Lilly's Donanemab Slows Clinical Decline of Alzheimer's Disease in Positive Phase 2 Trial

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INDIANAPOLIS, Jan. 11, 2021 /PRNewswire/ -- Donanemab, an investigational antibody that targets a modified form of beta amyloid called N3pG, showed significant slowing of decline in a composite measure of cognition and daily function in patients with early symptomatic Alzheimer's disease compared to placebo in results from Eli Lilly and Company's (NYSE: LLY) Phase 2 TRAILBLAZER-ALZ study. Donanemab met the primary endpoint of change from baseline to 76 weeks in the Integrated Alzheimer's Disease Rating Scale (iADRS), slowing decline by 32 percent relative to placebo, which was statistically significant. The iADRS is a clinical composite tool combining the cognitive measure ADAS-Cog13 and functional measure ADCS-iADL, two commonly used measures in Alzheimer's disease. Donanemab also showed consistent improvements in all prespecified secondary endpoints measuring cognition and function compared to placebo, but did not reach nominal statistical significance on every secondary endpoint.

"We are extremely pleased about these positive findings for donanemab as a potential therapy for people living with Alzheimer's disease, the only leading cause of death without a treatment that slows disease progression. We look forward to discussing the TRAILBLAZER-ALZ study data and next steps with global regulators. In addition, we are committed to reproducing and extending these important findings in our second ongoing pivotal donanemab trial, TRAILBLAZER-ALZ 2," said Mark Mintun, M.D., vice president of pain and neurodegeneration, Eli Lilly and Company. "With more than 30 years of dedication to finding solutions for this devastating disease, we are proud of our progress moving the field forward and advancing the science. These positive results give us hope for patients and their families."

By targeting N3pG beta amyloid, donanemab treatment has been shown to rapidly result in high levels of amyloid plaque clearance, as measured by amyloid imaging. In TRAILBLAZER-ALZ, donanemab-treated patients, on average, showed an 84 centiloid reduction of amyloid plaque at 76 weeks compared to a baseline of 108 centiloids (less than 25 centiloids is typical of a negative amyloid scan). In this study, patients stopped receiving donanemab and switched to placebo once their plaque level was below 25 centiloids for two consecutive measures or below 11 centiloids at any one measure.

"This unique mechanism and antibody for clearing plaques, discovered at Lilly, has the potential to provide high levels of durable amyloid plaque clearance after limited duration dosing," said Daniel Skovronsky, M.D., Ph.D., Lilly's chief scientific officer and president of Lilly Research Laboratories. "In conjunction with our expertise in amyloid and tau imaging, this allowed us to conduct a trial to test if reducing amyloid plaques in Alzheimer's patients to levels seen in scans of healthy individuals could result in clinically meaningful slowing of cognitive decline. The positive results we have obtained today give us confidence in donanemab and support its rapid and deep plaque clearance for the potential treatment of Alzheimer's disease."

The safety profile of donanemab was consistent with observations from Phase 1 data. Amyloid-related imaging abnormalities (ARIA) were observed, which is consistent with amyloid plaque clearing antibodies. In the donanemab treatment group, amyloid-related imaging abnormalities – edema (ARIA-E) occurred in 27 percent of treated participants, with an overall incidence of 6 percent experiencing symptomatic ARIA-E.

The full results of the TRAILBLAZER-ALZ study will be presented at a future medical congress and submitted for publication in a peer-reviewed clinical journal. Lilly plans to discuss these results with regulators to assess next steps for donanemab. In addition, TRAILBLAZER-EXT is an ongoing trial for those who participated in TRAILBLAZER-ALZ.

About TRAILBLAZER-ALZ Study
TRAILBLAZER-ALZ (NCT03367403) is a randomized, placebo-controlled, double-blind, multi-center Phase 2 study to assess the safety, tolerability and efficacy of donanemab in patients with early symptomatic Alzheimer's disease. The trial enrolled 272 patients who were selected based on cognitive assessments in conjunction with amyloid plaque imaging and tau imaging. The study's primary endpoint is change from baseline until 76 weeks in the Integrated Alzheimer's Disease Rating Scale (iADRS), a composite tool combining the Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog13) and the Alzheimer's Disease Cooperative Study - instrumental Activities of Daily Living (ADCS-iADL) for function. Key secondary endpoints include changes between baseline and 76 weeks in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog13), ADCS-iADL, MMSE, and Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) scores. Other secondary biomarker endpoints include changes from baseline to week 76 in brain amyloid deposition and brain tau deposition. The safety, tolerability and efficacy of donanemab are also being evaluated in the ongoing randomized, placebo-controlled, double-blind, multi-center Phase 2 study TRAILBLAZER-ALZ 2 (NCT04437511).

About Alzheimer's Disease
Alzheimer's disease is a fatal illness that causes progressive decline in memory and other aspects of cognition. Dementia due to Alzheimer's is the most common form of dementia, accounting for 60 to 80 percent of all cases.[1] There are currently over 50 million people living with dementia around the world, with numbers expected to increase to nearly 152 million by 2050.[2] Almost 10 million new cases of dementia are diagnosed each year worldwide, implying one new case every 3 seconds, and a significant increase in the caregiving burden placed on society and families. In the U.S. alone, there was an increase of 8 million new caregivers from 2015 to 2020.[3] The current annual societal and economic cost of dementia is estimated at $1 trillion, an amount that is expected to double by 2030 unless we find a way to slow the disease.[2]

About Eli Lilly and Company
Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at lilly.com and lilly.com/newsroom. P-LLY

Lilly Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about donanemab as a potential treatment for people with Alzheimer's disease, Lilly's Alzheimer's development efforts, Lilly's next steps in the development of donanemab, subsequent analyses and presentations of study data, and reflects Lilly's current beliefs and expectations. As with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug development and commercialization. Among other things, there is no guarantee that future study results will be consistent with study findings to date or that Lilly will successfully develop any therapies for the treatment of Alzheimer's. For further discussion of these and other risks and uncertainties, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

References

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