May 17, 2023

Market Update
- On Alzheimer's & AlzeCure's Alzheimer's projects

AlzeCure

Today's presenters

Bengt Winblad
MD, Ph.D,
Professor at KI

EXPERIENCES

- Professor in Geriatrics and Aging at Karolinska Institute (KI)
- Education: MD, PhDs from Umeå University
- Research focus on treatment & care of dementia with focus on Alzheimer's

Johan Sandin
CSO
Ph.D.

- Expert in in vivo Pharmacology with 16 years experience from the drug discovery industry within Neurology
- Education: Ph.D. in Neuropharmacology, Karolinska Institute

Pontus Forsell
Head of Discovery & Research,
Ph.D.

- Expert in drug screening with +20 years of experience from industrial research and drug development within CNS and Pain
- Education: Ph.D. in Medical Biochemistry & Biophysics from Karolinska Institute

Martin Jönsson
CEO

- Extensive experience in various senior management positions with >20 years of international experience in the industry
- Education: MSc in BA from Lund University, Ottawa, Canada & Freiburg, Germany

AlzeCure

MARKET UPDATE
- Alzheimer's Disease, Alzstatin & NeuroRestore

- 10:00 Welcome address & agenda – Martin Jönsson, CEO, AlzeCure
- 10:02 **AlzeCure Pharma: Overview, vision & update** – Martin Jönsson, CEO, AlzeCure
- 10:10 **Alzheimer's disease; Challenges & Opportunities** – Professor Bengt Winblad, M.D., PhD, Karolinska Institute
- 10:25 **Alzstatin: Background & evolution** - Johan Sandin, PhD, CSO, AlzeCure
- 10:45 **NeuroRestore: Background & data supporting disease modifying effects** Pontus Forsell, PhD, Head of Discovery & Research, AlzeCure
- 11:05 **Panel discussion & QnA** – Lead by Ludwig Sjöström, FinWire
- 11:25 **Concluding remarks** – Martin Jönsson, CEO, AlzeCure

AlzeCure

AlzeCure Pharma – in brief

- Working in **Alzheimer's Disease** (AD) and **Pain** – Hugh unmet medical need & multi-billion sales potential
- Spin-out from **AstraZeneca** – as a result of their exit from the CNS area
- Founded in **2016**, out of a research foundation sponsored by **Alzheimerfonden**
- **Experienced team** with extensive background within pharma industry
- Based at Novum Science Park, **Karolinska Institute**, Stockholm, Sweden

- Three project platforms with multiple **small molecule** candidates with **first-in-class properties**
  - **Alzstatin®** – An innovative preventive & disease-modifying treatment against Alzheimer's (AD)
  - **NeuroRestore®** – A novel symptomatic treatment for cognitive disorders, e.g. AD with disease modifying potential
  - **Painless** – Innovative projects for osteoarthritic & neuropathic pain
- Listed on **Nasdaq First North Premier** Growth Market since Nov. 2018 (Ticker: ALZCUR)

AlzeCure

Our Business Model

- We are a **Research & Development** company
- Research & **develop through early clinical phase** and then **to out-license** or partner on our projects
- Gain incomes through:
  - **Upfront payments**
  - **Milestone payments**
  - **Royalties** on sold products

AlzeCure

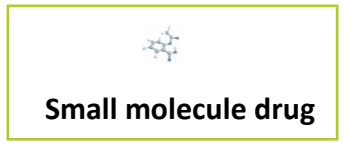
Small molecule drugs – AlzeCure's approach for increased success

DIFFERENCES BETWEEN SMALL MOLECULES & BIOLOGICS*

SMALL MOLECULE DRUG

LARGE BIOLOGIC

AlzeCure focus



Monoclonal antibody
c. 25,000 atoms

Additional benefits:
- Oral medications
- Low production costs
- …

Smaller molecules can have increased likelihood of penetrating the Blood Brain Barrier

*) Illustrative size

A pipeline of small-molecule programs

– Multiple candidates increase chance of success

Platform	Candidate	MoA	Indication	Research	Preclinical	Phase I	Phase II	Phase III
NeuroRestore®	ACD856	Positive allosteric modulator (PAM) of Trk-receptors	Alzheimer's Disease, Sleep disorders, TBI Parkinson's disease, Depression				**Positive read-out** Phase I trial Safety, Tolerability & Target engagement	
	ACD857	Positive allosteric modulator (PAM) of Trk-receptors	Alzheimer's Disease					
Alzstatin®	ACD679	Gamma secretase modulator (GSM)	Alzheimer's Disease					
	ACD680	Gamma secretase modulator (GSM)	Alzheimer's Disease			**New additional CD** ACD680		
PainLess	ACD440	TrpV1 antagonist	Neuropathic Pain					**Phase IIa** Planned read-out mid-2023
	TrkA-NAM	Negative allosteric modulator (NAM) of TrkA-receptors	Osteoarthritic Pain & other severe pain conditions					

Phase completed

Phase ongoing

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Progress & increased activity in the field of Alzheimer's disease

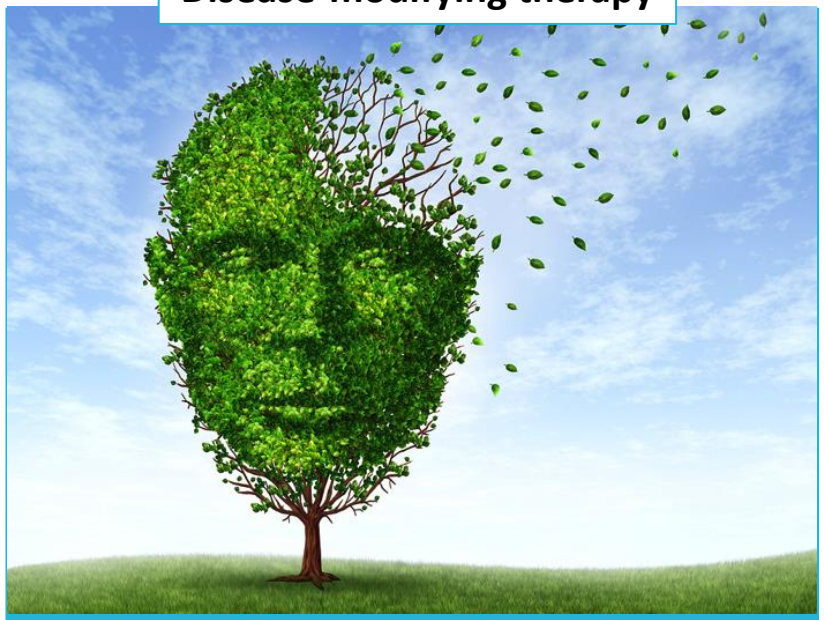
- Validation of the amyloid hypothesis
- Positive out-comes in clinical trials, incl in phase III
- New products being approved
- Vastly improved biomarkers & diagnostics
- Additional Big Pharma companies entering the field
- More funds and private equity investment in companies and projects
- …

AlzeCure

Two Alzheimer's platforms - 1st-in-class potentials & future game-changers

MEETING NEEDS OF AD PATIENTS – ADRESSING SHORT TERM NEEDS WITH LONG-TERM BENEFITS

Disease-modifying therapy



Alzstatin®

MoA: Gamma-secretase modulator

Targeting Amyloid Production

- *Novel Oral Small Molecule*

Symptomatic & pot. Disease-modifying therapy

NeuroRestore®

MoA: Trk-PAM

Improving Cognitive Function

- *Novel Oral Small Molecule*

AlzeCure

Karolinska Institutet Novum Science Park
Hälsovägen 7, 141 57 Stockholm
SWEDEN

www.alzecurepharma.com

AlzeCure

Alzheimer's disease;
Challenges & Opportunities

Bengt Winblad, Professor
Karolinska Institutet
Dept NVS
Center for Alzheimer Research
Div of Neurogeriatrics
Solna, Sweden

AlzeCure,
May 17, 2023

Dementia prevalence globally and in Sweden

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:

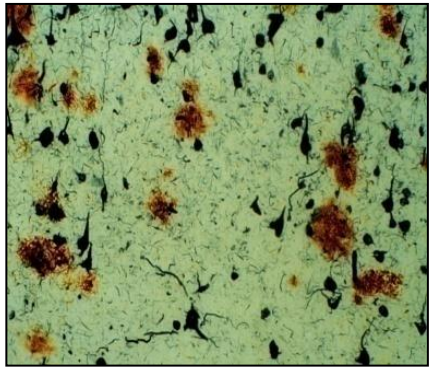
- 150 000 persons with dementia, out of which
  -120 000 with Alzheimer disease, (90 000 in mild to moderate stages)

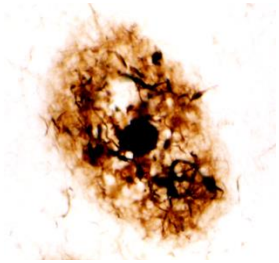
In addition;

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

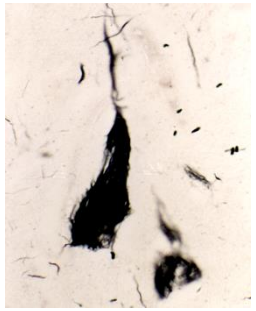
- The cost for our society (Sweden): Approx 80 billions SEK/yr

Alzheimer's disease

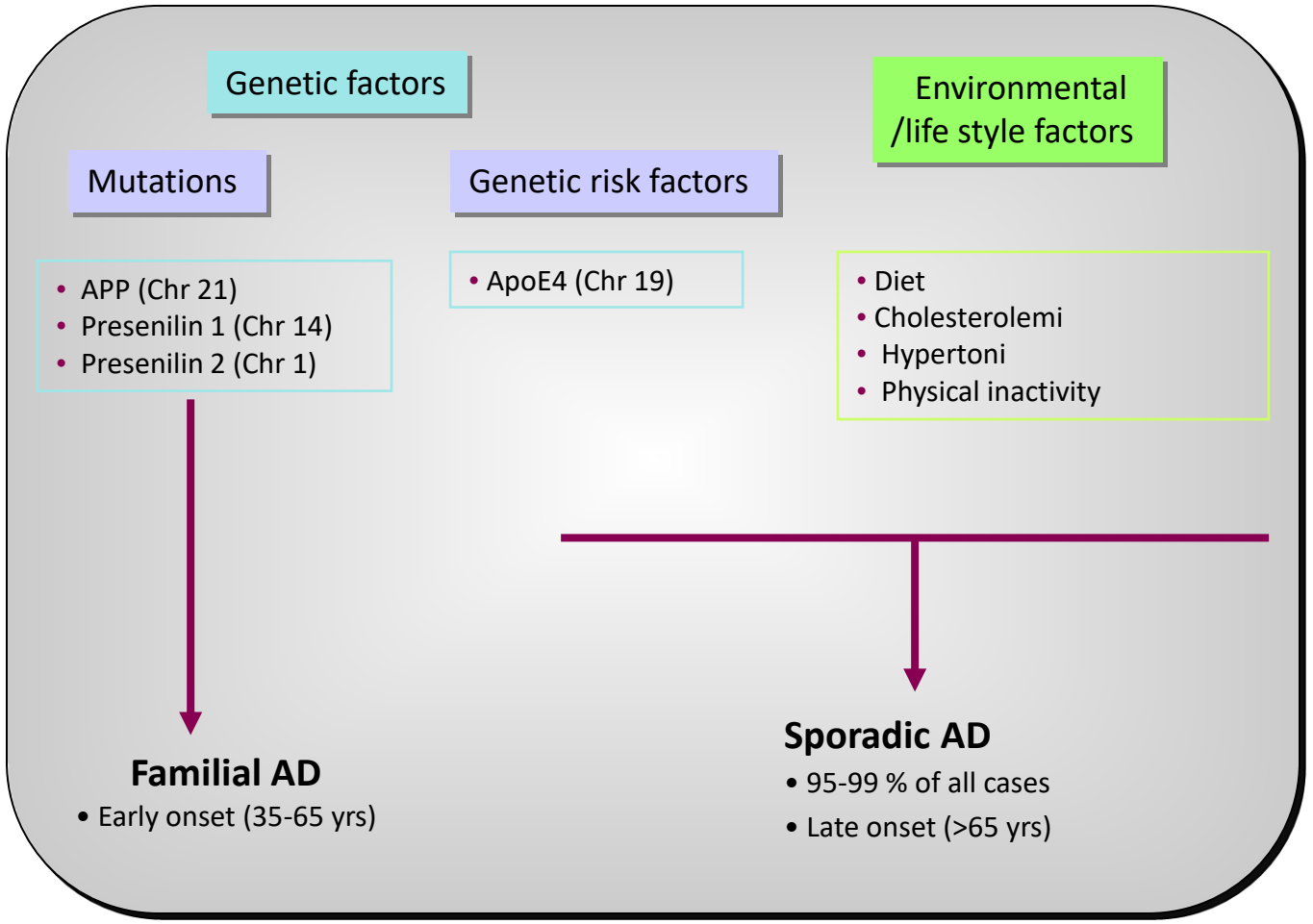




Amyloid beta plaques

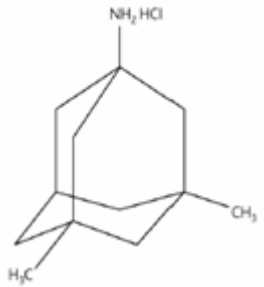


Neurofibrillary tangles



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

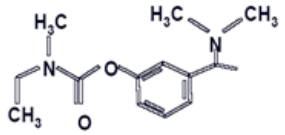
Memantine
NMDA
Uncompetitive
Receptor
Antagonist



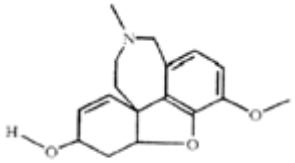
1906 1910 1974 1982 1997 2004 2010 2015 2021-2023

The cholinergic hypothesis

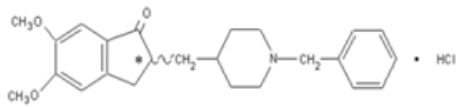
Acetylcholinesterase inhibitors



rivastigmine



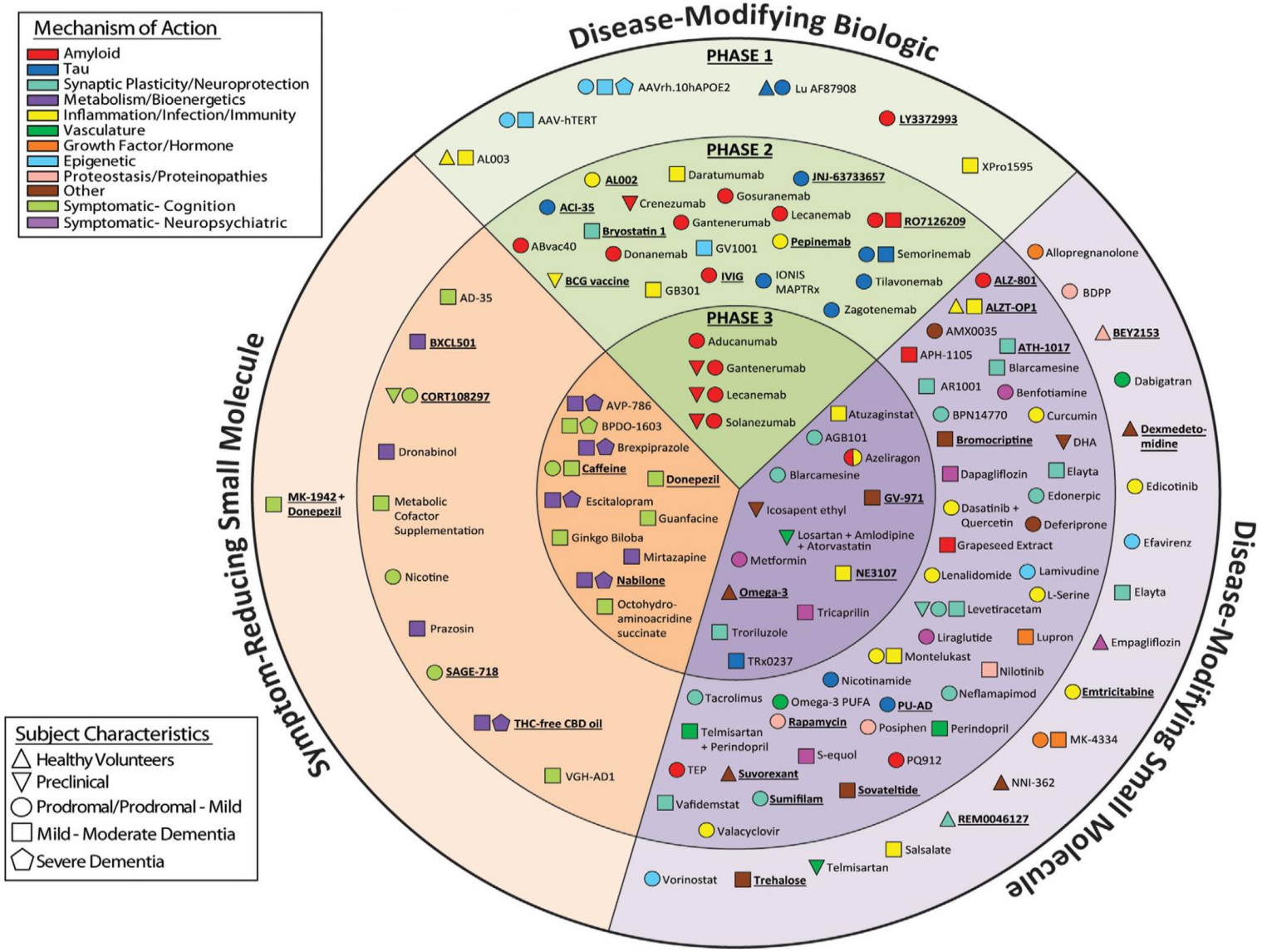
galantamine



donepezil

First Disease Modifying Rx
aducanumab & lecanemab approved
by FDA in US.
Donanemab pending.

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

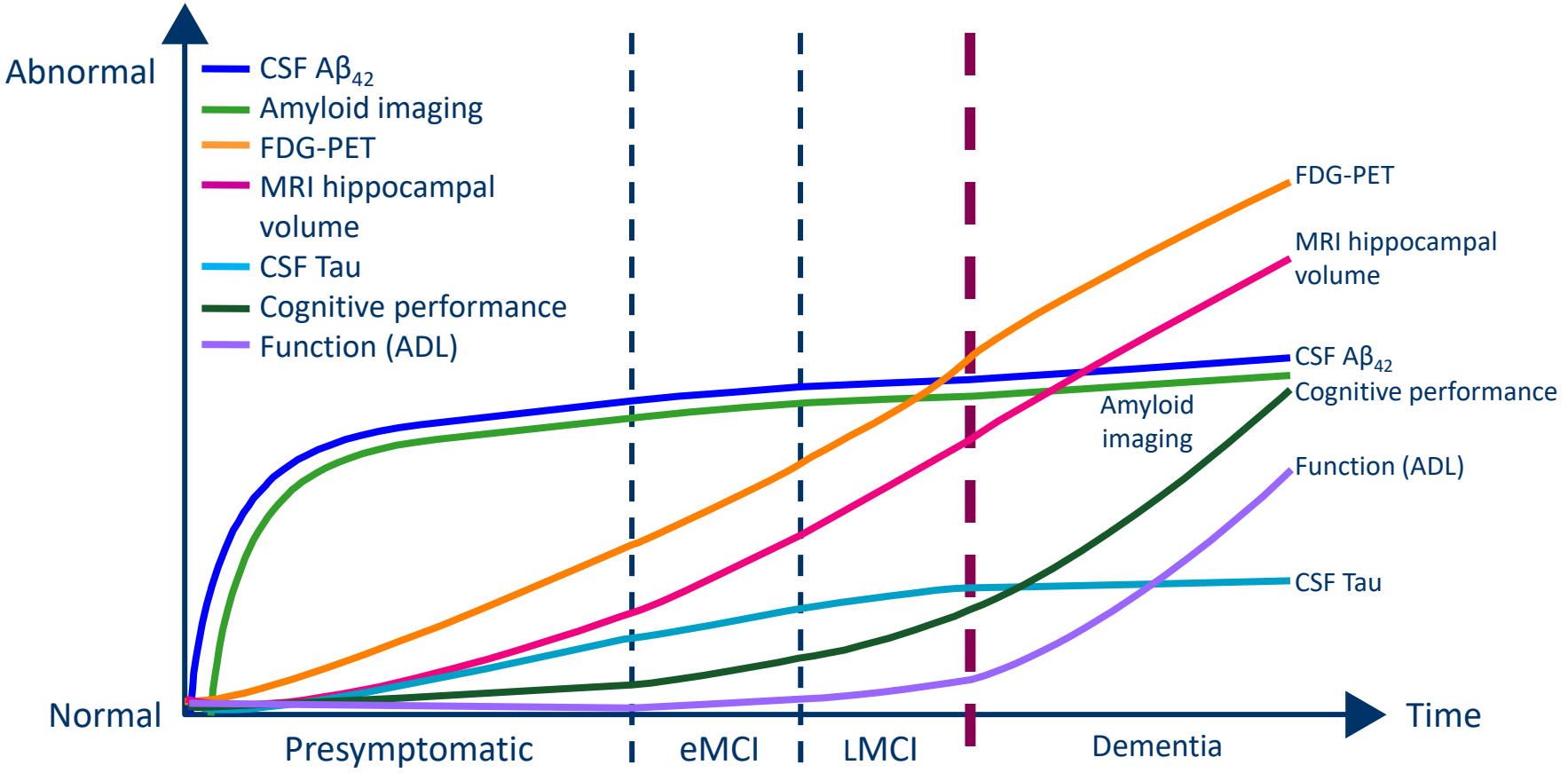
Important with early diagnosis!

- ***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

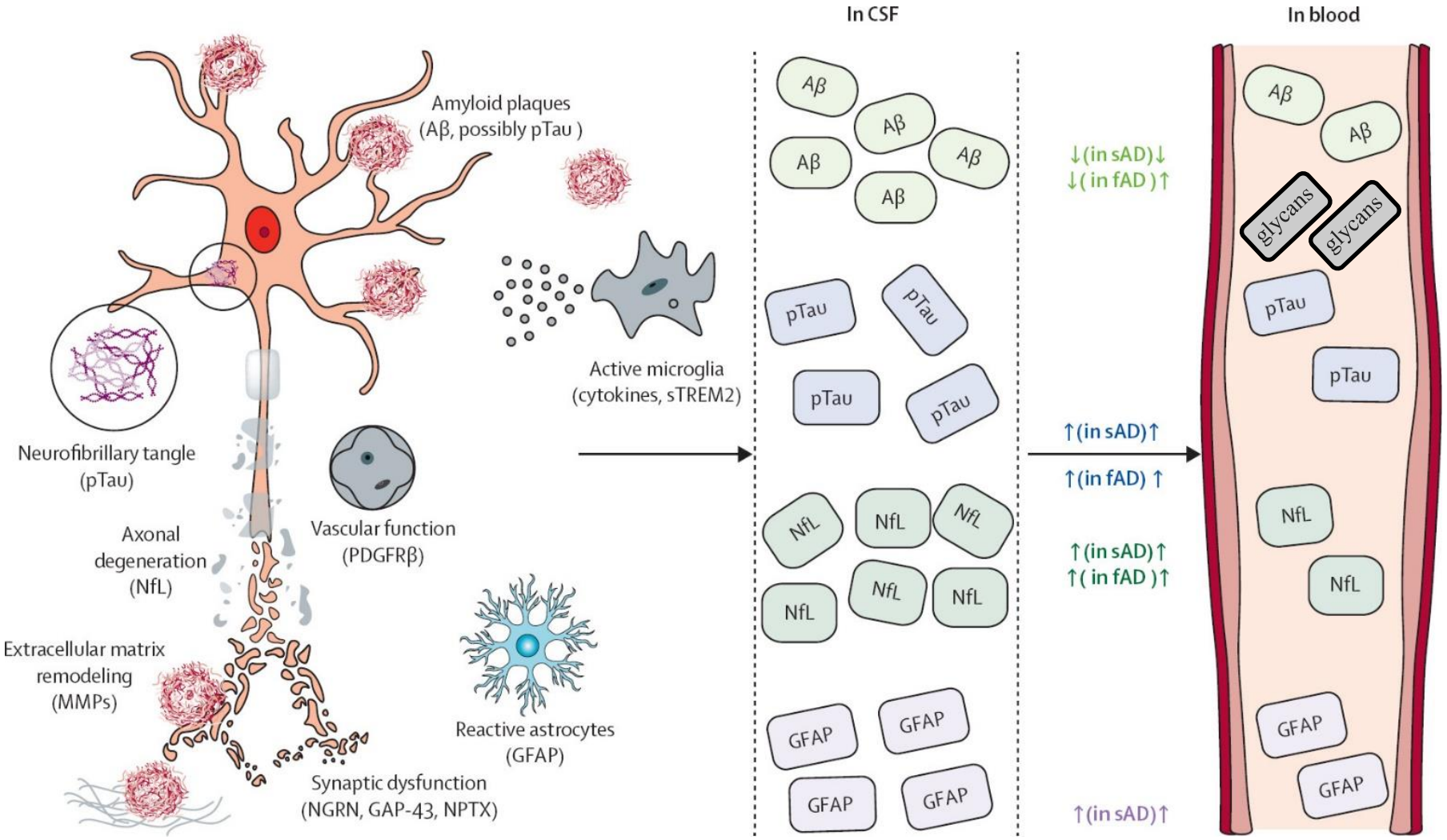
- ***For society;***
  - → Patient “in the system”
  - → Possibility to support the whole family
  - → More safe planning, cost awareness

AD progress and biomarkers enables early diagnosis



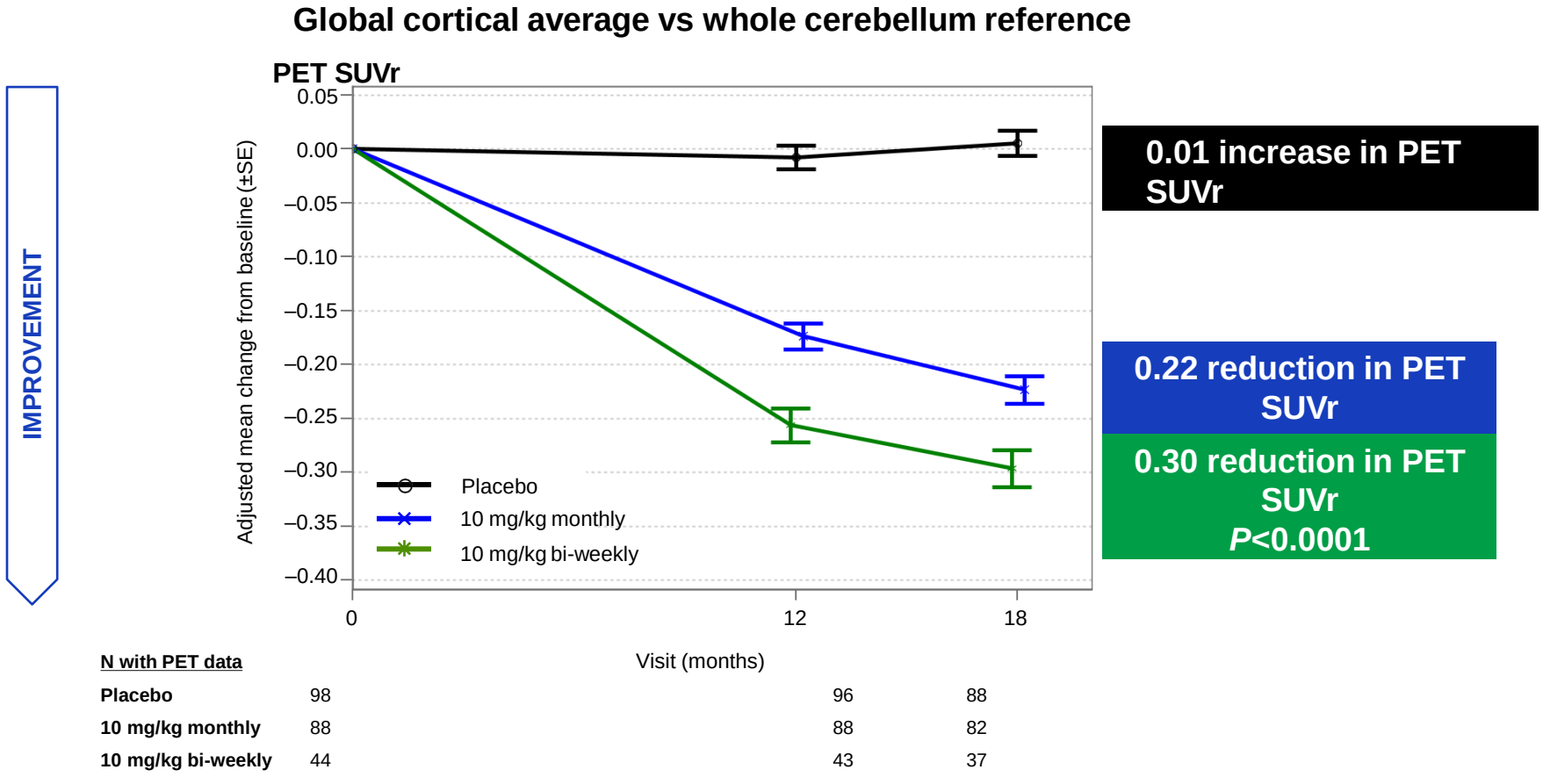
Aisen PS et al. Alzheimers Dement 2010

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)

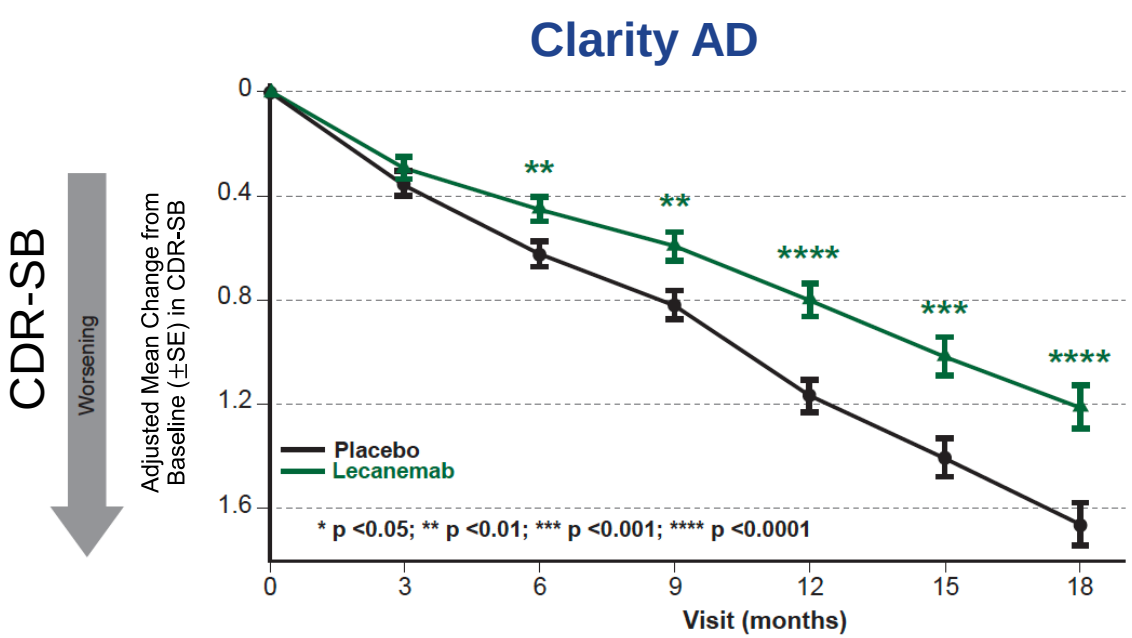


Both AUC and Cmax are important. 81% of amyloid positive converted back to negative at highest dose (visual read)

(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
	Favors lecanemab			
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

-0.16 -0.12 -0.08 -0.04 0 0.04

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:

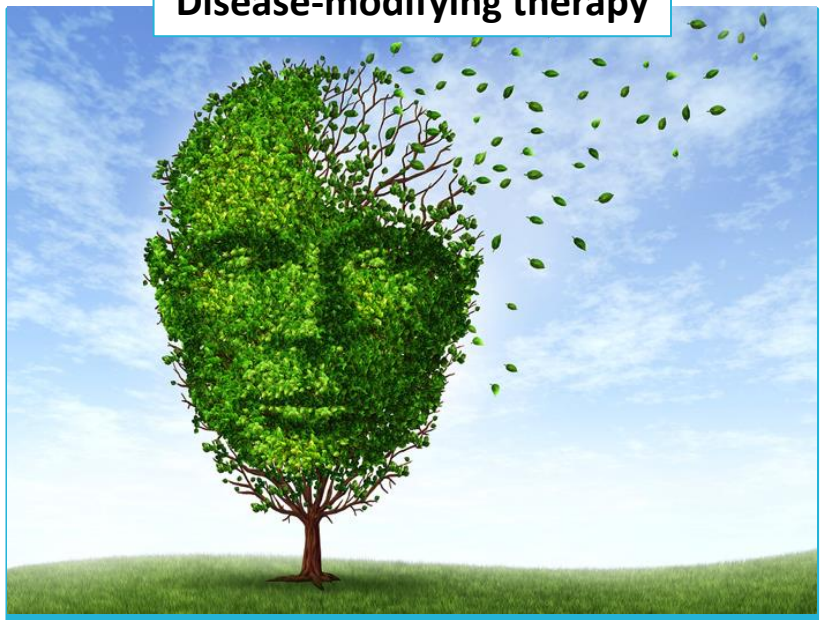
- Due to the same reasons, it is also difficult to properly evaluate the reported side effect from these two studies

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®

Gamma-Secretase-Modulators

Targeting Toxic Amyloid Production

- *Novel Oral Small Molecule*

Symptomatic therapy

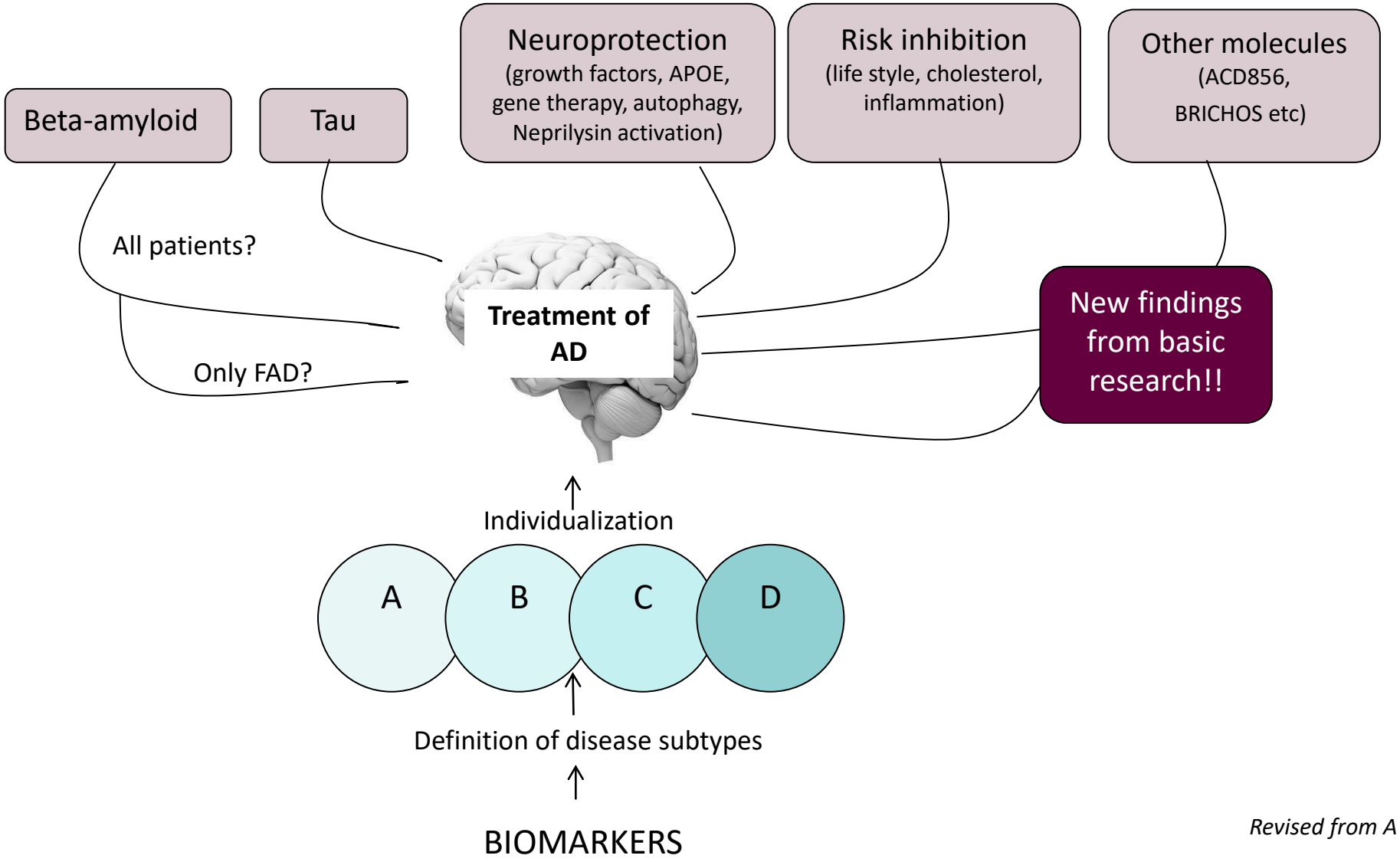
NeuroRestore®

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

Acknowledgement

- Angel Cedazo-Minguez
- Vesna Jelic
- Lars Lannfelt
- Anders Wimo
- Gunilla Johansson

May 17, 2023

Alzstatin®

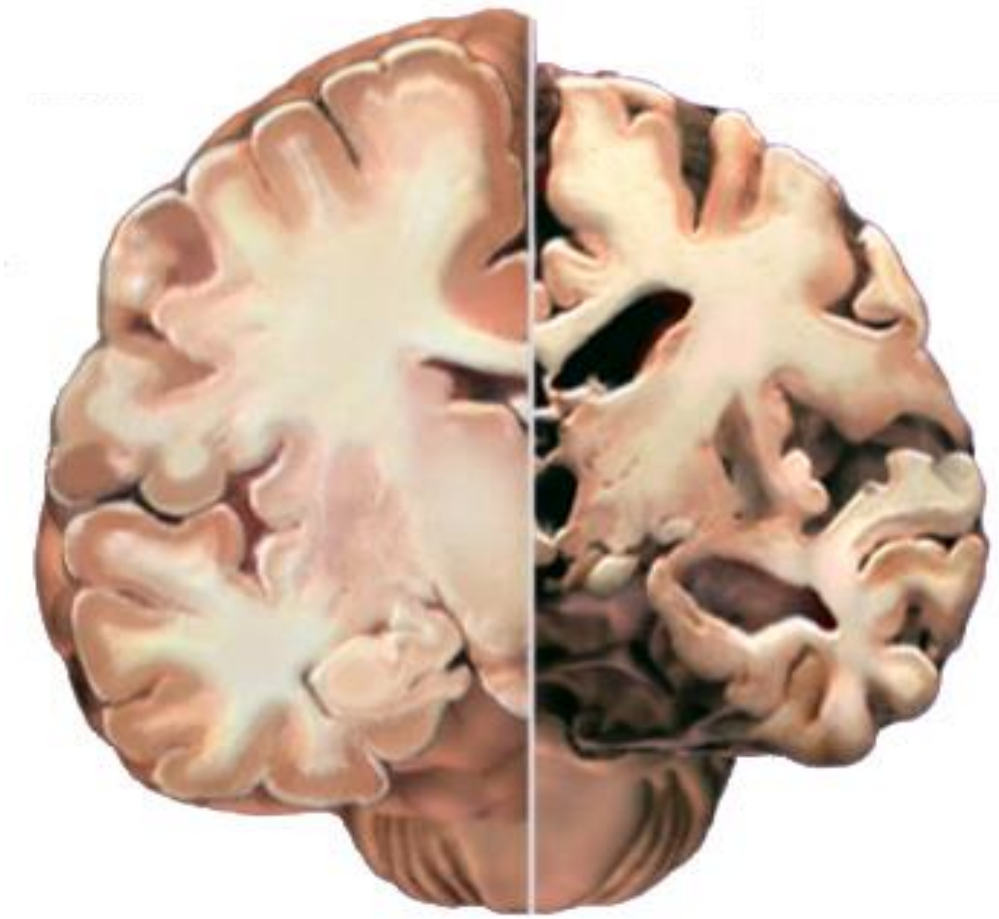
A preventive treatment against Alzheimer's

- Background & Evolution

Johan Sandin, PhD, CSO, AlzeCure Pharma

AlzeCure

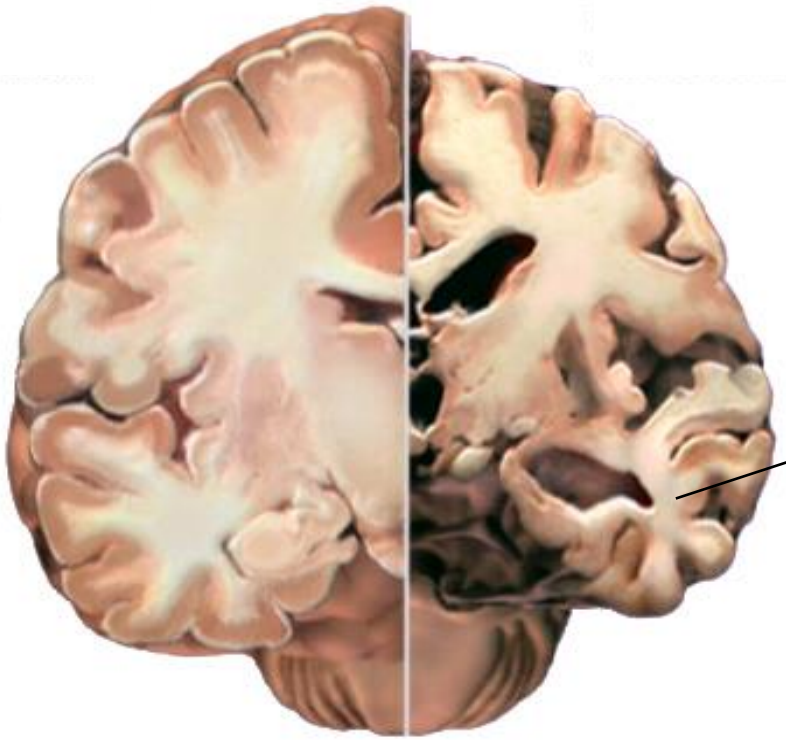
Amyloid plaques – a key hallmark of Alzheimer's

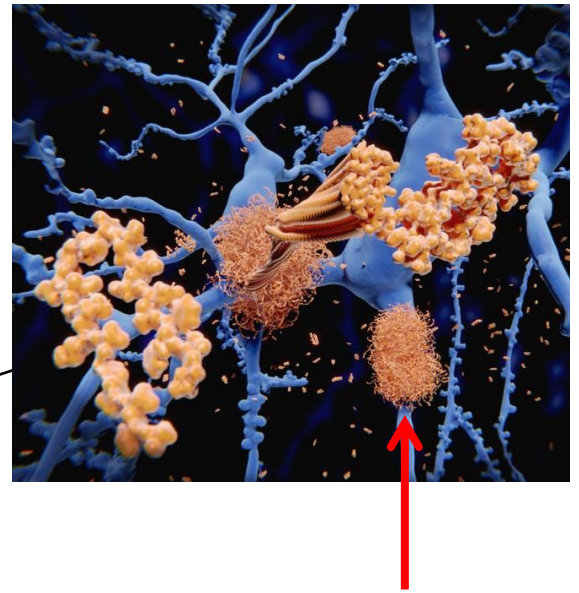


Healthy brain

Alzheimer's brain

Amyloid plaques – a key hallmark of Alzheimer's





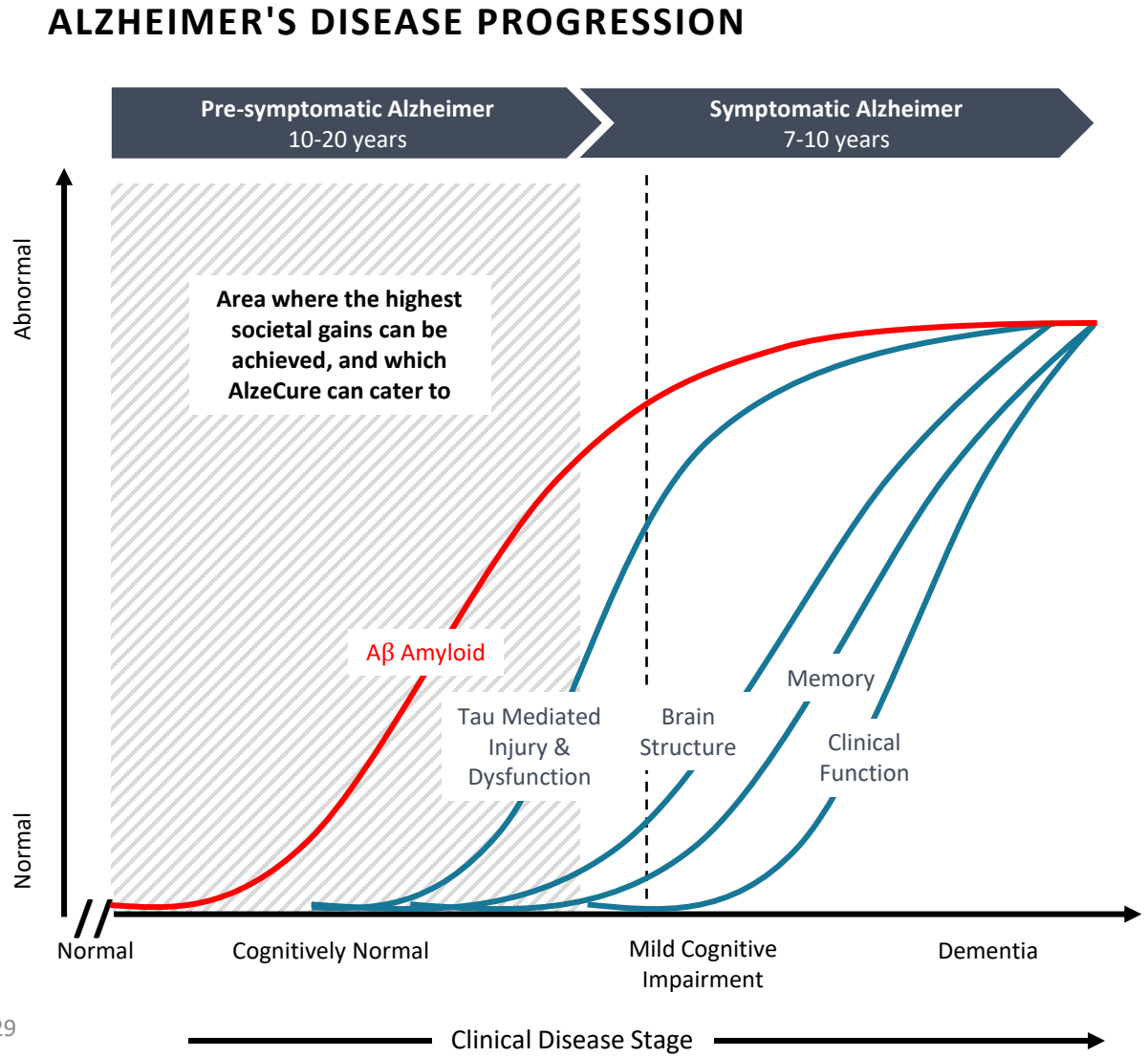
Aβ amyloid

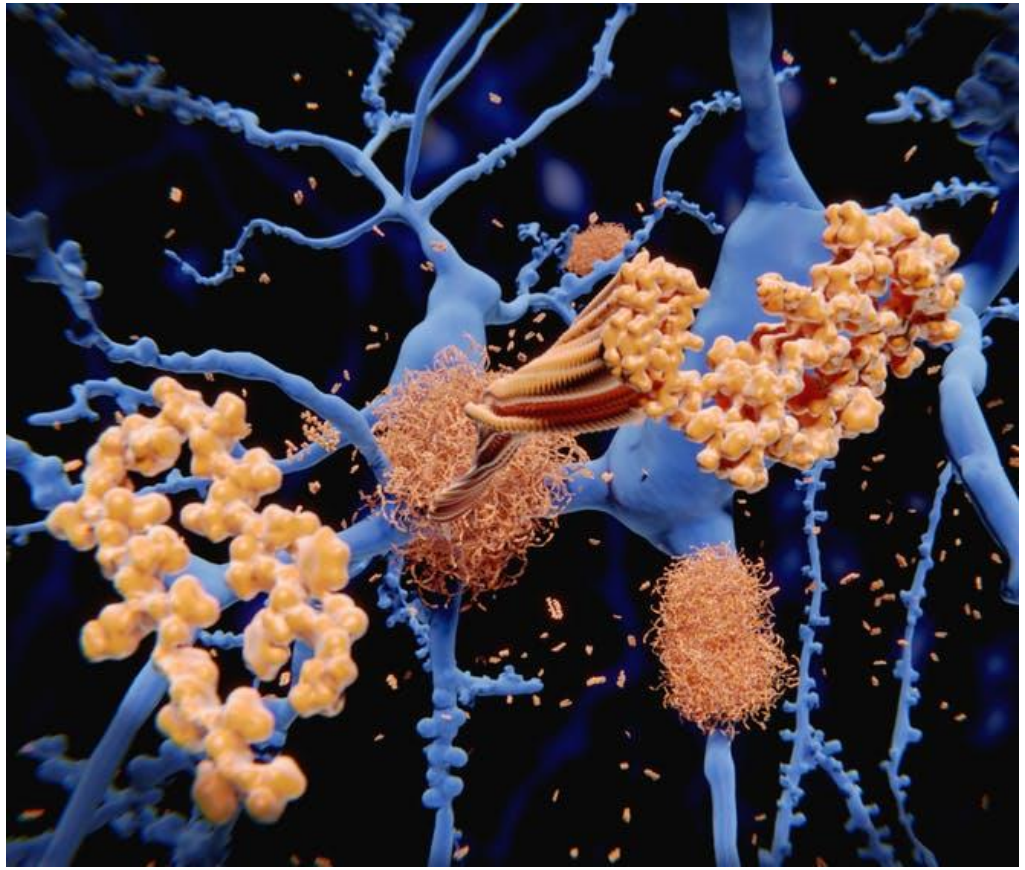
Healthy brain

Alzheimer's brain

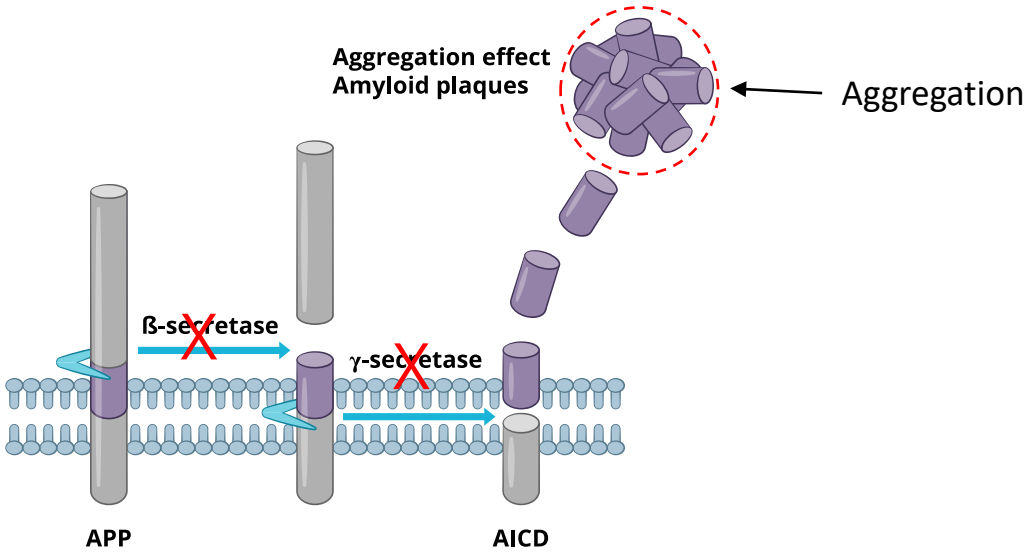
AlzeCure

Preventing or delaying Alzheimer's – reducing toxic Aβ42 production



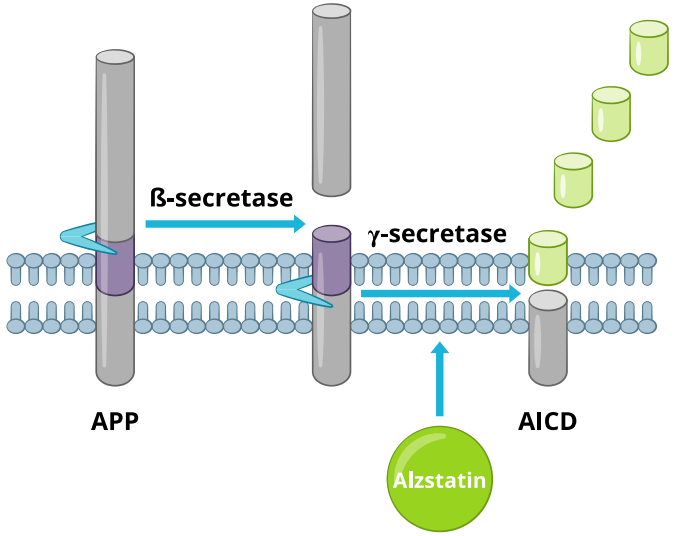


Preventing or delaying Alzheimer's – reducing toxic Aβ42 production



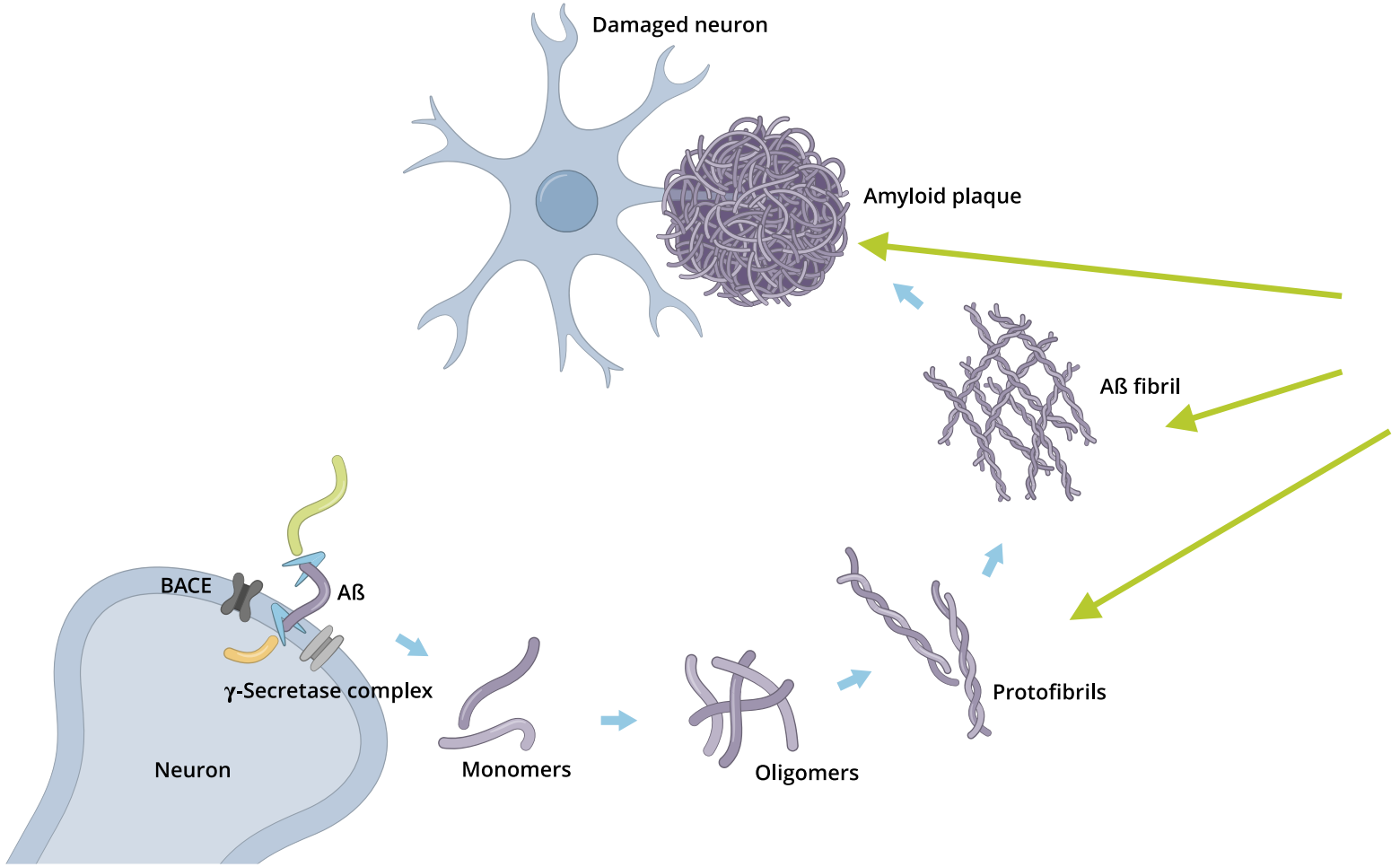
Aβ42 - main culprit in Alzheimer progression

Alzstatin® *modulates* the enzyme, alter its cleaving pattern and thereby **limits the aggregation**



*Alzstatin® **targets the gamma-secretase** as a **modulator** - does **not** block enzyme activity*

The Amyloid Cascade - Generates toxic & damaging fragments, including plaques, destroying neurons & brain structures

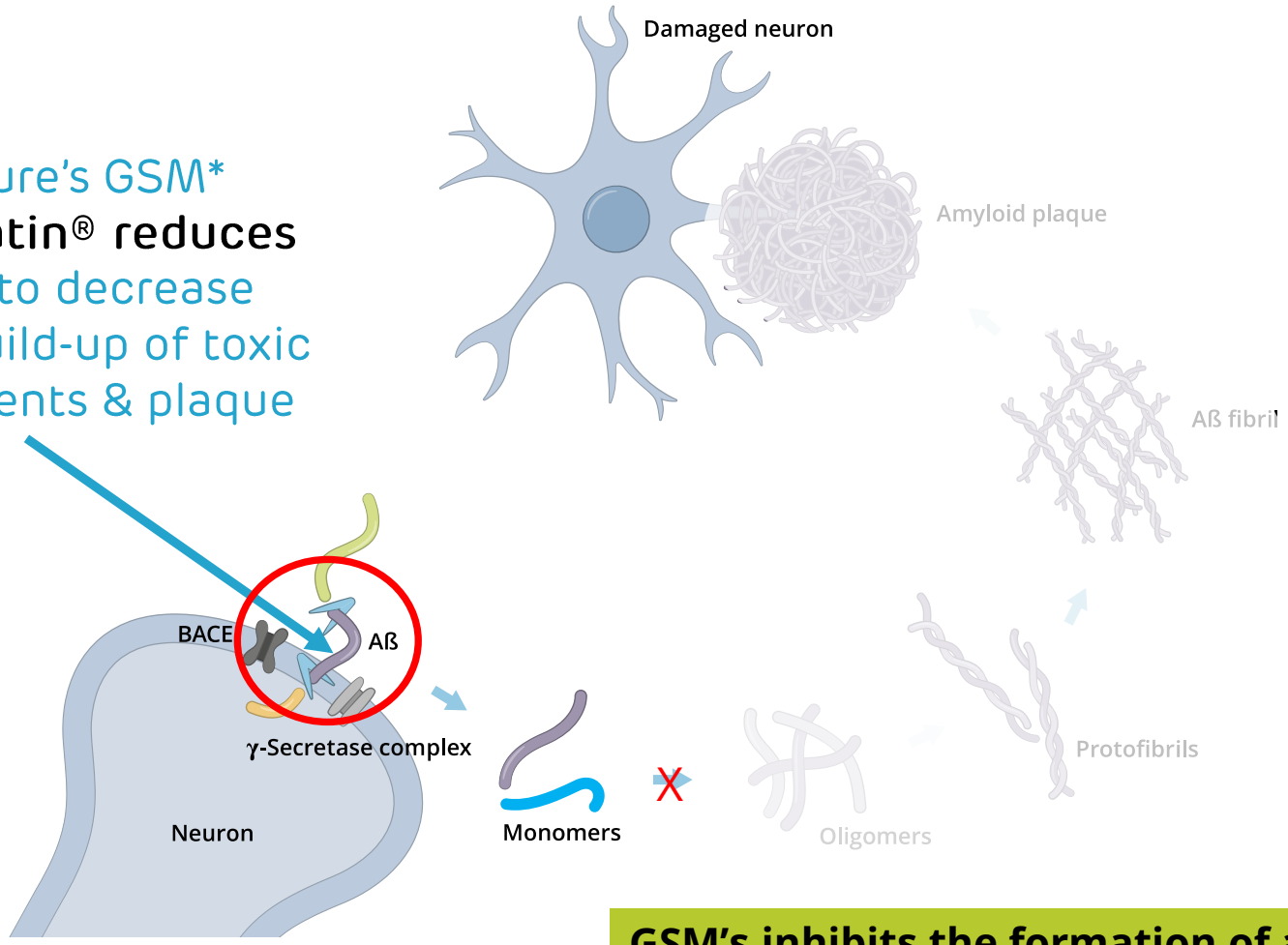


Aβ Antibodies bind and clear aggregated Aβ peptides.

AlzeCure

The Amyloid Cascade - Generates toxic & damaging fragments, including plaques, destroying neurons & brain structures

AlzeCure's GSM*
Alzstatin® reduces
Aβ42 to decrease
the build-up of toxic
fragments & plaque

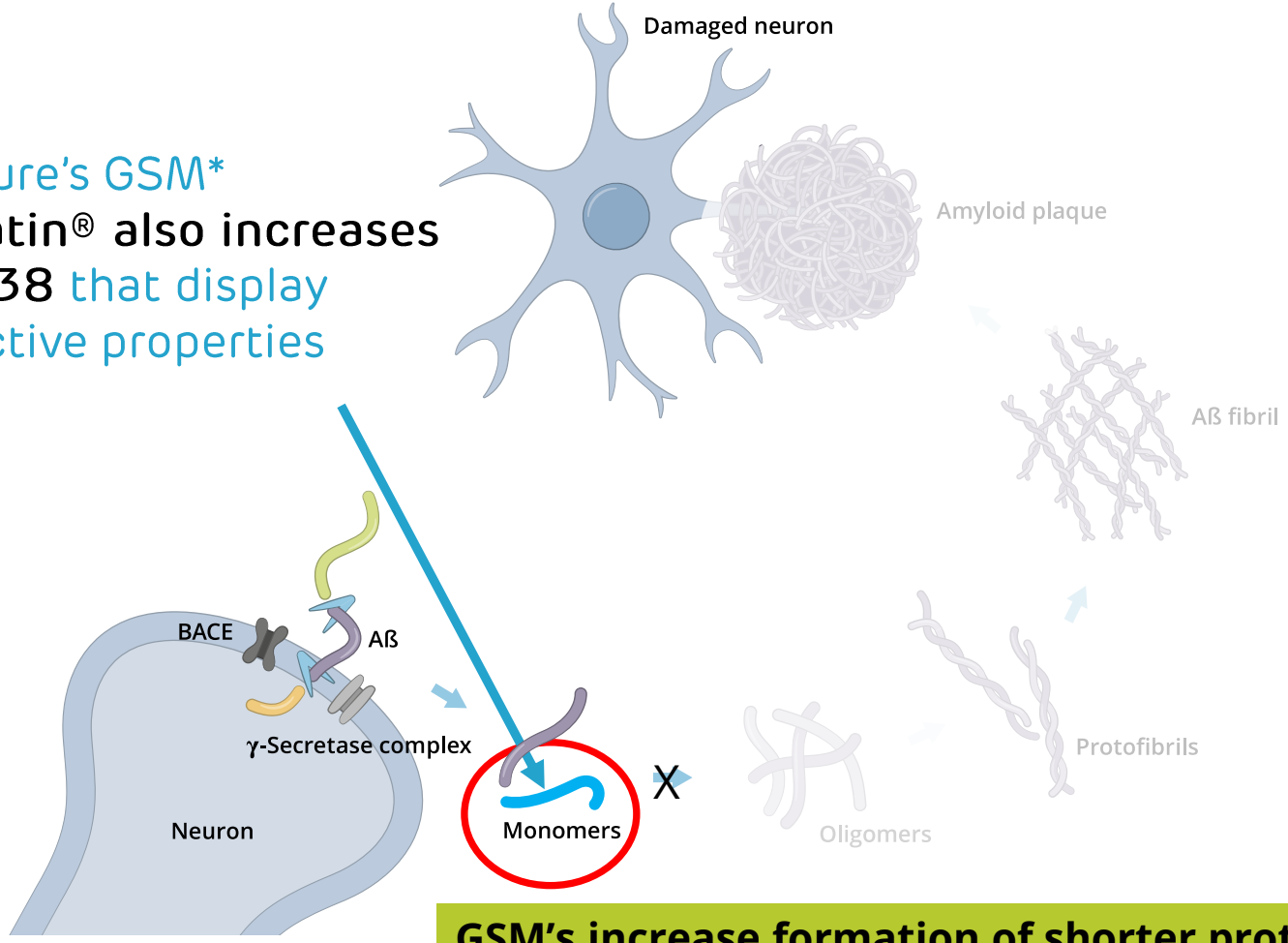


GSM's inhibits the formation of all Aβ aggregates

*) GSM = Gamma Secretase Modulator

The Amyloid Cascade - Generates toxic & damaging fragments, including plaques, destroying neurons & brain structures

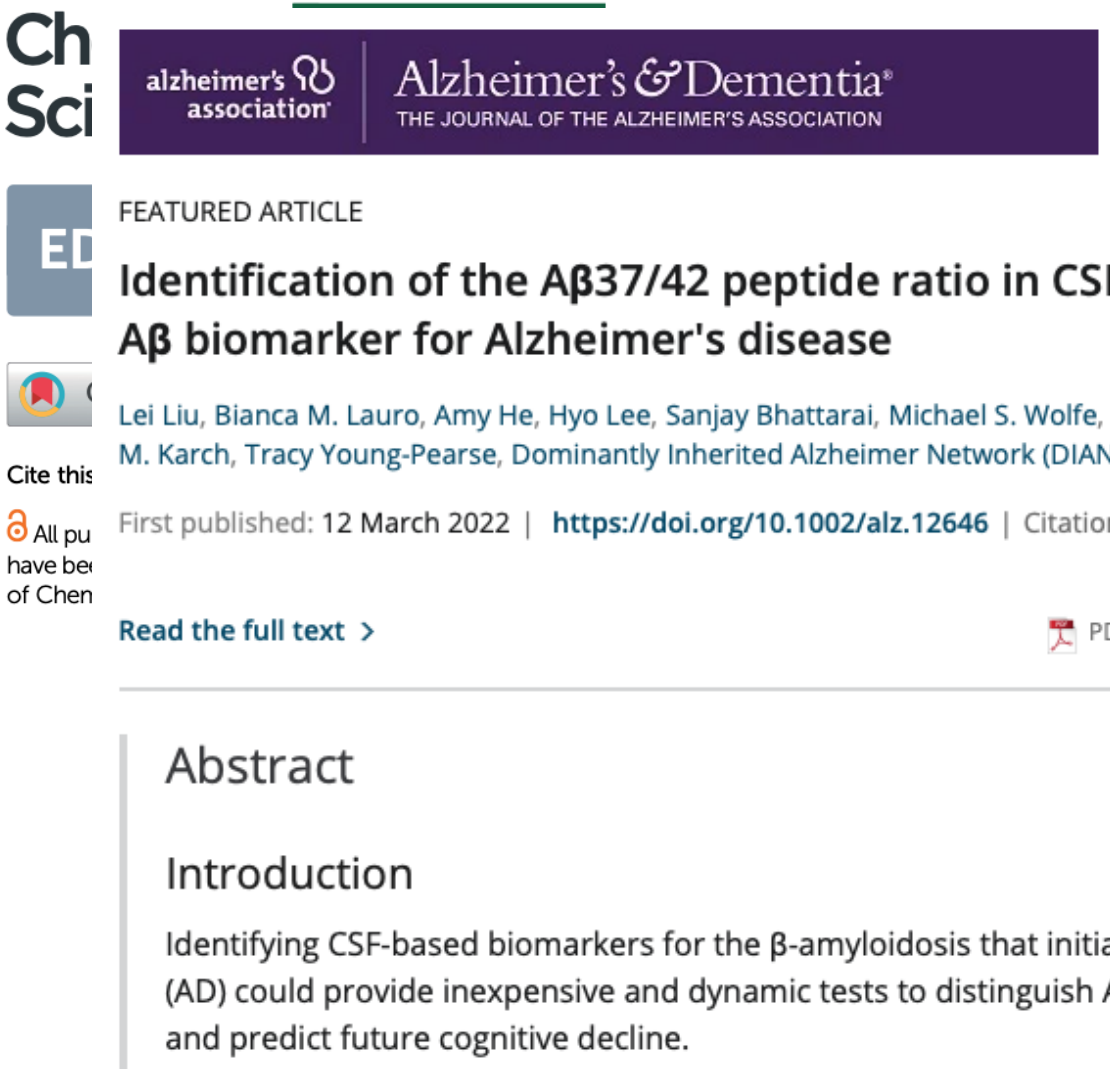
AlzeCure's GSM*
Alzstatin® also increases Aβ37/38 that display protective properties



GSM's increase formation of shorter protective Aβ fragments

*) GSM = Gamma Secretase Modulator

Recent data show that shorter Aβ peptides could have advantageous effects



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

FEATURED ARTICLE

Identification of the Aβ37/42 peptide ratio in CSF as an improved Aβ biomarker for Alzheimer's disease

Lei Liu, Bianca M. Lauro, Amy He, Hyo Lee, Sanjay Bhattarai, Michael S. Wolfe, David A. Bennett, Celeste M. Karch, Tracy Young-Pearse, Dominantly Inherited Alzheimer Network (DIAN), Dennis J. Selkoe

First published: 12 March 2022 | https://doi.org/10.1002/alz.12646 | Citations: 1

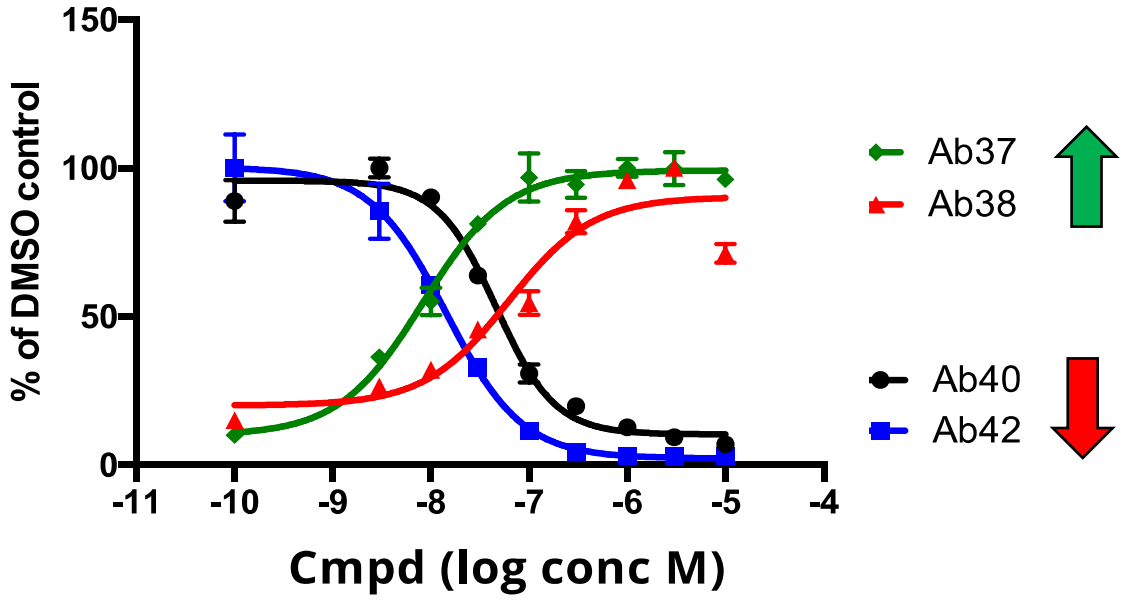
Read the full text > PDF TOOLS SHARE

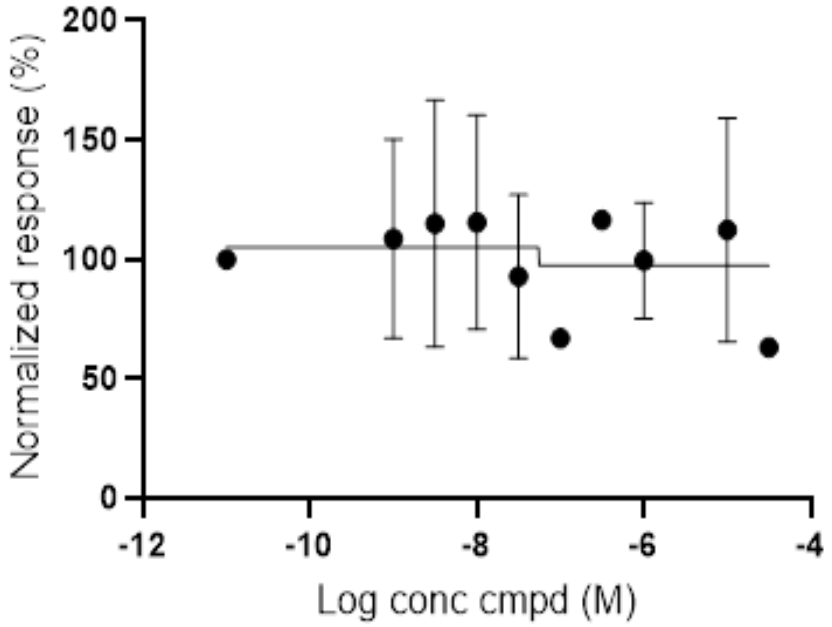
Abstract

Introduction

Identifying CSF-based biomarkers for the β-amyloidosis that initiates Alzheimer's disease (AD) could provide inexpensive and dynamic tests to distinguish AD from normal aging and predict future cognitive decline.

Alzstatin – potent reduction of toxic Aβ42



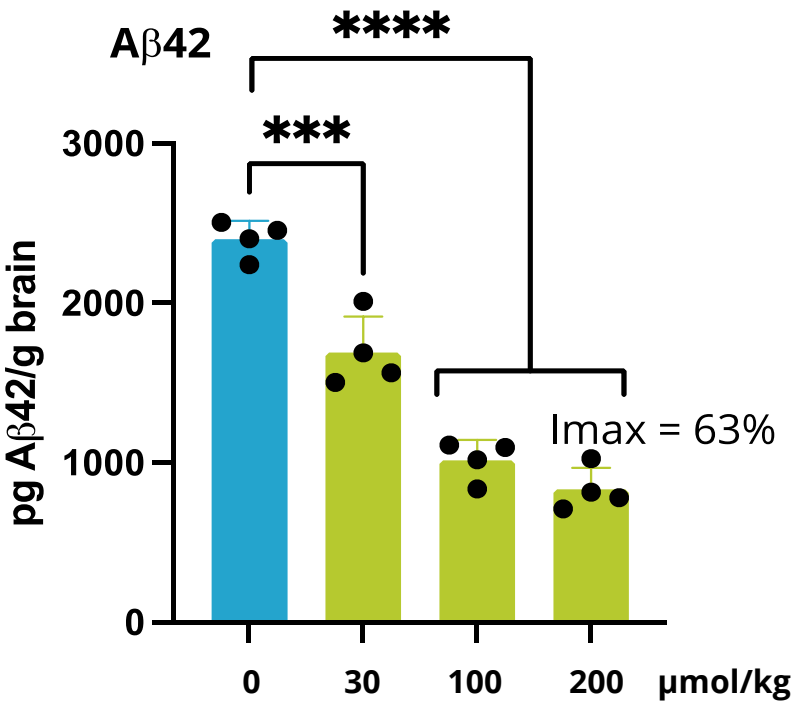


Alzstatin reduces toxic Aβ42 and Aβ40, while increasing protective Aβ38 and Aβ37 peptides

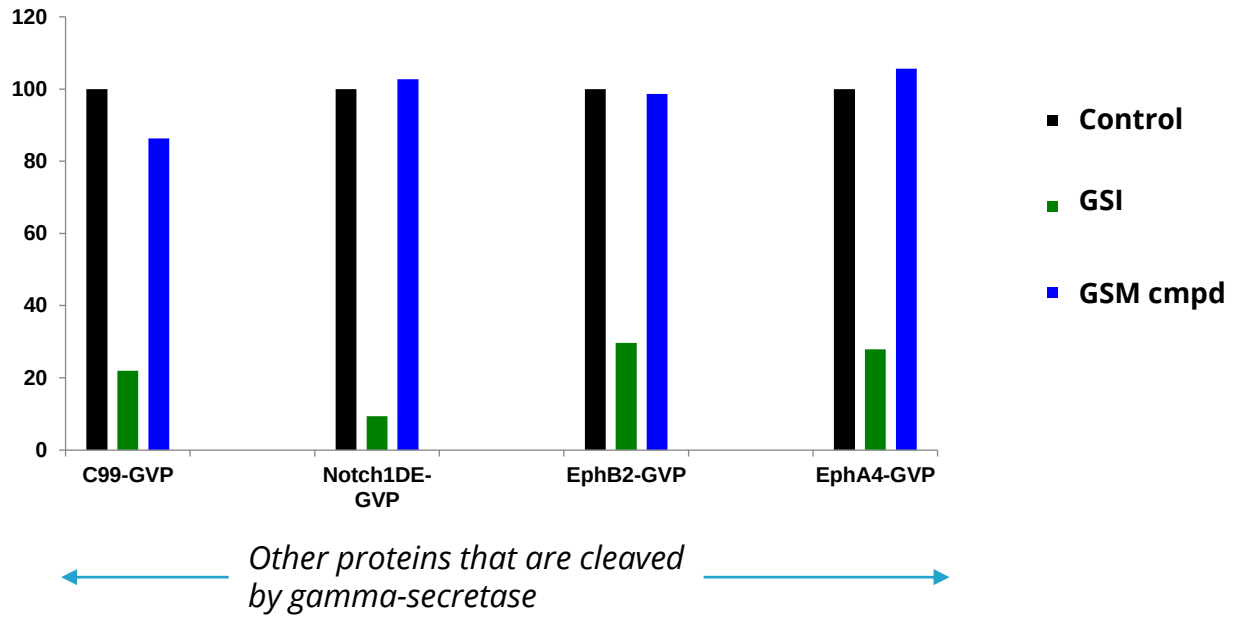
No effect on total Aβ
Consistent with a GSM

AlzeCure

Alzstatin – efficacious in vivo based on a safer mechanism-of-action



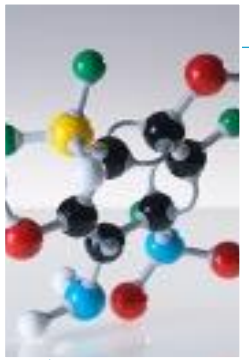
Alzstatin potently reduces the amount of toxic brain Aβ42 in mice



Alzstatin compounds do not affect the formation of other gamma-secretase substrates, e.g. Notch

AlzeCure

How Alzstatin is expected to differ from the Antibodies*
- Key advantages

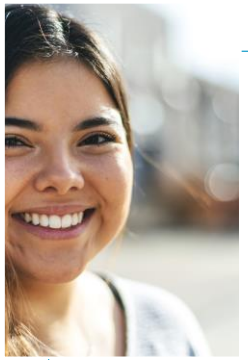


Small molecule therapy

- Small molecules generally pass much more readily across the BBB to its target site - the brain
- Provides a more cost-effective treatment for chronic use than biologics

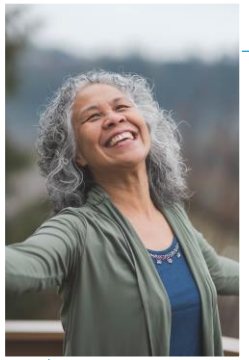
Oral formulation => Home treatment

- Don’t need to go to the hospital once or twice a month for an infusion of the drug



Early treatment

- Taken before the brain is heavily damaged and the patient is diagnosed with cognitive decline and Alzheimer’s disease, which is the case for the antibody



Fewer side effects

- Not expected to have the side effects of brain oedema and brain microbleedings (ARIA)
  - => Is not expected to demand regular brain scans, => minimizing hospital visits and costs

*) E.g. Aduhelm (aducanumab), Leqembi (lecanumab), Donanemab

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Attractive profile with early clinical proof-of-mechanism

- Clinical PoM **and** central target engagement already in Phase I
  - **SAD/MAD studies conducted in healthy volunteers**
    - Evaluation of safety and tolerability after single and repeated administration
    - Possibility to explore biomarker effects **showing central target engagement** already in Phase I
      - Aβ42/40 – show **reduction of toxic Aβ-peptides**
      - Aβ37/38 – show **increase of shorter protective Aβ-peptides**, establishing gamma-secretase involvement and MoA
      - Measurements done both in CSF and plasma – **biomarker kits available**

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Multiple target populations - preventive and maintenance therapy

Preventive therapy based on genetic risk factors* and biomarkers

- Early stand-alone treatment before onset of symptoms and any major neurodegeneration occurs
- Prevents build-up of amyloid – an early pathological feature of AD
- Suitable for preventive therapy - as a “statin” for Alzheimer’s disease
- Familiar forms of the disease (incl. Downs syndrome) suitable for initial proof of concept clinical studies

*) E.g. ApoE4

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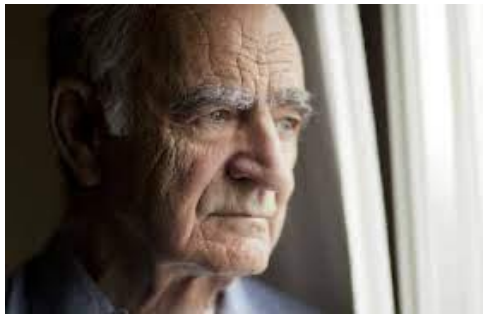
Multiple target populations - preventive and maintenance therapy

Preventive therapy based on genetic risk factors* and biomarkers

- Early stand-alone treatment before onset of symptoms and any major neurodegeneration occurs
- Prevents build-up of amyloid – an early pathological feature of AD
- Suitable for preventive therapy - as a “statin” for Alzheimer’s disease
- Familiar forms of the disease (incl. Downs syndrome) suitable for initial proof of concept clinical studies

Maintenance therapy in patients with established Alzheimer’s

- Potential for combination/maintenance treatment after initial plaque clearance provided by monoclonal antibody treatment (as initially proposed by Lilly) e.g., with:
  - Lecanemab (Eisai/Biogen/Bioartic)
  - Donanemab (Lilly)
  - Remternetug (Lilly)



*) E.g. ApoE4

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Competitive landscape

Main known competitors:

- UCSD-776890 (Steven Wagner)/NIH – Phase 1
- Roche RG6289 – Phase 1

Published data on Pfizer's PF-06648671 show that GSM's can display both potent efficacy and good safety in man. →

ARTICLE

Pharmacokinetic and Pharmacodynamic Effects of a γ-Secretase Modulator, PF-06648671, on CSF Amyloid-β Peptides in Randomized Phase I Studies

Jae Eun Ahn[1,*], Charles Carrieri[1], Fernando Dela Cruz[1], Terence Fullerton[1], Eva Hajos-Korcsok[1,3], Ping He[1,4], Constantino Kantaridis[2], Claire Leurent[1,5], Richann Liu[1,6], Jessica Mancuso[1], Laure Mendes da Costa[2] and Ruolun Qiu[1]

γ-Secretase modulators (GSMs) represent a promising therapy for Alzheimer's disease by reducing pathogenic amyloid-β (Aβ) peptide production. Three phase I studies (NCT02316756, NCT02407353, and NCT02440100) investigated the safety/tolerability, pharmacokinetics (PKs), and pharmacodynamics (PDs) of the oral GSM, PF-06648671. A PK/PD indirect-response model was developed (using biomarker data) to simultaneously characterize differential effects of PF-06648671 on multiple Aβ species in cerebrospinal fluid (CSF). Healthy subjects (n = 120) received single doses or multiple-ascending doses of PF-06648671/placebo for 14 days. No serious adverse events occurred; severe adverse events were deemed not drug related. PF-06648671 decreased Aβ42 and Aβ40 concentrations in CSF, with greater effects on Aβ42, and increased Aβ37 and Aβ38 levels, particularly Aβ37. No significant change in total Aβ was observed. The PK/PD model well described the tendency of observed CSF Aβ data and the steady-state effects of PF-06648671, supporting its use for predicting central Aβ effects and optimal dose selection for GSMs in future trials.

Development stage of Alzstatin in line with competitors

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Summary

Advantages with Alzstatin

- ✓ Reduces amyloidogenic Aβ42 production
- ✓ Increase the shorter peptides Aβ37 and Aβ38 - suggested to have protective properties
- ✓ Do not affect the total amount of Aβ – thus any physiological function likely not affected
- ✓ Mode of action is the reverse of most familiar Alzheimer mutations
- ✓ Alzstatin compounds such as ACD680 potently reduce Aβ42 production both in vitro and in vivo
- ✓ PoM data achievable already in phase 1 clinical trials
- ✓ Potential for both preventive and maintenance treatment

Bart De Strooper on Alzforum regarding Lecanemab Phase 3 results:
"These results strongly suggest that we revisit previous drug targets such as y-secretase and BACE, as small compounds modulating these activities might be, in the long run, the only cheap and feasible prevention for AD."

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Acknowledgement

- **Team at Alzecure Pharma**
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  - Sanja Juric
  - Cristina Parrado
  - Märta Segerdahl
- **Karolinska Institutet**
  - Prof. Bengt Winblad
  - Assoc. Prof. Lars Tjernberg
- **Göteborgs Universitet**
  - Prof. Henrik Zetterberg
  - Lotta Agholme, PhD
  - Stefanie Fruhwürth, PhD

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May 17, 2023

NeuroRestore ACD856
Background & data supporting disease modifying effects

Pontus Forsell, PhD, Head of Discovery & Research at AlzeCure Pharma

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Background: Neurotrophins and ACD856, a clinical stage cognitive enhancer with disease modifying potential

- ACD856 is a novel small molecule positive modulator of Trk receptors enhancing the signaling of neurotrophins, such as Nerve Growth Factor (NGF) and Brain-Derived Neurotrophic Factor (BDNF)
- The neurotrophins has been known for decades to play an essential role in neuronal survival and function as well as in learning, memory and mood
- ACD856 has been tested in a phase 0 micro-dose study, in a phase 1 single ascending dose study and in a phase 1 multiple ascending dose study
- ACD856 demonstrated excellent pharmacokinetic properties and bioavailability. It was safe, well tolerated with good blood-brain-barrier permeability. Quantitative EEG demonstrated evidence of a pharmacological effect in the CNS, suggesting target engagement.
- The role of neurotrophins and the mechanism of action of ACD856 implies that the compound could have disease modifying effects

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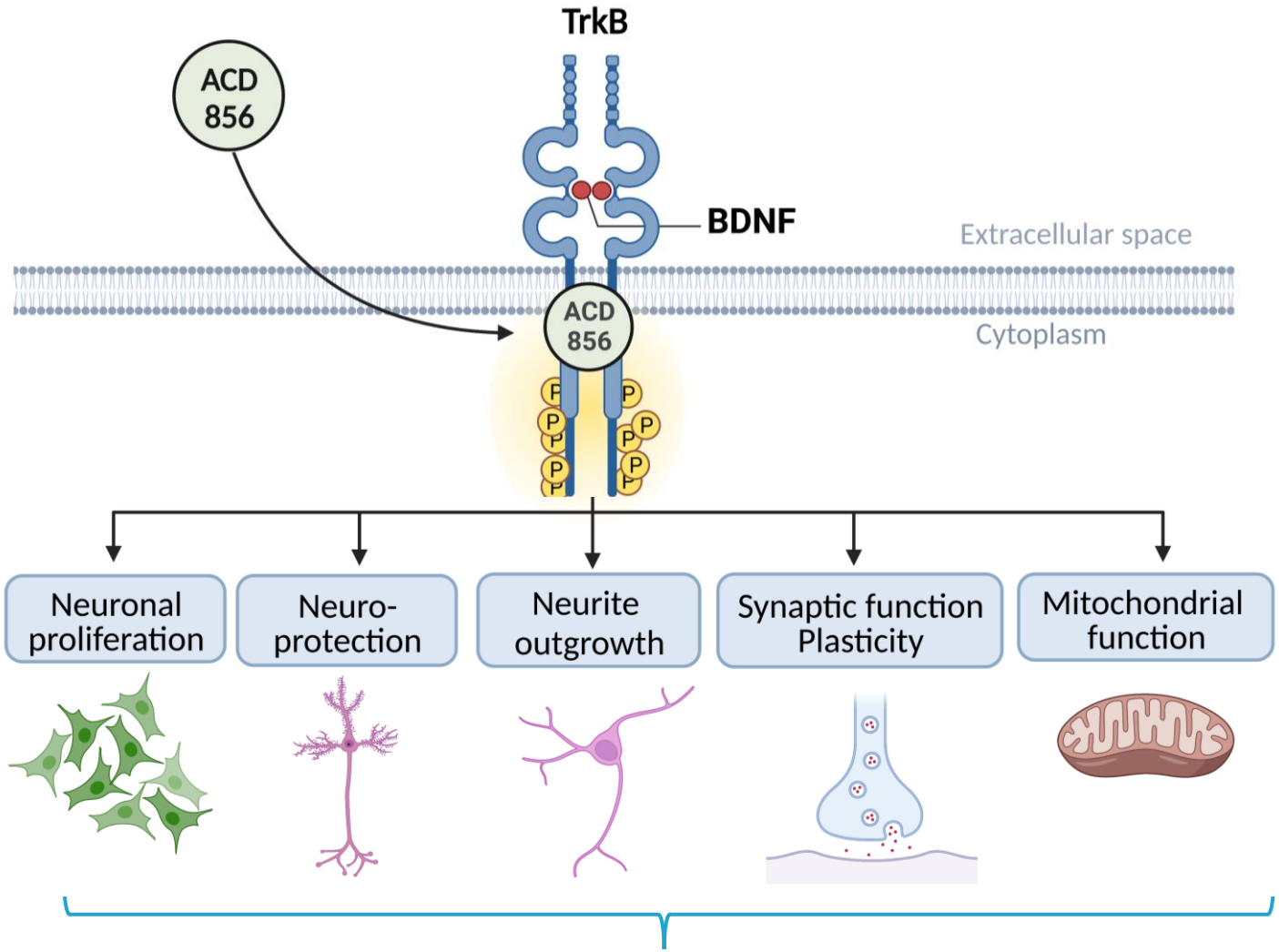
ACD856, mechanism of action supports disease modifying potential

- ACD856 is a novel small molecule positive modulator of Trk-receptors enhancing the signaling of neurotrophins such as NGF and BDNF
- The enhanced signaling leads to short term symptomatic effects with long term benefits
- The long-term effects of ACD856 could include improved neuronal function, increased mitochondrial function and improved cognition.



Results supporting disease modifying effects

- **In vitro**
  - Protection against amyloid-beta induced neurotoxicity
  - Potentiation of neuronal growth and neurite outgrowth
  - Increased levels of BDNF
- **In vivo**
  - Improved memory possibly through increased neuroplasticity
  - Long term antidepressant-like effect via a potential neuroplastic adaption

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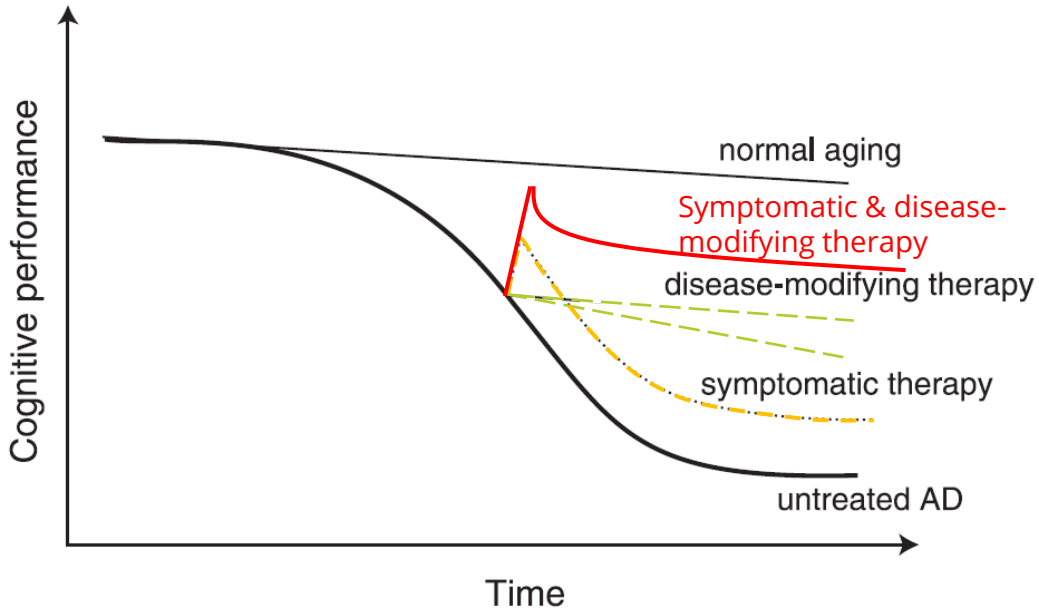
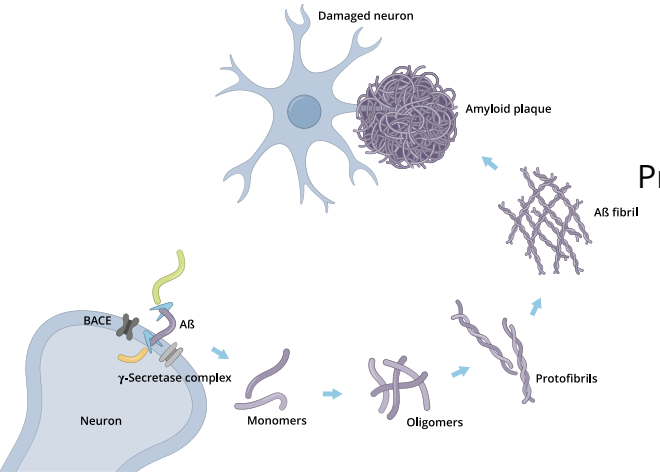
Amyloid toxicity and disease progression

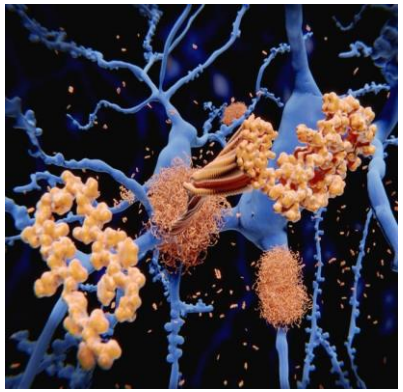
- Key pathological features of the Alzheimer's disease brain:
  - Amyloid plaque
  - Synapse dysfunction
  - Axon withdrawal
  - Mitochondrial dysfunction
- These events are closely correlated with the cognitive dysfunction that is characteristic for Alzheimer's disease.

Preventive, protective or restorative treatment will have a significant impact on disease progression, especially if combined with a symptomatic effect

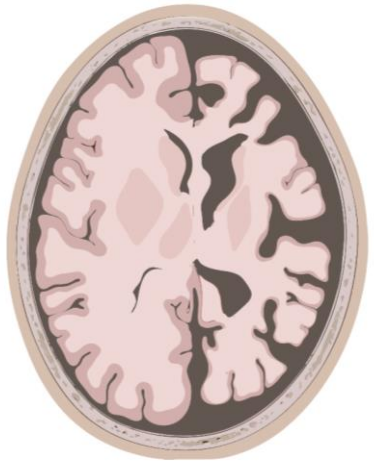




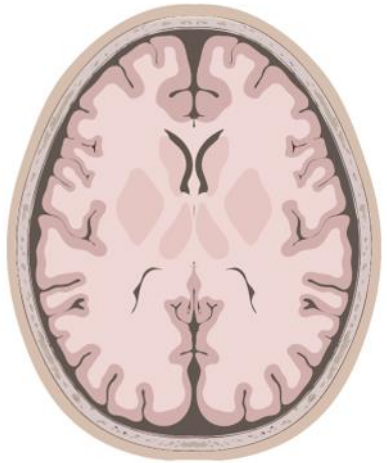
Preventive



Protective



Restorative



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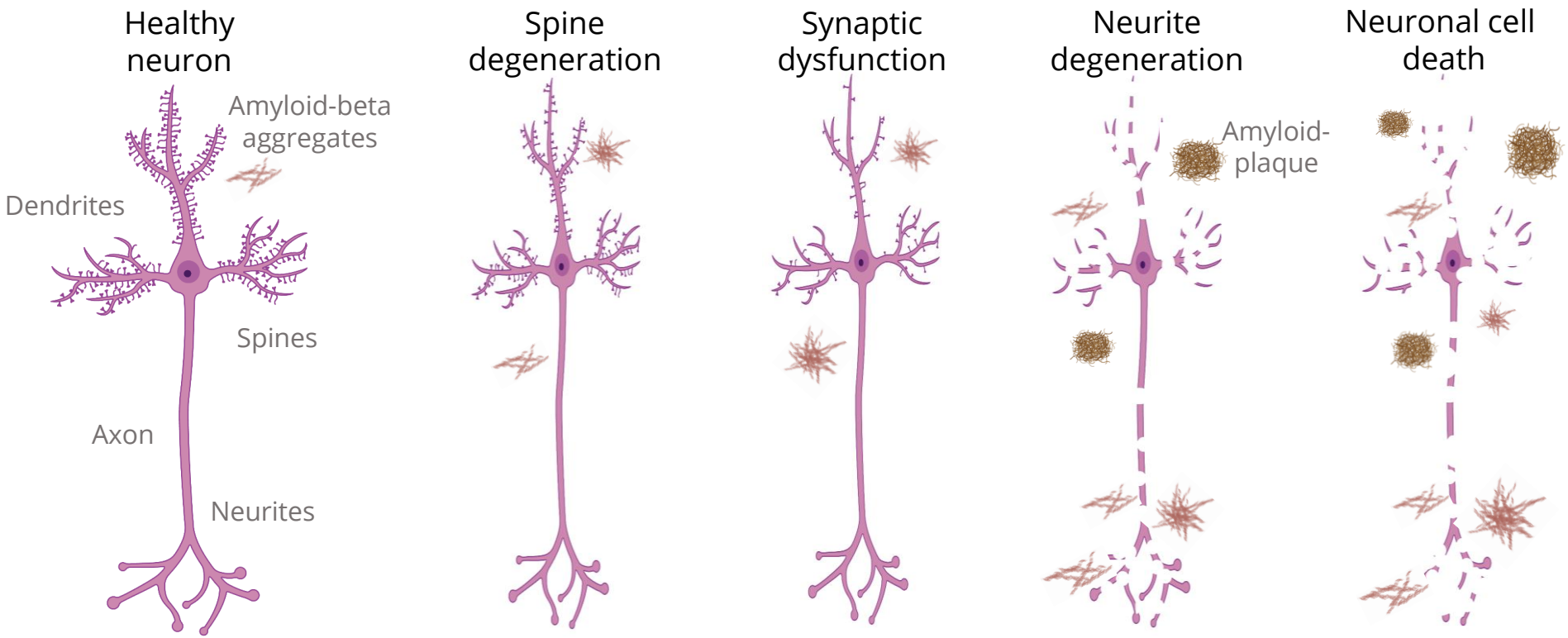
Amyloid-beta induced neurotoxicity

The life and death of a neuron



Neuronal function

Neuroprotective effects of ACD856

Synaptic dysfunction
Neurite degeneration
Neuronal cell death

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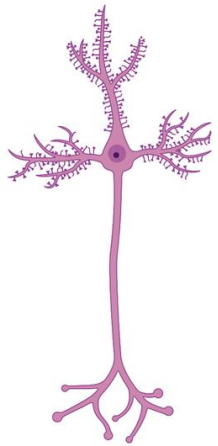
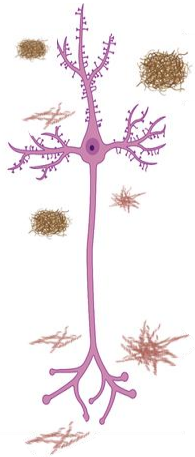
ACD856 and amyloid-beta induced neurotoxicity

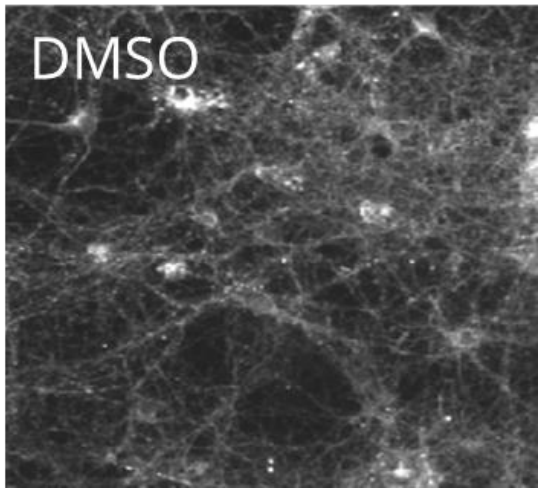
- Vehicle (DMSO) or $A\beta_{1-42}$ was added to neurons, with or without ACD856
- The neuronal content of a synaptic protein (SNAP25) was quantified by microscopy

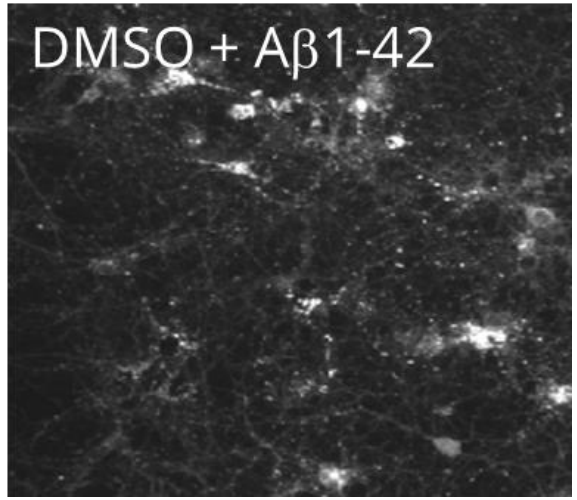


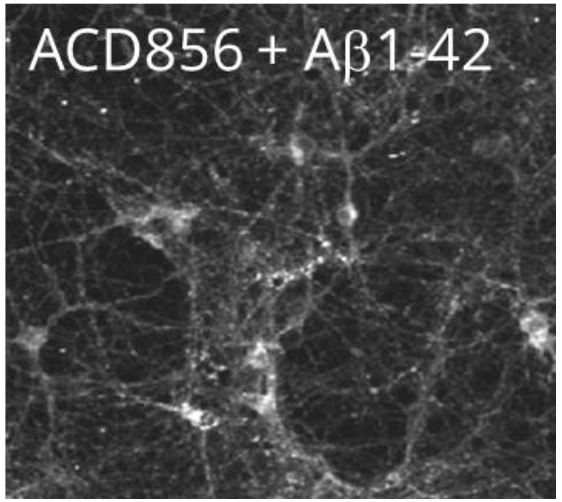
$A\beta_{1-42}$

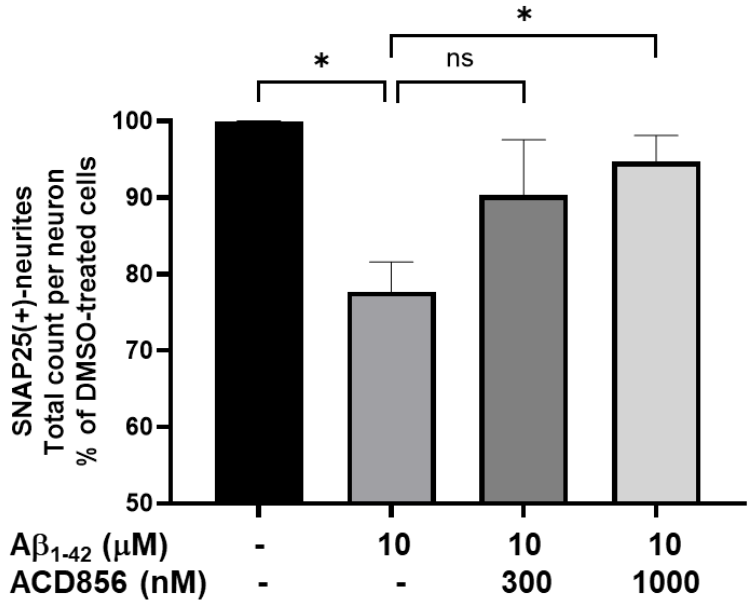
ACD856 + $A\beta_{1-42}$











ACD856 is protective against $A\beta_{1-42}$-induced neurotoxicity

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Results supporting disease modifying effects

- **In vitro**
  - Protection against amyloid-beta induced neurotoxicity
  - **Potentiation of neuronal growth and neurite outgrowth**
  - Increased levels of BDNF
- **In vivo**
  - Improved memory possibly through increased neuroplasticity
  - Long term antidepressant-like effect via a potential neuroplastic adaption

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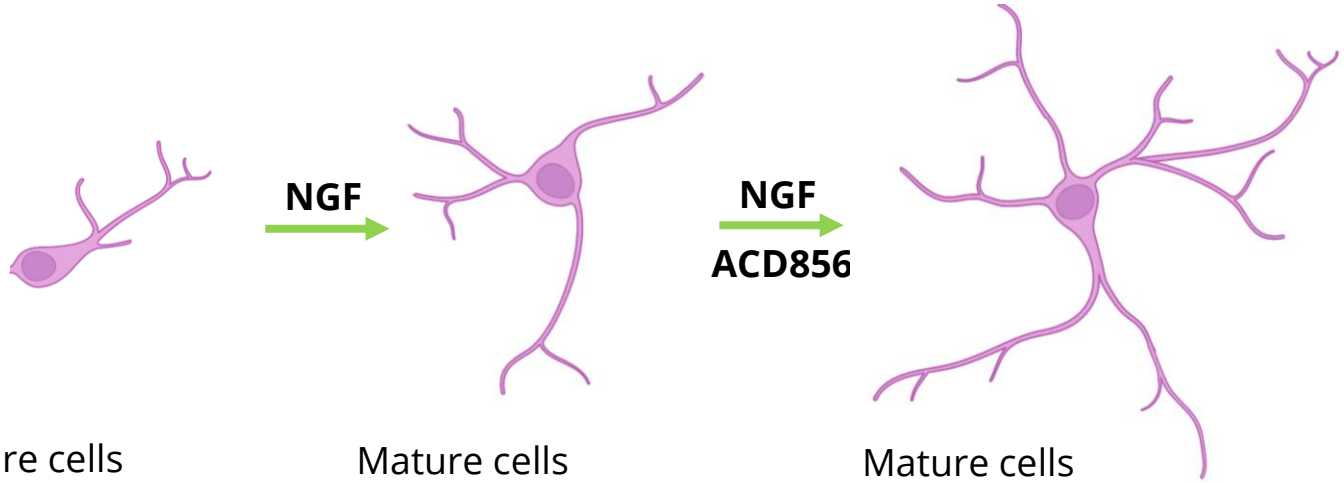
ACD856 and neurite outgrowth

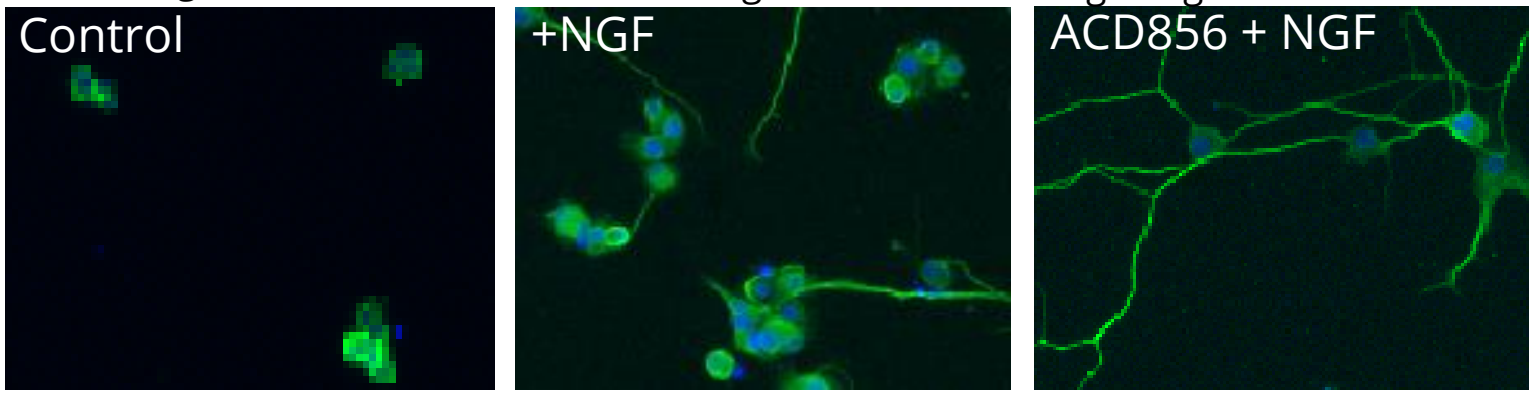
- Neurotrophins like NGF and BDNF are important for neurite outgrowth and neuronal proliferation
- Effects of ACD856 on cell number and neurite outgrowth was studied in immature neuronal-like cells

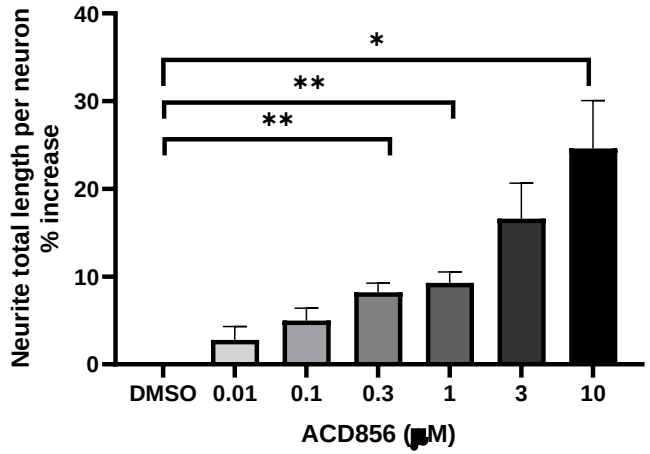


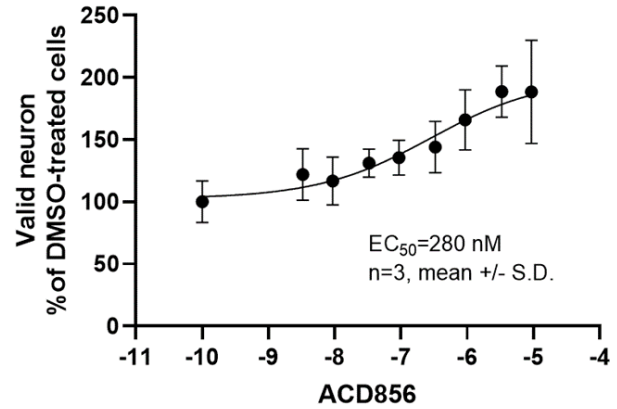
Immature cells
Low degree of neurites

Mature cells
Medium degree of neurites

Mature cells
High degree of neurites







ACD856 increase neuronal growth and neurite formation suggesting a potential for neurorestorative effects

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Results supporting disease modifying effects

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The importance of BDNF in brain function and memory

- BDNF stimulates neuroplasticity and synaptic function
- BDNF levels are increased in an activity-dependent manner. Exercise increase BDNF levels and it is believed to be one of the reasons for well-being after training
- Several lines of evidence point to the involvement of BDNF in Alzheimer's disease and in depression
- The BDNF-Val66Met polymorphism is associated with cognitive impairment and worsened amyloid pathology in Alzheimer's disease
- Carriers of ApoE4 and BDNF-Val66Met alleles have increased amyloid-beta pathology compared to non-carriers

BDNF-Val66Met heterozygotes

30% reduced BDNF secretion

- Increased rates of decline in memory
- Increased CSF Tau and p-Tau
- Reduced hippocampal glucose metabolism

"To date, this is the only genetic factor found to moderate downstream effects of amyloid-β levels in autosomal dominant Alzheimer's disease."

Bateman et al, Brain, 2016

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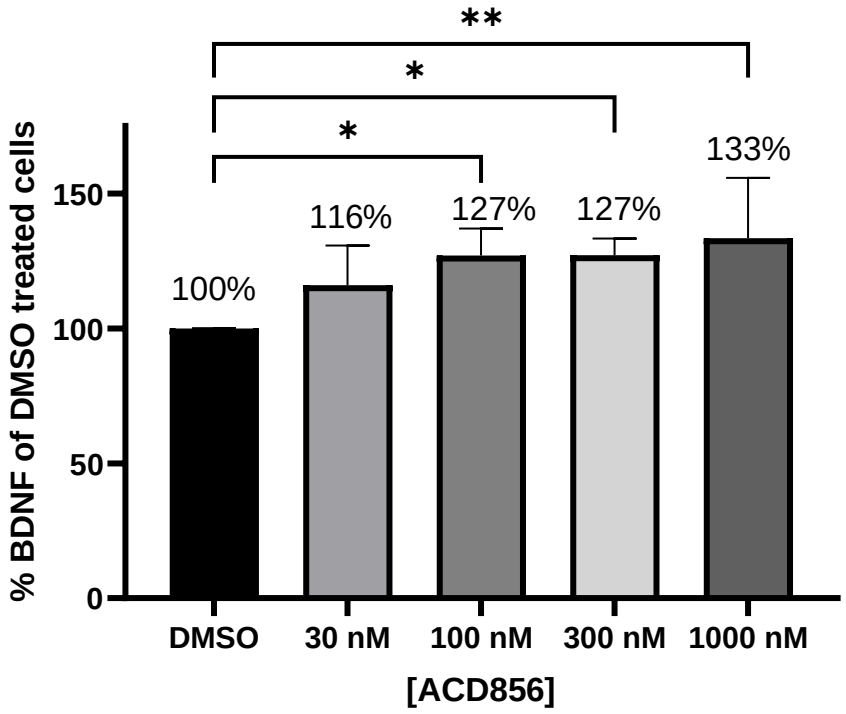
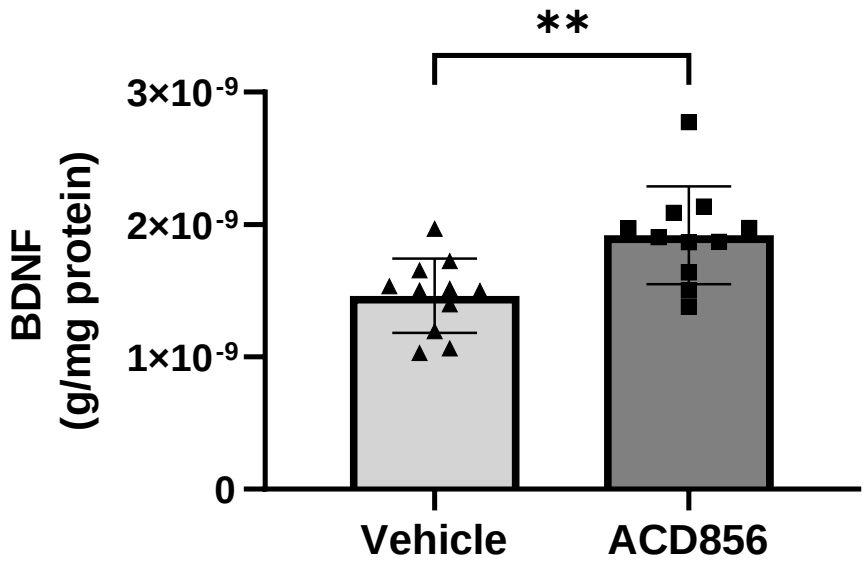
Effects of ACD856 on BDNF levels

- Cortical neurons were incubated with ACD856 for 6 hours
- Old animals were administered ACD856 once daily for 4 weeks

ACD856 increase BDNF levels in cortical neurons



ACD856 increase BDNF in brains of old mice



ACD856 significantly increase the levels of BDNF.

BDNF improves synaptic function and cognition

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Results supporting disease modifying effects

- **In vitro**
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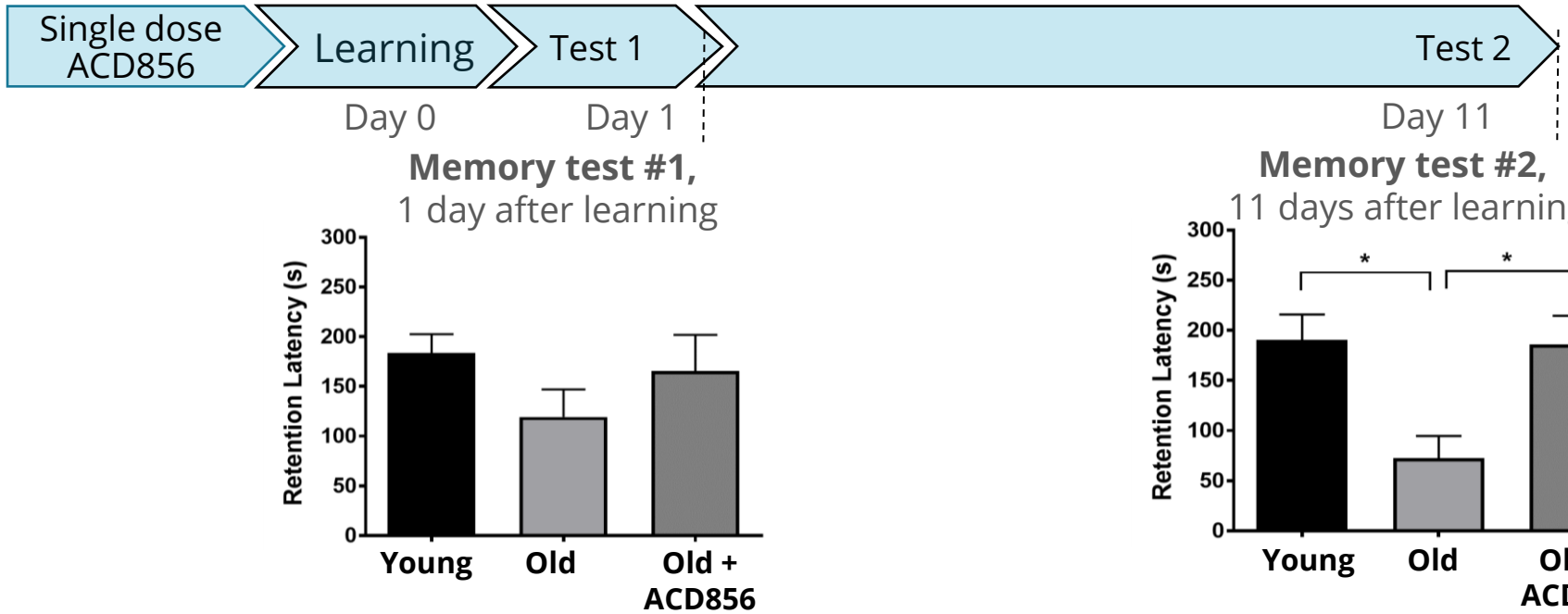
ACD856 and aged-induced memory impairment

- Old animals were used to study effects of ACD856 on age-induced memory impairment
- Two memory tests were performed at one or eleven days after a learning task



ACD856 improves age-induced memory impairment to a level similar to young animals

A single dose of ACD856 can improve the ability to both learn, store and remember information.
Repeated administration of ACD856 suggest improved neuroplastic adaption leading to better memory

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Results supporting disease modifying effects

- **In vitro**
  - Protection against amyloid-beta induced neurotoxicity
  - Potentiation of neuronal growth and neurite outgrowth
  - Increased levels of BDNF
- **In vivo**
  - Improved memory possibly through increased neuroplasticity
  - **Long term antidepressant-like effect via a potential neuroplastic adaption**

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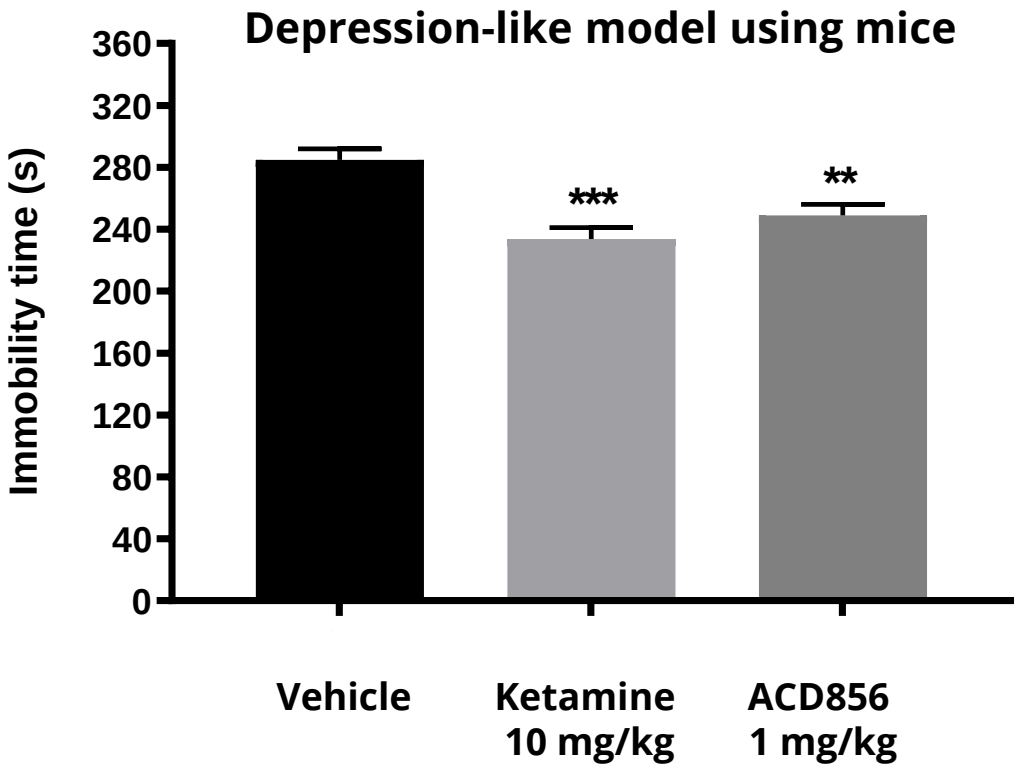
ACD856 and sustained antidepressant-like effects

- Mice were treated with ACD856 once daily for 5 days
- ACD856 was tested for antidepression-like effect 3, 5 or 7 days after the last dose



Repeated dosing of ACD856 leads to a sustained antidepressant-like effect lasting up to one week

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Summary of preclinical results – potential for disease modification

ACD856:

- ✓ Protects against amyloid-beta induced neurotoxicity
- ✓ Enhance neurite outgrowth and neuronal proliferation
- ✓ Increase the levels of BDNF in cortical neurons and in brains of aged mice
- ✓ Improves memory impairment, presumably via increased synaptic function/plasticity
- ✓ Demonstrate a sustained antidepressant-like effect

ACD856 has several short-term effects leading to memory improvement.
The presented long-term effects suggest a new potential disease modifying effect.

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Conclusions

- The preclinical data suggest a new potential use of ACD856
- The effect of ACD856 on BDNF levels are very encouraging and supports that ACD856 can improve learning and memory in multiple ways
- Neuroprotective and neurorestorative effects are add-on effects to the symptomatic effects previously seen with ACD856

The new presented data introduce a potential for disease modifying treatment to the already established symptomatic effects of ACD856.

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Acknowledgement

- **Team at Alzecure Pharma**
  - Cristina Parrado
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  - Magnus Halldin
  - Johan Sandin
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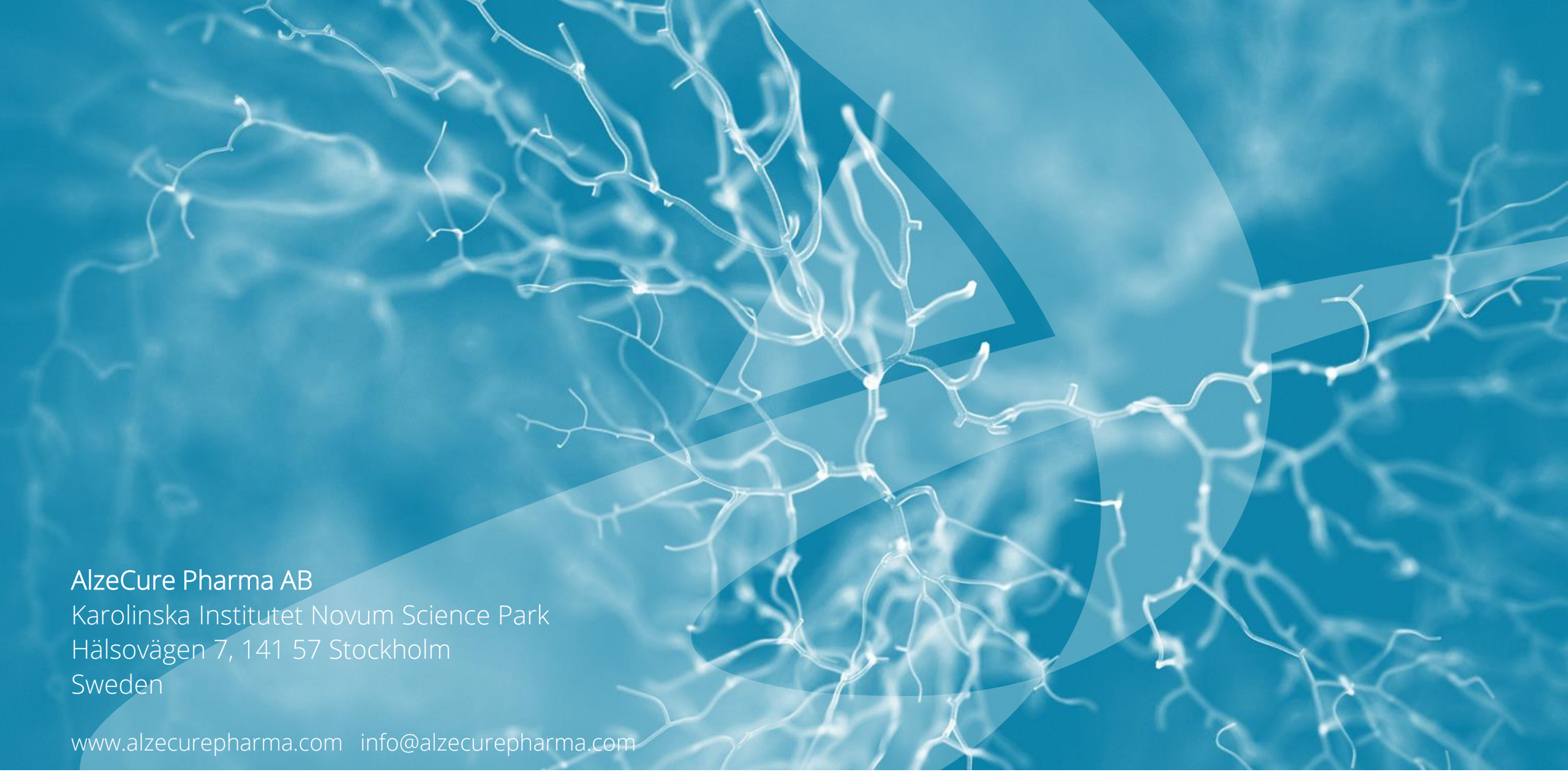
  - Prof. Bengt Winblad
  - Prof. Maria Eriksdotter
  - Assoc. Prof. Sumonto Mitra

Some of the artwork were performed by the use of BioRender.com



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Q&A session

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Today's panel in the Q&A

Bengt Winblad
MD, Ph.D.
Professor at KI

EXPERIENCES

- Professor in Geriatrics and Aging at Karolinska Institute (KI)
- Education: MD, PhDs from Umeå University
- Research focus on treatment & care of dementia with focus on Alzheimer's

Johan Sandin
CSO
Ph.D.

- Expert in in vivo Pharmacology with 16 years experience from the drug discovery industry within Neurology
- Education: Ph.D. in Neuropharmacology, Karolinska Institute

Pontus Forsell
Head of Discovery & Research
Ph.D.

- Expert in drug screening with +20 years of experience from industrial research and drug development within CNS and Pain
- Education: Ph.D. in Medical Biochemistry & Biophysics from Karolinska Institute

Martin Jönsson
CEO

- Extensive experience in various senior management positions with >20 years of international experience in the industry
- Education: MSc in BA from Lund University, Ottawa, Canada & Freiburg, Germany

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Take Home Messages

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Take home messages

- **Increased interest and activity level in the Alzheimer's field** - both with regard to investors and new pharma companies entering the area
- **Anti-bodies are very promising, slowing the disease progression**, - but not curing the disease or increasing patient's cognition
- => ***Huge need for new more effective, safer and more convenient treatment***

- **AlzeCure's projects continue to develop well**:
  - **NeuroRestore**, our cognitive enhancer, has **potentially disease modifying abilities** which can add additional opportunities for the project
  - **Alzstatin**, our **preventive therapy**, is developing according to plan, having a **new additional compound** in pre-clinical development, ACD680, to secure a **long patent time**

Learn more at: www.alzecurepharma.com

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Thank You
for attending

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