GeneTx and Ultragenyx Provide Preliminary Update on Phase 1/2 Clinical Study of GTX-102 in Canada and U.K. Patients with Angelman Syndrome

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SARASOTA, Fla. and NOVATO, Calif., Jan. 05, 2022 (GLOBE NEWSWIRE) -- 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 four patients in the Phase 1/2 study have received multiple doses of GTX-102 and regular assessments for safety. To date three have also received a preliminary assessment of clinical response. There have been no treatment-related serious adverse events of any type nor adverse events related to lower extremity weakness observed in these patients, and initial assessments have shown early signs of clinical activity.

The data safety monitoring board (DSMB) met to discuss the assessments for the first two patients in Cohort 4 (ages 4 to <8 years) and recommended that dose escalation may proceed as planned and the study may enroll the remaining four patients in this cohort. Since then, both patients in Cohort 4 met the criteria to increase their doses and have each escalated to the 5 mg dose, and Cohort 4 has been expanded and an additional patient has received their first dose. The DSMB for Cohort 5 (ages 8 to <18 years) is expected to meet soon and confirm whether enrollment for the remaining four patients in that group may commence. Data on full Cohorts 4 and 5 in the Canada/U.K. arm of the study is anticipated in mid 2022 after completing Day 128 of the protocol.

“We are encouraged by the safety, the initial impressions from the investigators and the improvements observed in the clinical global impression scale from early assessments. The changes in multiple functional domains are encouraging and similar to the reported early changes in the original patients from the initial part of the study at these doses,” said Scott Stromatt, M.D., Chief Medical Officer of GeneTx. “It is still early in the study and we look forward to the full assessments at the completion of the Day 128 study visit.”

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 – Improvement (CGI-I) scale of change at Day 58 and again at Day 128, at which time a panel of other efficacy assessments for the domains impacted in Angelman, including communication, sleep, behavior, gross motor skills, fine motor skills, and seizures will also be measured.

GTX-102 Phase 1/2 Study Design in Canada and the U.K.
Under the protocol approved in Canada and the U.K., 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. The starting doses in Cohort 4 and Cohort 5 are 3.3 and 5 mg, respectively. Patients will receive two doses and will be assessed for safety and efficacy, as measured by the CGI-I scale of change at Day 58, before moving to step-increases in dosing. Individual dose titration may continue if safety is sustained, and the clinical response is not scored as “much improved” or better by the CGI-I scale in at least two or more domains. If indicated, patients will increase one step for two more doses with dose increases based on clinical response and 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 based on the same criteria of sustained safety and clinical response.

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 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 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, the company's ability to achieve its projected development goals in its expected timeframes, risks and uncertainties related to the regulatory approval process, 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 November 3, 2021, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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-/mycompany/).

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