New Data from Biogen's Investigational Antisense Oligonucleotide (ASO) Targeting Tau Shows Promise for Potential New Generation of Treatments in Early Alzheimer's Disease

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- In the Phase 1b study, favorable trends were reported for the high-dose groups on multiple measures of cognition and function.
- First study of a tau targeting drug that shows reduction of aggregated tau pathology and favorable trends on clinical outcomes.
- Recruitment is underway for the Phase 2 CELIA study further investigating clinical efficacy and safety.

CAMBRIDGE, Mass., Oct. 25, 2023 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) reported new Phase 1b clinical data from the study of BIIB080, an investigational antisense oligonucleotide (ASO) therapy targeting tau, in mild Alzheimer's disease (AD). The data showed favorable trends on multiple exploratory endpoints of cognition and activities of daily living in AD (n=46), building upon prior results which showed a reduction of tau protein in the cerebral spinal fluid (CSF t-tau) and tau positron emission tomography (PET) across brain regions. The late-breaking results were presented at the 2023 Clinical Trials on Alzheimer's Disease (CTAD) meeting held in Boston, MA from October 24-27.

In AD, both tau and amyloid beta are linked to disease progression.[1] Tau protein can form tangles which progressively accumulate in brain regions involved in cognition.[2] The accumulation of pathological tau tangles has been shown to lead to neuronal loss. ASO therapies are seen as promising tools for modulating production of disease-associated proteins. Currently, the ASO approach underpins more than 60 treatments approved or in clinical trials for a variety of disease areas including a range of cancers, viral illnesses, and genetic conditions.[3]

"This is the first time we've seen both strong target engagement and favorable trends on clinical outcomes with a novel mechanism targeting tau," said Priya Singhal, M.D., M.P.H., Head of Development at Biogen. "While these are preliminary findings, we are excited about these results and continue to enroll the Phase 2 CELIA study. We believe defeating Alzheimer's disease will take different approaches and we are committed to exploring the targeting of tau as a new generation of treatment."

In results presented at CTAD, favorable trends were observed on the global Clinical Dementia Rating Sum of Boxes (CDR-SB), Mini-Mental State Exam (MMSE) cognitive scales and Functional Activities Questionnaire (FAQ) at week 100 in groups treated with a high-dose of BIIB080 (n=16). The results build on data presented at the International Conference on Alzheimer's and Parkinson's Disease (ADPD ^{TM} 2023) which showed that direct targeting of tau protein production had a substantial impact on tau biomarkers, reducing total and phosphorylated tau in the CSF and aggregated tau pathology as measured by PET across all brain regions assessed. The favorable trends suggest a potential link between a reduction in tau PET pathology and clinical outcomes.

Treatment was generally well tolerated throughout the study. The majority of adverse events were mild or moderate in severity, of which the most common were headache, back pain, pain in extremity, post-lumbar puncture syndrome and procedural pain.

BIIB080 is designed to target microtubule-associated protein tau (MAPT) mRNA and reduce production of tau protein. The Phase 1b trial and its long-term extension study (LTE) were designed to assess the safety and tolerability of multiple doses in patients with mild dementia due to AD. Participants were randomized to placebo or to four dose cohorts receiving 10mg once every 4 weeks [Q4W], 30mg Q4W, 60mg Q4W or 115mg Q12W. In the LTE, all participants received 60mg or 115mg every 12 weeks.

Recruitment for the Phase 2 CELIA study (NCT05399888), evaluating the potential for this ASO targeting tau to slow the worsening of mild cognitive impairment or mild dementia due to AD, is ongoing at sites across North America, Europe and Asia Pacific.

In December 2019, Biogen exercised a license option with Ionis and obtained a worldwide, exclusive, royalty-bearing license to develop and commercialize BIIB080.

About Antisense Therapies
Antisense therapies are designed to seek out, bind to and destroy a mRNA in a highly specific manner, so that the amount of disease-causing protein is dramatically decreased. Antisense therapies can also treat diseases caused by too little protein by increasing the production of the protein, thereby restoring the protein to normal levels.

About Biogen
Founded in 1978, Biogen is a leading global biotechnology company that has pioneered multiple breakthrough innovations including a broad portfolio of medicines to treat multiple sclerosis, the first approved treatment for spinal muscular atrophy, and two co-developed treatments to address a defining pathology of Alzheimer's disease. Biogen is advancing a pipeline of potential novel therapies across neurology, neuropsychiatry, specialized immunology and rare diseases and remains acutely focused on its purpose of serving humanity through science while advancing a healthier, more sustainable and equitable world.

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

Biogen Safe Harbor
This news release contains forward-looking statements, about the potential of BIIB080, including related to the Phase 2 CELIA study; 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; 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; and the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen's 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 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.

References:

1. BrightFocus Foundation. Tau Protein and Alzheimer's Disease: What's the Connection? https://www.brightfocus.org/alzheimers/article/tau-protein-and-alzheimers-disease-whats-connection. Accessed September 2023.
2. Moumné et al. Oligonucleotide Therapeutics: From Discovery and Development to Patentability. *Pharmaceutics* 2022, *14*(2), 260; https://doi.org/10.3390/pharmaceutics14020260
3. Alzheimer's Association. Tau Topic Sheet. https://www.alz.org/media/Documents/alzheimers-dementia-tau-ts.pdf. Accessed October 2023.

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