Ultragenyx Announces Completion of Enrollment in Global Phase 1/2 Trial of GTX-102 in Pediatric Patients with Angelman Syndrome

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Data from at least 20 patients enrolled in dose expansion cohorts anticipated in the first half of 2024

NOVATO, Calif., Jan. 03, 2024 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel therapies for serious rare and ultrarare genetic diseases, today announced the completion of patient enrollment in its Phase 1/2 clinical trial of GTX-102 for the treatment of pediatric patients with Angelman syndrome (AS). The dose-expansion cohorts (Cohorts A-E) have enrolled 53 patients for a total of 74 patients enrolled globally in the Phase 1/2 trial. GTX-102 is an investigational antisense oligonucleotide delivered via intrathecal administration and is designed to target and inhibit expression of *UBE3A* antisense transcript (*UBE3A-AS*).

“With completion of enrollment in the Phase 1/2 trial, we remain on track to report results in the first half of 2024 from at least 20 expansion cohort patients on therapy for a minimum of 6 months. We are confident that the cumulative safety and efficacy data will allow for dose and endpoint selection to support our Phase 3 program,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “We appreciate the support of the Angelman community, including the patients, families and healthcare providers, as we urgently work together to develop a new treatment option that may be able to improve the quality of life of those impacted by this devastating disease.”

In October 2023, interim data from the extension cohorts (Cohorts 4-7) of the ongoing Phase 1/2 study were announced and showed improvements across multiple domains compared to natural history data, where available, and clinical changes were associated with quantitative changes in EEG. Long-term data showed patients who stopped and restarted treatment reacquired previously gained developmental skills when they were re-dosed with the current regimen. As of the data cut-off, there have been no additional treatment-related SAEs, including lower extremity weakness, since November 2022.

About the Phase 1/2 study

The Phase 1/2, open-label, multiple-dose, dose-escalating study is evaluating the safety and tolerability of GTX-102 administered by intrathecal (IT) injection to pediatric patients with Angelman syndrome with a genetically confirmed diagnosis of full maternal UBE3A gene deletion. The study is also assessing clinical response as measured by a panel of efficacy assessments for the functional domains impacted in Angelman syndrome. Patients in the earlier extension cohorts (Cohorts 4-7) of the study have moved into long-term maintenance dosing, and the study has completed enrollment for the new expansion cohorts to verify the GTX-102 dose range and treatment regimen that will be used in the Phase 3 program.

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 (CNS), 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 generally 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 FDA.

Ultragenyx Forward-Looking Statements and Use of Digital Media

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, future clinical and regulatory developments for GTX-102, the clinical benefit, tolerability and safety of GTX-102, timing for enrollment, dosing and data for GTX-102 and the company’s other investigational therapies and regulatory meetings 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 uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals, the ability of the company to successfully develop GTX-102, the company’s ability to achieve its projected development goals in its expected timeframes, risks related to adverse side effects, risks related to reliance on third-party partners to conduct certain activities on the company’s behalf, the potential for any license or collaboration agreement, 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 product 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 (SEC) on November 3, 2023, and its subsequent periodic reports filed with the SEC.

In addition to its SEC filings, press releases and public conference calls, Ultragenyx uses its investor relations website and social media outlets to publish important information about the company, including information that may be deemed material to investors, and to comply with its disclosure obligations under Regulation FD. Financial and other information about Ultragenyx is routinely posted and is accessible on Ultragenyx's Investor Relations website (https://ir.ultragenyx.com/) and LinkedIn website (https://www.linkedin.com/company/ultragenyx-pharmaceutical-inc-/).

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