

# Memory Magic: Let's Explore Forgetfulness Together!



# Alzheimer's: not so forgetful huh?



**55 Mn+**

People have dementia\* (memory-loss) worldwide



**10 Mn+**

New cases every year



**60-70%**

Of all dementia cases are due to Alzheimer's disease

- Alzheimer's is a type of dementia that affects memory, thinking, and behavior. It is caused by damage to nerve cells (neurons) in the brain
- It is a progressive disease, meaning it gets worse with time; more neurons are damaged, and more areas of the brain are affected
- Eventually, the damage extends to parts of the brain that enable basic bodily functions such as walking and swallowing. Individuals become bed-bound and require around-the-clock care

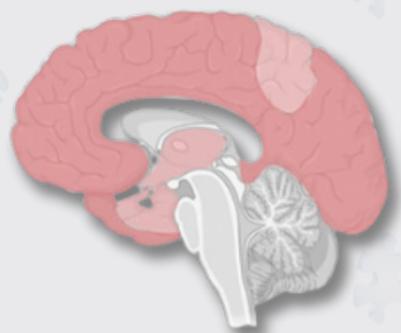
\*Dementia is a term for several diseases that affect memory, thinking, and the ability to perform daily activities.

# This is how it gets worse if not treated timely



## Preclinical AD

No symptoms but possible biological changes in the brain



## Mild cognitive Impairment Due to AD

Very mild symptoms that may not interfere with everyday activities

## Dementia due to AD mild

Symptoms interfere with some everyday activities



## Dementia due to AD Moderated

Symptoms interfere with many everyday activities

## Dementia due to AD Severe

Symptoms interfere with most everyday activities

**Amyloid plaques and neurofibrillary tangles of tau protein accumulate with the progression of the disease**

# Let us take you down memory lane to see the advancements in Alzheimer's treatment so far

## Memantine is Approved

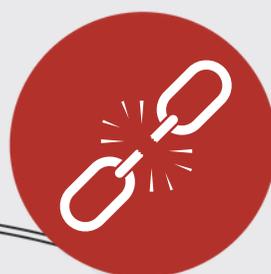
Memantine is approved, representing a second therapeutic class for AD

2003

1993

## First Drug Approved

Tacrine is approved; three similar drugs follow



For almost 2 decades, there have been no significant developments in the treatment of Alzheimer's. Multiple studies were going on to find the cure, but could not gain success.

2021

The FDA approved aducanumab (Aduhelm), First of its kind Alzheimer's drug that targets the fundamental pathophysiology of the disease

2023

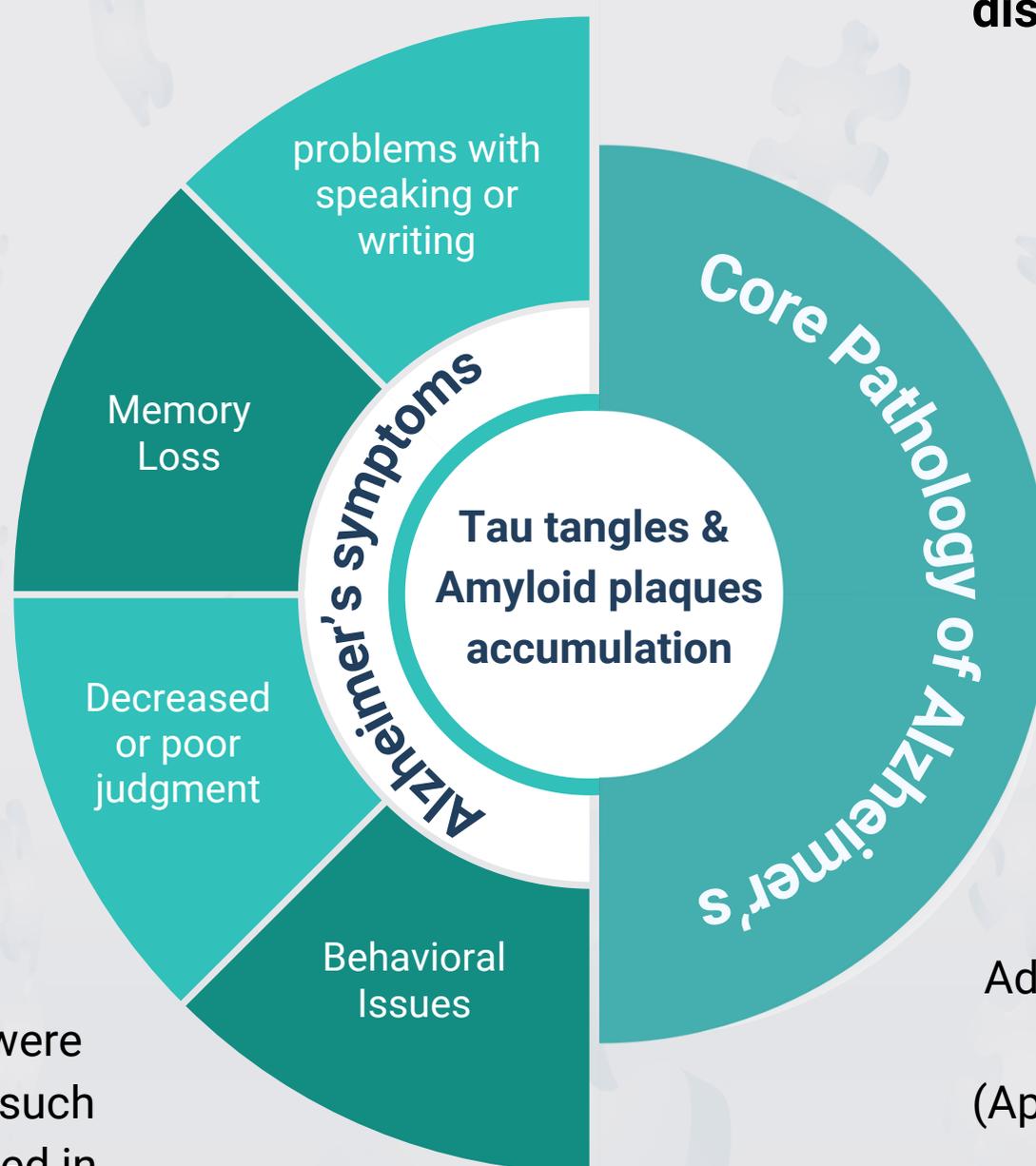
Aduhelm was followed by Leqembi, the second of the same category and the first one to get a traditional full approval\* by FDA

# 2021 was the onset of a new era for Alzheimer's treatment with the launch of the 1st drug that slows the progression

Previous Era drugs used to target only symptoms



New Era drugs target core pathology to slow down the disease progression



Only symptomatic therapeutic drugs were there before 2021, such as Tacrine (Approved in 1993) and Memantine (Approved in 2003). They provide temporary relief from symptoms but do not work on core pathology

Aduhelm (Approved in 2021) and Leqembi (Approved in 2023) act on the underlying pathology of the disease and lower levels of not just amyloid beta but also levels of tau and neurodegeneration in the blood and cerebrospinal fluid

# Aduhelm, the first-of-its-kind breakthrough drug, failed to live up to the hype

Jun,  
2021

The FDA approved Biogen's Aduhelm (aducanumab), becoming the first new Alzheimer's drug approved in 18 years. The FDA placed no restriction on which Alzheimer's patients can get the drug

Jun,  
2021

FDA released documents that revealed disagreements within the agency over the decision to approve the drug. At least three members from a panel of outside advisers to the regulator resigned in protest

Jul,  
2021

FDA changed its initial broad decision and restricted the drug to patients with mild stage of Alzheimer's



Sep,  
2021

U.S. lawmakers launched an investigation on the accelerated approval of the drug and requested documents from the FDA related to the decision

Dec,  
2021

The European Medicines Agency rejected Aduhelm, saying the link between the drug's reduction of amyloid beta and a clinical improvement in the disease had not been established

# ..and then enters **Leqembi**, which could be the first to actually make an impact

**Accelerated Approval:** Leqembi, from Eisai and Biogen, received accelerated approval in January 2023 as the drug found to slow memory and thinking declines by about 27 percent in 18 months

**Traditional or Full Approval:** In July 2023, It received full or traditional approval after the drug is shown to preserve memory and thinking

## Big Milestone

- Alzheimer's drugs have had a long, difficult history until Leqembi. Some drugs failed trials repeatedly or, in the case of Aduhelm, produced conflicting results. Hence, The approval of Leqembi is significant milestone for a condition that has largely been untreatable



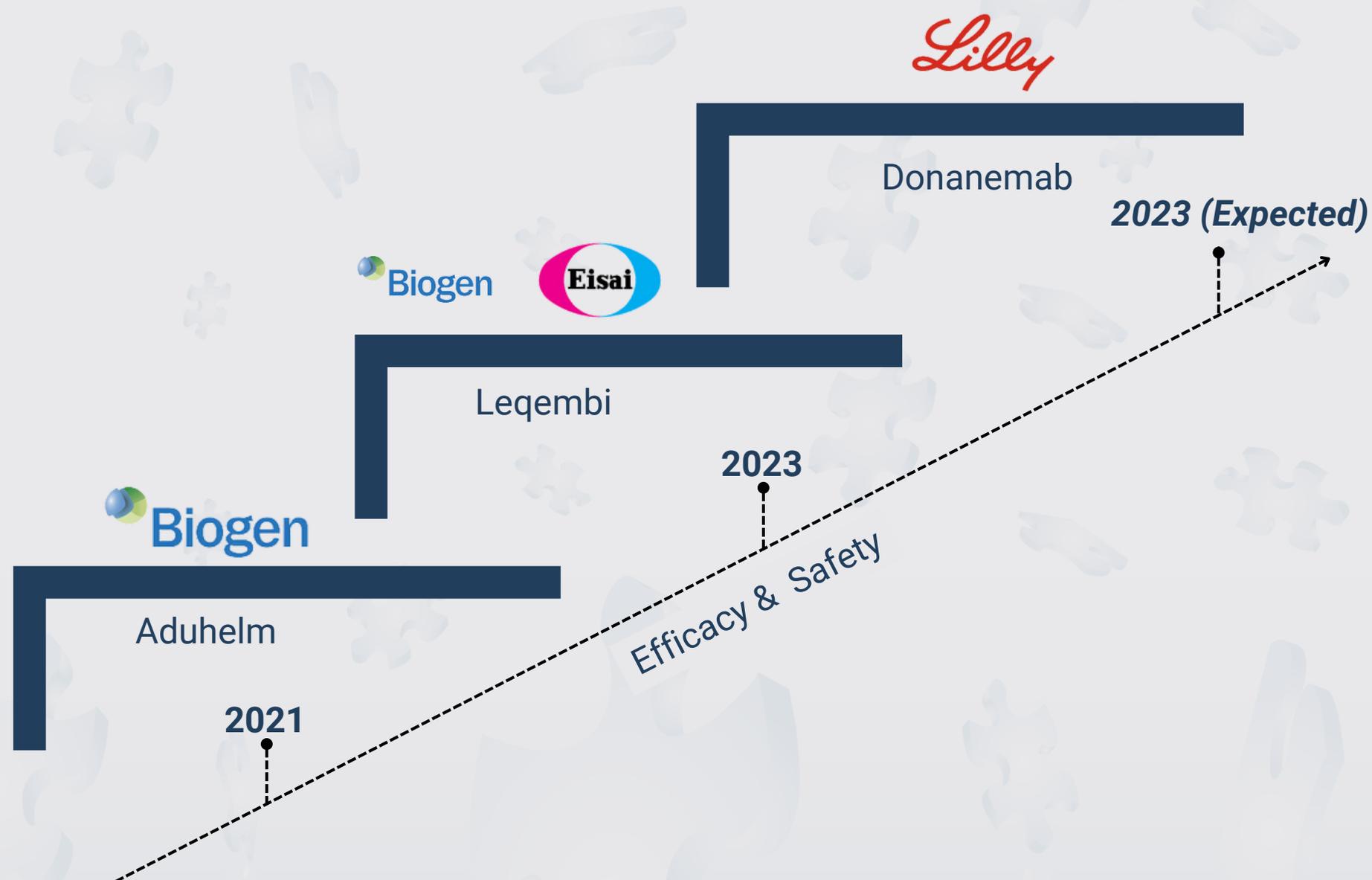
## Still challenges exist

- There may be a few side effects, such as swelling or bleeding in the brain, and in a worst-case scenario, there can be a hemorrhagic stroke
- Even with Medicare coverage, patients could be responsible for more than \$5,000 per year in out-of-pocket costs for the drug

# Leqembi has got the ball rolling, let's see what the future holds

An upcoming Alzheimer's drug outperforms even Leqembi

*Eli Lilly has completed the phase III trial of a new drug, Donanemab, which shows even more promising results*



## Way Forward...

*Some industry leaders predict that combination therapies (New Era drugs + Previously used symptomatic drugs) can be the future of Alzheimer's treatment*

*A new study, AHEAD, is a Phase 3 clinical trial that will test whether the study drug, Leqembi, reduces brain amyloid buildup in people with an increased risk of Alzheimer's disease. If this is successful, the prevention of Alzheimer's will be possible*