SPINRAZA (nusinersen): Setting The Standard For Dynamic Collaboration

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We are led by great science

Committed to areas of high unmet need

Opening up new therapeutic options like Spinraza
A STORY OF COLLABORATION

BIOGEN: We saw an unmet need

PATIENTS: Guided our path

FDA: Made it a reality

A Relationship Of Mutual Respect
SPINRAZA

SMA

Spinraza: A Case Study
PATIENTS ARE OUR SMEs

- Partners in research
- Advisors in development
- Most important stakeholders
OUR FOUNDATION

Do it right the first time

1. Partner with the patient community
2. Follow the science
3. Start with rigorous trial design
4. Employ flexibility in trial design and analysis
5. Use FDA’s expedited programs – Priority Review and Fast Track
WHAT WE LEARNED

Effective Communication + Collaboration = Speed
WE ARE JUST GETTING STARTED

- PRESYMPTOMATIC SMA
- SYMPTOMATIC – INFANTILE-ONSET SMA
- SYMPTOMATIC – LATER-ONSET SMA
NURTURE PRIMARY ENDPOINT: NO DEATHS OR CHRONIC RESPIRATORY SUPPORT AMONG SMA PATIENTS TREATED IN PRE-SYMPTOMATIC PERIOD

At the time of the interim analysis, infants had been on study for a median (range) of 317.5 (2–524) days.
All infants were alive and none had required respiratory intervention.⁹

<table>
<thead>
<tr>
<th>Nusinersen-treated infants, n (%)</th>
<th>2 SMN2 copies n=13</th>
<th>3 SMN2 copies n=7</th>
<th>Total n=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>13 (100)</td>
<td>7 (100)</td>
<td>20 (100)</td>
</tr>
<tr>
<td>Required invasive ventilation or tracheostomy</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Required noninvasive ventilation for ≥6 hours/day continuously for ≥7 days</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

NURTURE study interim analysis data cut-off date: October 31, 2016. aRespiratory intervention was defined as invasive or noninvasive ventilation for ≥6 hours/day continuously for ≥7 days or tracheostomy.
IMPROVEMENTS IN MOTOR MILESTONE SCORES ACROSS STUDIES OF PRE-SYMPTOMATIC AND SYMPTOMATIC SMA INFANTS

<table>
<thead>
<tr>
<th>Trial</th>
<th>Group Description</th>
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<tbody>
<tr>
<td>NURTURE</td>
<td>(OL, presymptomatic infantile-onset SMA; 2 or 3 SMN2 copies)</td>
</tr>
<tr>
<td>CS3A</td>
<td>(OL, infantile-onset SMA)</td>
</tr>
<tr>
<td>NURTUREb</td>
<td>(10/31/2016 data cut)</td>
</tr>
<tr>
<td>CS3Ac</td>
<td>(1/2016 data cut)</td>
</tr>
<tr>
<td>Nusinersen</td>
<td>(N=73)</td>
</tr>
<tr>
<td>Sham control</td>
<td>(N=37)</td>
</tr>
<tr>
<td>ENDEAR</td>
<td>(infantile-onset SMA; 2 SMN2 copies)</td>
</tr>
<tr>
<td>Nusinersen</td>
<td>(N=73)</td>
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<tr>
<td>Sham control</td>
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</tbody>
</table>

Mean (SE) total HINE motor milestone score

0 2 4 6 8 10 12 14 16 18 20 22 24 26
1 29 64 92 183 302 394 505 568 631 694 757

Biogen
IMPROVEMENT IN MOTOR FUNCTION AMONG SMA INFANTS TREATED AFTER SYMPTOM ONSET AND REQUIRE PERMANENT VENTILATION

Nusinersen-treated infants demonstrated more improvement and less worsening in motor function.\textsuperscript{b}

ENDEAR end-of-study analysis. CHOP INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders. An increase of ≥4 points in CHOP INTEND score from baseline is generally considered to be outside the range of test variability. Permanent ventilation was defined as tracheostomy or ≥16 hours ventilatory support per day for >21 days in the absence of acute reversible event in the determination of an independent endpoint adjudication committee.
OUR FUTURE, TOGETHER

We are putting the best practices in place to speed our efforts to bring transformative therapies to patients with few or no treatment options.