Agilis Biotherapeutics and National Taiwan University Enter Into Worldwide, Exclusive License Agreement for the Gene Therapy Treatment of AADC Deficiency

Phase II Program for Rare CNS Disease Expands Agilis' Pipeline

Cambridge, MA, January 28, 2016 7:30 am EST --(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 the Company has entered into an exclusive worldwide license agreement with National Taiwan University (NTU) for the treatment of Aromatic L-Amino Acid Decarboxylase (AADC) Deficiency using gene therapy developed by Dr. Paul Hwu, Professor of Pediatrics at NTU Hospital. AADC Deficiency is a rare CNS disorder arising from a reduction in the enzyme, aromatic L-amino acid decarboxylase (AADC), caused by 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. In an effort to address the high unmet medical need in AADC patients, Dr. Hwu and colleagues have developed a novel gene therapy targeted to restore deficient AADC and have successfully treated 18 subjects in two prospective clinical studies.

"Dr. Hwu's pioneering studies in the treatment of AADC Deficiency using gene therapy have shown great promise in treating this devastating disease and represent a seminal step for CNS gene therapy," said Dr. Mark Pykett, Agilis President and CEO. "To our knowledge, this is the most advanced CNS gene therapy program in the world, with available long-term follow-up data for over five years in some subjects. We believe this program represents an important catalyst for Agilis and an important validation of the potential for gene therapy in treating rare CNS disorders. Pending successful completion of a pivotal

clinical trial in subjects with AADC Deficiency and favorable regulatory review, we anticipate that AADC gene therapy could be the first CNS gene therapy product approved anywhere in the world."

A single administration of gene therapy, containing an adeno-associated virus (AAV) delivering the human AADC gene, has been evaluated to date in two prospective clinical studies enrolling 18 subjects with severe AADC Deficiency. Treated subjects exhibited *de novo* dopamine production, as 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 treatment. In contrast, untreated subjects routinely show continued deterioration as the disease progresses, as observed in natural history cases. All treatments have been performed at National Taiwan University Hospital.

Dr. Hwu commented, "Clinical studies have demonstrated strong safety and promising efficacy to date, with patients showing persistent improvements in functional, biomarker and imaging measures. These studies represent the first time gene therapy has been demonstrated as a potential durable treatment for AADC deficiency. On the basis of these results, a pivotal trial has been planned."

Under the terms of the agreement with NTU, Agilis will sponsor ongoing research and development of the AADC gene therapy in collaboration with Dr. Hwu, including the conduct of ongoing clinical work on AADC gene therapy and completion of nonclinical testing in advance of the pivotal clinical study, anticipated to begin in 2017. Agilis will also support ongoing manufacturing efforts for the gene therapy.

Christopher Silber, M.D., Agilis Chief Medical Officer, noted, "The potential to impact function, demonstrate evidence of *de novo* dopamine production, and mitigate the adverse consequences of AADC Deficiency with a single gene therapy treatment, is encouraging. Given the devastating clinical course of disease for patients with severe AADC deficiency, their poor quality of life and refractoriness to standard therapy, any intervention to improve the most severe forms of this disorder represents a critical advance for these patients and their families."

About AADC Deficiency

Aromatic L-amino acid decarboxylase (AADC) Deficiency is a rare genetic condition resulting from deficits in the enzyme, AADC, which is 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, long-lasting seizures 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 six-seven 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. Our therapies are engineered to impart sustainable clinical benefits, and potentially a functional cure, by inducing persistent expression of a therapeutic gene. The Company's technology is aimed at the precise targeting and restoration of a lost gene function, while avoiding unintended off-target effects. Our integrated strategy increases the efficiency of developing DNA therapeutics into safe, targeted gene therapies that achieve long-term efficacy and enable patients to remain asymptomatic without continuous invasive treatment. 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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