Autologous Transplantation of Mesenchymal Stem Cells Secreting Neurotrophic Factors (NurOwn®) In ALS: Results of a Phase 2 Clinical Trial

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Objective
To evaluate the safety and efficacy of transplantation of NurOwn® (MSC-NTF cells), autologous bone marrow-derived mesenchymal stem cells (MSC) induced to secrete neurotrophic factors (NTFs), in amyotrophic lateral sclerosis (ALS). ClinicalTrials.gov identifier: NCT01777646.

Background
MSC-NTF cells secreting GDNF, BDNF, VEGF and HGF have been shown to have neuroprotective effects in-vitro and in animal models of neurodegenerative diseases, including ALS. A prior phase 1/2 study showed a single intrathecal (IT) or intramuscular (IM) administration of MSC-NTF cells to be safe and well tolerated, and several subjects receiving IT administration showed stabilization of ALSFRS scores.

Design/Methods
The study enrolled 14 ALS patients in three ascending dose cohorts. During a three month run-in period, ALS Functional Rating Scale-Expanded (ALSFRS-R) and forced vital capacity (FVC) were assessed monthly and bone marrow cells were isolated, expanded ex-vivo and induced to secrete NTFs. Subjects then received a single dose of MSC-NTF cells via IT and IM administration to the right biceps and triceps, and were followed for safety and efficacy measures, including ALSFRS-R and FVC, for six months after administration.

Results

Progression Rate for all IT-Treated Subjects in Phase 2a and Prior Phase 1/2 Study

<table>
<thead>
<tr>
<th>Pre-Treatment (per month)</th>
<th>Post-Treatment (per month)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>ALSFRS-R</td>
<td>-1.2</td>
<td>0.052</td>
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<tr>
<td>FVC (% predicted)</td>
<td>-0.5</td>
<td>0.008</td>
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Change in Arm Muscle Volume by HRTI-Based 3D Volumetric Analysis

Change in CMAP of the Musculocutaneous Nerve

Conclusions
- The study met its primary objective in demonstrating that a single simultaneous intrathecal (up to 2 million cells/kg) and intramuscular (up to 48 million cells to the upper arm) administration of MSC-NTF cells was safe and well-tolerated.
- A strong efficacy signal was observed as subjects in the study experienced a clinically meaningful reductions in their rate of disease progression, as assessed by both ALSFRS-R and FVC, for 6 months after treatment.
- A piecewise linear regression model of these data pooled with results from our earlier phase 1/2 study revealed a statistically significant reduction in the rate of FVC decline (p=0.036) and a nearly significant reduction in the rate of ALSFRS-R decline (p=0.052) for the 6-month post treatment period.
- The results of these studies indicate that MSC-NTF cells show promise as a potential treatment for ALS, and possibly other neurodegenerative diseases.