Agilis Biotherapeutics Announces Data Presentations on AADC Deficiency at the American Society of Gene and Cell Therapy 2018 Annual Meeting

Independent Studies Highlight Sustainable Improvements in Children Treated with Investigational Gene Therapy, AGIL-AADC

Prevalence of AADC Deficiency Reported

Lynnfield, MA, May 14, 2018 -- Agilis Biotherapeutics, Inc. (Agilis), a biotechnology company advancing innovative DNA therapeutics for rare genetic diseases that affect the central nervous system (CNS), announced that multiple abstracts by its collaborators and partners were selected for presentation at the American Society of Gene and Cell Therapy (ASGCT) taking place May 16-19, 2018, in Chicago, IL. Agilis’ gene therapy candidate, AGIL-AADC, is an investigational therapeutic administered as a one-time, low dose treatment of AAV2-AADC delivered by targeted micro-dosing to the putamen by an established stereotactic procedure. Agilis is advancing AGIL-AADC toward the submission of a Biologics License Application (BLA) to the United States Food and Drug Administration (FDA). Abstracts from the Company’s collaborators and partners focusing on progress in gene therapy for AADC deficiency and on disease epidemiology will be presented as follows:

A poster presentation entitled “Gene Therapy for AADC Deficiency Results in De Novo Dopamine Production and Supports Durable Improvement in Major Motor Milestones” will be presented by Ni-Chung Lee, M.D., on Wednesday, May 16, 2018. The presentation details 25 children with severe AADC deficiency treated using a single administration of AGIL-AADC gene therapy delivered bilaterally to the putamen by stereotactic infusion during a single, operative session. Of the 25 children given AGIL-AADC, three are now more than seven-years post-gene therapy and seven are more than six-years post-
A platform presentation entitled “Gene Therapy Improves Cerebral White Matter Microstructures in Patients with Aromatic L-Amino Acid Decarboxylase Deficiency” will be given by Wuh-Liang Hwu, M.D., Ph.D., principal investigator on Agilis’ AGIL-AADC gene therapy clinical trials for AADC deficiency, on Wednesday, May 16, 2018. The presentation details patients (1.67 to 8.42 years of age) enrolled in a study evaluating the investigational gene therapy treatment, AGIL-AADC. Administration of a low dose of AGIL-AADC bilaterally to the putamen increased dopamine levels. Following gene therapy, patients exhibited marked improvements in motor function. Of the 25 children given AGIL-AADC to date, white matter structure was evaluated in eight patients by fractional anisotropy measures from magnetic resonance brain imaging. After gene therapy, total mean fractional anisotropy values increased ($p=0.012$), indicating an improvement in functional white matter structure. The data suggest that an increase in patients’ motor activity brought on by focal delivery of a gene therapy to the putamen to improve dopamine activity is associated with improvements in the microstructure of white matter tracts throughout the brain involving the motor and premotor cortices, thereby supporting clinical improvements.

A poster entitled “Improvement of Motor and Cognitive Function by Gene Therapy for Patients with AADC Deficiency” will be presented by Karin Kojima, M.D., on Friday, May 18, 2018. The presentation details five patients ages 4, 10, 12, 15 and 19 with severe AADC deficiency and one patient age 5 with moderate disease treated with AAV2-AADC via bilateral intraputaminal infusions by stereotactic neurosurgery. By two years after gene therapy, all patients showed improved motor function and no dystonia. Two severe patients walked with a walker, and the moderate patient could run and ride a bicycle. Regarding mental development, the moderate phenotype patient could converse. The 12-year-
old female with severe phenotype responded quickly to spoken orders. Positron emission tomography with 6-[18F]fluoro-L-m-tyrosine, a tracer of AADC, showed persistent AADC expression after gene therapy.

A poster entitled “Prevalence of Aromatic L-Amino Acid Decarboxylase Deficiency in At-Risk Populations” will be presented by Keith Hyland, Ph.D., on Friday, May 18, 2018. The presentation details an initial review of the screening of 18,647 samples received for cerebrospinal fluid (CSF) neurotransmitter metabolite analysis from patients with neurological deficits of unknown origin at Medical Neurogenetics Laboratories in the US. Patients with CSF neurotransmitter metabolite profiles consistent with AADC deficiency, together with studies examining AADC plasma enzyme assay and Sanger sequencing of the DDC gene, were used to estimate prevalence of AADC deficiency. Thirty-six new cases of AADC deficiency were identified. Of the 36, 22 were initially identified from CSF analysis, nine from plasma AADC enzyme assay, and five following sequencing of the DDC gene. In previous studies, screening for AADC deficiency in an at-risk population in Asia identified a prevalence of 0.25%, and newborn screening in Taiwan established the overall incidence at 1:32,000 births. In the present study of an at-risk population, an estimated prevalence frequency of 0.193% was calculated. Assuming that prevalence frequencies in at-risk populations are indicative of newborn incidence rates, newborn incidence in an at-risk population is extrapolated at approximately 1:41,000 births. If the patients diagnosed initially by sequencing or plasma enzyme assay are not included with those diagnosed by CSF testing, the prevalence estimate is 0.117%, and the newborn incidence estimate is approximately 1:68,000 births. The estimated prevalence from an at-risk population suggests that AADC deficiency is not uncommon, especially in an at-risk population tested for possible biogenic amine neurotransmitter disorders. This raises the possibility that there are patients with AADC deficiency who have not been identified.

Details on these abstracts accepted for presentation at the American Society of Gene and Cell Therapy 2018 Annual Meeting can be found at the ASGCT website: https://plan.core-apps.com/asgct2018.

Agilis’ investigational gene therapy AGIL-AADC has been administered to twenty-five children with severe AADC deficiency ranging in age from approximately 21 months to 8.5 years to date, the first of whom were treated in 2010, under the guidance of Paul Hwu, M.D., Ph.D., principal investigator and Professor of Pediatrics at National Taiwan University Hospital. At time of treatment, none of the
children had developed any functional motor movement or achieved any motor development milestones, including head control, self-feeding, or sitting, consistent with the natural history of this devastating disease in which children never develop meaningful motor movement. All children have shown improved motor function as measured on the Peabody Development Motor Scale, Second Edition, and the Alberta Infant Motor Scale, two independent, validated, standardized measures of motor function in children. Recent data analyses demonstrate that of the first 18 patients who are now two years after AGIL-AADC administration, approximately 45 percent of patients gained full head control (p<0.0001), approximately 35 percent could sit unassisted (p<0.0001), and 20 percent could stand with support (p=0.005). Motor function was sustained or continued to improve in the eight patients who are now five years post AGIL-AADC administration, with half of all patients achieving full head control (p<0.0001) and the ability to sit unassisted (p<0.0001), thereby allowing children to sit without support and use their hands for independent activities such as being able to feed themselves, and one-third of patients achieving standing with support (p=0.007), enabling independent activities of locomotor activity with a wheeled walker or learning to walk. No serious adverse events attributable to the AGIL-AADC gene therapy or to the administration procedure were reported.

“We are delighted to witness the progress of this pioneering gene therapy effort and related disease epidemiology for this devastating disease where no approved treatment options are available,” said Mark Pykett, President and CEO of Agilis. “Ongoing development of AGIL-AADC remains promising, as we strive to position the gene therapy for registration and commercialization to potentially bring this important, innovative therapy to patients.” Pursuant to a successful end-of-phase 2 meeting on available data in the AADC program with the FDA, Agilis is preparing a BLA for AGIL-AADC for submission. If approved, AGIL-AADC may be the first gene therapy approved anywhere in the world for a disorder of the central nervous system.

About AADC Deficiency

Aromatic L-amino acid decarboxylase (AADC) deficiency is a rare genetic condition resulting in lack of functioning AADC enzyme responsible for the final step in the synthesis of key neurotransmitters dopamine (a precursor of norepinephrine and epinephrine) and serotonin (a precursor of melatonin). AADC deficiency results in developmental failure, global muscular hypotonia, severe, seizure-like episodes known as oculogyric crises, autonomic abnormalities, and the need for life-long care. Given
this neurologically devastating illness, patients with severe AADC deficiency have a high risk for death during childhood. Treatment options for patients with AADC deficiency are limited and there are currently no approved therapies.

About Agilis Biotherapeutics, Inc.

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, for which the company is preparing regulatory filings in the US and EU, Friedreich ataxia and Angelman syndrome, rare genetic diseases that include 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 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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