



Passage Bio Announces Publication of Preclinical Data That Show Single Injection of Optimized AAV Vector into Cerebral Spinal Fluid Corrects Neurological Disease, Supporting Advancement of PBGM01 into Clinic

October 13, 2020

The study conducted by the University of Pennsylvania's Gene Therapy Program supports the potential of Passage Bio's PBGM01 to correct the underlying genetic defect of GM1 gangliosidosis, a rare, life-threatening disease most common in infants

PHILADELPHIA, Oct. 13, 2020 (GLOBE NEWSWIRE) -- Passage Bio, Inc. (NASDAQ: PASG), a genetic medicines company focused on developing transformative therapies for rare, monogenic central nervous system disorders, today announced publication of data in a murine model of GM1 gangliosidosis (GM1) demonstrating that a single intracerebroventricular injection of an optimized adeno-associated virus (AAV) into the cerebral spinal fluid (CSF) resulted in significant expression of Beta-galactosidase (β -gal) in the brain and peripheral tissues, and demonstrated dose-related reductions in neuronal lysosomal storage lesions, neurological impairment and improvement in survival. These data were published online ahead of print in the November issue of the peer-reviewed scientific journal [Human Gene Therapy](#) (HGT).

"This study suggests that delivery of an AAV vector optimized to express b-gal directly into the CSF restored b-gal activity in the brain and, if further developed and tested in human clinical trials, may be effective in modifying and preventing the devastating effects of the genetic disease GM1," said James Wilson, M.D., Ph.D., director of the Gene Therapy Program at the University of Pennsylvania (Penn) and chief scientific advisor of Passage Bio. "The AAV vector used in the study is the same as Passage Bio's PBGM01 gene therapy, which is designed to deliver a functional human GLB1 gene into the brain and optimized to express β -gal. These preclinical study data support the further development of PBGM01 as a potential therapy for patients suffering from GM1."

GM1 is a rare and often life-threatening monogenic lysosomal storage disease caused by mutations in the GLB1 gene, which encodes lysosomal acid β -gal. Reduced β -gal activity results in the accumulation of toxic levels of GM1 in neurons throughout the brain, causing rapidly progressing neurodegeneration. GM1 manifests as a continuum of disease and is most severe in the infantile form, which is characterized by onset in the first six months of life with hypotonia (reduced muscle tone), progressive CNS dysfunction, and rapid developmental regression. Life expectancy for infants with GM1 is two to four years, and infantile GM1 represents approximately 60 percent of the incidence of 0.5 to 1 in 100,000 live births. Currently, there are no approved disease-modifying therapies available.

Results of the PBGM01 preclinical study were reported in the paper titled, "A single injection of an optimized AAV vector into cerebrospinal fluid corrects neurological disease in a murine model of GM1 gangliosidosis," by Christian Hinderer, M.D., Ph.D., and colleagues, including gene transfer pioneer Dr. Wilson, from the Gene therapy Program, Department of Medicine, University of Pennsylvania Perelman School of Medicine. The study in part was previously presented at the 22nd annual Meeting of the American Society for Cell and Gene Therapy (ASCGT) in 2019.

This research evaluated the impact of single intracerebroventricular administration of the human β -gal containing AAV vector on β -galactosidase enzyme activity in the murine brain and peripheral tissues, lysosomal storage lesions, neurological function (including neurological exams and gait analysis) and survival in mice lacking the β -galactosidase gene. The mice received the single administration at age one month and were evaluated over 300 days. β -gal activity was increased significantly in the cerebral spinal fluid and serum of the vector-treated mice compared to vehicle control-treated mice. Significant improvements in gait assessments as measured by stride length and hind paw print length and significant preservation of neurological function as measured by neurological exam scores were observed throughout the study period in the human β -gal vector-treated mice. There were significant decreases in lysosomal storage lesions of vector-treated animals and by day 300 all animals that received the two highest doses were still alive, whereas none of the vehicle control-treated animals had survived.

"We're excited about being able to soon advance PBGM01 into the clinic, and the potential promise it holds for patients with GM1, the majority of whom are infants and for whom there are no approved disease modifying treatments," said Bruce Goldsmith, Ph.D., president and chief executive officer of Passage Bio. "Our plan is to administer PBGM01 through intra-cisterna magna delivery into the brain, which we believe may offer several benefits in terms of safety, efficiency and distribution compared to other approaches."

Passage Bio expects to initiate dosing of PBGM01 in a Phase 1/2 trial late in the fourth quarter of 2020 or early in the first quarter of 2021 and remains on track to report initial 30-day safety and biomarker data late in the first half of 2021.

This research was supported by a research, collaboration and license agreement with Passage Bio. *HGT* is the Official Journal of the European Society of Gene and Cell Therapy, British Society for Gene and Cell Therapy, French Society of Cell and Gene Therapy, German Society of Gene Therapy, and five other gene therapy societies. Click [here](#) to read the full-text article on the HGT website.

About PBGM01

PBGM01 is an AAV-delivery gene therapy currently being developed for the treatment of infantile GM1, in which patients have mutations in the GLB1 gene causing little or no residual β -gal enzyme activity and subsequent neurodegeneration. PBGM01 utilizes a next-generation AAVhu68 capsid administered through intra-cisterna magna (ICM) to deliver a functional GLB1 gene encoding β -gal to the brain and peripheral tissues. By reducing the accumulation of GM1 gangliosides, PBGM01 has the potential to halt or prevent neuronal toxicity, thereby restoring developmental potential. In preclinical models, PBGM01 has demonstrated broad brain distribution and wide uptake of the β -gal enzyme in both the central nervous system (CNS) and critical peripheral organs, suggesting potential treatment for both the CNS and peripheral manifestations of GM1. The Company has received Orphan Drug and Rare Pediatric Disease designation for PBGM01 for patients with GM1 and expects to initiate dosing of its Phase 1/2 trial late in the fourth quarter of 2020 or early in the first quarter of 2021 and remains on track to report initial 30-day safety and biomarker data late in the first half of

2021.

About Passage Bio

Passage Bio is a genetic medicines company focused on developing transformative therapies for rare, monogenic central nervous system disorders with limited or no approved treatment options. The company is based in Philadelphia, PA and has a research, collaboration and license agreement with the University of Pennsylvania and its Gene Therapy Program (GTP). The GTP conducts discovery and IND-enabling preclinical work and Passage Bio conducts all clinical development, regulatory strategy and commercialization activities under the agreement. The company has a development portfolio of six product candidates, with the option to license eleven more, with lead programs in GM1 gangliosidosis, frontotemporal dementia and Krabbe disease.

University of Pennsylvania (Penn) Financial Disclosure

Dr. Wilson is a Penn faculty member and also a scientific collaborator, consultant and co-founder of Passage Bio. As such, he holds an equity stake in the company, receives sponsored research funding from Passage Bio, and as an inventor of certain Penn intellectual property that is licensed to Passage Bio, he may receive additional financial benefits under the license in the future. He is an inventor of intellectual property covering the technology described in paper published in *HGT* that is licensed from Penn to Passage Bio, and he may receive financial benefits under this license in the future. Penn also holds equity and licensing interests in Passage Bio.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of, and made pursuant to the safe harbor provisions of, the Private Securities Litigation Reform Act of 1995, including, but not limited to: our expectations about timing and execution of anticipated milestones, including our planned IND submissions, initiation of clinical trials and the availability of clinical data from such trials; our expectations about our collaborators' and partners' ability to execute key initiatives; our expectations about manufacturing plans and strategies; our expectations about cash runway; and the ability of our lead product candidates to treat the underlying causes of their respective target monogenic CNS disorders. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "potential," "possible," "will," "would," and other words and terms of similar meaning. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: our ability to develop and obtain regulatory approval for our product candidates; the timing and results of preclinical studies and clinical trials; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events; the risk that positive results in a preclinical study or clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials; failure to protect and enforce our intellectual property, and other proprietary rights; our dependence on collaborators and other third parties for the development and manufacture of product candidates and other aspects of our business, which are outside of our full control; risks associated with current and potential delays, work stoppages, or supply chain disruptions caused by the coronavirus pandemic; and the other risks and uncertainties that are described in the Risk Factors section in documents the company files from time to time with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. Passage Bio undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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