Ultragenyx Receives PRIME Designation from European Medicines Agency (EMA) for GTX-102 for the Treatment of Angelman Syndrome

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GTX-102 is the first Angelman syndrome therapeutic candidate to receive PRIME designation

Phase 1/2 study fully enrolled; expansion data expected in first half of 2024

NOVATO, Calif., Feb. 05, 2024 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) today announced that the European Medicines Agency (EMA) has granted Priority Medicine (PRIME) designation to GTX-102 for the treatment of Angelman syndrome (AS). 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*). The EMA granted this designation in response to compelling early clinical data from the extension cohorts in the Phase 1/2 study of GTX-102 demonstrating clinically meaningful improvements in several neurodevelopmental domains including cognition, receptive communication and gross motor skills in individuals with Angelman syndrome.

"By granting PRIME designation, the EMA is recognizing the potential for GTX-102 to address the critical need for new treatments for children and families impacted by Angelman syndrome in the EU," said Eric Crombez, M.D., chief medical officer at Ultragenyx. "Our team is working with urgency on the development of GTX-102 for Angelman syndrome and looks forward to working closely with regulators in the U.S. and EU to bring this innovative treatment to patients."

PRIME designation is granted by the EMA to provide early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options. These medicines are considered priority medicines by the EMA, whose aim is to optimize development plans and speed up evaluations so these medicines that address significant unmet medical needs can reach patients faster.

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 one in 12,000 to one 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. Although 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 have shown that GTX-102 reduces 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, and Orphan Designation and PRIME designation from the EMA.

About Ultragenyx Pharmaceutical Inc.
Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultrarare 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.

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, risk that access to PRIME for our product candidates, if granted, may not lead to faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval; 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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