U.S. Food and Drug Administration Issues Complete Response Letter for Accelerated Approval of Donanemab

January 19, 2023

Accelerated approval application was based on Phase 2 trial showing amyloid plaque lowering

Complete response letter based on limited number of patients with 12-month drug exposure data in the accelerated approval submission; no other deficiencies were identified

Definitive Phase 3 readout and submission for traditional approval remain on track for mid-year 2023

INDIANAPOLIS, Jan. 19, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced the U.S. Food and Drug Administration (FDA) has issued a complete response letter for the accelerated approval submission of donanemab for the treatment of early symptomatic Alzheimer's disease due to the limited number of patients with at least 12 months of drug exposure data provided in the submission. No other deficiencies in the application were noted.

The confirmatory Phase 3 TRAILBLAZER-ALZ 2 trial remains ongoing, with topline data read-out expected in Q2 2023, and will form the basis of donanemab's application for traditional approval shortly thereafter. Lilly will continue to work with the FDA to evaluate the fastest pathway to make this potential treatment option widely available to patients.

In the complete response letter to the accelerated approval application, the FDA specifically requested that Lilly provide data from at least 100 patients who received a minimum of 12 months of continued treatment on donanemab. Donanemab's specificity to target deposited amyloid plaque informed the unique clinical trial design of TRAILBLAZER-ALZ, which allowed patients to complete their course of treatment when they reached a predefined level of amyloid plaque clearance. While the trial included more than 100 patients treated with donanemab, due to the speed of plaque reduction, many patients were able to stop dosing as early as 6 months of treatment, resulting in fewer than 100 patients receiving 12 months of donanemab. The FDA indicated that the data to meet the exposure expectation would likely need to include the unblinded controlled safety data from TRAILBLAZER-ALZ 2 upon completion.

The safety profile of donanemab was initially reported from the TRAILBLAZER-ALZ trial in the New England Journal of Medicine (Mintun et al, NEJM 2021)[1]. The safety profile of donanemab has remained consistent since our accelerated approval submission.

"We look forward to our upcoming confirmatory TRAILBLAZER-ALZ 2 Phase 3 results and subsequent FDA submission, which we've always seen as the most impactful next steps for patients. We anticipate this study will confirm the benefit and safety profile we observed in the TRAILBLAZER-ALZ Phase 2 study and believe that patients and physicians will be well served by having the full Phase 3 data available alongside our Phase 2 data when they need to make treatment decisions," said Anne White, executive vice president and president of Lilly Neuroscience, Eli Lilly and Company. "We are committed to working with the FDA to ensure the fastest possible path to bring this potential medicine to patients in need."

This action does not result in a change to Lilly's 2023 financial guidance.

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 disease is the most common form of dementia, accounting for 60 to 80 percent of all cases[1]. There are currently over 55 million people living with dementia around the world, with numbers expected to increase to nearly 139 million by 2050[2]. Over 10 million new cases of dementia are diagnosed each year worldwide, implying one new case every 3.2 seconds and a significant increase in the caregiving burden placed on society and families. In the U.S. alone, there was an increase of nearly 10 million new caregivers from 2015 to 2020[3]. The current annual societal and economic cost of dementia is estimated at $1.3 trillion, an amount that is expected to double by 2030 unless we find a way to slow the disease[2].

About Lilly
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 47 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/newsroom or follow us on Facebook, Instagram, and LinkedIn. P-LLY

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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 early symptomatic Alzheimer's disease, and reflects Lilly's current beliefs and expectations. However, as with any such undertaking, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that future study results will be consistent with study findings to date, that donanemab

will prove to be a safe and effective treatment, or that donanemab will receive regulatory approval. 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.

1. *Mintun M, Lo A, Evans C, et al. Donanemab in Early Alzheimer's Disease. N Engl J Med. 2021. 384:1691-1704. doi: 10.1056/NEJMoa2100708.*
2. *Alzheimer's Association. 2022 Alzheimer's Disease Facts and Figures. https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf. Accessed May 12, 2022.*
3. *Alzheimer's Disease International. Dementia Statistics. https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/. Accessed May 12, 2022.*
4. *AARP. 2020 Report: Caregiving in the U.S. . https://www.aarp.org/content/dam/aarp/ppi/2020/05/full-report-caregiving-in-the-united-states.doi.10.26419-2Fppi.00103.001.pdf. Accessed May 12, 2022.*

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