GeneTx and Ultragenyx Receive Approval from U.K. Regulatory Agency to Begin Clinical Study of GTX-102 for the Treatment of Angelman Syndrome

June 10, 2021

Patient enrollment to begin in early second half of 2021 in U.K. and Canada

GeneTx to submit revised protocol to U.S. Food and Drug Administration seeking study resumption in U.S. following May meeting

SARASOTA, Fla. and NOVATO, Calif., June 10, 2021 (GLOBE NEWSWIRE) -- GeneTx Biotherapeutics LLC and Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), companies partnered in the development of intrathecally administered GTX-102, an investigational treatment for Angelman syndrome, today announced that the U.K. Medicines and Healthcare Products Regulatory Agency (MHRA) has approved the Clinical Trial Application (CTA) for the Phase 1/2 study of GTX-102 in pediatric patients with Angelman syndrome in the U.K. The companies previously received clearance to enroll patients in the Phase 1/2 study in Canada. The first patients from these regions are expected to be enrolled in the study early in the second half of 2021, with clinical data from some patients in the study expected before the end of the year.

Additionally, GeneTx and Ultragenyx recently met with the U.S. Food and Drug Administration (FDA) and had a productive discussion regarding the Phase 1/2 study. Based on the outcome of the meeting, GeneTx will submit an amended protocol to FDA that addresses key FDA issues.

“We’ve made significant progress on the regulatory front over the past few weeks with the Phase 1/2 study cleared to begin enrollment in two countries. Based on our recent discussions, we are encouraged about our proposal to begin redosing patients in the U.S. pending FDA agreement,” said Scott Stromatt, M.D., Chief Medical Officer of GeneTx. “GTX-102 has demonstrated clinical activity in the first five patients dosed in the study, and the modified trial design approved by the MHRA and Health Canada intends to explore the benefit of repeat doses at the lower end of the dosing range previously tested in order to help mitigate the risk for serious adverse events caused by localized inflammation.”

Phase 1/2 study design in U.K. and Canada

The Phase 1/2, open-label, multiple-dose, dose-escalating study evaluates the safety, tolerability, and plasma and cerebrospinal fluid concentrations of GTX-102 in pediatric patients with Angelman syndrome with a genetically confirmed diagnosis of full maternal *UBE3A* gene deletion. Under the amended protocol approved in the U.K. and Canada, approximately 12 patients will be enrolled into two cohorts split by age: patients ages 4 to 7 years will be enrolled into Cohort 4, and patients ages 8 to 17 years will be enrolled into Cohort 5.

The starting doses in Cohorts 4 (<8 years old) and 5 (>8 years old) will be 3.3 and 5 mg, respectively. Patients will receive 3 to 4 monthly doses, titrated individually through smaller steps than the first three cohorts in the original study with dose increases based on response and enhanced safety monitoring. Patients will then move to a maintenance 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 if the clinical response is not much improved in at least 2 domains up to a maximum dose of 14 mg.

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 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 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 10Q filed with the Securities and Exchange Commission on May 5, 2021, and its subsequent periodic reports filed with the Securities and Exchange Commission.

Contacts

Ultragenyx Pharmaceutical Inc.
Investors
Joshua Higa

415-660-0951

Media
Carolyn Wang
415-225-5050

GeneTx
Paula Evans
630-639-7271
Paula.Evans@GeneTxBio.com