PHASE I-II FIRST-IN-MAN CLINICAL TRIAL OF INTRAPUTAMENAL CDNF IN PARKINSON'S DISEASE: EXPLORATORY FLUID-BASED BIOMARKER ENDPOINTS OF THE 12-MONTH TREATMENT PERIOD

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Aims: Cerebral dopamine neurotrophic factor (CDNF) is an unconventional neurotrophic factor that in preclinical models of Parkinson's disease (PD) protects dopamine neurons via a unique multi-modal mechanism of action. As part of the first-in-man clinal study of intermittent bilateral intraputamenal monthly infusions of CDNF in subjects with moderately advanced PD, we explored cerebrospinal fluid (CSF) biomarkers before and after treatment.

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. Lumbar CSF samples were collected at baseline and at 20 and 45 weeks after first dosing. As an exploratory endpoint, the levels of total, oligomeric and Ser129-phosphorylated α-synuclein were determined by ELISA. The aggregation propensity of CSF α-synuclein was determined by RT-QuiC assay. A proteomic biomarker screen was performed using mass spectrometric methods.

Results: The data for the α-synuclein analyses and proteomics screen will be available in Q4 2020. In the discovery phase of the proteomic screen, the PD subjects (n=15) at baseline were compared to healthy, age-matched controls (n=14). Based on the results, a panel 50 proteins were selected for a targeted proteomics screen to be conducted with CSF samples collected at different timepoints. In addition, a method was developed for enrichment of five cytokines (TNF-α, IL-1β, IL-6, IL-10 and CCL2) from CSF for quantitative proteomic analysis.

Conclusions: The results from these exploratory CSF analyses are expected to provide further insight into the biological responses to intraputamenal CDNF infusions in PD patients.