



**Karolinska  
Institutet**

# **Alzheimer's disease; Challenges & Opportunities**

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*AlzeCure,  
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# Dementia prevalence globally and in Sweden

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Globally, more than 55 million people have dementia, of which Alzheimer disease may contribute to 60–70% of cases.

- Every year, there are nearly 10 million new cases.

Sweden:

- 150 000 persons with dementia, out of which
  - 120 000 with Alzheimer disease, (90 000 in mild to moderate stages)

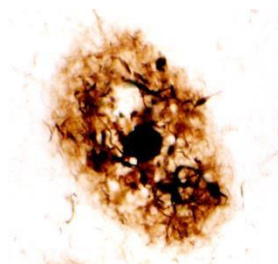
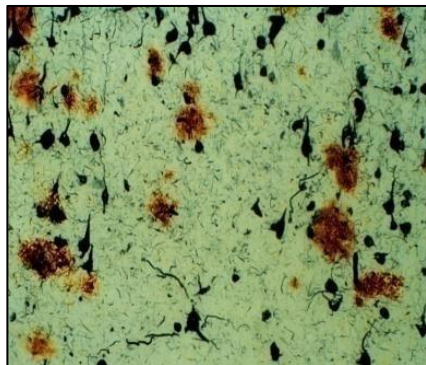
In addition;

- 100 000 persons with mild cognitive impairment, (MCI)

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- The cost for our society (Sweden): Approx 80 billions SEK/yr

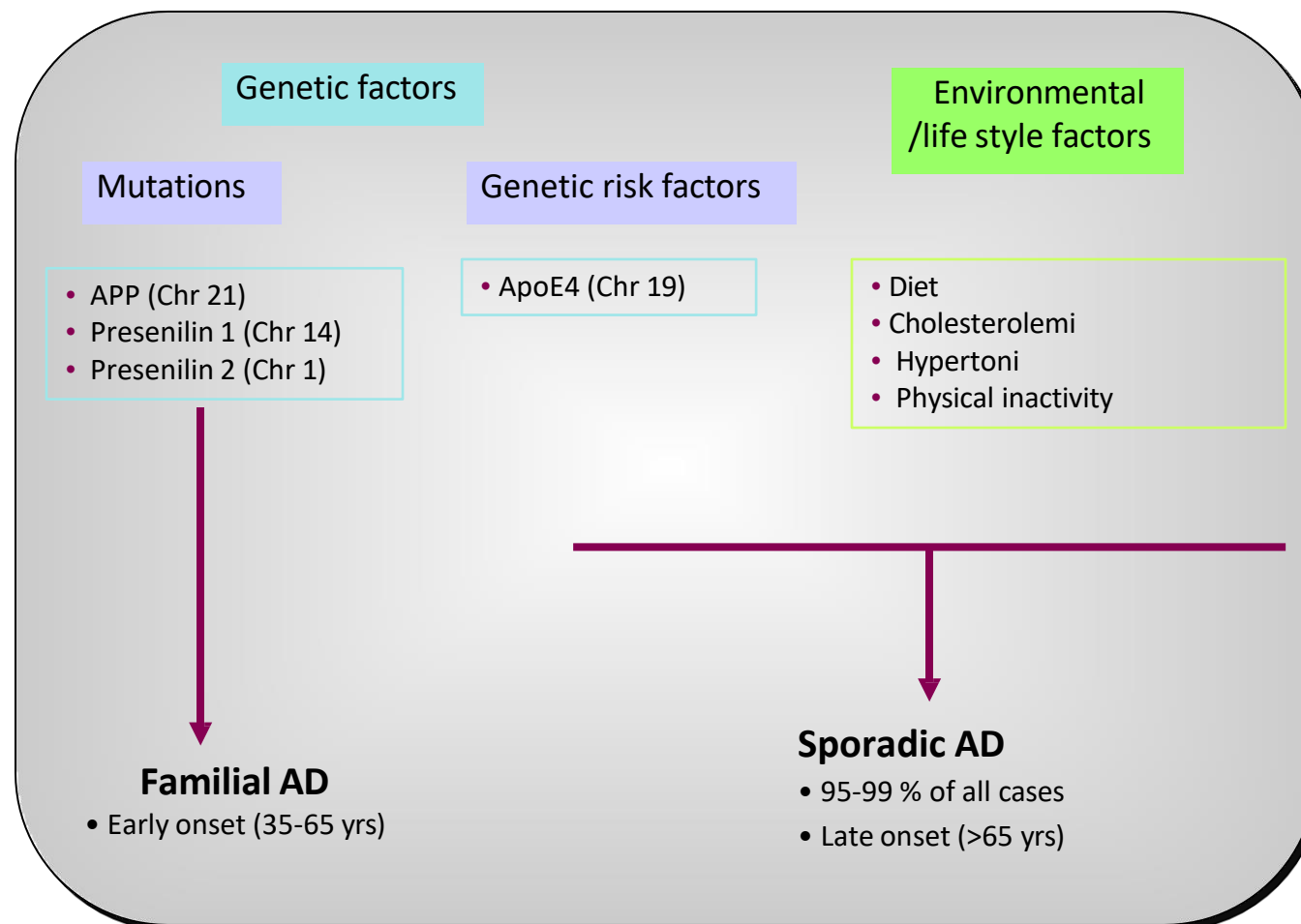
# Alzheimer's disease



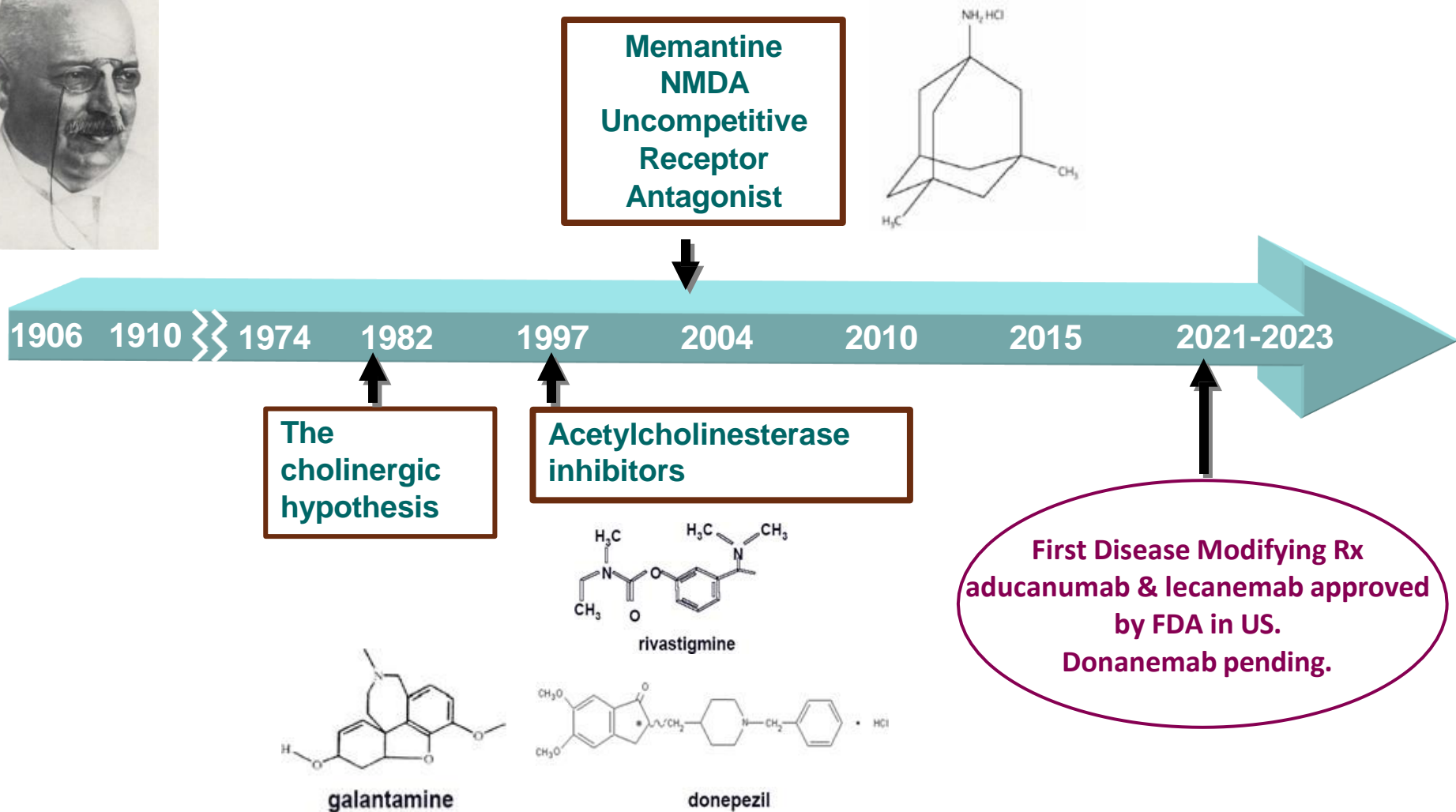
Amyloid beta plaques



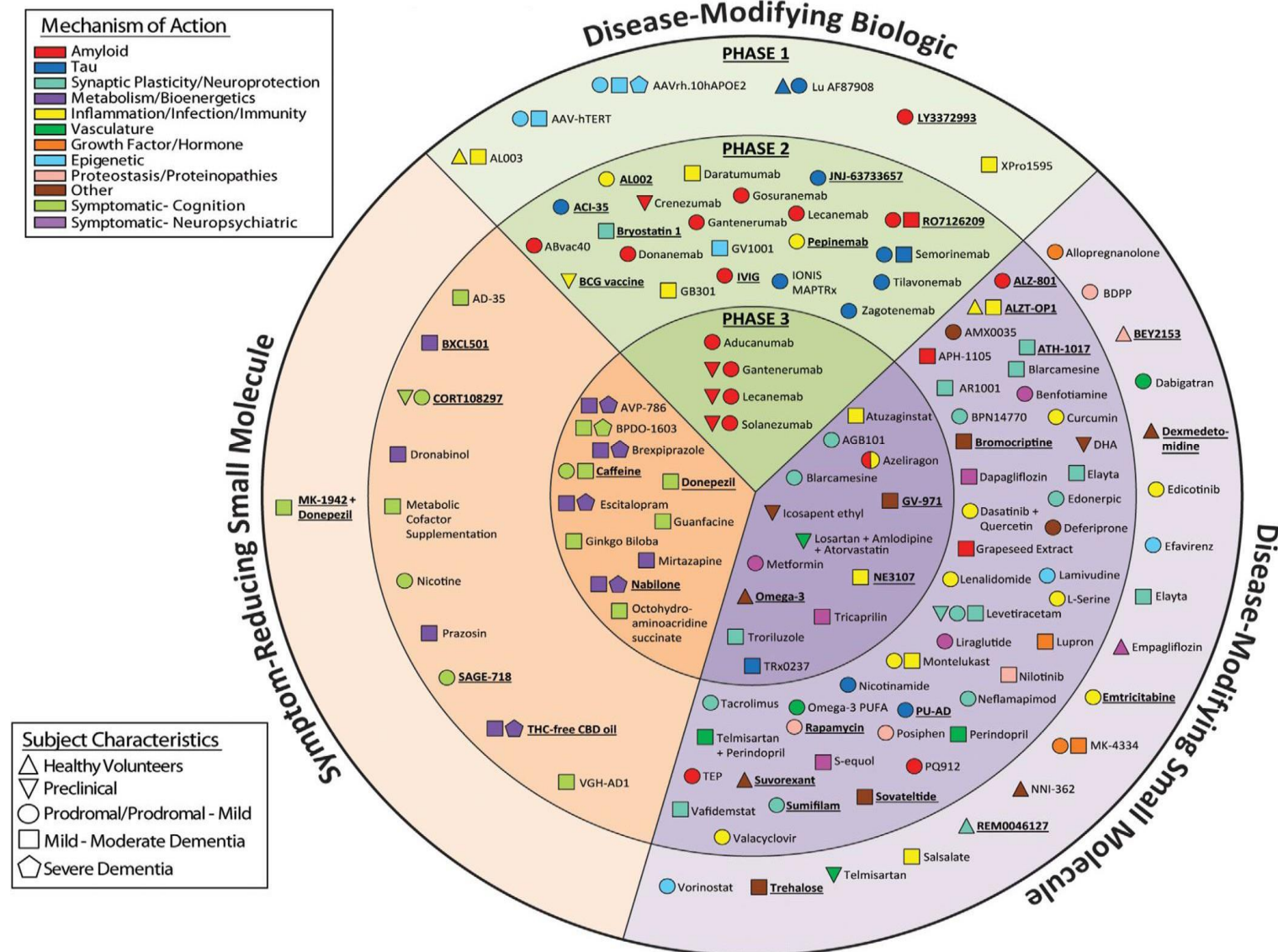
Neurofibrillary tangles



# Therapy in AD: The first hundred years and looking forward.....



## 2021 Alzheimer drug development pipeline



- “Biologics” are generally derived from living organisms and include antibodies, vaccines, antisense oligonucleotides, and therapeutic proteins.
- “Small molecules” refers to drugs taken orally that are typically <500 daltons in size and can regulate a biological process.

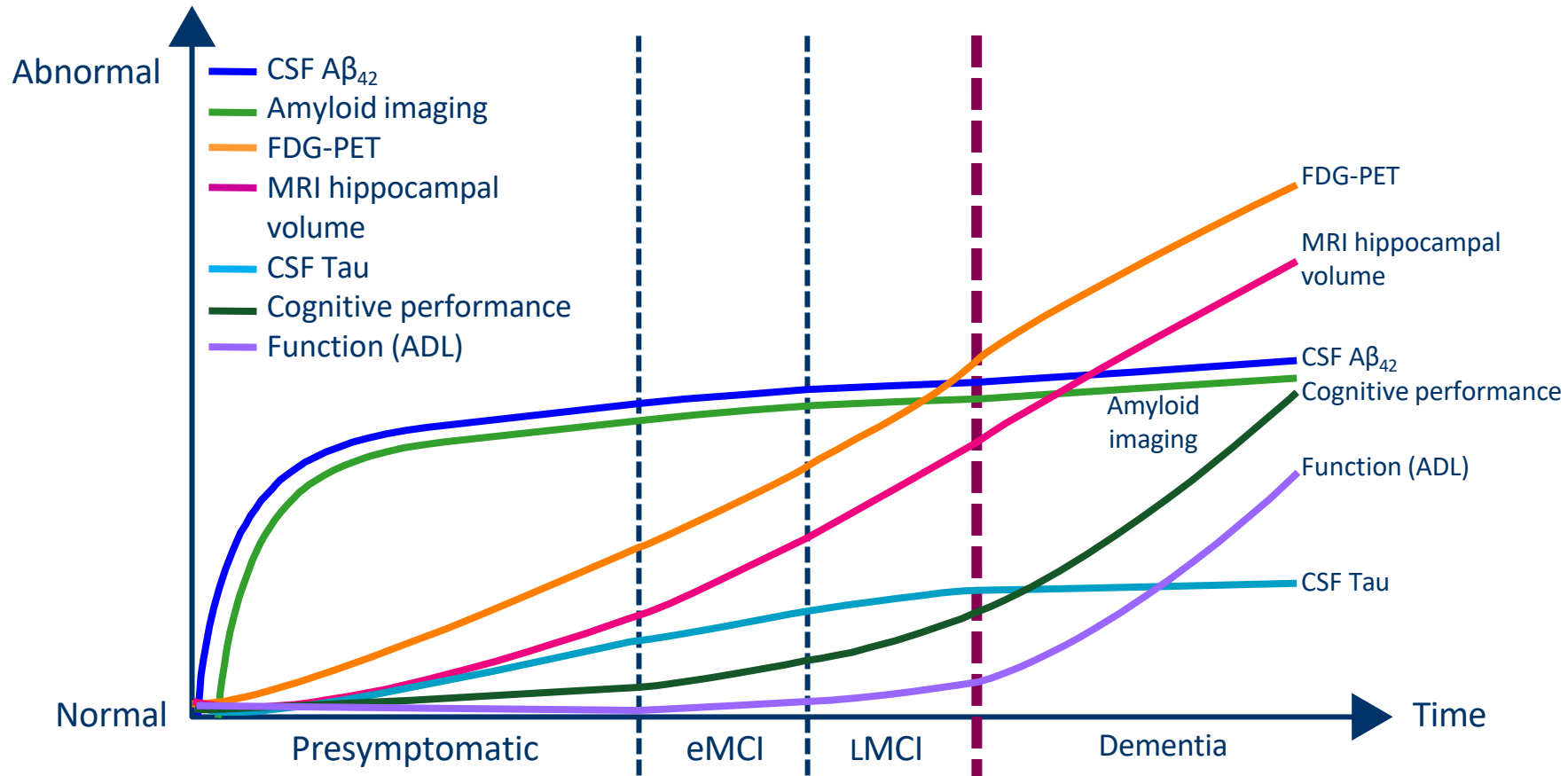
Cummings J et al. *Alzheimers Dement* (NY). 2021

# Important with early diagnosis!

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- ***For the patient;***
  - ➔ Explanation of symptoms
  - ➔ Practical future planning (eg economy, travels, retirement)
  - ➔ **Access to treatment before too much damage, take part in clinical trials**
- ***For the relatives;***
  - ➔ Same as above
  - ➔ Increased understanding
- ***For society;***
  - ➔ Patient “in the system”
  - ➔ Possibility to support the whole family
  - ➔ More safe planning, cost awareness

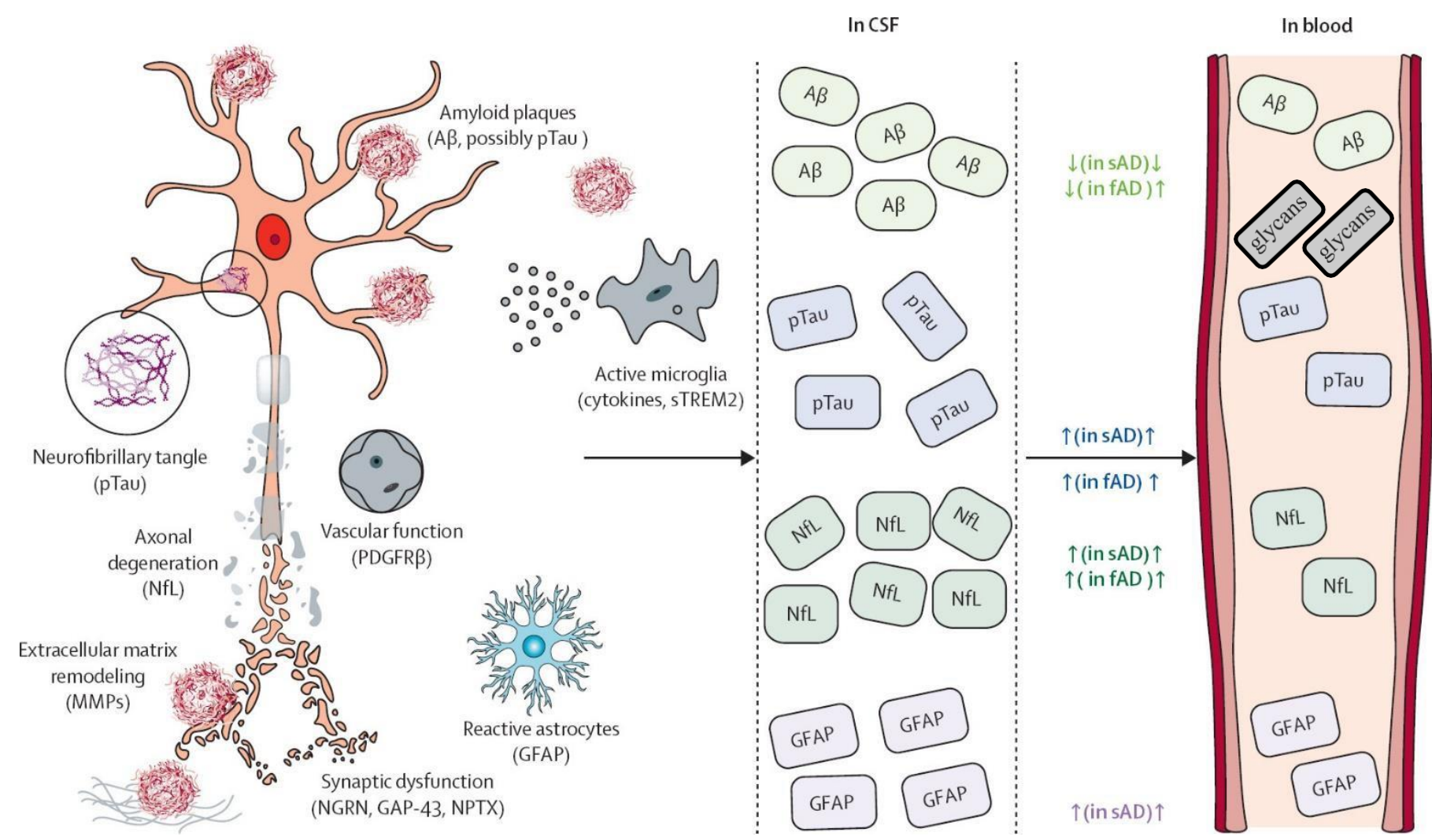
# AD progress and biomarkers enables early diagnosis



Aisen PS et al. *Alzheimers Dement* 2010



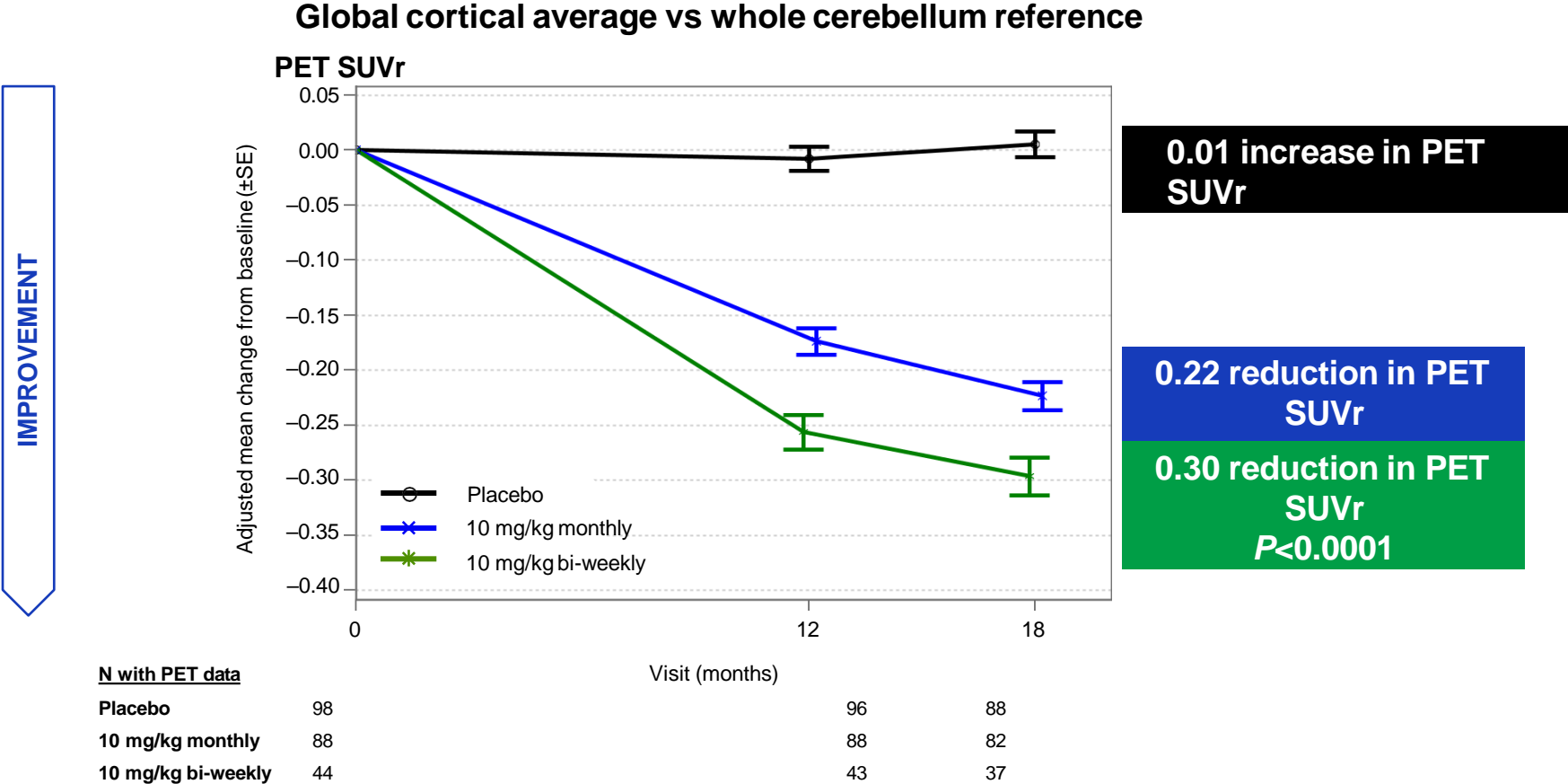
# Addition of blood/plasma biomarkers



C Teunissen, 2022, rev S Schedin-Weiss



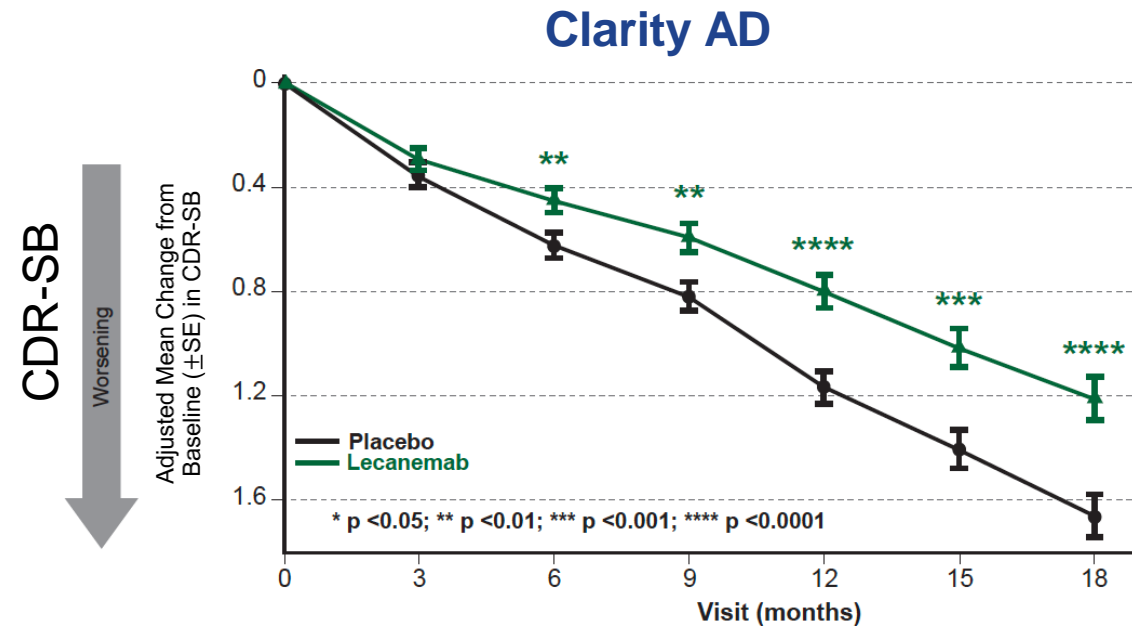
# Lecanemab phase 2 study showed reduced amyloid burden over 18 months (developed by BioArctic, Sweden)



Both AUC and Cmax are important. 81% of amyloid positive converted back to negative at highest dose (visual read) (presented at CTAD Oct 2018 by Eisai)

# Clarity AD (phase 3) Treatment Effect: CDR-SB

(Global Measure of Cognition and Function)



CDR-SB Domains	No. of Participants (placebo, lecanemab)		Adjusted Mean Difference	% Slowing	P Value
		<b>Favors lecanemab</b>			
Memory	875, 859		-0.077	27.5	0.00117
Orientation	875, 859		-0.081	28.1	0.00044
Judgement/Problem Solving	875, 859		-0.053	23.6	0.01008
Community Affairs	875, 859		-0.070	21.2	0.00524
Home and Hobbies	875, 859		-0.098	28.8	0.00018
Personal Care	875, 859		-0.067	29.9	0.01325

Adjusted Mean Difference versus Placebo (95% CI)

## Lecanemab Effect

- 27% slowing on CDR-SB
- Increased magnitude of separation over time (0.45 at 18 months)
- Effect seen across all CDR-SB domains

## CDR-SB Scale

- Patient and caregiver interview
- Rates 6 cognitive and functional domains
- Each domain scored from 0, 0.5, 1, 2 for range of 0-18
- Mild cognitive impairment and mild AD dementia tend to score 0.5 or 1 in each domain
- Baseline CDR-SB was 3.2

# Donanemab – last reported positive immunotherapy study

- Eli-Lilly, US reported in a press release May 3, 2023 positive top-line results of donanemab, from the phase 3 TRAILBLAZER-ALZ2 study
- Antibody treatment during 18 months targeting amyloid beta aggregates (plaques) in the brain
- 1,736 persons with mild cognitive impairment / mild dementia due to AD
- Result: 35% less cognitive and functional decline
- 31.4% reported side effects such as brain microbleeds (ARIA-H), (13.6% on placebo). Two cases of deaths related to treatment

# Lecanemab vs Donanemab

- Difference in study populations
- Different cognitive and ADL scales
- The only common scale is CDR-SB, but the outcome from this scale is also influenced by the different study populations

## In summary:

- These differences makes it difficult to properly compare the results from these two studies

## Side effects:

- Due to the same reasons, it is also difficult to properly evaluate the reported side effect from these two studies

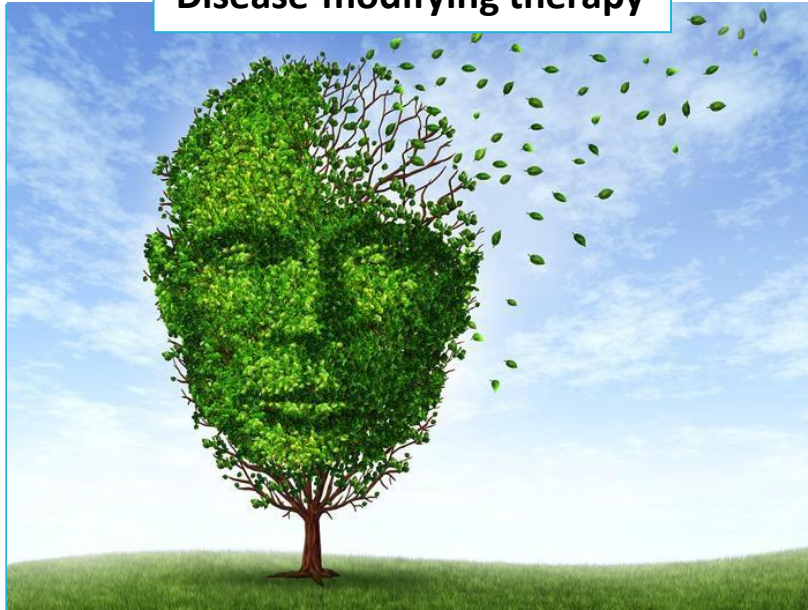
*However – these two studies represent very positive findings, giving hope for future treatment of AD. Most probably, a combined treatment with small molecules necessary.*

# AlzeCure Pharma's two Alzheimer platforms

- 1st-in-class properties & potential game-changers



Disease-modifying therapy



**Alzstatin<sup>®</sup>**

Gamma-Secretase-Modulators  
**Targeting Toxic Amyloid Production**  
- Novel Oral Small Molecule

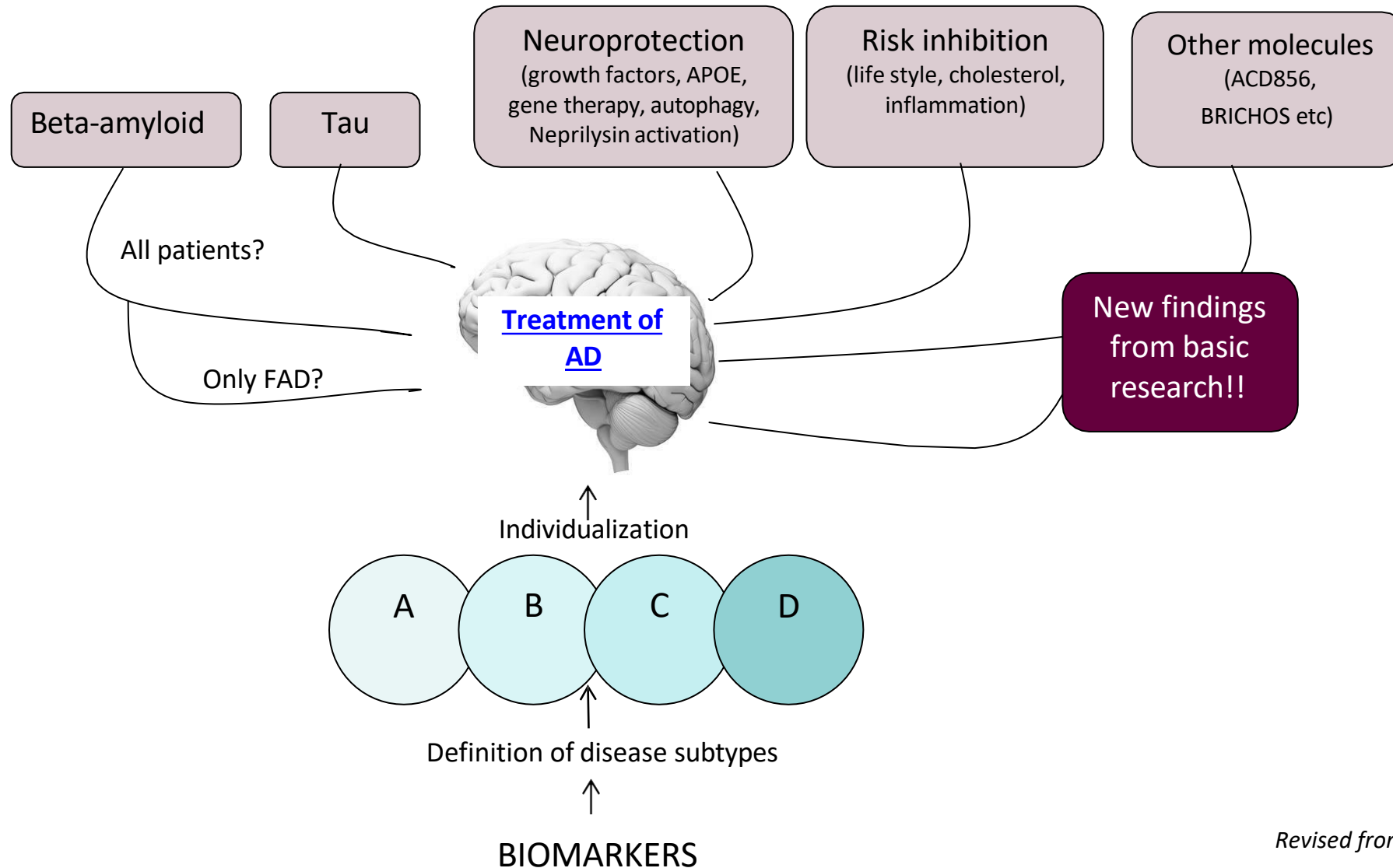
Symptomatic therapy



**NeuroRestore<sup>®</sup>**

Trk-PAMs  
**Improving Neuronal Function & Cognition**  
- Novel Oral Small Molecule

# Research – still needed & the only way forward to new treatment



*Revised from A Cedazo-Minguez*



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