Novel Investigational Gene-Based Therapy for X-Linked Retinitis Pigmentosa Demonstrates Functional Rescue of Photoreceptor Structure and Function in Canine Model

Research led by scientists from the University of Pennsylvania presented at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting

SEATTLE, May 02, 2016 (GLOBE NEWSWIRE) -- Researchers from the University of Pennsylvania today announced new animal study data evaluating the efficacy of an investigational adeno-associated virus (AAV) vector gene therapy treatment for X-linked retinitis pigmentosa (XLRP), a rare inherited retinal disease that causes progressive vision loss in boys and young men. The investigational gene therapy was developed by Applied Genetic Technologies Corporation (Nasdaq:AGTC), a biotechnology company conducting human clinical trials of gene therapies for the treatment of rare diseases. Study results were presented in a poster session at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, taking place from May 1 – 5.

The abstract (# 785-C0074), titled “Two AAV2/5-mediated RPGR gene augmentation constructs driven by the GRK1 promoter rescue photoreceptor structure and function in a canine model of RPGR X-linked retinitis pigmentosa,” describes a study conducted at the University of Pennsylvania and the University of Florida comparing the short-term efficacy of two different AAV2/5 constructs carrying either a codon-optimized RPGR cDNA (RPGR1) or a previously evaluated RPGR cDNA (RPGR2) in the functional rescue of photoreceptors in a canine model of XLRP. Seven dogs affected with XLRP were treated with a subretinal injection of either AAV2/5-GRK1-RPGR1 (5 eyes) or AAV2/5-GRK1-RPGR2 (4 eyes) and followed up for 12 or 18 weeks post-injection. Rescue of photoreceptor structure and function was assessed by retinal imaging, electroretinography (ERG) and histology/immunohistochemistry (IHC) at termination.

Rod-mediated ERG function was improved in 4 out of 5 RPGR1-treated eyes, and 3 out of 3 RPGR2-treated eyes, in comparison to untreated eyes. Significant preservation of outer nuclear layer thickness was seen in all treated eyes. IHC testing confirmed that RPGR transgene expression was found predominantly in rods, but associated with improved structure of both rods and cones, and correction of rod and cone opsin mislocation.

Study researchers concluded that rescue of both rods and cones was achieved following treatment with both vectors, with no significant efficacy differences observed.

“These study results demonstrate that a human optimized version of this novel AAV-based gene therapy approach could have clinical potential in treating XLRP, a severe inherited retinal disease without adequate treatment options,” said lead study investigator William Beltran, DVM, Ph.D., Associate Professor of Ophthalmology, University of Pennsylvania School of Veterinary Medicine. "We have made significant progress in advancing the field of ocular gene therapy and these data confirming efficacy in a large animal model suggest a future path for human clinical studies."

XLRP is an inherited condition that causes progressive vision loss in boys and young men, beginning with night blindness in young boys followed by progressive constriction of the field of vision. Affected men become legally blind at an average of about 45 years of age. The most common form of XLRP is caused by mutations in the RPGR gene, and AGTC is developing a gene therapy product for this form of XLRP.

“We are encouraged by these additional results supporting a potential role for gene therapy in treating rare and serious eye diseases, and are grateful for the continued support of our academic research partners,” said Sue Washer, President and CEO of AGTC. “The gene therapy landscape has evolved significantly in recent years and we are excited to be reaching a point where these approaches are shifting towards becoming a viable clinical reality.”

About the University of Pennsylvania School of Veterinary Medicine

Penn Vet is a global leader in veterinary medicine education, research, and clinical care. Founded in 1884, Penn Vet is the only veterinary school developed in association with a medical school. The school is a proud member of the One Health Initiative, linking human, animal, and environmental health.
Penn Vet serves a diverse population of animals at its two campuses, which include extensive diagnostic and research laboratories. Ryan Hospital in Philadelphia provides care for dogs, cats, and other domestic/companion animals, handling more than 31,000 patient visits a year. New Bolton Center, Penn Vet's large-animal hospital on nearly 700 acres in rural Kennett Square, PA, cares for horses and livestock/farm animals. The hospital handles more than 4,000 patient visits a year, while the Field Service treats nearly 36,000 patients at local farms. In addition, New Bolton Center's campus includes a swine center, working dairy, and poultry unit that provide valuable research for the agriculture industry.

For more information, visit [www.vet.upenn.edu](http://www.vet.upenn.edu).

About AGTC

AGTC is a clinical-stage biotechnology company that uses its proprietary gene therapy platform to develop products designed to transform the lives of patients with severe diseases, with an initial focus in ophthalmology. AGTC's lead product candidates are designed to treat inherited orphan diseases of the eye, caused by mutations in single genes that significantly affect visual function, and which currently lack effective medical treatments.

AGTC's product pipeline includes six named ophthalmology development programs across five targets (X-linked retinoschisis, X-linked retinitis pigmentosa, achromatopsia, wet age-related macular degeneration and blue cone monochromacy), two non-ophthalmology programs (alpha-1 antitrypsin deficiency and adrenoleukodystrophy) and early research studies in additional indications. AGTC employs a highly targeted approach to selecting and designing its product candidates, choosing to develop therapies for indications having high unmet medical need, clinical feasibility and commercial potential. AGTC has a significant intellectual property portfolio and extensive expertise in the design of gene therapy products including capsids, promoters and expression cassettes, as well as, expertise in the formulation, manufacture and physical delivery of gene therapy products.

Forward Looking Statements

This release contains forward-looking statements that reflect AGTC's plans, estimates, assumptions and beliefs. These statements relate to a variety of matters, including but not limited to, the anticipated utility of AAV vectors made using AGTC's proprietary manufacturing method in the treatment of XLRP and other therapeutic indications and the viability of gene therapy in treating rare and serious eye diseases. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "could," "seeks," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would" or similar expressions and the negatives of those terms. Actual results could differ materially from those discussed in the forward-looking statements, due to a number of important factors, which include, but are not limited to, the following: success in animal studies or early clinical trials may not be indicative of results obtained in later trials, no gene therapy products have been approved in the United States and AGTC cannot predict when or if it will obtain regulatory approval to commercialize a product candidate; AGTC relies on third parties to conduct research, conduct, supervise and monitor its clinical trials and to conduct certain aspects of its product manufacturing and protocol development; and increased regulatory scrutiny of gene therapy, we may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates, and genetic research could damage public perception of AGTC's product candidates or adversely affect AGTC's ability to conduct its business. Additional factors that could cause actual results to differ materially from those described in the forward-looking statements are set forth under the heading "Item 1A—Risk Factors" in AGTC's Annual Report on Form 10-K for the fiscal year ended June 30, 2015, as filed with the SEC. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent management's plans, estimates, assumptions and beliefs only as of the date of this release. Except as required by law, AGTC assumes no obligation to update these forward-looking statements publicly or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

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