# New Biomarker Data Add Further Evidence Supporting the Potential Benefit of SPINRAZA® (nusinersen) in Infants and Toddlers with Unmet Clinical Needs after Gene Therapy

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- New data from the RESPOND study show that neurofilament levels, an indicator of neurodegeneration, were reduced in nearly all study participants treated with SPINRAZA
- Reductions in biomarker complement previously reported RESPOND efficacy results showing improved motor function in most participants treated with SPINRAZA after gene therapy

CAMBRIDGE, Mass., March 06, 2024 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) announced interim 6-month biomarker data from the initial 29 participants in the open-label RESPOND study.* The Phase 4 study evaluates clinical outcomes and safety following treatment with SPINRAZA over a 2-year period in infants and toddlers with spinal muscular atrophy (SMA) who have unmet clinical needs after treatment with Zolgensma® (onasemnogene abeparvovec). The new data show that plasma neurofilament light chain (NfL) levels, an objective biomarker of axonal injury and neurodegeneration, were reduced in nearly all study participants treated with SPINRAZA. These data will be presented at the 2024 Muscular Dystrophy Association (MDA) Clinical & Scientific Conference (March 3-6, 2024).

“Our evolving understanding of gene therapy indicates there may be an opportunity for better outcomes,” said Crystal Proud, M.D., Pediatric Neurologist at Children’s Hospital of the King’s Daughters. “Improvements in motor function together with decreases in neurofilament levels seen after treatment with SPINRAZA in RESPOND show that we may be able to further maximize benefits for patients.”

Today NfL data are being presented from study participants treated with SPINRAZA for 6 months showing:

Among participants with 2 SMN2 copies:

- All participants had elevated baseline NfL levels relative to healthy children of similar age
- In infants (n=11) who were 9 months or younger at first SPINRAZA dose (mean baseline NfL: 148.3 pg/mL), NfL levels decreased by a mean of 70% from baseline.
- In children (n=11) over 9 months of age at first SPINRAZA dose (mean baseline NfL: 121.8 pg/mL), NfL levels decreased by a mean of 78% from baseline.

Among participants with 3 SMN2 copies:

- Baseline NfL levels were elevated in 2 of 3 children (mean: 60.6 pg/mL).
- NfL reductions were observed in those with elevated levels at baseline and remained stable in the participant without an elevated level at baseline.

“Biogen is at the forefront of pioneering research aimed at advancing biomarkers to accelerate development of drugs for people living with devastating neurodegenerative diseases like SMA and ALS,” said Priya Singhal, M.D., M.P.H., Head of Development and interim Chief Medical Officer at Biogen. “Prior to receiving SPINRAZA at the start of RESPOND, we saw that participants had elevated neurofilament levels, as compared to healthy children suggesting ongoing neuronal injury. The RESPOND findings underscore the value of neurofilament as an objective marker for assessing remaining unmet needs in SMA patients who have previously received gene therapy.”

As reported at the SMA Research & Clinical Care Meeting in June 2023 from the same 29 participants, improvements in motor function were observed in most participants as measured by increased mean total Hammersmith Infant Neurological Examination Section 2 (HINE-2) score from baseline.[1] No new emerging safety concerns have been identified in enrolled RESPOND participants who received SPINRAZA after Zolgensma. After a median of 230.5 days in the study, serious adverse events (AEs) were reported in 13/38 (34%) participants. Any AEs were reported in 31/38 (81.6%) participants. No serious AEs were considered related to SPINRAZA or led to study withdrawal, although some were related to administration.

These data and additional data from the RESPOND study will be presented at subsequent conferences this year including the 4th International Congress on Spinal Muscular Atrophy hosted by SMA Europe.

**About SPINRAZA® (nusinersen)**
SPINRAZA is approved in more than 71 countries to treat infants, children and adults with spinal muscular atrophy (SMA). As a foundation of care in SMA, more than 14,000 individuals have been treated with SPINRAZA worldwide.[2]

SPINRAZA is an antisense oligonucleotide (ASO) that targets the root cause of SMA by continuously increasing the amount of full-length survival motor neuron (SMN) protein produced in the body.[3] It is administered directly into the central nervous system, where motor neurons reside, to deliver treatment where the disease starts.[3]

SPINRAZA has demonstrated sustained efficacy across ages and SMA types with a well-established safety profile based on data in patients treated up to 8 years,[3] combined with unsurpassed real-world experience. The nusinersen clinical development program encompasses more than 10 clinical studies, which have included more than 460 individuals across a broad spectrum of patient populations, including two randomized controlled studies (ENDEAR and CHERISH). The SHINE and NURTURE open-label extension studies are evaluating the long-term impact of SPINRAZA. The most common adverse events observed in clinical studies were respiratory infection, fever, constipation, headache, vomiting and back pain. Laboratory tests can monitor for renal toxicity and coagulation abnormalities, including acute severe low platelet counts, which have been observed after administration of some ASOs.

Biogen licensed the global rights to develop, manufacture and commercialize SPINRAZA from Ionis Pharmaceuticals, Inc. (Nasdaq: IONS). Please click here for Important Safety Information and full Prescribing Information for SPINRAZA in the U.S., or visit your respective country's product website.

**About Biogen**
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patient's lives and to create value for shareholders and our communities. We apply deep understanding of human biology and leverage different modalities to advance first-in-class treatments or therapies that deliver superior outcomes. Our approach is to take bold risks, balanced with return on investment to deliver long-term growth.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media - Facebook, LinkedIn, X, YouTube.

**Biogen Safe Harbor**
This news release contains forward-looking statements, the potential clinical effects of SPINRAZA; the potential benefits, safety and efficacy of SPINRAZA; the clinical development program for SPINRAZA; the identification and treatment of SMA; our research and development program for the treatment of SMA; the potential of our commercial business and pipeline programs, including SPINRAZA; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will," "would" and other words and terms of similar meaning.
Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on our forward-looking statements.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation, uncertainty of success in the development and potential commercialization of SPINRAZA; the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected; unexpected concerns may arise from additional data, analysis or results obtained during our clinical trials; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including SPINRAZA; the occurrence of adverse safety events; the risks of unexpected hurdles, costs or delays; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; results of operations and financial condition. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from our expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements speak only as of the date of this news release.

We do not undertake any obligation to publicly update any forward-looking statements.

*References:*


1. Proud C. Interim results from the ongoing RESPOND study evaluating nusinersen in children with spinal muscular atrophy previously treated with onasemnogene abeparvovec. June 2023. SMA Research & Clinical Care Meeting. Orlando, Fla.
2. Based on commercial patients, early access patients, and clinical trial participants through December 31, 2022.
3. SPINRAZA U.S. Prescribing Information. Available at: https://www.spinraza.com/content/dam/commercial/specialty/spinraza/caregiver/en_us/pdf/spinraza-prescribing-information.pdf. Accessed: February 2024.
4. Core Data sheet, Version 13, October 2021. SPINRAZA. Biogen Inc, Cambridge, MA.


* Clinical outcomes and NfL were analyzed in the 29 participants who had the opportunity for at least six months of treatment at the time of the interim analysis. Analysis of mean change in NfL includes participants with baseline and Day 183 assessments; a mean change from baseline was not reported in the 3 SMN2 copies group, due to the small number of participants. Safety data are reported in all participants (n=38) who received at least one dose of SPINRAZA in the trial.


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