Results of an Open Label, Dose Escalating, Phase 1 Clinical Trial Evaluating the Safety of a Human Neural Stem Cell Based Therapy in Parkinson’s Disease
Russell Kern¹, Ibon Garitaonandia¹, Rodolfo Gonzalez¹, Glenn Sherman¹, Andrey Semechkin¹, Emma Braine², Girish Nair², Andrew Evans²
¹International Stem Cell Corporation, ²The Royal Melbourne Hospital

Objective:
Evaluate the safety and tolerability of transplanting human pluripotent stem cell derived neural stem cells (ISC-hpNSC) into patients with Parkinson’s disease (PD).

Background: Transplantation of clinical grade ISC-hpNSC in preclinical PD models ameliorates symptoms and increases dopaminergic neuron innervation by providing neurotrophic support, immunomodulation, and cell replacement. ISC-hpNSC cells are safe, well tolerated, and do not induce systemic toxicity or tumors in PD models. A Phase 1 clinical trial is currently underway evaluating the safety and tolerability of ISC-hpNSC in PD patients (ClinicalTrials.gov Identifier: NCT02452723).

Design/Methods:
In this open label, single arm, dose escalating, Phase 1 clinical trial, 12 participants are recruited into three cohorts of four participants each. Patients receive stereotactic bilateral injections into the caudate nucleus, putamen and substantia nigra of 3x10⁷ (1st cohort), 5x10⁷ (2nd cohort), and 7x10⁷ (3rd cohort) ISC-hpNSC cells. Participants are evaluated for 12 months in the active phase and five years in the safety follow-up phase. The primary endpoint evaluates the incidence of treatment-emergent adverse events (AEs) and serious adverse events (SAEs). Secondary endpoints evaluate preliminary efficacy by comparing neurological scores to baseline.

Results:
Ten subjects have been successfully transplanted with ISC-hpNSC and eight subjects (full 1st and 2nd cohorts) have completed the 12 month active phase and entered the five year safety follow-up phase. The transplanted cells seem to be well tolerated and no tumors, infection, or test article related SAEs have been reported thus far. Preliminary efficacy measures show a dose-dependent improvement, with the 2nd cohort on average outperforming the 1st cohort, in Hauser Motor Diary, PD Quality of Life Score-39, and Clinical Global Impression at six months post-transplantation.

Conclusions:
Interim results of the world’s first human pluripotent stem cell based therapy for PD show that transplantation of ISC-hpNSC is safe, well tolerated, and can potentially improve the quality of life of patients.