Agilis Biotherapeutics Announces Authorization of Phase IIb Clinical Study of Gene Therapy for AADC Deficiency

Study to Advance Novel AAV Gene Therapy, Explore Dose Increase

Cambridge, MA, October 11, 2016 (BUSINESS WIRE) — Agilis Biotherapeutics, LLC (Agilis), a biotechnology company advancing innovative gene therapies for rare genetic diseases that affect the central nervous system (CNS), announced today that a Phase IIb clinical study for its gene therapy treatment of Aromatic L-Amino Acid Decarboxylase (AADC) deficiency, AGIL-AADC, has been authorized by the Taiwan Food and Drug Administration (TFDA) and the ethics committee at National Taiwan University (NTU). The study will be performed under the direction of Paul Hwu, M.D., Ph.D., Professor of Pediatrics at NTU Hospital. AGIL-AADC is an adeno-associated virus (AAV) vector containing the human gene for the AADC enzyme. Dr. Hwu and colleagues have treated 18 subjects to date in two prospective clinical studies using a single administration of the gene therapy. The present Phase IIb study will enroll a third cohort of patients into two parts, one evaluating the AGIL-AADC gene therapy dose used in prior studies and a second exploring single administration of an increased dose.

Dr. Hwu said, “We are pleased to embark on this important clinical study of AGIL-AADC in an effort to expand the promising safety and efficacy observed in studies to date in which AADC deficiency patients have exhibited persistent improvements in functional, biomarker and imaging measures. Our combined studies have collected more than five years of data in some cases, providing support for this gene therapy as a potential durable treatment for AADC deficiency.”

AADC deficiency is a rare CNS disorder arising from a reduction in the enzyme aromatic L-amino acid decarboxylase that results from mutations in the dopa decarboxylase (DDC) gene. This reduction leads to deficits in the neurotransmitters dopamine, norepinephrine, epinephrine, serotonin and melatonin.

In its profound forms, AADC deficiency causes severe developmental delays, the inability to develop motor strength and control (global muscular hypotonia/dystonia) resulting in breathing, feeding, and swallowing problems, frequent hospitalizations, and the need for life-long care that ultimately culminates in premature death within the first decade of life.

Subjects treated with AGIL-AADC in prior studies have exhibited *de novo* dopamine production visualized by F-DOPA PET imaging, the emergence of dopamine metabolites, and substantial gains in motor function and cognitive scales over multiple years following the single gene therapy administration. In contrast, untreated subjects typically do not achieve critical developmental milestones, as observed in natural history cases. The University of Florida Powell Gene Therapy Center was instrumental in the manufacturing and toxicology work of the initial product.

"The AADC gene therapy program started by Dr. Hwu over six years ago continues to make great strides in clinical development," said Barry Byrne, M.D., Ph.D., Director, UF Powell Gene Therapy Center, Professor, Pediatrics and Molecular Genetics & Microbiology and Associate Chair, Department of Pediatrics, College of Medicine, University of Florida. "Dr. Hwu's pioneering gene therapy is a clinically relevant approach to treating this devastating disease and one of the most advanced CNS gene therapies in development today. My team and I at the University of Florida and the Powell Gene Therapy Center are proud to have supported Dr. Hwu's efforts at multiple stages. We look forward to continuing to work with him and Agilis to bring this important, novel treatment to the United States for AADC patients here."

Christopher Silber, M.D., Agilis Chief Medical Officer, noted, "Clinical development of AGIL-AADC continues to be very encouraging, with long-term follow-up and data collection for treated patients providing an opportunity for ongoing assessment of the durability of functional improvements and safety profile. Advancing our understanding of dose range will be informative as we continue to strive to position AGIL-AADC for registration. Given the devastating clinical course of AADC deficiency and refractoriness to standard therapies, our mission for these patients is to provide a novel intervention to improve their condition and enhance their lives."

About AADC Deficiency

Aromatic L-amino acid decarboxylase (AADC) deficiency is a rare genetic condition resulting from deficits in the AADC responsible for the final step in the synthesis of the neurotransmitters dopamine (a precursor of norepinephrine and epinephrine) and serotonin (a precursor of melatonin). AADC deficiency arises from mutations in the dopa decarboxylase (DDC) gene. In its profound forms, AADC deficiency results in severe developmental failures, global muscular hypotonia and dystonia, severe, seizure-like episodes known as oculo-gyric crises, frequent hospitalizations (including prolonged stays in intensive care), and the need for life-long care. Symptoms and severity vary depending on the type of underlying genetic mutation which abrogates AADC enzyme function. Severe forms of the disease can arise from specific DNA mutations. Patients with severe forms usually die before the age of 7 years due to profound motor dysfunction, autonomic abnormalities, and secondary complications such as choking, hypoxia, and pneumonia. No treatment options other than palliative care currently exist for patients with severe AADC deficiency.

About Agilis Biotherapeutics

Agilis is advancing innovative gene therapies designed to provide long-term efficacy for patients with debilitating, often fatal, rare genetic diseases that affect the central nervous system. Agilis' gene therapies are engineered to impart sustainable clinical benefits by inducing persistent expression of a therapeutic gene through precise targeting and restoration of lost gene function to achieve long-term efficacy. Agilis' rare disease programs are focused on gene therapy for AADC deficiency, Friedreich's ataxia, Angelman syndrome, and Fragile X syndrome, rare genetic diseases that include severe neurological deficits and result in physically debilitating conditions.

We invite you to visit our website at www.agilisbio.com

Safe Harbor Statement

Some of the statements made in this press release are forward-looking statements. These forward-looking statements are based upon our current expectations and projections about future events and generally relate to our plans, objectives and expectations for the development of our business. Although management believes that the plans and objectives reflected in or suggested by these forward-looking statements are reasonable, all forward-looking statements involve risks and uncertainties and actual future results may be materially different from the plans, objectives and expectations expressed in this press release.

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