Acumen R&D Day

October 2, 2024

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Any statement describing Acumen's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Words such as "believes," "expects," "anticipates," "could," "would," "seeks," "aims," "plans," "potential," "will" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements concerning Acumen's business, and Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the expected sufficiency of its cash resources into the first half of 2027, the therapeutic potential of Acumen's product candidate, sabirnetug (ACU193), including against other antibodies, the anticipated timeline for announcing the top-line results from our Phase 1 trial of a subcutaneous dosing option of sabirnetug, and the anticipated timeline for completing enrollment in our Phase 2 trial. These statements are based upon the current beliefs and expectations of Acumen management, and are subject to certain factors, risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing safe and effective human therapeutics. Such risks may be amplified by the impacts of the COVID-19 pandemic. These and other risks concerning Acumen's programs are described in additional detail in Acumen's filings with the Securities and Exchange Commission ("SEC"), including in Acumen's most recent Annual Report Form 10-K and future filings and reports by Acumen. Copies of these and other documents are available from Acumen. Additional information will be made available in other filings that Acumen makes from time to time with the SEC. These forward-looking statements speak only as of the date hereof, and Acumen expressly disclaims any obligation to update or revise any forward-looking statement, except as otherwise required by law, whether, as a result of new information, future events or otherwise. In this presentation, references to cash also include cash equivalents.

Dan O'Connell

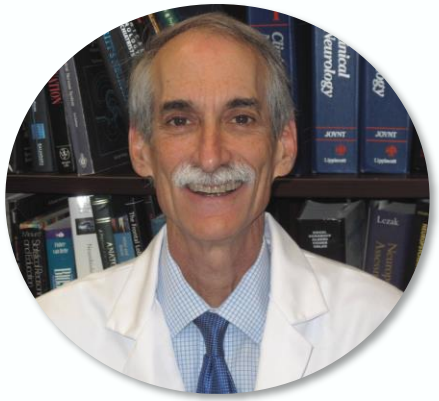
Chief Executive Officer, Acumen Pharmaceuticals

Dr. Jim Doherty

President and Chief Development Officer, Acumen Pharmaceuticals

Dr. Eric Siemers

Chief Medical Officer, Acumen Pharmaceuticals



Dr. Stephen Salloway

Founding Director of the Memory and Aging Program at Butler Hospital in Providence, Rhode Island, and Professor of Psychiatry and Neurology at the Warren Alpert Medical School of Brown University

Dr. Paul Solomon

Founder and Clinical Director of the Boston Center for Memory, professor in the Department of Neurology at Boston University School of Medicine and an investigator at Boston University Alzheimer's Disease Center

Agenda

Welcome	Alex Braun, Head of IR
Introduction to Acumen	Dan O'Connell
Amyloid Beta Oligomers & Nonclinical Profile of Sabirnetug	Dr. Jim Doherty
INTERCEPT-AD Phase 1 Results	Dr. Stephen Salloway
INTERCEPT-AD Fluid Biomarker Results & ALTITUDE-AD Design	Dr. Eric Siemers
AD Landscape & ALTITUDE-AD Enrollment Progress	Dr. Paul Solomon
Milestones and Concluding Remarks	Dan O'Connell
Q&A	All speakers

Introduction to Acumen

ACUMEN

Acumen's Mission: to Develop Innovative Treatments that *Preserve Quality Time* for all People Impacted by Alzheimer's Disease (AD) and Other Forms of Neurodegeneration

Alzheimer's disease affects more than

55M people worldwide…

…and the number is expected to grow

3x over the next 25 years*

Acumen is leveraging:

- A dedicated team with extensive CNS/AD drug-development experience who are fully committed to better treatment options for people living with AD
- Decades of novel discoveries, methods and IP that inform the therapeutic rationale for targeting toxic amyloid beta oligomers (AβOs) in AD
- A potentially differentiated product candidate with positive Phase 1 results in Alzheimer's patients, now advancing in Phase 2 as a potential next generation treatment

*Lancet Public Health 2022; 2023 Alzheimer's Association Facts and Figures

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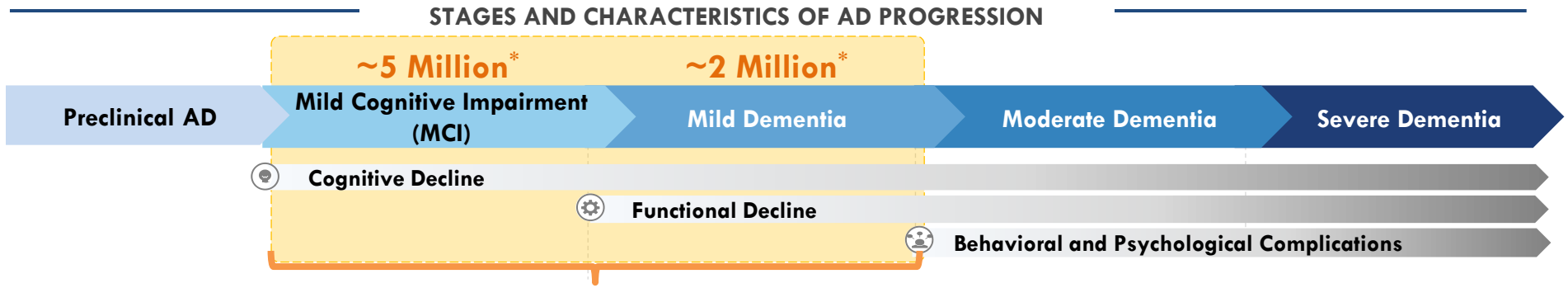
Early AD Patient Population Represents Significant and Growing Market



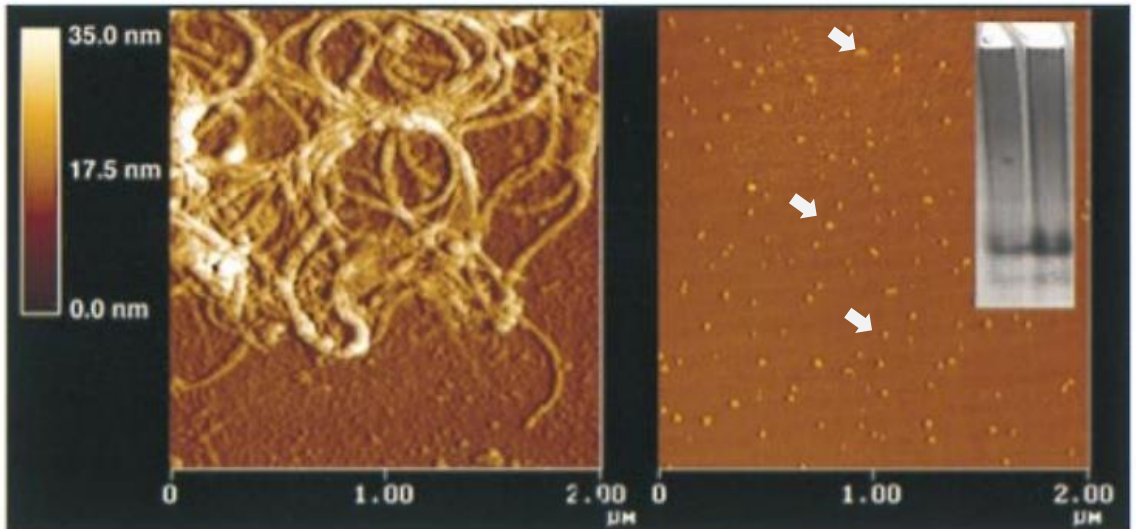
Early Alzheimer's Disease in the U.S.

Higher prevalence due to aging population → More diagnosed cases driven by improved ability to diagnose in earlier stages of AD → More treated cases due to availability of treatment options and favorable shifts around adoption = **Growing Market**

*Alzheimer's Association

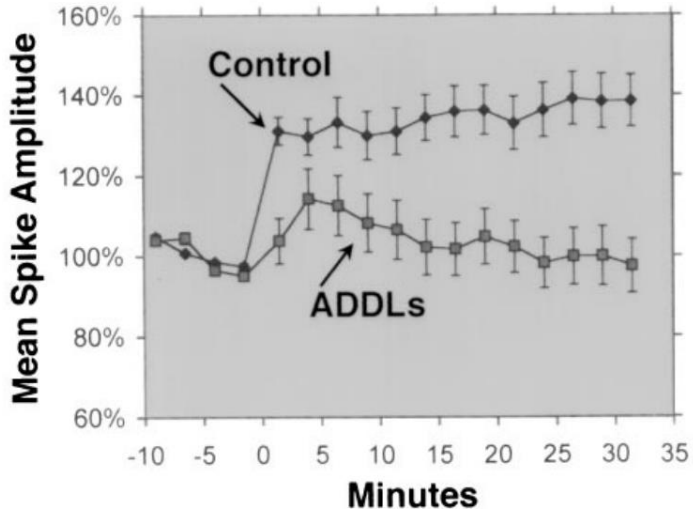
Acumen Founders Contributed to the Seminal Work Informing AβO Toxicity

Large, non-diffusible fibrillar Aβ species vs. **Small, diffusible, globular ADDLs (AβOs)**



- Early experiments characterized Aβ-derived diffusible ligands, or ADDLs (synthetic AβOs), which were shown to be synaptotoxic in contrast to Aβ fibrils, such as those found in amyloid plaques

ADDLs (AβOs) block long-term potentiation (LTP)



- ADDLs rapidly inhibited LTP, a classic model for synaptic plasticity and a surrogate for cognitive function
  - After only 45 min, ADDLs completely blocked LTP in rat hippocampal slices before any overt signs of cell degeneration

These results and related discoveries supported novel IP and served as the scientific cornerstone of Acumen, leading to an AβO-directed drug-discovery effort that continues today

Lambert M.P., et al. Diffusible, nonfibrillar ligands derived from AB1-42 are potent central nervous system neurotoxins. Proc. Natl. Acad. Sci. USA Vol. 95, 6448–6453, May 1998 Neurobiology.

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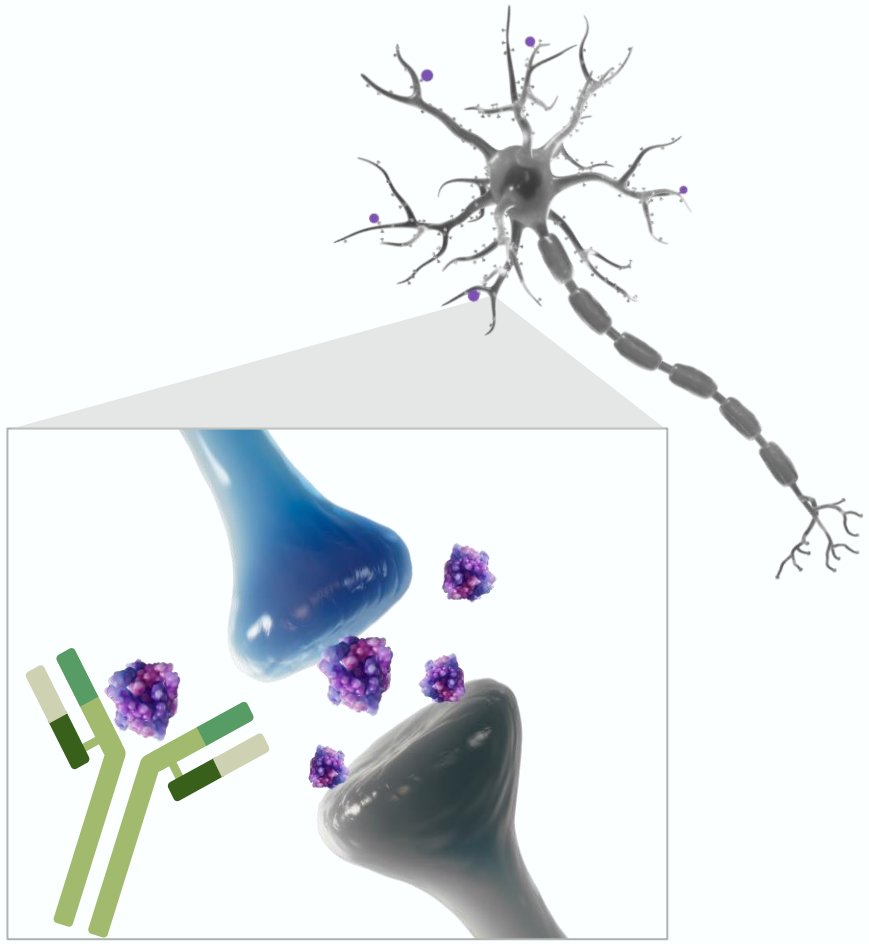
Sabirnetug: Potential Next Generation Immunotherapy for Early AD

Large Pharma Collaboration	• **Discovered in collaboration with Merck & Co.** Acumen holds exclusive program rights with no future financial or other obligations due to Merck
Designed for Improved Efficacy & Safety	• **Humanized, affinity matured mAb developed to target toxic Aβ oligomers** • **IgG2 subclass mAb with reduced effector function**
Encouraging FDA Interactions	• **FDA Fast Track designation for the treatment of early Alzheimer's disease** • **FDA End of Phase 2 meeting in 4Q 2023**
Positive Phase 1 in AD	• **Successful Phase 1 exclusively in early AD patients** • **Phase 2 initiated in 2Q 2024**



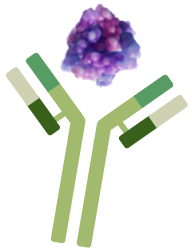
Opportunity for a Next Generation Treatment Option for Early AD

Disease Burden

- Alzheimer's disease was the fifth-leading cause of death among individuals age 65 and older in 2021[1]
- WW economic burden of AD and other related dementias projected to rise from $3T in 2019 to $17T by 2050[2]

Differentiation Opportunities

- Novel mechanism (AβOs) within anti-amyloid landscape
- Improved efficacy
- Improved safety: Lower rate of ARIA-E



Sabirnetug Target Patient Population

Sabirnetug has the potential to be a treatment of choice for both treatment naïve patients and ones requiring chronic treatment, especially in sub-populations who are at high risk of ARIA-E (e.g., ApoE4 homozygotes) and/or would prefer a safer option

1. Centers for Disease Control and Prevention, National Center for Health Statistics. National Vital Statistics System, Mortality 2018-2021 on CDC WONDER Online Database, released in 2021; 2. Nandi et al 'Global and regional projections of the economic burden of Alzheimer's disease and related dementias from 2019 to 2050: A value of statistical life approach', The Lancet, 2022.

Amyloid Beta Oligomers and the Nonclinical Profile of Sabirnetug

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Soluble Amyloid Beta Oligomers (AβOs)

A low abundance, toxic target when compared to insoluble, high concentration amyloid plaque deposits in the diseased brain

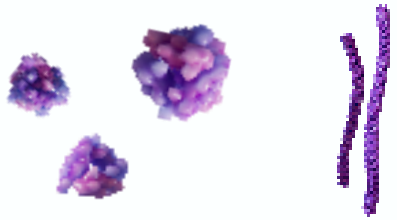
Disease progression

Monomer

Soluble Aβ 1-40
2712 pM (CSF)

Oligomers

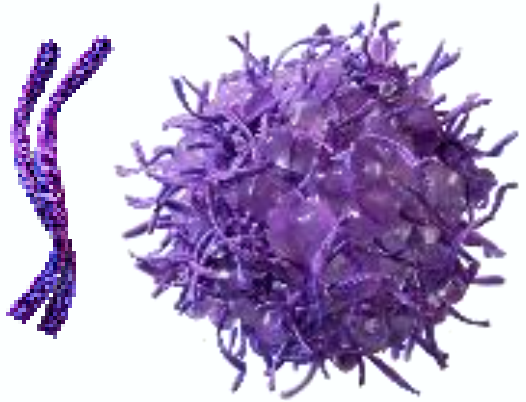
Protofibrils



Soluble AβO/Protofibril
0.02-2 pM (CSF)

Fibrils

Plaques



Insoluble Amyloid
1818 pmol/g (brain)

Images not to scale.

Walsh et al. 1997 J Biol Chem; Harper et al. 1997 Chem Biol; Nilsberth et al. 2001 Nat Genet; O'Nuallain et al. 2010 J Neurosci; Lannfelt et al. 2013 J Intern Med; Lannfelt et al. 2014 AlzRes Ther; Willemse 2021 Alzheimers Dement; Wang 1999 Exp Neurol; Savage 2014 Neurobiol Dis.

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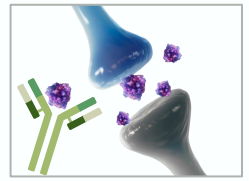
Targeting Soluble AβOs: An Early and Continuous Intervention in AD

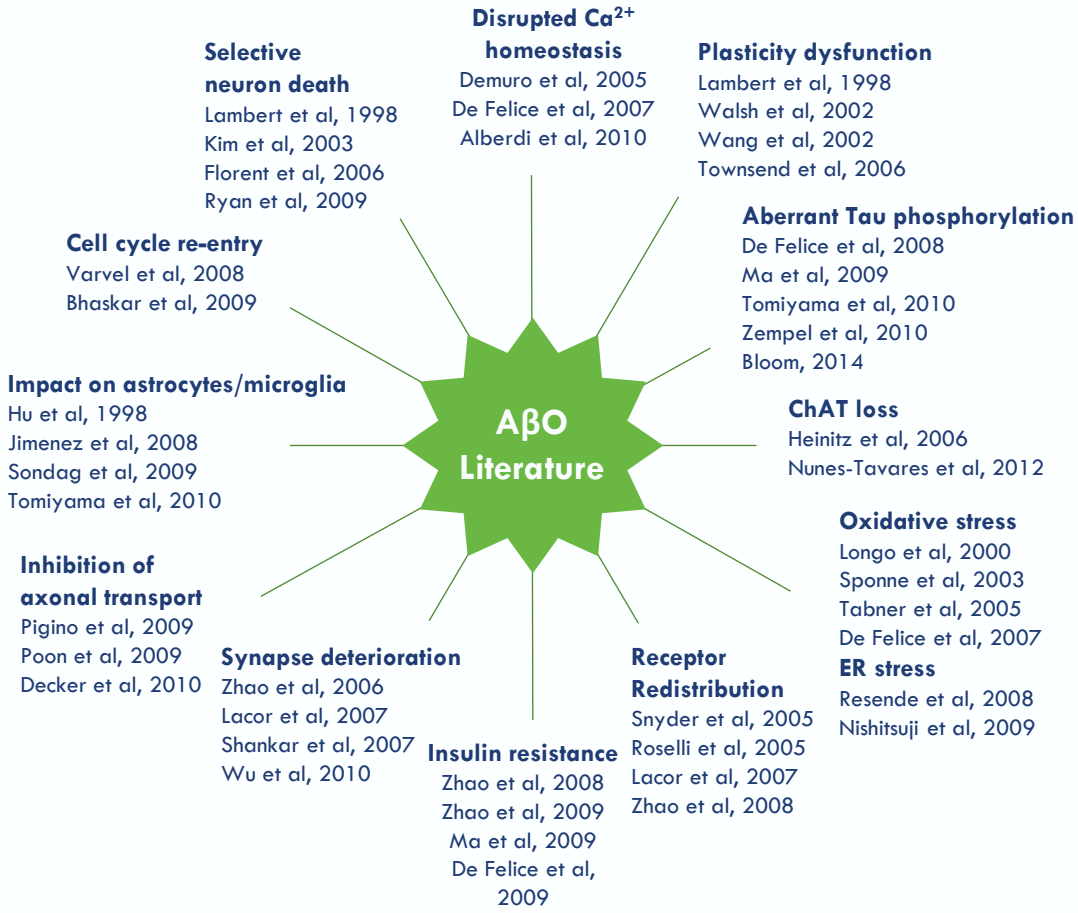


Why focus on soluble forms of Aβ?

- Soluble Aβ forms appear early in the course of disease pathophysiology
- Reduced neuronal toxicity and intervention at the synaptic level may prevent irreversible neuronal cell death
- Production of toxic soluble Aβ persists after plaque removal

Consequences of soluble Aβ oligomer production:

- x Synapses dysfunction and loss
- x Tau hyperphosphorylation
- x Immune cell activation
- x Functional impairment



Adapted from Cline et al. 2018

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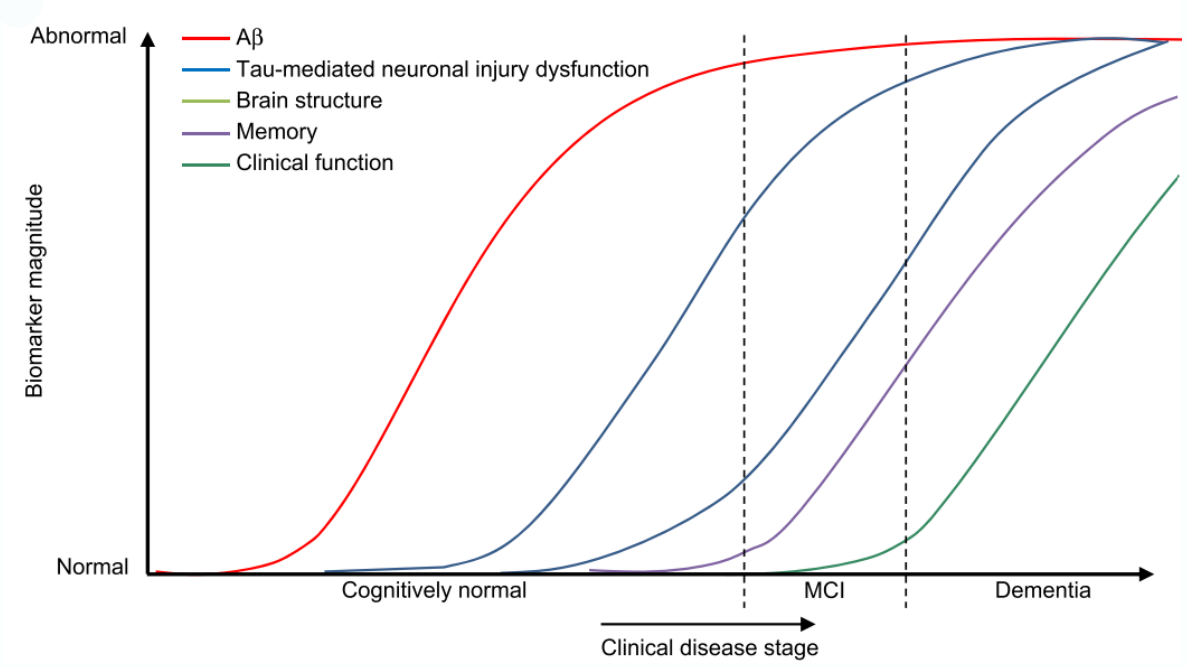
AβO Concentrations Peak in Early Alzheimer's Disease

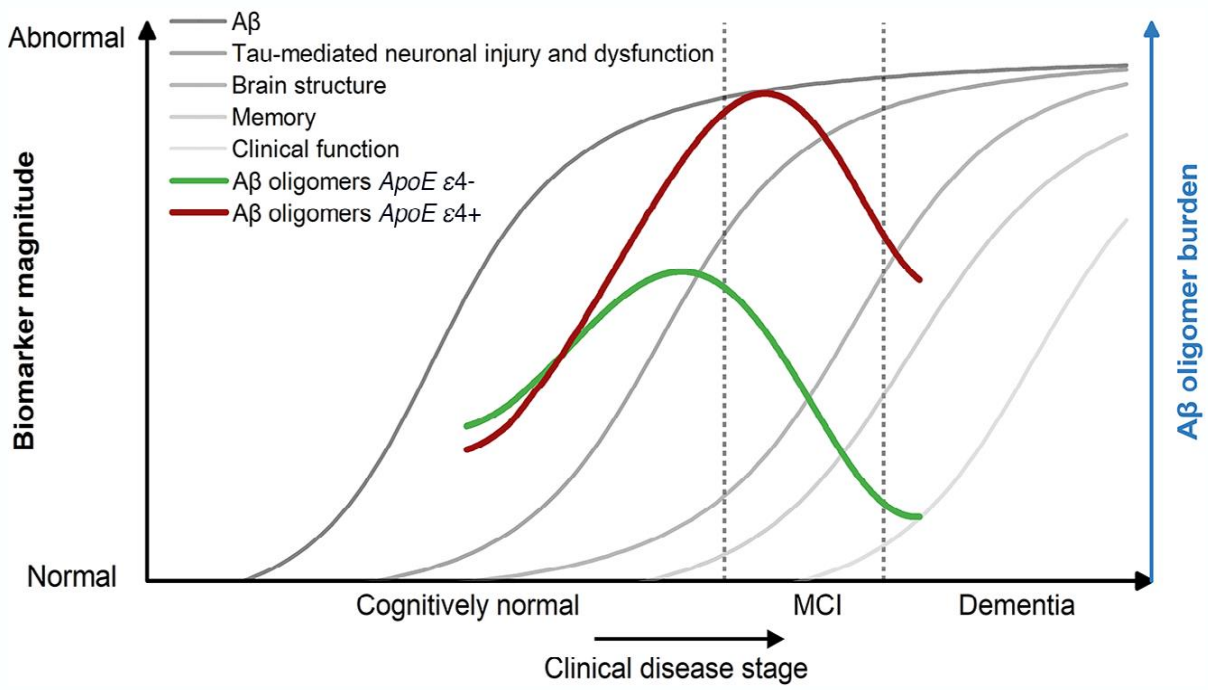
Soluble Aβ forms appear early in disease

A temporal model of Alzheimer's disease biomarkers



Adapted from Aisen et al. 2017

Model of Aβ oligomer levels in CNS across the Alzheimer's disease continuum



Adapted from Blomeke et al. 2024

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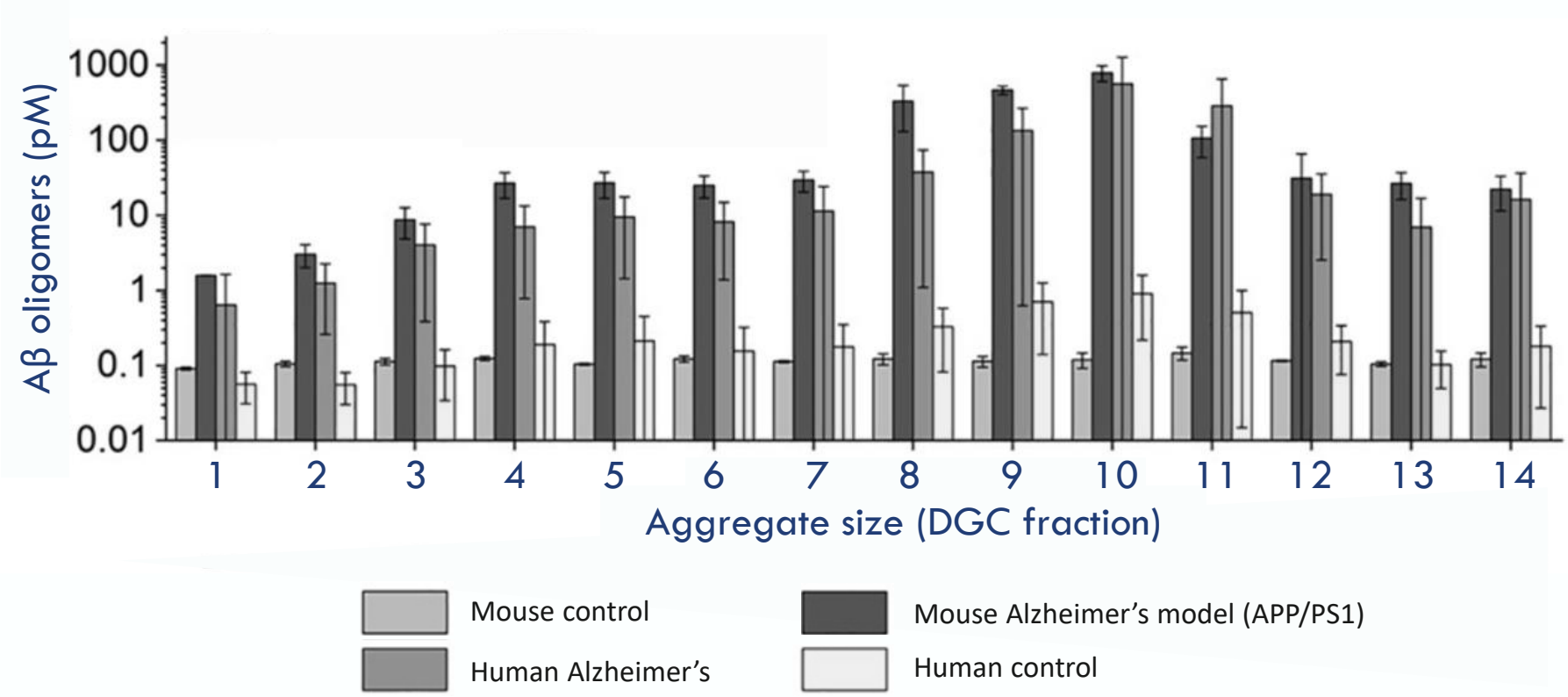
Quantitation of AβOs of Different Sizes in Brain Homogenates

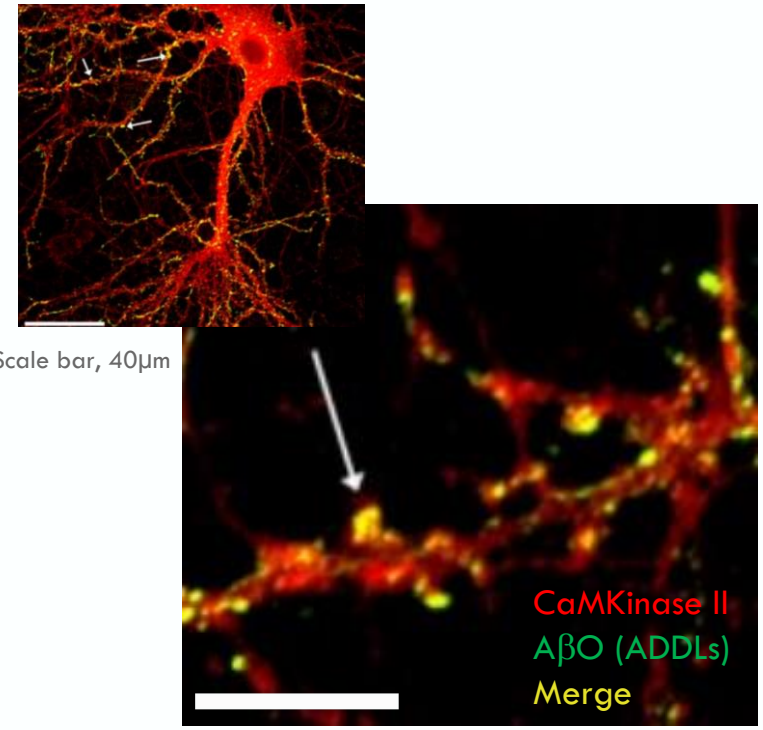
Size distribution of AβOs in murine and human brain homogenates by sFIDA assay



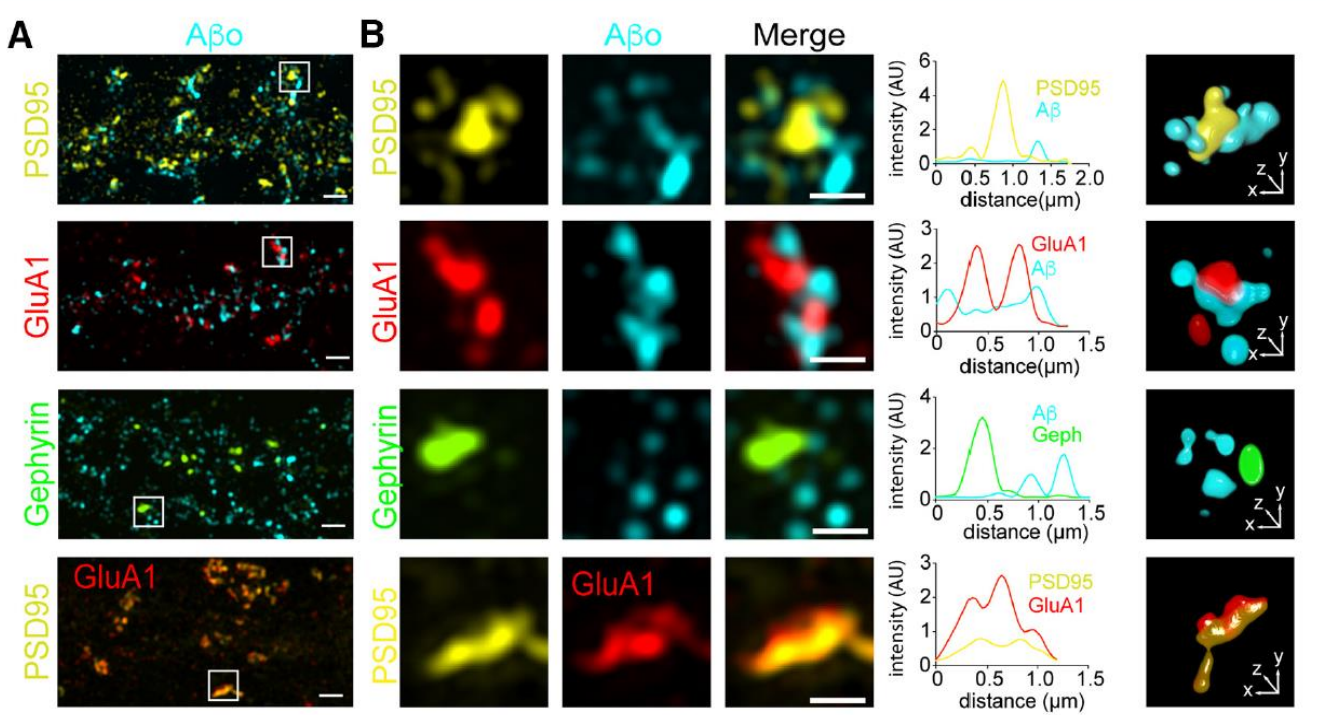
Adapted from Kass et al. 2022

Perisynaptic Localization of Aβ Oligomers in Rat Neurons

AβOs form nanoscale clusters adjacent to excitatory synapses



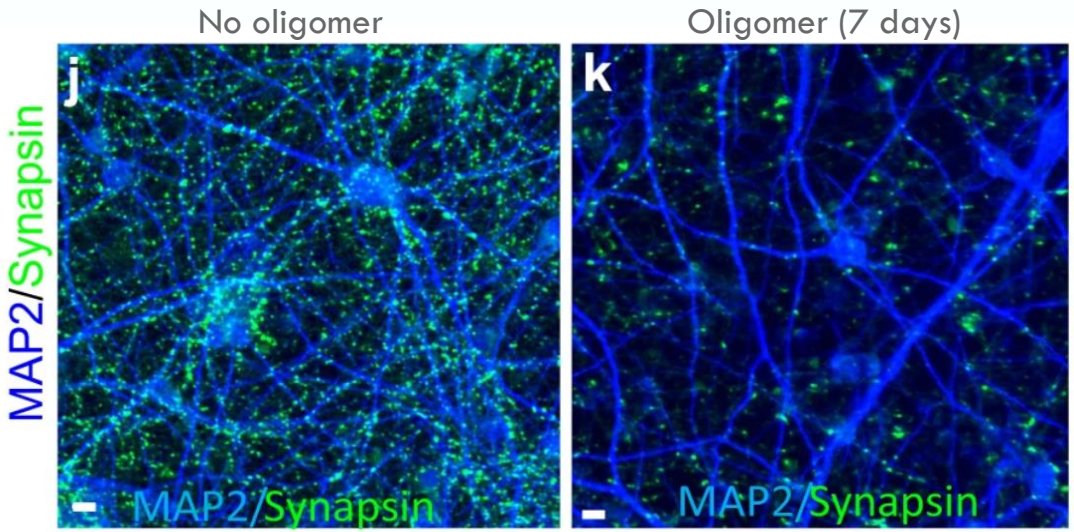
Adapted from Lacor et al. 2004

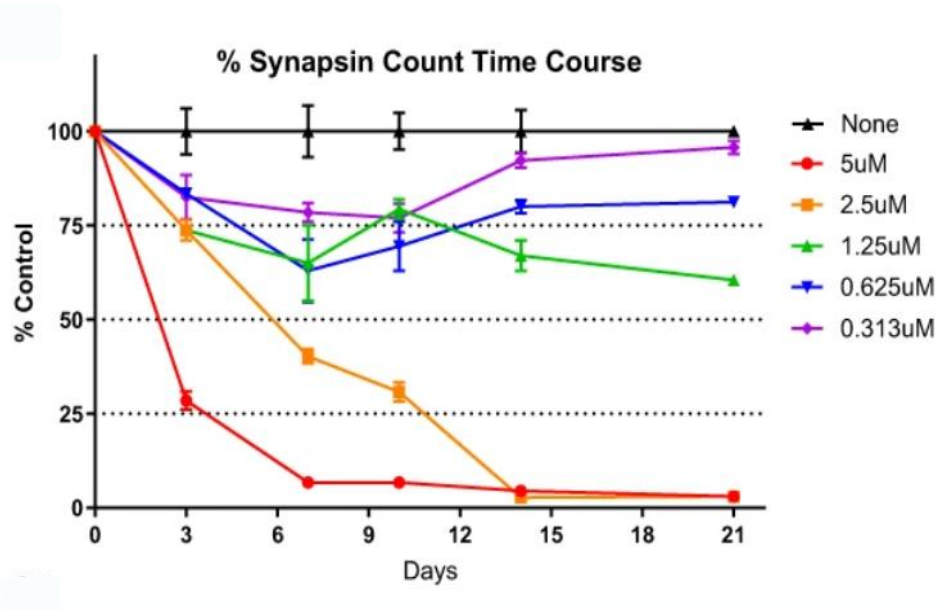


Adapted from Actor Engel et al. 2021

AβOs Cause Synaptic Damage

Synthetic AβOs applied to human iPSC neurons cause synapse loss





Adapted from Bassil et al. 2021

Functional disruption of synapses by AβOs may provide a molecular basis for impaired memory function in early AD

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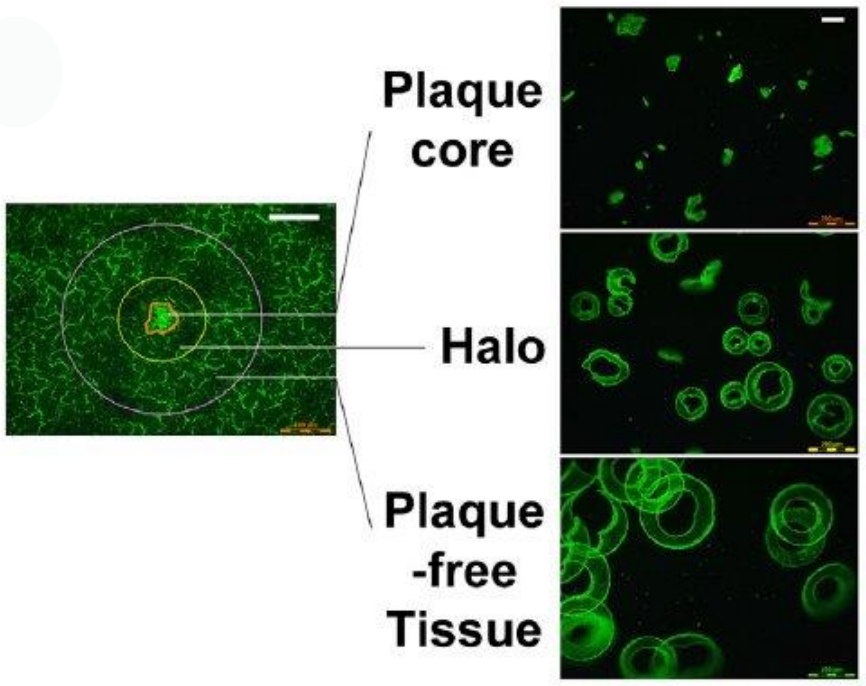
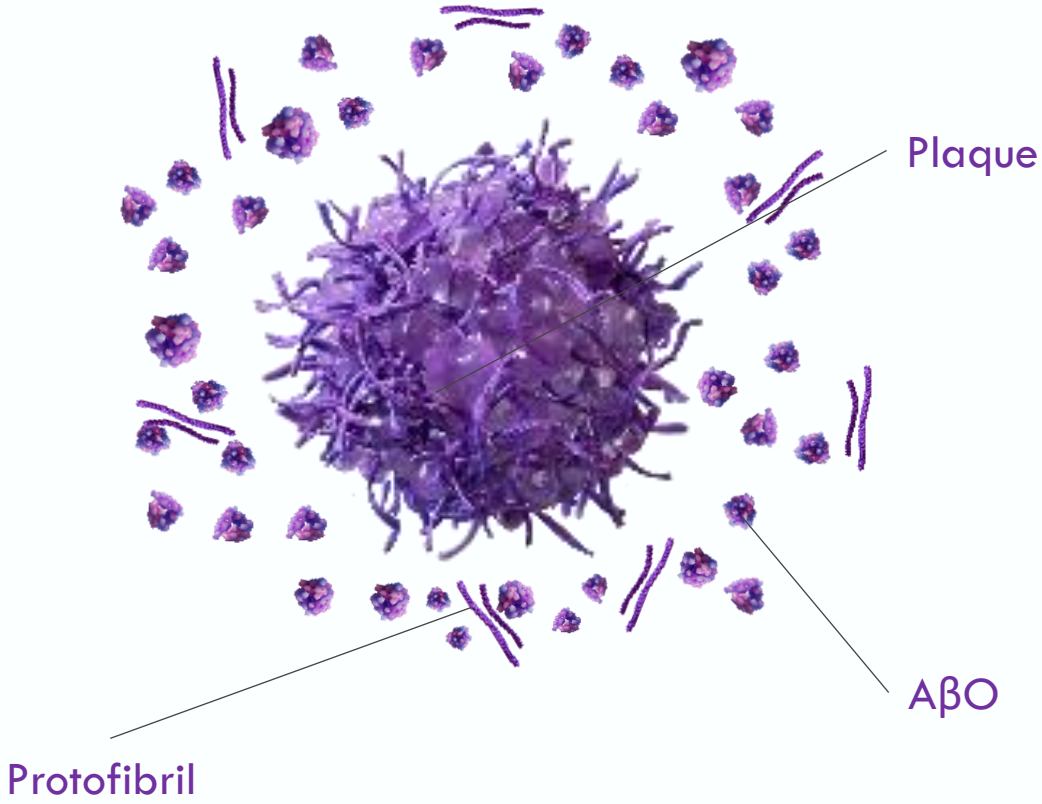
AβOs are Associated with Amyloid Plaques

AβOs form halos of soluble aggregates around dense core of plaque



Adapted from Liu et al. 2015



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AβOs Induce Tau Hyperphosphorylation

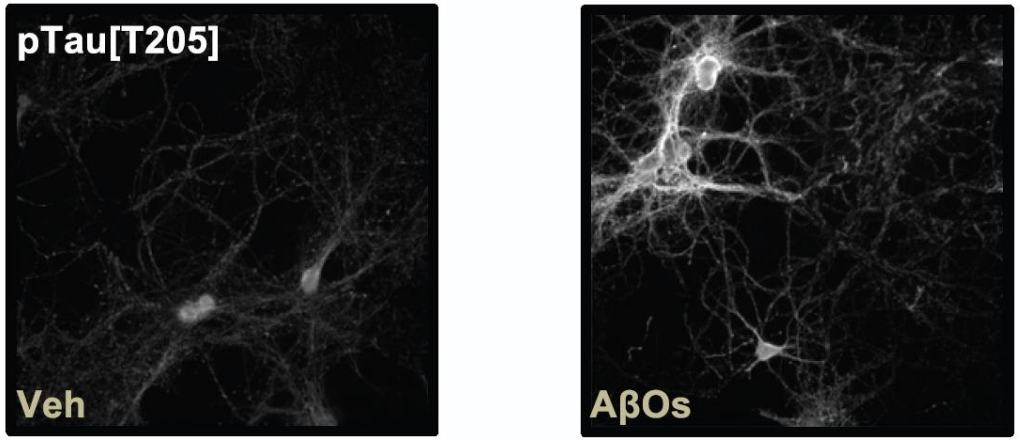
ADDLs increase pTau in rat hippocampal neurons

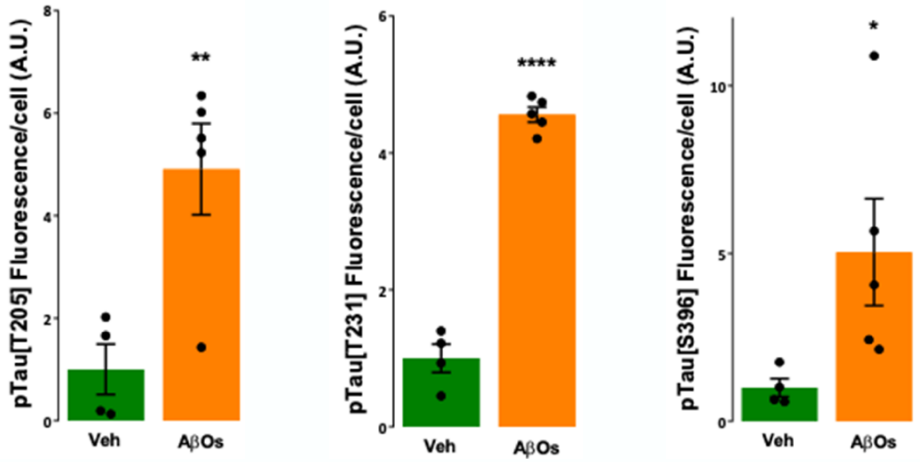
- pTau levels were markedly increased in neurons that exhibited ADDL binding but not in neurons that were ADDL-free
- Tau hyperphosphorylation can be induced by ADDLs, as well as by soluble extracts containing oligomers obtained from AD brains

De Felice et al. 2008

Vehicle-treated neurons exhibited low pTau immunofluorescence

500 nM AβOs (ADDLs) for 6 hours significantly increased pTau immunofluorescence

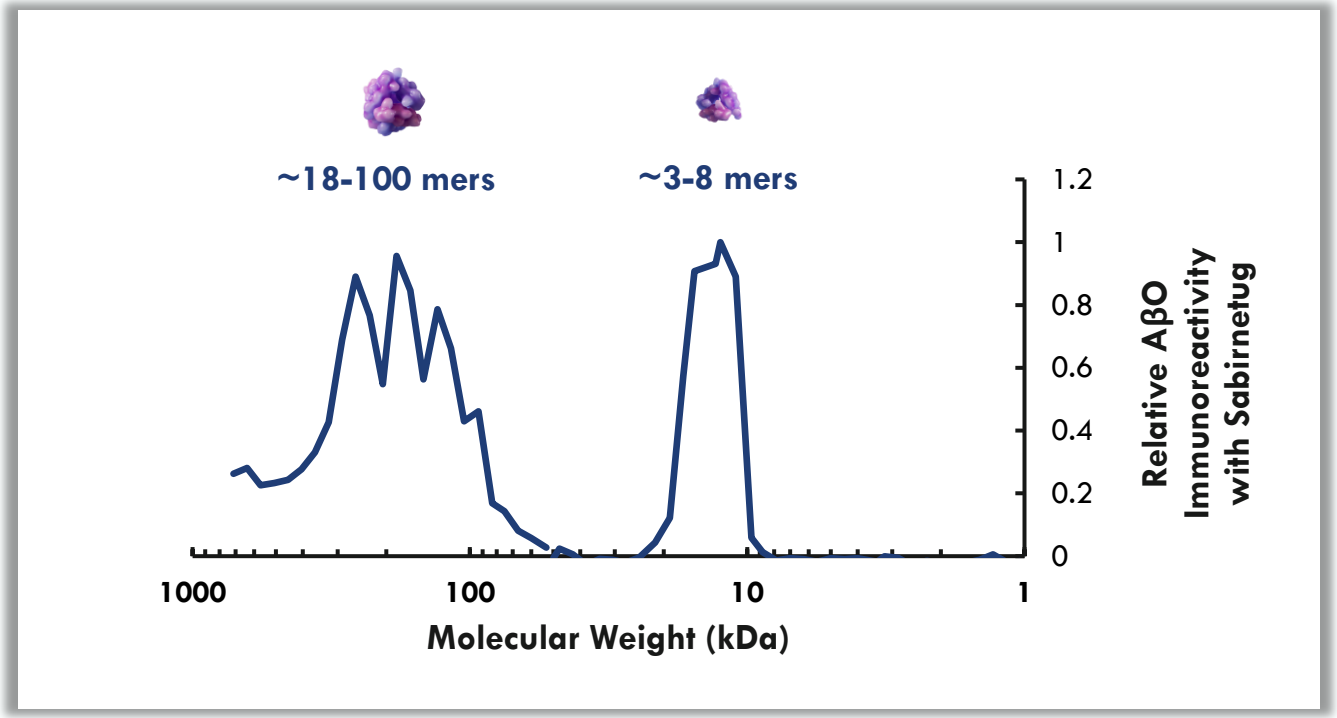




Adapted from Cline et al. 2019

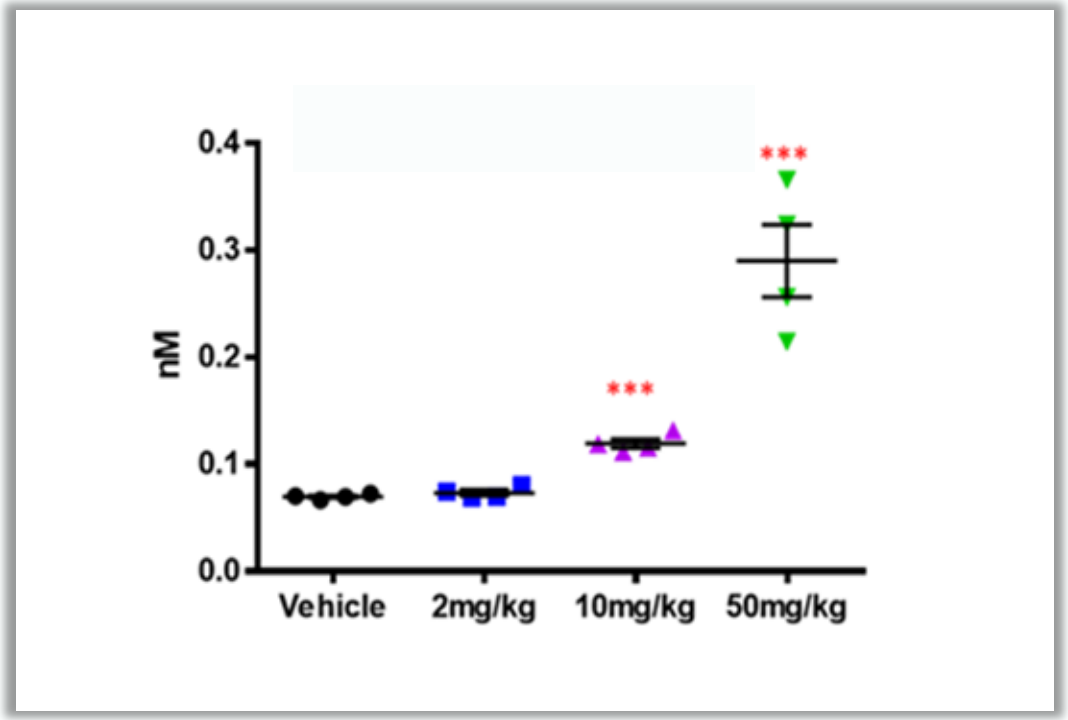
Sabirnetug Recognizes a Wide Range of Oligomeric Species of Aβ

Broad AβO size distribution recognized by sabirnetug in human AD brain



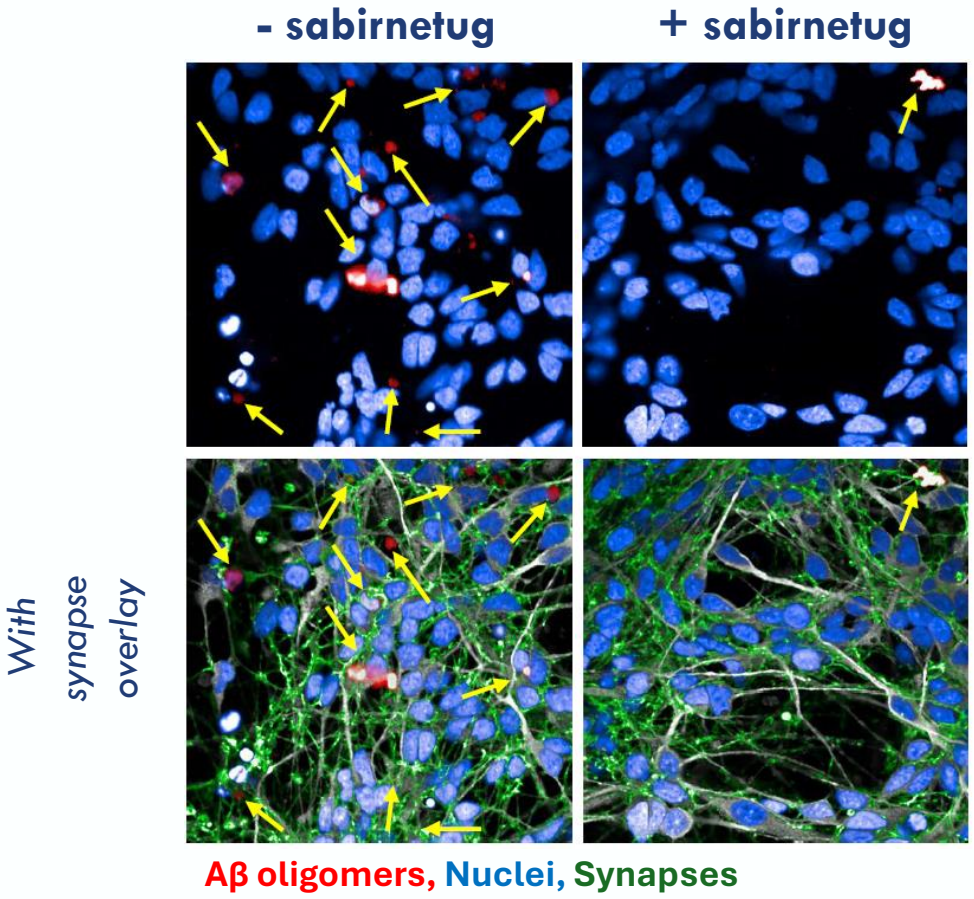
Data from lab of William Klein, NU, 2018

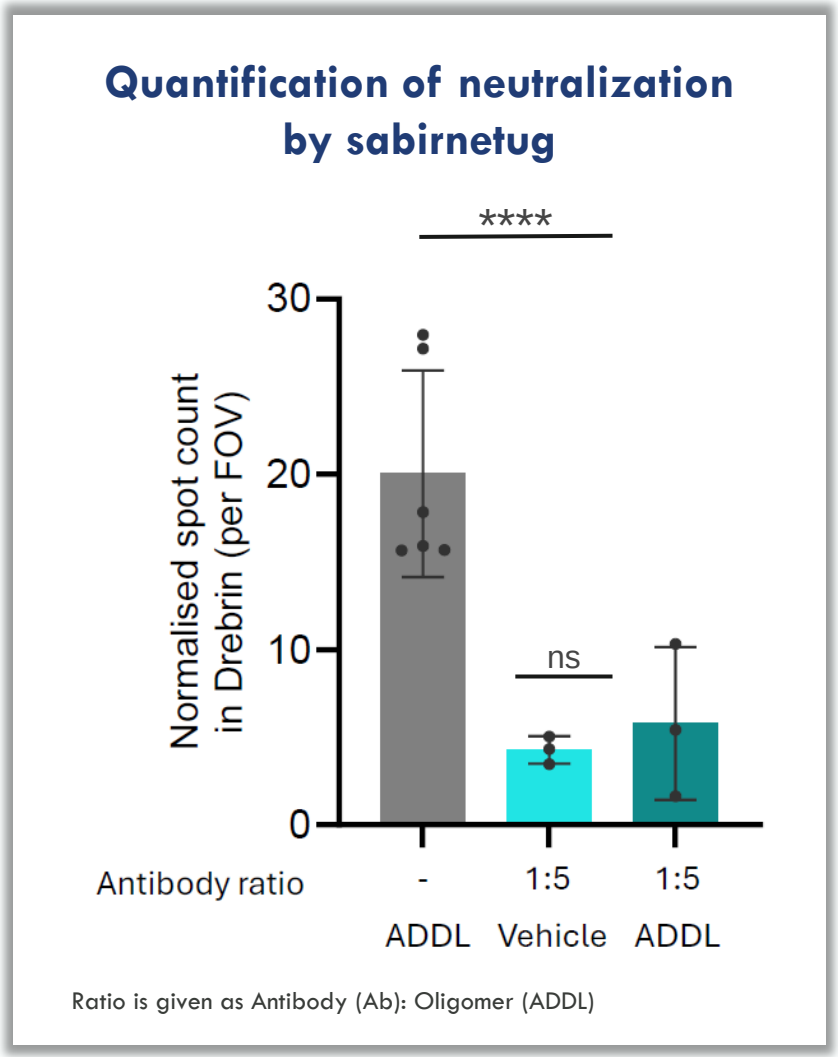
Sabirnetug dose dependently binds to AβOs in brain tissue from Tg2576 mice



Merck internal data, 2011

Sabirnetug Prevents Oligomer Synaptic Binding to iPSC-derived Human Neurons

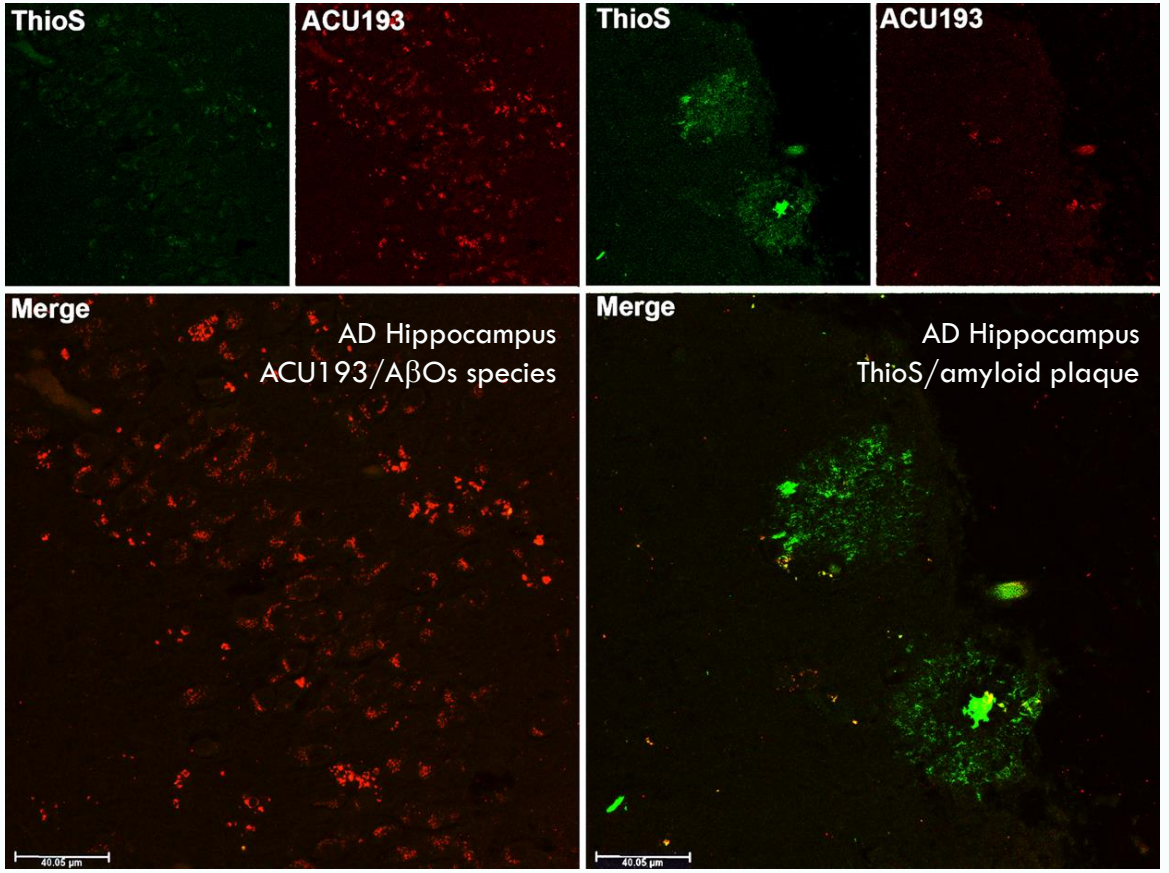




Internal data, 2024

Sabirnetug is Highly Selective for AβOs Versus Aβ Plaques

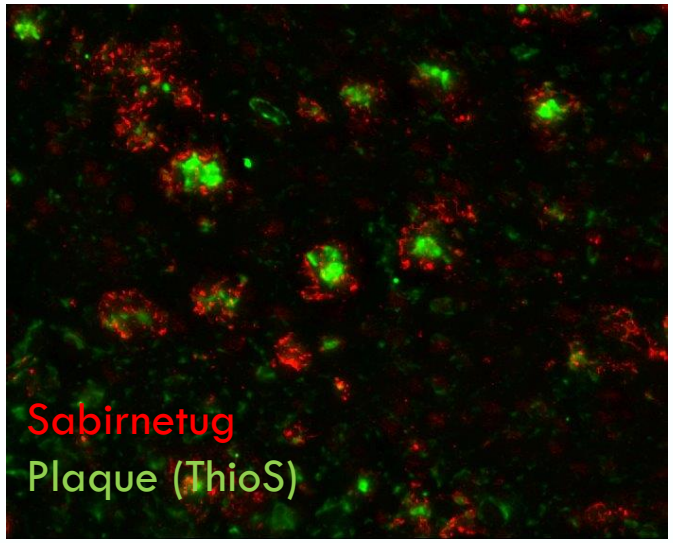
Sabirnetug staining in human AD brain slices



Adapted from Krafft et al. 2022

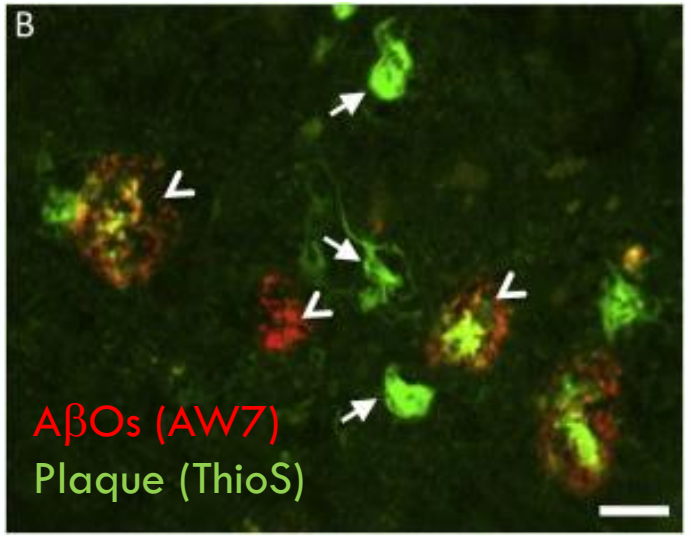
Amyloid Plaques are Surrounded by a Halo of AβOs

Transgenic mouse model of AD



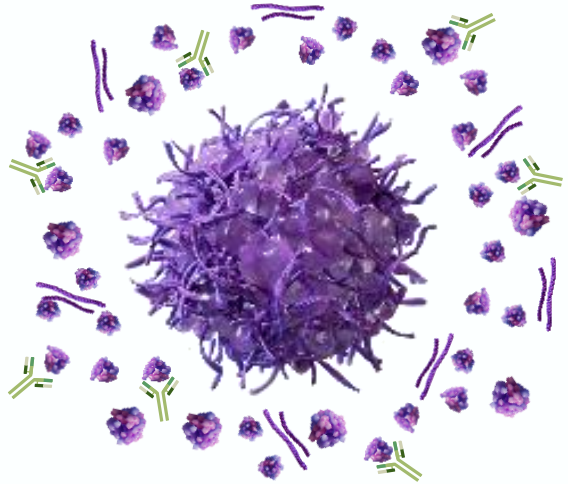
Lab of William Klein, NU

AD brain tissue



Spires-Jones et al. 2016

Sabirnetug targets AβOs that form halos of soluble aggregates around dense core of plaques

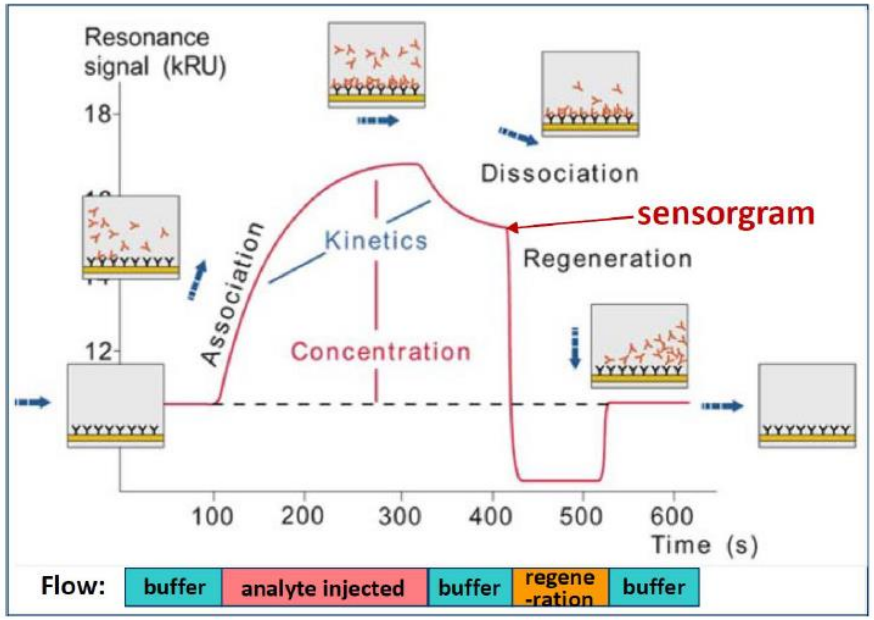


Sabirnetug binding to soluble AβOs

Defining Sabirnetug AβO Selectivity

Measurement of binding to Aβ conformers with SPR

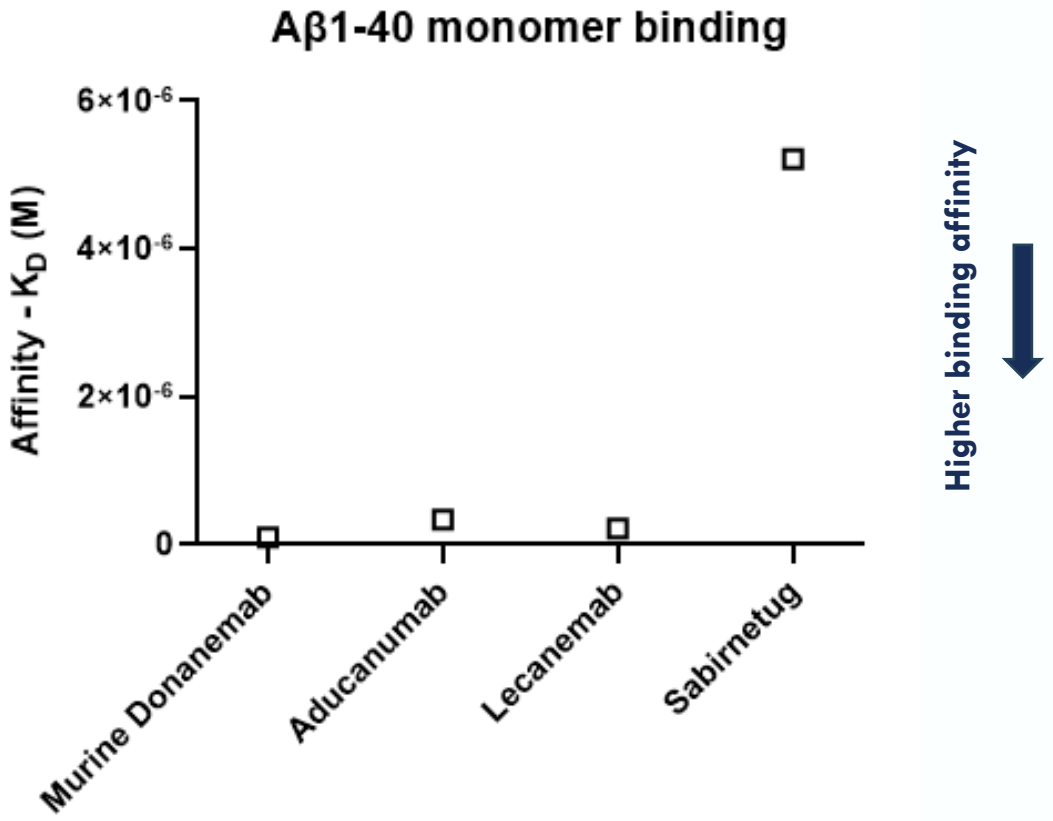
Multi Cycle Kinetic SPR



- Surface Plasmon Resonance (SPR) exploits physical properties of light to measure binding kinetics between two proteins
- The SPR setup immobilizes a pan-Aβ antibody on the chip to capture Aβ prior to adding the test antibody
- For Aβ monomers, we utilized the commonly used Multi Cycle Kinetic SPR setup

Sabirnetug was Developed to Selectively Target AβOs

High selectivity for AβOs versus monomeric Aβ



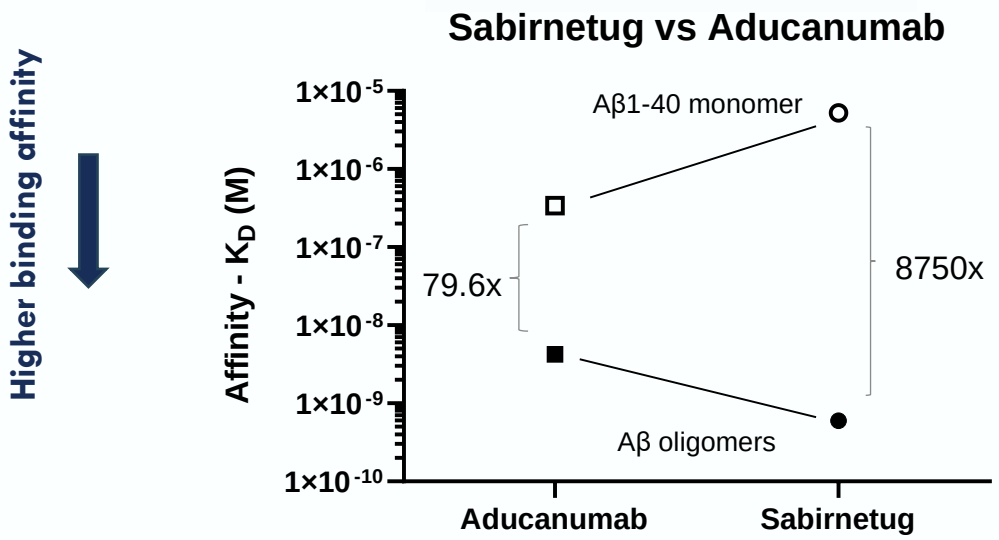
Internal data, 2024

- Aβ monomers are ~7000x fold higher concentration than AβOs in AD CSF
- Higher affinity for monomeric Aβ will reduce functional selectivity due to high monomer levels
- Sabirnetug has much lower affinity than other mAbs for Aβ monomers

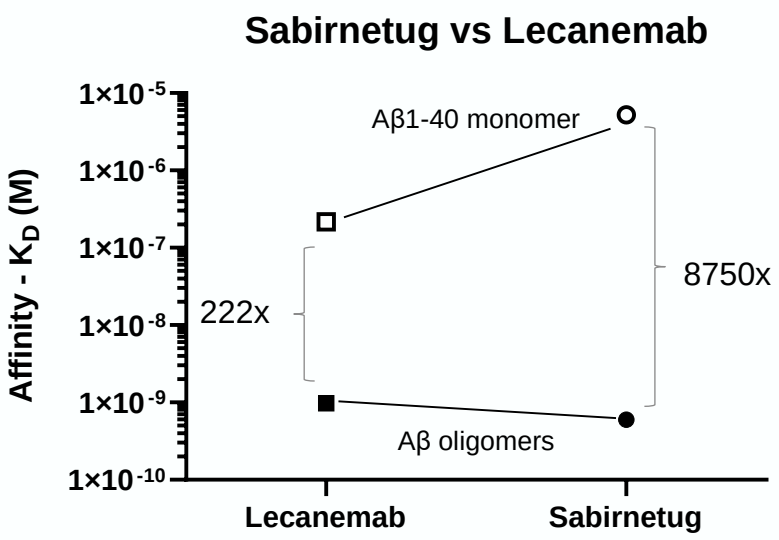
Sabirnetug is Highly Selective for Aβ Oligomers

Relative selectivity for AβO versus monomeric Aβ measured with SPR

Sabirnetug is more selective for AβOs than aducanumab



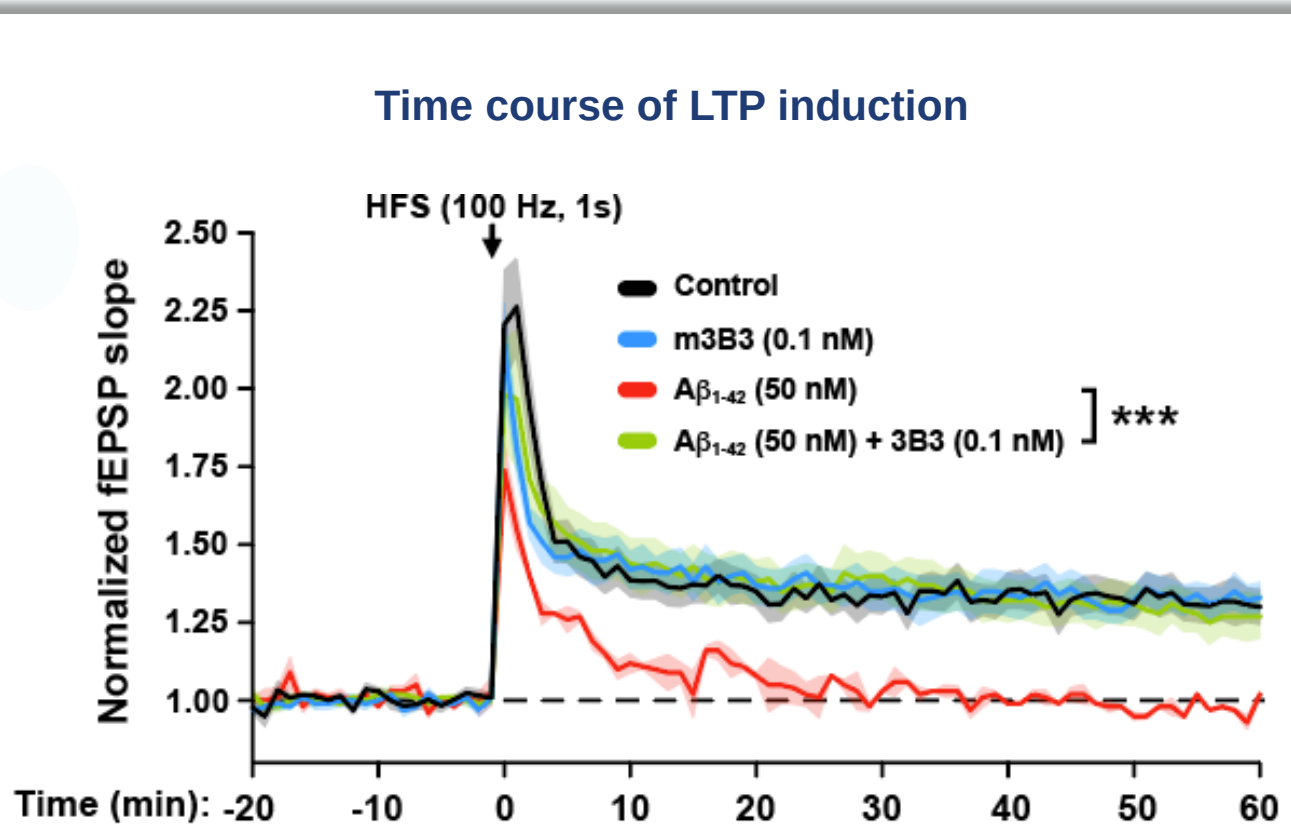
Sabirnetug is more selective for AβOs than lecanemab



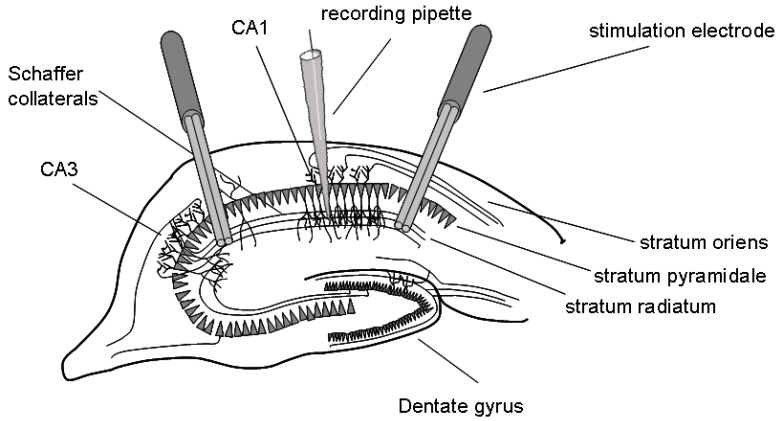
Internal data, 2024

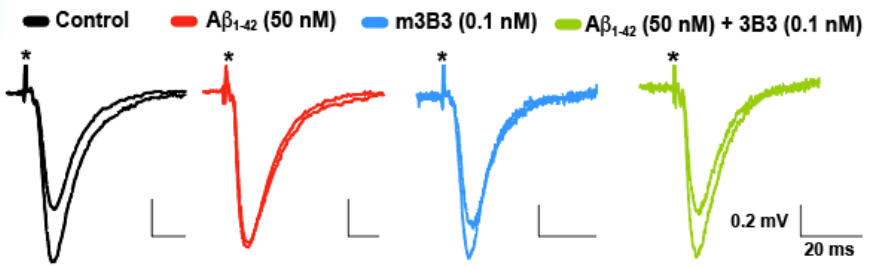
Functional Consequences of AβO Clearance: Restoring Plasticity

1. Prevention of hippocampal LTP impairment



- Aβ at 50 nM markedly reduced HFS-induced LTP in wildtype slices
- Pre-treatment with ACU3B3 oligomer-selective antibody prevented $A\beta_{1-42}$-induced LTP deficits

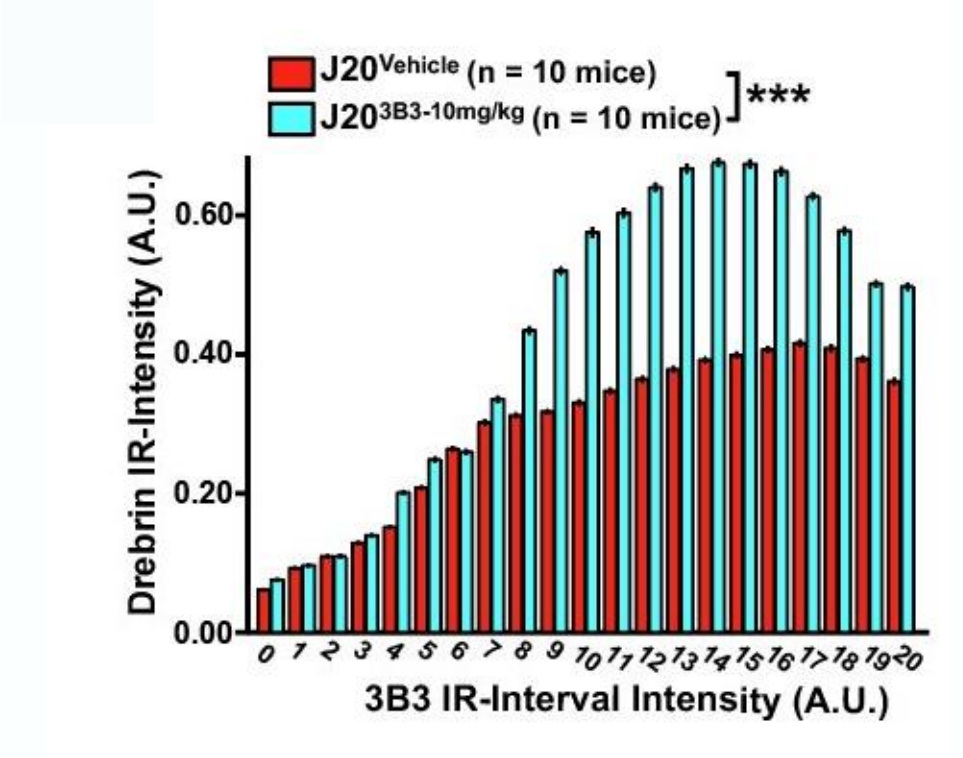




From manuscript in prep; data collected by lab of Gerhard Rammes, University of Regensburg, Max-Planck Institute of Psychiatry, Germany

Functional Consequences Following ACU3B3 Treatment

2. Reduced amyloid deposition and increased spine density



From manuscript in prep; data collected by lab of Jorge Palop, Gladstone Institute

- ACU3B3 (murine oligomer selective antibody) treatment ***prior*** to plaque pathology leads to reduced amyloid deposition in J20 Tg model (5-7 months)
- Treatment effects are less prominent in aged animals (16-23 months)
- Evidence of synaptic recovery in advanced stages of pathology in contrast to minor effects on plaque deposition

Summary and Conclusions

- Soluble oligomers are a low abundance, highly toxic target in the pathophysiology of AD
- Soluble oligomers exist in a range of sizes from 10s to 100s of kDa and bind to excitatory synapses to form nanoscale clusters that can disrupt synaptic plasticity and impair network function
- Soluble oligomers levels increase during the early phases of AD and are associated with both excitatory synapses in limbic and cortical circuitry as well as with amyloid plaques
- Sabirnetug binds to soluble oligomers with high affinity and is highly selective for soluble oligomers relative to monomeric Aβ
- Sabirnetug delivered either acutely or chronically can prevent pathophysiological effects on synaptic plasticity in nonclinical models of AD

INTERCEPT-AD Phase 1 Results

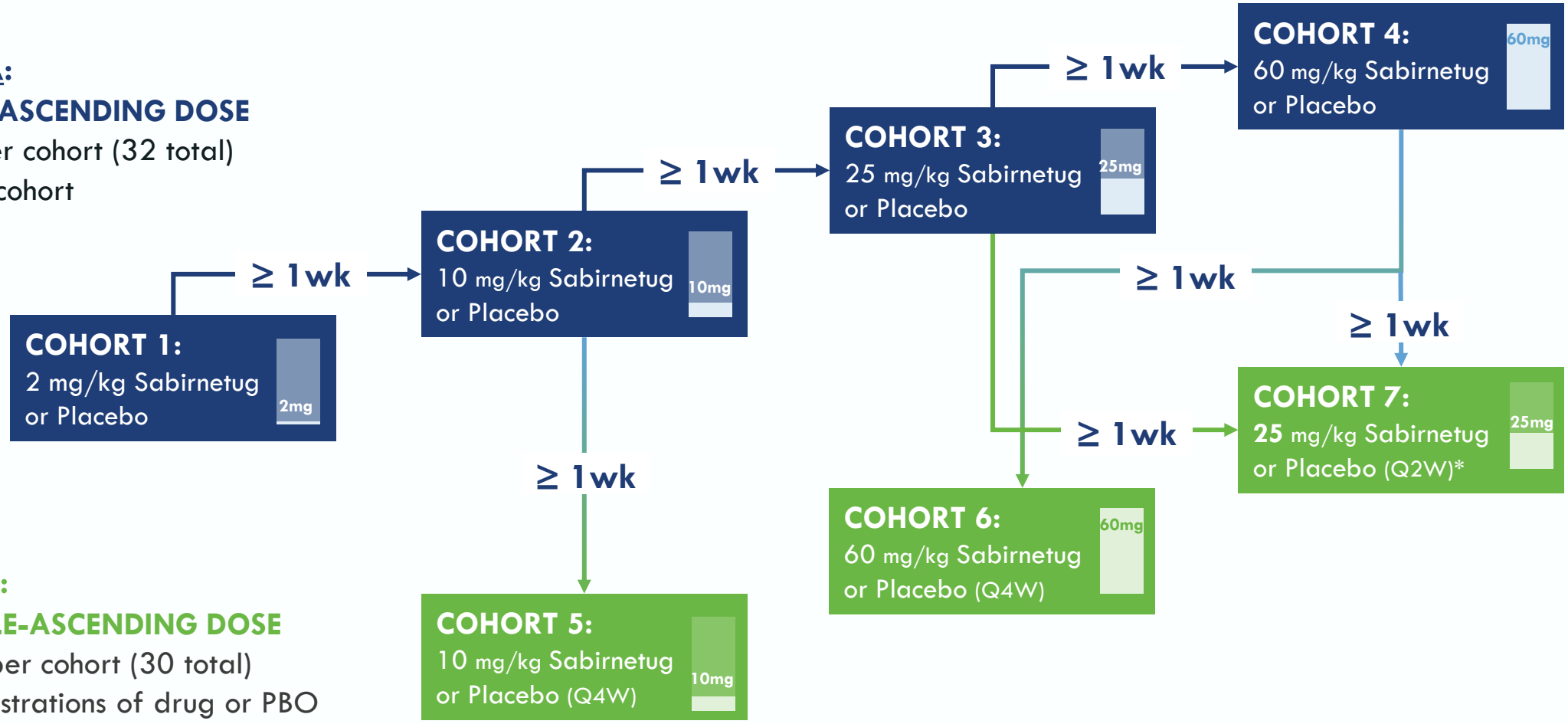
ACUMEN

Disclosures

Stephen Salloway, MD, MS

- Butler Hospital receives research support for clinical trials from Janssen, Lilly, Eisai, Genentech, Roche, and Biogen
- Dr. Salloway has provided consultation to Eisai, Biogen, Lilly, Roche, Genentech, Bolden, Novo Nordisk, Prothena, Acumen, Labcorp, Alector, Corium, Kisbee and AbbVie
- Dr. Salloway is a member of the ADRD Therapeutic Working Group and an author on the Appropriate Use Recommendations for lecanemab and aducanumab. He is also a member of the Editorial Board of the Journal of Alzheimer's Disease Prevention and Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring
- Dr. Salloway owns no stocks or equity in any pharmaceutical company and has no patents or royalties

INTERCEPT-AD: A Randomized Placebo Controlled Phase 1 in Early AD Patients



Q2W: Dosing every two weeks; Q4W: Dosing every four weeks

Study Population

- Diagnosis of MCI or Mild AD dementia (NIA-AA criteria)

- Key Inclusion criteria:
  - Age 55-90 years
  - MMSE total score 18-30 inclusive
  - CDR Global Score 0.5 or 1
  - Confirmation of amyloid pathology via Amyloid PET
  - Apolipoprotein E (*APOE*) genotype is recorded

- Measures of cognition, function, and behavior were obtained and include:
  - MMSE
  - CDR
  - ADAS-Cog_{13}
  - ADCS-ADL
  - iADRS
  - NPI-10
  - C-SSRS (children's version)
  - Brief computerized neuropsychological test battery

Baseline Demographics

Characteristic	ACU193 (N=49)	Placebo (N=15)
Age, median (range), years	72.3 (56,85)	71.5 (59,83)
Female, n (%)	27 (55.1)	7 (46.7)
Race, n (%)		
Asian	0 (0)	0 (0)
Black/African American	2 (4.1)	1 (6.7)
Caucasian	46 (93.9)	14 (93.3)
American Indian/Alaskan	1(2.0)	0 (0)
Ethnicity, n (%)		
Hispanic or Latino	8 (16.3)	2 (13.3)
Not Hispanic or Latino	41 (83.7)	13 (86.7)
Height in centimeters, n (%)	168.7 (8.7)	166.6 (9.3)
Weight in kilograms, n (%)	80.1 (16.6)	79.9 (13.9)
BMI in kg/m^2 , n (%)	28.0 (5.4)	28.9 (5.7)

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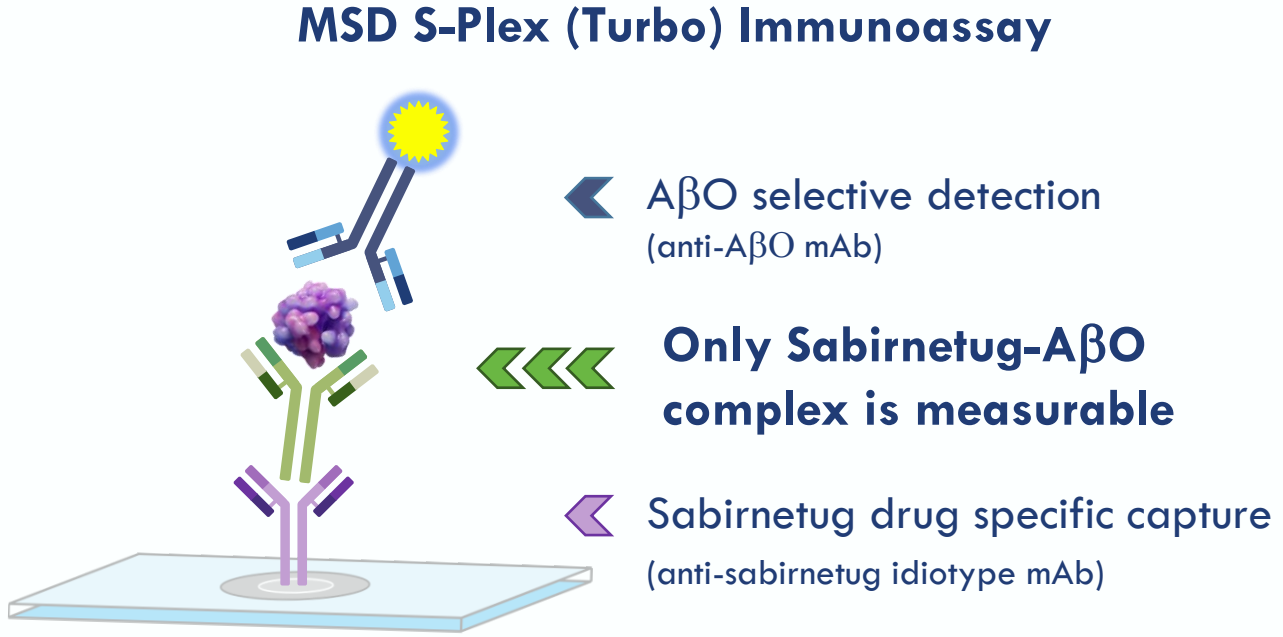
Baseline Clinical Characteristics

Characteristic	ACU193 (N=49)	Placebo (N=15)
APOE4 Status, n (%)		
Noncarrier	21 (43.75)	4 (28.6)
Heterozygous Carrier	21 (43.75)	8 (57.1)
Homozygous Carrier	6 (12.5)	2 (14.3)
CDR-GS, mean (SD)	0.6 (0.3)	0.6 (0.2)
CDR-SB, mean (SD)	3.6 (1.9)	3.2 (1.8)
MMSE, mean (SD)	24.1 (3.7)	24.8 (3.6)
iADRS, mean	111.5	110.6
PET SUVr, mean (SD)	1.42 (0.25)	1.33 (0.19)
PET Centiloids, mean (SD)	64.8 (42.8)	48.5 (33.4)

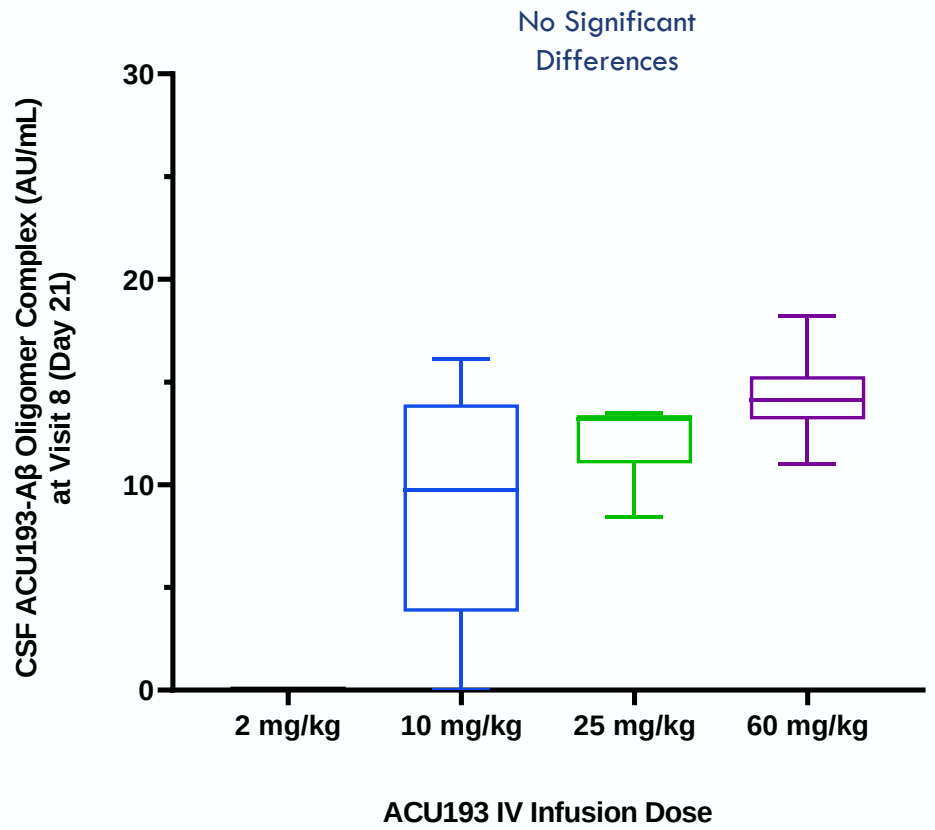
Target Engagement Assessed by Measuring Sabirnetug-AβO Complex in CSF

- Novel assay configuration tailored to selectively detect sabirnetug-AβO complex in CSF as direct measure of target engagement
- Translated for clinical use from a preclinical assay developed by Merck that showed sabirnetug engages target AβOs in transgenic mouse brain (tg2576) in dose dependent manner

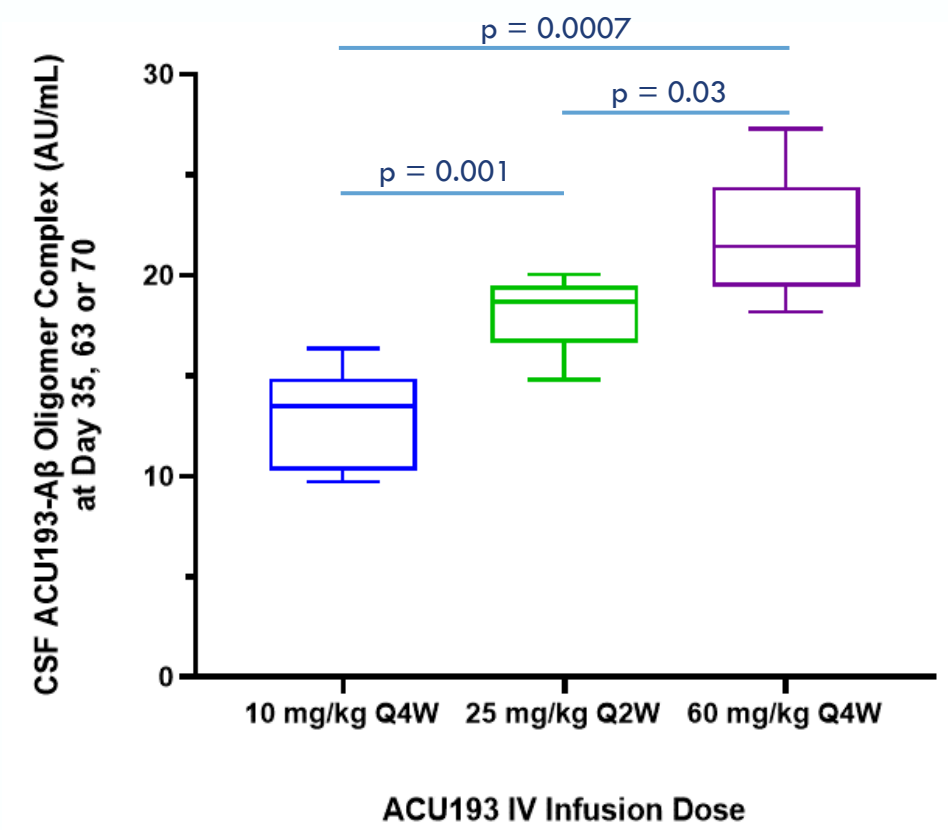


Target Engagement of Sabirnetug with AβOs is Dose Proportional

Single Dose Cohorts



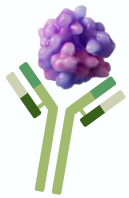
Multiple Dose Cohorts*



*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).
P-values not corrected for multiple comparisons.

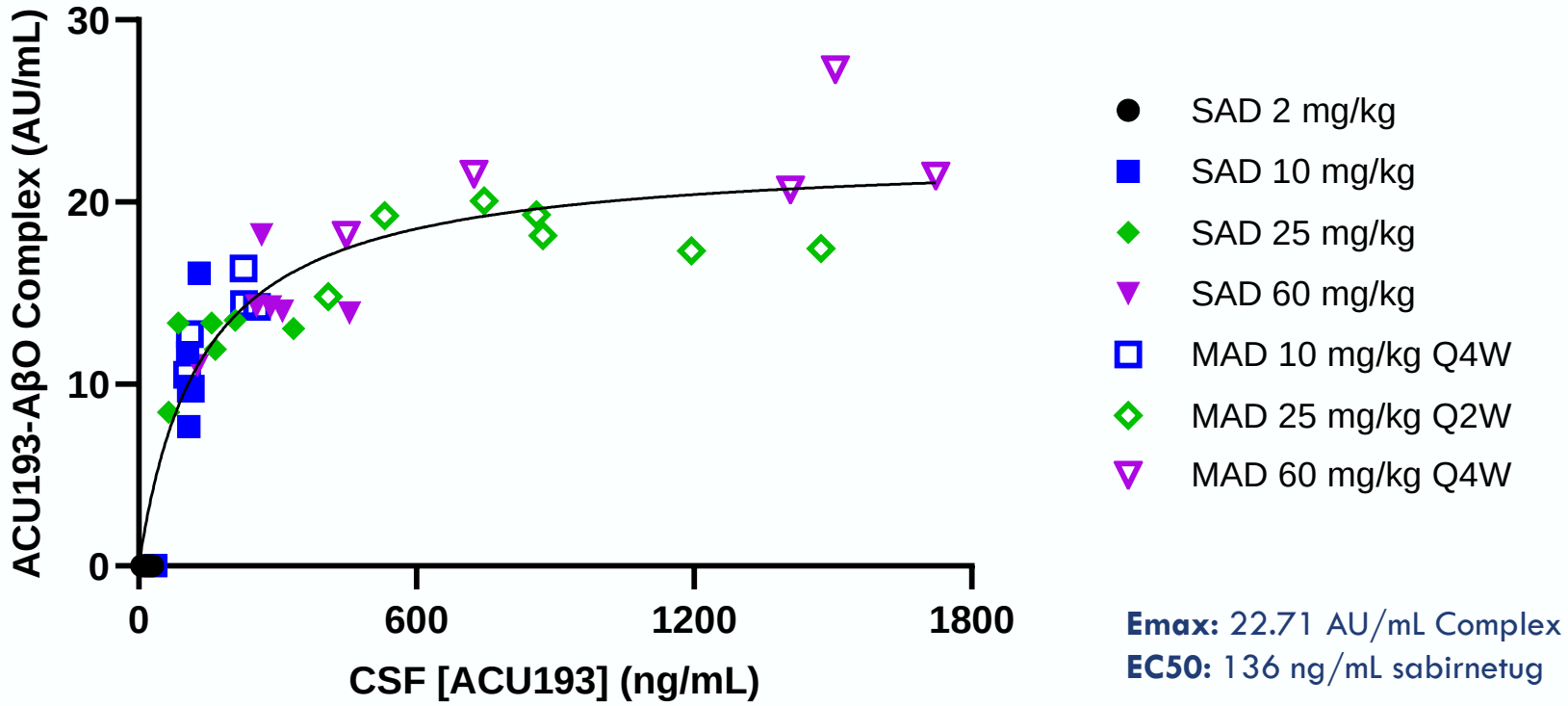
Doses Approaching Maximal Target Engagement Support Sabirnetug AβO Mechanism and Helped Guide Dose Selection for Next Study Phase

Target Engagement



Sabirnetug-AβO Complex

Single & Multiple Dose Cohorts - Exposure Response Relationship (Emax Model)

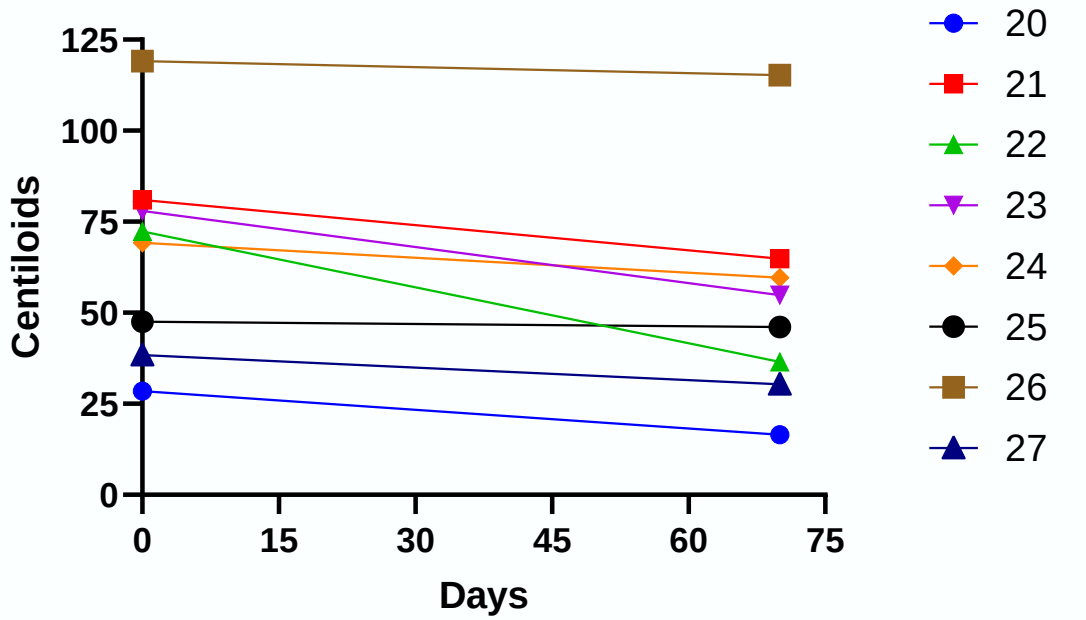


Emax: 22.71 AU/mL Complex
EC50: 136 ng/mL sabirnetug

*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).
P-values not corrected for multiple comparisons.

Nearly All Sabirnetug-Treated Patients in High Dose MAD Cohorts Showed Reductions in Plaque Load After Three Doses at 63 or 70 days

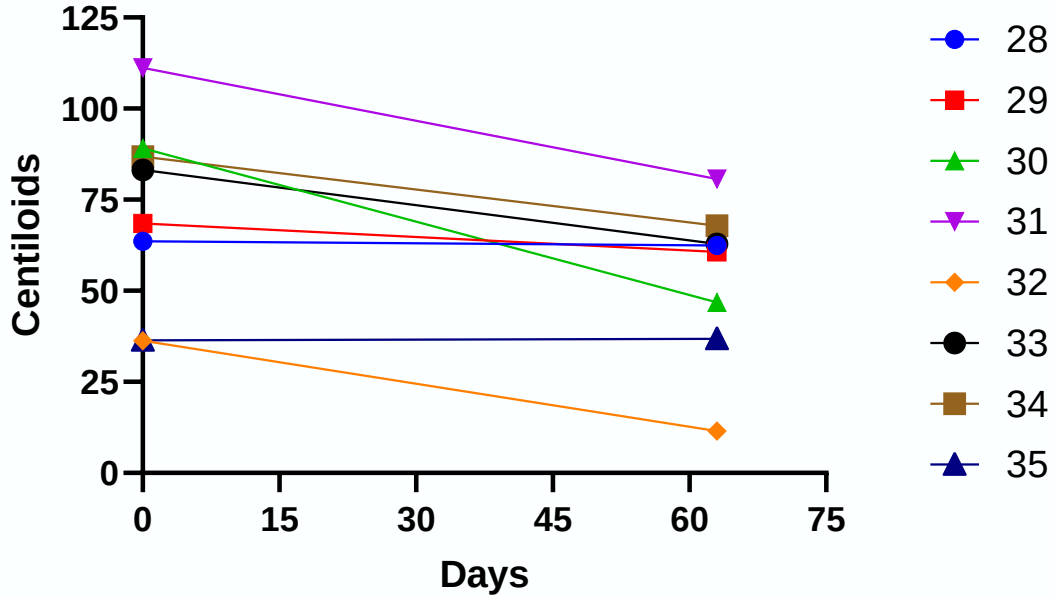
25 mg/kg Q2W MAD



Mean reduction in amyloid plaque

Δ (absolute value, centiloids)	13.7
Δ (%, centiloids)	20.6%

60 mg/kg Q4W MAD



Mean reduction in amyloid plaque

Δ (absolute value, centiloids)	18.1
Δ (%, centiloids)	25.6%

Plaque load based on florbetapir PET

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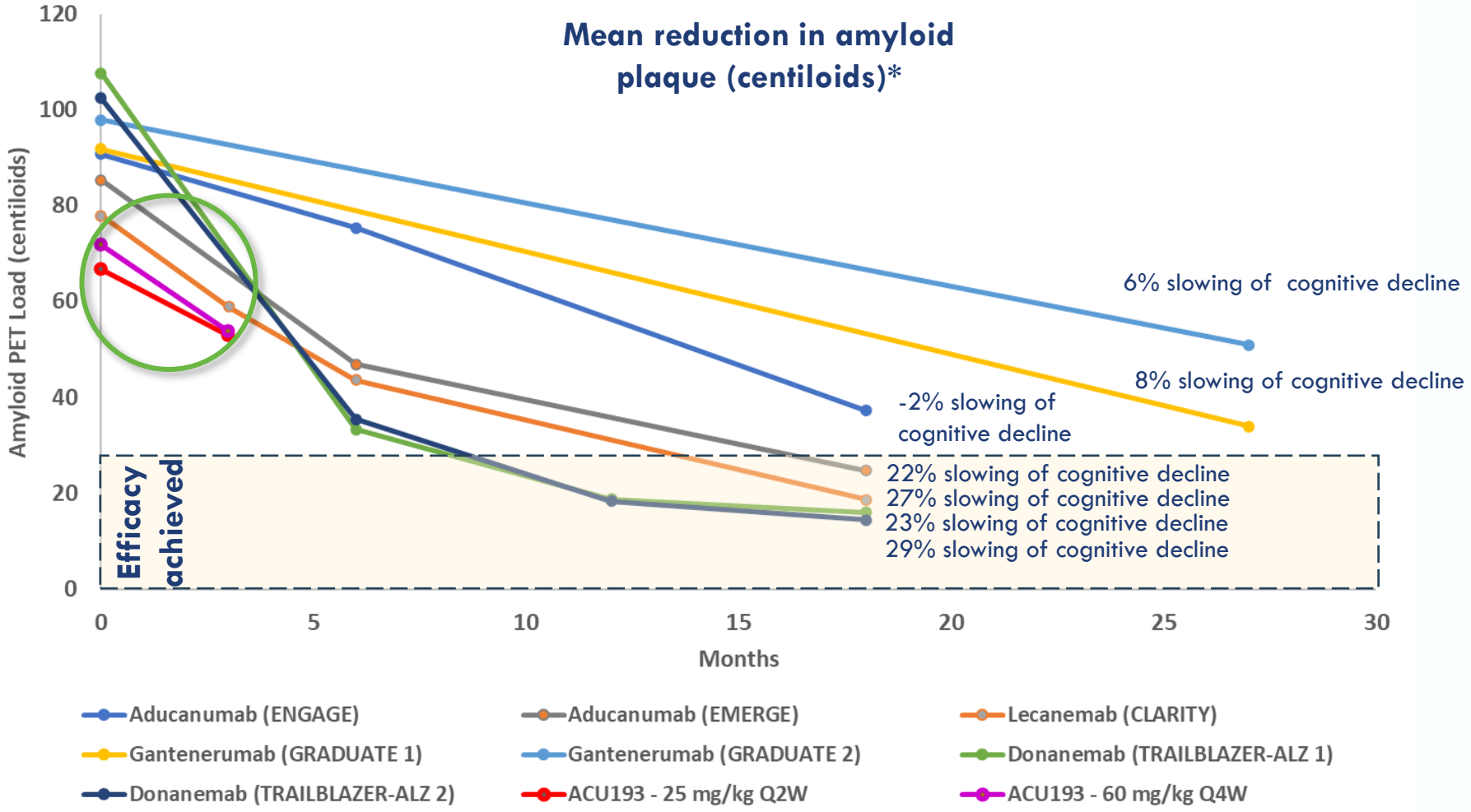
Highest Doses of INTERCEPT-AD Reduced Amyloid Plaque at Similar Rate and Magnitude to Lecanemab at Comparable Timepoints

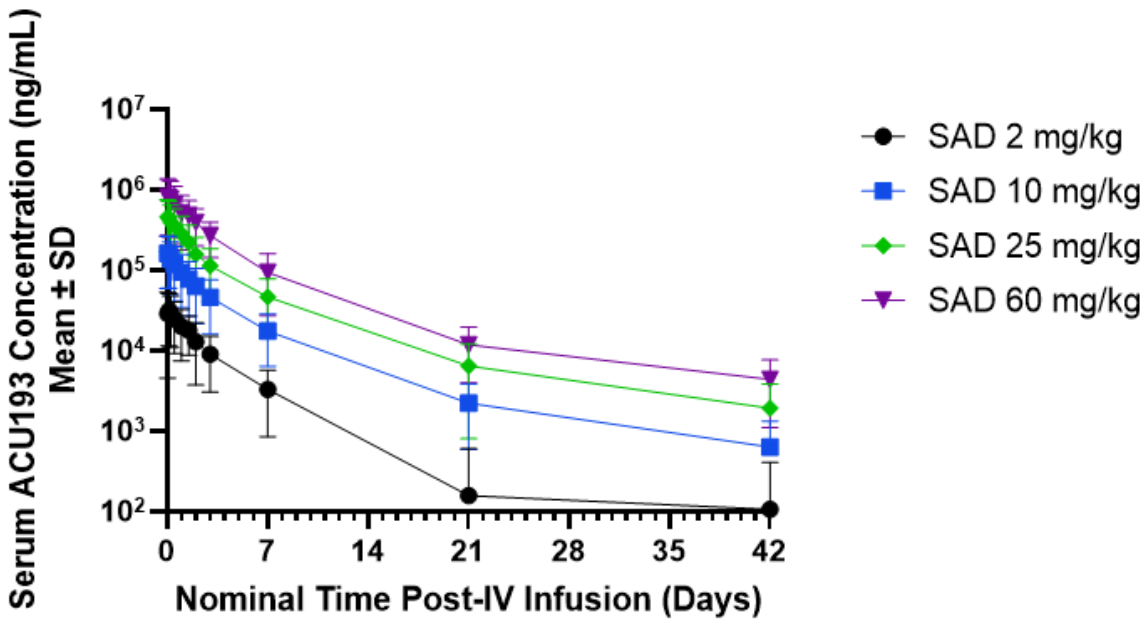


Acumen Pharmaceuticals, data on file; van Dyck (2023), NEJM (amyloid PET reduction estimated from graphs).

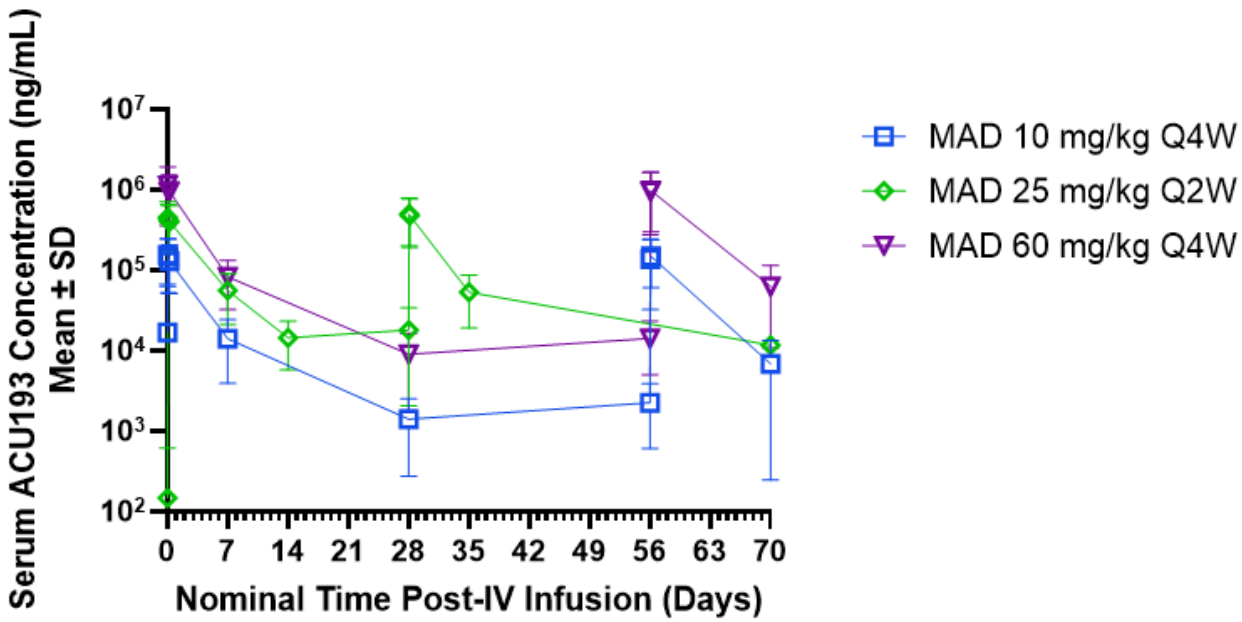
*There have been no head-to-head clinical trials between the product candidates listed above. Study designs and protocols for each product candidate were different, and as a result, results may not be comparable between product candidates.

Sabirnetug Serum Exposure is Dose Proportional Without Accumulation

Single Dose Cohorts



Multiple Dose Cohorts



Estimated serum terminal $T_{1/2}$ of 5-7 days

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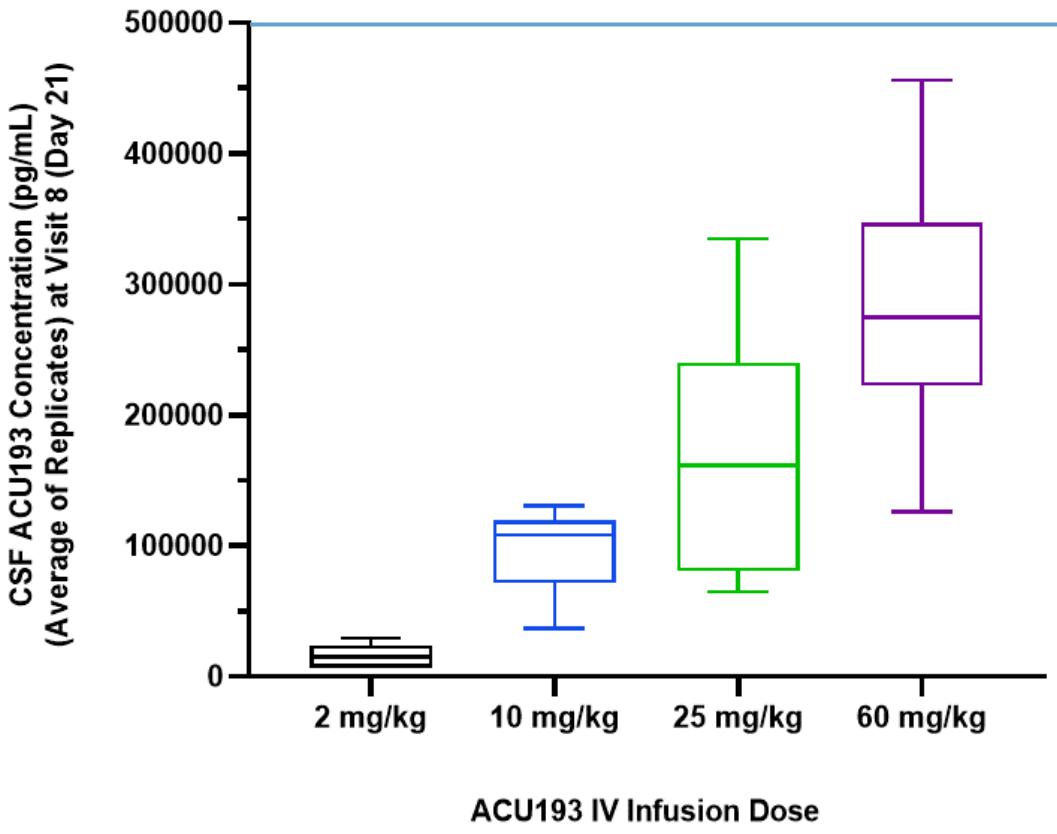
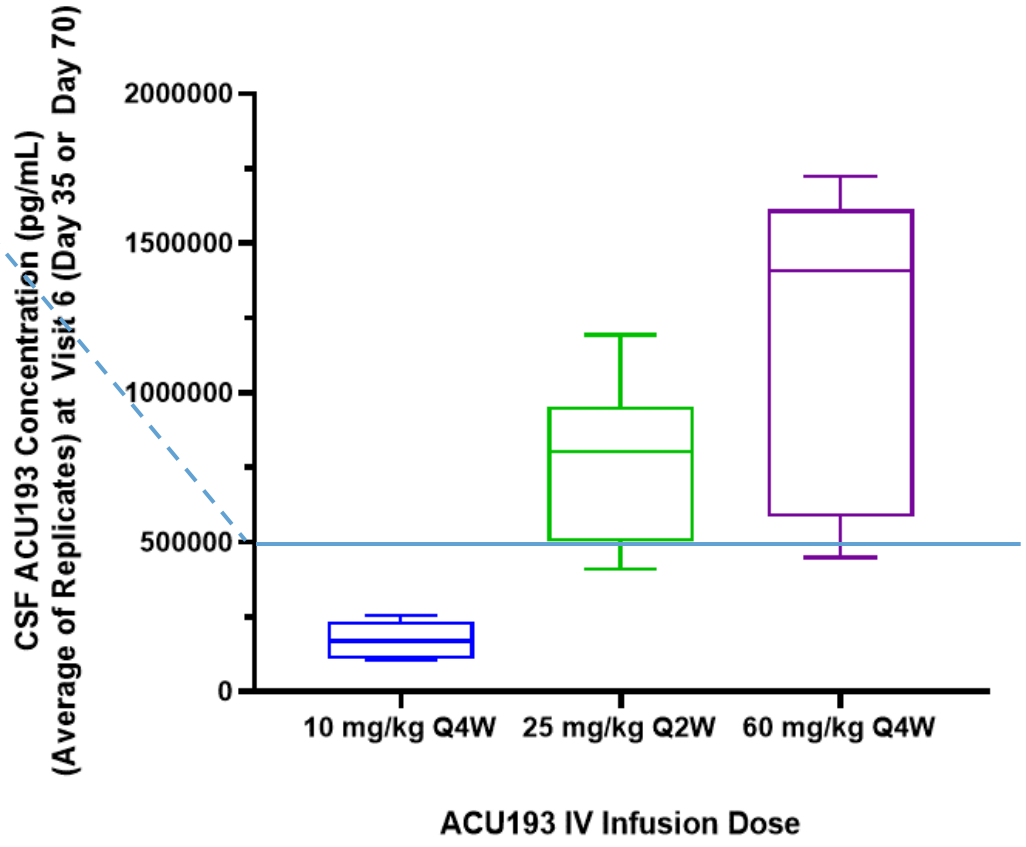
Sabirnetug CSF Exposure is Dose and Dose-Regimen Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

INTERCEPT-AD: ARIA-E Summary

SAD

2 mg/kg
Cohort 1

ApoE	D21	D140
3,4		
3,3	PBO	PBO
3,4		
2,3		
3,4	PBO	PBO
3,3		
3,3		
3,3		

10 mg/kg
Cohorts 2, 5

ApoE	D21	D140
3,4	PBO	PBO
3,3		
3,3		
3,4		
3,4	PBO	PBO
3,4		
3,4		
3,4		

25 mg/kg
Cohorts 3, 7

ApoE	D21	D140
3,3		
3,3	PBO	PBO
4,4		
3,3		
2,4		
3,3	PBO	PBO
3,4		
3,3		

60 mg/kg
Cohorts 4, 6

ApoE	D21	D140
4,4	PBO	PBO
3,4		
3,4	PBO	PBO
3,3		
3,3		
3,4		
2,4		
3,4		

MAD

ApoE	D28	D70	D196
2,3			
3,3			
3,3			
4,4			
3,3	PBO	PBO	PBO
3,4			
4,4			
3,4			
3,3			
3,4	PBO	PBO	PBO

ApoE	D28	D70	D98
3,3			
3,4			
3,4			
3,4			
3,4			
3,4	PBO	PBO	PBO
3,3			
3,4	PBO	PBO	PBO
4,4			
4,4			

ApoE	D28	D63	D126
3,4			
3,3			
3,3			
4,4			
4,4	PBO	PBO	PBO
3,3			
3,4			
3,4			
3,4	PBO	PBO	PBO
3,3			

NO ARIA-E
Asymptomatic ARIA-E
Symptomatic ARIA-E
Discontinued

PBO: Participant on placebo

No ε4 homozygotes developed ARIA-E despite comprising 6 individuals (13%) in study; 4/5 ARIA-E cases are ε4 heterozygotes and 1/5 (at 60 mg/kg) was a non-carrier

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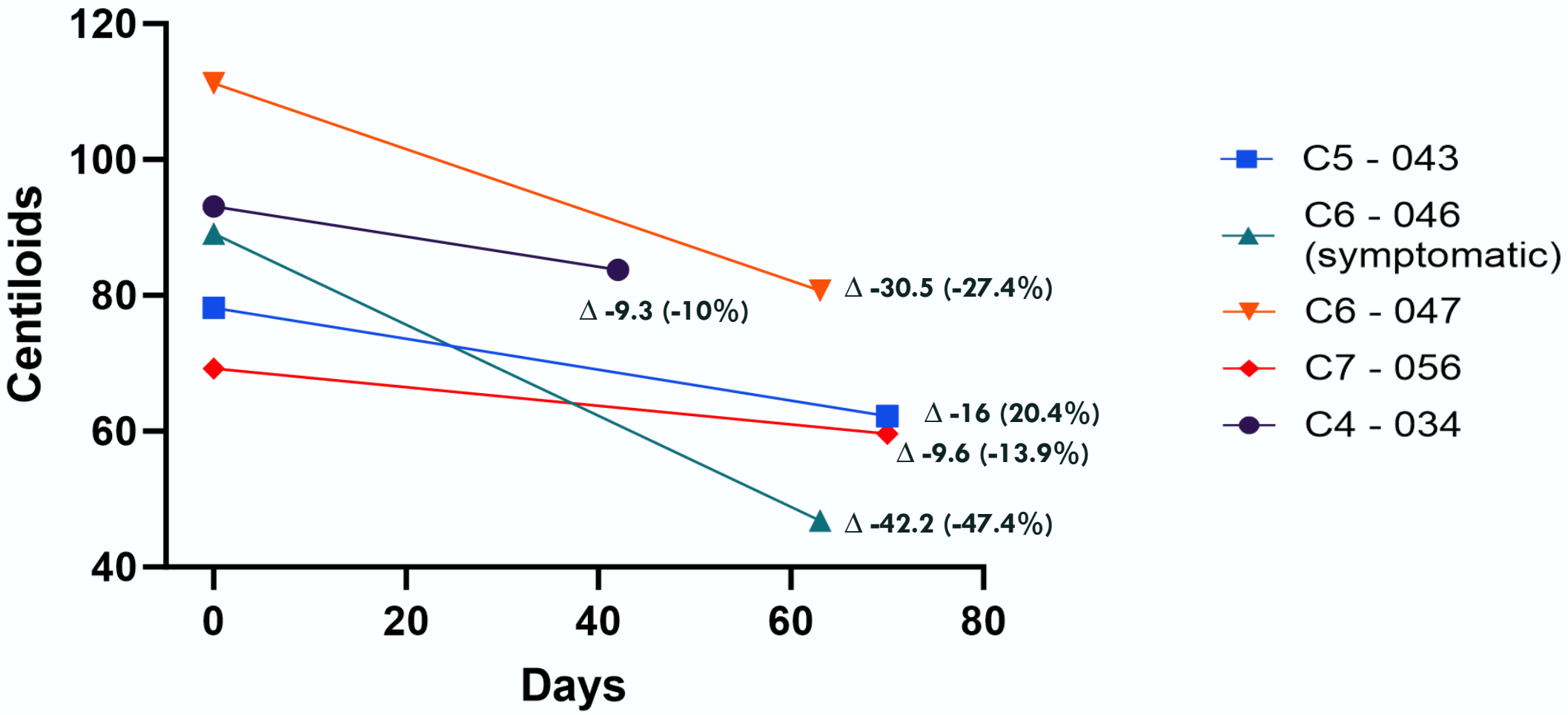
ARIA-E: Patient Details

Cohort	ApoE4	Gender	Age	Baseline/Endpoint Plaque Load (Centiloids)	Severity by FDA Criteria
C4 SAD 60 mg/kg	**Heterozygote**	**F**	**58**	93.1/83.8	Moderate - Asymptomatic
C5 10 mg/kg Q4W	**Heterozygote**	**F**	**72**	78.2/62.2	Mild - Asymptomatic 3rd/final dose on D56
C6 60 mg/kg Q4W	**Heterozygote**	**F**	**80**	89.1/46.9	Moderate - **Symptomatic** (R leg dysfunction) 1 dose at BL; 2 remaining doses withheld
C6 60 mg/kg Q4W	**NonCarrier**	**F**	**56**	111.2/80.7	Mild - Asymptomatic 3rd/final dose on D56
C7 25 mg/kg Q2W	**Heterozygote**	**F**	**70**	69.3/59.6	Moderate - Asymptomatic 3rd/final dose on D28 D28 ARIA-E (mild) noted in retrospective review

Of 5 total ARIA-E cases, 1 was symptomatic (2.1% overall) and symptoms resolved with resolution of radiographic ARIA-E. All cases showed radiographic resolution.

ACUMEN

Change in Amyloid Burden in Participants with ARIA-E



Baseline mean = 88.2 Centiloids

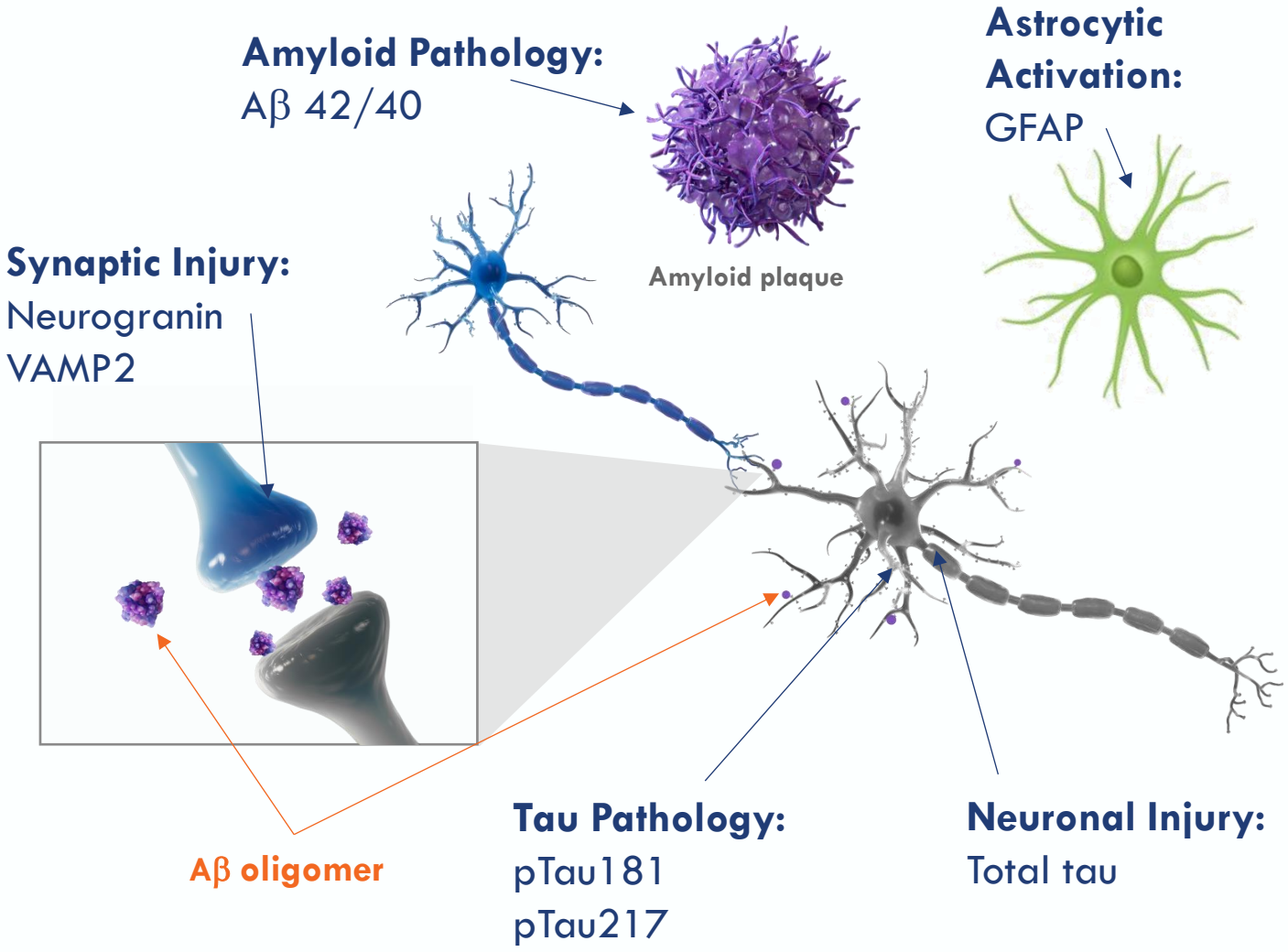
Endpoint mean = 66.6 Centiloids

INTERCEPT-AD Fluid Biomarker Results & Phase 2 ALTITUDE-AD Design

ACUMEN

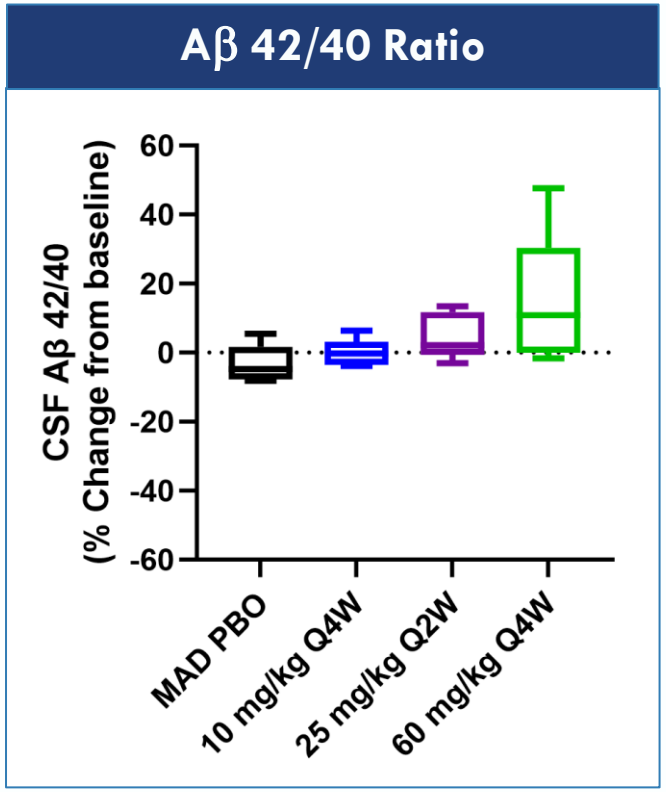
Importance of Key Fluid Biomarkers Associated with AD Pathology

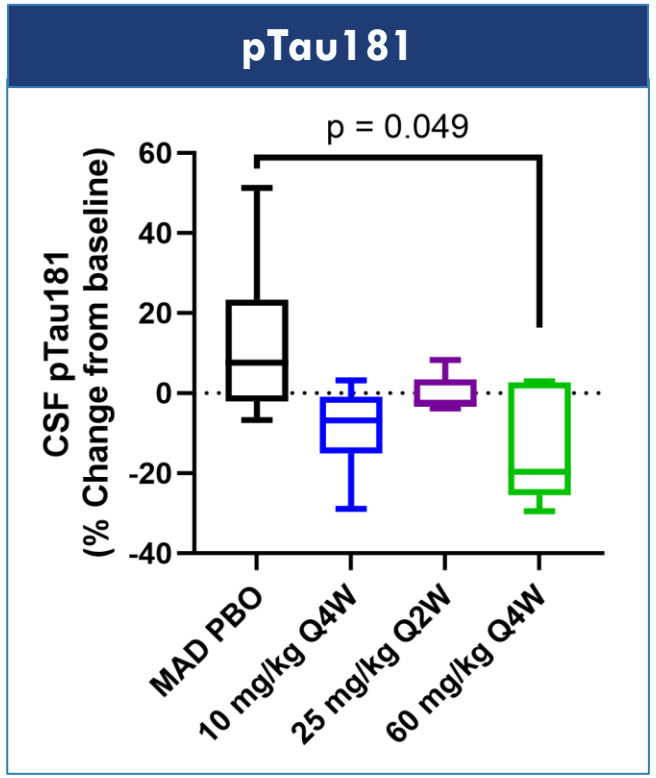
- Biomarkers from cerebrospinal fluid and plasma capture neuronal, synaptic, and axonal injury and reflect the cumulative outcome of different pathological substrates in AD[1]
- Evidence suggests that biomarkers are likely to be better predictors of the underlying pathology of AD than imaging alone[2]
- **After just three administrations of sabirnetug, patients with early AD demonstrated improvements in biomarkers associated with AD pathology**

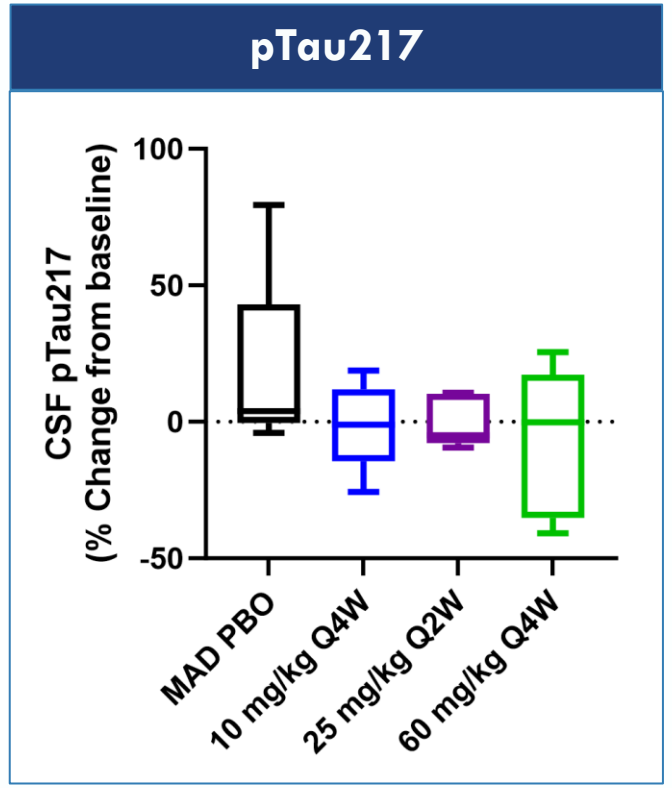


1. Tarawneh, R. Biomarkers: Our Path Towards a Cure for Alzheimer Disease. Biomarker Insights Volume 15: 1–15. 2020; 2. Blennow K, Zetterberg H. The Past and the Future of Alzheimer's Disease Fluid Biomarkers. J Alzheimers Dis. 2018;62(3):1125-1140.

Consistent Improvement in CSF Amyloid and Tau Biomarkers Indicate Downstream Pharmacology of Sabirnetug After Only Three Doses







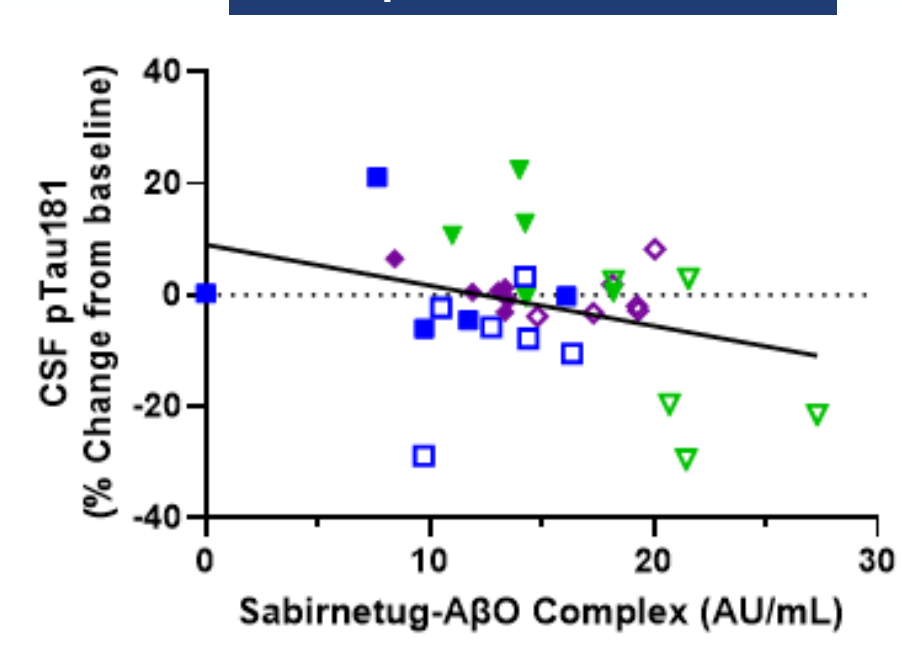
Amyloid pathology

Tau pathology

- *n = 8 participants/treated group; 6 participants in pooled placebo (PBO)*
- *p-values from unpaired, 2-sided Student's t test*

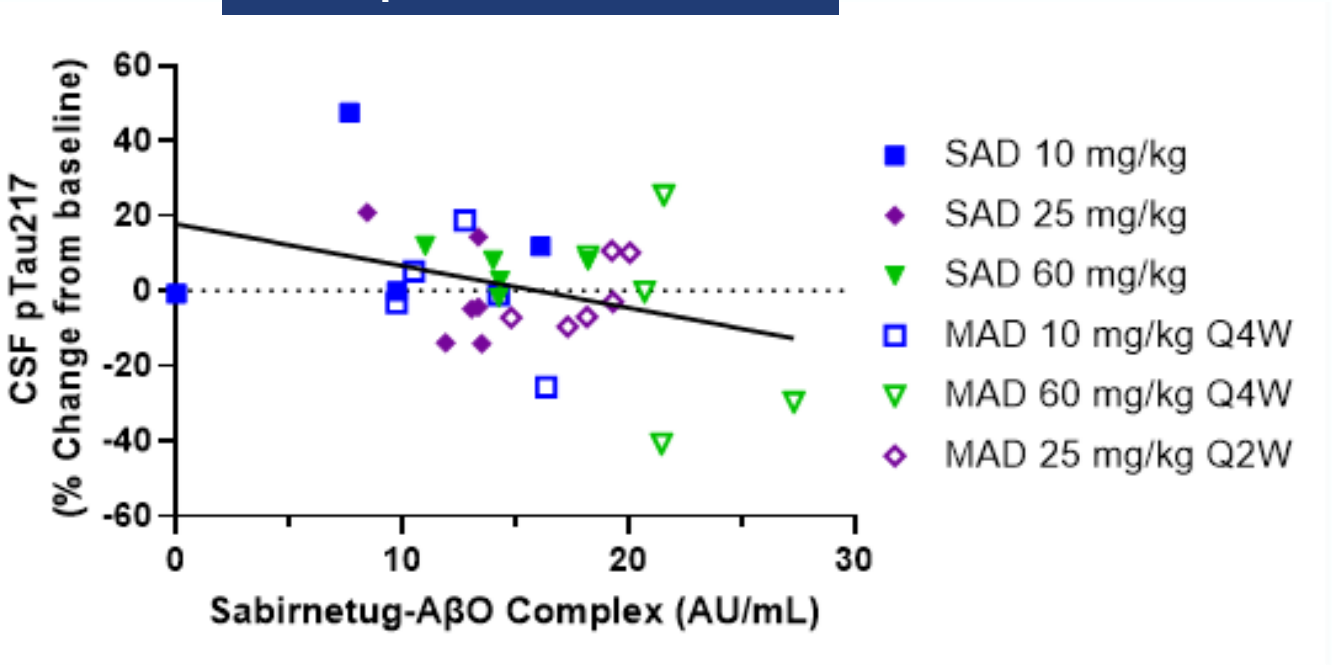
Improvements in CSF pTau181 and pTau217 Correlate with Target Engagement (Sabirnetug Binding to CSF Aβ Oligomers)

pTau181 vs. TE



R^2= 0.25 p = 0.001

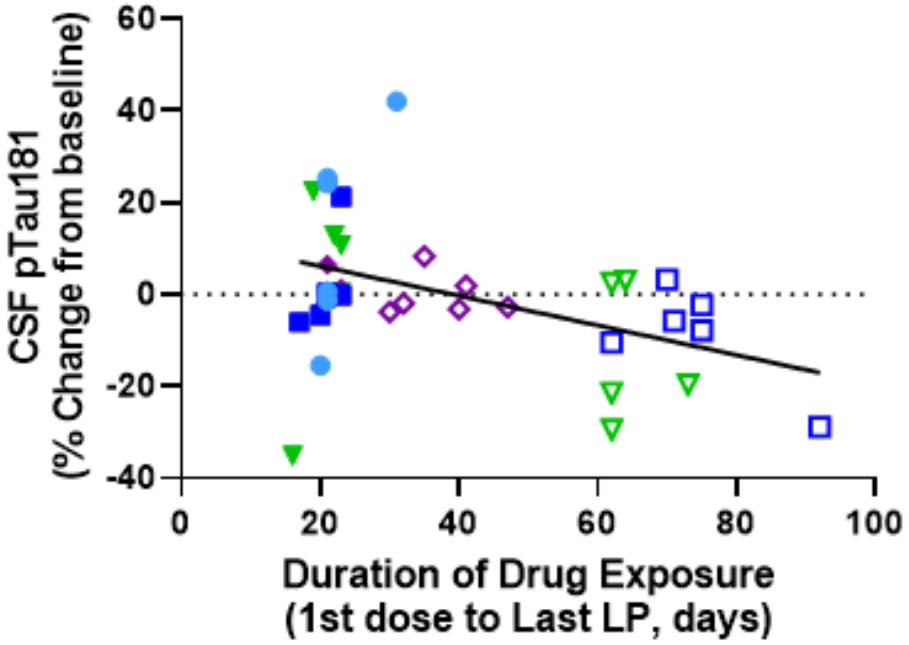
pTau217 vs. TE



R^2= 0.04 p = 0.27

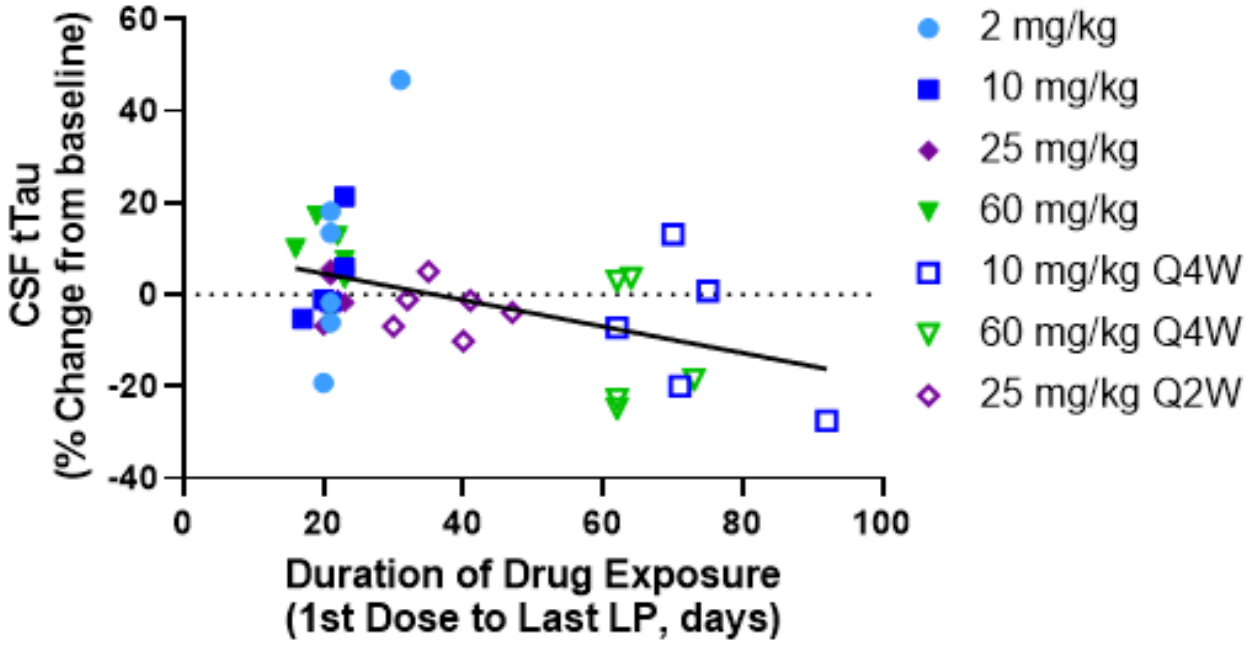
Percent Change from Baseline in CSF pTau181 and tTau Correlate with Duration of Drug Exposure

pTau181 vs. Sabirnetug Exposure Duration



R^2= 0.25 p = 0.001

tTau vs. Sabirnetug Exposure Duration

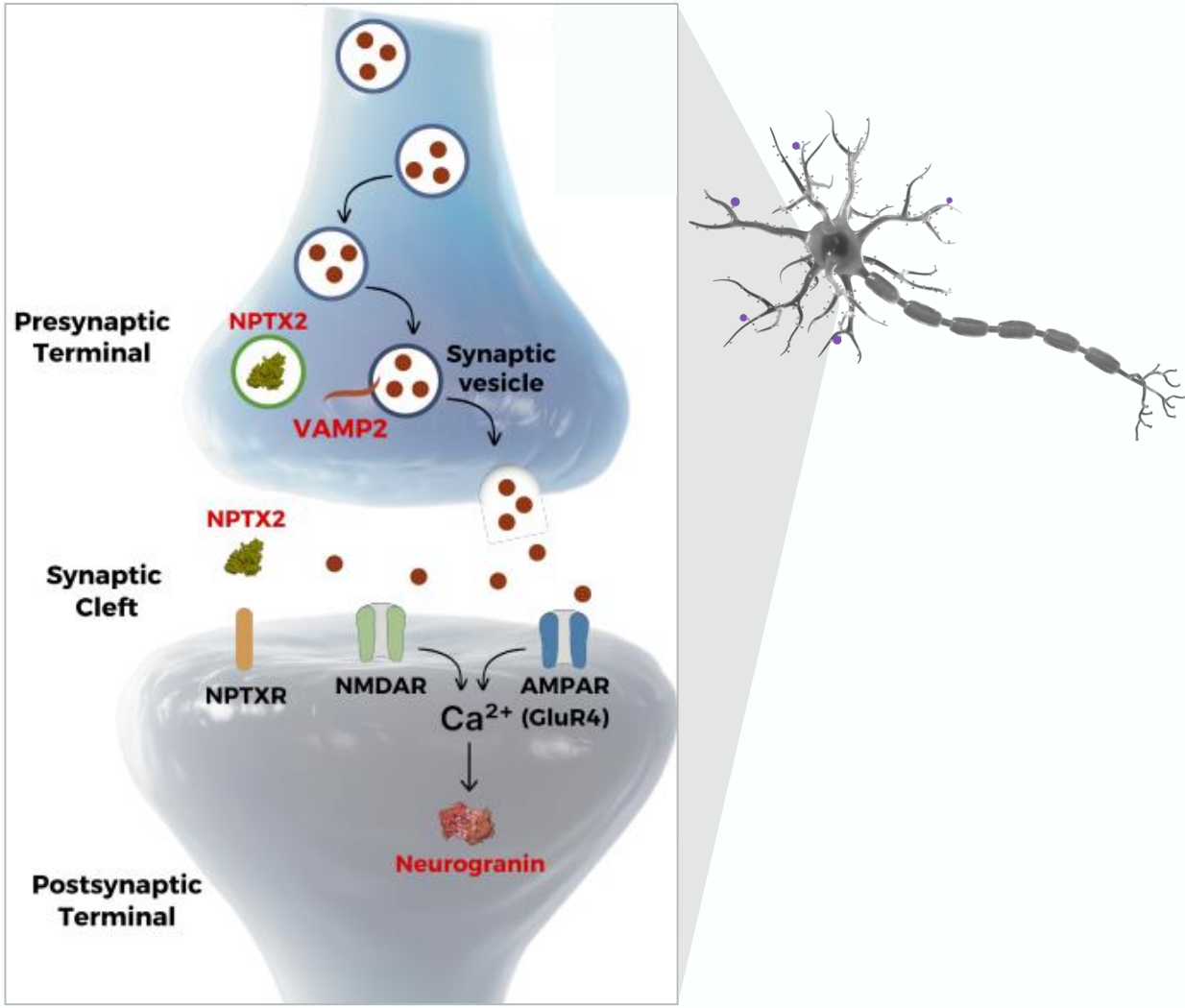


R^2= 0.19 p = 0.005

Improvements in Synaptic Biomarkers Observed in AD Patients from INTERCEPT-AD Study

- Increased understanding of pre- and post-synaptic fluid proteins as biomarkers of synaptic health
  - Vesicle-associated membrane protein 2 (VAMP-2), is a component of synaptic vesicles, functioning in neurotransmitter release and the post-synaptic vesicle trafficking of glutamate receptor subunits[1]
  - Neuropentraxin 2 (NPTX2) is a pre-synaptic protein that acts on post-synaptic excitatory synapses[2]
  - Neurogranin is a postsynaptic, calcium regulating protein that is predominantly expressed in dendritic spines, and plays a role in LTP[3]

Improvements in these synaptic biomarkers align with sabirnetug's ability to bind synaptotoxic AβOs

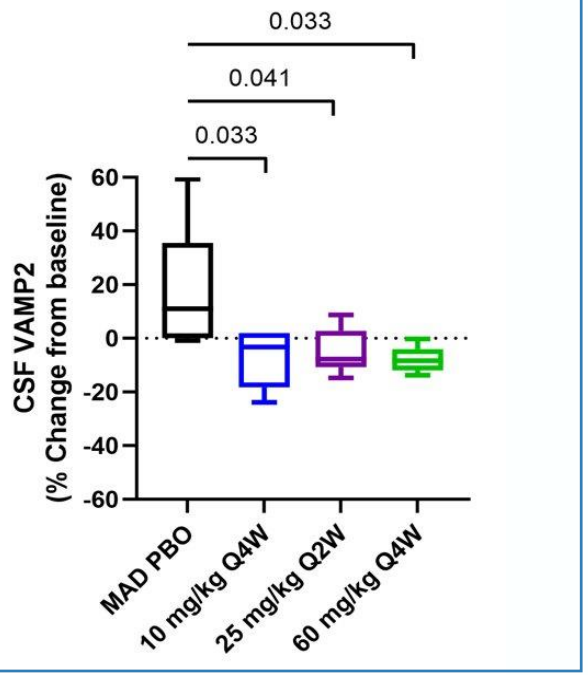


Adapted from Das et al. 2023

1. Goossens et al. Alzheimers Res Ther 2023;15:186. 2. Das et al. Alzheimers Res Ther, 2023;15:62. 3. O'Day. Int J Mol Sci. 2020;21(19):7344.

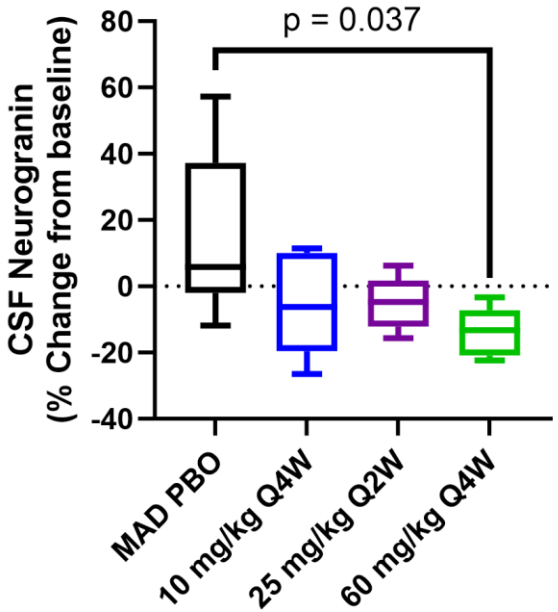
Synaptic Biomarkers Improved After Only Three Administrations of Sabirnetug

VAMP2



- *n = 8 participants/treated group; 6 participants in pooled placebo (PBO)*

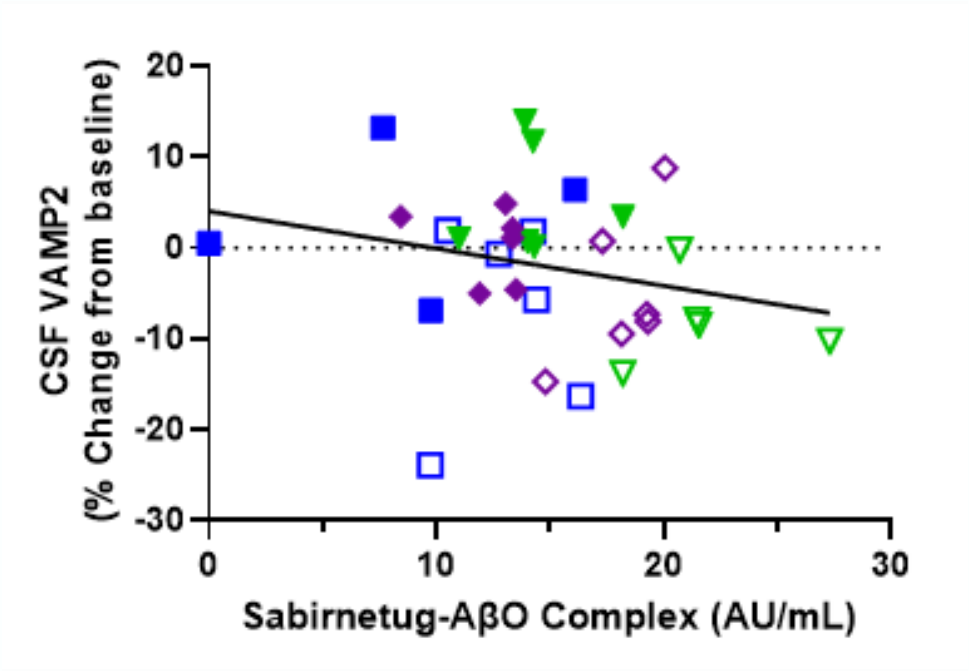
Neurogranin



- *p-values from unpaired, 2-sided Student's t test*

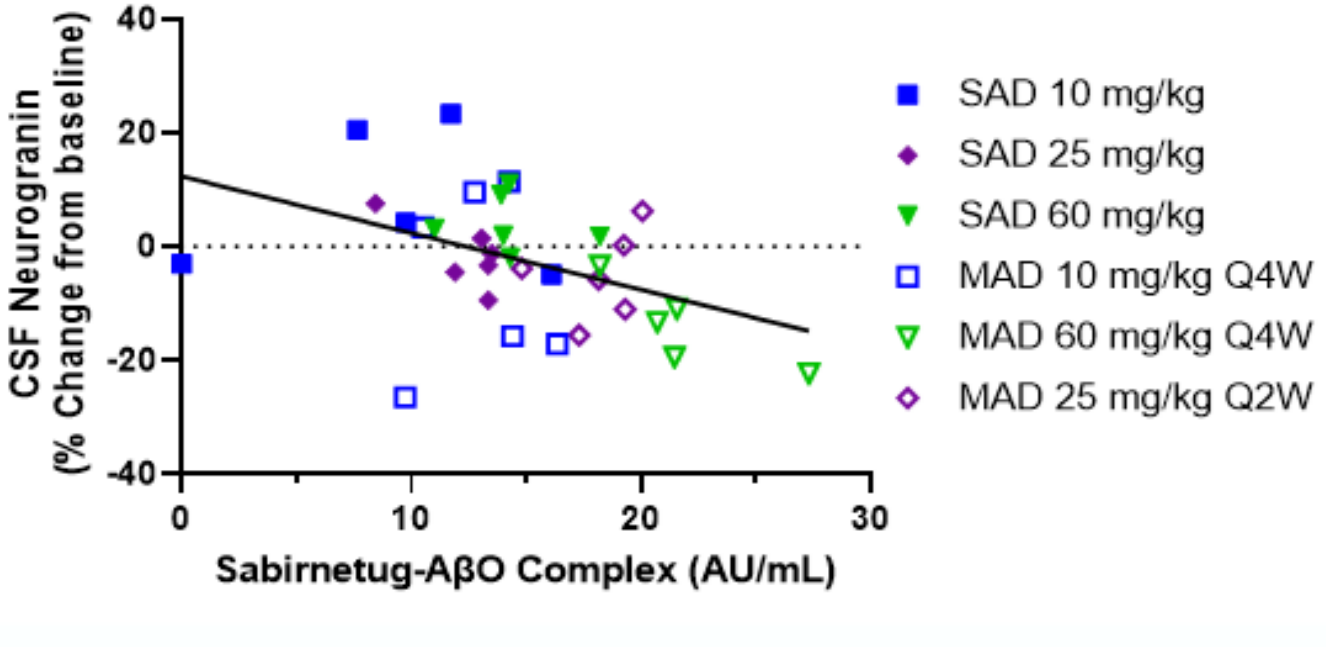
Changes in CSF VAMP2 and Neurogranin Correlate with Target Engagement (Sabirnetug Binding to CSF Aβ Oligomers)

VAMP2 vs. TE



R^2= 0.18 p = 0.007

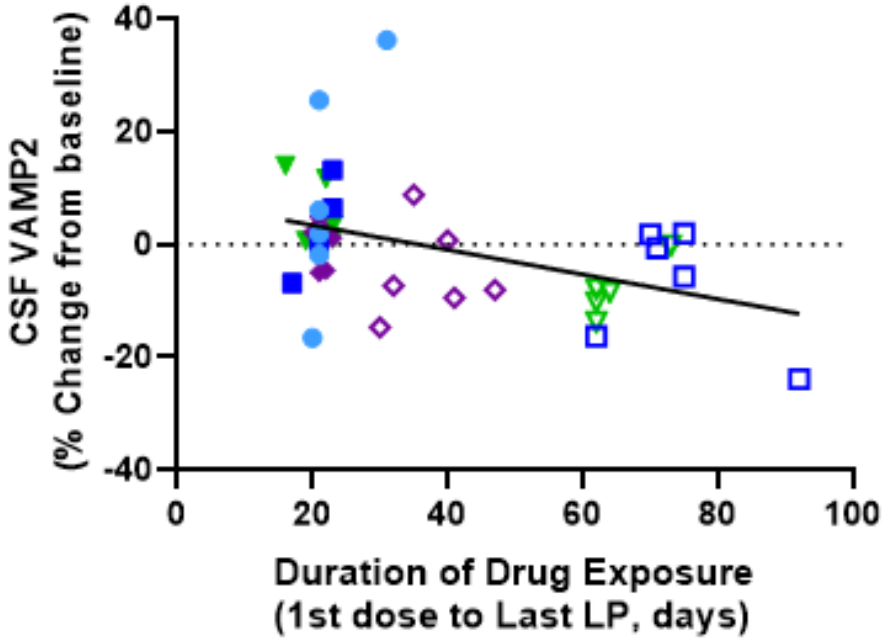
Neurogranin vs. TE



R^2= 0.18 p = 0.007

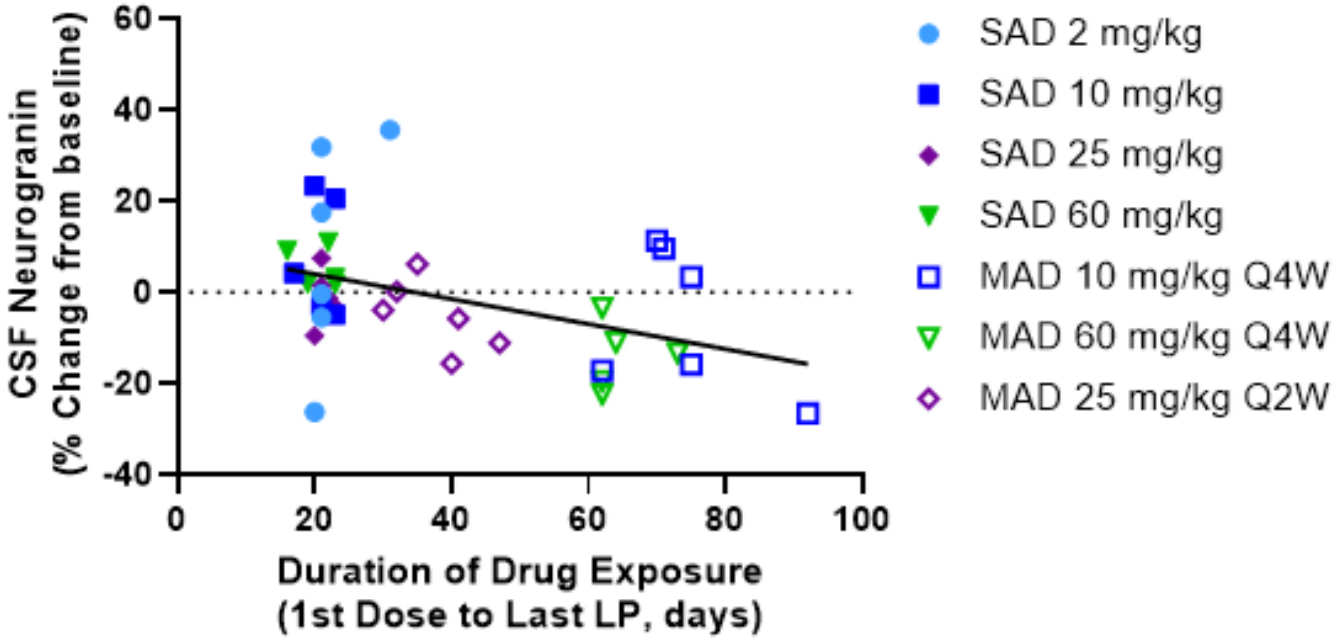
Percent Change from Baseline in CSF Synaptic Biomarkers VAMP2 and Neurogranin Correlate with Duration of Drug Exposure

VAMP2 vs. Sabirnetug Drug Exposure



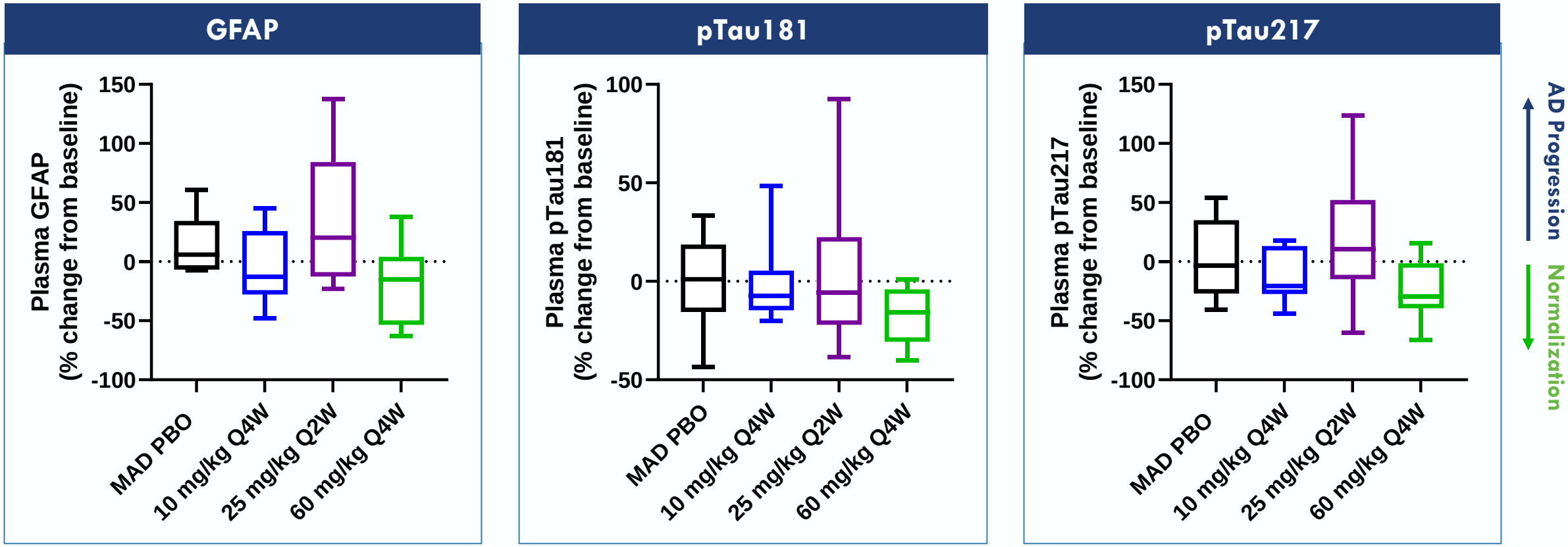
R^2= 0.18 p = 0.007

Neurogranin vs. Sabirnetug Drug Exposure



R^2= 0.18 p = 0.007

Trends Toward Normalizing Plasma GFAP, pTau181 and pTau217 with 10 mg/kg and 60 mg/kg Q4W



Samples taken 1-6 weeks following third administration of sabirnetug

INTERCEPT-AD Phase 1 Data Support Potential for Sabirnetug to Offer Best-in-Class Efficacy and Safety

Key Takeaways from INTERCEPT-AD

Potential for Differentiated Efficacy

- ✓ First mAb to demonstrate selective target engagement of AβOs (most toxic form of Aβ)
- ✓ Rapid, significant plaque reduction comparable to the current market front-runners at similar timepoints
- ✓ Improvement of AD biomarkers in CSF and plasma are a strong indication of downstream effects

Potential for Differentiated Safety

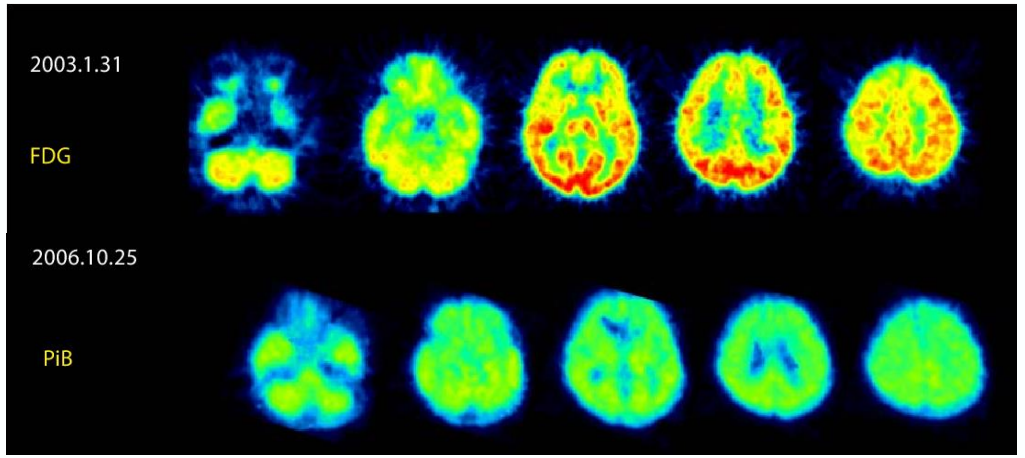
- ✓ Compelling safety profile with low incidence of ARIA-E
- ✓ Absence of ARIA-E observed in ApoE4 homozygotes
  - Differentiated from other antibodies with ARIA-E rates of ~30% to ~40% in ApoE4 homozygotes
- ✓ Broad therapeutic index with convenient monthly dosing

Human Genetic Data with Osaka Mutation Consistent with Hypothesis that Soluble Amyloid is an Instigator in Underlying AD Pathology

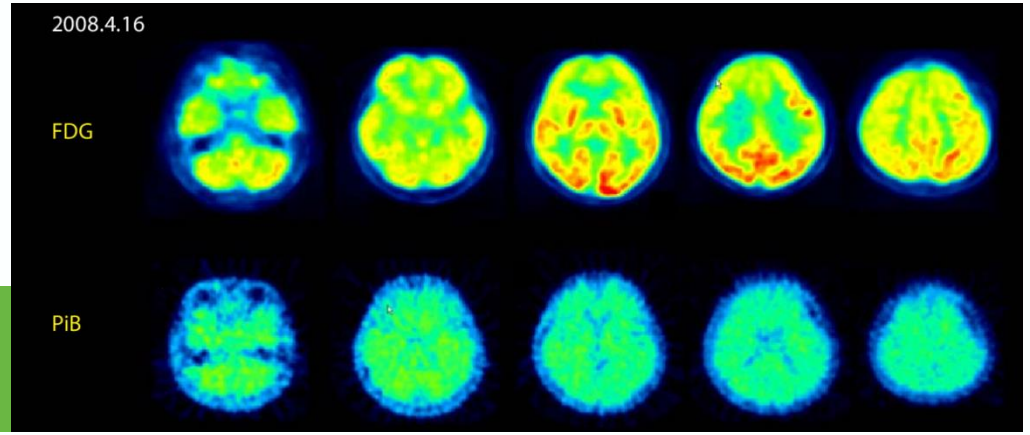
- Osaka familial AD mutation showed **extremely low levels of senile plaques despite severe cognitive impairment**
    - Cerebrospinal fluid (CSF) manifested **low levels of overall amyloid, but elevated levels of AβOs**
- Transgenic (Tg) mice carrying this mutation, or a closely related one, likewise manifest AβOs and other major forms of AD neuropathology but not plaques

Toxicity in the AD brain appears to be mediated by Aβ species not detected by amyloid PET

Cline et al., 2018 JPAD; Tomiyama et al., 2008; Kutoku et al., 2015



Patient 1: FDG showed hypometabolism in the posterior cingulate cortex, which was similar to that seen in patients with sporadic AD. PiB PET images show no accumulation of amyloid in her brain.



Patient 2: FDG and PiB PET images show no accumulation of amyloid in her brain similar to that seen in patient 1.

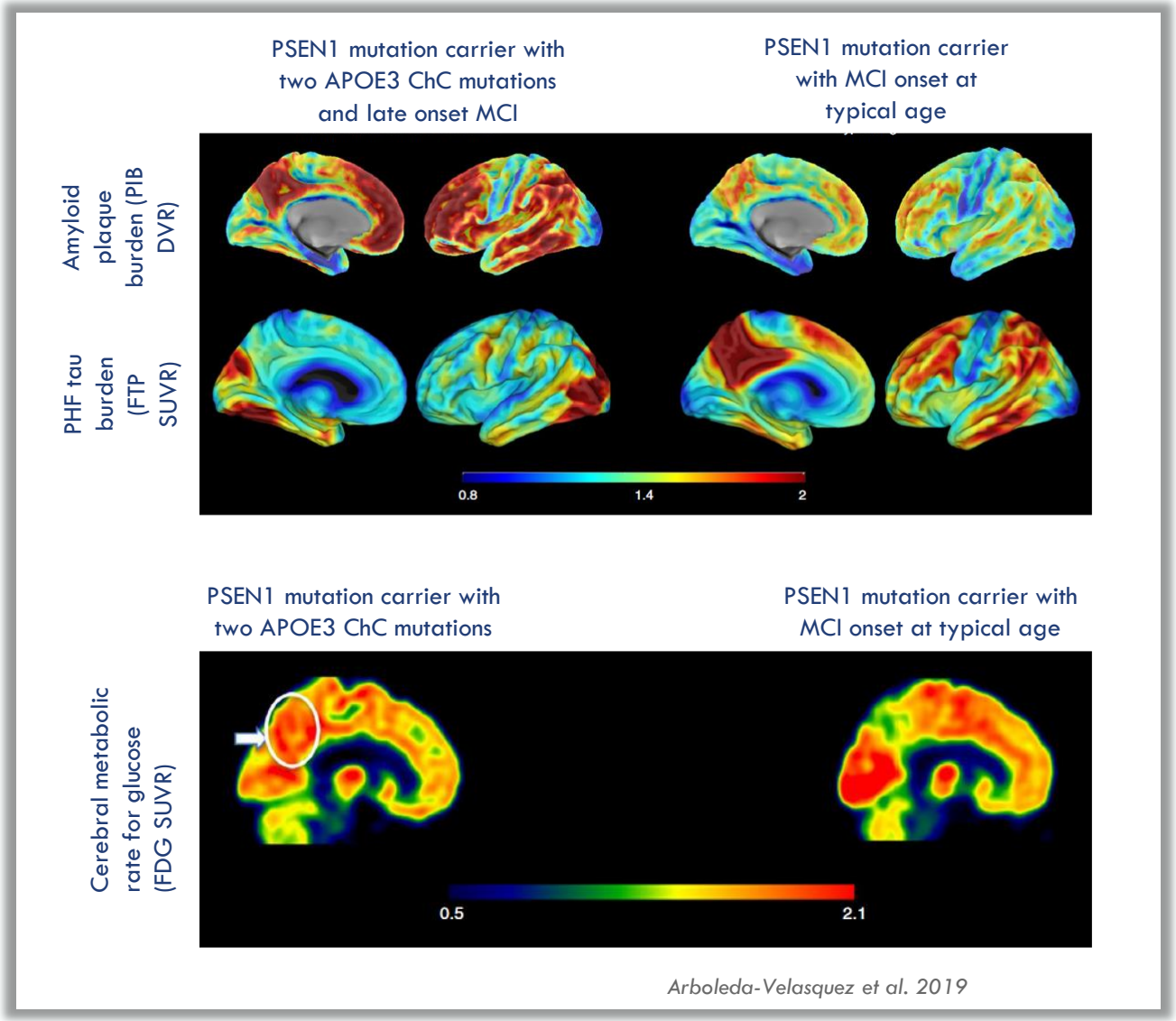
Shimada et al., 2011

Human Genetic Data with Christchurch Mutation Consistent with Concept that Amyloid Plaque is Correlative, Not Causative, of Cognitive Decline

- Christchurch AD mutation presents with two copies of the APOE3 Christchurch (R136S) mutation, **unusually high brain amyloid levels and limited tau and neurodegenerative measurements**

- PSEN1 (presenilin 1) mutation carrier from the world's largest autosomal dominant Alzheimer's disease kindred, who **did not develop mild cognitive impairment** until her seventies, three decades after the expected age of clinical onset

	PSEN1 alone	PSEN1 and ChC
Amyloid plaque	present	marked
PHF tau	present	minimal
FDG PET	impaired	preserved



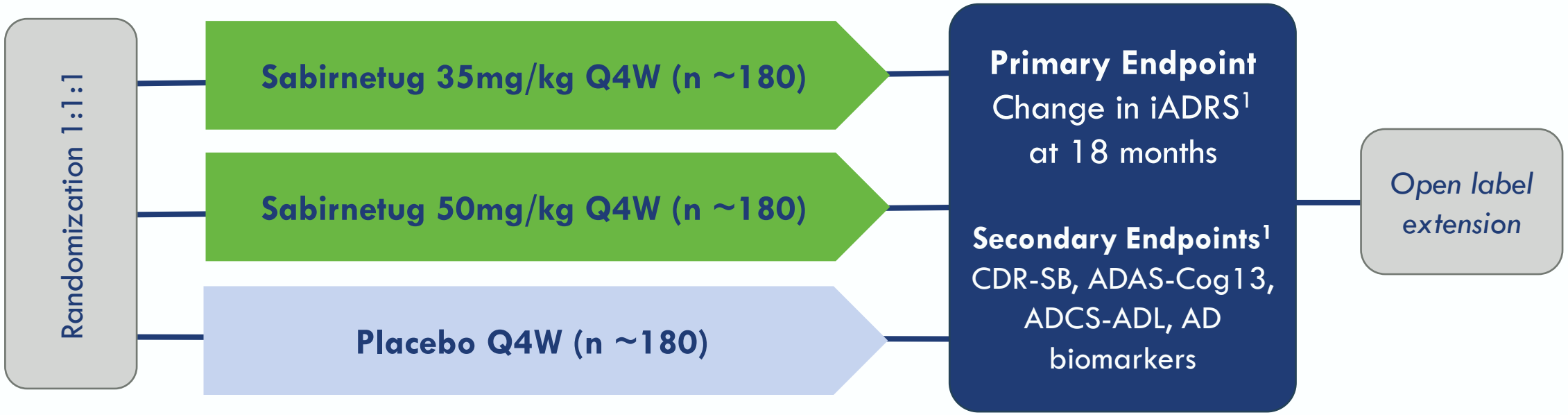
Arboleda-Velasquez et al. 2019

ALTITUDE-AD Study

Currently Enrolling

Objective: To evaluate the clinical efficacy, safety and tolerability of sabirnetug

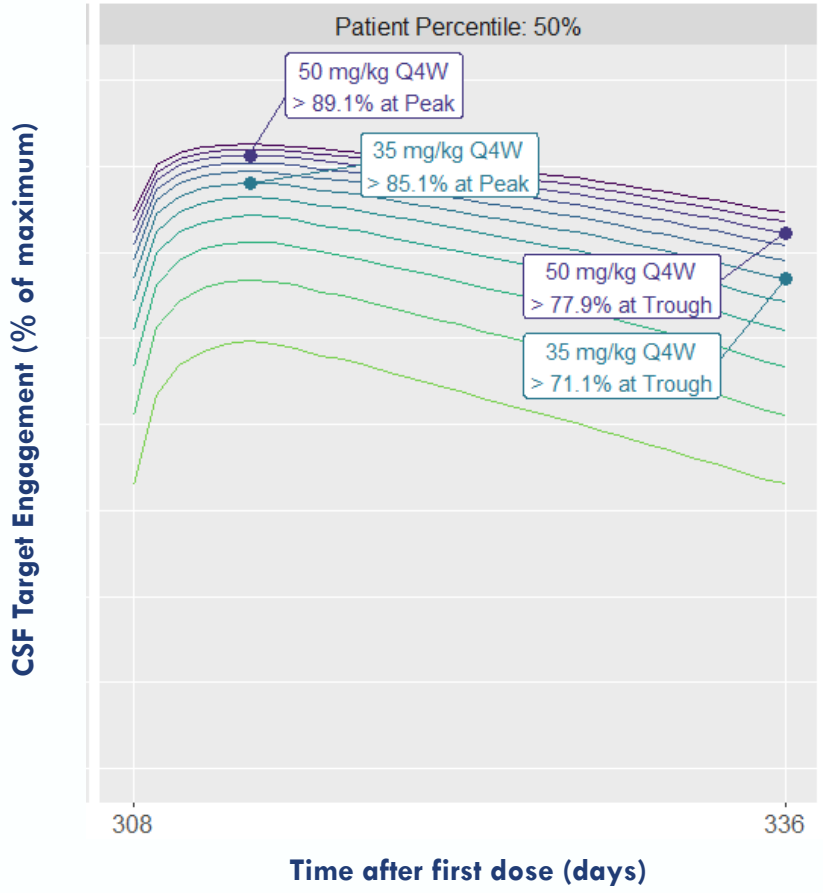
Patient population: Patients with early AD (MCI or mild dementia due to early AD)



1. iADRS: Integrated Alzheimer's Disease Rating Scale; CDR-SB: Clinical Dementia Rating – Sum of Boxes; ADAS-cog: Alzheimer's Disease Assessment Scale – Cognitive Subscale; ADCS-ADL: Alzheimer's Disease Cooperative Study – Activities of Daily Living

Simulated CSF Target Engagement at Steady-State for ALTITUDE-AD Doses

CSF target engagement was simulated at a candidate list of doses given Q4W at steady-state



Ph2 Dosing Strategy (ALTITUDE-AD)

lower dose: 35 mg/kg Q4W

upper dose: 50 mg/kg Q4W

- Notable **diminishing differentiation** as dose increases
- Doses were selected with **peak-trough** variation in mind: select doses based on trough (end of dosing interval) CSF engagement

Regimen: 10 mg/kg Q4W, 15 mg/kg Q4W, 20 mg/kg Q4W, 25 mg/kg Q4W, 30 mg/kg Q4W, 35 mg/kg Q4W, 40 mg/kg Q4W, 45 mg/kg Q4W, 50 mg/kg Q4W, 55 mg/kg Q4W, 60 mg/kg Q4W

60

AD Landscape & ALTITUDE-AD Enrollment Progress

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Disclosures

Paul Solomon, PhD

- Boston Center for Memory currently receives support for clinical trials from Eisai, Eli Lilly, UCB Biopharma, Cassava Sciences, Cognito Therapeutics, Biogen, AriBio USA, Acumen, Bristol Myers Squibb
- Dr. Solomon has provided consultation to AbbVie, Astellis, Avanir, AVID, Axovant, Biogen, Boxer Capital, Bristol Myers Squibb, Cognito, Eli Lilly, Eisai, EPIX, Kisbee, Pfizer, Toyoma, Virogenics
- Dr. Solomon receives royalties from Elsevier for "Memory Loss, Alzheimer's disease and dementia. A Practical Guide for Clinicians, third edition
- Dr. Solomon owns no stocks or equity in any pharmaceutical company and has no patents

Current Therapeutic Options for AD Patients and Room for Growth

AD prevalence predicted to increase

- Lecanemab and donanemab current marketed disease-modifying therapies in AD after decades of failures
  - Current clinical use increasing as infrastructure and education proceeds
- Advances in diagnosis and fluid biomarkers will contribute to heightened understanding of disease pathophysiology
- Opportunity for novel therapeutics to improve upon both efficacy and safety parameters
  - Potential for differentiation via patient genomic subgroups, such as APoE4 status

Lancet Public Health 2022; 2023 Alzheimer's Association Facts and Figures.

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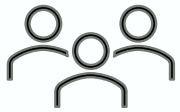
Amyloid Beta (Aβ) Therapies Will Remain Primary Form of Treatment for Early AD for a Significant Period of Time



Current state

Aβ Therapies

Includes:

- Plaque-targeting
- Protofibril-targeting
- **AβO-targeting** ACUMEN

Aβ therapies will be the primary treatment option for early AD (induction/maintenance)

Future additions

Non-Aβ Therapies

Includes:

- Tau-directed
- TREM2-targeting
- Other investigative therapies

Non-Aβ therapies will potentially be used as second-line (non-amyloid treatment) and may be good candidates for combination therapy in the future

"Given the high failure rates historically, don't expect more than 3-4 treatment options to emerge over the next 5 years."[1]

"Expect Aβ therapies to be the primary treatment option. Potential for newer MoAs (e.g. tau) to be used in combination with Aβ therapies." [1]

1. Deloitte interviews with Alzheimer's thought leaders on behalf of Acumen market analysis, conducted in 2023.

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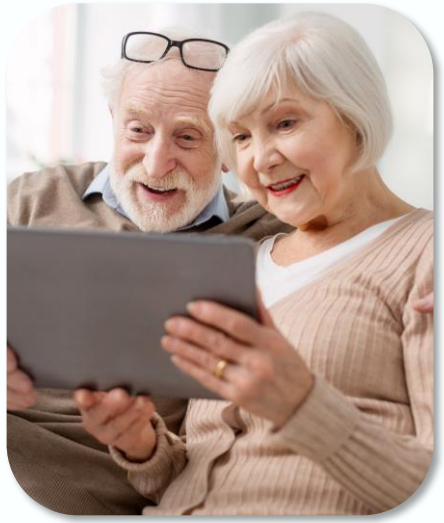
Trial Selection for Alzheimer's Disease Patients

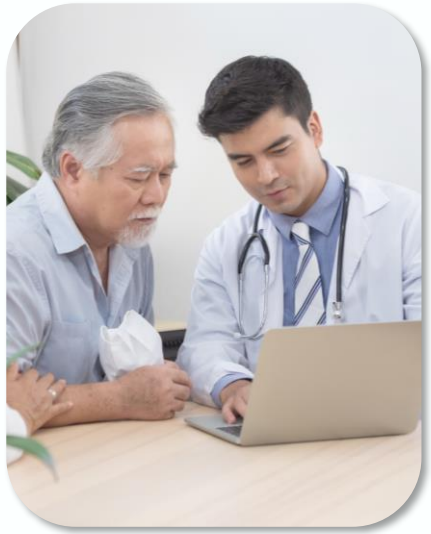
Considerations in trial selection:

- In search of next-generation, novel approaches
- AD patients more willing to 'take a risk' than patients in other disease areas
- ARIA-E a manageable side effect



Why we chose to participate in ALTITUDE-AD:

- Protocol design & influence from Phase 1 results
- Caliber and experience of Acumen team
- Potential of a novel target in AD



Current Enrollment Status of ALTITUDE-AD

- 70 sites activated since initiation in May 2024* in U.S., Canada, EU and U.K.
- Rapid enrollment likely due to:
  - Backlog of demand from patients and caregivers for additional novel options with the potential to treat AD
  - Experienced CRO and trial sites that have strong relationships with patients and Acumen
  - Potential for patients to receive a dose of sabirnetug that is efficacious, based on the Phase 1 results in patients that solidified dose ranges via target engagement of oligomers

Completion of enrollment in ALTITUDE-AD expected in the first half of 2025

*As of Sept. 25, 2024

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Milestones and Concluding Remarks

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Sabirnetug Subcutaneous Formulation Under Development in Collaboration with Halozyme

Potential to Broaden Patient Access and Increase Treatment Convenience

- Announced partnership with Halozyme in November 2023 to develop subcutaneous dosing option for sabirnetug
- Halozyme's drug delivery technology, ENHANZE®, is commercially validated in eight approved therapies available in 100+ countries, with >800,000 patients treated
- Current sabirnetug potential target product profile inclusive of no more than single weekly injection

Phase 1 bioavailability study ongoing to compare the pharmacokinetics of subcutaneous form of sabirnetug to the IV form

Ongoing Phase 1 Subcutaneous Healthy Volunteer Study

Topline Results Expected in Q1 2025

Population:

- Healthy volunteers
- Age matched to AD population in sabirnetug Phase 1 (INTERCEPT-AD) study

IV dose (1/month)

(n = 12)

Subcutaneous dose (1/week)

(n = 16)

Output:

- Safety
- Subcutaneous bioavailability
- Information on flat dosing

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Milestones Achieved in 2024 and Anticipated in 2025

MILESTONES	STATUS/ EXPECTED TIMING
Initiation of ALTITUDE-AD Phase 2 trial	✓
Initiation of Phase 1 subcutaneous trial	✓
Expected Phase 1 subcutaneous topline results	1Q25
Expected completion of enrollment of ALTITUDE-AD	1H25

Cash & marketable securities

$281M

As of June 30, 2024

=

Projected runway into

1H 2027

Summary

Key Takeaways

- ✓ Significant and growing Alzheimer's population in need of additional treatment options
- ✓ Sabirnetug demonstrates high selectivity for toxic AβOs in nonclinical and clinical data
- ✓ Positive Phase 1 data strengthen potential for sabirnetug to offer best-in-class efficacy and safety
- ✓ Phase 2 IV study and Phase 1 subcutaneous study ongoing

Q&A

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