New data highlight potential benefit of SPINRAZA® (nusinersen) in infants and toddlers with unmet medical needs after gene therapy

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- *Interim results from RESPOND study show improved motor function in most participants treated with SPINRAZA after Zolgensma® (onasemnogene abeparvovec)*

CARLSBAD, Calif., June 30, 2023 /PRNewswire/ -- Ionis Pharmaceuticals (Nasdaq: IONS) today announced that its partner Biogen presented new data highlighting the potential benefit of SPINRAZA® (nusinersen) in infants and toddlers living with spinal muscular atrophy (SMA). Interim results from the RESPOND study showed improved motor function in most participants treated with SPINRAZA following treatment with Zolgensma® (onasemnogene abeparvovec). The data were presented today at the SMA Research & Clinical Care Meeting hosted by Cure SMA.

RESPOND is an ongoing two-year, Phase 4 open-label study to evaluate clinical outcomes and safety following treatment with SPINRAZA in infants and toddlers with SMA who have unmet medical needs after treatment with Zolgensma. Interim efficacy results at six months from 29* study participants treated with SPINRAZA show:

- Improvements in motor function in most participants as measured by increased mean total Hammersmith Infant Neurological Examination Section 2 (HINE-2) score from baseline.
  - Participants with two SMN2 copies (n=24) improved by a mean of over 5 points on HINE-2.
  - All participants with three SMN2 copies (n=3) improved; a mean change from baseline was not calculated due to the small number of participants.
- Most participants (25/27) with investigator-reported suboptimal motor function at baseline improved.

After a median of 230.5 days in the study, serious adverse events (AEs) were reported in 13/38 (34%) participants. No serious AEs were considered related to SPINRAZA or led to study withdrawal. No new emerging safety concerns have been identified in enrolled participants who received SPINRAZA after Zolgensma. Additional interim clinical outcomes from the RESPOND study are being presented at the conference.

"SPINRAZA is a foundation of care for people living with spinal muscular atrophy. The early results from RESPOND show that SPINRAZA may further improve muscle performance in patients treated with gene therapy whose outcomes have not met clinical expectations," said C. Frank Bennett, Ph.D., executive vice president and chief scientific officer of Ionis.

New Analysis Evaluating Real-World Impact of SPINRAZA

A systematic literature review and meta-analysis evaluating real-world impact of SPINRAZA for infantile-onset SMA was presented and highlights the importance of generating real-world evidence to achieve a comprehensive understanding of the treatment benefits of SPINRAZA. Improvements in motor function and motor milestones observed in real-world studies were greater than or comparable to those observed in clinical trials, and patients continued to improve with longer duration of SPINRAZA treatment.

About SPINRAZA® (nusinersen)

SPINRAZA is approved in more than 60 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.[1]

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.[2] 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,[4] 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. 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 Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been a leader in RNA-targeted therapy, pioneering new markets and changing standards of care. Ionis currently has four marketed medicines and a promising late-stage pipeline highlighted by cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision to become the leader in genetic medicine, utilizing a multi-platform approach to discover, develop and deliver life-transforming therapies.

To learn more about Ionis visit www.ionispharma.com and follow us on Twitter @ionispharma.

Ionis' Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of SPINRAZA®, Ionis' technologies and other products in development. Any statement describing Ionis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties including those related to our commercial products and the medicines in our pipeline, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Ionis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on Form 10-K for the year ended Dec. 31, 2022, and the most recent Form 10-Q quarterly filing, which are on file with the Securities and Exchange Commission. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" all refer to Ionis Pharmaceuticals and its subsidiaries.

*Two participants in the RESPOND study were not assessed at Day 183 and, therefore, not included in the mean calculation.

[1] Based on commercial patients, early access patients, and clinical trial participants through December 31, 2022.

[2] 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: June 2023.

[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: June 2023.

[4] Core Data sheet, Version 13, October 2021. SPINRAZA. Biogen Inc, Cambridge, MA.

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Ionis Investor Contact: D. Wade Walke, Ph.D., info@ionisph.com, 760-603-2331; Ionis Media Contact: David Polk, J.D., ionis_ca@ionisph.com, 760-603-4679