Biogen and Ionis Announce Topline Phase 1 Study Results of Investigational Drug in C9orf72 Amyotrophic Lateral Sclerosis

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- *BIIB078, an investigational antisense oligonucleotide for C9orf72-associated amyotrophic lateral sclerosis (ALS), did not show clinical benefit; clinical program will be discontinued*
- *Biogen and Ionis remain committed to their decade-long pursuit of advancing ALS research and developing therapies for all forms of this progressive and fatal neurodegenerative disease*

CAMBRIDGE, Mass. and CARLSBAD, Calif. , March 28, 2022 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced topline results from the Phase 1 study of BIIB078 (IONIS-$C9_{Rx}$), an investigational antisense oligonucleotide (ASO) for people with C9orf72-associated amyotrophic lateral sclerosis (ALS).

In this Phase 1 study, BIIB078 was generally well-tolerated. The adverse events (AEs) were mostly mild to moderate in severity and occurred at a similar rate across BIIB078 and placebo groups. The most common AEs were fall, procedural pain and headache.

BIIB078 did not meet any secondary efficacy endpoints and it did not demonstrate clinical benefit. In the dose cohorts up to 60 mg there were no consistent differences between the BIIB078 group and the placebo group. Participants in the BIIB078 90 mg dose cohort trended toward a greater decline than those in the placebo group across secondary endpoints. Based on these results, the BIIB078 clinical development program will be discontinued, including its ongoing open-label extension study.

“We are incredibly grateful for the selfless commitment of the individuals with ALS who participated in the study, and the community’s dedication to advancing research for this devastating disease,” said Toby Ferguson, M.D., Ph.D., Vice President and Head of the Neuromuscular Development Unit at Biogen. “While these were not the results we were hoping for, they are clear and will inform future research across our broad pipeline of investigational ALS therapies. We remain focused on pioneering new treatments that will positively impact people living with this debilitating disease.”

“C9orf72-associated ALS is a complex genetic form of ALS and there are multiple mechanisms by which the scientific community believes the *C9orf72* gene causes disease. We designed BIIB078 to test the prevailing hypothesis that the mechanisms of disease for C9orf72-associated ALS were caused by toxicity associated with the repeat containing RNA and corresponding dipeptides. Unfortunately, this Phase 1 study did not support the hypothesis, suggesting that the disease mechanism is much more complex. While these results do not support further development of BIIB078, we anticipate they will provide valuable learnings that lead to a deeper understanding of this form of ALS,” said C. Frank Bennett, Executive Vice President, Chief Scientific Officer and Franchise Leader for Neurological Programs at Ionis.

This Phase 1 study was a randomized, placebo-controlled, dose-escalating trial to evaluate BIIB078 administered intrathecally to adults (n=106) with C9orf72-associated ALS. Within each of the six study treatment cohorts, participants were randomized to receive BIIB078 or placebo (3:1 ratio). The primary objective of the study was to assess safety and tolerability. Secondary efficacy endpoints included ALS Functional Rating Scale–Revised, Slow Vital Capacity, Hand-Held Dynamometry, and the Iowa Oral Pressure Instrument.

The companies will present the BIIB078 Phase 1 data at a future scientific forum.

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. Today, the company has a pipeline of several investigational drugs being evaluated in ALS, including tofersen, BIIB105 and BIIB100.

About Biogen
As pioneers in neuroscience, Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological diseases as well as related therapeutic adjacencies. One of the world’s first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Sir Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today, Biogen has a leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, and is providing the first and only approved treatment to address a defining pathology of Alzheimer’s disease. Biogen is also commercializing biosimilars and focusing on advancing the industry’s most diversified pipeline in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

In 2020, Biogen launched a bold 20-year, $250 million initiative to address the deeply interrelated issues of climate, health, and equity. Healthy Climate, Healthy Lives™ aims to eliminate fossil fuels across the company’s operations, build collaborations with renowned institutions to advance the science to improve human health outcomes, and support underserved communities.

The company routinely post information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow Biogen on social media – Twitter, LinkedIn, Facebook, YouTube.

About Ionis Pharmaceuticals, Inc.
For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming a leading, fully integrated biotechnology company.

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

Biogen Safe Harbor Statement
This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including statements about results from the Phase 1 study of BIIB078; the potential clinical effects of BIIB078; the potential benefits, safety and efficacy of BIIB078; the clinical development program for BIIB078; the identification and treatment of ALS; our research and development program for the treatment of ALS; the potential of our commercial business and pipeline programs, including BIIB078; 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 these statements or the scientific data presented.

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 BIIB078; 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 BIIB078; 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; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, 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 are based on our current beliefs and expectations and speak only as of the date of this news release.

Ionis Forward-looking Statement
This press release includes forward-looking statements regarding Ionis' business, and the therapeutic and commercial potential of Ionis' technologies, IONIS-C9$_{Rx}$ (BIIB078) 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 the impact COVID-19 could have on our business, and including but not limited to 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 December 31, 2021, and the most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available from the Company.

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