AGTC Announces Publication of Positive Preclinical Data that Provides Foundational Scientific Evidence for its Ongoing Clinical Program in Patients with X-Linked Retinitis Pigmentosa (XLRP)

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- *Administration of AGTC's proprietary adeno-associated virus (AAV) vectors expressing variants of the RPGR gene corrected early markers of disease and provided evidence of a rescue effect in an animal model of XLRP, with a favorable safety profile* -

GAINESVILLE, Fla., and CAMBRIDGE, Mass., May 20, 2020 (GLOBE NEWSWIRE) -- Applied Genetic Technologies Corporation (Nasdaq: AGTC), a biotechnology company conducting human clinical trials of adeno-associated virus (AAV)-based gene therapies for the treatment of rare diseases, today announced the publication of positive preclinical data that provide the foundation for the vector and starting dose used in its ongoing Phase 1/2 clinical trial in patients with XLRP due to mutations in the RPGR gene. The data, which demonstrate that the company's proprietary AAV vector and engineered RPGR constructs were well tolerated and had beneficial effects on markers of disease in a canine model of XLRP, were published online in *Human Gene Therapy*.[1]

"The development of safe and effective gene-based therapies requires optimization of multiple vector components, including the capsid, promoter, transgene and other regulatory elements, and the studies reported in this publication were undertaken to identify an optimal construct for XLRP gene therapy," said Mark S. Shearman, Ph.D., Chief Scientific Officer, AGTC, and an author on the publication. "The results of this study identified an AAV-RPGR vector construct that has optimized safety and efficacy in a highly relevant animal model of human XLRP disease and that large-scale manufacturing that will be essential for making XLRP gene therapy available to the patients who may benefit from it."

The DNA sequence encoding the full length RPGR protein contains repetitive sequences that can lead to instability during vector engineering and manufacturing. One approach to overcoming this challenge is to remove the repetitive sequence, which results in a truncated RPGR protein. Another approach is to change the repetitive sequence to reduce instability while producing the full-length RPGR protein. The publication reports data from dose-ranging studies utilizing AGTC's proprietary rAAV2tYF capsid to deliver either a truncated RPGR DNA sequence (hRPGRstb) or an RPGR sequence encoding full-length RPGR protein optimized for stability (hRPGRco) in a canine model of XLRP.

"AGTC is a leader in designing and optimizing critical gene therapy elements and combining them to develop customized therapies that address real patient needs," said Sue Washer, President and CEO of AGTC. "The results of these studies demonstrate our ability to integrate advances in vector and disease biology with expertise in DNA engineering to enable gene-based therapies that are safe, effective and amenable to our proprietary and industry-leading AAV manufacturing process. The data presented to date from our ongoing Phase 1/2 clinical program in XLRP using rAAV2tYF-GRK1-hRPGRco demonstrate the power of patent-protected technology platform."

Following subretinal injection, both transgenes showed similar levels of efficacy as assessed by fundus reflectivity, outer nuclear layer thickness, correction of opsin mislocalization and length of cone inner segments at all doses tested; in some cases, hRPRGco showed superior efficacy. Both vectors were generally well tolerated, with retinal detachment and inflammation observed only in the high dose group. The results supported the selection of rAAV2tYF-GRK1-hRPGRco as the optimized vector to advance to clinical trials and informed the dosing schedule for the company's ongoing Phase 1/2 XLRP clinical trial.

In January 2020, AGTC announced positive interim six-month data from its ongoing Phase 1/2 clinical program in XLRP. The results show that four of eight evaluable patients treated centrally with its product candidate demonstrated durable improvement in visual sensitivity six months after dosing. All patients demonstrated a favorable safety profile for the XLRP candidate, with no dose-limiting inflammatory responses observed and no secondary inflammatory responses requiring re-administration of steroids in any patients. Preliminary data also showed that all nine centrally dosed patients had stable or improving visual acuity at the six-month time point, a result that has not been reported by others.

Reference

[1]Song C, Dufour VL, Cideciyan AV, et al. Dose range finding studies with two RPGR transgenes in a canine model of X-linked retinitis pigmentosa treated with subretinal gene therapy. Hum Gen Ther. 2020. Published online May 15, 2020.

About AGTC

AGTC is a clinical-stage biotechnology company developing genetic therapies for people with rare and debilitating ophthalmic, otologic and central nervous system (CNS) diseases. AGTC is a leader in designing and constructing all critical gene therapy elements and bringing them together to develop customized therapies that address real patient needs. Initially focusing on ophthalmology, our goal is to preserve or, hopefully, be able to improve vision in some cases. AGTC has active clinical trials in X-linked retinitis pigmentosa and achromatopsia (ACHM CNGB3 & ACHM CNGA3). Our pre-clinical programs build on our industry leading AAV manufacturing technology and expertise. AGTC is advancing multiple important pipeline candidates to address substantial unmet clinical need in optogenetics, otology and CNS disorders.

About X-linked Retinitis Pigmentosa (XLRP)

XLRP is an inherited condition that causes progressive vision loss in boys and young men. Characteristics of the disease include night blindness in early childhood and progressive constriction of the visual field. In general, XLRP patients experience a gradual decline in visual acuity over the disease course, which results in legal blindness around the 4th decade of life. AGTC was granted U.S. Food and Drug (FDA) orphan drug designation in 2017, as well as European Commission orphan medicinal product designation in 2016, for its gene therapy product candidate to treat XLRP caused by mutations in the RPGR gene.

Forward-Looking Statements

This release contains forward-looking statements that reflect AGTC's plans, estimates, assumptions and beliefs. Forward-looking statements include

information concerning possible or assumed future results of operations, financial guidance, business strategies and operations, preclinical and clinical product development and regulatory progress, potential growth opportunities, potential market opportunities, the effects of competition and the impact of the COVID-19 pandemic. 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. Risks and uncertainties that may cause actual results to differ materially include, among others: gene therapy is still novel with only a few approved treatments so far; AGTC cannot predict when or if it will obtain regulatory approval to commercialize a product candidate or receive reasonable reimbursement; uncertainty inherent in clinical trials and the regulatory review process; risks and uncertainties associated with drug development and commercialization; the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations, and financial condition; factors that could cause actual results to differ materially from those described in the forward-looking statements are set forth under the heading "Risk Factors" in our most recent annual or quarterly report and in other reports we have 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, we assume 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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