Biogen and Ionis Announce Topline Phase 1/2 Study Results of Investigational Drug in Amyotrophic Lateral Sclerosis

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- Development of BIIB105, an investigational antisense oligonucleotide for amyotrophic lateral sclerosis (ALS), will be discontinued based on data from the Phase 1/2 ALSpire study
- Biogen and Ionis continue their long-standing commitment to developing therapies for ALS given the devastating impact of this progressive, fatal neurodegenerative condition

CAMBRIDGE, Mass. and CARLSBAD, Calif., May 16, 2024 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced the decision to terminate development of BIIB105 (ION541) an investigational antisense oligonucleotide (ASO) for amyotrophic lateral sclerosis (ALS) based on topline results from the Phase 1/2 ALSpire study. BIIB105 was designed to reduce expression of ataxin-2 (ATXN2) protein and demonstrated statistically significant cerebrospinal fluid (CSF) ATXN2 protein reductions in the study. However, over the 6-month placebo-controlled period, treatment with BIIB105 did not result in a reduction in levels of plasma neurofilament light chain (NfL), a marker of neurodegeneration and neuronal damage. Additionally, BIIB105 did not demonstrate an impact on clinical outcome measures of function, breathing, and strength.

“While BIIB105 lowered ATXN2 protein, it did not reduce neurofilament, which gives us confidence that BIIB105 did not slow the disease process,” said Stephanie Fradette, Pharm.D., Head of the Neuromuscular Development Unit at Biogen. “We are deeply grateful for the contributions of the study participants and remain committed to developing treatments that can meaningfully change the disease trajectory for people living with ALS.”

“We are very appreciative of the people with ALS and investigators who participated in this study and were critical to advancing our scientific understanding of ALS,” said Frank Bennett, Ph.D., executive vice president and chief scientific officer of Ionis. ”Ionis continues to be committed to the ALS community and is advancing our Phase 3 ulefnersen program for people with the genetic form of the disease known as FUS-ALS.”

Longer-term biomarker and efficacy data from the open-label-extension were similar to those seen during the 6-month placebo-controlled treatment period, with sustained reductions in ATXN2 but no impact on NfL or clinical outcome measures over 40+ weeks of follow up. No evidence of benefit was observed in any subgroup evaluated, including those participants with a Poly-CAG expansion in the *ATXN2* gene.

The Phase 1/2 study was a randomized, placebo-controlled, dose-escalating trial to evaluate BIIB105 administered intrathecally to adults (n=99) with ALS. Participants were randomized to receive BIIB105 or placebo (3:1 or 2:1 ratio) for 3 to 6 months. Participants who completed the placebo-controlled period were eligible to enroll in the open-label extension.

During the 6-month placebo-controlled portion of the study, the most common adverse events (AEs) in BIIB105 treated participants were procedural pain, headache and fall. AEs leading to study discontinuation were higher in the BIIB105 group (8.3%) compared with the placebo group (3.6%).

Analyses of data from the study are ongoing to further understanding of the underlying disease process and effects of BIIB105. The companies will present the BIIB105 Phase 1/2 data at the upcoming European Network to Cure ALS (ENCALS) meeting in Stockholm, Sweden in June.

Biogen’s Continuous Commitment to ALS
For over a decade, Biogen has been committed to advancing ALS research to provide a deeper understanding of all forms of the disease. The company has continued to invest in and pioneer research despite making the difficult decision to discontinue a late-stage ALS asset in 2013. Biogen has applied important learnings to its portfolio of assets for genetic and other forms of ALS, with the goal of increasing the probability of bringing a potential therapy to patients in need. These applied learnings include evaluating genetically validated targets in defined patient populations, pursuing the most appropriate modality for each target and employing sensitive clinical endpoints. In addition to QALSODY® (tofersen), the first treatment to target a genetic cause of ALS, which was discovered by Ionis, the company has a robust discovery pipeline including efforts to address TDP43 pathology for the broad ALS population. TDP43 pathology is seen in 97% of ALS cases and is considered a hallmark of the disease.

About Biogen
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patients’ 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.

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has five marketed medicines and a leading pipeline in neurology, cardiology, and other 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 Ionispharma.com and follow us on X (Twitter) and LinkedIn.

About Ionis' Neurology Franchise
Ionis' neurology franchise addresses all major brain regions and central nervous system cell types and currently has three Phase 3 studies ongoing with 11 therapies in clinical development, several of which Ionis plans to commercialize directly. Ionis is discovering and developing potential treatments for many neurological diseases for which there are few or no disease modifying treatments, including common diseases like Alzheimer's and Parkinson's as well as rare diseases such as amyotrophic lateral sclerosis (ALS) and Alexander disease. Ionis has discovered and developed

three commercially available neurological disease medicines, including the first approved treatment for spinal muscular atrophy, a medicine to treat hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN), and, most recently, QALSODY for SOD1-ALS.

Biogen Safe Harbor
This news release contains forward-looking statements, about the treatment of ALS; the anticipated benefits and potential of Biogen's collaboration arrangements with Ionis; the potential of Biogen's commercial business and pipeline programs; and risks and uncertainties associated with drug development and commercialization. These statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "possible," "potential," "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 studies may not be indicative of full results or results from later stage or larger scale clinical studies and do not ensure regulatory approval. You should not place undue reliance on these statements.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation unexpected concerns that may arise from additional data, analysis or results obtained during clinical studies; the occurrence of adverse safety events; risks of unexpected costs or delays; the risk of other unexpected hurdles; regulatory submissions may take longer or be more difficult to complete than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates, including lecanemab; actual timing and content of submissions to and decisions made by the regulatory authorities regarding lecanemab; uncertainty of success in the development and potential commercialization of lecanemab; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; and third party collaboration risks, 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 Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements.

Ionis Forward-looking Statements
This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of 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, 2023, 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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