Passage Bio Announces Publication of Preclinical Gene Therapy Study Data from Frontotemporal Dementia Program

September 17, 2020

Data Show Single Injection of AAV-Granulin Gene Therapy into Central Nervous System

Reverses Frontotemporal Dementia Pathology Caused by Granulin Mutations and is Well Tolerated

Study Conducted by the University of Pennsylvania's Gene Therapy Program Supports Further Development of Passage Bio's PBFT02

PHILADELPHIA, Sept. 17, 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 supporting development of its gene therapy PBFTO2 for patients with frontotemporal dementia caused by mutations in the granulin gene (FTD-GRN). In the study, a single administration of an optimized adeno-associated virus (AAV) containing the GRN gene resulted in elevated levels of progranulin (PGRN) in the brain and cerebral spinal fluid (CSF), reduced lysosomal storage lesions, normalized lysosomal enzyme expression and corrected microgliosis in a mouse model of progranulin deficiency. These data were published online September 16 in the peer-reviewed scientific journal *Annals of Clinical and Translational Neurology* (ACTN).

To identify a vector capable of achieving optimal expression levels of GRN, the study also evaluated three AAV serotypes (1, 5, and hu68) in non-human primates. Following a single intra-cisterna magna (ICM) injection of the AAV-GRN vectors, all non-human primates, regardless of AAV serotype, showed increased PGRN levels in the CSF. The injections were also well tolerated across serotypes. However, a single administration of an optimized AAV1-GRN vector (PBFT02) showed the greatest CSF expression levels, reaching more than 50-fold the normal expression level. AAV1 also appeared to demonstrate extensive transduction of the ependymal cells that line the ventricles of the brain and are involved in the production of CSF.

"These findings suggest that the highly transduced ependymal cells achieved with AAV1 could be the primary source of PGRN in the CSF, which also could make it the ideal choice for GRN gene therapy," said James Wilson, M.D., Ph.D., director of the Gene Therapy Program at the University of Pennsylvania and chief scientific advisor of Passage Bio. "Of course, more study is needed, which is why we look forward to Passage Bio's clinical development of PBFT02 for patients with FTD-GRN."

FTD is one of the more common causes of early-onset (midlife) dementia, causing impairment in behavior, language and executive function, and occurs at similar frequency to Alzheimer's disease in patients younger than 65 years. In approximately 5% to 10% of individuals with FTD, the disease occurs because of mutations in the GRN gene, causing a deficiency of PGRN. PGRN is a complex and highly conserved protein thought to have multiple roles in cell biology, development and inflammation. Emerging evidence suggests that PGRN's pathogenic contribution to FTD and other neurodegenerative disorders relates to its critical role in lysosomal function.

"This study also demonstrates that the route of administration – ICM – that we plan to use for PBFT02 in our clinical studies was minimally invasive and well tolerated in animal models," said Bruce Goldsmith, Ph.D., CEO of Passage Bio. "Using this approach with PBFT02 may allow us to determine empirically the levels of brain progranulin required to overcome intracellular lysosomal deficiency. Based on the encouraging pre-clinical data, we plan to initiate a Phase 1/2 trial in the first half of 2021. Our aim is to one day offer a transformative therapy to patients with FTD-GRN, who currently suffer profound impairments and have no treatment options available to them."

Results of the PBFT02 preclinical study were reported in the paper titled, "Adeno-associated virus serotype 1-based gene therapy for FTD caused by *GRN* mutations," by Christian Hinderer, M.D., Ph.D., and colleagues, including Dr. Wilson, from the Gene Therapy Program, Department of Medicine, University of Pennsylvania Perlman School of Medicine, Philadelphia, PA., an expert in gene transfer technologies. *ACTN* is an Official Journal of the American Neurological Association. Click here to read the full-text article.

About PBFT02
Passage Bio is developing PBFT02 to treat FTD-GRN with a single dose of PBFT02 by intra-cisterna magna injection. PBFT02 is a gene therapy that utilizes an AAV1 viral vector to deliver a modified DNA encoding the granulin (GRN) gene to a patient's cells. The goal of this vector and delivery approach is to provide higher than normal levels of progranulin (PGRN) to the central nervous system to overcome the progranulin deficiency in GRN mutation carriers, who have been observed to have reduced cerebrospinal fluid PGRN levels ranging from 30% to 50% of the PGRN levels observed in normal, mutation non-carriers.

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.

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. The University of Pennsylvania 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; gene therapies are novel, complex and difficult to manufacture; 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.

For further information, please contact:

Investors:
Sarah McCabe and Zofia Mita
Stern Investor Relations, Inc.
sarah.mccabe@sternir.com
zofia.mita@sternir.com

Media:
Gwen Fisher
Passage Bio
215.407.1548
gfisher@passagebio.com