Eisai Presents Data on Benefits of Long-Term Administration of Dual-Acting Lecanemab at the 17th Clinical Trials for Alzheimer's Disease (CTAD) Conference

October 30, 2024

-New testing method highlights link between protofibrils and biomarkers for neurodegeneration-
-Patient and caregiver perspectives on five-year treatment with lecanemab -
- Utilization of blood biomarkers to predict brain amyloid accumulation in AHEAD study of preclinical AD-

TOKYO and CAMBRIDGE, Mass., Oct. 30, 2024 (GLOBE NEWSWIRE) -- Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq: BIIB, Corporate headquarters: Cambridge, Massachusetts, CEO: Christopher A. Viehbacher, "Biogen") announced today that the latest findings for lecanemab-irmb (U.S. brand name: LEQEMBI®), an anti-amyloid beta (Aβ) protofibril* antibody for the treatment of early Alzheimer's disease (AD), were presented at the Clinical Trials for Alzheimer's Disease Conference (CTAD), held in Madrid, Spain, and virtually.

Benefits of Continued Treatment with Lecanemab for People with Early AD
In July 2024 at the Alzheimer's Association International Conference (AAIC) 2024, results from the open-label long-term extension study (OLE) following the core study of the lecanemab Phase 3 Clarity AD study were presented, showing that the mean change from baseline in CDR-SB (global cognitive and functional scale) in the lecanemab treated group relative to the placebo group was -0.45 at 18 months, and at 36 months, this expanded to -0.95 compared to a prespecified natural history** cohort of AD. There was a 30% reduction in the relative risk of progressing to the next disease stage In addition, the tau PET substudy of the lecanemab Phase 3 Clarity AD clinical study showed that with three (3) years of continuous treatment with lecanemab, 59% of patients with no or low tau accumulation in the brain (no tau/low tau) at baseline showed improvement or no decline, and 51% showed improvement from baseline on the Clinical Dementia Rating-Sum of Boxes (CDR-SB) global cognitive and functional scale.[1]

Clarity AD data presented at CTAD expand on these initial results to include additional measurements resulting from three (3) years of continuous lecanemab treatment in patients with low levels of amyloid accumulation in the brain at baseline (less than 60 Centiloids: low amyloid). These data show that 46% of patients improved or had no decline, and 33% showed improvement from baseline on the CDR-SB. On the ADAS-Cog14 measurement scale, 46% of patients showed improvement or no decline and 43% showed improvement. On the ADCS MCI-ADL, 51% of patients showed improvement or no decline and 48% showed improvement. These results – from no tau/low tau population and low amyloid populations – suggest that earlier initiation of lecanemab treatment may have a positive impact on disease progression of early AD patients and may provide continued benefits to patients with early AD over the long term.[2]

No new safety findings were observed with continued lecanemab treatment over three (3) years. Most amyloid-related imaging abnormalities (ARIA) occurred in the first six (6) months of treatment. After the first six (6) months, ARIA rates were low and similar to ARIA rates on placebo during the placebo-controlled period. With regards to the incidence of ARIA by ApoEε4 status during the continuous treatment, the incidence was higher in ApoE4 homozygotes than in heterozygotes or non-carriers, but rates of new ARIA were decreased after the completion of the 18 months core study as treatment continued, regardless of ApoEε4 status.[2]

Correlation between Protofibrils and Biomarkers for Neurodegenerative Disease in the AD Brain
Dual-acting lecanemab is the only early AD treatment available to support neuronal function by clearing the highly toxic protofibrils that continue to cause neuronal injury and death even after plaques have been cleared from the brain. Protofibrils accumulate early in the AD brain and lead to nerve cell function loss, abnormal nerve processes, inflammation, and memory loss. In non-clinical studies, antibodies against protofibrils prevented protofibril-mediated neuronal dysfunction and memory loss.

Accurately quantifying the amount of protofibrils in human cerebrospinal fluid (CSF) has been challenging due to their low concentration. As such, a new measurement method was developed by researchers at Eisai to accurately quantify protofibrils in CSF.

Utilizing this new method of measurement, the amount of protofibrils in AD CSF correlated more strongly with neurodegenerative disease biomarkers (CSF total tau and neurogranin) than with CSF Aβ42, a biomarker associated with Aβ plaques accumulation, indicating that protofibrils are closely related to synaptic dysfunction. Furthermore, it was observed that protofibrils, unlike plaques, are diffusible. These results suggest that protofibrils induce synaptic dysfunction, playing an important role in neurodegeneration in AD brains.[3]

Lecanemab Treatment for Early AD: Insights from Long-Term U.S. Clinical Studies
Dr. Marwan Noel Sabbagh, Moreno Family Chair for Alzheimer's Research and Vice Chairman for Research and Professor, Department of Neurology, Barrow Neurological Institute, presented outcomes of an analysis of the use of lecanemab treatment between January 6, 2023, and July 30, 2024, based on payment claims data from the Komodo Research Database, a medical database in the U.S. In the U.S., lecanemab is used in accordance with the US FDA-approved indication, dosing, and monitoring guidelines. The analysis found that access to lecanemab treatment is expanding and highlighted opportunities to improve access in rural areas and educational outreach for underserved populations.[4]

Dr. David Watson of the Alzheimer's Research and Treatment Center reported on patients who continued to receive lecanemab treatment following the Phase II Study 201 and Phase III Clarity AD study. A total of 136 patients participated in both studies at this center, and 66 patients chose to continue lecanemab therapy, with 13 patients receiving treatment for more than five (5) years and 40 patients receiving treatment for more than three (3) years. More than half of the patients (15/24) who continued treatment with lecanemab for more than three (3) years after the core phase remained in their initial stage of disease. Further, in a survey of 11 patients (or their caregivers) who received lecanemab treatment for more than five (5) years, all patients responded that they were "very satisfied" or "satisfied" with lecanemab treatment. In addition, between 45% and 73% of patients responded that lecanemab treatment made them feel more positive about their daily life, social activities, memory, etc. "frequently" or "very often."[5]

No new long-term safety findings were observed in these multi-year studies.[5]

Progress in the AHEAD 3-45 Study: Improving Screening Eligibility Using Blood Biomarkers and Completing Patient Enrollment
AHEAD 3-45 is a Phase 3 clinical study for individuals with preclinical AD, meaning they are clinically unimpaired but have intermediate or elevated levels of amyloid in their brains. In the study, blood tests, cognitive function tests (PACC-5***), amyloid PET, MRI, and tau PET were used for

screening. Based on the amount of Aβ accumulation in the brain as determined by amyloid PET, subjects were assigned to two (2) trials with different dose settings: the A3 trial, for those with borderline Aβ levels in the brain, and the A45 trial, for those with positive Aβ levels in the brain.[6]

Screening with blood biomarker tests was important to improve eligibility for amyloid PET testing in subjects without cognitive impairment. Using plasma Aβ42/40 ratio and p-tau217/tau217 ratio in the initial screening reduced screening failure on amyloid PET from more than 70% to less than 30%. In particular, plasma p-tau217 was shown to correlate with amyloid PET, supporting its role as a useful blood biomarker to identify elevated amyloid in the brain.[6]

Enrollment for the AHEAD 3-45 study was completed in October 2024.

Lifetime Achievement Award Presented to Professor Lannfelt
Professor Emeritus Lars Lannfelt of Uppsala University received the CTAD Lifetime Achievement Award in recognition of his pioneering work in scientific discovery and drug development in AD. As part of this award ceremony, he delivered a keynote speech outlining the discovery of the arctic mutation in familial AD, its application to therapeutic strategies targeting protofibrils for AD treatment, and the development of lecanemab.

Eisai serves as the lead for lecanemab's development and regulatory submissions globally with both Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority.

*Protofibrils are believed to contribute to the brain injury that occurs with AD and are considered to be the most toxic form of Aβ, having a primary role in the cognitive decline of this progressive, debilitating condition.[7] Protofibrils cause injury to neurons in the brain which, in turn, can negatively impact cognitive function through multiple mechanisms, not only increasing the development of insoluble Aβ plaques but also increasing direct damage to brain cell membranes and the connections that transmit signals between nerve cells or nerve cells and other cells. It is believed the reduction of protofibrils may prevent the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.[8]

**ADNI is a clinical research project launched in 2005 to develop methods to predict the onset of AD and to confirm the effectiveness of treatments. The ADNI observational cohort was pre-specified and used during the design of Clarity AD. The cohort represents the exact population of those in Clarity AD study; matched ADNI participants show similar degree of decline to placebo group out to 18 months.

***PACC-5 is a composite measure that provides a highly sensitive measure of changes in cognitive function in individuals with preclinical AD.

Please see full Prescribing Information for LEQEMBI, including Boxed WARNING.

U.S. INDICATION
LEQEMBI® [(lecanemab-irmb) 100 mg/mL injection for intravenous use] is indicated for the treatment of Alzheimer's disease (AD). Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

IMPORTANT SAFETY INFORMATION

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES (ARIA)

- **Monoclonal antibodies directed against aggregated forms of amyloid beta, including LEQEMBI, can cause ARIA, characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Serious intracerebral hemorrhages >1 cm, some fatal, have been observed with this class of medications.**
  - **Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients who are ApoE ε4 homozygotes (~15% of patients with AD) treated with this class of medications have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with LEQEMBI; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.**
- **Consider the benefit of LEQEMBI for the treatment of AD and the potential risk of serious ARIA events when deciding to initiate treatment with LEQEMBI**.

CONTRAINDICATION
LEQEMBI is contraindicated in patients with serious hypersensitivity to lecanemab-irmb or to any of the excipients of LEQEMBI. Reactions have included angioedema and anaphylaxis.

WARNINGS AND PRECAUTIONS
AMYLOID-RELATED IMAGING ABNORMALITIES
LEQEMBI can cause ARIA-E and ARIA-H, which can occur together. ARIA-E can be observed on magnetic resonance imaging (MRI) as brain edema or sulcal effusions and ARIA-H as microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with AD. With this class of medications, ARIA-H generally occurs in association with ARIA-E. Reported ARIA symptoms may include headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms usually resolve over time.

Incidence of ARIA
Symptomatic ARIA occurred in 3% (29/898) and serious ARIA symptoms in 0.7% (6/898) with LEQEMBI. Clinical ARIA symptoms resolved in 79% (23/29) of patients during the period of observation. ARIA, including asymptomatic radiographic events, was observed: LEQEMBI, 21% (191/898); placebo, 9% (84/897). ARIA-E was observed: LEQEMBI, 13% (113/898); placebo, 2% (15/897). ARIA-H was observed: LEQEMBI, 17% (152/898); placebo, 9% (80/897). No increase in isolated ARIA-H was observed for LEQEMBI vs placebo.

ApoE ε4 Carrier Status and Risk of ARIA
Of the patients taking LEQEMBI, 16% (141/898) were ApoE ε4 homozygotes, 53% (479/898) were heterozygotes, and 31% (278/898) were noncarriers. With LEQEMBI, the incidence of ARIA was higher in ApoE ε4 homozygotes (LEQEMBI: 45%; placebo: 22%) than in heterozygotes (LEQEMBI: 19%; placebo: 9%) and noncarriers (LEQEMBI: 13%; placebo: 4%). Symptomatic ARIA-E occurred in 9% of ApoE ε4 homozygotes vs 2% of heterozygotes and 1% of noncarriers. Serious ARIA events occurred in 3% of ApoE ε4 homozygotes and in ~1% of heterozygotes and noncarriers. The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers.

Radiographic Findings
The majority of ARIA-E radiographic events occurred within the first 7 doses, although ARIA can occur at any time, and patients can have >1 episode. Maximum radiographic severity of ARIA-E with LEQEMBI was mild in 4% (37/898), moderate in 7% (66/898), and severe in 1% (9/898) of patients. Resolution of ARIA-E on MRI occurred in 52% of patients by 12 weeks, 81% by 17 weeks, and 100% overall after detection. Maximum radiographic severity of ARIA-H microhemorrhage with LEQEMBI was mild in 9% (79/898), moderate in 2% (19/898), and severe in 3% (28/898) of patients; superficial siderosis was mild in 4% (38/898), moderate in 1% (8/898), and severe in 0.4% (4/898) of patients. With LEQEMBI, the rate of severe radiographic ARIA-E was highest in ApoE ε4 homozygotes (5%; 7/141) vs heterozygotes (0.4%; 2/479) or noncarriers (0%; 0/278). With LEQEMBI, the rate of severe radiographic ARIA-H was highest in ApoE ε4 homozygotes (13.5%; 19/141) vs heterozygotes (2.1%; 10/479) or noncarriers (1.1%; 3/278).

Intracerebral Hemorrhage
Intracerebral hemorrhage >1 cm in diameter was reported in 0.7% (6/898) with LEQEMBI vs 0.1% (1/897) with placebo. Fatal events of intracerebral hemorrhage in patients taking LEQEMBI have been reported.

Concomitant Antithrombotic Medication:
In Clarity AD, baseline use of antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) was allowed if the patient was on a stable dose. The majority of exposures to antithrombotic medications were to aspirin. Antithrombotic medications did not increase the risk of ARIA with LEQEMBI. The incidence of intracerebral hemorrhage was 0.9% (3/328) in patients taking LEQEMBI with a concomitant antithrombotic medication at the time of the event vs 0.6% (3/545) in those who did not receive an antithrombotic. Patients taking LEQEMBI with an anticoagulant alone or combined with an antiplatelet medication or aspirin had an incidence of intracerebral hemorrhage of 2.5% (2/79) vs none in patients receiving placebo. Caution should be exercised when considering the administration of anticoagulants or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI.

Other Risk Factors for Intracerebral Hemorrhage:
Patients were excluded from enrollment in Clarity AD for findings on neuroimaging that indicated an increased risk for intracerebral hemorrhage. These included findings suggestive of cerebral amyloid angiopathy (prior cerebral hemorrhage >1 cm in greatest diameter, >4 microhemorrhages, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation). The presence of an ApoE ε4 allele is also associated with cerebral amyloid angiopathy. Caution should be exercised when considering the use of LEQEMBI in patients with factors that indicate an increased risk for intracerebral hemorrhage and in patients who need to be on anticoagulant therapy.

ARIA Monitoring and Dose Management Guidelines
Obtain a recent baseline brain MRI prior to initiating treatment with LEQEMBI and prior to the 5th, 7th, and 14th infusions. Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment with LEQEMBI. Depending on ARIA-E and ARIA-H clinical symptoms and radiographic severity, use clinical judgment when considering whether to continue dosing or to temporarily or permanently discontinue LEQEMBI. If a patient experiences ARIA symptoms, clinical evaluation should be performed, including MRI if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment.

HYPERSENSITIVITY REACTIONS
Hypersensitivity reactions, including angioedema, bronchospasm, and anaphylaxis, have occurred with LEQEMBI. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate therapy.

INFUSION-RELATED REACTIONS (IRRs)
IRRs were observed—LEQEMBI: 26% (237/898); placebo: 7% (66/897)—and the majority of cases with LEQEMBI (75%, 178/237) occurred with the first infusion. IRRs were mostly mild (69%) or moderate (28%) in severity. IRRs resulted in discontinuation of LEQEMBI in 1% (12/898). Symptoms of IRRs included fever and flu-like symptoms (chills, generalized aches, feeling shaky, and joint pain), nausea, vomiting, hypotension, hypertension, and oxygen desaturation.

In the event of an IRR, the infusion rate may be reduced or the infusion may be discontinued and appropriate therapy initiated as clinically indicated. Consider prophylactic treatment prior to future infusions with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids.

ADVERSE REACTIONS
The most common adverse reaction leading to discontinuation of LEQEMBI was ARIA-H microhemorrhages that led to discontinuation in 2% (15/898) with LEQEMBI vs <1% (1/897) with placebo.

The most common adverse reactions reported in ≥5% with LEQEMBI (N=898) and ≥2% higher than placebo (N=897) were IRRs (LEQEMBI: 26%; placebo: 7%), ARIA-H (LEQEMBI: 14%; placebo: 8%), ARIA-E (LEQEMBI: 13%; placebo: 2%), headache (LEQEMBI: 11%; placebo: 8%), superficial siderosis of central nervous system (LEQEMBI: 6%; placebo: 3%), rash (LEQEMBI: 6%; placebo: 4%), and nausea/vomiting (LEQEMBI: 6%; placebo: 4%).

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[Notes to editors]

1. About lecanemab (LEQEMBI®)

Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. It is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). Lecanemab is approved in the U.S.,[9] Japan,[10] China,[11] South Korea,[12] Hong Kong,[13] Israel,[14] the United Arab Emirates[15] and Great Britain.[16] Eisai has also submitted applications for approval of lecanemab in 10 countries and regions, including the European Union (EU).

LEQEMBI's approvals in these countries were based on Phase 3 data from Eisai's, global Clarity AD clinical trial, in which it met its primary endpoint and all key secondary endpoints with statistically significant results. The primary endpoint was the global cognitive and functional scale, Clinical Dementia Rating Sum of Boxes (CDR-SB). In the Clarity AD clinical trial, treatment with lecanemab reduced clinical decline on CDR-SB by 27% at 18 months compared to placebo.[17,18] The mean CDR-SB score at baseline was approximately 3.2 in both groups. The adjusted least-squares mean change from baseline at 18 months was 1.21 with lecanemab and 1.66 with placebo (difference, −0.45; 95% confidence interval [CI], −0.67 to −0.23; P<0.001). In addition, the secondary endpoint from the AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS-MCI-ADL), which measures information provided by people caring for patients with AD, noted a statistically significant benefit of 37% compared to placebo. The adjusted mean change from baseline at 18 months in the ADCS-MCI-ADL score was −3.5 in the lecanemab group and −5.5 in the placebo group (difference, 2.0; 95% CI, 1.2 to 2.8; P<0.001). The ADCS MCI-ADL assesses the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities. The most common adverse events (>10%) in the lecanemab group were infusion reactions, ARIA-H (combined cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis), ARIA-E (edema/effusion), headache, and fall.

In July 2024 Eisai presented 36-month data from the Phase 3 Clarity AD Open-Label Extension Study demonstrating that LEQEMBI-treated patients continued to show benefit at 36 months of treatment. In the 18-month core study of Clarity AD, there was a statistically significant difference in global cognition and function as measured by CDR-SB between the LEQEMBI and placebo groups. The separation in CDR-SB between the group that continued to receive LEQEMBI (early start group) and the group who switched from placebo to LEQEMBI (delayed start group) was maintained during the 6-month OLE following the core study. This indicates that similar disease trajectory for both early and delayed start groups occurred with LEQEMBI administration. The blood biomarker results (plasma Aβ42/40 ratio, ptau181, GFAP and NfL) showed improvement even after delayed initiation of treatment with LEQEMBI.

Since July 2020 the Phase 3 clinical study (AHEAD 3-45) for individuals with preclinical AD, meaning they are clinically normal and have intermediate or elevated levels of amyloid in their brains, is ongoing. AHEAD 3-45 is conducted as a public-private partnership between the Alzheimer's Clinical Trial Consortium that provides the infrastructure for academic clinical trials in AD and related dementias in the U.S, funded by the National Institute on Aging, part of the National Institutes of Health, Eisai, and Biogen. Since January 2022, the Tau NexGen clinical study for Dominantly Inherited AD (DIAD), that is conducted by Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis, is ongoing and includes lecanemab as the backbone anti-amyloid therapy.

2. About the Collaboration between Eisai and Biogen for AD

Eisai and Biogen have been collaborating on the joint development and commercialization of AD treatments since 2014. Eisai serves as the lead of lecanemab development and regulatory submissions globally with both companies co-commercializing and co-promoting the product and Eisai having final decision-making authority.

3. About the Collaboration between Eisai and BioArctic for AD

Since 2005, Eisai and BioArctic have had a long-term collaboration regarding the development and commercialization of AD treatments. Eisai obtained the global rights to study, develop, manufacture and market lecanemab for the treatment of AD pursuant to an agreement with BioArctic in December 2007. The development and commercialization agreement on the antibody back-up was signed in May 2015.

4. About Eisai Co., Ltd.

Eisai's Corporate Concept is "to give first thought to patients and people in the daily living domain, and to increase the benefits that health care provides." Under this Concept (also known as *human health care* (*hhc*) Concept), we aim to effectively achieve social good in the form of relieving anxiety over health and reducing health disparities. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to create and deliver innovative products to target diseases with high unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.
In addition, we demonstrate our commitment to the elimination of neglected tropical diseases (NTDs), which is a target (3.3) of the United Nations Sustainable Development Goals (SDGs), by working on various activities together with global partners.

For more information about Eisai, please visit www.eisai.com (for global headquarters: Eisai Co., Ltd.), and connect with us on X, LinkedIn and Facebook. The website and social media channels are intended for audiences outside of the UK and Europe. For audiences based in the UK and Europe, please visit www.eisai.eu and Eisai EMEA LinkedIn.

5. 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.

The company routinely posts information that may be important to investors on its website at www.biogen.com. Follow Biogen on social media – Facebook, LinkedIn, X, YouTube.

Biogen Safe Harbor

This news release contains forward-looking statements, including about the potential clinical effects of lecanemab; the potential benefits, safety and efficacy of lecanemab; potential regulatory discussions, submissions and approvals and the timing thereof; the treatment of Alzheimer's disease; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; the potential of Biogen's commercial business and pipeline programs; including lecanemab; 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 the medicine; 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.

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