Passage Bio Receives FDA Clearance of IND Application for PBFT02 Gene Therapy Candidate for Treatment of Patients with Frontotemporal Dementia with Granulin Mutations

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– Second Product Candidate Expected to Enter Clinic in First Half of 2021

– Preclinical Data Underscore Treatment Potential for PBFT02 in Frontotemporal Dementia with Granulin (GRN) Mutations, a Devastating, Progressive Disorder Impacting Adults with No Approved Disease-Modifying Therapy Options

PHILADELPHIA, Jan. 28, 2021 (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 announced that the U.S. Food and Drug Administration (FDA) has cleared an investigational new drug (IND) application for PBFT02, an adeno-associated virus (AAV)-delivery gene therapy that is being studied for the treatment of patients with Frontotemporal Dementia (FTD) with granulin (GRN) mutations. FTD is a debilitating form of early onset dementia that currently has no approved disease-modifying therapies.

“We are pleased to be advancing our second therapy into clinical development in our quest to bring transformative medicines to patients who need them,” said Bruce Goldsmith, Ph.D., chief executive officer of Passage Bio. “FTD can have a devastating impact on a person’s quality of life and create a substantial caregiving and economic burden for families. We are excited to investigate the potential of PBFT02 as a treatment for FTD-GRN as we initiate our clinical development program in the coming months.”

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 percent of individuals with FTD – 3,000 to 6,000 in the United States – the disease occurs because of mutations in the GRN gene, causing a deficiency of progranulin (PGRN). PGRN is a complex and highly conserved protein. The mechanism by which PGRN deficiency results in FTD is uncertain, but increasing evidence points to PGRN’s role in lysosomal function. The rapid progression of FTD results in an average survival of eight years after onset of symptoms.

Passage Bio is developing PBFT02 to treat FTD-GRN as a single dose delivered via intra-cisterna magna (ICM) injection. The gene therapy utilizes an AAV1 viral vector to deliver a modified DNA encoding the GRN gene to a patient's cells. The goal of this vector and delivery approach is to provide higher than normal levels of 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.

Clinical Development of PBFT02 Supported by University of Pennsylvania’s Gene Therapy Program (GTP) Pre-Clinical Data

Passage Bio is advancing PBFT02 into the clinic supported by preclinical data generated by its collaborator, University of Pennsylvania’s Gene Therapy Program (GTP). The data, published in the peer-reviewed scientific journal *Annals of Clinical and Translational Neurology*, showed that a single administration of an optimized AAV containing the GRN gene resulted in elevated levels of 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. A single administration of PBFT02 via the optimized AAV1-GRN vector demonstrated transduction broadly across the brain, including a very high transduction of ependymal cells that line the ventricles of the brain and are involved with CSF production, resulting in CSF progranulin levels of more than 50-fold normal.

The FDA has granted an Orphan Drug designation for PBFT02 for the treatment of FTD-GRN.

Phase 1/2 Study Initiation Anticipated for 1H21

Passage Bio expects to initiate a Phase1/2 clinical trial for PBFT02 in the first half of 2021. The trial is designed as a dose-escalation study of a single ICM dose of PBFT02 in subjects with FTD and heterozygous mutations in the GRN gene. The primary endpoint of the Phase 1/2 study is safety and tolerability; secondary endpoints include CSF progranulin levels, disease biomarkers, and clinical outcome measure. Initial data from the trial is anticipated to potentially readout in late 2021 or early 2022, depending on the timing of when the first patient is treated in the study.

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 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.

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.

For further information, please contact:

Passage Bio Investors:

Sarah McCabe and Zofia Mita
Stern Investor Relations, Inc.
212-362-1200
sarah.mccabe@sternir.com
Zofia.mita@sternir.com

Passage Bio Media:

Gwen Fisher
Passage Bio
215-407-1548
gfisher@passagebio.com