



Alzheimer's Updates and New Medications

Courtney Kloske, Ph.D.
Director, Scientific Engagement
Medical & Scientific Relations

Our Time Today

1 About Alzheimer's & Dementia

2 Early Detection & Diagnosis

3 Treatment

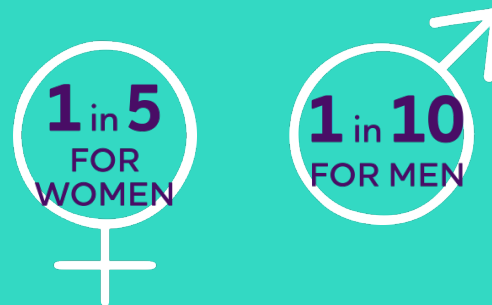
4 Alzheimer's Association Initiatives

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



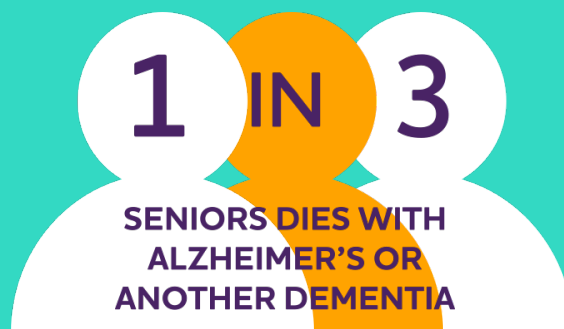
Older Black Americans are
2X AS LIKELY
to have Alzheimer's or other
dementia than Whites.

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

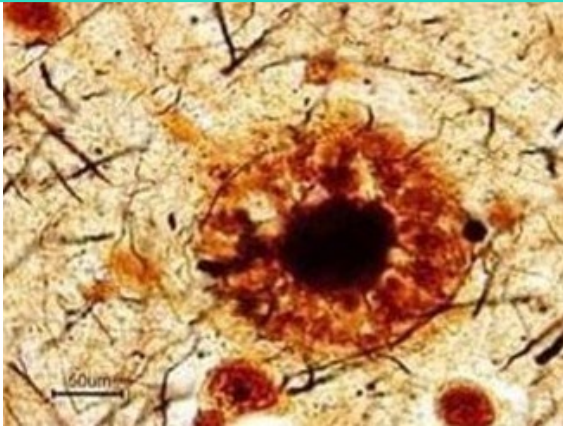
— + —
COMBINED



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

The Hallmarks of Alzheimer's

1 Plaques



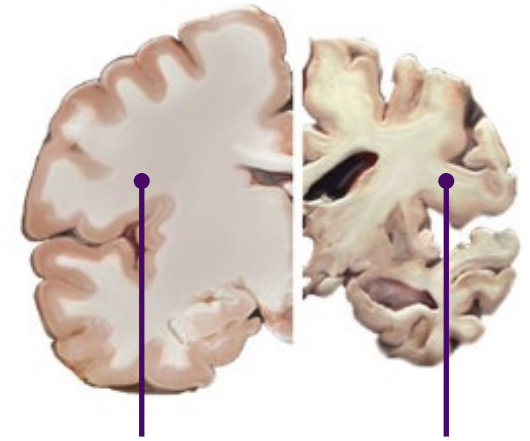
Made up of **beta amyloid**

2 Tangles



Made up of **tau**

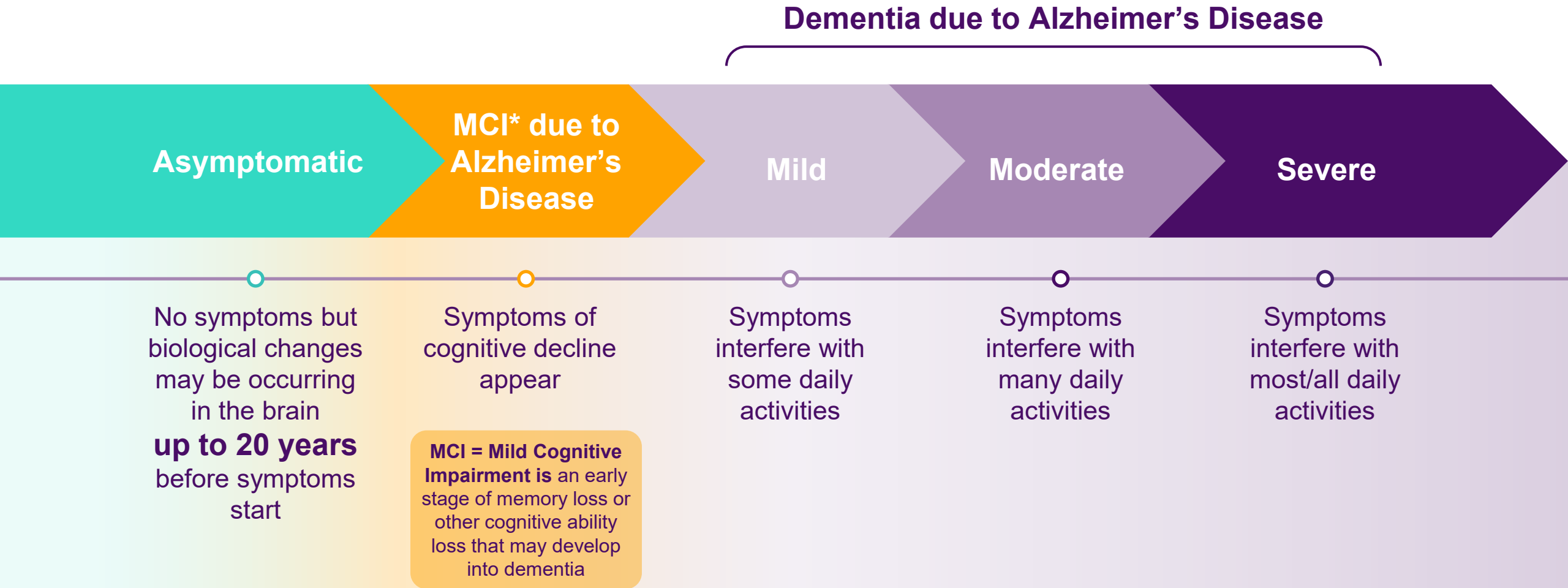
3 Brain Cell Death



Healthy
brain

Advanced
Alzheimer's

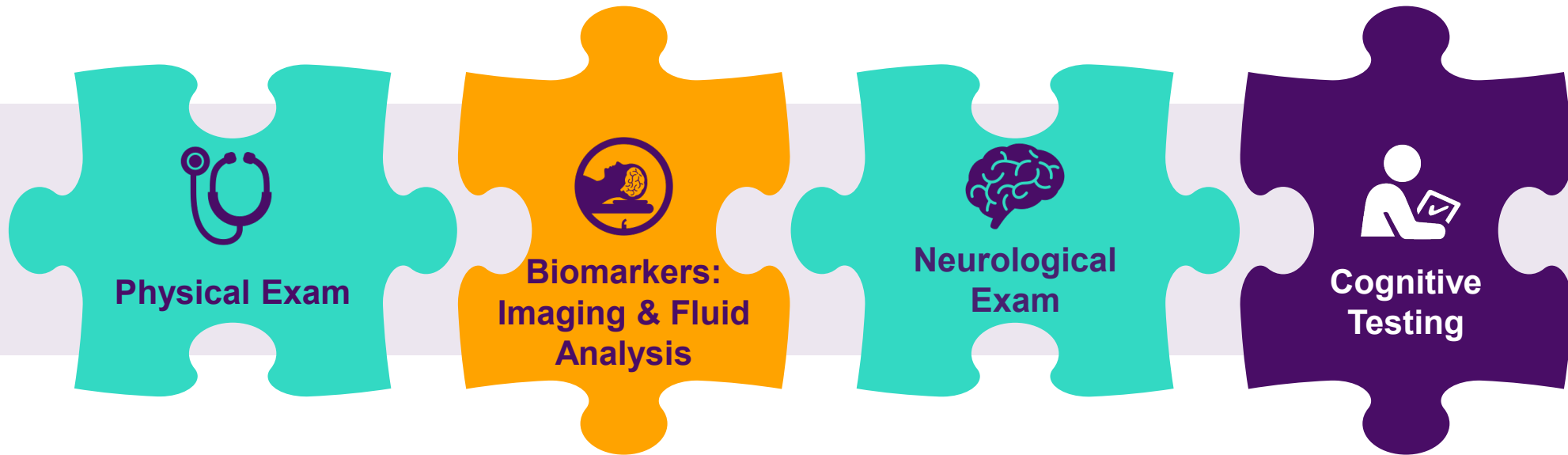
Alzheimer's Disease is a Continuum



How is Alzheimer's Currently Diagnosed?

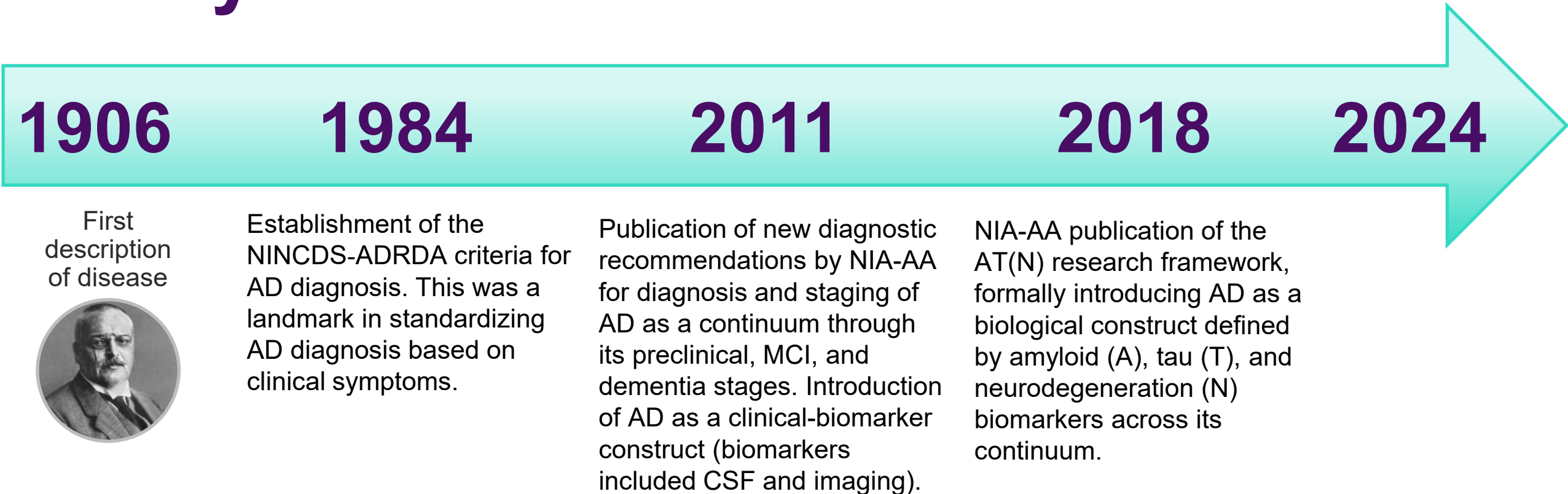
There is no single test that can determine if a person is living with Alzheimer's disease or another dementia.

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

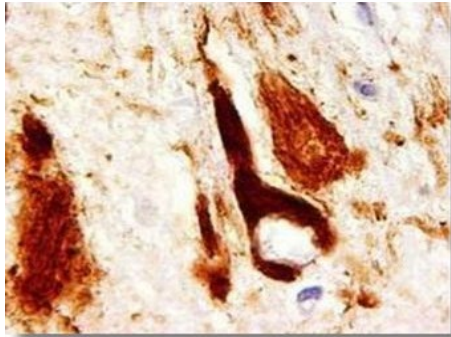
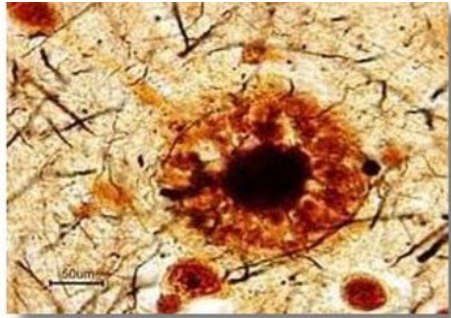
RESEARCH ARTICLE

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

Clifford R. Jack Jr.¹ | J. Scott Andrews² | Thomas G. Beach³ | Teresa Buracchio⁴ | Billy Dunn⁵ | Ana Graf⁶ | Oskar Hansson^{7,8} | Carole Ho⁹ | William Jagust¹⁰ | Eric McDade¹¹ | Jose Luis Molinuevo¹² | Ozioma C. Okonkwo¹³ | Luca Pani¹⁴ | Michael S. Rafii¹⁵ | Philip Scheltens¹⁶ | Eric Siemers¹⁷ | Heather M. Snyder¹⁸ | Reisa Sperling¹⁹ | Charlotte E. Teunissen²⁰ | Maria C. Carrillo¹⁸

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

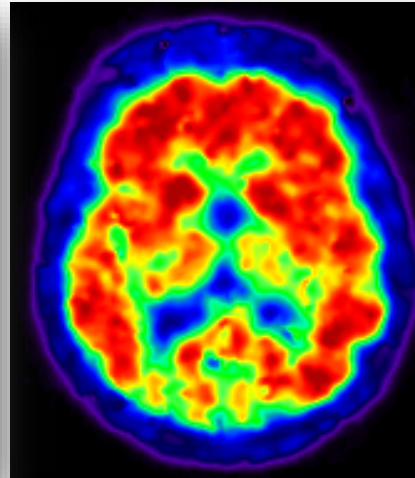
Biomarker Development for Hallmark Brain Changes



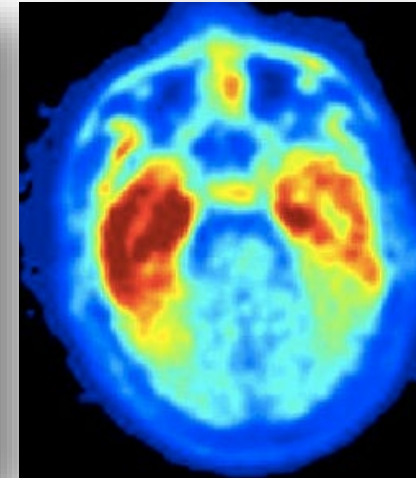
1906
Amyloid and Tau
Pathology



Late 1990s
CSF A β ,
Tau, p-Tau



Mid-late
2000s
Amyloid PET



Mid-late
2010s
Tau PET



2020s
Plasma A β ,
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

REVIEW ARTICLE

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

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

Oskar Hansson^{1,2} | Rebecca M. Edelmayer³ | Adam L. Boxer⁴ | Maria C. Carrillo³ | Michelle M. Mielke⁵ | Gil D. Rabinovici⁴ | Stephen Salloway⁶ | Reisa Sperling⁷ | Henrik Zetterberg^{8,9,10,11,12} | Charlotte E. Teunissen¹³

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

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RESEARCH ARTICLE

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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

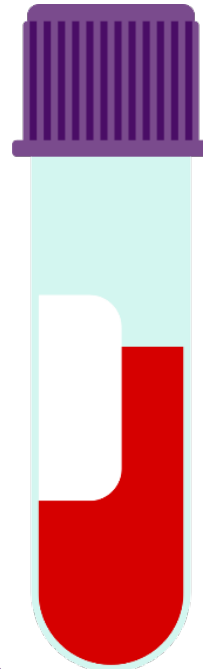
Blood tests are demonstrating to be valuable tool to help streamline clinical trials enrollment

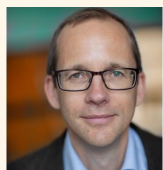
Commercial

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
Oskar Hansson, MD, PhD



Co-Chair
Heather Whitson, MD



Henrik Zetterberg, MD, PhD



Charlotte Teunissen, PhD



Hamid Okhravi, MD



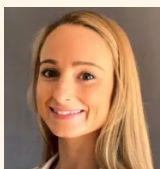
Laura Allen, NP



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



Co-Chair
Dorene Rentz, PhD



Co-Chair
Fred Ko, MD



Ambar Kulshreshtha, MD



Brent Forester, MD



Sharon Brangman, MD



Jennifer Gatchel, MD, PhD



Karen Bell, MD



Maria Carrillo, PhD



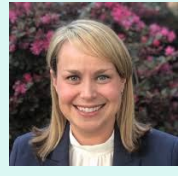
Dana Jones, F-NPC



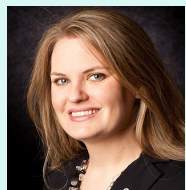
Martin Sliwinski, PhD



Peter Snyder, PhD



Noelle L. Fields,
PhD, LCSW



Heather Snyder, PhD



Eric Tangelos, MD



Malavika Tampi, MPH

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)

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)					

* Suvorexant approved for insomnia not AD but safe and effective in AD population.

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

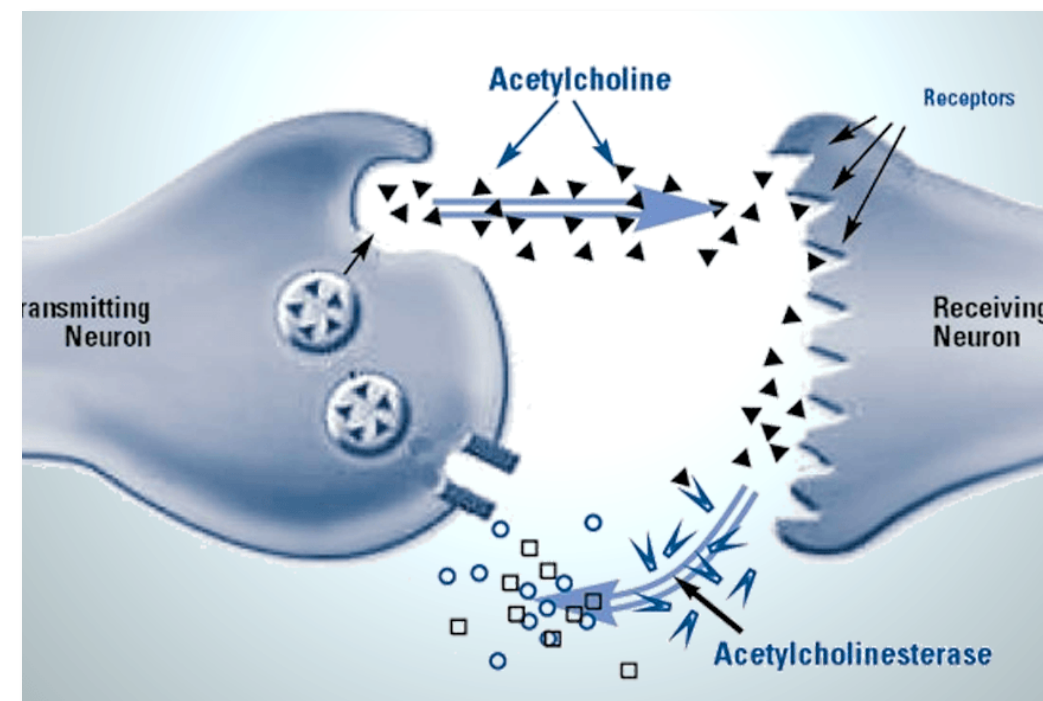
Cholinesterase inhibitors:

- 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



FDA-Approved Therapies for Alzheimer's

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2020	suvorexant* (Belsomra)					
2023	brexpiprazole (Rexulti)					

* Suvorexant approved for insomnia not AD but safe and effective in AD population.

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

suvorexant (Belsomra®)

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

Merck gets Alzheimer's label claim for insomnia drug Belsomra

Alzheimer's patients typically experience poor sleep



Article by
[Phil Taylor](#)

4th February 2020

brexpiprazole (Rexulti®)

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

PSYCHIATRICNEWS

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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>

FDA-Approved Therapies for Alzheimer's

First description of disease 1906



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Cognition and Function

Treat Symptoms:
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2020	suvorexant* (Belsomra)					
2023	lecanemab (Leqembi)					
2023	brexpiprazole (Rexulti)					
2024	donanemab (Kisunla)					

* Suvorexant approved for insomnia not AD but safe and effective in AD population.



Deeper Dive: A New Phase of Treatment



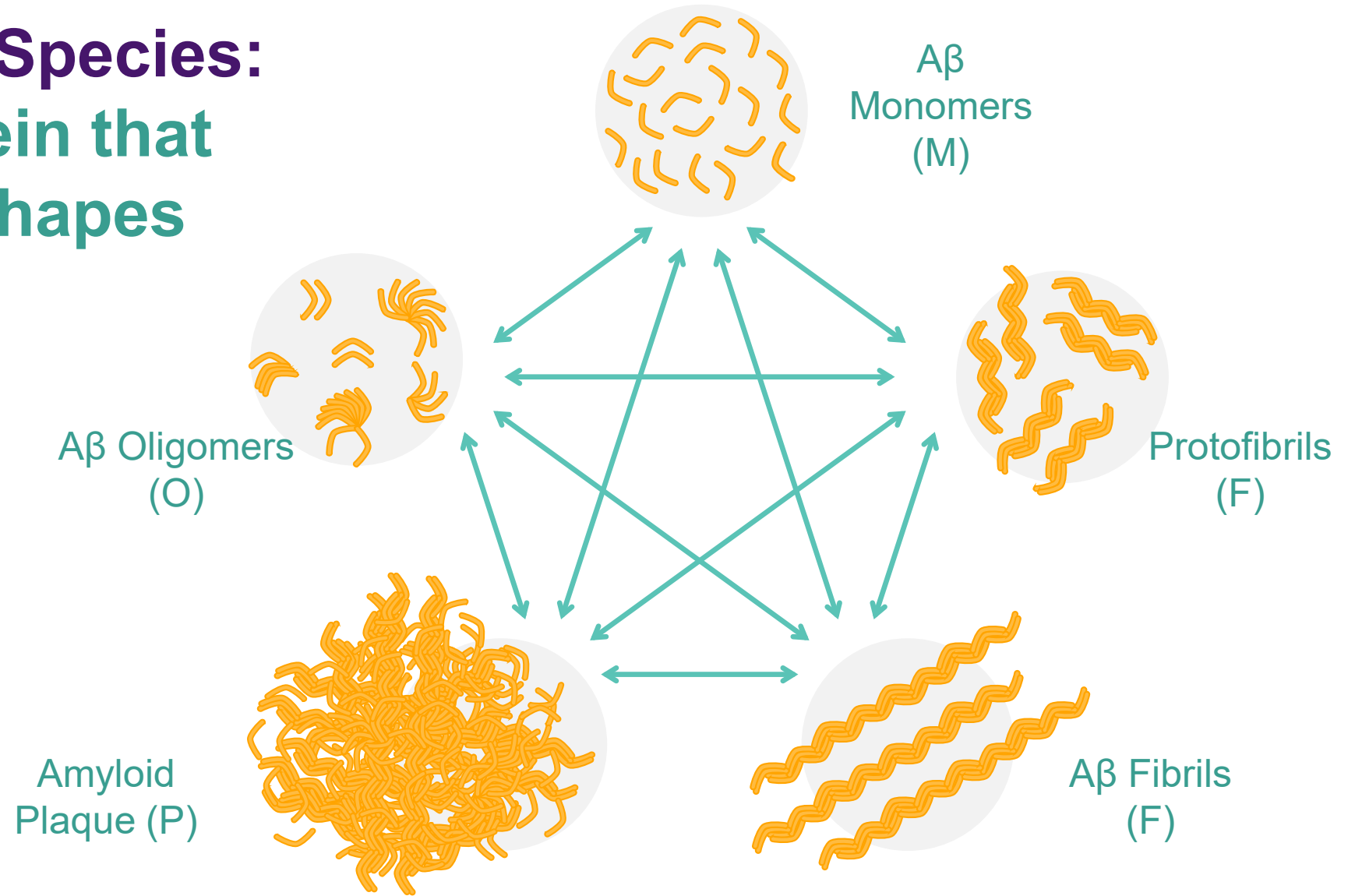
**lecanemab
(Leqembi)**

Approved in 2023
Targets Beta Amyloid

**donanemab
(Kisunla)**

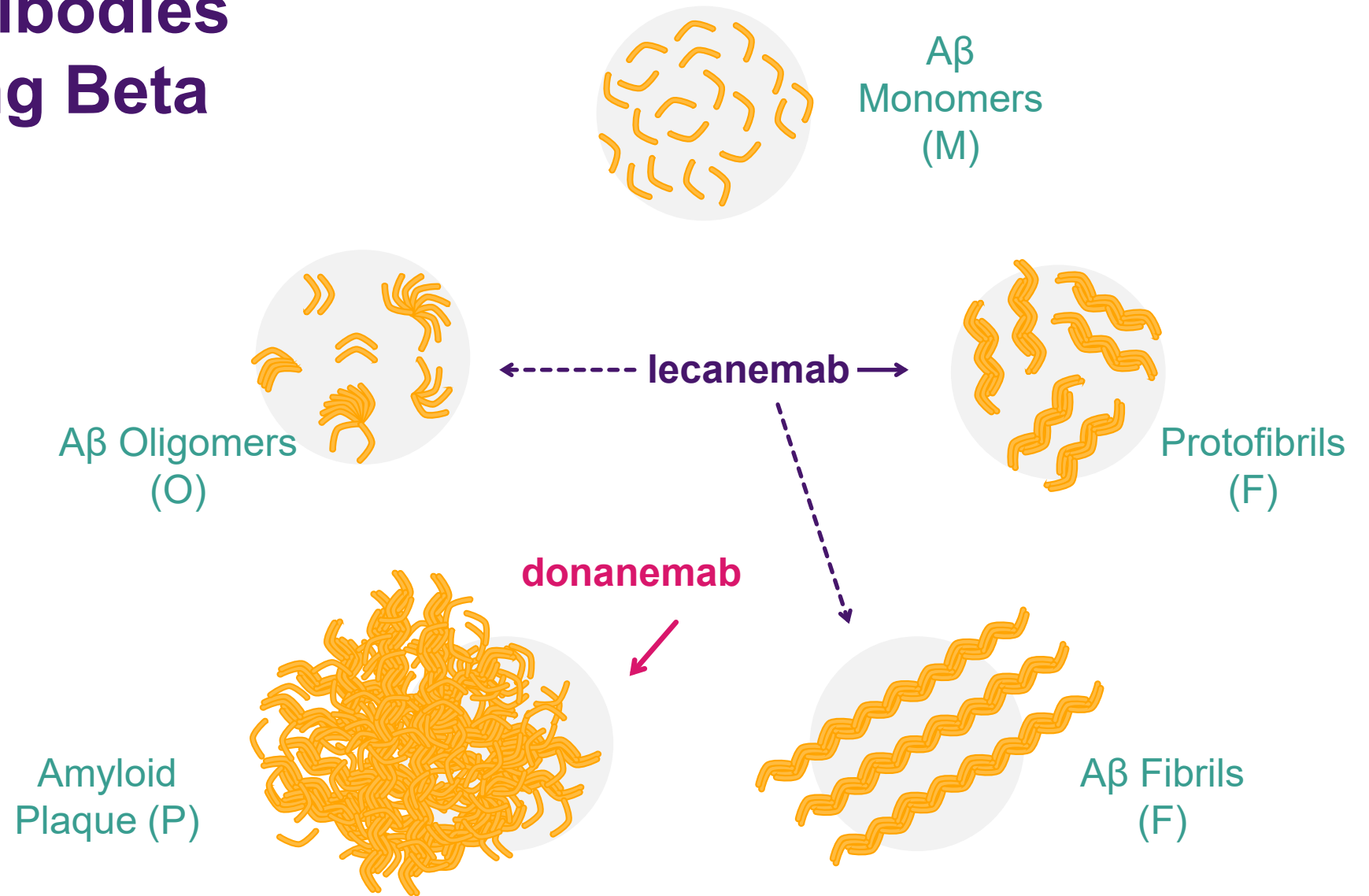
Approved in 2024
Targets Beta Amyloid

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



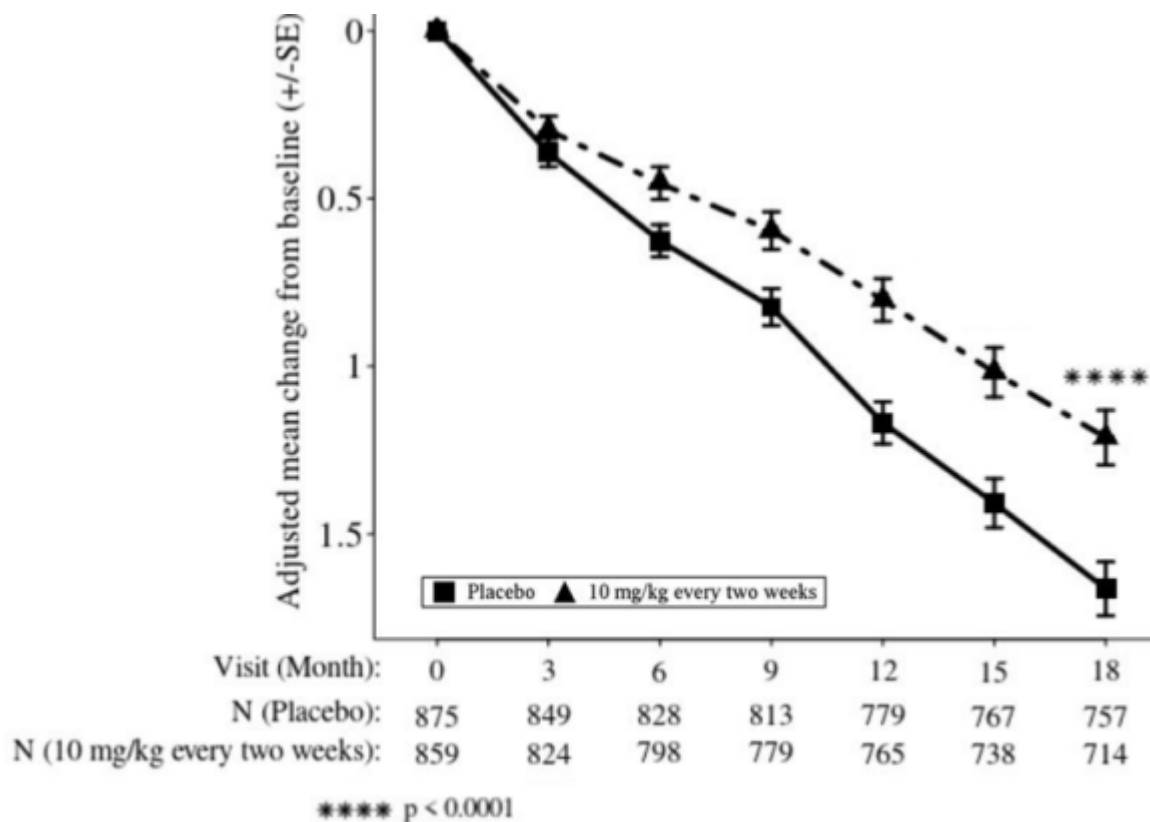
Monoclonal Antibodies (mAbs) Targeting Beta Amyloid

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

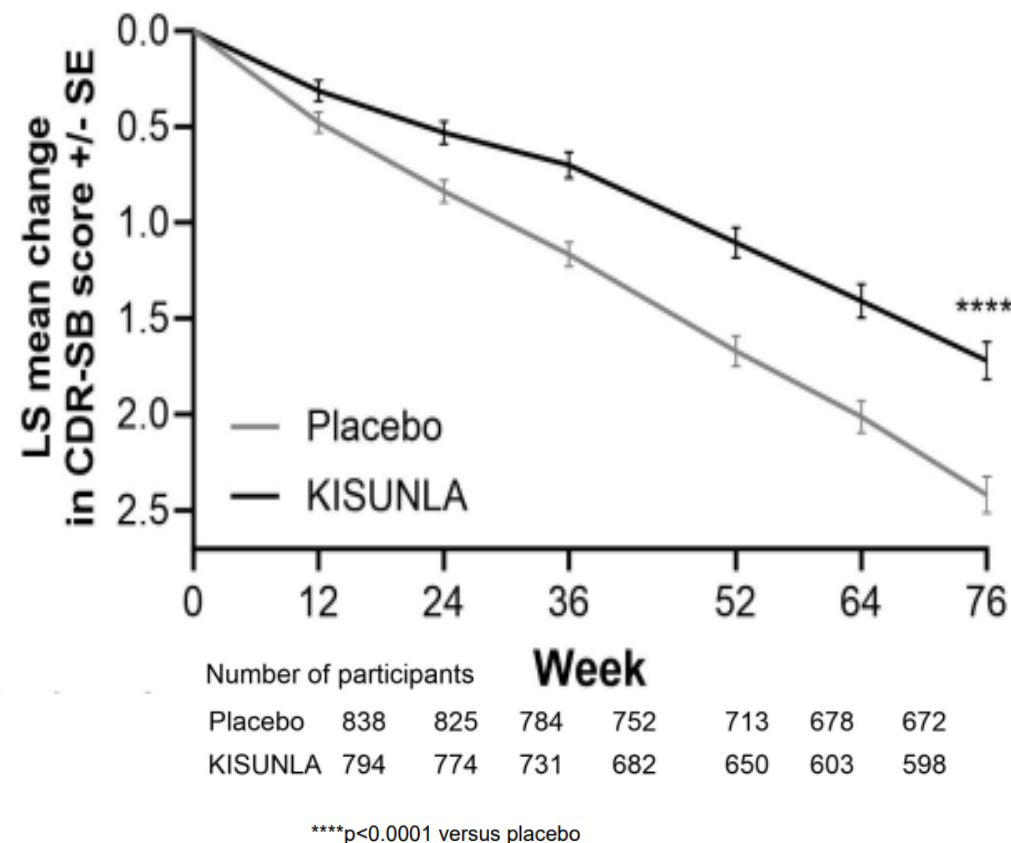


CDR-SB across FDA-approved anti-amyloid therapies

lecanemab (Leqembi)



donanemab (Kisunla)



Prescribing Information for Newly Approved Treatments: Warnings & Precautions

Amyloid Related Imaging Abnormalities

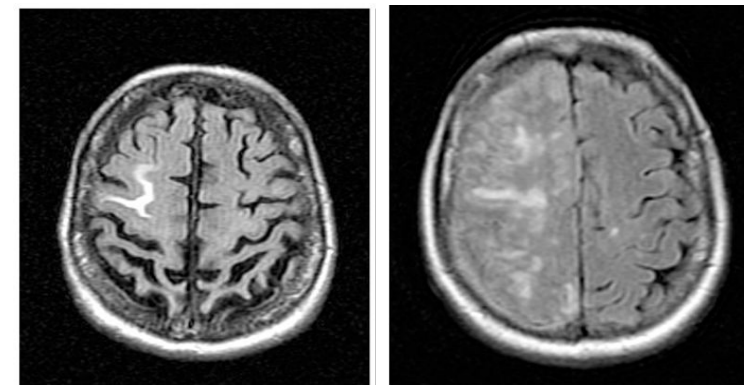
(ARIA): Enhanced vigilance monitoring for ARIA is recommended during first 14 weeks

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

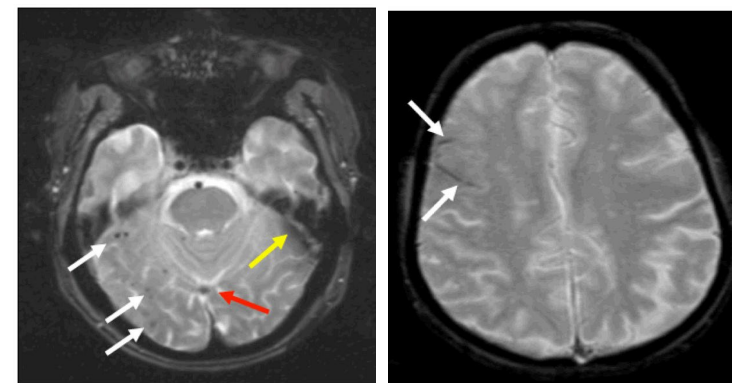
Amyloid-Related Imaging Abnormalities (ARIA)

- **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* ϵ 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

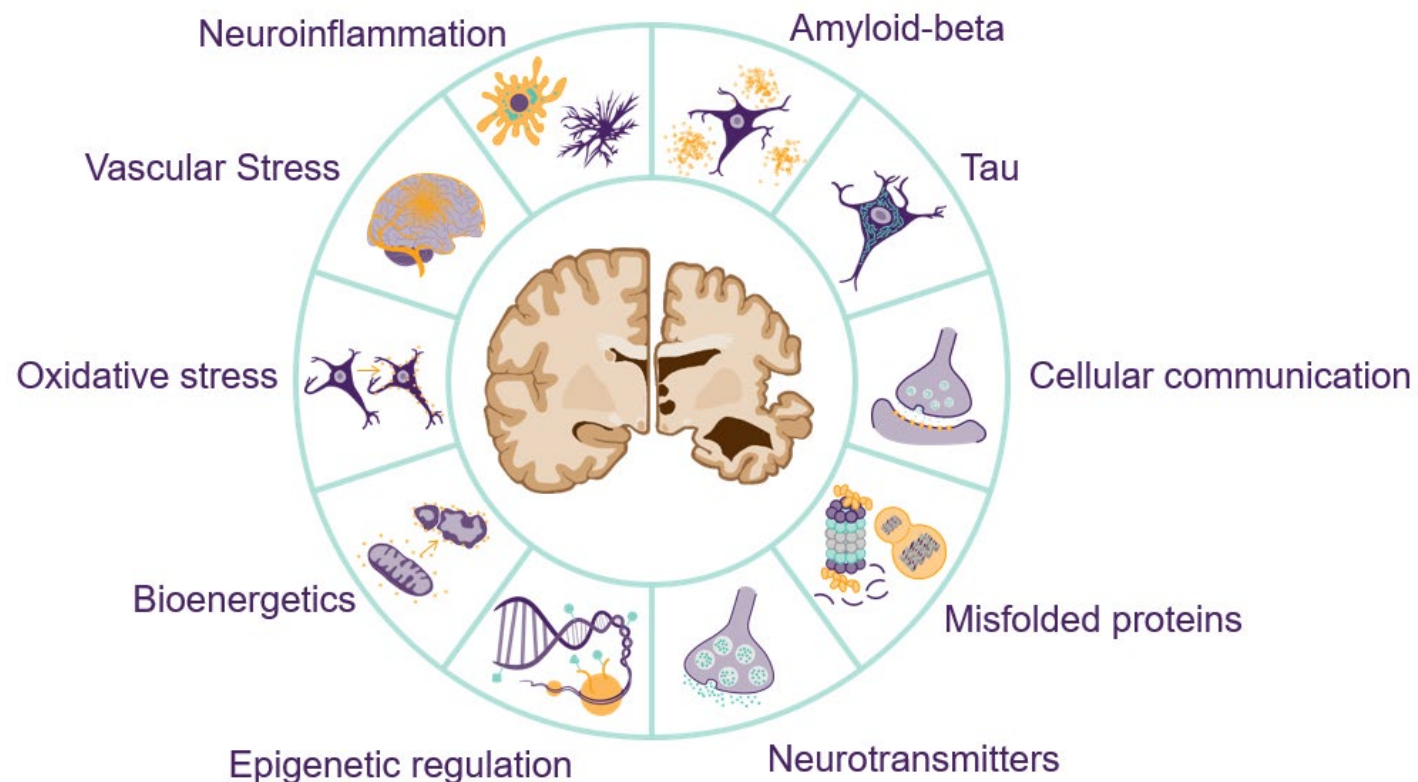
lecanemab
(Leqembi®)

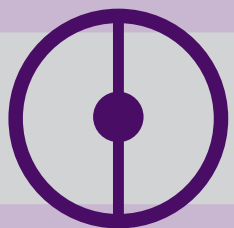
Targets
amyloid



2024

donanemab
(Kisunla™)





2024 Alzheimer's Drug Development Pipeline

148

Phase 1 Clinical Trials

221

Phase 2 Clinical Trials

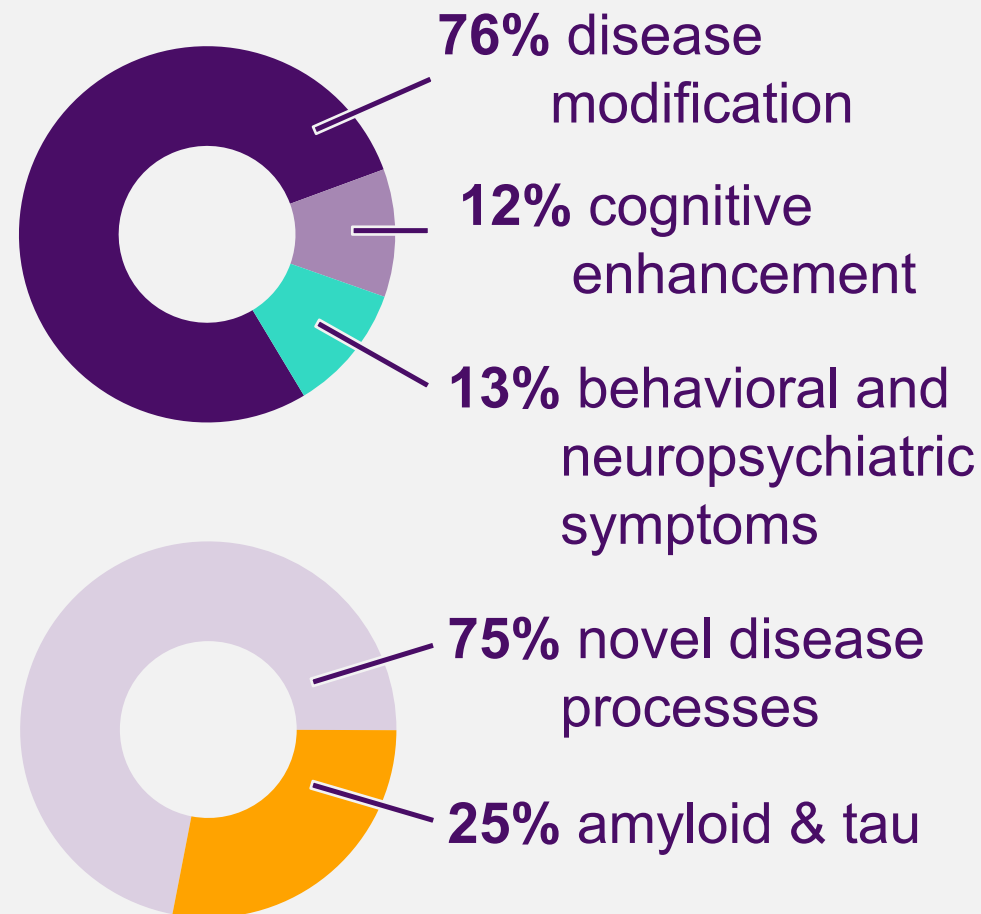
64

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.

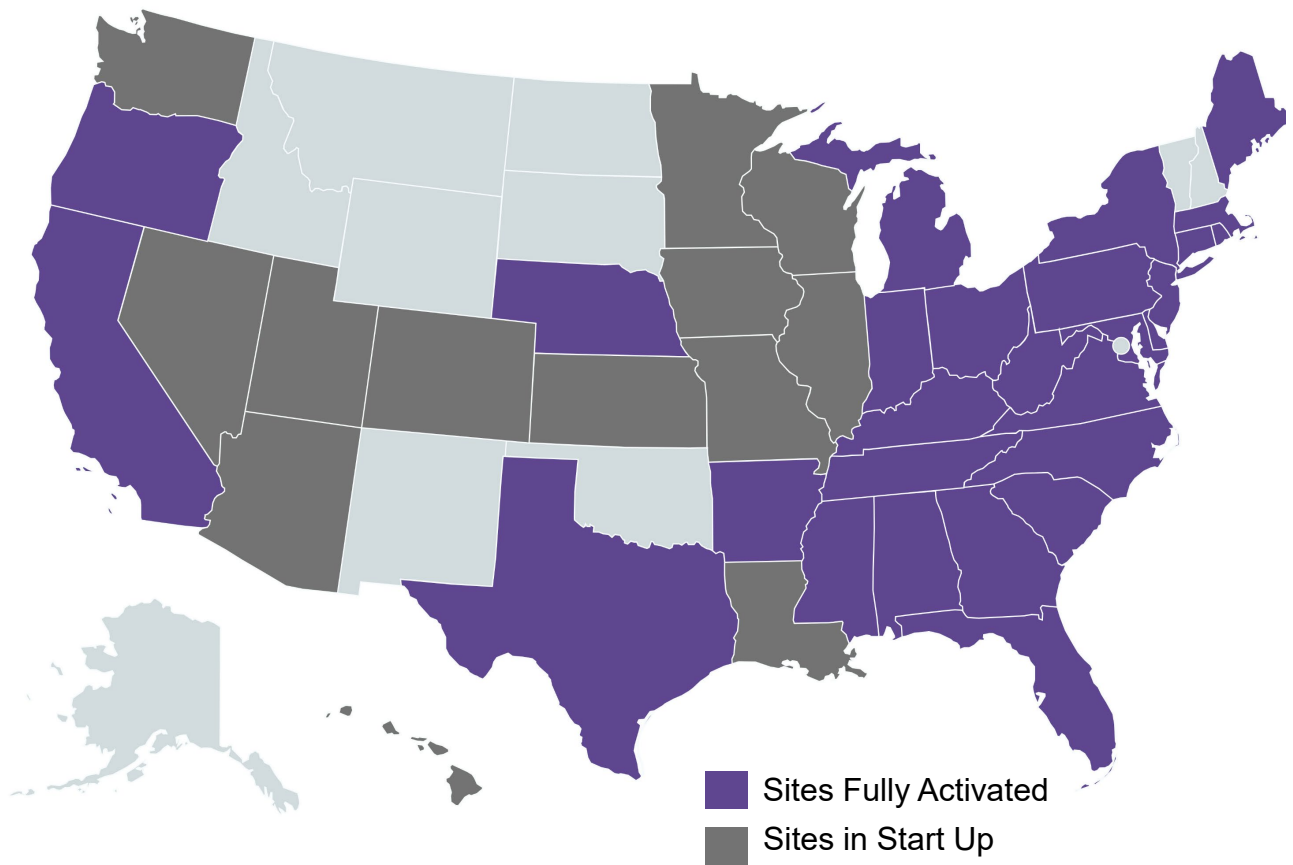


Questions ALZ-NET could address:

- 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

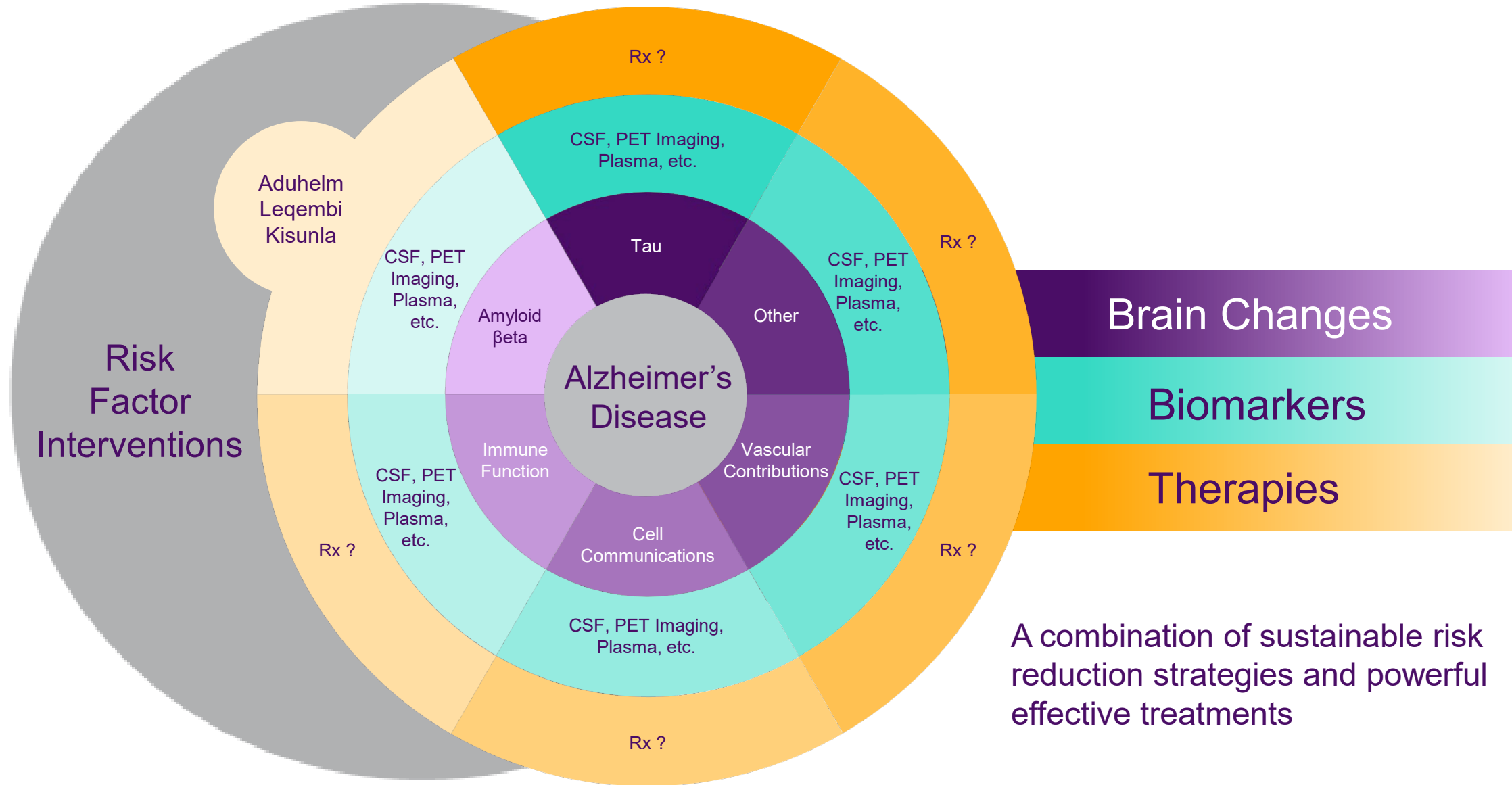
More than **165 additional clinical sites** are in various stages of startup

10 new sites likely to activate within the next few weeks

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

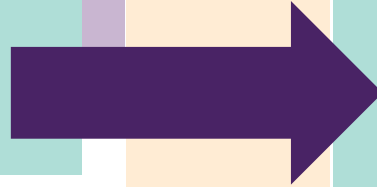


New Era of Research, Treatment and Care...



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[®]

ALZHEIMER'S  ASSOCIATION[®]

POWERED BY CenterWatch iConnect[™]

**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



Research at the Association | alz.org/research



Join a Clinical Trial | 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 INTERNATIONAL CONFERENCE®

SAVE THE DATE

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

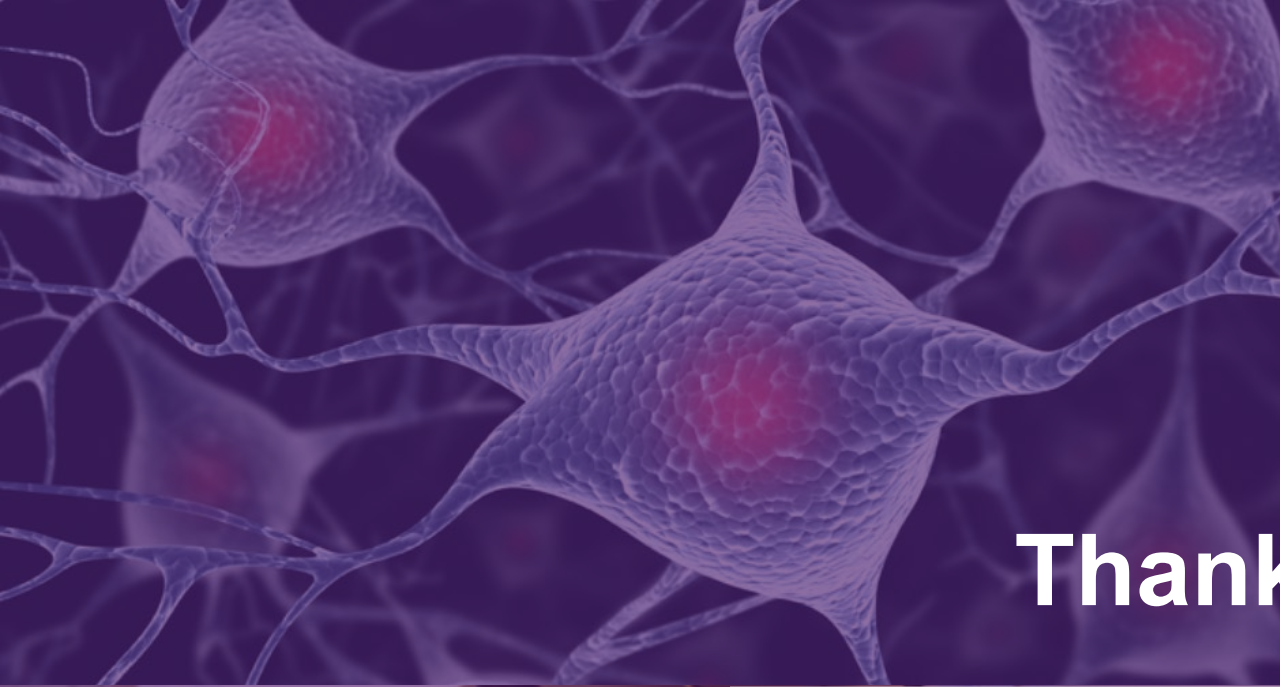
July 25-26

Educational Workshops and Preconferences

July 27-30

Exhibits

alz.org/AAIC



Thank You!



Questions & Discussion

