PHASE I-II FIRST-IN-MAN CLINICAL TRIAL OF INTRAPUTAMENAL CDNF IN PARKINSON'S DISEASE: TOPLINE RESULTS OF THE 12-MONTH TREATMENT PERIOD

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Objective: To assess the safety and tolerability and to explore the efficacy of intermittent bilateral intraputamenal monthly infusions of cerebral dopamine neurotrophic factor (CDNF) in subjects with advanced Parkinson's disease (PD).

Background: CDNF is an unconventional neurotrophic factor that in preclinical models of PD protects dopamine neurons via a unique multi-modal mechanism of action.

Methods: A randomized, placebo-controlled, double-blind phase I-II trial in 17 patients with moderate PD, comprising placebo or incremental CDNF dosing for six-month followed by an active treatment six-month extension study. A drug delivery system (Renishaw) was implanted into putamina in all patients. Primary endpoint was safety and tolerability. Secondary and exploratory endpoints included UPDRS, dopamine transporter (DAT) PET, actigraphy and CSF biomarkers.

Results: At screening, the patients had on average disease duration of 10.6±2.6 years, H&Y 2.4±0.4 and >5 h daily off-time. Two patients discontinued in the first 6-month period due to serious adverse events (SAE) related to infusion procedures with the implanted device. Study drug-related AEs were mild to moderate. The primary endpoint was met. At the 12-month timepoint, the least square means change in UPDRS III (off) from baseline in all patients receiving CDNF was -2.2 points ($p>0.05$, repeated-measures ANCOVA). Increased DAT availability in the putamen was observed at 6 and 12-month timepoints in some patients that received CDNF.

Conclusions: Intraputamenal CDNF infusions were safe and well tolerated despite the AEs and SAEs related to the route of administration. Signs of potential clinical and biological response to the treatment were observed in some patients.