AGIL-AADC Gene Therapy Results in Sustained Improvements in Motor and Developmental Milestones Over 5 Years in Children With AADC Deficiency
Yin-Hsiu Chien¹, Ni-Chung Lee¹, Sheng-Hong Tseng¹, Chun-Hwei Tai¹, Anne Marie Conway², Mark Pykett², Wuh-Liang Hwu¹
¹National Taiwan University Hospital, ²PTC Therapeutics, Inc.

Objective: To evaluate clinical outcomes through 5 years in children with aromatic l-amino acid decarboxylase (AADC) deficiency treated with AGIL-AADC, a recombinant adeno-associated virus vector containing the human cDNA encoding the AADC enzyme.

Background: AADC deficiency is a rare genetic disorder of neurotransmitter synthesis. In this update, we present 2-year posttreatment data with AGIL-AADC in 18 patients, and 5-year posttreatment data for 8 patients.

Design/Methods:
In 2 single-arm, open-label clinical studies, children with AADC deficiency received AGIL-AADC (total dose, 1.8x10¹¹ vg) as bilateral, intraputaminal, stereotactic infusions during a single operative session. The primary endpoint was achievement of motor developmental milestones on the Peabody Developmental Motor Scale, Second Edition (PDMS-2; total and single-item subscale scores). Total and subscale scores on the Alberta Infant Motor Scale (AIMS) and Bayley-III also assessed developmental milestones. De novo dopamine production was evaluated with F-DOPA PET imaging. Adverse events (AEs) were recorded. Findings were compared with a natural history cohort of severe AADC patients (N=82) using the Fisher exact test (α=0.05).

Results:
Patients aged 21 months to 8.5 years (N=18) received AGIL-AADC. None had full head control or could sit unassisted or stand at baseline. At the time of this analysis, all patients had 2 years of posttreatment data; 8 patients had 5 years of posttreatment data. Clinically meaningful improvements were observed in PDMS-2 total score and single-item motor developmental milestones versus natural history controls. Improvements were observed in AIMS scores and Bayley-III total and cognitive and language subscale scores. All patients demonstrated sustained de novo dopamine production. All AEs were associated with the disease; no new safety signals were observed over 5 years.

Conclusions: In children with AADC deficiency, AGIL-AADC gene therapy achieved clinically meaningful, sustained improvements in motor, cognitive, and language milestones for up to 5 years, with no new safety signals identified.