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

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SARASOTA, Fla. and NOVATO, Calif., March 16, 2020 (GLOBE NEWSWIRE) -- GeneTx Biotherapeutics LLC and Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel products for serious rare and ultra-rare diseases, today announced that it has dosed the first patient in its KIK-AS (**K**nockdown of *UBE3A*-antisense **i**n **K**ids with **A**ngelman **S**yndrome**)** study of GTX-102, an experimental antisense oligonucleotide being evaluated for the treatment of Angelman syndrome (AS).

The Phase 1/2 open-label, multiple-dose, dose-escalating study will enroll 20 patients to evaluate the safety, tolerability, and potential efficacy of GTX-102 in pediatric patients with Angelman syndrome. This is the first investigational study testing an antisense oligonucleotide as a potential therapy to treat AS. Further details can be referenced at: https://clinicaltrials.gov/ct2/show/NCT04259281.

"Today is an important milestone with the dosing of the first patient in the KIK-AS study," stated Dr. Scott Stromatt, GeneTx's Chief Medical Officer "GTX-102 has the potential to address the underlying deficiency that causes Angelman syndrome and we are excited, grateful and humbled to be leading this scientific quest. We look forward to the results of this study and sharing them with the Angelman community."

"The GeneTx team has achieved a tremendous accomplishment rapidly advancing this program into the clinic, and GTX-102 may one day provide patients with Angelman syndrome with the first targeted therapy and a potentially transformative option for this devastating disease," said Camille L. Bedrosian, M.D., Chief Medical Officer of Ultragenyx.

Chicago's Rush University Medical Center is the first clinical site to begin enrolling patients in the KIK-AS study, with additional sites being planned in Boston, Cincinnati, Denver, Los Angeles, New York and Ottawa, Canada.

"When I held the syringe with this investigational treatment in my hand to inject it for the first time, I thought about the scientific advances in genomic and molecular medicine to produce potential treatments that bring hope of changing the disease course and ameliorating severity of symptoms in those with Angelman syndrome," said Elizabeth Berry-Kravis, site principal investigator at Rush. "This is an exciting time for the field of neurodevelopmental disorders as we embark on a path to understanding the outcomes of treatments directed at correcting the underlying molecular causes of disease."

Pending additional site activation, GeneTx Biotherapeutics expects to report preliminary data from the first cohorts in the study in early 2021.

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.

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 and Rare Pediatric Disease 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 patients novel products for the treatment of serious rare and ultra-rare 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

Except for the historical information contained herein, the matters set forth in this press release, including statements related to Ultragenyx's expectations regarding 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, including our partnership with GeneTx, 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 uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of regulatory filings and approvals (including whether such approvals can be obtained), and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations and the availability or commercial potential of our 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 Annual Report filed on Form 10-K with the Securities and Exchange Commission on February 14, 2020, and its subsequent periodic reports filed with the Securities and Exchange Commission.

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