Passage Bio Announces Presentation of Data from Animal Models of Krabbe Disease at the American Society of Gene & Cell Therapy (ASGCT) 23rd Annual Meeting

May 12, 2020

– Preclinical data from University of Pennsylvania's Gene Therapy Program demonstrate single injection of AAVhu68 carrying a functional GALC gene resulted in normalization of GALC enzyme activity and improved all parameters in animal models of Krabbe disease –

– Treated Krabbe dogs showed nerve conduction normalization, CSF psychosine levels normalization, improved brain histopathology, phenotypic correction and increased survival –

– Twitcher mouse model demonstrated peripheral nerve correction, a dose-dependent correction of phenotype and increased survival –

PHILADELPHIA, May 12, 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 the presentation of preclinical data for its Krabbe disease program. This data was presented today in an virtual oral presentation at the American Society of Gene and Cell Therapy (ASGCT) 23rd Annual Meeting by Juliette Hordeaux, D.V.M., Ph.D., senior director of translational research at the University of Pennsylvania's Gene Therapy Program.

"The data presented today showcase the promising potential of pairing CSF administration with high potency vectors to achieve robust, scalable effects utilizing cross-correction on central and peripheral nerve function," 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. "The marked improvements on critical markers of disease such as myelination and neuroinflammation as well as, and perhaps more importantly, phenotypic improvements in function and ultimately prolonged survival suggest that ICM gene therapy may be incredibly efficacious for rare CNS indications such as Krabbe disease."

"We are extremely excited about this data for our Krabbe program. We believe it demonstrates the potential of the AAVhu68 GALC therapeutic PBKR03 as a life-altering therapy for patients with infantile Krabbe disease, and we look forward to advancing this program into the clinic," said Bruce Goldsmith, Ph.D., president and chief executive officer of Passage Bio. "These findings suggest that PBKR03 may be able to normalize GAL-C activity and restore myelination and nerve function in both the brain and key peripheral tissues that would have otherwise resulted in neurodegeneration and eventual death. We believe these data strongly support the continued development of PBKR03 and look forward to continuing to build and evaluate our preclinical models as we prepare for our IND submission in the second half of this year."

In the Twitcher mouse model of Krabbe, CSF delivery of AAVhu68 encoding GALC showed substantial increases in GALC enzyme activity, improved myelination of peripheral nerves, improved neuromotor function and increased survival. In the naturally occurring Krabbe canine model, a single ICM injection of AAVhu68 encoding GALC showed normalization of GALC activity, reduction of CSF psychosine levels, normalization of peripheral nerve conduction velocity, improvement in brain myelination, reduction in brain inflammation, phenotypic correction and increased survival. Treatments in both the mouse and canine models were shown to be well-tolerated with no observed toxicities.

Presentation details

Presentation title: Evaluating the Efficacy and Safety of Cerebrospinal Fluid-Delivered Gene Therapy for Krabbe Disease in Murine and Canine Models
Presentation date and time: Tuesday, May 12, 2020 4:30pm - 4:45pm ET
Presenter: Juliette Hordeaux, D.V.M., Ph.D., University of Pennsylvania
Session title: AAV Gene Delivery for CNS Disorders
Session date and time: Tuesday, May 12, 2020 3:45pm - 5:30pm ET
Abstract number: 95

About Krabbe Disease
Krabbe disease is a rare and often life-threatening lysosomal storage disease caused by mutations in the GALC gene, which encodes galactosylceramidase, an enzyme that breaks down galactosylceramide and psychosine. Without adequate levels of galactosylceramidase, psychosine accumulates, causing widespread death of myelin-producing cells and progressive damage to nerves in both the brain and peripheral tissues. The early infantile form of the disease is the most severe and common, typically manifesting before six months of age and accounting for 60% to 70% of diagnoses. In these patients, the disease course is highly predictable and rapidly progresses to include loss of acquired milestones, staring episodes, apnea, peripheral neuropathy, severe weakness, unresponsiveness to stimuli, seizures, blindness, deafness and eventual death by two years of age. Late infantile patients, defined by onset between seven to twelve months of age, present similar symptoms and a median survival of approximately five years from onset of symptoms. There are currently no disease-modifying therapies for Krabbe disease, and we believe incidence may be 2.6 in 100,00 births, which is higher than reported due to lack of adequate screening at birth.

About PBKR03
PBKR03 is an AAV-delivered gene therapy encoding GALC currently in late preclinical development for the treatment of infantile Krabbe disease, in which patients have a mutations in the gene that codes for galactosylceramidase (GAL-C). Low GAL-C activity results in accumulation of psychosine which is toxic to the myelin producing oligodendrocytes of the CNS and Schwann cells in the periphery, resulting in damage to both the central and peripheral nervous systems. PBKR03 utilizes a next-generation proprietary AAVhu68 capsid to deliver, through intra-cisterna magna administration, a functional GALC gene. In preclinical models, PBKR03 has shown meaningful transduction of both the central and peripheral nervous system, with restoration of myelination in the brain and peripheral nerves. PBKR03 thus has the potential to treat both the central nervous system and peripheral

nerve manifestations observed in Krabbe disease patients. We expect to submit an IND for PBKR03 in the second half of 2020 and to initiate a Phase 1/2 trial 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.

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; 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, obtain regulatory approval for and commercialize our product candidates; the timing and results of preclinical studies and clinical trials; 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; 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; failure to protect and enforce our intellectual property, and other proprietary rights; failure to successfully execute or realize the anticipated benefits of our strategic and growth initiatives; risks relating to technology failures or breaches; our dependence on collaborators and other third parties for the development 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; risks associated with current and potential future healthcare reforms; risks relating to attracting and retaining key personnel; failure to comply with legal and regulatory requirements; risks relating to access to capital and credit markets; 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
Stern Investor Relations, Inc.
212-362-1200
sarah.mccabe@sternir.com

Media:
Emily Maxwell
HDMZ
312-506-5220
emily.maxwell@hdmz.com