NurOwn® Phase 2 ALS study: ALSFRS-R subscale responder analysis

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Objective

To evaluate the contribution of the four ALSFRS-R subscales to the overall ALSFRS-R efficacy outcomes in the NurOwn® U.S. Phase 2 ALS multicenter, double-blind, placebo-controlled trial

* [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) identifier NCT02017912
ALSFRS-R subscale slopes decline at different rates and by region of onset.

*Fig. 1. Cross-sectional mean (±SEM) change from baseline to 9 months for each of the four factors of the ALSFRS-R.*
NurOwn® Phase 2 Study Met Primary Safety Outcomes

Study Design
- 48 participants (16 per site)
- Randomized 3:1
- Blinded to allocation

- No deaths or treatment related SAEs
- No drop outs related to SAEs
- Most common adverse events transient and mild/moderate severity and procedure related

**Efficacy**
- ALSFRS-R
- SVC

*IT 125M cells/4 ml and IM (R biceps and R triceps)
Phase 2 Subgroups: 
(>= or < 1 point/month decline pre-treatment*)

<table>
<thead>
<tr>
<th>Group</th>
<th>MSC-NTF</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>Rapid progressors</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Slow progressors</td>
<td>21</td>
<td>6</td>
</tr>
</tbody>
</table>

*Prespecified
ALSFRS-R Total Score and Subscale Responder Definitions

- ≥ 1.5* points/month improvement in ALSFRS-R total score (slope)
- ≥ 0.375* points/month for each of the subscales improvement (25% of 1.5 point/month improvement in total score)
  - Bulbar
  - Gross Motor
  - Fine Motor
  - Breathing

*Post hoc
Responder Analysis:
≥1.5 points/month improvement (Rapid Progressors)
Comparison of Phase 2 Placebo and Historical Placebo Groups

Phase 2 Placebo Group n=6

ProACT Placebo Group n= 103**

**Matched rapid progressor placebo group by inclusion/exclusion criteria

* p<0.05 (two-sided Fisher’s exact test)
MCP-1 reduction correlates with ALSFRS-R slope improvement

**MCP-1/ALSFRS-R Delta slope at 12wks**

- **MCP-1**
  - NurOwn®
  - Placebo

Mean ± SEM

\* p<0.05 ** p<0.01 *** p< 0.001

- Pre transplantation
- Post transplantation
Subscale responder analysis: ≥ 0.375 point/month improvement (rapid progressors)

MSC-NTF Subscale Responders (%)

Placebo Subscale Responders (%)

* p<0.10: treated vs. placebo
Conclusions

• Evaluation of ALSFRS-R subscale outcomes is important to fully understand the impact of NurOwn® in ALS

• In the NurOwn® single dose phase 2 study, ALSFRS-R improvement in the rapid progressor subgroup is reflected in all four subscales, particularly in the bulbar and fine motor subscales

• A Phase 3 multicenter repeat dose placebo controlled study* is currently underway at 6 US medical centers to confirm and extend these observations

* [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) identifier NCT03280056