

**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): October 07, 2021

Ultragenyx Pharmaceutical Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-36276
(Commission File Number)

27-2546083
(IRS Employer
Identification No.)

60 Leveroni Court
Novato, California
(Address of Principal Executive Offices)

94949
(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 October 7, 2021, Ultragenyx Pharmaceutical Inc. (the “**Company**”) and GeneTx Biotherapeutics LLC (“**GeneTx**”) issued a press release (the “**Press Release**”) announcing that the first patient has been dosed in the Phase 1/2 study of GTX-102, an investigational treatment for Angelman syndrome, with three other patients enrolled and scheduled to begin dosing. A copy of the Press Release is filed as Exhibit 99.1

Item 9.01 Financial Statements and Exhibits.**(d) Exhibits**

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release, dated October 7, 2021.
104	The cover page from the Company’s Current Report on Form 8-K dated October 7, 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 thereunto duly authorized.

Ultragenyx Pharmaceutical Inc.

Date: October 7, 2021

By: /s/ Mardi C. Dier

Mardi C. Dier

Executive Vice President & Chief Financial Officer



GeneTx and Ultragenyx Announce First Patient Dosed in Canada in Phase 1/2 Clinical Trial of GTX-102 in Patients with Angelman Syndrome

SARASOTA, Fla., and NOVATO, Calif. — October 7, 2021 — GeneTx Biotherapeutics LLC and Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), companies partnered in the development of GTX-102, an investigational treatment for Angelman syndrome, today announced that the first patient has been dosed in the Phase 1/2 study in Canada with three other patients enrolled and scheduled to begin dosing.

“We have been actively working with our principal investigators across all three regions over the past several months to efficiently execute this Phase 1/2 trial and can now move forward rapidly with study enrollment,” said Scott Stromatt, M.D., Chief Medical Officer of GeneTx. “This is an in-depth study to evaluate both safety and measures of efficacy across multiple domains in Angelman Syndrome that will inform us on the optimal endpoints to evaluate in the registrational program.”

The open-label, multiple-dose, dose-escalating Phase 1/2 study is evaluating the safety, tolerability and efficacy of GTX-102 in pediatric patients with Angelman syndrome who have a genetically confirmed diagnosis of full maternal *UBE3A* gene deletion. The study will evaluate the overall clinical global impression scale of change after the first two doses, along with a panel of other efficacy assessments for the domains impacted in Angelman, including communication, sleep, behavior, gross motor skills, fine motor skills, and seizures, which will be measured at Day 128.

“The dosing schedule across the three arms of this study, in the U.K., Canada, and the U.S., is designed to achieve a cumulative dose range similar to the original study where we saw impact across domains beginning at the lowest dose of 3.3 mg and meaningful improvements at 13-20 mg of cumulative dosing in younger patients,” said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. “Based on the prior data, we believe this study should contribute meaningfully to our understanding of dose response and safety in this program.”

About the GTX-102 Phase 1/2 Study Design in Canada and the U.K.

Under the protocol approved in the U.K. and Canada, 12 patients will be enrolled into two cohorts split by age: patients ages 4 to <8 years will be enrolled into Cohort 4, and patients ages 8 to <18 years will be enrolled into Cohort 5. Two in the younger cohort and two in the older cohort will be enrolled first and assessed after two doses by a data safety monitoring board (DSMB). The DSMB will review the available safety data and provide a recommendation on the enrollment for the remaining 8 patients

The starting doses in younger cohort 4 and older cohort 5 will be 3.3 and 5 mg, respectively. Patients will receive two doses and will be assessed for safety and efficacy before moving to step-increases in dosing. If indicated, they will increase one step for two more doses with dose increases based on response and enhanced safety monitoring. Patients will then transition to a maintenance dose phase during which they will receive GTX-102 every three months and continue to be monitored for response and safety. In this phase, individual dose titration may continue up to a maximum dose of 14 mg if safety is sustained, and the clinical response is not scored as “much improved” by the clinical global impression scale in at least two or more domains.

A preliminary update on the first few patients will be available at the end of the year, and complete data on all 12 patients in the UK/Canada arm of the study is anticipated in mid 2022 after completing day 128 of the protocol.

About Angelman Syndrome

Angelman syndrome is a rare, neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the *UBE3A* gene. The maternal-specific inheritance pattern of Angelman syndrome is due to genomic



imprinting of *UBE3A* in neurons of the central nervous system, a naturally occurring phenomenon in which the maternal *UBE3A* allele is expressed and the paternal *UBE3A* is not. Silencing of the paternal *UBE3A* allele is regulated by the *UBE3A* antisense transcript (*UBE3A-AS*), the intended target of GTX-102. In almost all cases of Angelman syndrome, the maternal *UBE3A* allele is either missing or mutated, resulting in limited to no protein expression. This condition is typically not inherited but instead occurs spontaneously. It is estimated to affect 1 in 12,000 to 1 in 20,000 people globally.

Individuals with Angelman syndrome have developmental delay, balance issues, motor impairment and debilitating seizures. Some individuals with Angelman syndrome are unable to walk and most do not speak. Anxiety and disturbed sleep can be serious challenges in individuals with Angelman syndrome. While individuals with Angelman syndrome have a normal lifespan, they require continuous care and are unable to live independently. Angelman syndrome is not a degenerative disorder, but the loss of the *UBE3A* protein expression in neurons results in abnormal communications between neurons. Angelman syndrome is often misdiagnosed as autism or cerebral palsy. There are no currently approved therapies for Angelman syndrome; however, several symptoms of this disorder can be reversed in adult animal models of Angelman syndrome suggesting that improvement of symptoms can potentially be achieved at any age.

About GTX-102

GTX-102 is an investigational antisense oligonucleotide delivered via intrathecal administration and designed to target and inhibit expression of *UBE3A-AS*. Nonclinical studies show that GTX-102 reduces the levels of *UBE3A-AS* and reactivates expression of the paternal *UBE3A* allele in neurons of the CNS. Reactivation of paternal *UBE3A* expression in animal models of Angelman syndrome has been associated with improvements in some of the neurological symptoms associated with the condition. GTX-102 has been granted Orphan Drug Designation, Rare Pediatric Disease Designation, and Fast Track Designation from the U.S. Food and Drug Administration (FDA). In August 2019, GeneTx and Ultragenyx announced a partnership to develop GTX-102, with Ultragenyx receiving an exclusive option to acquire GeneTx.

About GeneTx Biotherapeutics

GeneTx Biotherapeutics LLC is a startup biotechnology company singularly focused on developing and commercializing a safe and effective antisense therapeutic for the treatment of Angelman syndrome. GeneTx was launched by FAST, a patient advocacy organization and the largest non-governmental funder of Angelman syndrome research. GeneTx licensed the rights to antisense technology intellectual property from the Texas A&M University System in December 2017.

About Ultragenyx Pharmaceutical Inc.

Ultragenyx is a biopharmaceutical company committed to bringing novel therapies to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved medicines and treatment candidates aimed at addressing diseases with high unmet medical need and clear biology, 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 and projections regarding its business plans and objectives for GTX-102, the therapeutic potential and clinical benefits of GTX-102, expectations regarding the safety and



tolerability of GTX-102, and future clinical developments for GTX-102 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 ability of the company and GeneTx to successfully develop GTX-102 at lower doses, including the resolution of adverse events that were seen at higher doses, whether lower doses of GTX-102 are sufficiently effective to support the continued development of the program, 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 August 3, 2021, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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