# Agilis Biotherapeutics Announces FDA Orphan Drug Designation for the Treatment of Aromatic L-amino Acid Decarboxylase Deficiency

**Cambridge, MA**, June 29, 2016 (BUSINESS WIRE)—Agilis Biotherapeutics, LLC (Agilis), a biotechnology company advancing innovative DNA therapeutics for rare genetic diseases that affect the central nervous system (CNS), announced today that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to Agilis' gene therapy product candidate, AGIL-AADC, being developed for the treatment of Aromatic L-amino Acid Decarboxylase (AADC) deficiency, a genetic disorder that results in severe developmental failure, global muscular hypotonia and dystonia, severe, long-lasting episodes known as oculogyric crises, frequent hospitalizations, and the need for life-long care. The gene therapy has been evaluated in 18 patients in two prospective clinical cohorts in Taiwan under the direction of Paul Hwu, MD, PhD, Professor of Pediatrics at National Taiwan University (NTU) Hospital.

"Receiving orphan drug designation from the FDA is another step on our path to bringing this important new medicine to patients in dire need of an effective, durable treatment," said Mark Pykett, President and CEO of Agilis. "Given the profound clinical course for patients with severe AADC deficiency, their poor quality of life, and refractoriness to standard therapy, any intervention to improve the condition of these patients represents an important advance in the fight against this disease. We are pleased that we continue to make important clinical and regulatory progress, positioning us to advance this new treatment to address this devastating disease."

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. Agilis entered into an exclusive

worldwide license agreement with NTU for the treatment of AADC-D using gene therapy technology evaluated by Dr. Paul Hwu and colleagues. A single administration of gene therapy, containing an adeno-associated virus (AAV) delivering the human AADC gene, has been evaluated in two prospective clinical cohorts 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. In preparing the program for clinical trials, The University of Florida Powell Gene Therapy Center was instrumental in the development of the initial product manufacturing and toxicology work.

"Preliminary clinical findings are encouraging and appear to support a positive impact on function, de novo dopamine production, and potential mitigation of the significant consequences of severe AADC deficiency with a single gene therapy treatment," said Christopher Silber, MD, Chief Medical Officer at Agilis. "These cohorts represent the first assessment of gene therapy as a potential durable treatment for AADC deficiency and we look forward to reviewing the ongoing data from these patients, and others."

FDA Orphan Drug Designation is evaluated for drugs from all classes (e.g. small molecules, proteins, and gene or cell therapies) that are intended for the treatment of rare diseases, defined as diseases affecting fewer than 200,000 people in the United States. The designation provides sponsors with development and commercial incentives, including seven years of market exclusivity in the US, prioritized consultation by FDA on clinical studies, and certain exemptions from or reductions in regulatory fees.

**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 failure, global muscular hypotonia and dystonia, severe, long-lasting 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 seven years due to extreme 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

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