A NEW ERA OF TREATMENT FOR ALZHEIMER'S DISEASE

Gil Rabinovici, MD
LEADS MPI and PET Core Lead
Professor of Neurology & Radiology
University of California San Francisco

A New Era in Alzheimer's Disease Care

Alzheimer's drug lecanemab hailed as momentous breakthrough

🕐 6 days ago

BBC NEWS

The New York Times

Treating Alzheimer's Very Early Offers Better Hope of Slowing Decline, Study Finds

CNN health — Life, But Better   Fitness   Food   Sleep   Mindfulness   Relationships

With new therapies that promise to slow Alzheimer's disease, researchers race to reform how patients are diagnosed

By Brenda Goodman, CNN
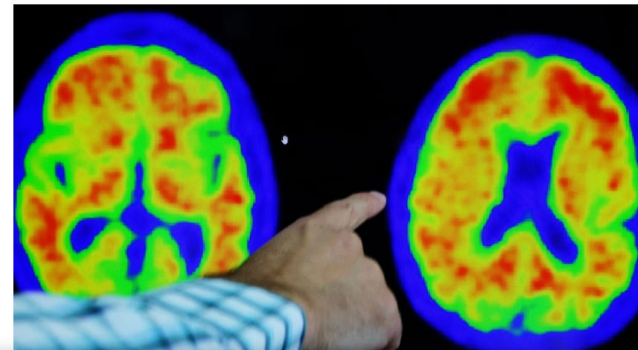Published 10:15 AM EDT, Sun July 16, 2023

Eli Lilly's experimental Alzheimer's drug slows disease, data sho

The Washington Post
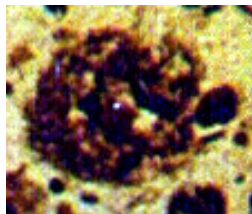*Democracy Dies in Darkness*
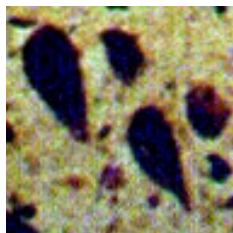
By Laurie McGinley

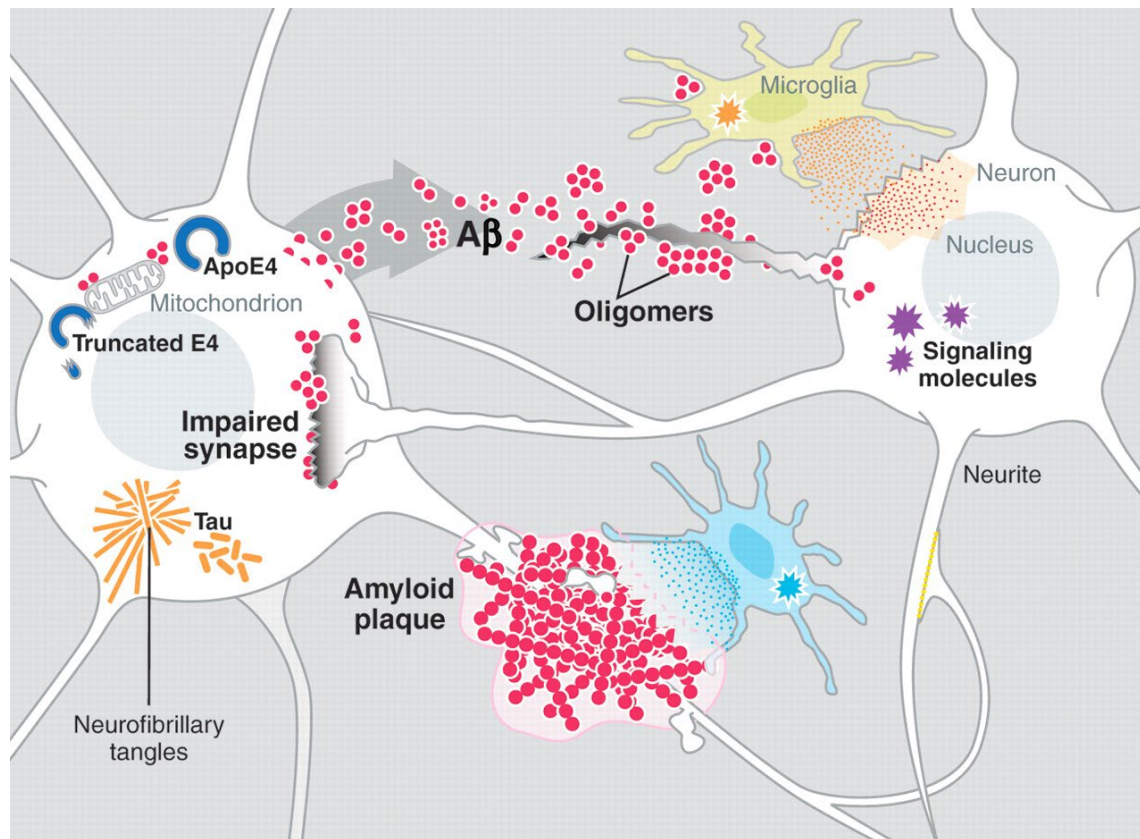Updated July 17, 2023 at 6:11 p.m. EDT | Published July 17, 2023 at 10:15 a.m. EDT
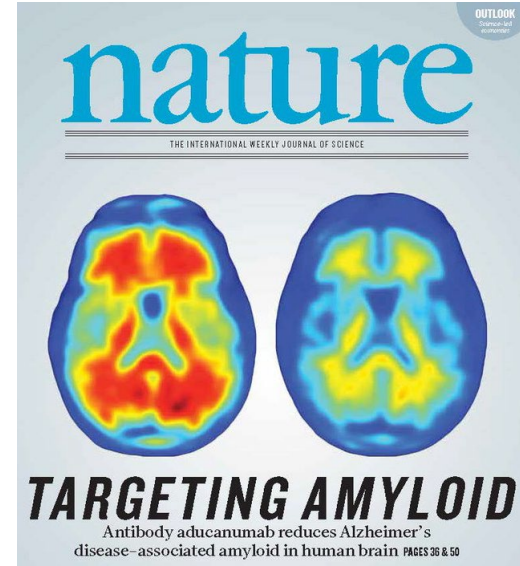
Biology of Alzheimer's Disease

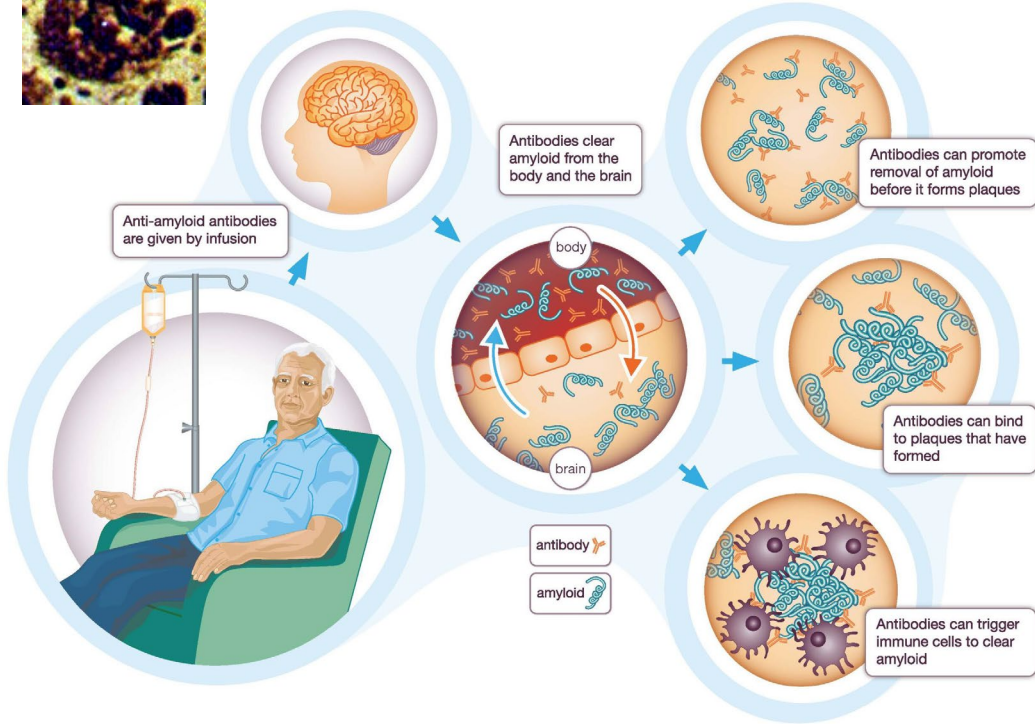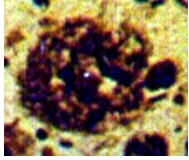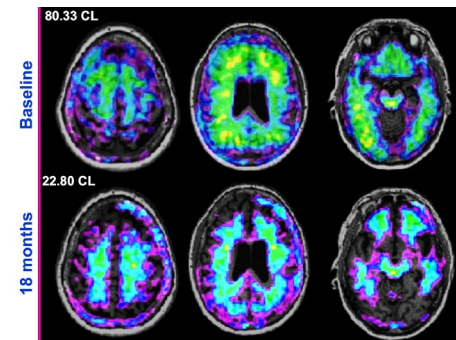
Amyloid plaques

Tau tangles

Anti-Amyloid Antibodies

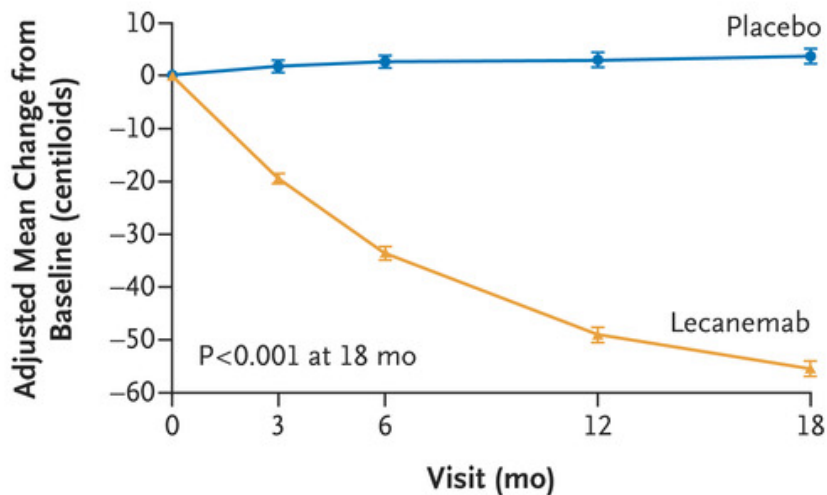Image credit: Alzheimer's Research UK

Two anti-amyloid antibodies have received full FDA approval

- Lecanemab (Leqembi^{TM}) – July 2023
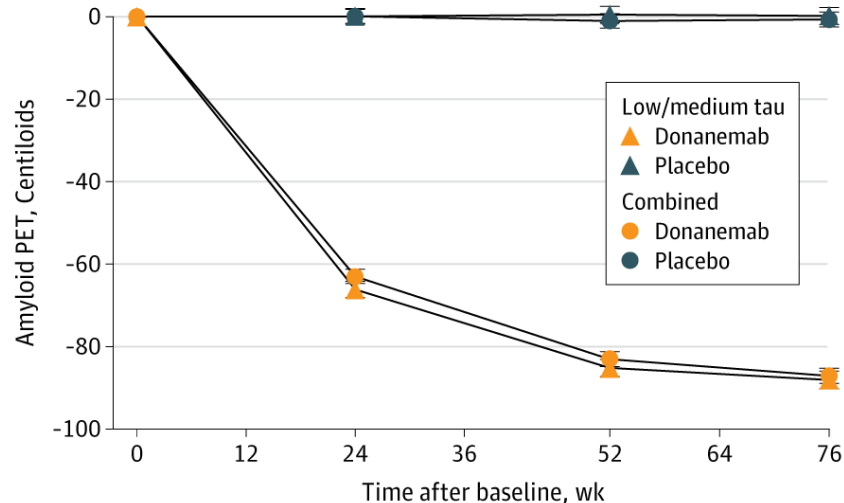- Donanemab (Kisunla^{TM}) – July 2024

Antibodies Remove Plaques

Lecanemab (Leqembi™)

Donanemab (Kisunla™)

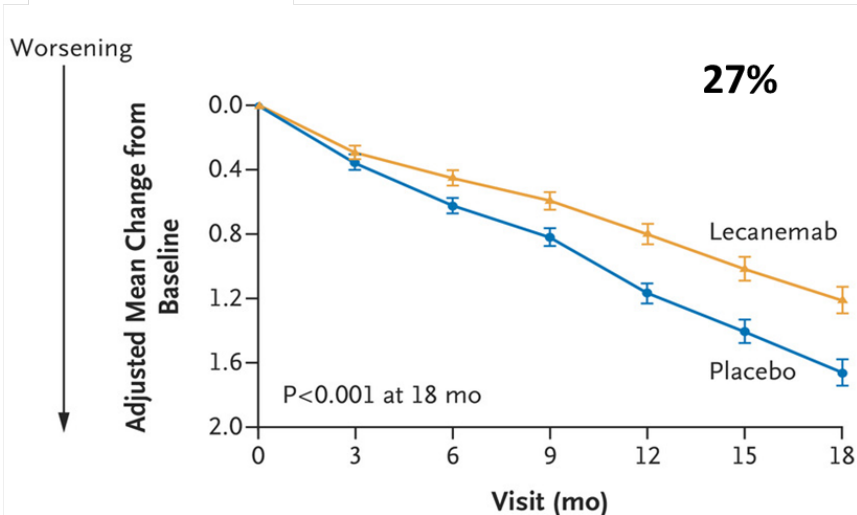van Dyck et al. New Eng J Med 2022; Sims et al. JAMA 2023

Antibodies Slow Cognitive Decline

Clinical Dementia Rating Sum-of-Boxes: Measures cognition (memory, orientation, judgment & problem solving) and function (community affairs, home & hobbies, personal care)
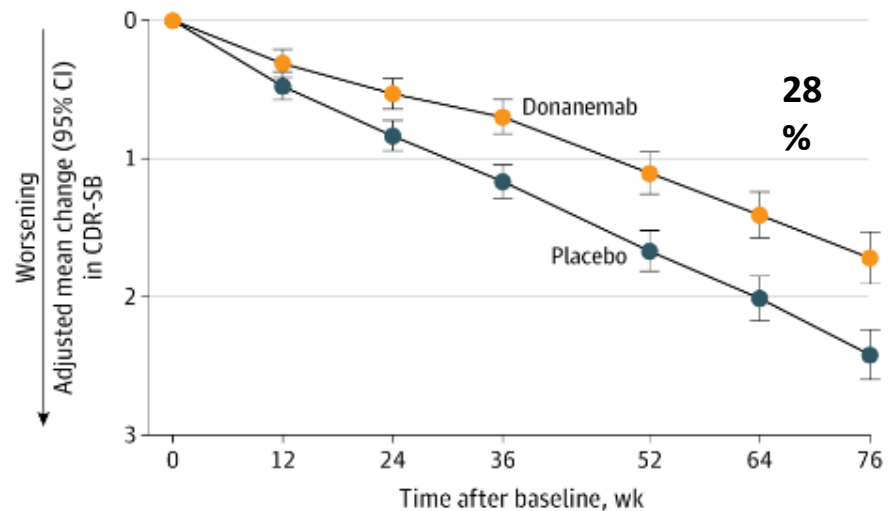
Lecanemab (Leqembi™)

Donanemab (Kisunla™)

van Dyck et al. New Eng J Med 2022; Sims et al. JAMA 2023

Treatment Effects: Patient Perspective

- **What does this degree of slowing mean for patients?**
  - "Benign forgetfulness" vs. "moderate memory loss… interferes with daily functions"
  - "Slight impairment" vs. "unable to function independently" in community affairs
  - "Slight impairment in home and hobbies" vs. "mild but definite impairment of function at home; more difficult chores and complicated hobbies abandoned"
  - **31% - 37% lower chance** of progressing from **Mild Cognitive Impairment** to **Mild Dementia**, or from **Mild Dementia** to **Moderate Dementia** over 18 months

Petersen et al. Alzheimer's & Dementia 2023

Following Treatment Response in LEADS

**Baseline visit
118 CL**
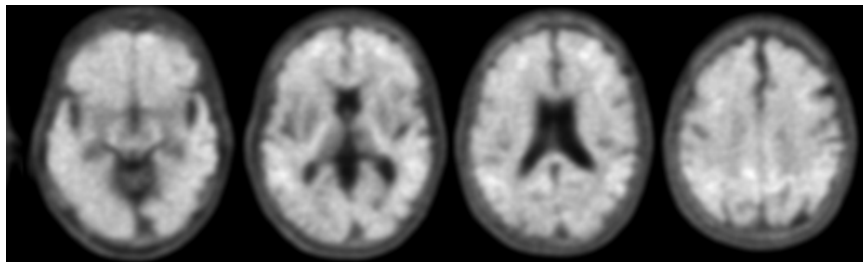
**12 months visit
78 CL**
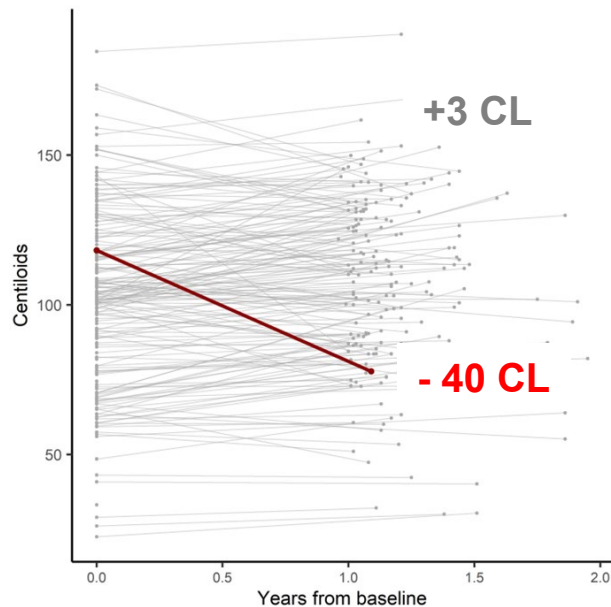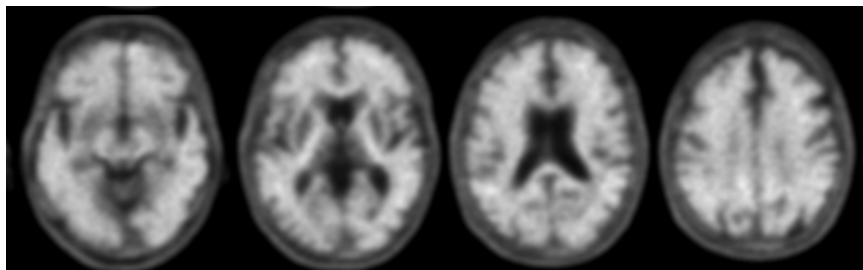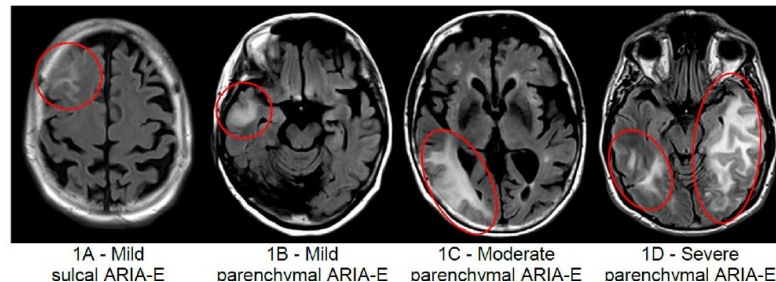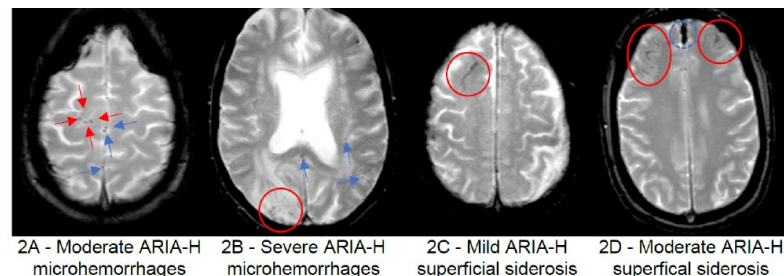
Amyloid Related Imaging Abnormalities (ARIA)

- **Class effect of anti-Aβ antibodies**
- **ARIA-E**: fluid shifts, swelling
- **ARIA-H**: microbleeds, superficial bleeds
- **Risk factors**
  - APOE4 gene, baseline MRI findings suggestive of previous bleeding
- 75%-80% have no symptoms
  - When present, symptoms usually mild (headache, dizziness, confusion)
  - ~1% experience serious symptoms (seizure, stroke, large hemorrhage, rarely death)

ARIA-E

1A - Mild sulcal ARIA-E · 1B - Mild parenchymal ARIA-E · 1C - Moderate parenchymal ARIA-E · 1D - Severe parenchymal ARIA-E

ARIA-H

2A - Moderate ARIA-H microhemorrhages · 2B - Severe ARIA-H microhemorrhages · 2C - Mild ARIA-H superficial siderosis · 2D - Moderate ARIA-H superfical siderosis

Sperling RA et al. Alzheimer's & Dementia 2011
Salloway S et al. JAMA Neurol 2022

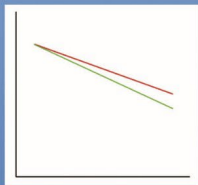**Treatment aims**
- Intervene at early symptomatic stages
- Remove brain amyloid-β plaques
- Slow disease-related cognitive decline

Treatment caveats
- The disease is more than just amyloid
- Treatment does not cure the disease
- Genetic factors influence side effects

Are monoclonal anti-amyloid therapies for Alzheimer disease an option for me?

Treatment risks
- High test and visit burden
- Potentially high financial costs
- Infusion reactions
- Brain swelling or bleeding (ARIA)

Alternatives
- Existing oral medications
- Lifestyle modifications
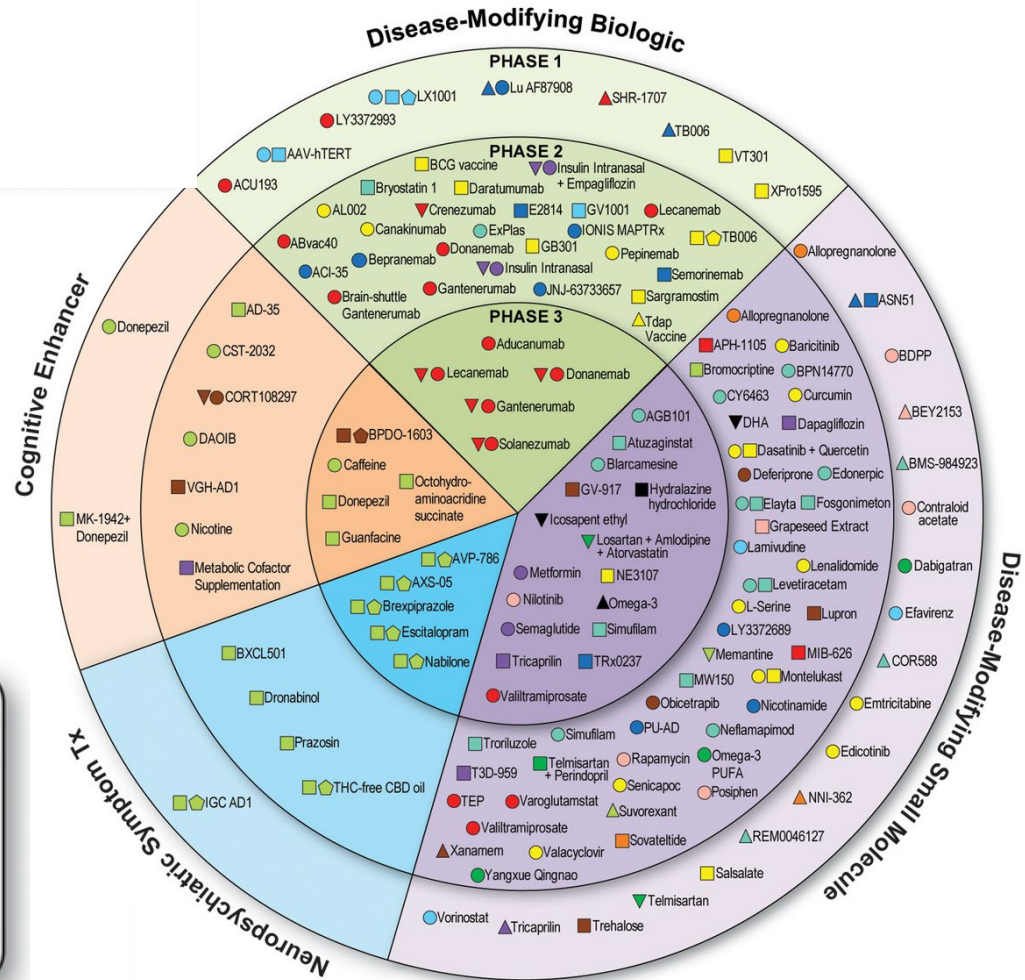- Future approved drugs
- Clinical trials

Ramanan et al. Neurology 2023

AD Drug Development: Diverse targets and approaches

Cummings et al. Alzheimer's & Dementia 2024

Alzheimer's National Registry for Treatment and Diagnostics

ALZ-NET
Alzheimer's National Registry for Treatment and Diagnostics
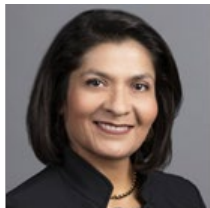
Maria Carrillo, Ph.D.

Gil Rabinovici, M.D.

Michael Rafii, M.D., Ph.D.

Develop a multi-site network for enrollment and data collection.

Collect patient data at the start and over time, including measures of cognition, function and safety.

Track health outcomes and resource utilization of participants.

Collect and archive brain scans, as well as genetic and biomarker data and blood samples.

Share de-identified data, brain scans and blood samples with the research community.

ACR® AMERICAN COLLEGE OF RADIOLOGY

CRITICAL PATH INSTITUTE

ALZHEIMER'S ASSOCIATION™

BROWN School of Public Health

ASNR American Society of Neuroradiology

Thank you to LEADS participants and family members!

Together, we can improve early diagnosis, deepen our understanding, and ultimately build the foundation for a cure for early-onset AD