Biogen and Ionis report positive topline clinical data on investigational Alzheimer's disease treatment at AAIC

July 26, 2021

- Phase 1b study of BIIB080/IONIS-MAPT Rx met primary objective of safety and tolerability
- Study demonstrated durable, robust, time and dose dependent lowering of tau protein in cerebrospinal fluid

CAMBRIDGE, Mass. and CARLSBAD, Calif., July 26, 2021 /PRNewswire/ -- Biogen Inc. (Nasdaq: BIIB) and Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that topline data from a Phase 1b placebo-controlled, multiple ascending dose clinical study showed that BIIB080/IONIS-MAPT$_{Rx}$ met its primary objective of safety and tolerability in patients with mild Alzheimer's disease. The study demonstrated robust time and dose dependent lowering of tau protein in cerebrospinal fluid (CSF) over the three-month treatment period and sustained reductions during the six-month post-treatment period.

In patients receiving BIIB080, there were dose-dependent decreases in the concentration of total-tau in CSF eight weeks post-last dose (Day 141) with a mean percentage reduction of 30 percent, 40 percent and 49 percent in the low, medium and high dose groups treated every four-weeks, respectively, and 42 percent in the group treated every 12 weeks. Total-tau in the CSF continued to decline 16 weeks post-last dose in patients treated with BIIB080 in the high dose four-week and 12-week dose groups, showing a 55 percent and 49 percent mean reduction from baseline, respectively. CSF was not collected 16 weeks post-last dose in the low and medium four-week dose groups. There were similar dose-dependent decreases in the levels of phosphorylated tau. All participants (n=46) completed the Multiple Ascending Dose (MAD) period and 43 participants completed the Post-Treatment (PT) period (3 participants voluntarily withdrew). These data were presented in a poster session at the 2021 Alzheimer's Association International Conference (AAIC) held virtually and in Denver, Colo., July 26 – 30.

"There is clearly an urgent need to develop and deliver effective treatments for Alzheimer's disease, a devastating disorder for which there currently are limited therapeutic options. We are encouraged by the topline results from this study of BIIB080, which demonstrate the potential of Ionis' antisense technology to successfully target what we believe is a root cause of Alzheimer's disease," said C. Frank Bennett, Ph.D., Ionis' chief scientific officer and franchise leader for neurological programs. Dr. Bennett added, "These study results support further investigation of BIIB080 for the treatment of Alzheimer's disease and suggest that antisense-mediated suppression of tau protein may be a feasible therapeutic approach for other tauopathies."

"Biogen is deeply committed to the development of novel treatments for patients with Alzheimer's disease. This commitment extends across multiple modalities, including antisense oligonucleotides, as with BIIB080," said Alfred Sandrock, Jr., M.D., Ph.D., Head of Research and Development at Biogen. "Biogen is encouraged by the results of this trial, and we look forward to our continued research in future clinical studies with this promising investigational asset."

Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive and functional decline resulting in significant disability. Until recently, treatment was limited to management of symptoms. BIIB080 is an investigational antisense therapy designed to target microtubule-associated protein tau (MAPT) mRNA and prevent production of tau protein. Growing evidence suggests that aggregated, hyperphosphorylated tau may be a key driver of neurodegeneration in Alzheimer's disease as well as other tauopathies including progressive supranuclear palsy and frontotemporal degeneration. In preclinical studies in MAPT transgenic mice, MAPT-targeted antisense treatment demonstrated robust tau-lowering in CNS tissues and prevention and reversal of disease.

The primary objective of the Phase 1b first-in-human study was to assess safety and tolerability of multiple intrathecal (IT) bolus administrations of BIIB080. The study was divided into two parts: Part 1, a MAD study of 46 patients with mild Alzheimer's disease comprising a three-month Treatment Evaluation Period and a six-month PT period; Part 2, an open label long-term extension study comprising a 12-month Treatment Evaluation Period and a four- or six-month PT period. Four ascending dose cohorts were enrolled sequentially and randomized 3:1 to IT bolus administrations of BIIB080 or placebo. Patients aged 50-74 years with mild Alzheimer's disease and confirmed amyloid positivity (via CSF) at screening were considered eligible. Part 1 is now complete; Part 2 is currently ongoing (EudraCT: 2016-002713-22; NCT03186989).

The characteristics of patients at baseline were representative of relatively younger, mild Alzheimer's disease patients and were generally similar across trial groups. All adverse events were mild to moderate in severity with no serious adverse events occurring in any patients that received BIIB080. There were no deaths, dose-limiting adverse events or dosing discontinuations.

About Ionis' Neurology Franchise

The Ionis neurology franchise addresses all major brain regions and central nervous system cell types and currently has three Phase 3 studies ongoing with 11 medicines in clinical development, three of which are wholly owned. Ionis is leading the way in treating root causes of many neurological diseases and developing antisense medicines for common diseases like Alzheimer's and Parkinson's as well as rare diseases like amyotrophic lateral sclerosis (ALS) and Alexander disease. Ionis' marketed neurological disease medicines include SPINRAZA®, a global foundation of care for spinal muscular atrophy (SMA), commercialized by Biogen, and TEGSEDI®, the first and only self-administered, subcutaneous treatment for the polyneuropathy of hereditary ATTR amyloidosis in adults.

About Biogen

At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative 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, Kenneth Murray and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, neuropsychiatry, immunology, acute neurology and neuropathic pain.

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

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, relating to the potential clinical effects of BIIB080; the potential benefits, safety and efficacy of BIIB080; the results of the Phase 1b study of BIIB080; the clinical development program for BIIB080; the identification and treatment of Alzheimer's disease; the potential of Biogen's commercial business and pipeline programs, including BIIB080; the anticipated benefits and potential of Biogen's collaboration arrangements with Ionis; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "potential," "possible," "prospect," "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 unexpected concerns that may arise from additional data, analysis or results obtained during clinical trials; the occurrence of adverse safety events; risks of unexpected costs or delays; the risk of other unexpected hurdles; uncertainty of success in the development and potential commercialization of BIIB080; 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; third party collaboration risks; the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen's business, results of operations and financial condition; and any other risks and uncertainties that are described in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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 neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

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

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of Ionis' technologies, IONIS-MAPT$_{Rx}$/BIIB080 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, 2020, 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.

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

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