR) approach. As a result, the actual highest Phase 1/2 dose and planned Phase 3 dose for DTX301 is 1.7 x 10^13 GC/kg (from 1.0 x 10^13 GC/kg) and for DTX401 is

1.0 x 10^13 GC/kg (from 6.0 x 10^12 GC/kg). This change in dose designation of the same product does not represent a change in dose but a more accurate estimate of the actual GC content of the product relative to qPCR, the prior method.

UX701 (Wilson Disease) Program using HeLa PCL Platform

Ultragenyx submitted an Investigational New Drug (IND) application in December as planned for UX701, an AAV9 gene therapy for the treatment of Wilson Disease. The company expects to initiate a seamless single-protocol Phase 1/2/3 study in the first half of 2021. Manufacture and testing of GMP grade drug product to supply the clinical study are complete using the company's proprietary HeLa 2.0 PCL process at the 2,000 liter scale.

Ultragenyx previously reported that UX701 has received orphan drug designation by the FDA. The European Commission has since also granted orphan drug designation for the gene therapy.

Advancing HeLa Producer Cell Line (PCL) Platform and Programs

Ultragenyx continues to advance the proprietary HeLa producer cell line (PCL) platform with recent HeLa 3.0 improvements. The platform enables large 2,000 liter commercial-scale manufacturing and yields high-quality product from a highly reproducible, highly scalable platform, and less expensive process.

Breaking Ground on Gene Therapy Manufacturing Plant

Ultragenyx recently broke ground on its new manufacturing facility to provide important internal capacity to develop and manufacture supply of the company's gene therapies for both clinical-stage and approved products. The initial 100,000 square foot facility will be able to support two independent manufacturing suites with an initial capacity of 30 runs per year and is expected to be complete in 2023.

DTX201 / BAY 2599023 (Hemophilia A) Program Partnered with Bayer AG and Currently Manufactured in HeLa PCL System

Updated Phase 1/2 data through three cohorts were presented at the American Society of Hematology Annual Meeting & Exposition in December 2020 for DTX201 / BAY 2599023, an AAVhu37 gene therapy in development by Bayer, using Ultragenyx's HeLa PCL platform. The data demonstrate dose-responsive and sustained FVIII levels with no evidence of loss of expression through follow-up between 40 and 80 weeks after treatment. Patients in Cohorts 2 and 3 were on FVIII prophylaxis prior to gene therapy, which they have discontinued since approximately 6 weeks after receiving treatment. No spontaneous bleeds have been reported after achieving protective FVIII levels of greater than 15 IU/dL.

No treatment-emergent serious adverse events have been reported. ALT elevations have been observed in three patients at higher doses, which were managed with corticosteroid treatment.

Preclinical HeLa PCL Programs Progress

Earlier-stage preclinical programs utilizing the HeLa PCL platform continue to advance, including:

· The collaboration with Solid Biosciences to develop new gene therapies for Duchenne muscular dystrophy using Solid's novel microdystrophin with AAV8 variants and the HeLa 3.0 platform for cost-effective manufacturing.

· The platform-based partnership with Daiichi Sankyo Company, which provides a non-exclusive license to Ultragenyx's AAV-based gene therapy manufacturing technologies.

About GSDIa and DTX401

GSDIa is the most severe genetically inherited glycogen storage disease. It is caused by a defective gene coding 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.
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, and Regenerative Medicine Advanced Therapy (RMAT) designation and Fast Track designation in the United States.

About OTC Deficiency and DTX301

OTC deficiency, the most common urea cycle disorder, is caused by a genetic defect in a liver enzyme responsible for detoxification of ammonia. Individuals with OTC deficiency can build up excessive levels of ammonia in their blood, potentially resulting in acute and chronic neurological deficits and other toxicities. It is estimated that more than 10,000 people are affected by OTC deficiency worldwide, of whom approximately 80 percent are classified as late-onset and represent a clinical spectrum of disease severity. In the late-onset form of the disease, elevated ammonia can lead to significant medical issues for patients. Neonatal onset disease occurs only in males, presents as severe disease, and can be fatal at an early age. Approved therapies, which must be taken multiple times a day for the patient's entire life, do not eliminate the risk of future metabolic crises. Currently, the only curative approach is liver transplantation.

DTX301 is an investigational AAV type 8 gene therapy designed to deliver stable expression and activity of OTC following a single intravenous infusion. It has been shown in preclinical studies to normalize levels of urinary orotic acid, a marker of ammonia metabolism. DTX301 was granted Orphan Drug Designation in both the United States and Europe.

About Wilson Disease and UX701

Wilson disease is a rare inherited disorder caused by mutations in the ATP7B gene, which results in deficient production of ATP7B, a protein that transports copper. Loss of function of this copper-binding protein results in the accumulation of copper in the liver and other tissues, most notably the central nervous system. Patients with Wilson disease experience hepatic, neurologic and/or psychiatric problems. Those with liver disease can experience such symptoms as fatigue, lack of appetite, abdominal pain and jaundice, and can progress to fibrosis, cirrhosis, life-threatening liver failure and death. Wilson disease can be treated by reducing copper absorption or removing excess copper from the body using life-long chelation therapy, but unmet needs exist

because some treated patients experience clinical deterioration and severe side effects. Wilson disease affects more than 50,000 individuals in the developed world.

UX701 is an investigational AAV type 9 gene therapy designed to deliver stable expression of a truncated version of the ATP7B copper transporter following a single intravenous infusion. It has been shown in preclinical studies to normalize copper trafficking and excretion from the body. UX701 was granted Orphan Drug Designation in the United States and European Union.

About Ultragenyx

Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients 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 and ensuring majority access to its therapies for patients who can benefit.

For more information on Ultragenyx, please visit the company's website at www.ultragenyx.com.

Ultragenyx 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 and projections regarding its future operating results and financial performance, anticipated cost or expense reductions, the timing, progress and plans for its clinical programs and clinical studies, future regulatory interactions, and the components and timing of regulatory submissions 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, collaboration with third parties, 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 effects from the COVID-19 pandemic on the company's clinical activities, business and operating results, risks related to reliance on third party partners to conduct certain activities on the company's behalf, uncertainty and potential delays related to clinical drug development, smaller than anticipated market opportunities for the company's products and product candidates, manufacturing risks, competition from other therapies or products, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's 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 October 27, 2020, and its subsequent periodic reports filed with the Securities and Exchange Commission.

# # #