Lilly's Kisunla™ (donanemab-azbt) Approved in Japan for the Treatment of Early Symptomatic Alzheimer's Disease

September 24, 2024

Japan is the second major market where Kisunla has received approval

Kisunla was first approved in the United States in July 2024

INDIANAPOLIS, Sept. 24, 2024 /PRNewswire/ -- The Ministry of Health, Labour and Welfare Japan has approved Kisunla™ (donanemab-azbt, 350 mg/20 mL every four weeks injection for IV infusion), Eli Lilly and Company's (NYSE: LLY) Alzheimer's treatment for adults with early symptomatic Alzheimer's disease (AD), which includes people with mild cognitive impairment (MCI) as well as people with the mild dementia stage of AD, with confirmed amyloid pathology.

Japan is the second major market in which Kisunla has been approved for use. In Japan, by 2030, the number of patients with dementia is estimated to be more than 5 million[1], and AD is the most common cause of dementia, accounting for more than 67% of cases[2]. The number of AD patients is expected to increase significantly compared with other dementias.[3]

"Lilly scientists have been dedicated to research in Alzheimer's disease for more than 35 years, and this news is testament to their ingenuity, perseverance, and commitment to helping people with this disease," said Ilya Yuffa, executive vice president and president of Lilly International, Eli Lilly and Company. "Kisunla demonstrated very meaningful results for people with early symptomatic Alzheimer's disease by significantly slowing cognitive and functional decline in our TRAILBLAZER-ALZ 2 study, which included participants from Japan. People around the world want and deserve access to treatment options for this devastating disease. Today's news is another critical step in ensuring patients with Alzheimer's disease can receive treatment with these first class of amyloid therapies, which could give them more time to do what matters most to them."

Amyloid is a protein produced naturally in the body that can clump together to create amyloid plaques. The excessive buildup of amyloid plaques in the brain may lead to memory and thinking issues associated with Alzheimer's disease.[4,5] Kisunla can help the body remove the excessive buildup of amyloid plaques and slow the decline that may diminish people's ability to remember new information, important dates, and appointments; plan and organize; make meals; use household appliances; manage finances; and be left alone.[4-7]

"Alzheimer's disease is a significant healthcare burden in Japan due to the rapidly aging population. We are excited to make Kisunla available in Japan as a new treatment option for early symptomatic Alzheimer's disease," said Yanping Wang, senior vice president of Drug Development and Medical Affairs at Eli Lilly Japan. "Patients treated with Kisunla may have the option to stop treatment once the amyloid plaques are removed, which could help reduce the infusion burden for eligible patients."

Results from the TRAILBLAZER-ALZ 2 Phase 3 Study
The application to the PMDA was based on the efficacy and safety data from TRAILBLAZER-ALZ 2 Phase 3 clinical study.

In the TRAILBLAZER-ALZ 2 Phase 3 study, people who were the least advanced in the disease experienced the strongest results with Kisunla. Trial participants were analyzed over 18 months in two groupings: one group who was less advanced in their disease (those with low to medium levels of tau protein) and the overall population, which also included participants with high tau levels.[8-10] Treatment with Kisunla significantly slowed clinical decline in both groups.[8] Those individuals treated with Kisunla who were less advanced in their disease showed a significant slowing of decline of 35% compared with placebo on the integrated Alzheimer's Disease Rating Scale (iADRS), which measures memory, thinking, and daily functioning. In the overall population, the response to treatment was also statistically significant using the iADRS at 22%.[8, 11] Among the two groups analyzed, participants treated with Kisunla had up to a 39% lower risk of progressing to the next clinical stage of disease than those taking placebo.[12]

Among the overall population of participants, Kisunla reduced amyloid plaques on average by 61% at 6 months, 80% at 12 months, and 84% at 18 months compared to the start of the study.[8, 13] One of the treatment goals of the study was to remove amyloid plaques to minimal levels consistent with a visually negative scan using amyloid positron emission tomography (PET). If participants were confirmed to have reached these levels, they were able to complete treatment with Kisunla and switch to placebo for the remainder of the study. In the TRAILBLAZER-ALZ 2 study, 66% of patients achieved plaque clearance (based on above criteria) at one year.[14]

Kisunla can cause amyloid-related imaging abnormalities (ARIA), which is a potential side effect with amyloid plaque-targeting therapies that does not usually cause symptoms. It can be detected via magnetic resonance imaging (MRI) scans and, when it does occur, may present as temporary swelling in an area or areas of the brain, which usually resolves over time, or as small spots of bleeding in or on the surface of the brain. Infrequently, larger areas of bleeding in the brain can occur.[8,15] ARIA can be serious, and life-threatening events can occur. Kisunla can also cause certain types of allergic reactions, some of which may be serious and life-threatening, that typically occur during infusion or within 30 minutes post-infusion. Headache is another commonly reported side effect. See the *Indication and Safety Summary with Warnings* below for additional information.

About Kisunla™(donanemab)
Kisunla™ (donanemab-azbt) (pronounced kih-SUHN-lah) is an amyloid-targeting treatment for people with mild cognitive impairment (MCI) as well as people with mild dementia stage of early symptomatic Alzheimer's disease, with confirmed amyloid pathology. Kisunla can cause serious side effects, including amyloid-related imaging abnormalities, or ARIA, and infusion-related reactions. Kisunla is a prescription medicine administered intravenously every four weeks, 700 mg for the first three doses and 1400 mg thereafter.

About TRAILBLAZER-ALZ 2 Study and the TRAILBLAZER-ALZ program
TRAILBLAZER-ALZ 2 (NCT04437511) is a Phase 3, double-blind, placebo-controlled study to evaluate the safety and efficacy of donanemab in participants with early symptomatic Alzheimer's disease (MCI or mild dementia due to Alzheimer's disease) with the presence of confirmed Alzheimer's disease neuropathology. The trial enrolled 1,736 participants, across 8 countries, selected based on cognitive assessments in conjunction evidence of Alzheimer's disease pathology. The Phase 3 TRAILBLAZER-ALZ 2 study results were published in the *Journal of the American Medical Association* (JAMA).

Lilly continues to study donanemab in multiple clinical trials, including TRAILBLAZER-ALZ 3, which is focused on preventing symptomatic Alzheimer's disease in participants with preclinical AD; TRAILBLAZER-ALZ 5, a registration trial for early symptomatic AD currently enrolling in China and Korea; and TRAILBLAZER-ALZ 6, which is focused on expanding our understanding of ARIA through novel MRI sequences, blood-based biomarkers, and different dosing regimens of donanemab.

U.S. INDICATION AND SAFETY SUMMARY WITH WARNINGS

Kisunla™ (donanemab-azbt) pronounced kih-SUHN-lah, is used to treat adults with early symptomatic Alzheimer's disease (AD), which includes mild cognitive impairment (MCI) or mild dementia stage of disease.

Warnings - Kisunla can cause Amyloid-Related Imaging Abnormalities or "ARIA." This is a common side effect that does not usually cause any symptoms, but serious symptoms can occur. ARIA can be fatal. ARIA is most commonly seen as temporary swelling in an area or areas of the brain that usually goes away over time. Some people may also have spots of bleeding on the surface of or in the brain and infrequently, larger areas of bleeding in the brain can occur. Although most people do not have symptoms, some people have headaches, dizziness, nausea, difficulty walking, confusion, vision changes and seizures.

Some people have a genetic risk factor (homozygous apolipoprotein E ε4 gene carriers) that may cause an increased risk for ARIA. Talk to your healthcare provider about testing to see if you have this risk factor.

You may be at higher risk of developing bleeding in the brain if you take medicines to reduce blood clots from forming (antithrombotic medicines) while receiving Kisunla. **Talk to your healthcare provider to see if you are on any medicines that increase this risk.**

Your healthcare provider will do magnetic resonance imaging (MRI) brain scans before and during your treatment with Kisunla to check you for ARIA. You should carry information that you are receiving Kisunla, which can cause ARIA, and that ARIA symptoms can look like stroke symptoms.
Call your healthcare provider or go to the nearest hospital emergency room right away if you have any of the symptoms listed above.

There are registries that collect information on treatments for Alzheimer's disease. Your healthcare provider can help you become enrolled in these registries.

Warnings - Kisunla can cause serious allergic and infusion-related reactions. Do not receive Kisunla if you have serious allergic reactions to donanemab-azbt or any of the ingredients in Kisunla. Symptoms may include swelling of the face, lips, mouth, or eyelids, problems breathing, hives, chills, irritation of skin, nausea, vomiting, sweating, headache, or chest pain. You will be monitored for at least 30 minutes after you receive Kisunla for any reaction. **Tell your healthcare provider right away if you have these symptoms or any reaction during or after a Kisunla infusion.**

Other common side effects

- Headache

Tell your healthcare provider right away if you have any side effects. These are not all of the possible side effects of Kisunla. **You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch**.

Before you receive Kisunla, tell your healthcare provider:

- About all medicines you take, including prescription and over-the-counter medicines, as well as vitamins and herbal supplements. Especially tell your healthcare provider if you have medicines to reduce blood clots from forming (antithrombotic medicines, including aspirin).
- About all of your medical conditions including if you are pregnant, breastfeeding, or plan to become pregnant or breastfeed. Kisunla has not been studied in people who were pregnant or breastfeeding. It is not known if Kisunla could harm your unborn or breastfeeding baby.

How to receive Kisunla
Kisunla is a prescription medicine given through an intravenous (IV) infusion using a needle inserted into a vein in your arm. Kisunla is given once every 4 weeks. Each infusion will last about 30 minutes.

Learn more
For more information about Kisunla, call 1-800-LillyRx (1-800-545-5979) or go to **kisunla.lilly.com**.

This summary provides basic information about Kisunla. It does not include all information known about this medicine. Read the information given to you about Kisunla. This information does not take the place of talking with your healthcare provider. Be sure to talk to your healthcare provider about Kisunla. Your healthcare provider is the best person to help you decide if Kisunla is right for you.

Please see full Prescribing Information including boxed warning for ARIA and Medication Guide for Kisunla.

About Lilly
Lilly is a medicine company turning science into healing to 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 51 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/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

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 Kisunla (donanemab-azbt) as a treatment for people with early symptomatic Alzheimer's disease, the supply and commercialization of Kisunla, and future readouts, presentations, and other milestones relating to Kisunla and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study findings to date, that Kisunla will receive additional regulatory approvals or that Kisunla will be commercially successful. 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

1. *https://www.eph.med.kyushu-u.ac.jp/jpsc/uploads/resmaterials/0000000111.pdf?1715072186*
2. *https://www.tsukuba-psychiatry.com/wp-content/uploads/2013/06/H24Report_Part1.pdf*
3. *https://mhlw-grants.niph.go.jp/system/files/2014/141031/201405037A/201405037A0001.pdf*
4. *Porsteinsson AP, Isaacson RS, Knox S, et al. Diagnosis of early Alzheimer's disease: clinical practice in 2021. J Prev Alzheimers Dis. 2021;8:371-386.*
5. *Alzheimer's Association. 2023 Alzheimer's disease facts and figures. Alzheimers Dement. 2023;19(4):1598-1695*
6. *Ross EL, Weinberg MS, Arnold SE. Cost-effectiveness of Aducanumab and Donanemab for Early Alzheimer Disease in the US. JAMA Neurol. 2022;79(5):478-487. doi:10.1001/jamaneurol.2022.0315.*
7. *Wessels AM, Dennehy EB, Dowsett SA, et al. Meaningful clinical changes in Alzheimer disease measured with the iADRS and illustrated using the donanemab TRAILBLAZER-ALZ study findings. Neurol Clin Pract. 2023;13(2):e200127. doi:10.1212/CPJ.0000000000200127*
8. *Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC.*
9. *Bucci M, Chiotis K, Nordberg A; Alzheimer's Disease Neuroimaging Initiative. Alzheimer's disease profiled by fluid and imaging markers: tau PET best predicts cognitive decline. Mol Psychiatry. 2021 Oct;26(10):5888-5898. doi: 10.1038/s41380-021-01263-2.*
10. *Boccalini C, Ribaldi F, Hristovska I, Arnone A, Peretti DE, Mu L, Scheffler M, Perani D, Frisoni GB, Garibotto V. The impact of tau deposition and hypometabolism on cognitive impairment and longitudinal cognitive decline. Alzheimers Dement. 2023 Aug 9. doi: 10.1002/alz.13355.*
11. *Data on File. Lilly USA, LLC. DOF-DN-US-0053.*
12. *Data on File. Lilly USA, LLC. DOF-DN-US-0055.*
13. *Data on File. Lilly USA, LLC. DOF-DN-US-0029.*
14. *Sims JR, Zimmer JA, Evans CD, et al. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. JAMA. 2023;330(6):512-527. doi:10.1001/jama.2023.13239.*
15. *Kisunla (donanemab-azbt). Medication Guide. Lilly USA, LLC.*

Refer to: J.K. Wall; jkwall@lilly.com; 317-433-5328 (Media)
Joe Fletcher; jfletcher@lilly.com; 317-296-2884 (Investors)

View original content to download multimedia:https://www.prnewswire.com/news-releases/lillys-kisunla-donanemab-azbt-approved-in-japan-for-the-treatment-of-early-symptomatic-alzheimers-disease-302255834.html

SOURCE Eli Lilly and Company