FDA Clears IND Application for Passage Bio's Gene Therapy Candidate PBKR03 for Treatment of Patients with Early Infantile Krabbe Disease, A Rare Pediatric Disorder with No Approved Disease-Modifying Treatment Options

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- Phase 1/2 trial expected to commence in first half of 2021

- Company has three INDs cleared for rare monogenic CNS disorders

PHILADELPHIA, Feb. 08, 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 PBKR03, an adeno-associated virus (AAV)-delivery gene therapy being studied for the treatment of early infantile Krabbe disease (Globoid Cell Leukodystrophy). Currently, there are no approved disease-modifying therapies available for Krabbe disease, a rare lysosomal storage disease that most often presents early in a child's life, resulting in rapid progressive damage to both the brain and peripheral nervous system and mortality by two years of age. Underscoring the urgent medical need in the patient population, the FDA has previously granted Passage Bio both Orphan Drug and Rare Pediatric Disease designations for PBKR03 for treatment in Krabbe disease.

"As part of our commitment to deliver a transformative, one-time gene therapy to the children and their families who suffer from the devastating effects of Krabbe disease, we are excited to advance toward clinically evaluating the potential life-changing benefits of PBKR03," said Bruce Goldsmith, Ph.D., chief executive officer of Passage Bio. "The FDA clearance of our IND for PBKR03 is an important milestone for Passage Bio, paving the way for the start of our third clinical program in rare monogenic CNS disorders in the first half of 2021. Having solidified our clinical trial preparedness and manufacturing readiness during the past year, we are well-positioned to move with urgency to advance PBKR03 into the clinic."

PBKR03 utilizes a next-generation proprietary AAV capsid to deliver, through intra-cisterna magna (ICM) administration, a functional GALC gene to Krabbe patients with 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 has the potential to treat both the central nervous system and peripheral nerve manifestations observed in Krabbe disease patients.

Compelling preclinical data support advancement into clinical trials

PBKR03 is supported by extensive preclinical studies, conducted by our collaborator, the University of Pennsylvania's Gene Therapy Program, showing meaningful transduction of both the central and peripheral nervous system in animal models, with restoration of myelination in the brain and peripheral nerves. In a naturally occurring Krabbe animal model, a single ICM injection of an AAVhu68 capsid containing the normal canine GALC gene showed normalization of GALC activity, reduction of cerebral spinal fluid psychosine levels, normalization of peripheral nerve conduction velocity, improvement in brain myelination, reduction in brain inflammation and increased survival.

Phase 1/2 study anticipated for 1H21

Passage Bio expects to initiate a Phase1/2 clinical trial for PBKR03 in the first half of 2021. The trial is designed as a dose escalation study of a single ICM dose of PBKR03 in pediatric subjects with early infantile Krabbe disease. The primary endpoint of the Phase 1/2 study is safety and tolerability; secondary endpoints include CSF and serum GALC levels, disease biomarkers, and clinical outcome measures. 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.

PENN Financial Disclosure

The University of Pennsylvania (Penn) and its Gene Therapy Program receives sponsored research funding from Passage Bio, and Penn has licensed intellectual property to Passage Bio that may result in future financial returns to Penn.

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 percent to 70 percent 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 have a median survival of approximately five years from onset of symptoms. The estimated worldwide incidence of Krabbe disease is 2.6 in 100,000 births, which is higher than reported due to lack of adequate screening at birth.

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 enhanced 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.

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