Ionis announces Biogen to advance salanersen into SMA registrational studies based on positive interim Phase 1 results

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– Investigational salanersen (ION306/BIIB115) developed using novel Ionis antisense chemistry with the potential to achieve high efficacy and once-yearly dosing –

– Interim Phase 1 data show children with SMA previously treated with gene therapy experienced a substantial slowing of neurodegeneration and clinically meaningful improvements in motor function following initiation of salanersen –

– Biogen is engaging with regulators to advance salanersen to registrational stage studies –

CARLSBAD, Calif.--(BUSINESS WIRE)--Jun. 25, 2025-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that its partner, Biogen, shared positive topline results from the Phase 1 study of salanersen (ION306/BIIB115), an investigational antisense oligonucleotide (ASO) being developed for the potential treatment of spinal muscular atrophy (SMA). Leveraging the same mechanism of action as SPINRAZA® (nusinersen) but designed to achieve greater potency, salanersen has the potential to achieve high efficacy and enable once-yearly dosing. Both dose levels tested, 40 mg and 80 mg, given once a year, were generally well-tolerated and led to substantial slowing of neurodegeneration, as shown by reductions in neurofilament. Exploratory clinical outcome data show clinically meaningful improvements in function and attainment of new World Health Organization (WHO) milestones over one year. These data will be presented today at the SMA Research & Clinical Care Meeting hosted by Cure SMA in Anaheim, Calif.

The Phase 1 single ascending dose study was designed to evaluate the safety, tolerability and pharmacokinetics of salanersen. The trial consisted of two parts: Part A, a randomized and placebo-controlled segment in healthy adult male volunteers and Part B, an open-label segment in pediatric participants with SMA who previously received ZOLGENSMA® (onasemnogene abeparvovec) and had investigator-reported suboptimal clinical status. Interim results are from Part B (n=24) in individuals who received either 40 mg or 80 mg salanersen once a year. In participants with elevated baseline concentrations of neurofilament light chain (NfL), indicating ongoing neurodegeneration, initiation of salanersen led to mean reductions in NfL of 70% at 6-months which were sustained through the one-year dosing interval.

“These encouraging interim results reflect the potential of Ionis’ leading technology to continue to improve the lives of people living with SMA,” said Holly Kordasiewicz, Ph.D., senior vice president of neurology, Ionis. “We’re proud to have discovered salanersen, which builds on the foundation we established with SPINRAZA and further supports Ionis’ long-standing leadership in neurology and innovative RNA-targeted medicines. We are deeply grateful to the patients, families and investigators who participated in this study and look forward to continuing to work with Biogen to support the SMA community.”

Salanersen was invented by Ionis using a novel antisense chemistry designed to enhance potency, stability and durability. This advanced molecular design has the potential to deliver long-term results with long-interval dosing.

In addition to safety and NfL, exploratory clinical outcome data were evaluated for the subgroup of participants with at least one year of follow-up at the time of the interim analysis (n=8 participants aged 2-12 who received 40 mg of salanersen). Half (4/8) of these participants achieved new WHO motor milestones that they previously could not achieve on their own or for which they required assistance, such as walking, crawling, standing or sitting. Furthermore, these participants experienced clinically meaningful improvements in motor function from baseline to one year, including a 3.3-point (SD 4.46) mean improvement from baseline on the Hammersmith Functional Motor Scale – Expanded (HFMSE) and a 5.3-point (SD 4.75) improvement on the Revised Upper Limb Module (RULM).

“Despite the remarkable therapeutic advancements in the field of SMA over the past decade, there remains critical unmet needs. Salanersen represents the next phase of Biogen's ongoing pursuit to address these needs,” said Stephanie Fradette, Pharm.D., Head of the Neuromuscular Development Unit at Biogen. “We are encouraged by the available data and eager to move salanersen into the next stage of development as quickly as possible. We are deeply grateful for the trial participants and their families, investigators, and site staff.”

The cumulative interim data from the Phase 1 study indicate that salanersen was generally well tolerated at the 40 mg and 80 mg doses, with most adverse events (AEs) mild to moderate in severity. The most common AEs were pyrexia and upper respiratory tract infection.

Biogen is currently engaging with global health authorities regarding the design of the Phase 3 studies. Ionis discovered salanersen and licensed the global development, manufacturing and commercialization rights to Biogen Inc.

About Spinal Muscular Atrophy (SMA)

SMA is a rare, genetic, neuromuscular disease that affects individuals of all ages. It is characterized by a loss of motor neurons in the spinal cord and lower brain stem, resulting in progressive muscle atrophy and weakness. SMA is caused by a deficiency in the production of survival motor neuron (SMN) protein due to a damaged or missing *SMN1* gene, with a spectrum of disease severity. Some individuals with SMA may never sit; some sit but never walk; and some walk but may lose that ability over time. In the absence of treatment, children with the most severe form of SMA would usually not be expected to reach their second birthday.

SMA impacts approximately 1 in 10,000 live births, is a leading cause of genetic death among infants and causes a range of disability in teenagers and adults.

About SPINRAZA

SPINRAZA® (nusinersen) 12 mg/5 mL injection 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.

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

SPINRAZA has shown efficacy across ages and SMA types with a well-established safety profile based on data in patients treated up to 10 years, combined with unsurpassed real-world experience. 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 Ionis Neurology

Ionis has been at the forefront of discovering and developing leading neurological disease medicines, including SPINRAZA® (nusinersen), the first approved treatment for spinal muscular atrophy, WAINUA™ (eplontersen), a medicine to treat hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN), and QALSODY® (tofersen) for SOD1-ALS. The clinical-stage portfolio includes 13 therapies, of which eight are wholly owned by Ionis. Ionis' investigational portfolio includes medicines for which there are few or no disease modifying treatments, such as rare diseases including Angelman syndrome, Prion disease and Alexander disease and more common conditions such as Alzheimer's and Parkinson's disease.

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has six marketed medicines and a leading pipeline in neurology, cardiology, and select areas of high patient need. As the pioneer in RNA-targeted medicines, Ionis continues to drive innovation in RNA therapies in addition to advancing new approaches in gene editing. A deep understanding of disease biology and industry-leading technology propels our work, coupled with a passion and urgency to deliver life-changing advances for patients. To learn more about Ionis, visit Ionis.com and follow us on X (Twitter), LinkedIn and Instagram.

Ionis Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of salanersen (ION306/BIIB115), our commercial medicines, additional medicines in development and technologies. 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 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. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. 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 December 31, 2024, and most recent Form 10-Q, 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.

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