PD-1102: A Phase 1 study of VY-AADC01 Administered Using a Posterior Approach in Patients with Parkinson’s Disease and Motor Fluctuations

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Objective: Evaluate safety, putaminal coverage, aromatic L-amino acid decarboxylase (AADC) activity, and clinical outcomes at 12 months in patients with Parkinson’s disease and motor fluctuations treated with VY-AADC01, an AAV2-AADC vector-based therapy administered to bilateral putamen.

Background: The phase 1 study (PD-1101) showed improved putaminal coverage, AADC activity, and clinical outcomes with dose escalation and improved administration of VY-AADC. This study (PD-1102) changed to a single administration trajectory per putamen targeting the posterior tail, with a goal of increasing coverage and improving clinical outcomes.

Design/Methods:
Eight subjects with similar baseline characteristics to those in PD-1101 were administered up to 2.6x10¹² vg/mL in up to 1.8 mL per putamen (total dose up to 9.4x10¹² vg) using a single parietal-occipital trajectory per putamen, optimizing vector delivery to motor areas in postcommisural putamen. VY-AADC01 was admixed with gadoteridol, allowing real-time MR imaging of the location and volume of infusate; AADC activity was assessed by (18)F-DOPA PET at baseline and <7 months. Clinical measures included change in antiparkinsonian medications, subject-reported diary ON and OFF times, and UPDRS.

Results: At baseline, mean age was 56.8 years and mean PD duration 9.2 years; subjects reported a mean 6.8 hours of diary OFF time and 9.1 hours of diary ON time. There were no vector-related serious adverse events; two subjects experienced mild surgical intra-cerebral hemorrhage, which resolved without residual deficits. Mean VY-AADC01 coverage of the putamen was 53.5%. AADC activity by (18)F-DOPA PET increased to levels similar to healthy adults (Feigin, 2002) and there was a 33% reduction in the need for antiparkinsonian medications. Diary ON and OFF times, and UPDRS at 12 months will be reported.

Conclusions: Modifying the neurosurgical administration of VY-AADC01 resulted in increased putaminal coverage and associated AADC activity. Together with the reductions in antiparkinsonian medications, these findings suggest potential clinical benefit.