



# Alzheimer's Updates and New Medications

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Director, Scientific Engagement  
Medical & Scientific Relations

# Our Time Today

1 About Alzheimer's & Dementia

2 Early Detection & Diagnosis

3 Treatment

4 Alzheimer's Association Initiatives

2024  
ALZHEIMER'S DISEASE  
FACTS AND FIGURES



NEARLY  
**7 MILLION**  
AMERICANS ARE LIVING  
WITH ALZHEIMER'S

THE LIFETIME RISK FOR  
ALZHEIMER'S AT AGE 45 IS

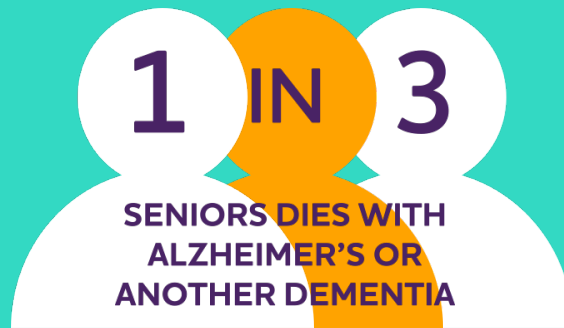


Older Black Americans are  
**2X AS LIKELY**  
to have Alzheimer's or other  
dementia than Whites.

BETWEEN 2000 AND 2021, DEATHS  
FROM HEART DISEASE HAVE  
**DECREASED 2.1%**



WHILE DEATHS FROM  
ALZHEIMER'S DISEASE HAVE  
**INCREASED 141%**



IT KILLS MORE THAN  
BREAST CANCER AND  
PROSTATE CANCER

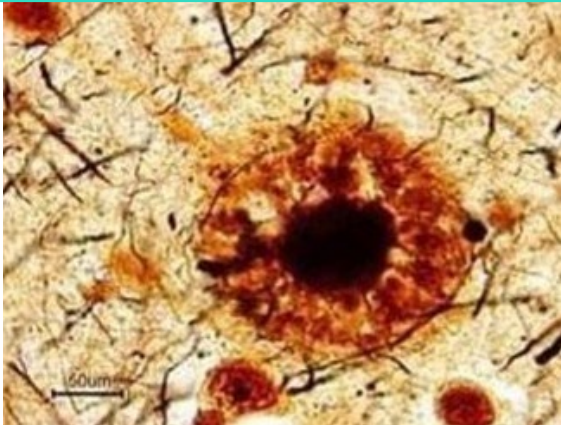
— + —  
**COMBINED**



Older Hispanic Americans are  
**1.5X AS LIKELY**  
to have Alzheimer's or other  
dementia than Whites.

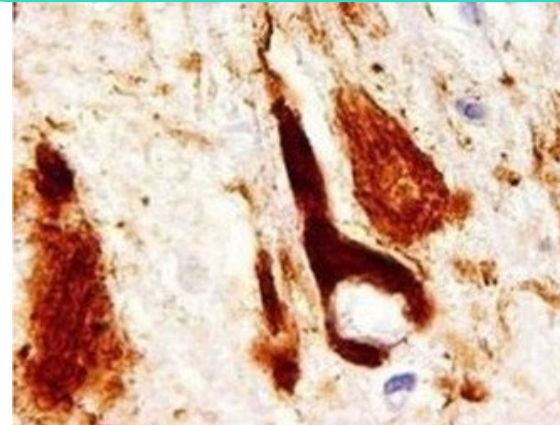
# The Hallmarks of Alzheimer's

## 1 Plaques



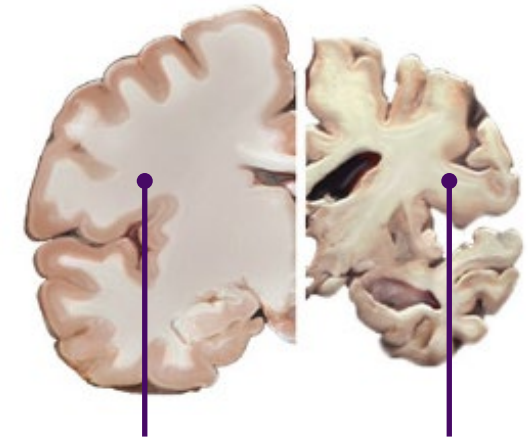
Made up of **beta amyloid**

## 2 Tangles



Made up of **tau**

## 3 Brain Cell Death

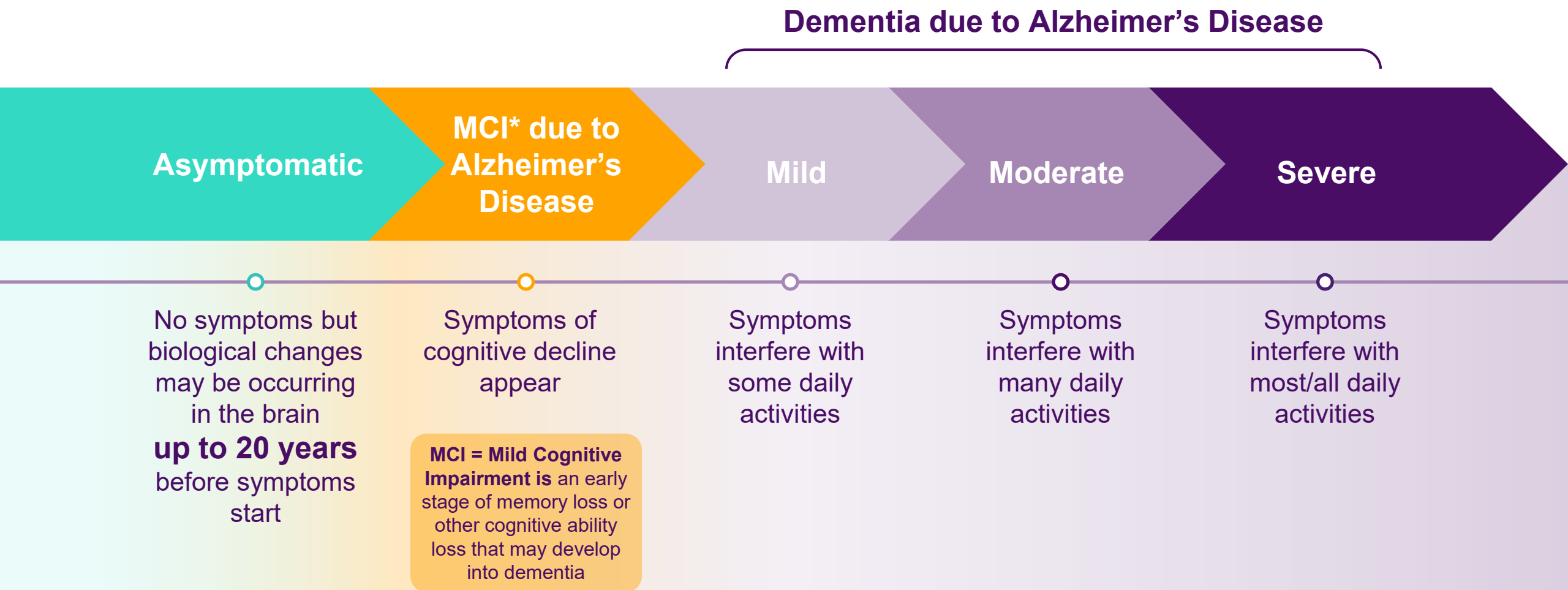


**Healthy**  
brain

**Advanced**  
Alzheimer's

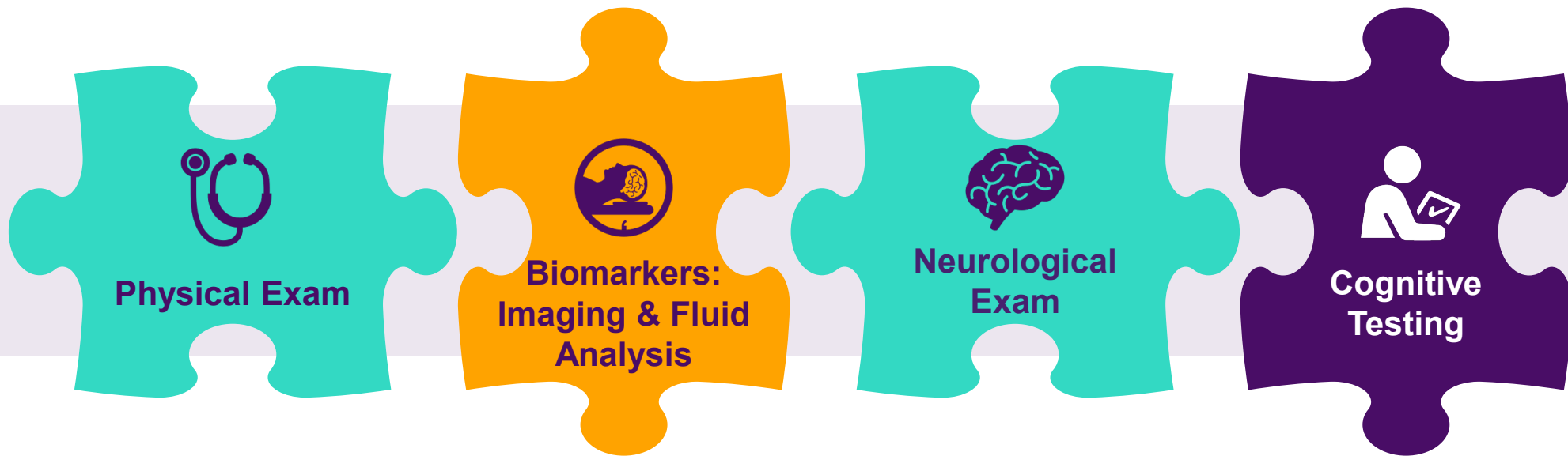


# Alzheimer's Disease is a Continuum



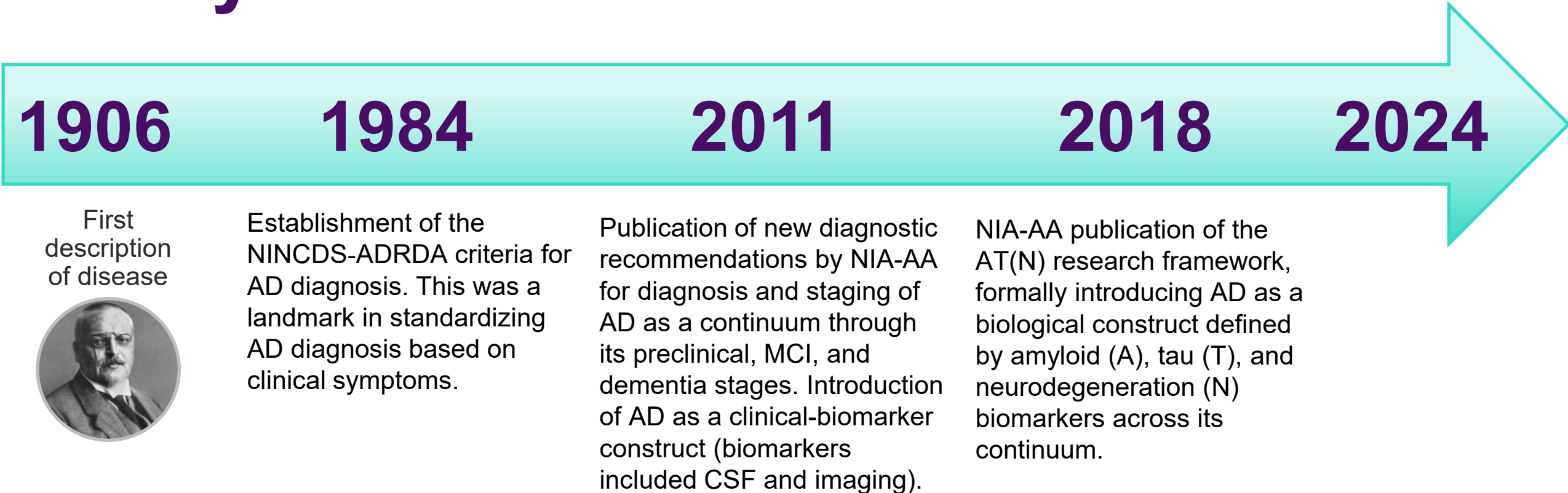
# How is Alzheimer's Currently Diagnosed?

There is no single test that can determine if a person is living with Alzheimer's disease or another dementia. Doctors use a combination of diagnostic tools combined with medical history to make an accurate diagnosis.



# History of Guidance on Diagnosis and Staging of Alzheimer's

## Nearly 120 Years ...



# Revised Criteria For Diagnosis and Staging of Alzheimer's Disease: Published 2024

Received: 7 February 2024 | Revised: 21 March 2024 | Accepted: 4 April 2024

DOI: 10.1002/alz.13859

Alzheimer's & Dementia®  
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

## RESEARCH ARTICLE

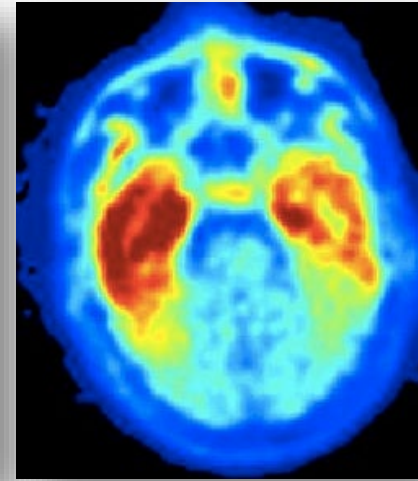
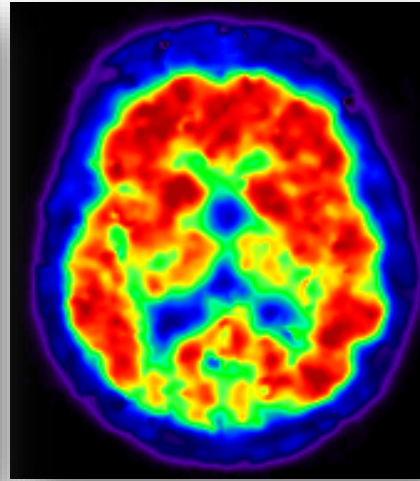
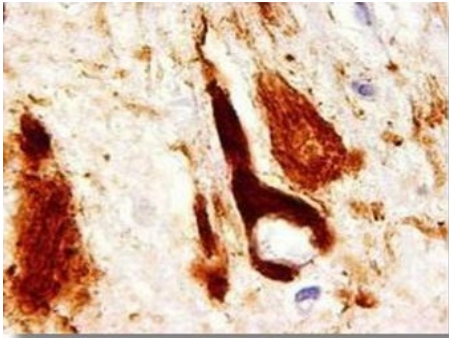
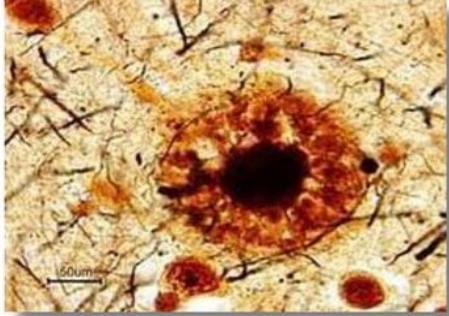
### Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup

Clifford R. Jack Jr.<sup>1</sup> | J. Scott Andrews<sup>2</sup> | Thomas G. Beach<sup>3</sup> | Teresa Buracchio<sup>4</sup> | Billy Dunn<sup>5</sup> | Ana Graf<sup>6</sup> | Oskar Hansson<sup>7,8</sup> | Carole Ho<sup>9</sup> | William Jagust<sup>10</sup> | Eric McDade<sup>11</sup> | Jose Luis Molinuevo<sup>12</sup> | Ozioma C. Okonkwo<sup>13</sup> | Luca Pani<sup>14</sup> | Michael S. Rafii<sup>15</sup> | Philip Scheltens<sup>16</sup> | Eric Siemers<sup>17</sup> | Heather M. Snyder<sup>18</sup> | Reisa Sperling<sup>19</sup> | Charlotte E. Teunissen<sup>20</sup> | Maria C. Carrillo<sup>18</sup>

Objective criteria for diagnosis and staging of Alzheimer's, incorporating recent advances in biomarkers which create an integrated biological and clinical staging scheme, to serve as a bridge between research and clinical care



# Biomarker Development for Hallmark Brain Changes



**1906**  
**Amyloid and Tau**  
**Pathology**

**Late 1990s**  
**CSF A $\beta$ ,**  
**Tau, p-Tau**

**Mid-late**  
**2000s**  
**Amyloid PET**

**Mid-late**  
**2010s**  
**Tau PET**

**2020s**  
**Plasma A $\beta$ ,**  
**Tau, p-Tau**

# Latest advancements drive need for blood-based biomarker guidelines

Received: 11 May 2022 | Revised: 28 June 2022 | Accepted: 8 July 2022

DOI: 10.1002/alz.12756

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THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

REVIEW ARTICLE

## The Alzheimer's Association appropriate use recommendations for blood biomarkers in Alzheimer's disease

Oskar Hansson<sup>1,2</sup> | Rebecca M. Edelmayer<sup>3</sup> | Adam L. Boxer<sup>4</sup> | Maria C. Carrillo<sup>3</sup> | Michelle M. Mielke<sup>5</sup> | Gil D. Rabinovici<sup>4</sup> | Stephen Salloway<sup>6</sup> | Reisa Sperling<sup>7</sup> | Henrik Zetterberg<sup>8,9,10,11,12</sup> | Charlotte E. Teunissen<sup>13</sup>

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RESEARCH ARTICLE

## Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup

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- In 2022, recommendations were published that indicated blood biomarkers show promise for improving, and possibly even redefining, the diagnostic work-up for Alzheimer's. This is a rapidly evolving field.
- The 2024 revised criteria included an updated biomarker classification system that includes blood-based biomarkers (BBM) and a revised disease staging system.
- The accuracy of some emerging Alzheimer's blood tests needs to be considered, and researchers and clinicians made aware and properly educated and guided on their use
- **There is a need to update the 2022 AUR for blood and create formal clinical guidance on BBM, and a need to distill the best available evidence and translate it into clear and actionable recommendations for clinical practice**

# New Era of Diagnostics: Blood Tests

## Urgent

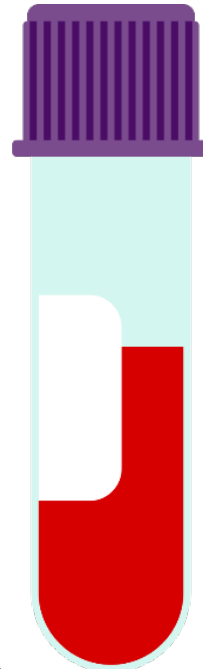
Global Race to uncover and develop blood-based biomarkers for Alzheimer's and other dementia

## Range

More than beta amyloid and tau; emerging tests to measure alpha synuclein, markers of cell death, inflammation and vascular related changes

## Clinical Guidance

Appropriate Use Recommendations – Published 2022  
Blood Biomarker Guidelines – In Progress



## Valuable

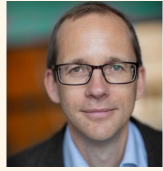
Blood tests are demonstrating to be valuable tool to help streamline clinical trials enrollment

## Commercial

A variety of blood tests that predict the presence of Alzheimer's amyloid brain plaques have hit the commercial market. Must be prescribed by healthcare providers to individuals with a cognitive concern.

## Emerging

While not ready for broad use in the clinic, blood-based biomarkers are making remarkable progress.



Co-Chair  
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Hamid Okhravi, MD



Laura Allen, NP



Suzanne Schindler, MD, PhD



Maria Carrillo, PhD



Madeline Paczynski, PA



Marc Suárez-Calvet, MD, PhD



Thomas Karikari, PhD



Douglas Galasko, MD



Rebecca Edelmayer, PhD



Malavika Tampi, MPH

# Clinical Practice Guideline in Development: Blood Biomarkers in Alzheimer's Disease

- Building a clinical guidance that distills the best available evidence and translates it into clear and actionable recommendations for clinical practice
- A collaboration between the Alzheimer's Association, a guideline panel of clinical and subject-matter experts, partner organizations, and patient representatives
- Using a transparent guideline development framework and GRADE methodology to move the panel from the evidence to decisions (or recommendations)

## Deliverables



Systematic review



Clinical practice guideline



Clinical tools



Educational courses and presentations



# Clinical Practice Guideline in Development: Cognitive Assessment Tools for Cognitive Impairment

- Building a clinical guidance that distills the best available evidence and translates it into clear and actionable recommendations for clinical practice
- A collaboration between the Alzheimer's Association, a guideline panel of clinical and subject-matter experts, partner organizations, and patient representatives
- Using a transparent guideline development framework and GRADE methodology to move the panel from the evidence to decisions (or recommendations)



Co-Chair  
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Jennifer Gatchel, MD, PhD



Karen Bell, MD



Maria Carrillo, PhD



Dana Jones, F-NPC



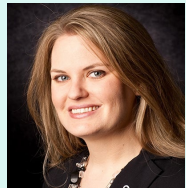
Martin Sliwinski, PhD



Peter Snyder, PhD



Noelle L. Fields,  
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Heather Snyder, PhD



Eric Tangalos, MD



Malavika Tampi, MPH

## Deliverables



Systematic  
review



Clinical practice  
guideline



Clinical  
tools



Educational courses  
and presentations

# The Right Test, For the Right Patient, at the Right Time



*“Doc, I’m worried I have Alzheimer’s disease.  
What testing do you recommend for me?”*



# FDA-Approved Therapies for Alzheimer's

First description of disease 1906



**Treat Symptoms:**  
Cognition and Function

**Treat Symptoms:**  
Mood or Behavior

**Slow Disease Progression:**  
Cognition, Function and Behavior

		Asymptomatic	MCI	Mild Dementia	Moderate Dementia	Severe Dementia
1996	donepezil (Aricept)					
2000	rivastigmine (Exelon)					
2001	galantamine (Razadyne)					
2003	memantine (Namenda)					
2014	memantine + donepezil (Namzaric)					

# FDA-Approved Therapies for Alzheimer's – Symptomatic: Cognition and Function

FDA approved therapies to temporarily improve symptoms

## Cholinesterase Inhibitors

- donepezil (Aricept)
- rivastigmine (Exelon)
- galantamine (Razadyne)

Mild - severe dementia due to Alzheimer's

Mild - moderate dementia due to Alzheimer's

Mild - moderate dementia due to Alzheimer's or Parkinson's

## Glutamate Moderators

- memantine (Namenda)

Moderate - severe dementia due to Alzheimer's

## Combination

- donepezil + memantine (Namzaric)

Moderate - severe dementia due to Alzheimer's

# How Cognitive Enhancing Drugs Work

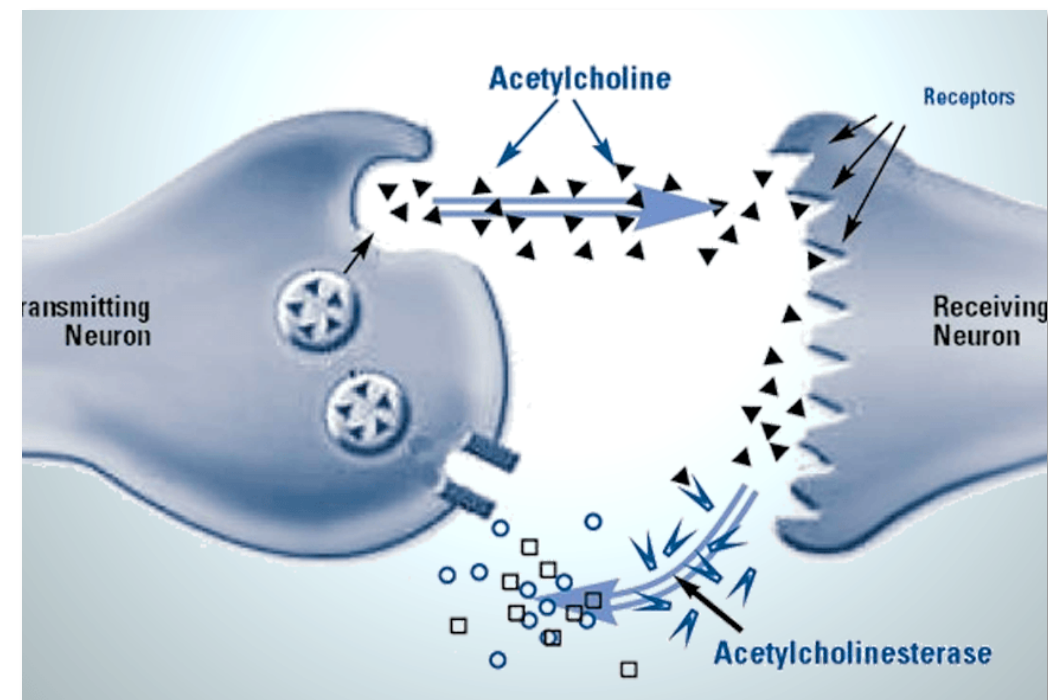
## Cholinesterase inhibitors:

- Acetylcholine is a chemical in the brain
- These drugs block the breakdown of acetylcholine
- Can restore neuronal communication by concentrating the available chemical

## Glutamate moderators:

- Glutamate is an excitatory chemical in the brain
- Glutamate can overstimulate cells leading to neuronal cell death
- These drugs block the glutamate receptors from being overstimulated

## Cholinesterase inhibitors and acetylcholine communication



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2020	suvorexant* (Belsomra)					
2023	brexpiprazole (Rexulti)					

# FDA-Approved Therapies for Alzheimer's – Symptomatic: Behavioral and Psychological Symptoms of Dementia

## suvorexant (Belsomra®)

- Insomnia
- 1<sup>st</sup> FDA-approved insomnia drug tested in a Mild-to-Moderate Alzheimer's dementia population

## brexpiprazole (Rexulti®)

- Agitation associated with dementia due to Alzheimer's disease
- 1<sup>st</sup> and only FDA-approved atypical antipsychotic for use in Alzheimer's
- Reduces frequency of agitation symptoms

### Merck gets Alzheimer's label claim for insomnia drug Belsomra

*Alzheimer's patients typically experience poor sleep*



Article by  
[Phil Taylor](#)

4th February 2020

PSYCHIATRIC NEWS

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FULL ACCESS | Clinical & Research | Published Online: 12 May 2023

## FDA Approves Rexulti for Agitation Associated With Dementia Due to Alzheimer's Disease

Mark Moran | [AUTHORS INFO & AFFILIATIONS](#)

Publication: Psychiatric News • Volume 58, Number 07 • <https://doi.org/10.1176/appi.pn.2023.07.7.17>

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2023	lecanemab (Leqembi)					
2023	brexpiprazole (Rexulti)					
2024	donanemab (Kisunla)					





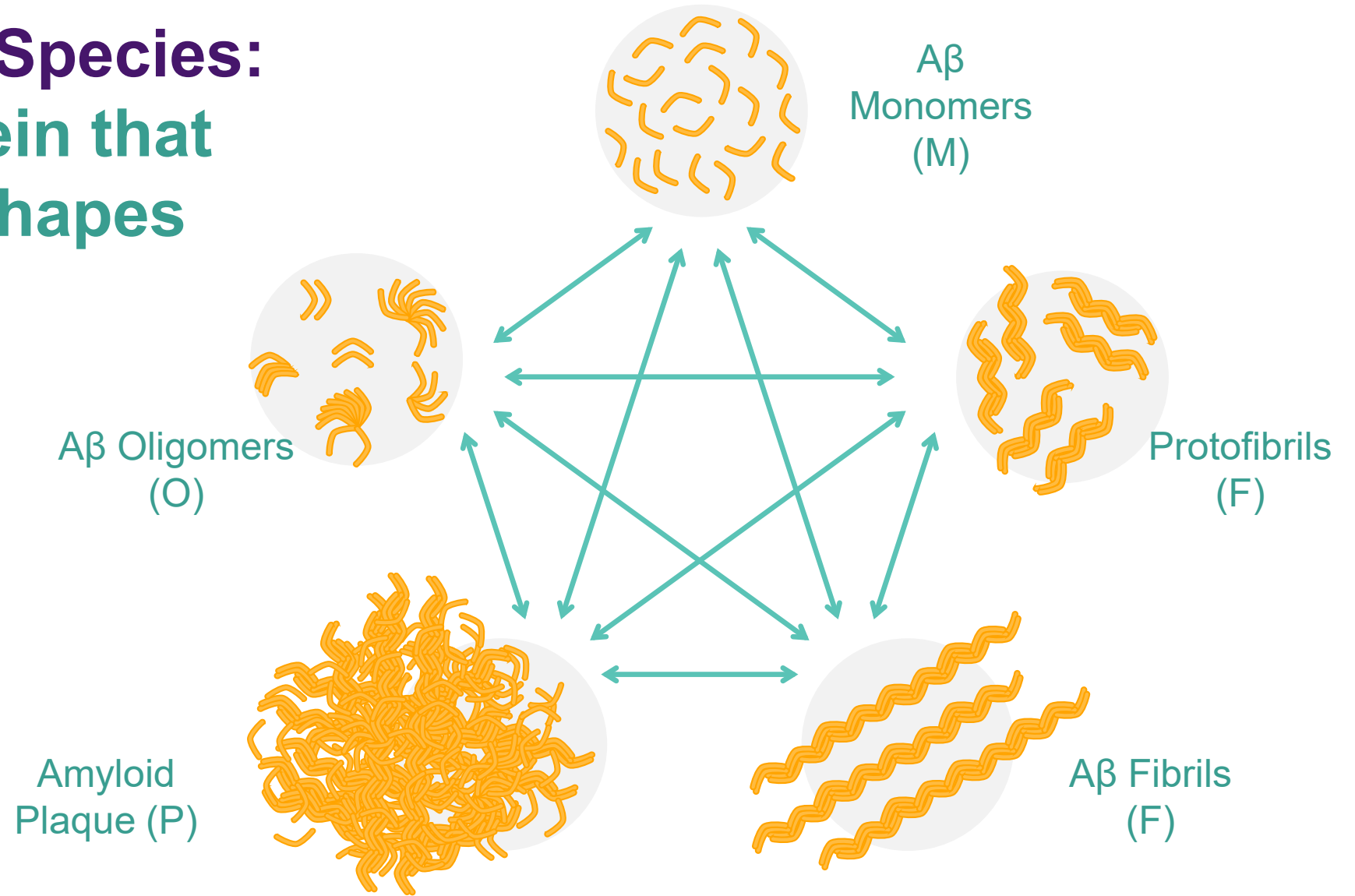
# Deeper Dive: A New Phase of Treatment



**lecanemab  
(Leqembi)**  
Approved in 2023  
Targets Beta Amyloid

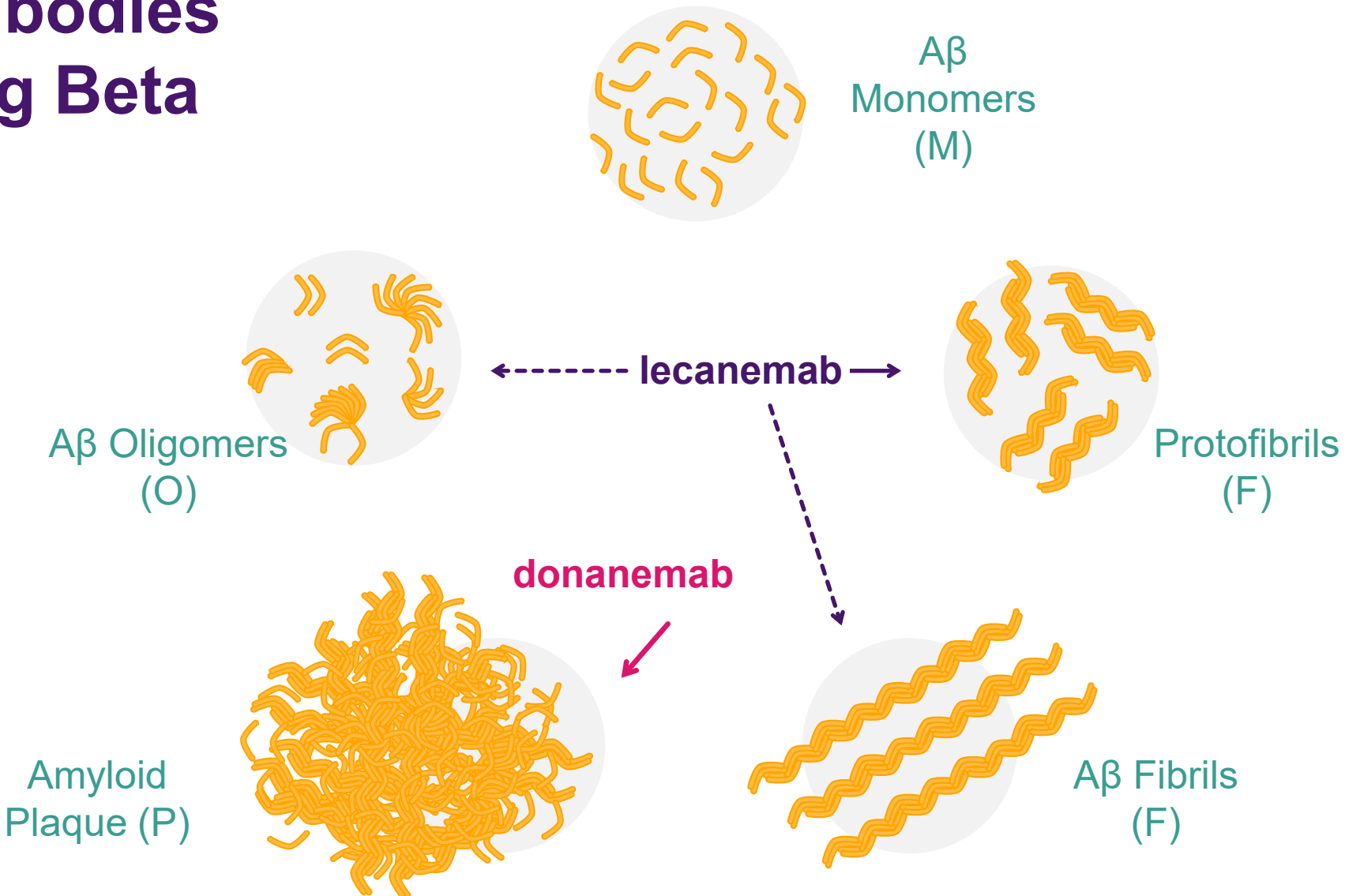
**donanemab  
(Kisunla)**  
Approved in 2024  
Targets Beta Amyloid

# Beta Amyloid Species: Dynamic protein that has multiple shapes and forms



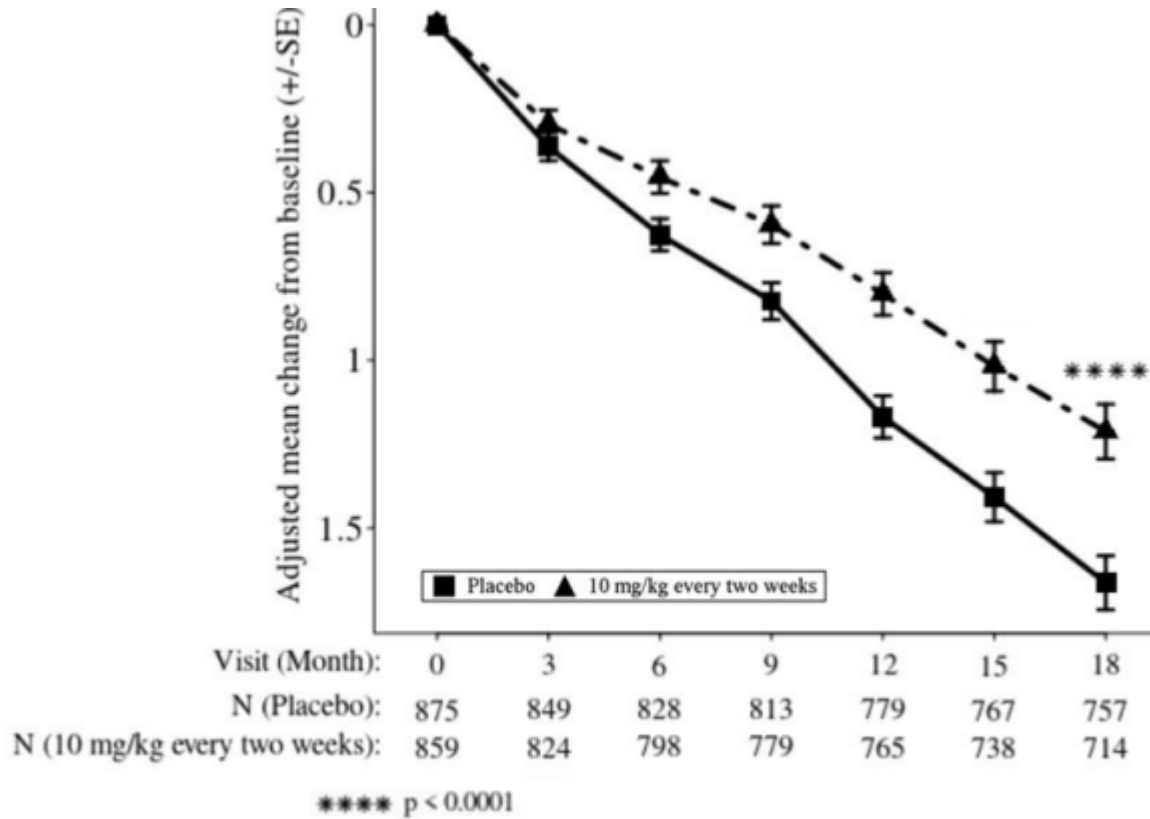
# Monoclonal Antibodies (mAbs) Targeting Beta Amyloid

strong binding ———  
weak binding - - - - -

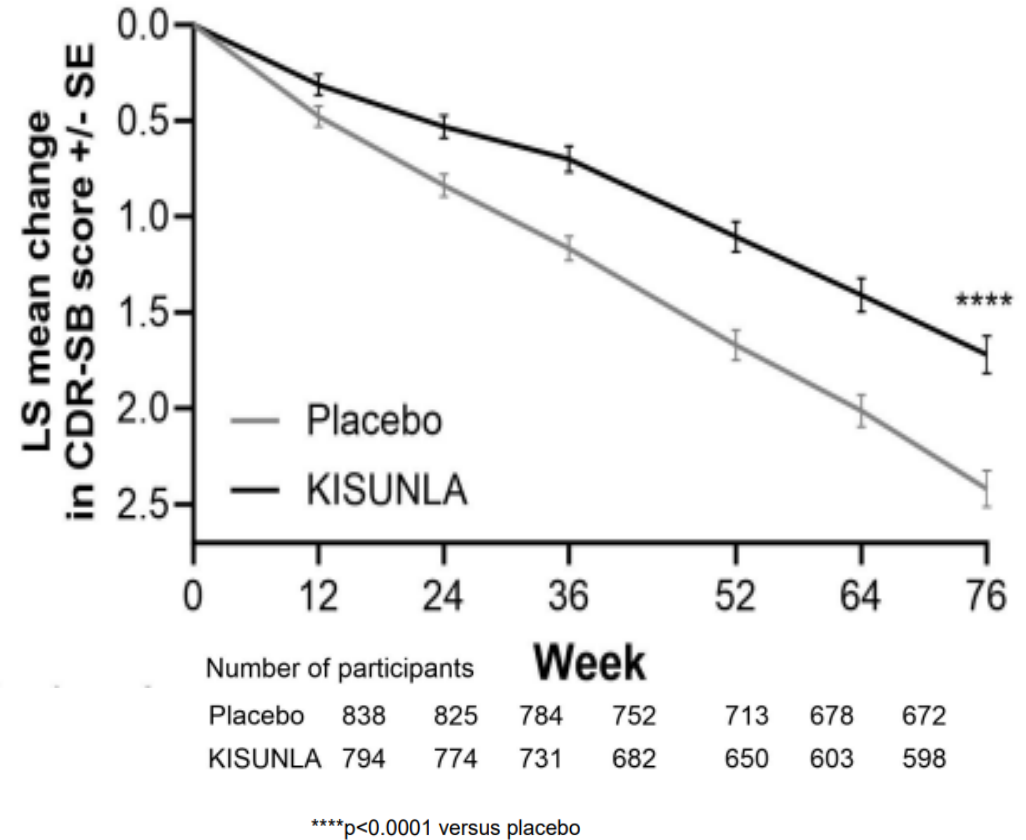


# CDR-SB across FDA-approved anti-amyloid therapies

## lecanemab (Leqembi)



## donanemab (Kisunla)



# Prescribing Information for Newly Approved Treatments: Warnings & Precautions

## **Amyloid Related Imaging Abnormalities**

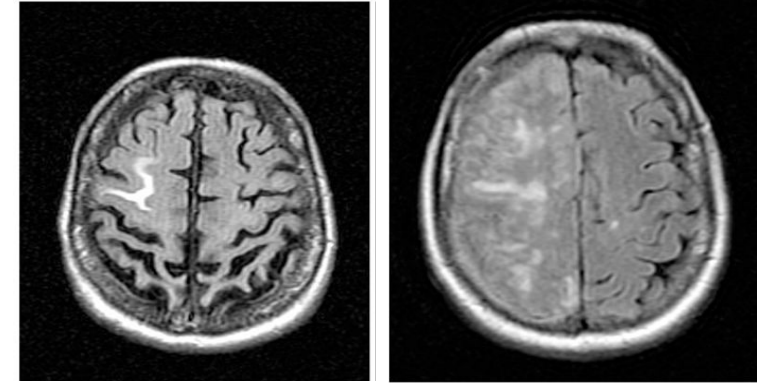
**(ARIA):** Enhanced vigilance monitoring for ARIA is recommended during first 14 weeks

**APOE genetic testing:** ARIA risk increased in individuals with two copies of the APOEε4 gene compared to others.

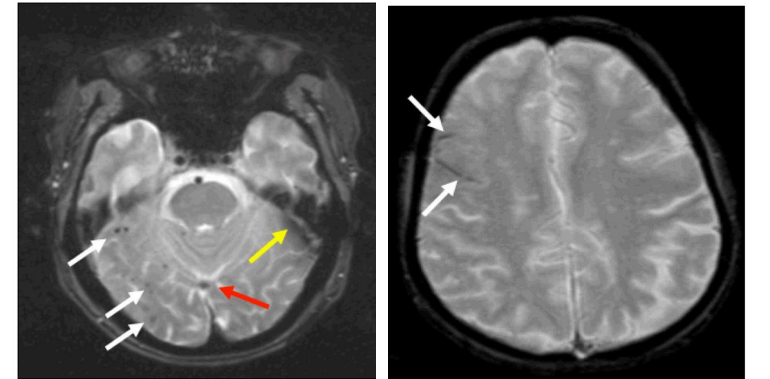
# Amyloid-Related Imaging Abnormalities (ARIA)

- **ARIA** - brain MRI abnormalities seen in patients undergoing amyloid targeting monoclonal antibody treatment: ARIA-E and ARIA-H
- **Incidence and clinical manifestation:**
  - Common manageable side effect
  - Typically asymptomatic and resolves over time
  - Can be serious in rare cases
- **Risk factors:** *APOE*  $\epsilon$ 4 carrier, microhemorrhages, superficial siderosis, and CAA
- **Monitoring:** essential with MRI before and during treatment

ARIA-E (Edema)



ARIA-H (Hemorrhage)



Sperling, RA., et al, *Alzheimer's & Dementia* (2011): 367-385.



# A New Phase of Treatment

Today, Over 120 Unique Therapies Being Tested in Clinical Trials that Target Multiple Aspects of Alzheimer's Biology

Targets  
*amyloid*



2023

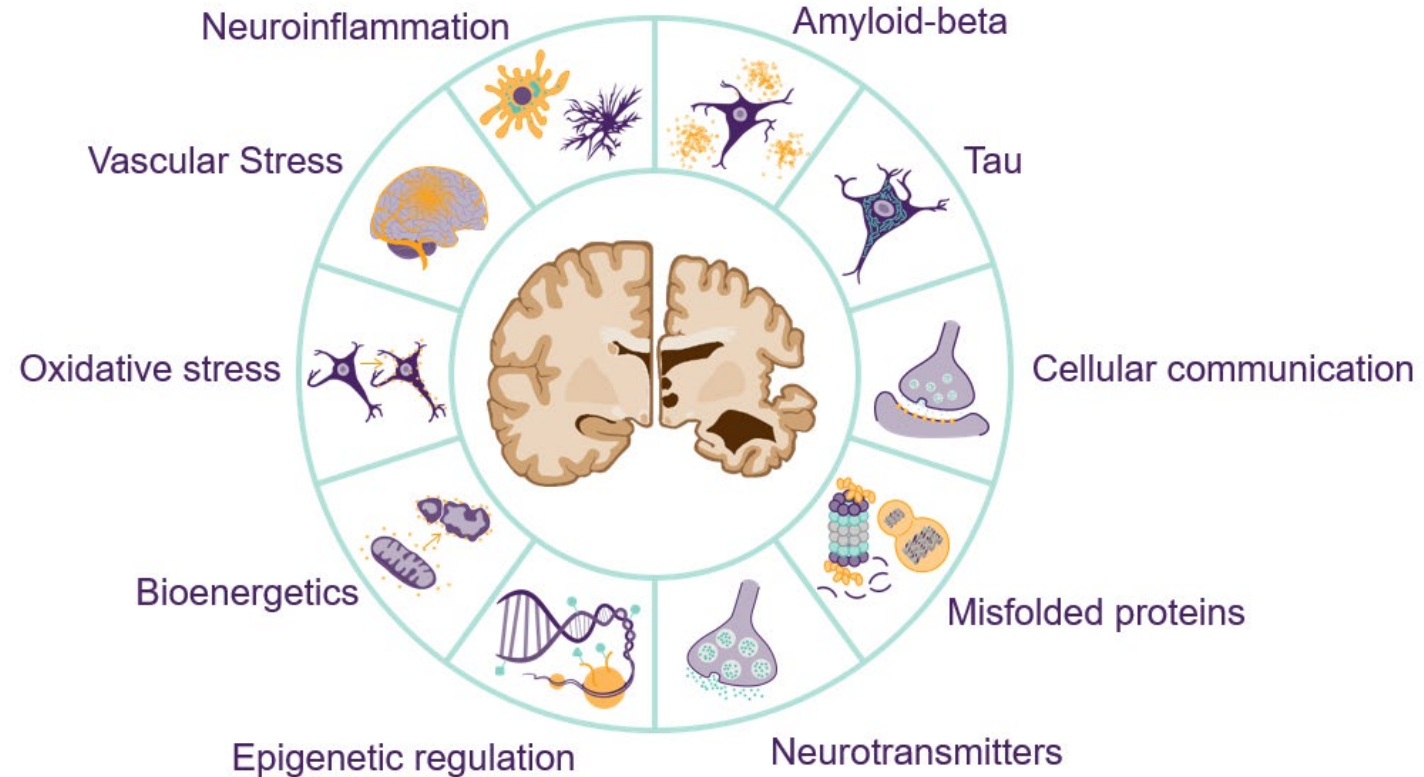
lecanemab  
(Leqembi®)

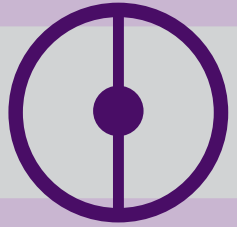
Targets  
*amyloid*



2024

donanemab  
(Kisunla™)





# 2024 Alzheimer's Drug Development Pipeline

148

Phase 1 Clinical Trials

221

Phase 2 Clinical Trials

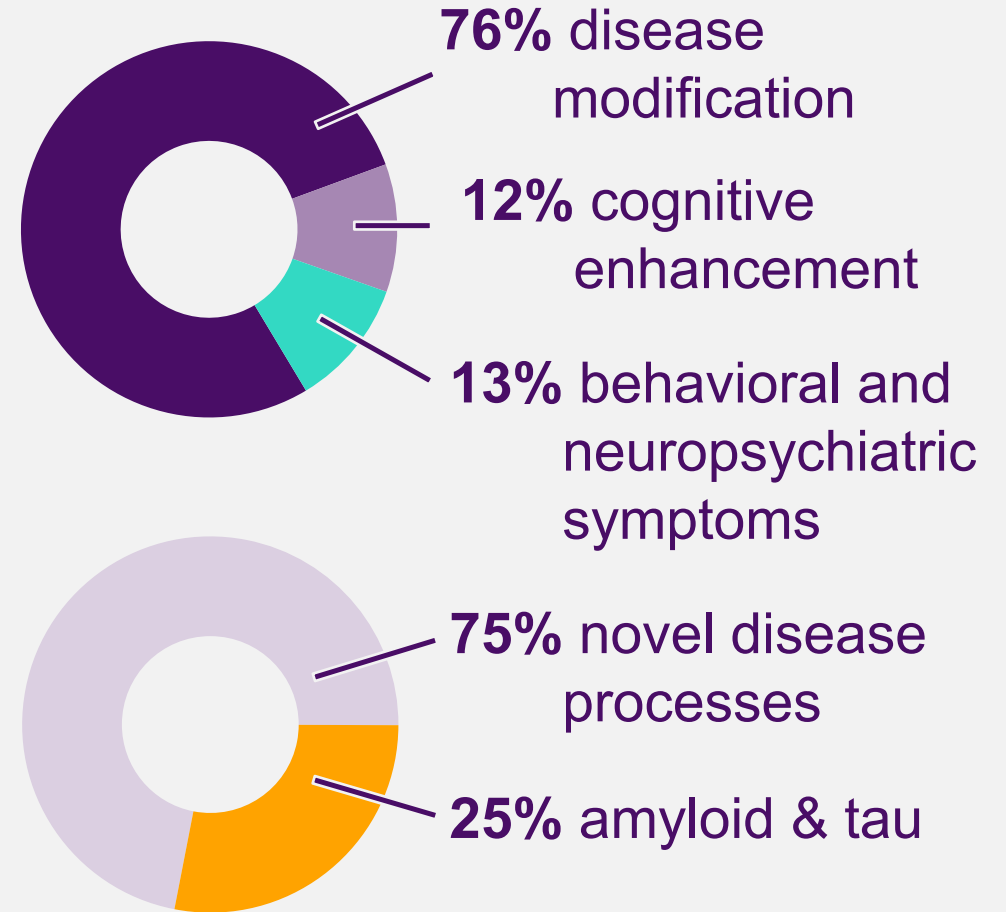
64

Phase 3 Clinical Trials

65,798

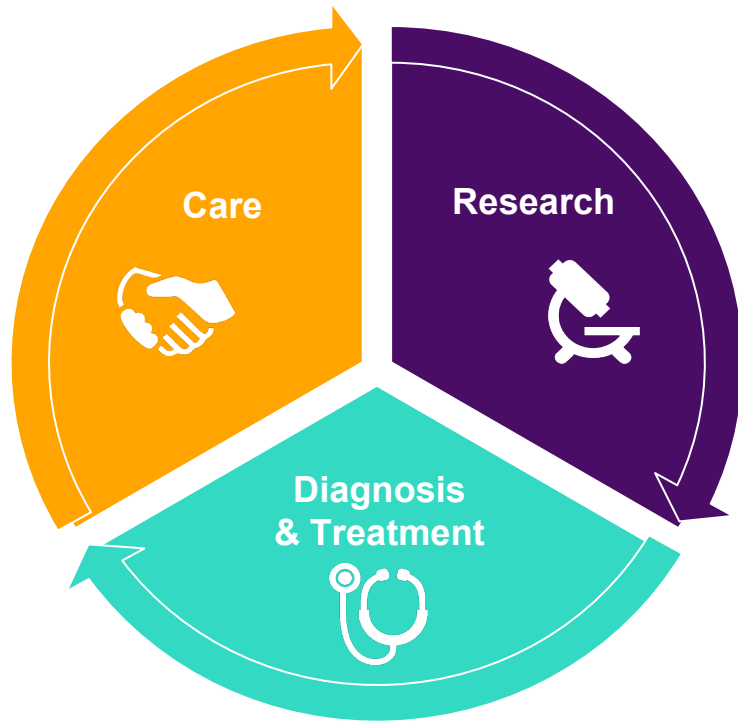
Total number of participants needed to populate all currently active trials (Phases 1, 2 and 3)

Targets of agents currently in clinical trials include:



# Translating Biomarker Results for the Patient: Diagnosis, Treatment and Care

We are in the midst of a paradigm shift



Clinicians must be ready to answer patient questions:

- Am I at risk?
- What is my diagnosis?
- What stage is my disease?
- How fast will I progress?
- What treatments are appropriate?
- Is the treatment working?
- Can my dosing be adjusted?
- Can my treatment be stopped?
- What are my next steps?



A Real World Network to Inform the  
Future of Alzheimer's Research,  
Treatment and Care





# Alzheimer's Network for Treatment and Diagnosis (ALZ-NET)



A **voluntary health care provider-enrolled patient network** that collects longitudinal data on patients being evaluated or treated for Alzheimer's disease.



**Enrolling patients being evaluated for or treated with novel Alzheimer's treatments** approved by the FDA in 2021 or after.



Implemented in real-world clinical practice, ALZ-NET is **not a clinical trial**. Sites are providers who provide routine clinical care.



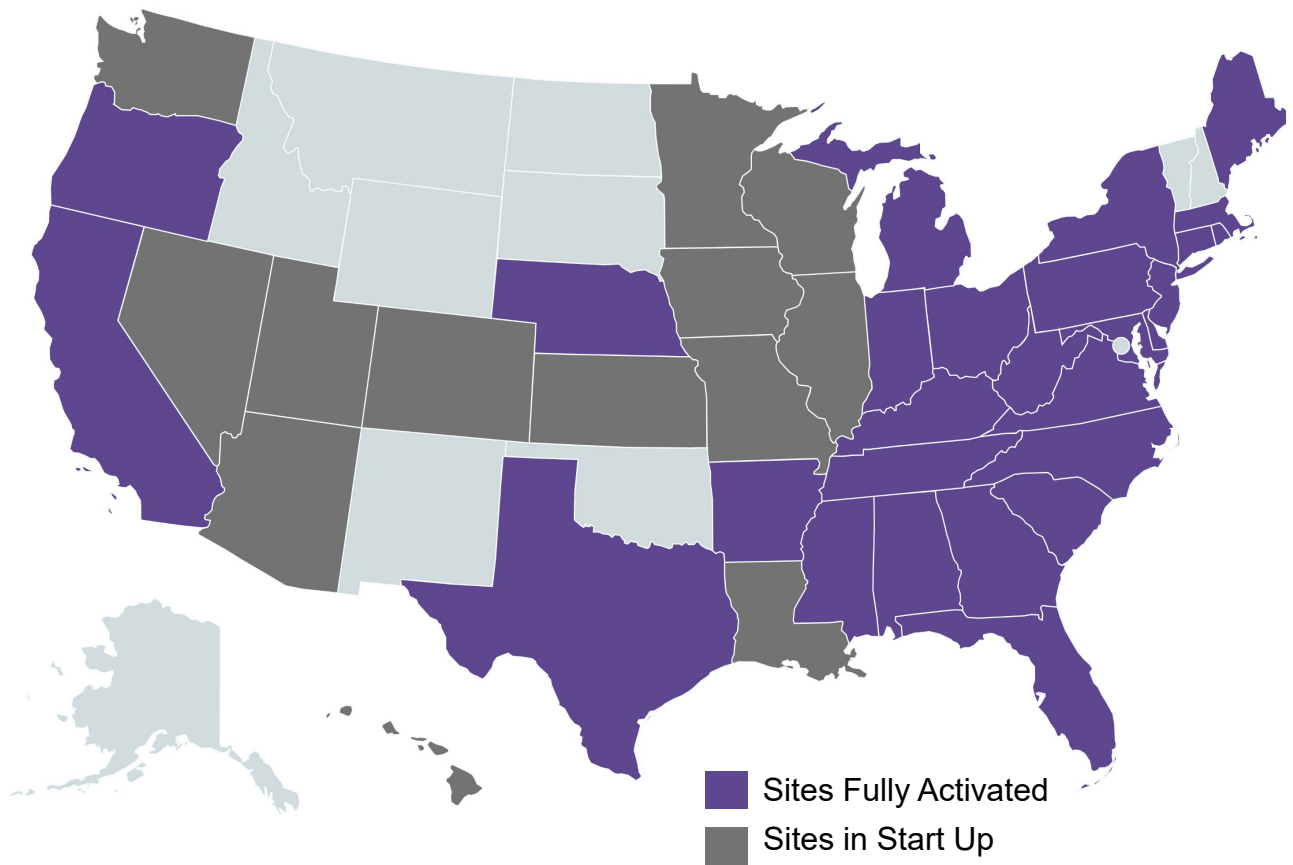
## Questions ALZ-NET could address:

- What is the long-term effectiveness of a treatment?
- What are long-term safety considerations?
- Who is most likely to respond well and benefit from different treatments?
- Who is most likely to have treatment-related side effects?
- Which treatments might work well together as combination therapies?
- And much more.





# ALZ-NET continues to grow, enrolling, activating and partnering with teams every day!



There are **887 patients enrolled** with numbers increasing every day as patients consent to being included during their regularly scheduled care and treatment visits.

There are **70 clinical sites activated** across the United States

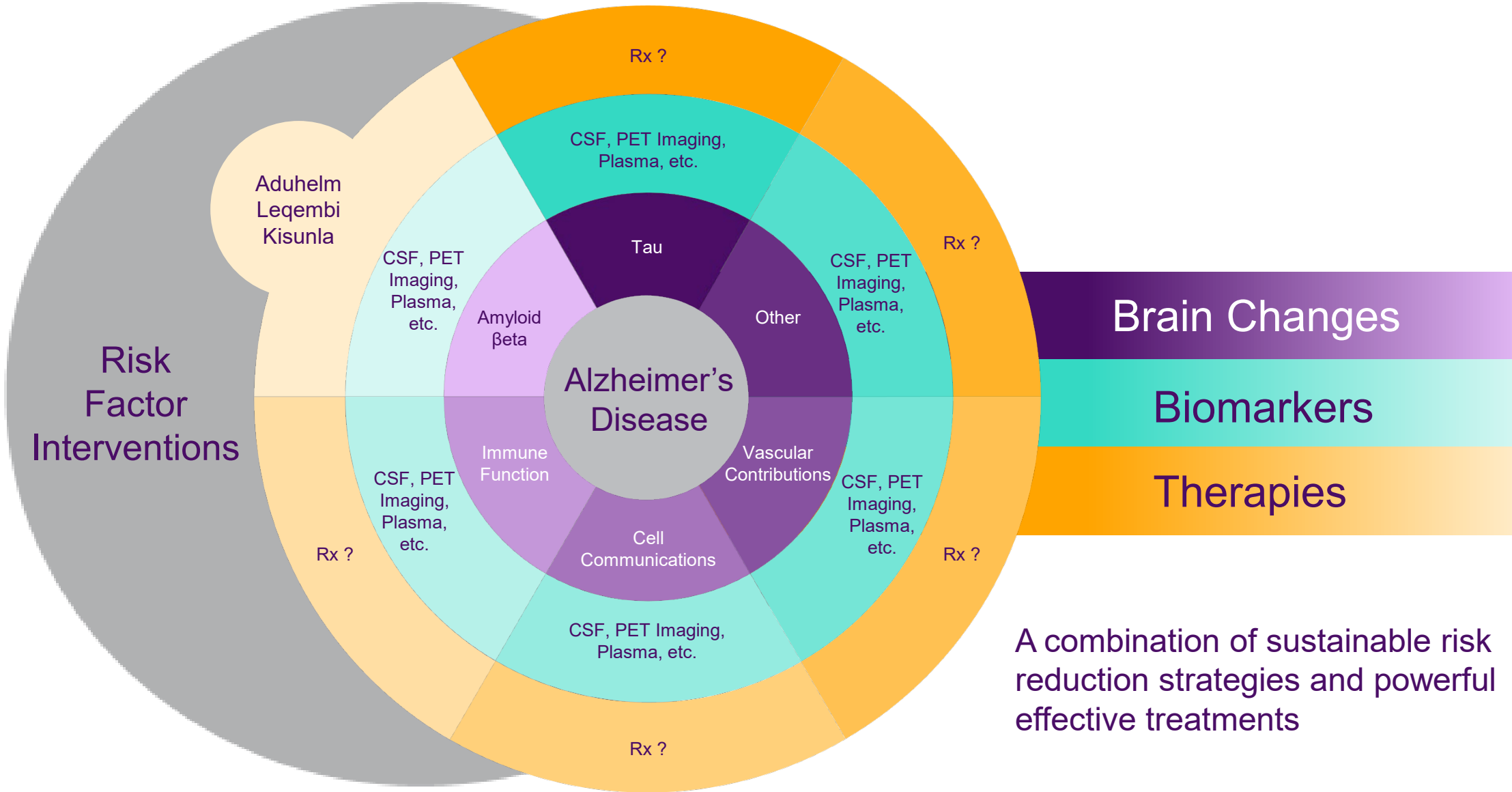
More than **165 additional clinical sites** are in various stages of startup

**10 new sites likely to activate** within the next few weeks

\* As of Site & Patient Tracker 10/23/24



# New Era of Research, Treatment and Care...



# Future of Treatment - Precision and Personalized Medicine

## New Era of Treatment



Researchers are exploring what treatment could look like in the future with **precision and personalized medicine** approaches to Alzheimer's and other dementia. While, the science is *not there yet*, it holds promise for the future.

# Get Involved in Research

- TrialMatch is a **free clinical studies matching service** designed to provide a **customized list** of potential study matches to each user.
- Healthy and cognitively impaired people from all backgrounds are needed to participate in Alzheimer's and dementia research.



**SCAN**  
to find  
out more

**trialmatch**<sup>®</sup>

ALZHEIMER'S  ASSOCIATION<sup>®</sup>

POWERED BY CenterWatch iConnect<sup>™</sup>

*\*Over 370,000 users and includes 863+ clinical studies around the world.*

**744** Alzheimer's Disease

**348** Mild Cognitive Impairment

**36** Vascular Dementia

**123** Other Dementia

# World's Largest Nonprofit Funder of Alzheimer's & All Dementia Research



**SEED**  
new ideas

**SPEED**  
the development of  
new therapies

**SCALE**  
to accelerate the  
science



**\$430M+**

currently  
active



**1110+** projects



**56** countries

# Research Resources



Association's Website | [alz.org](https://alz.org)



Research at the Association | [alz.org/research](https://alz.org/research)



Join a Clinical Trial | [alz.org/trialmatch](https://alz.org/trialmatch)



Contact the 24/7 helpline | 800-272-3900



# In Summary...

- **The Alzheimer's Association is the global leader for Alzheimer's and dementia science**
- **Exciting time in research**
- New tools for detection and diagnosis
- New approved treatments and more in the pipeline
- Strategies for risk reduction
- There is HOPE in research



**Care  
& Support**



**Advocacy**



**Education  
& Awareness**



**Research**



**Diversity, Equity  
& Inclusion**

ALZHEIMER'S ASSOCIATION

AAIC > 25

ALZHEIMER'S ASSOCIATION  
INTERNATIONAL CONFERENCE®

SAVE THE DATE

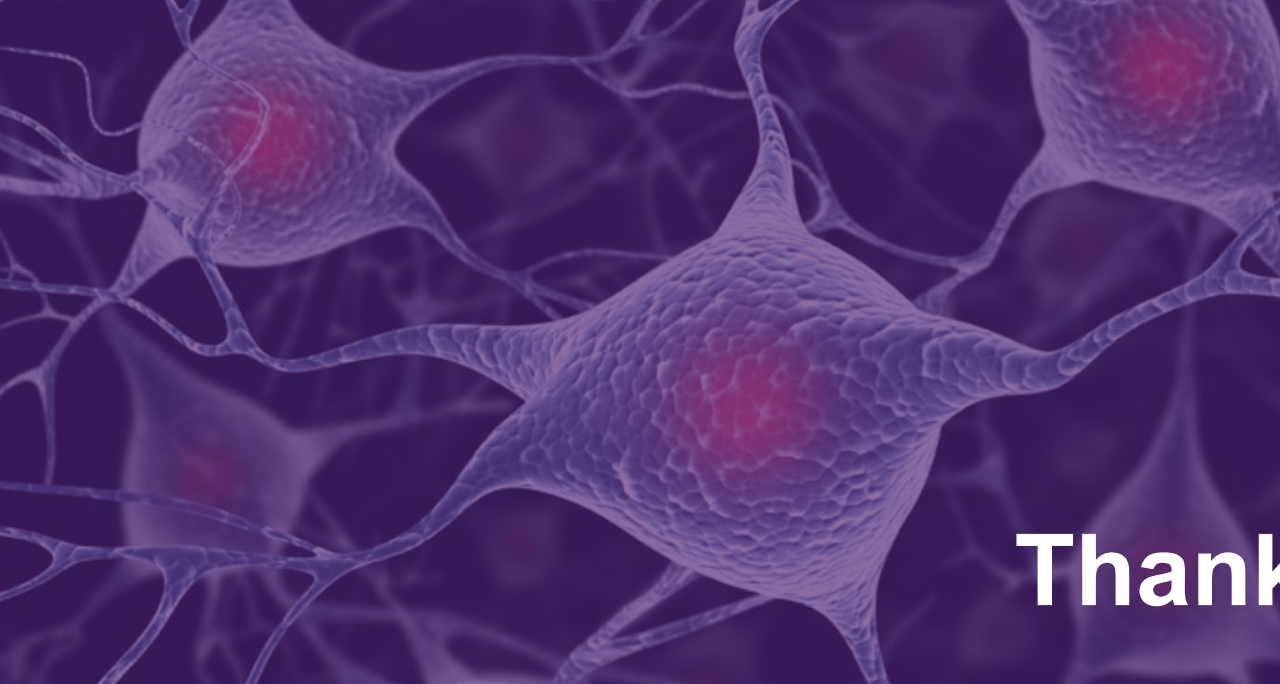
JULY 27-31 ANNUAL CONFERENCE > TORONTO, CANADA, AND ONLINE

July 25-26 Educational Workshops and Preconferences

July 27-30 Exhibits

[alz.org/AAIC](https://alz.org/AAIC)





**Thank You!**



**Questions & Discussion**

