Welcome!

The following **INTERACTIVE INFOGRAPHIC** provides detailed information on various important aspects of a clinical study on the Alzheimer drug lecanemab.

Harnessing the **POWER OF VISUAL STORYTELLING**, the **INTERACTIVE INFOGRAPHIC** features a well-structured narrative flow, eye-catching visuals, concise text and intuitive navigation.

The story of lecanemab can be told in 4 different **INTERACTIVE INFOGRAPHIC FORMATS**.

Here you can see the **INTERACTIVE PDF**.

START

Learn more about the different **INTERACTIVE INFOGRAPHIC FORMATS**

2201x25

INTERACTIVE INFOGRAPHIC FORMATS

ABOUT CAST PHARMA

Currently viewing

Interactive PDF

- ✓ Various sizes and aspect ratios possible
- ✓ Interactive

This format focuses on clear visual storytelling with basic interactivity. It is quick to create, and its small file size makes it ideal for emailing or downloading.

Interactive PPT

- ✓ Various sizes and aspect ratios possible
- ✓ Interactive
- ✓ Dynamic slide animations
- ✓ Audio
- ✓ Video

PowerPoint forms the foundation for many deliverables. A final product in PPT can include audio and/or videos, making it a dynamic format ideal for both self-study and presentations.

Download Interactive PPT

Interactive HTML

- ✓ Various sizes and aspect ratios possible
- ✓ Interactive
- ✓ Dynamic slide animations
- ✓ Audio
- ✓ Video
- ✓ Games/assessment/quizzes

This format offers additional interactive options. HTML deliverables can be uploaded to websites or made SCORM-compatible for use in a learning management system.

View Interactive HTML

Interactive Booklet

- ✓ Built on existing framework for responsive design (size and aspect ratio adapt to user's device)
- ✓ Interactive
- ✓ Dynamic slide animations
- ✓ Audio
- ✓ Video
- ✓ Games/assessment/quizzes

Not based on PPT, this framework allows for significant interactivity and has a built-in responsive design. It has fewer design options to maximize compatibility across devices.

View Interactive Booklet

CAST PHARMA
interactive infographic

ABOUT CAST PHARMA

We make complex medical science accessible!

Our mission

Empowering medical affairs, medical marketing, and scientific training teams to communicate key insights about their products and therapeutic areas.

Our approach

Combining medical and creative expertise to create materials that are scientifically accurate, visually engaging, and easy to understand.

Our ambition

Bridging the gap between scientific communication and graphic design.

Our team

70
Skilled experts for your projects

60%
Medical content developers with PhD degrees

1,000
Global projects completed

25
Years on the market

Our locations

ALK ABELLÓ · teva · GSK · AstraZeneca · BAYER · novo nordisk · Edwards · Lilly · Takeda · Daiichi-Sankyo · Karyopharm Therapeutics

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CAST PHARMA
interactive infographic

LECANEMAB REDUCED BRAIN AMYLOID IN EARLY ALZHEIMER DISEASE (AD)[1]

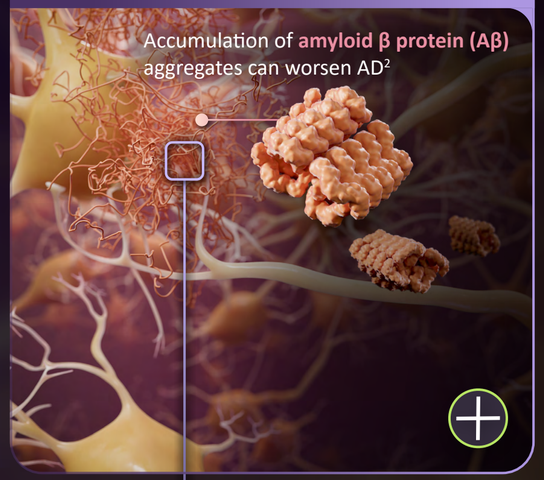
BACK

Alzheimer disease[1]

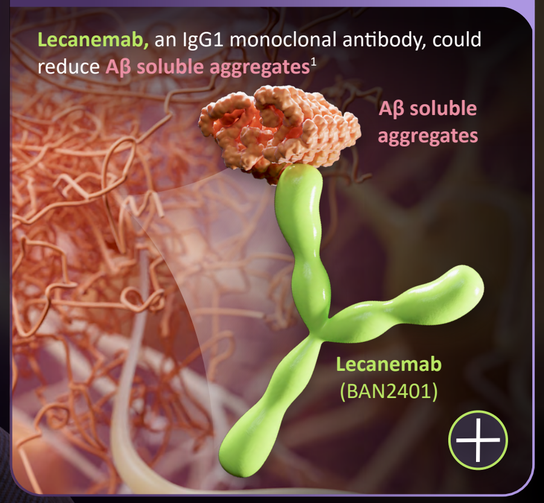
is a progressive, neurodegenerative disease that impairs cognition and function, with progression in 5 distinct stages:

Preclinical → Mild cognitive impairment → Mild AD dementia → Moderate AD dementia → Advanced AD dementia

MECHANISM OF DISEASE



MECHANISM OF ACTION



PROOF-OF-CONCEPT CLINICAL TRIAL IN EARLY AD WITH LECANEMAB

Objective[1]

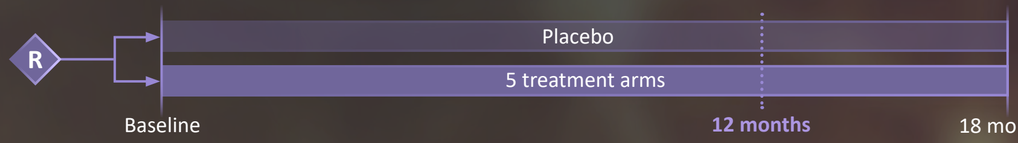
To assess safety and efficacy of response-adaptive randomization across 1 placebo and 5 lecanemab arms in participants with mild cognitive impairment due to AD or mild AD dementia

Primary endpoint[1]

Change from baseline to 12 months in ADCOMS, with an 80% chance of ≥25% reduction in clinical decline versus placebo

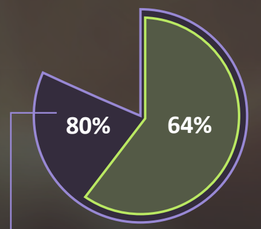
Study design[1]

multicenter · double blind · placebo controlled · phase 2b



Results - lecanemab[1]:

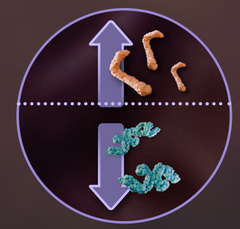
Has a 64% chance of being better than placebo with 25% less decline on ADCOMS[a]



The primary endpoint of 80% was not met

Significantly** decreases amyloid in the brain[a]

Significantly** increases $A\beta_{1-42}$ monomer in the CSF[b]



Significantly* decreases p-tau in the CSF[b]

THESE RESULTS LED TO ACCELERATED APPROVAL OF LECANEMAB IN THE US[3]

[a] At 10 mg/kg biweekly[1]; [b] For the combined lecanemab 10 mg/kg treatment arms vs placebo; *P=0.013; **P<0.001 (all nominal).[1]

Aβ, amyloid β protein; $A\beta_{1-42}$, amyloid beta 1–42; AD, Alzheimer disease; ADCOMS, Alzheimer's Disease Composite Score; CSF, cerebrospinal fluid; p-tau, phosphorylated tau; R, randomization.

1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80 [data republished under the Creative Commons Attribution (CC-BY 4.0): https://creativecommons.org/licenses/by/4.0/]; 2. van Dyck CH et al. *N Engl J Med*. 2023;388(1):9-21;
3. FDA. January 26, 2023. Accessed March 13, 2024. https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-disease-treatment.

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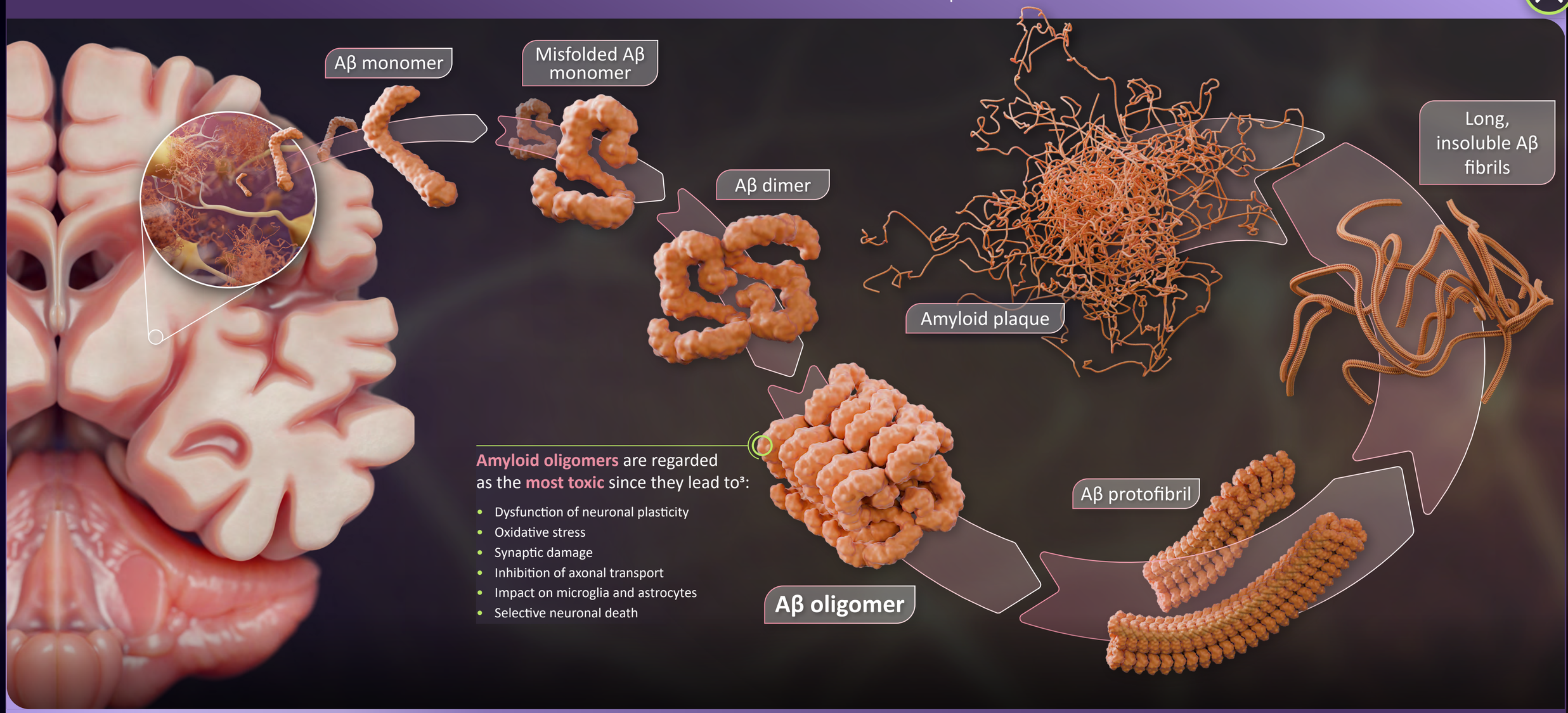
THE SEMINAL EVENT IN AD IS MISFOLDING AND DEPOSITION OF AMYLOID β PROTEIN TO FORM AMYLOID PLAQUES[1-3]



MECHANISM OF DISEASE

Aβ, amyloid β protein; AD, Alzheimer disease.

1. Rasmussen J et al. *Proc Natl Acad Sci U S A*. 2017;114(49):13018-13023; 2. Swanson CJ, et al. *Alzheimers Res Ther*. 2021;13(1):80; 3. Penke B et al. *Molecules*. 2020;25(7):1659.

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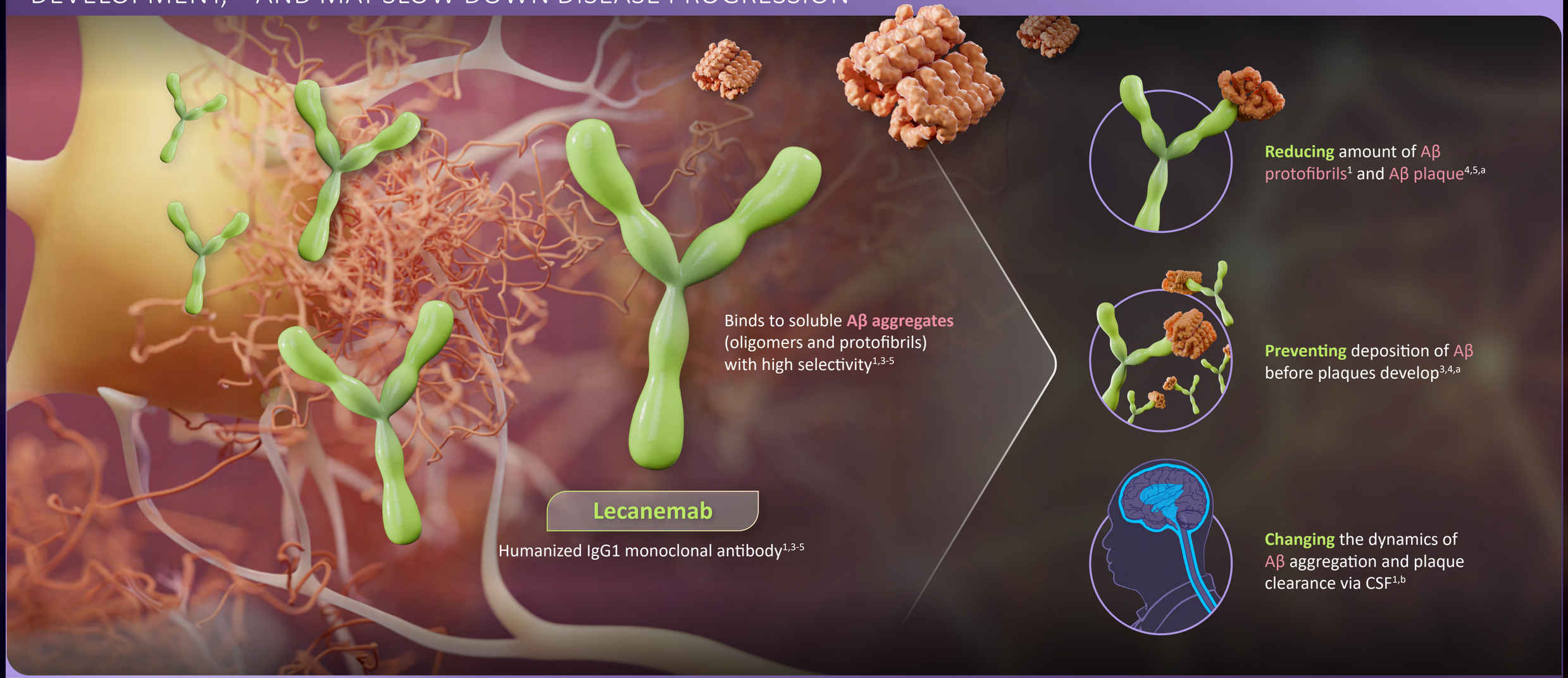
LECANEMAB **REDUCES THE AMOUNT OF AMYLOID β AGGREGATES,** WHICH IS ESSENTIAL TO PREVENTING PLAQUE DEVELOPMENT,[2,5] AND MAY SLOW DOWN DISEASE PROGRESSION[3]



MECHANISM OF ACTION

[a] Demonstrated in murine models[3,4]; [b] Mechanistic studies are needed to better understand the meaning of the increase in CSF $A\beta_{1-42}$ and how it relates to the treatment effect.[1]

Aβ, amyloid β protein; $A\beta_{1-42}$, amyloid beta 1–42; AD, Alzheimer disease; CSF, cerebrospinal fluid; IgG1, immunoglobulin G1.

1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80; 2. Sehlin D et al. *Neurodegener Dis*. 2011;8(3):117-123; 3. Lacor PN, et al. *J Neurosci*. 2004;24(45):10191-10200; 4. Tucker S et al. *J Alzheimers Dis*. 2015;43(2):575–588; 5. Lord A et al. *Neurobiol Dis*. 2009;36(3):425–434.

LECANEMAB'S IMPACT IN PARTICIPANTS WITH **EARLY AD** WAS ASSESSED IN A PHASE **2B PROOF-OF-CONCEPT** STUDY[1]

Key inclusion criteria[1]

- Mild cognitive impairment due to AD or mild AD dementia
- Objective impairment of episodic memory (on Wechsler Memory Scale-IV Logical Memory II)
- MMSE score ≥22 at screening and baseline
- Naive to or on stable dose of approved AD medications for 12 weeks

Endpoints measured[1]

Primary endpoint[1]:

- Change from baseline on ADCOMS

Key secondary endpoints[1]:

Change from baseline in:

- Brain amyloid by PET SUVr
- ADCOMS
- CDR-SB
- ADAS-Cog14
- CSF biomarker
- Total hippocampal volume using volumetric MRI

Evaluation of efficacy compared to placebo in both clinical sub-groups at 18 months

ADCOMS is an outcome approach **to detect AD-related clinical decline**. It is based on **12 items** of commonly used clinical trial instruments (ADAS-Cog, MMSE, CDR-SB).[2]

Scale	Item name
ADAS-Cog	• Delayed word recall • Orientation • Word recognition • Word-finding difficulty
MMSE	• Orientation time • Drawing
CDR-SB	• Personal care • Community affairs • Home hobbies • Judgment and problem-solving • Memory • Orientation

AD, Alzheimer disease; ADAS-Cog14, Alzheimer's Diseases Assessment Scale-Cognitive subscale with 14 competencies; ADCOMS, Alzheimer's Disease Composite Score; CDR-SB, Clinical Dementia Rating–sum of boxes; CSF, cerebrospinal fluid; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; PET SUVr, positron emission tomography standard uptake value ratio.

1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80; 2. Wang J et al. *J Neurol Neurosurg Psychiatry*. 2016;87(9):993-999.

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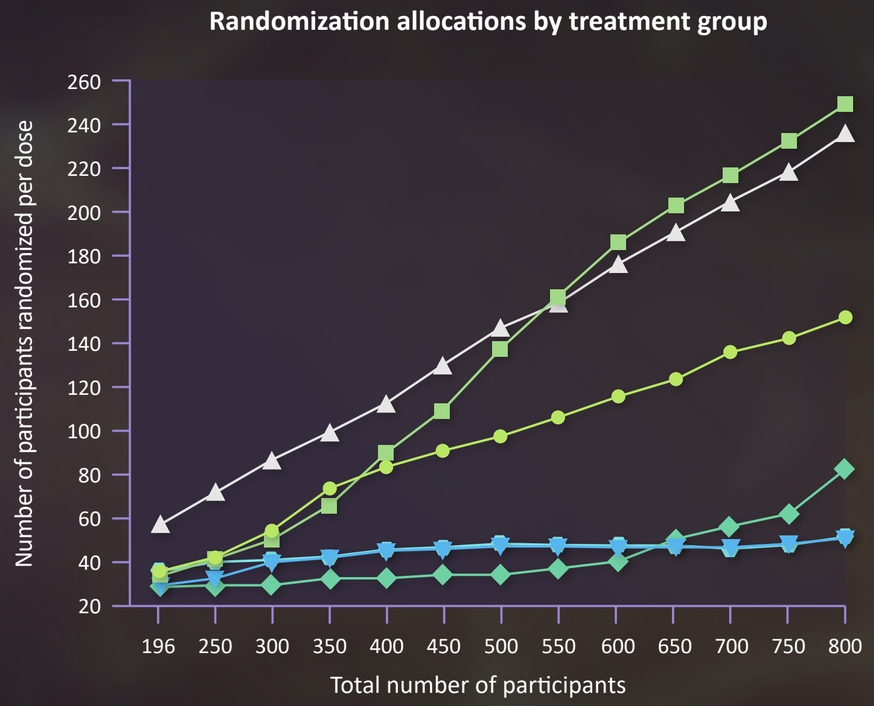
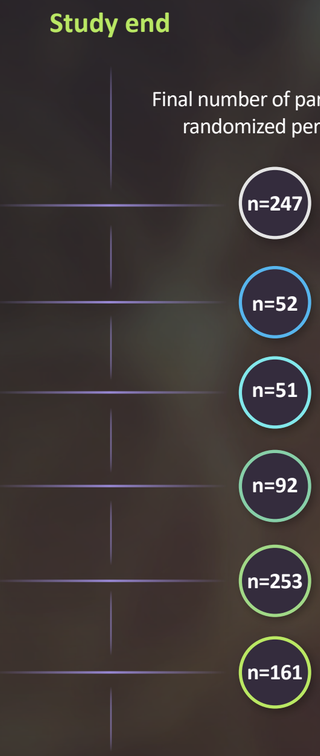
856 PARTICIPANTS WERE ALLOCATED VIA AN **ADAPTIVE RANDOMIZATION DESIGN** INTO 1 PLACEBO ARM AND 5 LECANEMAB DOSING ARMS[1]





Bayesian response-adaptive randomization was employed for efficient participant allocation to the most effective dose in the trial.[1]

R, randomization.

1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80.

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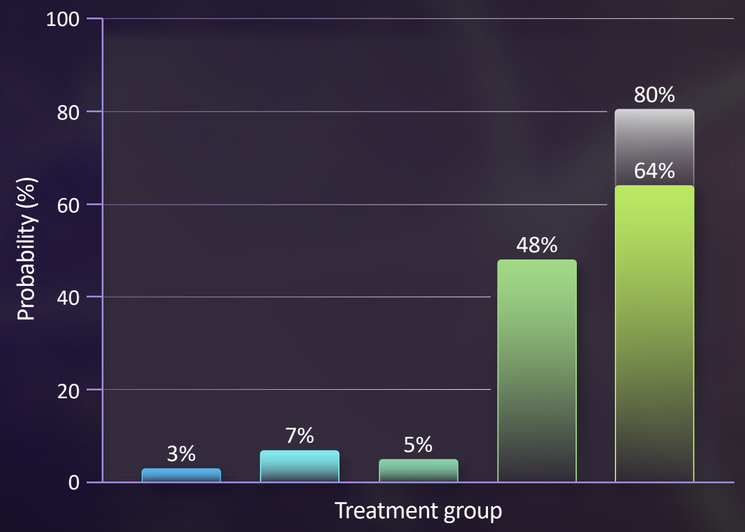
1 DECLINE IN ADCOMS | 2 Aβ REDUCTION IN PET | 3 CSF BIOMARKER CHANGE

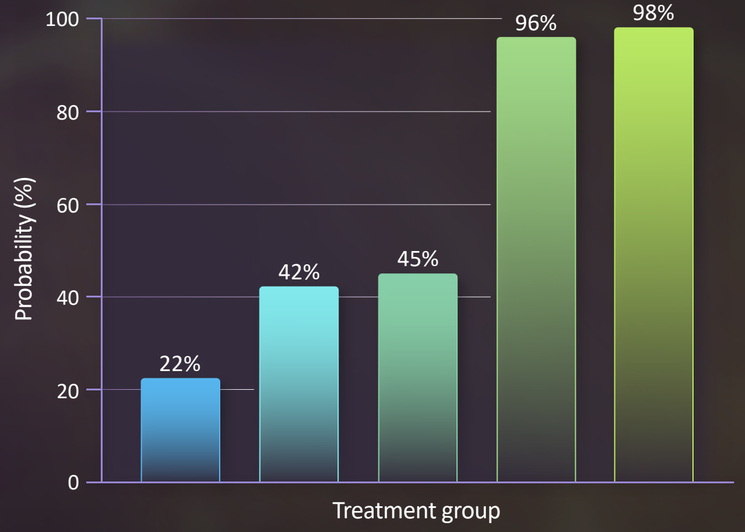
Though it did not meet the primary endpoint at 12 months, lecanemab demonstrated **consistent reduction of clinical decline in ADCOMS** over 18 months[1]

Probability of being better than placebo by 25% in ADCOMS at 12 months



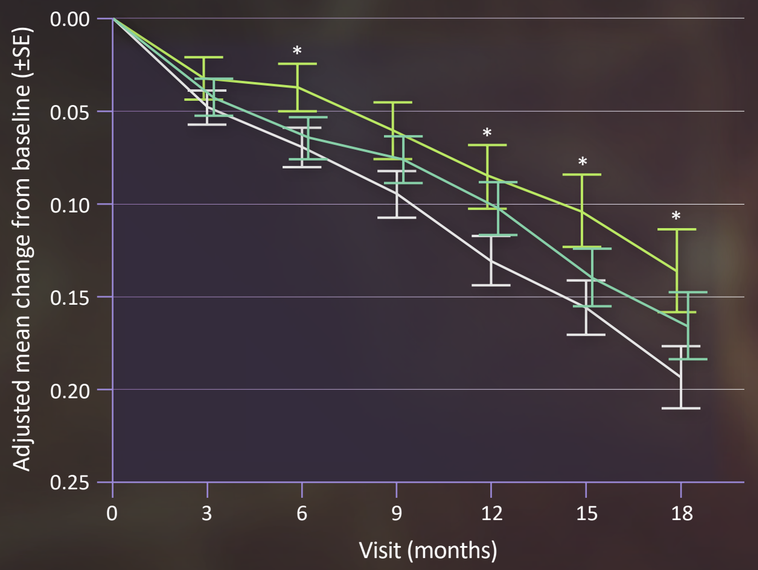
The primary analysis indicated that lecanemab had a 64% probability of being better than placebo by 25%. It thus **missed the prespecified 80% probability threshold for the primary outcome**.[1]

Probability of being better than placebo by any magnitude in ADCOMS at 12 months



Additional Bayesian analyses indicated a **98% probability of being superior to placebo by any magnitude** at month 12.[1]

Change in ADCOMS at 18 months



At 18 months, lecanemab showed a dose-dependent reduction in change from baseline on ADCOMS, with **30% less clinical decline compared to placebo** at 10 mg/kg biweekly.[1]

Placebo | 2.5 mg/kg biweekly | 5 mg/kg monthly | 5 mg/kg biweekly | 10 mg/kg monthly | 10 mg/kg biweekly

*$P<0.05$.
ADCOMS, Alzheimer's Disease Composite Score; SE, standard error.
1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80.

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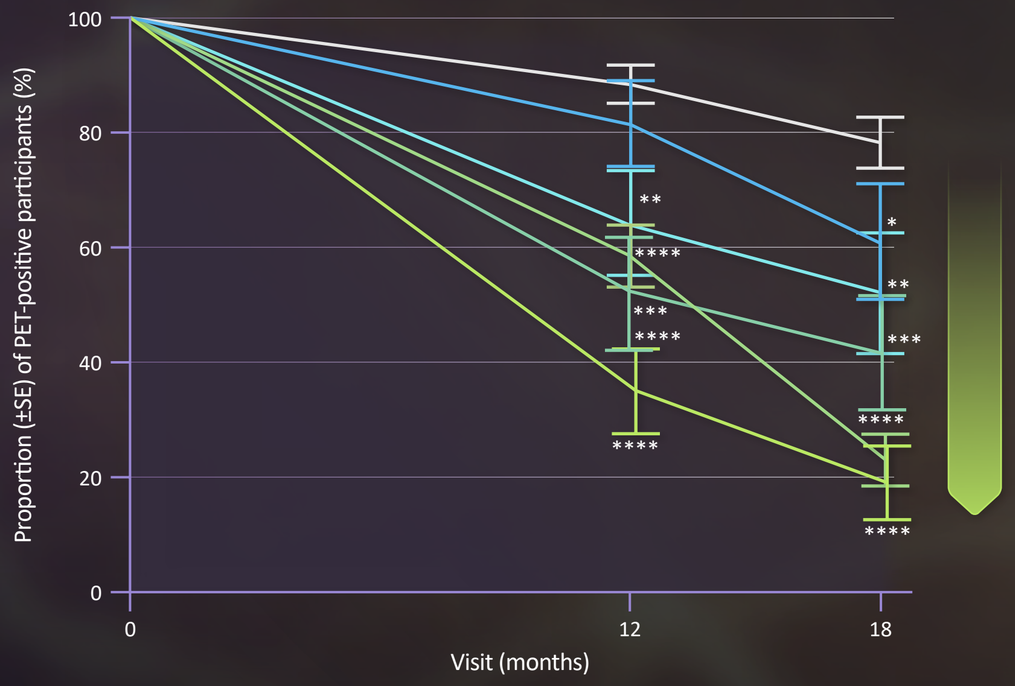
Lecanemab significantly **decreased Aβ in the brain** in a dose-dependent manner[1]

The conversion of brain amyloid pathology was evaluated via PET scans with florbetapir as the imaging agent and the whole cerebellum as the reference region.

When evaluating the effect of lecanemab over 18 months, a dose-dependent reduction in the proportion of PET-positive participants was observed.[1] This finding was the **basis for the accelerated approval of lecanemab by the FDA**.[2]

Conversion of brain amyloid pathology[a]



A decline in PET-positive signals indicates a reduction in brain amyloid.

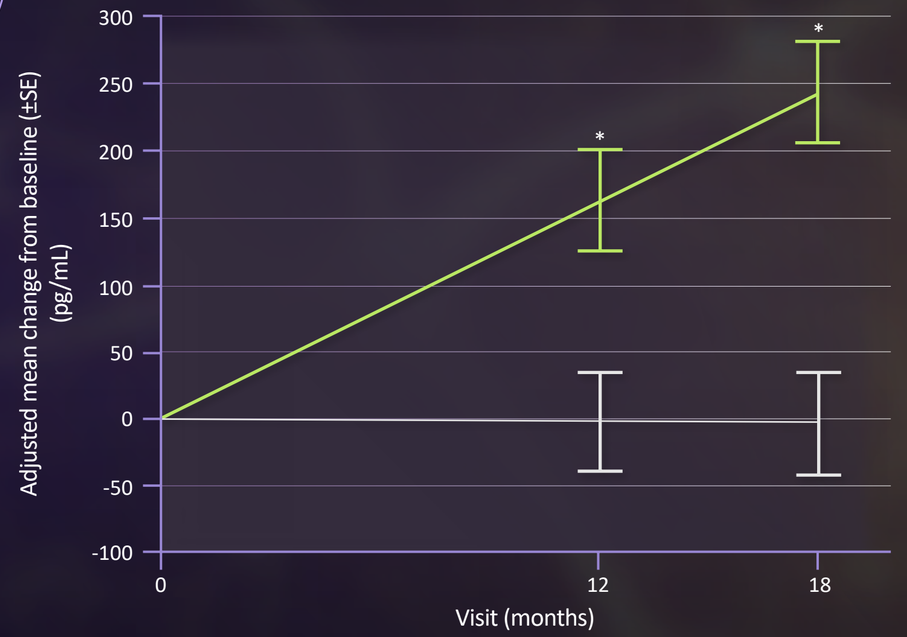
[a] For PET analysis, N=306 at 12 months and N=288 at 18 months. The PET substudy was optional, so only a portion of the total enrolled participant population opted to participate[1]; *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001 (all nominal).[1]

Aβ, amyloid β protein; FDA, US Food and Drug Administration; PET, positron emission tomography; SE, standard error.

1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80; 2. FDA. January 26, 2023. Accessed March 13, 2024. https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-disease-treatment.

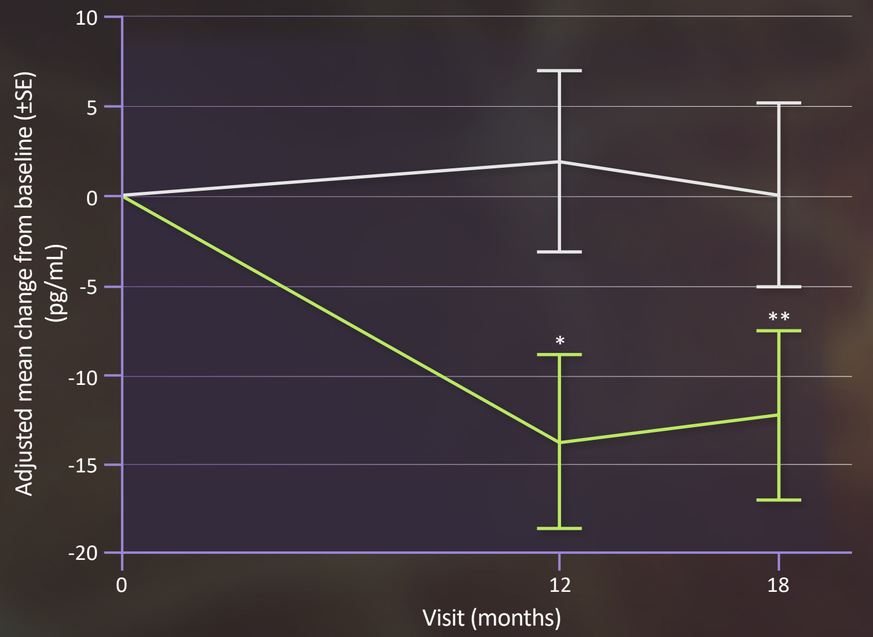
Lecanemab **significantly increased $A\beta_{1-42}$**, and **significantly decreased p-tau** in CSF vs placebo[1,a]

Change in $A\beta_{1-42}$ in CSF from baseline



For AD, a **decrease of $A\beta_{1-42}$** monomers in the CSF has been described due to **sequestration of these monomers into amyloid plaques**. When evaluating the amount of $A\beta_{1-42}$ in the CSF over 18 months, a significant increase in the pooled **lecanemab** 10 mg/kg **dosing arm** relative to placebo could be shown.[1]

Change in p-tau in CSF from baseline



For **p-tau protein**, whose **presence in the CSF is a key characteristic of AD**,[2] a decline in p-tau in the CSF of participants in the pooled **lecanemab** 10 mg/kg **dosing arm** relative to placebo could be shown.[1]

Placebo Lecanemab (10 mg/kg)

[a] For the combined lecanemab 10 mg/kg treatment arms[1]; *P<0.001, **P=0.005 (all nominal).[1]

$A\beta_{1-42}$, amyloid beta 1–42; AD, Alzheimer disease; CSF, cerebrospinal fluid; p-tau, phosphorylated tau; SE, standard error.

1. Swanson CJ et al. *Alzheimers Res Ther*. 2021;13(1):80; 2. McKhann GM et al. *Alzheimers Dement*. 2011;7(3):263-269.

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