Passage Bio Highlights University of Pennsylvania's Gene Therapy Program's Newly Published Research to Prevent Toxicity Associated with Gene Therapy

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Through its unique collaboration agreement, Passage Bio has certain rights to technology highlighted in the University's research, which has the potential to significantly advance nascent field of gene therapy

PHILADELPHIA, Nov. 11, 2020 (GLOBE NEWSWIRE) -- Passage Bio, Inc. (Nasdaq: PASG), a genetic medicines company focused on developing transformative therapies for rare, monogenic central nervous system (CNS) disorders, today commends the newly published research of the University of Pennsylvania's (Penn) Gene Therapy Program (GTP) regarding a novel targeted approach to prevent a selective neurotoxicity seen in the sensory neurons of dorsal root ganglia (DRG) after gene therapy treatment. As previously published, this DRG toxicity has been observed after both systemic and central nervous system (CNS) delivery of gene therapy and across a variety of vectors in pre-clinical models, but clinical manifestations have not been observed.[1]

As part of its unique collaboration agreement with Penn, Passage Bio has certain rights to this novel DRG technology for the indications the company progresses with Penn.

"Although our safety studies for our programs have not shown any clinical manifestations of DRG toxicity, we are excited about the promising approach developed by Penn's GTP," said Bruce Goldsmith, Ph.D., president and chief executive officer of Passage Bio. "As part of our mission to develop transformative therapies for patients, we remain committed to advancing the field of gene therapy. If in the future this new approach shows clinical benefit for patients, we will be in a strong position to incorporate it into our programs. Our relationship with Penn's GTP is an important distinguishing characteristic of Passage Bio. Through our collaboration, we have ready access to world-class expertise and groundbreaking research that we can rapidly apply, if appropriate, to our therapeutic programs."

GTP's research on preventing DRG toxicity published online this week in *Science Translational Medicine*. According to the researchers, DRG toxicity is the result of over expression of an introduced gene, known as a transgene, in cells in the DRG, a cluster of neural cells on the outside of the spinal cord responsible for transmission of sensory messages. To correct this over expression, the GTP research team modified a transgene with a microRNA target designed to reduce the level of the transgene expression in DRG neurons as well as toxicity in DRG neurons, without affecting transduction elsewhere in the brain. That alteration eliminated more than 80 percent of the transgene expression in DRG neurons and reduced the related DRG toxicity in preclinical studies with primates.

James M. Wilson, M.D., Ph.D., director of Penn's GTP and a chief scientific advisor at Passage Bio, served as a senior author of the published manuscript. Juliette Hordeaux, DVM, Ph.D., senior director of Translational Research in Penn's GTP is first author. They reported that their microRNA target approach may be a straightforward way to potentially make AAV therapy for the central nervous system more safe.

As previously reported, results from preclinical toxicology studies for Passage Bio's lead therapeutic programs, PBGM01 (GM1 gangliosidosis), PBKR03 (Krabbe disease), PBFT02 (FTD-GRN), were consistent with this overall AAV platform observation, and showed no clinical manifestations in detailed neurological examinations or daily observations. To proactively determine whether there is appearance of clinical signs of DRG toxicity in our clinical programs, Passage Bio will implement monitoring of patients, consisting of both nerve-conduction studies and neurological exams focused on sensory and peripheral nerve functions.

Passage Bio is advancing six programs, which include the lead programs for GM1 gangliosidosis (GM1), Krabbe disease, and frontotemporal dementia (FTD), as well as three additional programs for amyotrophic lateral sclerosis (ALS), metachromatic leukodystrophy (MLD) and Charcot-Marie-Tooth disease Type 2a (CMT2a). The company anticipates that the initial three clinical candidates will be in clinical trials in 2021. Through its collaboration agreement with Penn, Passage Bio has the option to license a total of 17 programs focused on rare, monogenic disorders of the CNS.

About Passage Bio

At Passage Bio (Nasdaq: PASG), we are on a mission to provide life-transforming gene therapies for patients with rare, monogenic CNS diseases that replace their suffering with boundless possibility, all while building lasting relationships with the communities we serve. Based in Philadelphia, PA, our company has established a strategic collaboration and licensing agreement with the renowned University of Pennsylvania's Gene Therapy Program to conduct our discovery and IND-enabling preclinical work. This provides our team with unparalleled access to a broad portfolio of gene therapy candidates and future gene therapy innovations that we then pair with our deep clinical, regulatory, manufacturing and commercial expertise to rapidly advance our robust pipeline of optimized gene therapies into clinical testing. As we work with speed and tenacity, we are always mindful of patients who may be able to benefit from our therapies. More information is available at www.passagebio.com.

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; 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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[1] Juliette Hordeaux, Elizabeth L. Buza, et al. “Adeno-Associated Virus-Induced Dorsal Root Ganglion Pathology,” *Human Gene Therapy*, published online June 25, 2020.