Corporate Presentation

March 2026

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 early 2027, the therapeutic potential of Acumen's product candidate, sabirnetug (ACU193), including against other antibodies, the timing of anticipated topline results of ALTITUDE-AD, the potential for additional development to support a subcutaneous dosing option of sabirnetug, and the potential to develop a candidate to treat Alzheimer's Disease utilizing EBD technology. 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.

Advancing Next Generation Treatments for Early Alzheimer's Disease (AD)

Targeting Toxic Amyloid Beta Oligomers (AβOs)

Large and growing market in need of additional treatment options

Sabirnetug (ACU193): monoclonal antibody (mAb) **highly selective for toxic AβOs** with positive Phase 1 clinical trial results in AD patients; **Phase 2 (IV) topline results expected late 2026**

Enhanced Brain Delivery (EBD™) program to develop oligomer-targeted antibodies with BBB-penetrating technology; **EBD pre-clinical candidate (PCC) data announced early 2026 & IND filing targeted for mid-2027**

Experienced leadership team with extensive AD drug development experience

Strong balance sheet supporting clinical development plans for sabirnetug (~$117M at 12/31/25)

BBB: blood-brain-barrier

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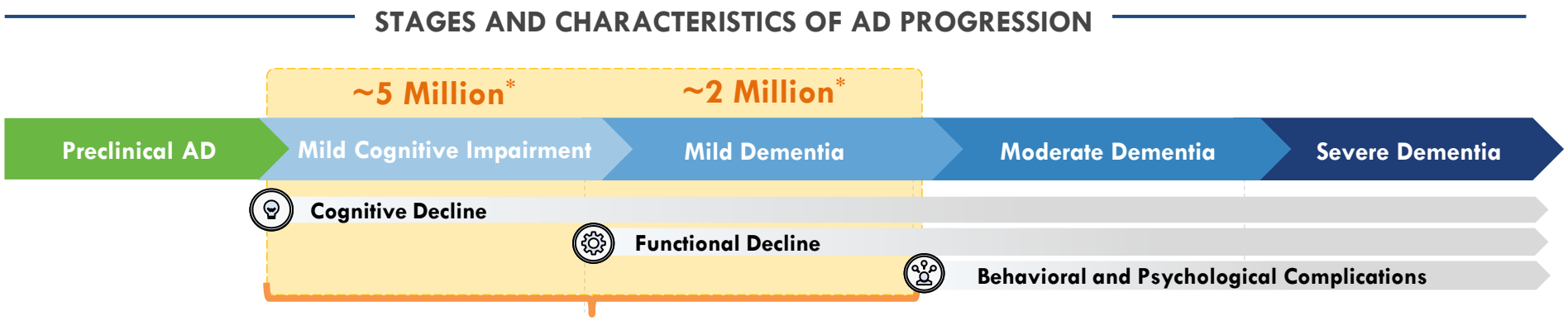
Early AD Patient Population Represents Significant and Growing Market



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 via increased understanding of blood-based biomarkers → More treated cases due to availability of treatment options and favorable shifts around adoption = **Growing Market**

*Alzheimer's Association

AD Treatment Landscape Continues to Evolve

Approved Therapies Establish Momentum and Next-generation Approaches Expand Impact

Current AD Treatments

Offer Hope for People Living with AD

- First approved anti-amyloid therapies steadily growing
- Education and infrastructure buildout allowing for greater access to treatments by the addressable patient population

Opportunities for New Anti-amyloid Therapies

to Strengthen Risk-Benefit Tradeoff

- Increase efficacy
- Reduce ARIA-E* risk
- Provide more convenient delivery options
- Target amyloid that occurs earlier in disease course

Future of AD Landscape

Broadens Growth Prospects

- New blood-based biomarkers and imaging tools will improve diagnostic and monitoring capabilities
- Expansion into preclinical AD will significantly increase the addressable population
- Combinations with other targets, such as tau, hold promise

*ARIA-E: Amyloid-related imaging abnormalities - edema

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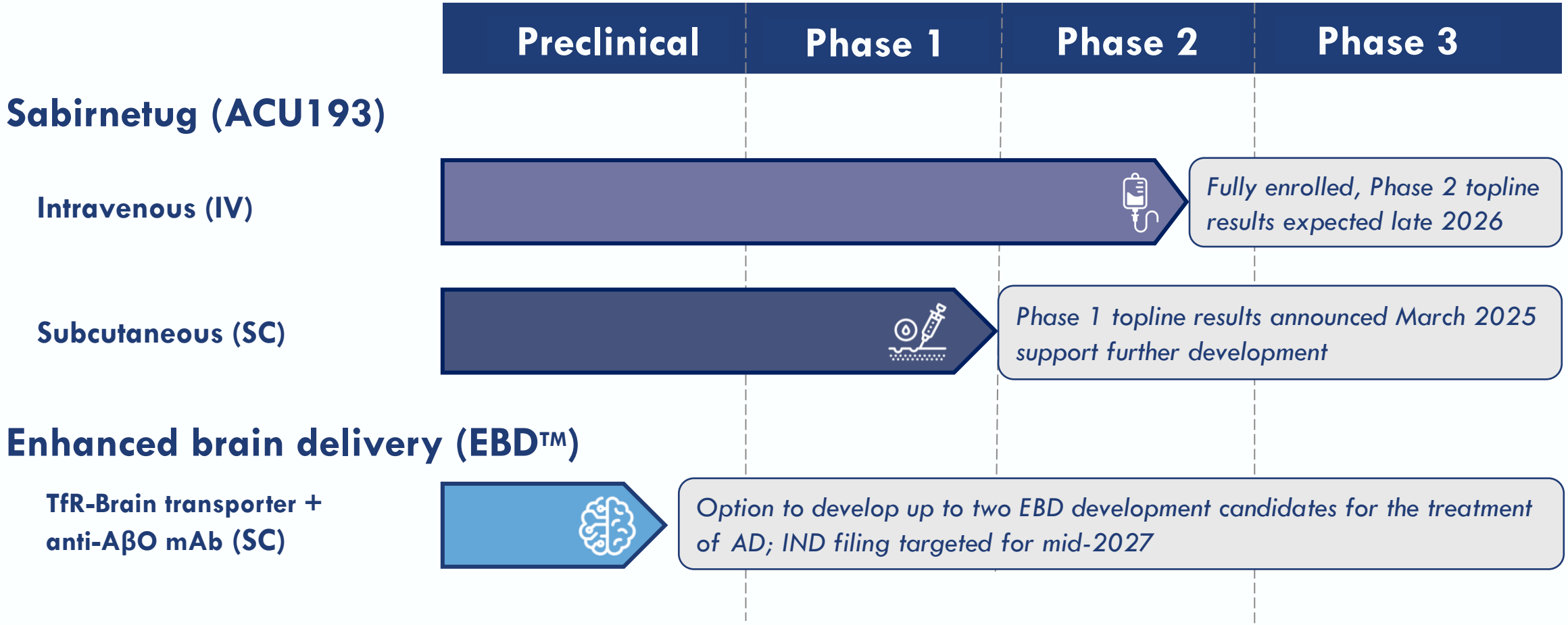
2026 a Pivotal Year for Acumen's Pipeline

Sabirnetug Global Phase 2 Study Results & Next Generation EBD™ Candidate Selection



Acumen Leadership Team

Experienced in AD/Neuro Drug Development

DANIEL O'CONNELL
Chief Executive Officer
ACUMEN
neuroventures

JAMES DOHERTY, PHD
President &
Chief Development Officer
ACUMEN
Sage Therapeutics
AstraZeneca

ERIC SIEMERS, MD
Chief Medical Officer
ACUMEN
Lilly

MATT ZUGA
Chief Financial Officer &
Chief Business Officer
ACUMEN
HIGHCAPE PARTNERS

RUSSELL BARTON
Chief Operating Officer
ACUMEN
Lilly

LIEAN SCHENK
SVP, Head of CMC
ACUMEN
Lilly Lonza
NOVAVAX

LAURA ROSEN, MD, PHD
SVP, Clinical Development
ACUMEN MERCK
Takeda Shire

AMY SCHACTERLE, PHD
Chief Regulatory Officer,
Head of Quality
Sage Therapeutics
ACUMEN sunovion

SIEW TIN GAN
Head of Clinical
Operations
ACUMEN
Lundbeck Takeda

JASNA JERECIC, PHD
Disease Area Strategy Lead
ACUMEN

PAUL SHUGHRUE, PHD
VP, Research & Strategy
ACUMEN
MERCK prothena
Allergan

DEREK MEISNER, JD
Chief Legal Officer
ACUMEN
X4 PHARMACEUTICALS

JULIE BOCKENSTETTE
Chief People Officer
ACUMEN
Roche Lilly

Acumen team has decades of experience in Alzheimer's drug discovery and development

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Milestones Achieved and Upcoming

MILESTONES	TIMING	STATUS
Initiation of ALTITUDE-AD Phase 2 trial	**2Q2024**	✓
Completion of enrollment of ALTITUDE-AD	**1Q2025**	✓
Phase 1 subcutaneous topline results	**1Q2025**	✓
EBD™ non-clinical data package	**Early 2026**	✓
ALTITUDE-AD topline results	**Late 2026**	☐

~$117M

Cash, cash equivalents and marketable securities as of Dec. 31, 2025

On March 16, 2026, the Company completed a private placement, with gross proceeds totaling $35.75M

Acumen expects its cash runway to extend into early 2027

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Amyloid Beta Oligomers in AD

Sabirnetug (ACU193): monoclonal antibody (mAb) highly selective for toxic AβOs

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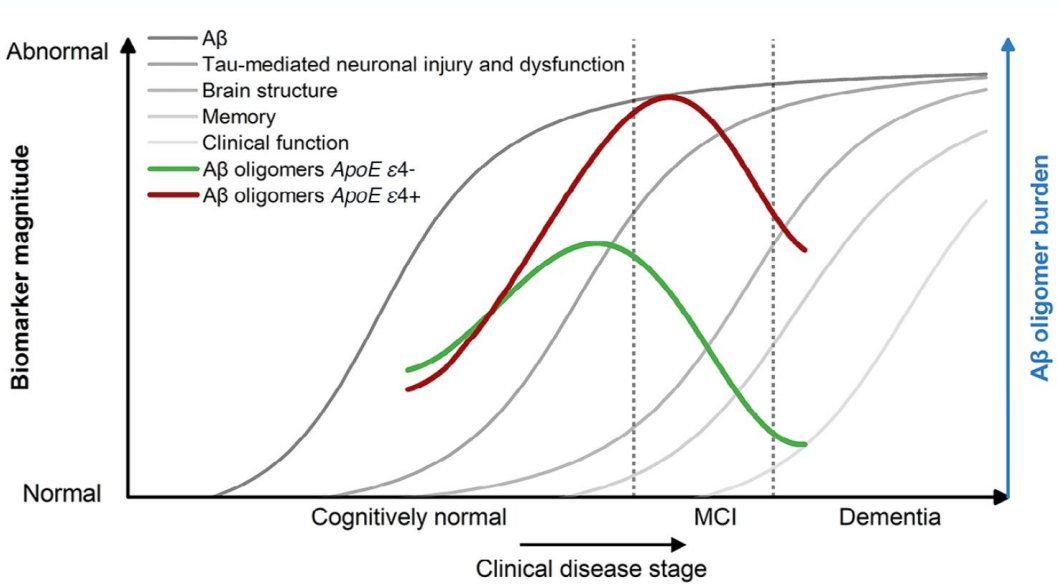
Soluble AβOs Contribute to Pathophysiological Processes Associated with Alzheimer's Disease

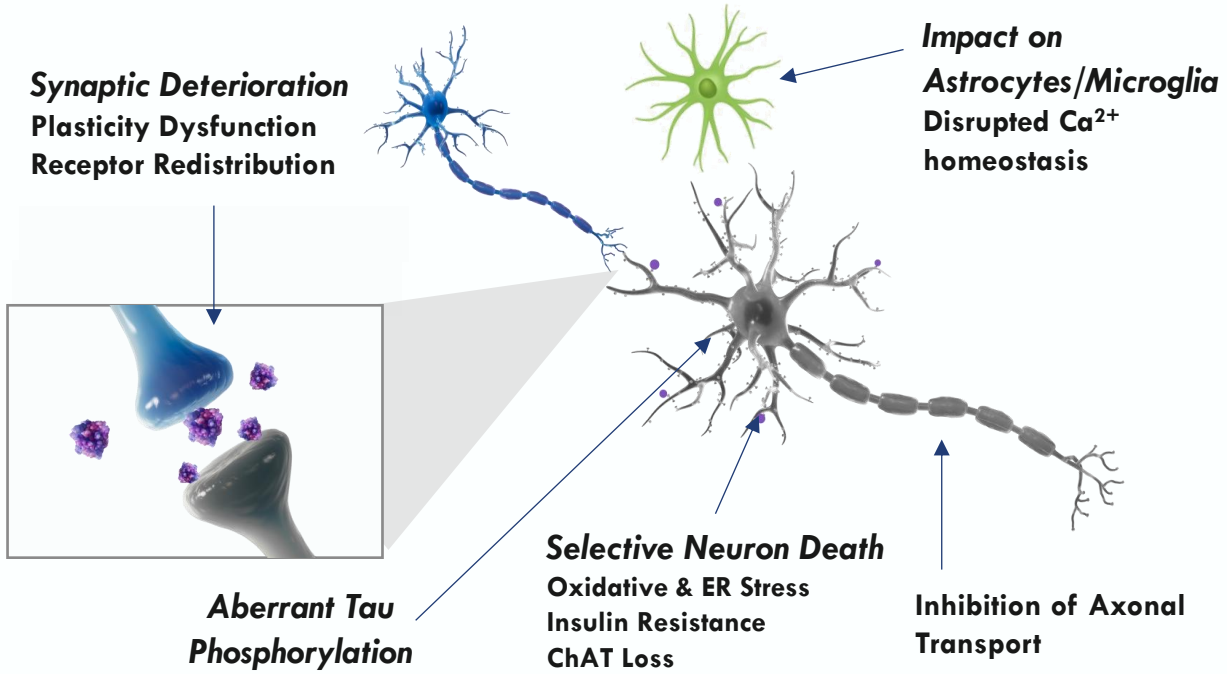
Model of Aβ oligomer levels



Adapted from Blomeke et al. 2024

- Soluble Aβ forms appear early in the course of disease pathophysiology
- Production of toxic soluble Aβ persists after plaque removal

- Toxic consequences of soluble Aβ oligomer production include synapse dysfunction and loss, tau hyperphosphorylation, immune cell activation and functional impairment
- Reduced neuronal toxicity and intervention at the synaptic level may prevent irreversible neuronal cell death



Sabirnetug: Potential Next Generation Immunotherapy for Early AD

Designed for Improved Efficacy & Safety

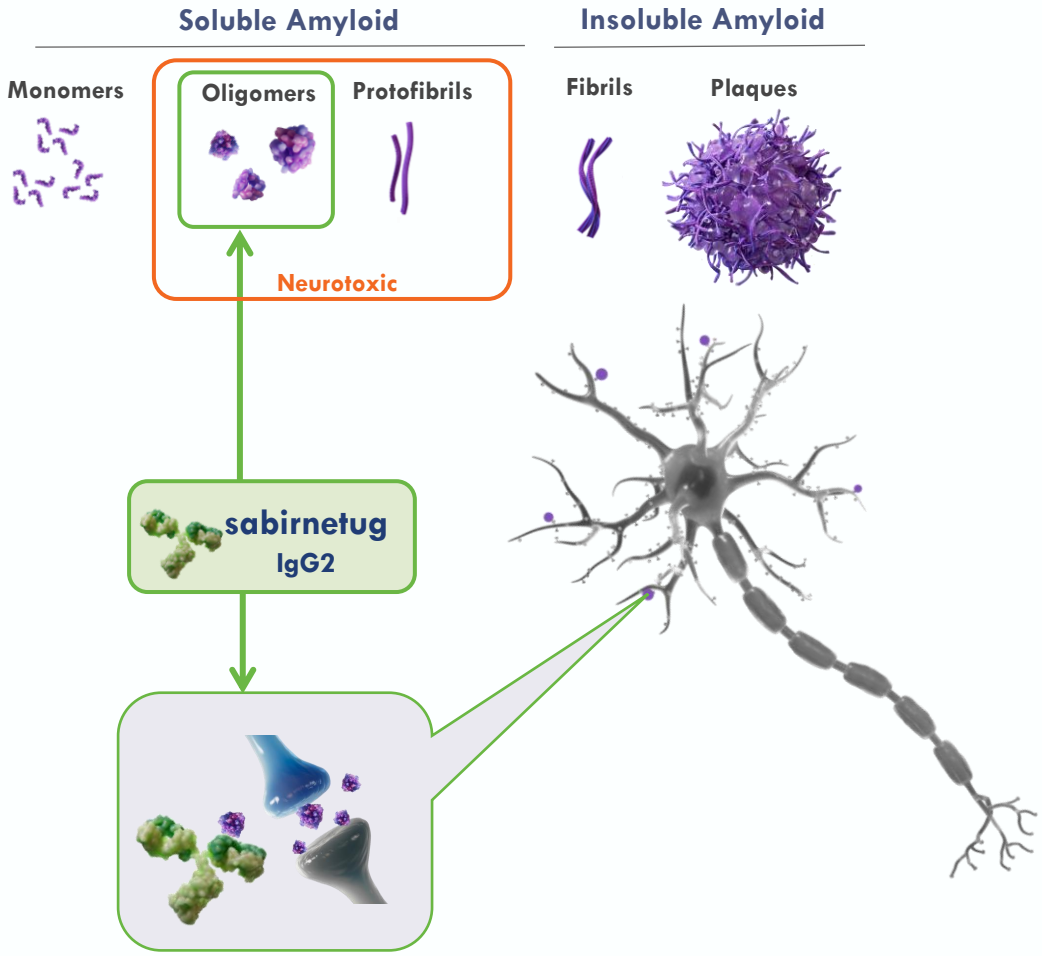
- Humanized, affinity matured mAb developed to target toxic Aβ oligomers
- IgG2 subclass mAb with reduced effector function

Encouraging Regulatory Interactions

- FDA Fast Track designation for the treatment of early AD
- Phase 2 implemented as a registration-quality study

Positive Ph1 in AD Patients & Encouraging Ph2 Enrollment

- Successful Phase 1 exclusively in early AD patients
  - ✓ Safety, target engagement, biomarker effects
- Phase 2 (n=542) enrollment complete in March 2025; topline results expected in late 2026



Sabirnetug

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

PART A:
SINGLE-ASCENDING DOSE
n = 8 per cohort (32 total)
6:2 per cohort

COHORT 1: 2 mg/kg sabirnetug or Placebo — 2mg

≥ 1wk

COHORT 2: 10 mg/kg sabirnetug or Placebo — 10mg

≥ 1wk

COHORT 3: 25 mg/kg sabirnetug or Placebo — 25mg

≥ 1wk

COHORT 4: 60 mg/kg sabirnetug or Placebo — 60mg

PART B:
MULTIPLE-ASCENDING DOSE
n = 10 per cohort (30 total)
3 administrations of drug or PBO
8:2 per cohort

≥ 1wk

COHORT 5: 10 mg/kg sabirnetug or Placebo (Q4W)* — 10mg

≥ 1wk

COHORT 6: 60 mg/kg sabirnetug or Placebo (Q4W)* — 60mg

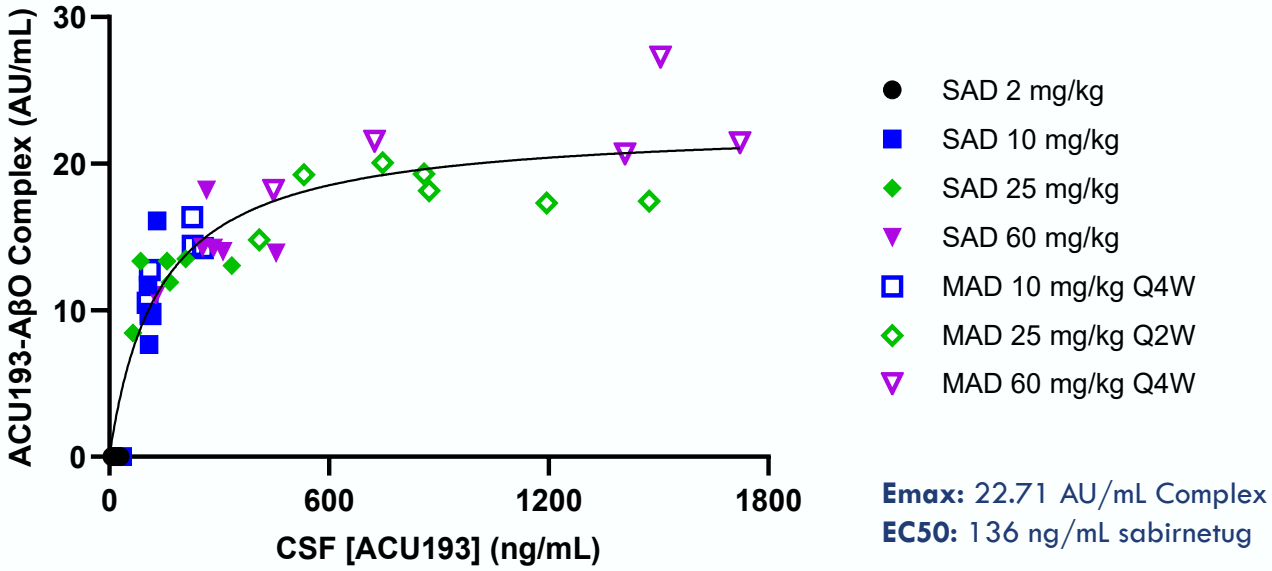
≥ 1wk

COHORT 7: 25 mg/kg sabirnetug or Placebo (Q2W)* — 25mg

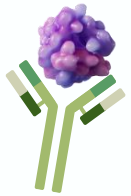
Q2W: Dosing every two weeks; Q4W: Dosing every four weeks.

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

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



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



Sabirnetug-AβO Complex

- Acumen developed a novel assay to measure the complex of AβOs bound to sabirnetug in cerebrospinal fluid
- Observed target engagement with oligomers that increased across a range of doses
- Achieved saturation point between 25 mg/kg and 60 mg/kg

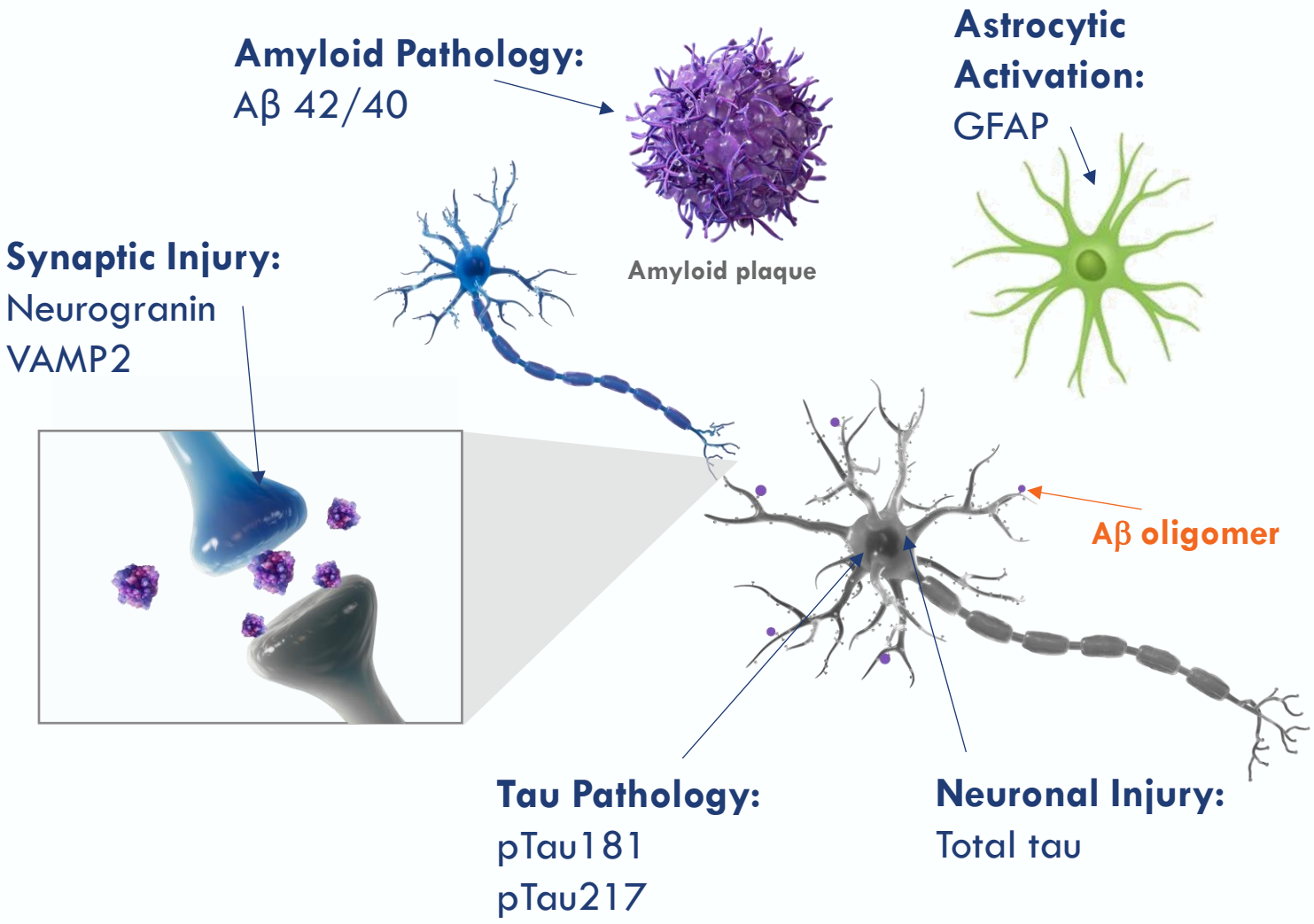
*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

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]

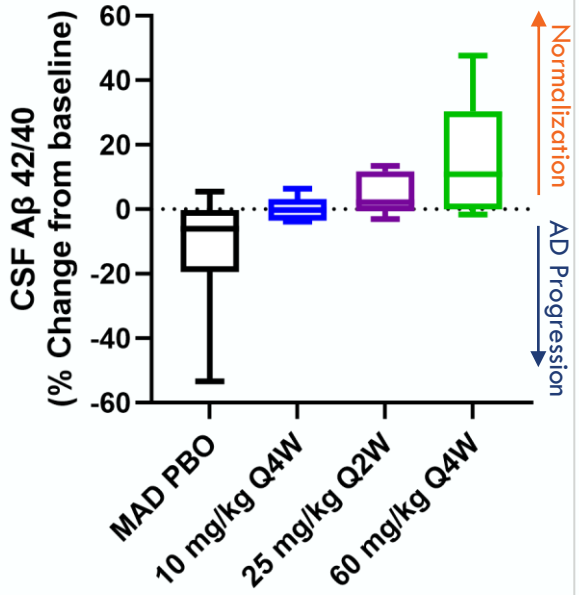
- **After just three administrations of sabirnetug, patients with early AD demonstrated improvements in biomarkers associated with AD pathology**



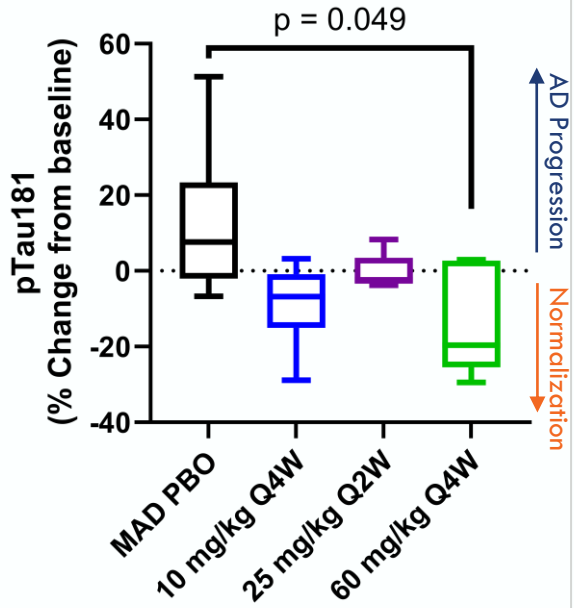
1. Tarawneh, R. Biomarkers: Our Path Towards a Cure for Alzheimer Disease. Biomarker Insights Volume 15: 1–15. 2020; 2. Blennow K, Zetterberg H. The Past and the Future of Alzheimer's Disease Fluid Biomarkers. J Alzheimer's Dis. 2018;62(3):1125-1140.

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

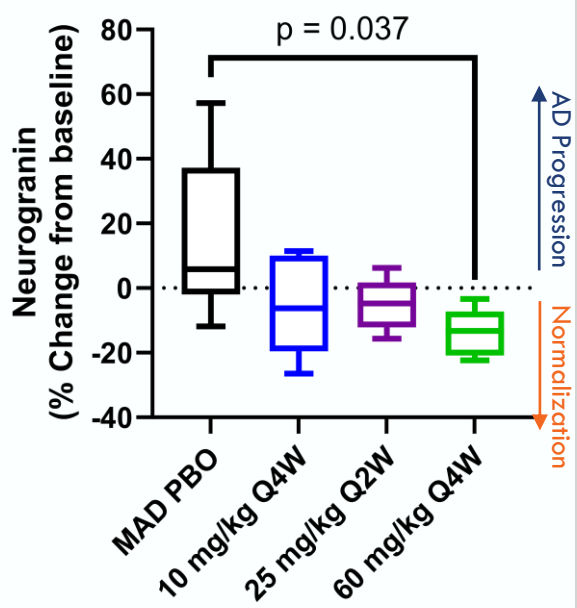
Aβ 42/40 Ratio



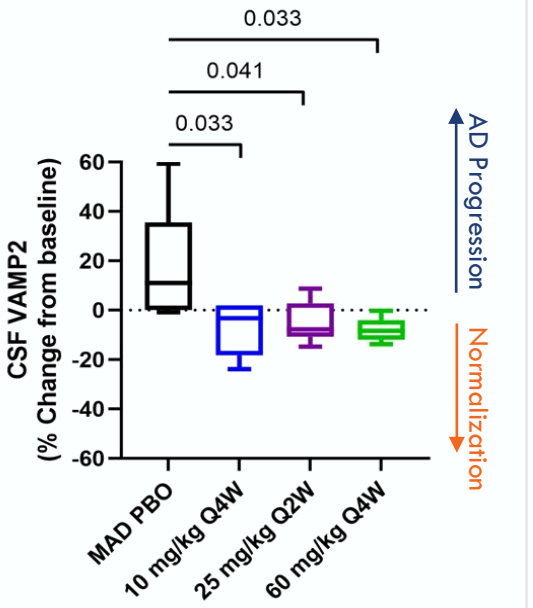
pTau181



Neurogranin



VAMP2



Amyloid pathology

Tau pathology

Synaptic injury

E. Cline, et al, Biofluid biomarker changes following treatment with sabirnetug (ACU193) in INTERCEPT-AD, a phase 1 trial in early Alzheimer's disease. JPAD 2025.

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

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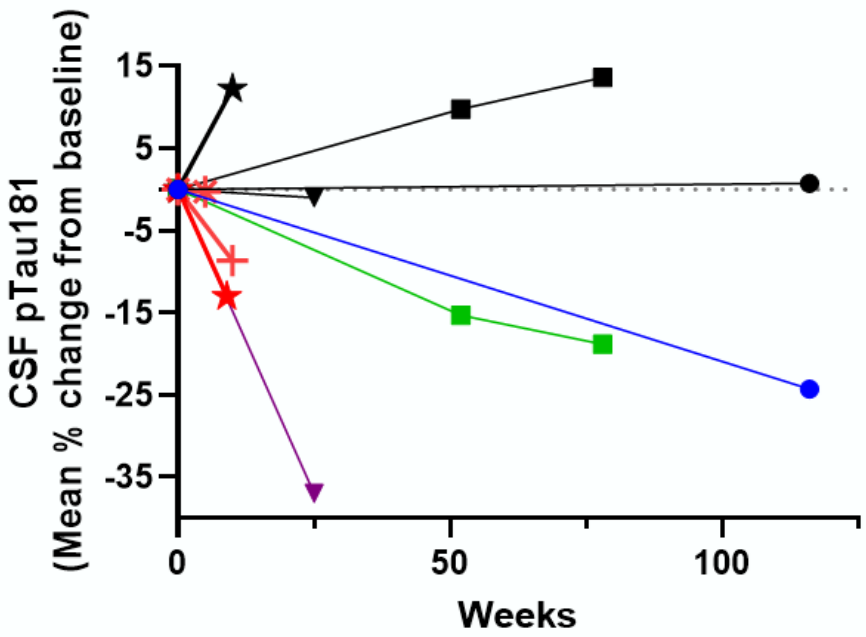
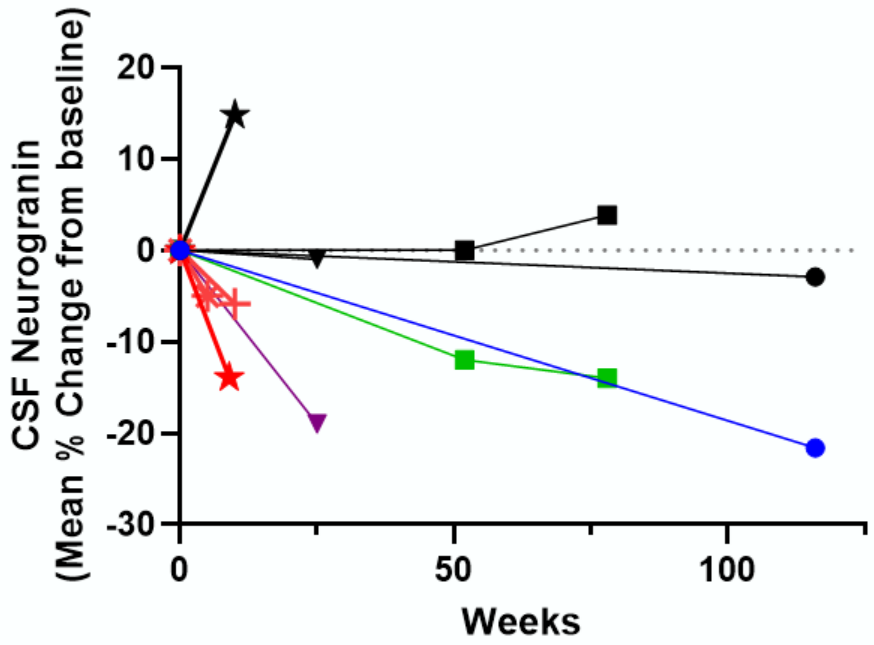
Sabirnetug Shows Greater or Similar Improvement in Multiple CSF Biomarkers as Compared to Other Aβ Agents

CSF pTau181



CSF Neurogranin



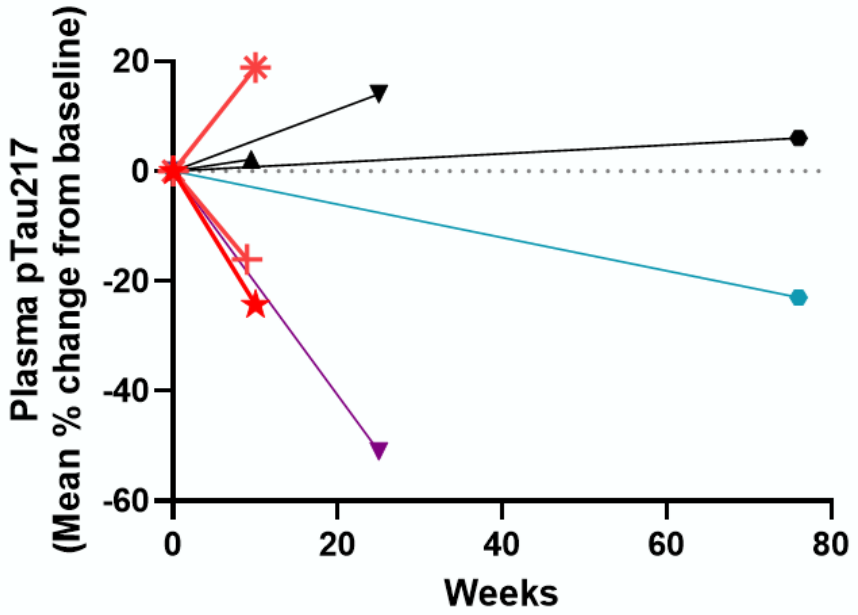
- ★ ACU193 (60 mg/kg Q4W)
- ✳ ACU193 (25 mg/kg Q2W)
- \+ ACU193 (10 mg/kg Q4W)
- ★ Pooled Placebo ACU193
- ● Gantenerumab (510 mg Q2W)
- ● Gantenerumab Placebo
- ■ Lecanemab (10 mg/kg Q2W)
- ■ Lecanemab Placebo
- ▼ Trontinemab (3.6 mg/kg Q4W)
- ▼ Trontinemab Placebo

Acumen Pharmaceuticals, data on file; AAIC 2023; Bateman et al 2023 NEJM; ADPD 2025.

*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 Shows Greater or Similar Improvement in Plasma pTau217 Biomarker as Compared to Other Aβ Agents

Plasma pTau217



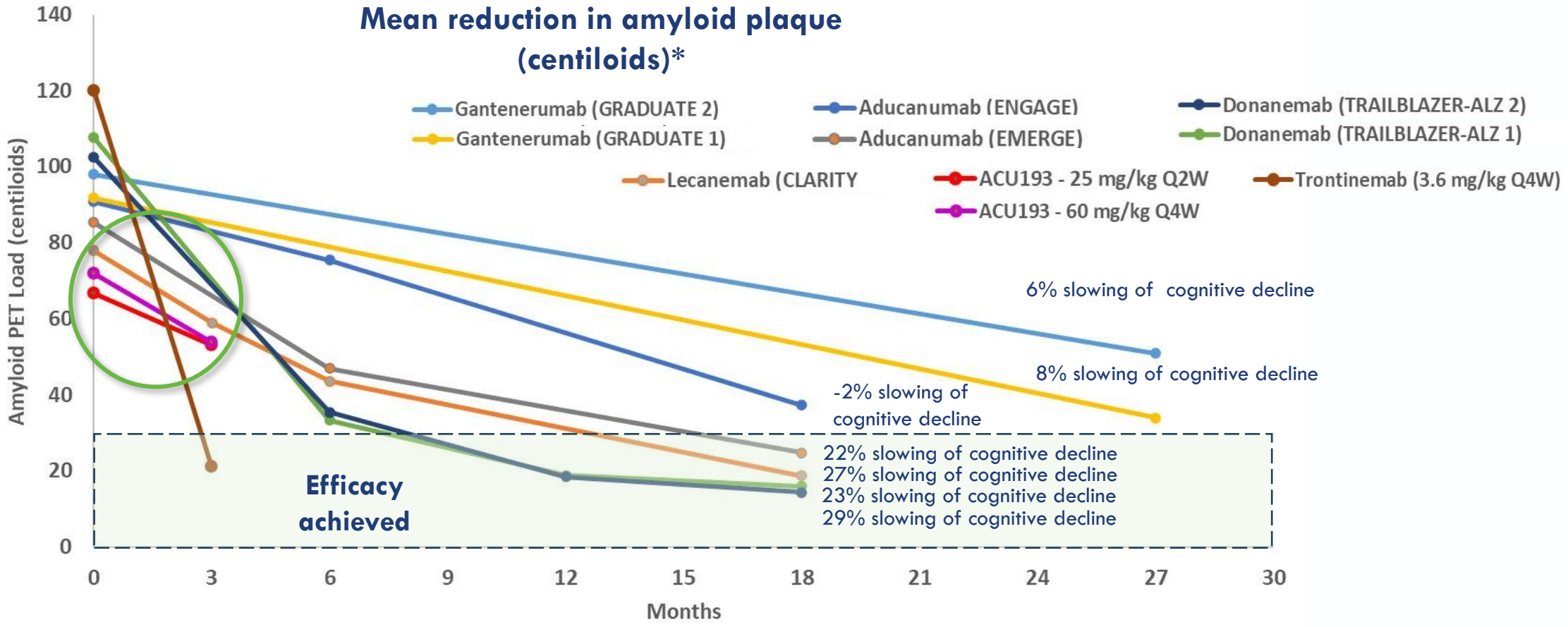
- ACU193 (60 mg/kg Q4W)
- ACU193 (25 mg/kg Q2W)
- ACU193 (10 mg/kg Q4W)
- ACU193 Pooled Placebo*
- Donanemab
- Donanemab Placebo
- Trontinemab (3.6 mg/kg Q4W)
- Trontinemab Placebo

Acumen Pharmaceuticals, data on file; AAIC 2023; Sims et al 2023 JAMA; ADPD 2025.

Note: More impact to fluid biomarkers was observed with longer dosing duration; the 25 mg/kg Q2W cohort differed in dose and sample timing, with drug on board for less time than the 10 mg/kg & 60 mg/kg Q4W cohorts

*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.

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 Demonstrates Potential for Best-in-Class Safety Profile

Compelling Overall Safety Profile, with Low Incidence of ARIA-E in the INTERCEPT-AD study

INTERCEPT-AD Phase 1 Safety Data

5 Total ARIA-E cases, or ~10%

0 Cases of ARIA-E in ApoE4 homozygotes N=6

0 Deaths, SAEs Related to Study Drug

✓ **Limited incidence of ARIA-E**

- 10 mg/kg Q4W: 1 asymptomatic case
- 25 mg/kg Q2W: 1 asymptomatic case
- 60 mg/kg Q4W: 2 asymptomatic cases; 1 symptomatic case

✓ **No ARIA-E observed in ApoE4 homozygotes (n=6), despite comprising 13% of study**

- Differentiated from other antibodies that have ARIA-E rates ~30% to ~40% in participants who are E4-homozygotes

✓ **Broad therapeutic index** with convenient monthly dosing

- Safety profile may support attractive benefit/risk option for large portion of patients

E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

ApoE4: ε4 allele of Apolipoprotein E

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INTERCEPT-AD Phase 1 Data Support Potential for Sabirnetug to Offer Next Generation 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
- ✓ Broad potential therapeutic index with convenient monthly dosing

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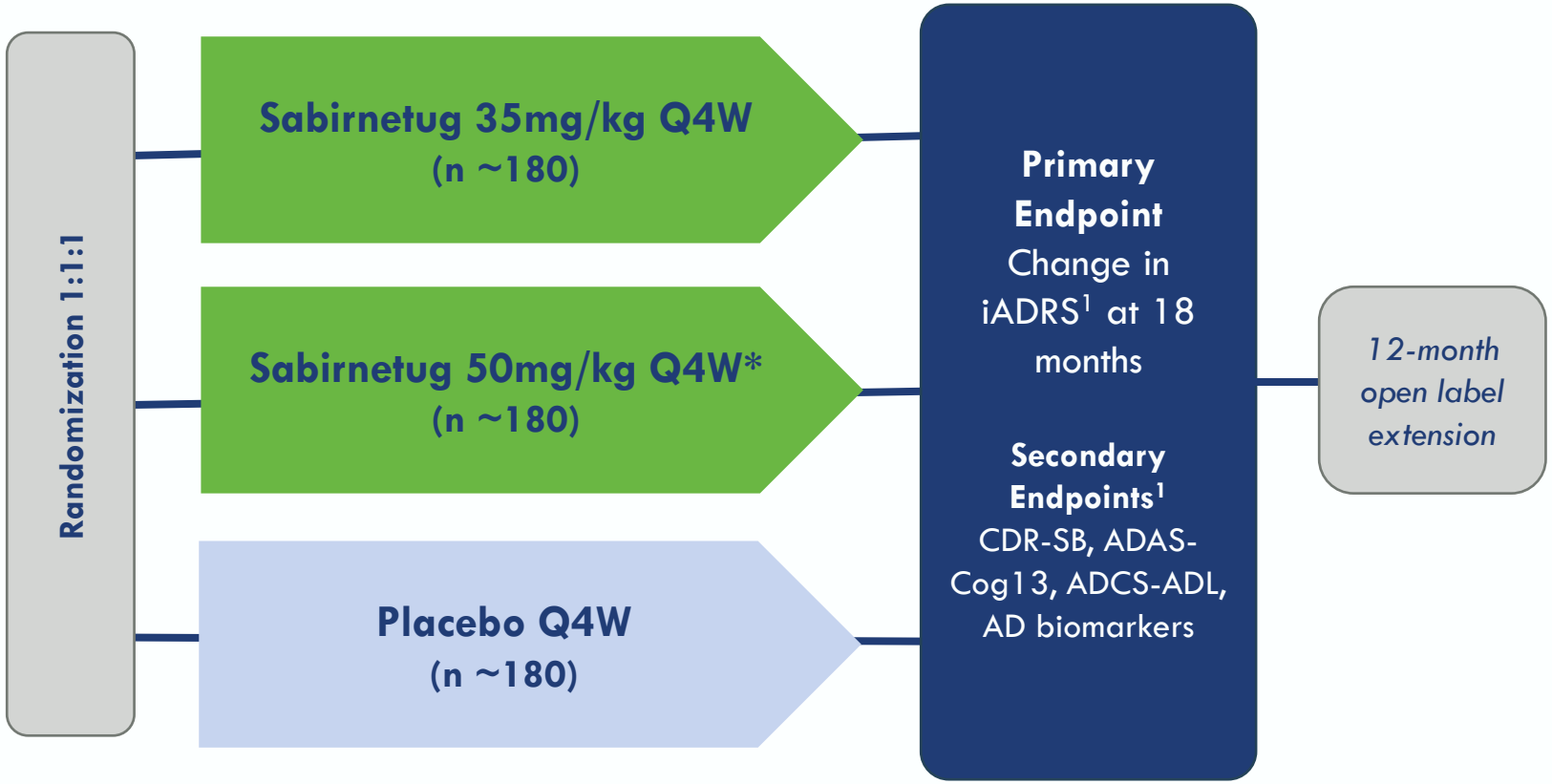
ALTITUDE-AD Phase 2 Study Results Expected in Late 2026

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)



*Titration of sabirnetug 35mg/kg Q4W for two doses.

Key Highlights

- 542-participant study fully enrolled in March 2025 (U.S., Canada, U.K., Germany, Spain)
- Open label extension portion of ALTITUDE-AD initiated in November 2025
- Topline results expected in late 2026

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

Subcutaneous Formulation Well-Tolerated in Phase 1 Healthy Volunteer Study

Potential to Dose Once-Weekly with Single Injection to Broaden Patient Access and Increase Treatment Convenience

Phase 1 Subcutaneous Healthy Volunteer Study

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

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

IV dose (single dose) (n = 12)

Subcutaneous dose (4 doses, 1/week) (*n = 16*)

Outcomes:
- Safety
- Subcutaneous bioavailability
- Information on flat dosing

Topline results announced in March 2025 show systemic exposure supports further clinical development of the subcutaneous formulation

Halozyme

Announced partnership with Halozyme in November 2023 to develop subcutaneous dosing option for sabirnetug using Halozyme's drug delivery technology, ENHANZE®

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Sabirnetug IP & Market Exclusivity

- Exclusive, perpetual, irrevocable, worldwide, royalty-free license from Merck to its Amyloid Derived Diffusible Ligand (ADDL) IP including issued sabirnetug patents
- Sabirnetug Global IP estate:
  - ✓ Issued patents in 19 countries
  - ✓ Composition of matter patents and methods of use run into July 2031
  - ✓ Patent term extensions may be available, 3-5 years depending on jurisdiction
- Biologics market exclusivity is expected for sabirnetug as a novel biologic drug
  - ✓ US provides 12 years market exclusivity for novel biologics
  - ✓ Europe provides 10 years of market exclusivity for novel biologics
- EBD™ program includes Acumen wholly-owned AβO-selective mAbs expected to generate novel IP including Composition of Matter Patent(s)

Enhanced Brain Delivery (EBD™)

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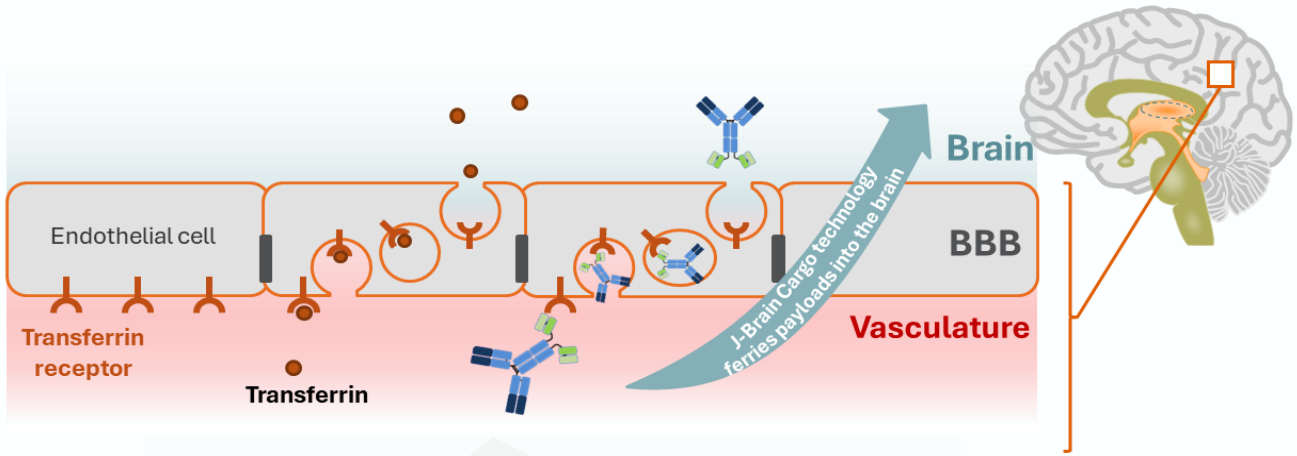
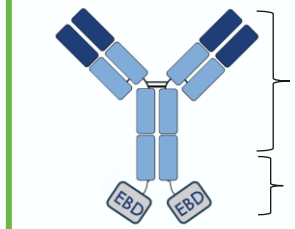
Delivering Antibodies to the Brain via the Transferrin Receptor (TfR)

Aim to Widen the Therapeutic Window to Increase Efficacy, Safety, and Convenience





Oligomer-targeted antibody

TfR-targeted carrier

Image courtesy of JCR Pharmaceuticals

Enhanced Brain Delivery (EBD) Opportunities:

- Increased brain exposure may enhance efficacy
- Wider capillary distribution may reduce ARIA-E risk
- Lower dose volumes enable convenient subcutaneous administration

JCR Pharmaceuticals

- ✓ Collaboration, option and license agreement announced in July 2025 with JCR Pharmaceuticals
- ✓ Acumen holds exclusive option to license and develop up to two candidates under terms of agreement

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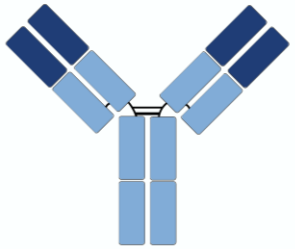
Acumen's EBD May Improve Efficacy, Safety and Delivery Compared to Non-AβO Selective Antibodies

Differentiated Cargo (AβO-selective mAb)



- **Targets synaptotoxic AβO species**
- **Robust fluid biomarker results** in Phase 1b INTERCEPT-AD trial
- Demonstrated **low ARIA-E** overall in Phase 1b, including no ARIA-E observed in APOE 4/4 carriers
- **Low rate of infusion related reactions** observed to date clinically
- Candidate mAbs: ACU193 and ACU234

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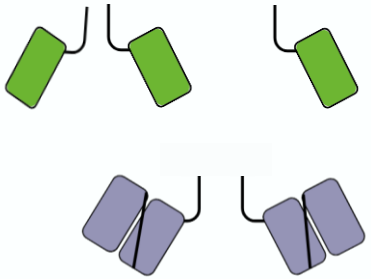
Validated BBB Carrier Technology (TfR-targeting)



- **Enhance brain penetration** versus native antibody to enable low-volume SC delivery
- **Potential for lower ARIA rate** due to TfR prevalence on capillary bed
- **Little to no anemia observed with JCR technologies**

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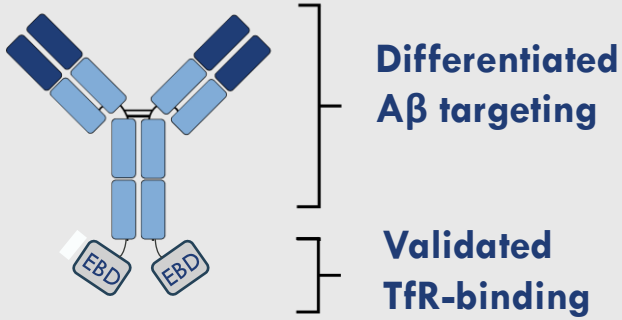
Acumen EBD Candidates



- **Enhanced efficacy:** Leverage improved brain delivery/ distribution and Aβ oligomer targeting
- **Best-in-class safety:** Lower ARIA, anemia, IRRs
- **Designed for SC administration:** Low dose, formulation, stability

ApoE4: ε4 allele of Apolipoprotein E

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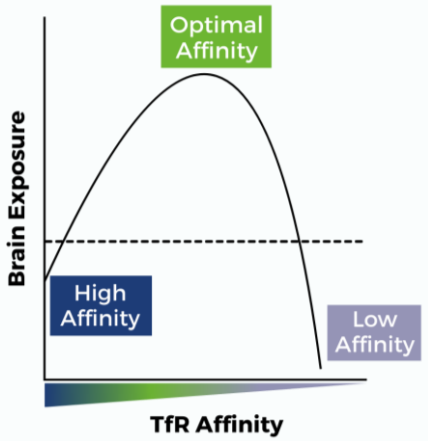
Acumen Explored Broad Parameters to Develop a TfR-Mediated AβO Product

TfR Affinity

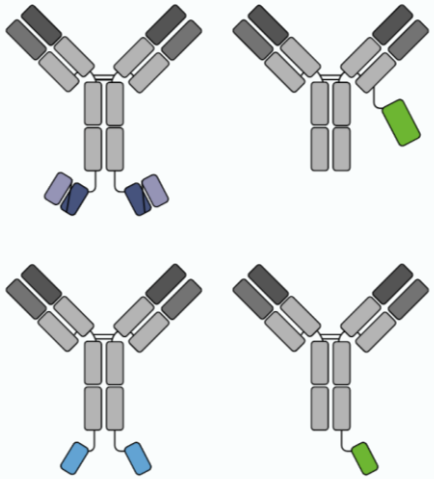
Affinity Range



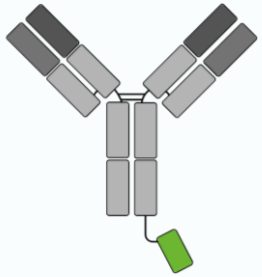
Architecture

scFv or VHH

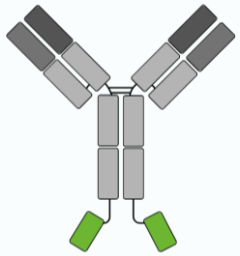
Heavy Chain vs Light Chain



Valency



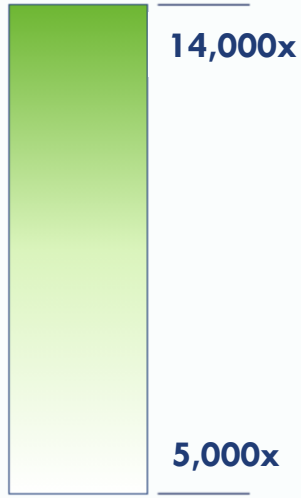
Monovalent



Bivalent

AβO Selectivity

Selectivity Range



SQ Properties

Dosing, Formulation, Stability

TfR: transferrin receptor; scFv: single chain variable fragment antibodies; VHHs: variable heavy domain antibodies; SQ: subcutaneous

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Phase 1 Results Provide Foundation for EBD™ Program

Half-life/Dosing Interval

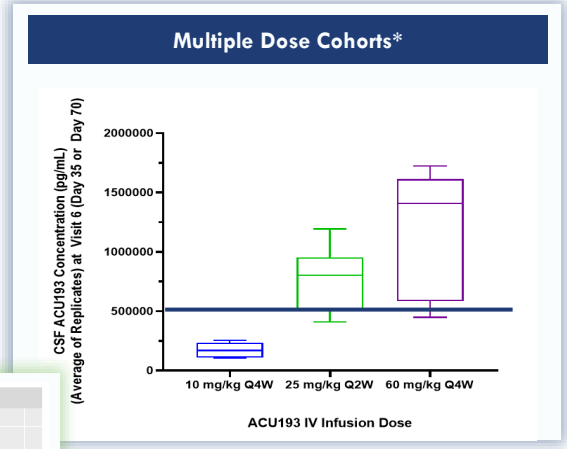
Once monthly dosing

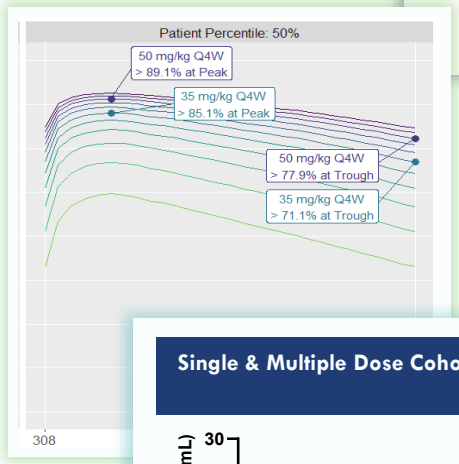
Dosing Exposure

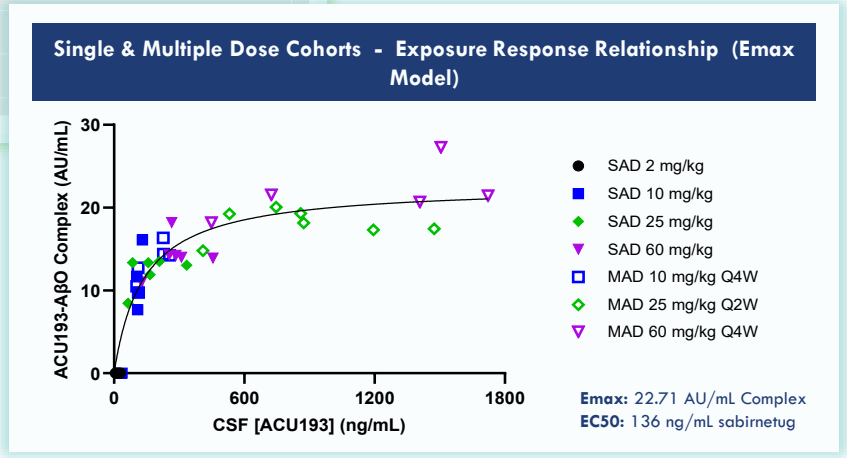
35 mg/kg and 50 mg/kg in Phase 2 IV

Target Engagement

Maximal TE of AβOs observed



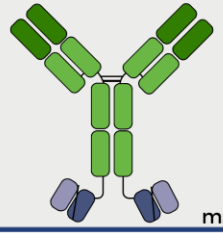
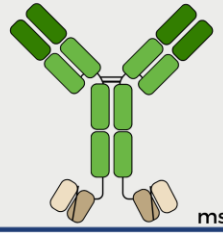
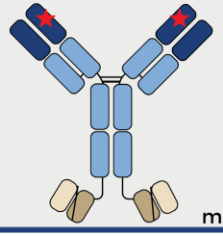
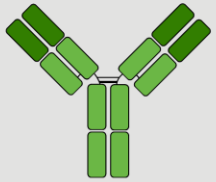




*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

Mouse Surrogate Antibodies Developed to Explore EBD™ and Target Engagement in a Mouse Model of Alzheimer's Disease

No.	mBBB.193-1	mBBB.193-2	mBBB.234-2	ACU193
Candidate Molecules 	ACU193 bivalent 	ACU193 bivalent 	ACU234 bivalent 	
Affinity to mTfR*	0.33 nM	5.34 nM	3.52 nM	0 nM
Oligomer Binding	0.60 nM	0.45 nM	2.48 nM	0.319 nM *
Monomer Binding	6.91 µM	5.87 µM	8.60 µM	3.76 µM

Cline et al., CTAD, 2025

*Cline et al., AAIC, 2025

The fusion of anti-oligomer antibodies and J-Brain Cargo (anti-TfR scFv) did not alter the ability of constructs to bind TfR or alter the preferential binding to AβOs

mTfR: murine transferrin receptor; mscFv: murine single chain variable fragment antibodies

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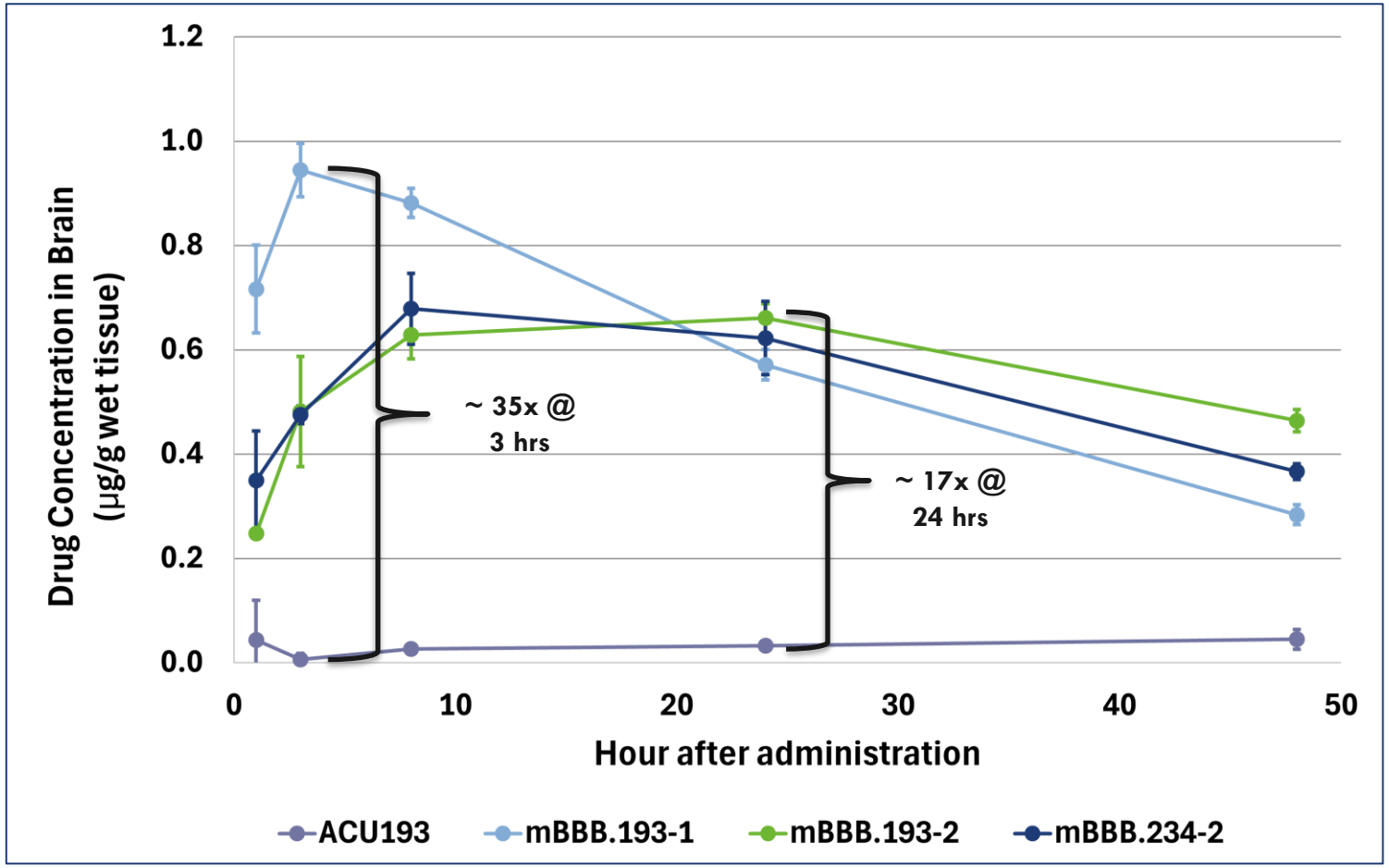
In Wild-Type Mice, All EBD™ Fusion Proteins Showed Increased Brain Exposure Compared to Sabirnetug (ACU193)



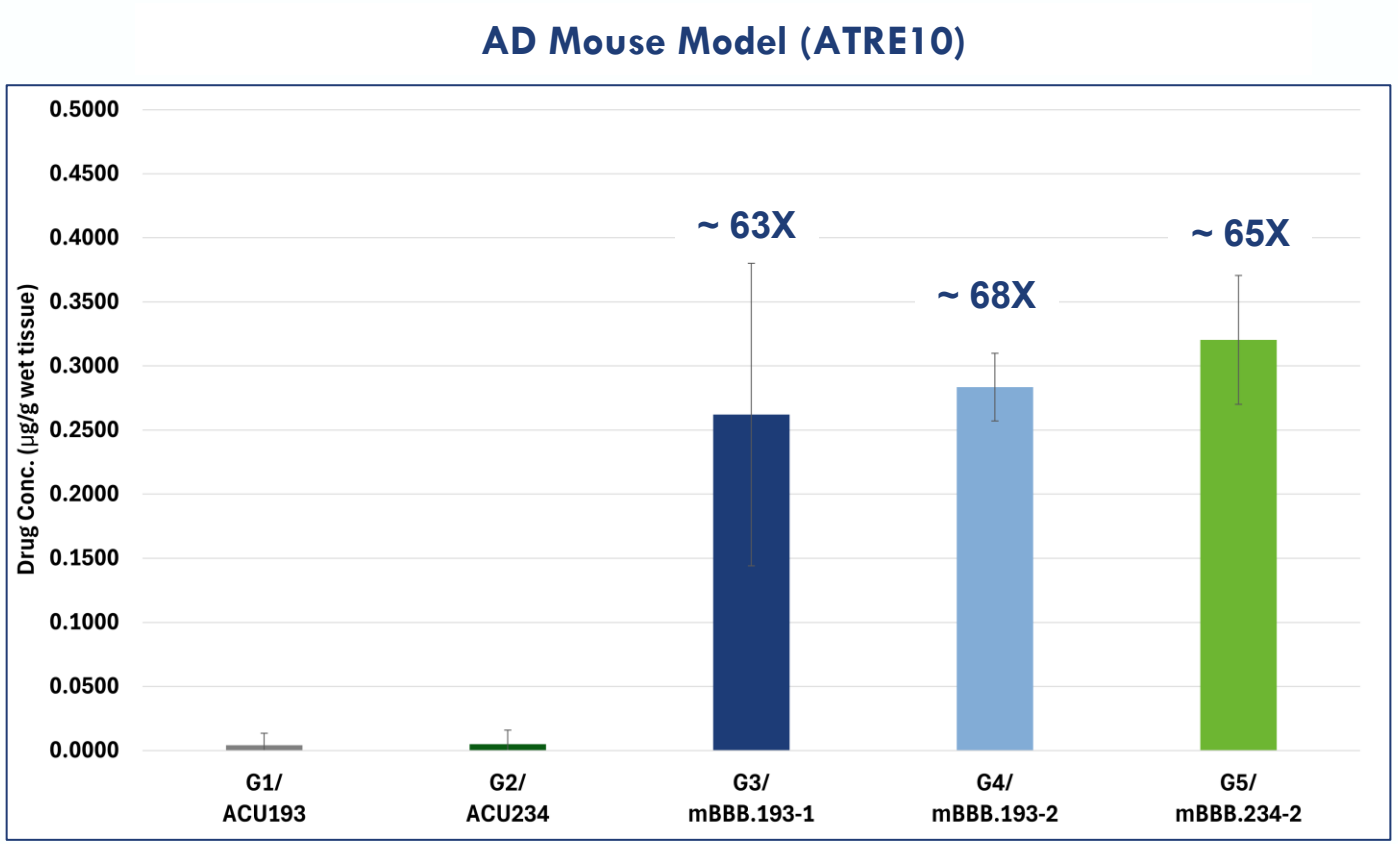
- Higher brain exposure was observed for all fusion proteins compared to ACU193:
  - mBBB.193-1 exhibited **~35-fold higher** brain exposure at 3 hours
  - mBBB.193-2 and mBBB.234-2 exhibited **~17-fold higher** brain exposure at 24 hours
- mBBB.193-2 and mBBB.234-2 showed the greatest cumulative exposure:
  - **32- to 55-fold higher** AUC than ACU193

Animals dosed IV at 2 mpk

Cline et al., CTAD, 2025

Surrogate Antibodies Show Enhanced Delivery to the AD Mouse Brain, when Compared with ACU193 and ACU234

- The brain exposure of the three fusion proteins was **63- to 68-fold higher** compared to ACU193 and ACU234
- Higher concentrations of all three fusion proteins seen in AD mouse brain compared to wild-type mice may be due to target engagement of AβOs and retention in brain



Animals dosed at IV 2 mpk

Cline et al., CTAD, 2025

Robust Data Package Supporting EBD™ Construct Selection

Inclusive of NHP Primate Data

- TfR Affinity
- Pharmacokinetics
- Aβ Oligomer Binding
- Stability & Manufacturability
- Brain Distribution
- Anemia Risk

Key Takeaways from NHP Study Results

✓ Enhanced Brain Penetration

EBD candidates achieved 14-40x higher brain levels in non-human primates compared to native antibodies 24 hours after dosing

✓ Low Anemia Risk

- Hematology data in non-human primates indicate low potential for anemia: At 24 hours after SC dosing, EBD candidates demonstrated no observed change in red blood cell count, hematocrit, hemoglobin or reticulocyte count
- No adverse events observed

✓ Subcutaneous Dosing Capability

Favorable stability profile and enhanced brain delivery support a path to subcutaneous administration with low-volume devices

Lead clinical candidate IND filing targeted for 2027

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Acumen Positioned to Deliver Potential Next-Gen Treatment for Early AD

Key Takeaways

- ✓ **Significant and growing Alzheimer's population** in need of additional treatment options
- ✓ **Synaptotoxic AβOs** appear early in Alzheimer's Disease and contribute to its pathophysiological processes; sabirnetug demonstrates **high selectivity for AβOs** in AD patients
- ✓ **Positive Phase 1 data** strengthen potential for sabirnetug to offer **next-generation** efficacy and safety
- ✓ Significant interest in ALTITUDE-AD, a **Phase 2 study** investigating sabirnetug, evidenced by **rapid enrollment**
- ✓ **Enhanced Brain Delivery™** program augments **portfolio optionality**, leveraging Acumen capabilities and assets

Next Steps

- ✓ EBD™ program pre-clinical candidate (PCC) data announced in **early 2026**
- ❑ Topline results from ALTITUDE-AD Phase 2 IV study evaluating the clinical efficacy and safety of sabirnetug in patients with MCI or mild dementia due to Alzheimer's expected in **late 2026**
- ❑ IND filing for EBD program targeted for **mid-2027**

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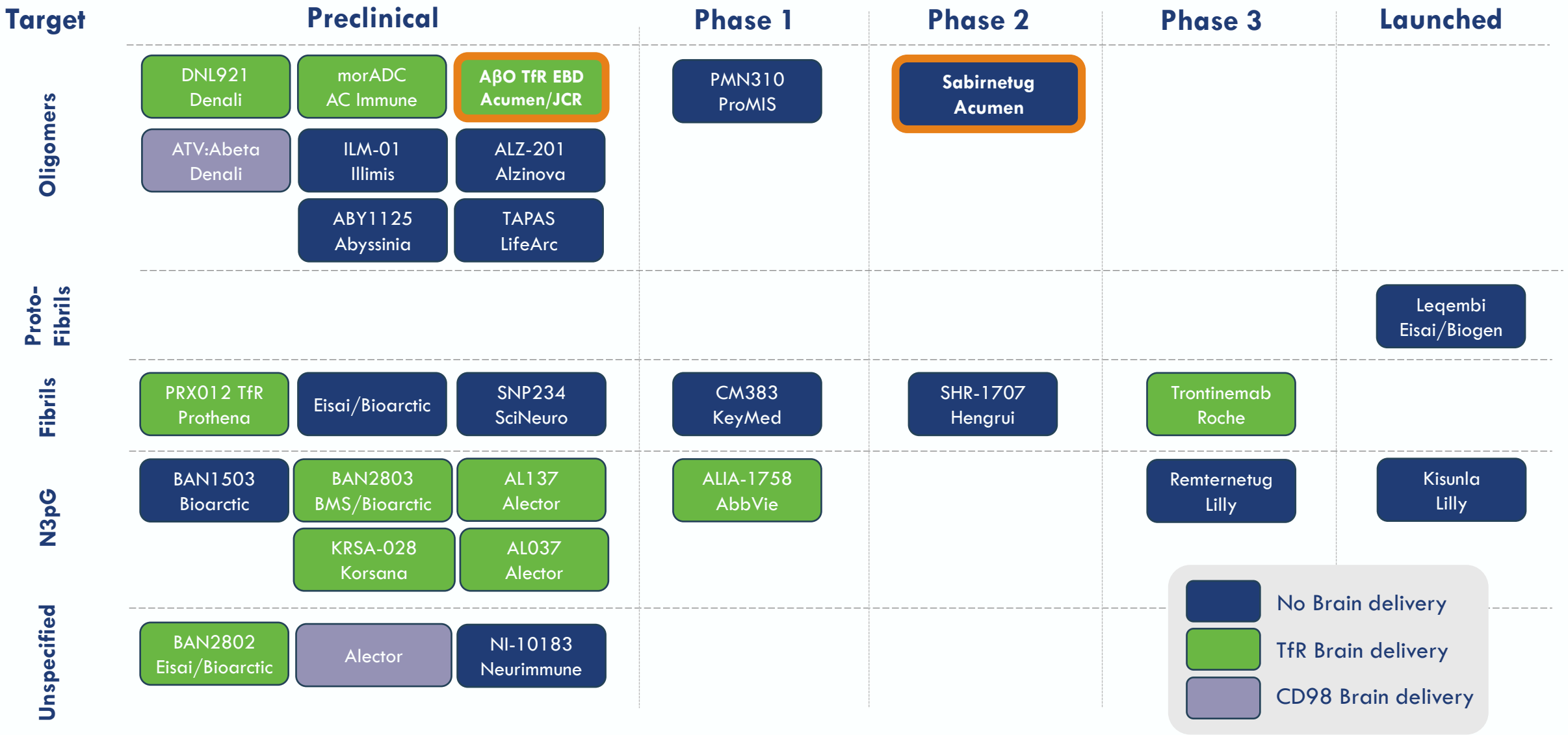
Appendix

www.acumenpharm.com

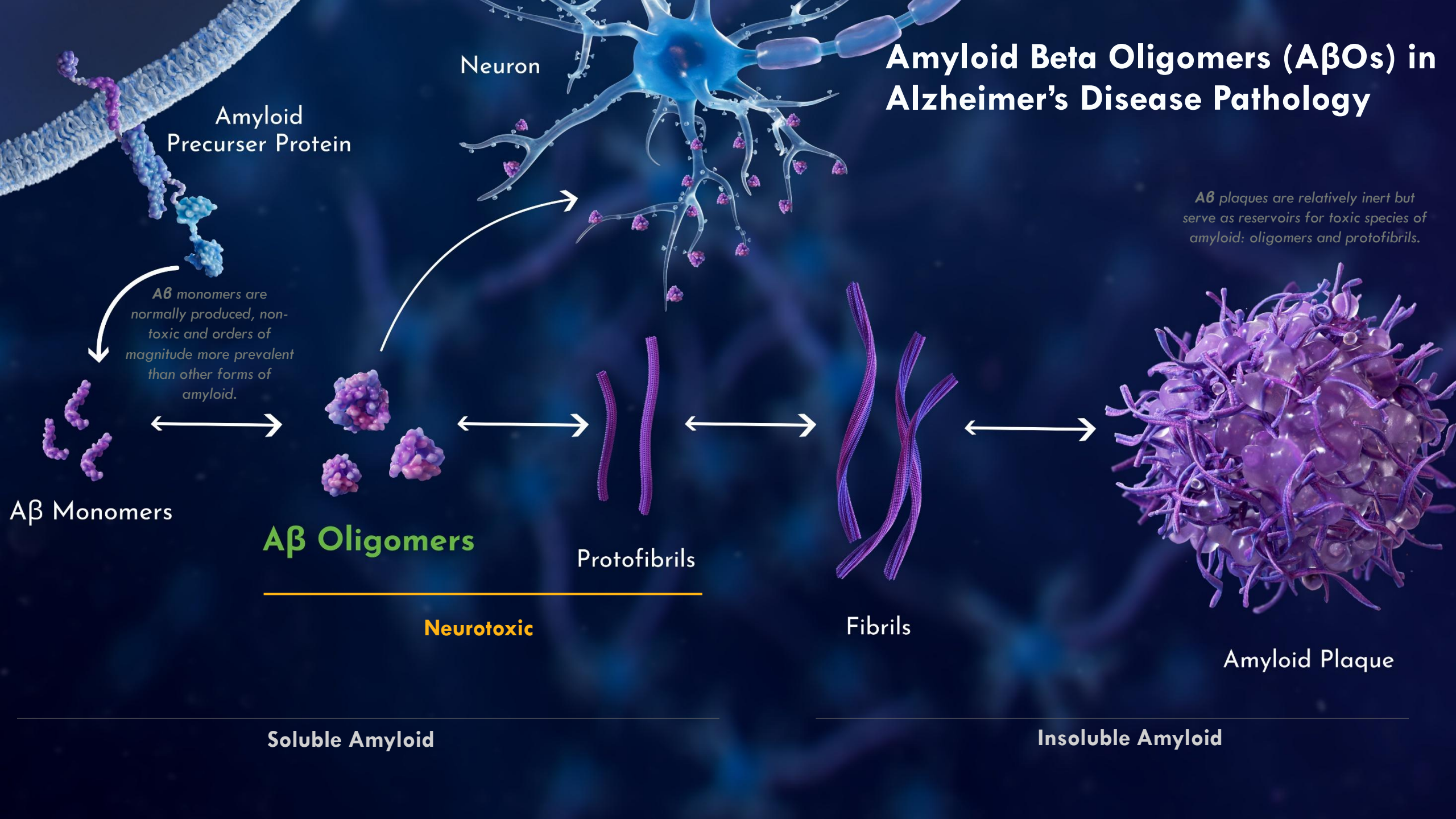
Current Anti-Aβ Antibodies in Preclinical/Clinical Development or Launched



TfR: Transferrin receptor; CD98: Cluster of differentiation 98; Adapted from DeMattos, R., CTAD 2025.

Non-clinical Sabirnetug Data

Amyloid Beta Oligomers (AβOs) in Alzheimer's Disease Pathology



Literature Selection: Soluble AβOs Contribute to Pathophysiological Processes Associated with Alzheimer's Disease

Synapse deterioration
Zhao et al, 2006
Lacor et al, 2007
Shankar et al, 2007
Wu et al, 2010
Brito-Moreira et al, 2017
Actor-Engel et al, 2021
Sackmann & Hallbeck, 2020
Limegrover et al, 2021

Receptor Redistribution
Snyder et al, 2005
Roselli et al, 2005
Lacor et al, 2007
Zhao et al, 2008

Impact on astrocytes/microglia
Hu et al, 1998
Jimenez et al, 2008
Sondag et al, 2009
Tomiyama et al, 2010

Selective neuron death
Lambert et al, 1998
Kim et al, 2003
Florent et al, 2006
Ryan et al, 2009
Lee et al, 2017
Komura, 2019

Oxidative stress
Longo et al, 2000
Sponne et al, 2003
Tabner et al, 2005
De Felice et al, 2007

ER stress
Resende et al, 2008
Nishitsuji et al, 2009

Plasticity dysfunction
Lambert et al, 1998
Walsh et al, 2002
Wang et al, 2002
Townsend et al, 2006
Yasumoto et al, 2019

Aberrant Tau phosphorylation
De Felice et al, 2008
Ma et al, 2009
Tomiyama et al, 2010
Zempel et al, 2010
Bloom, 2014
Forny-Germano et al, 2020
Wakeman et al, 2022
Darricau et al, 2023

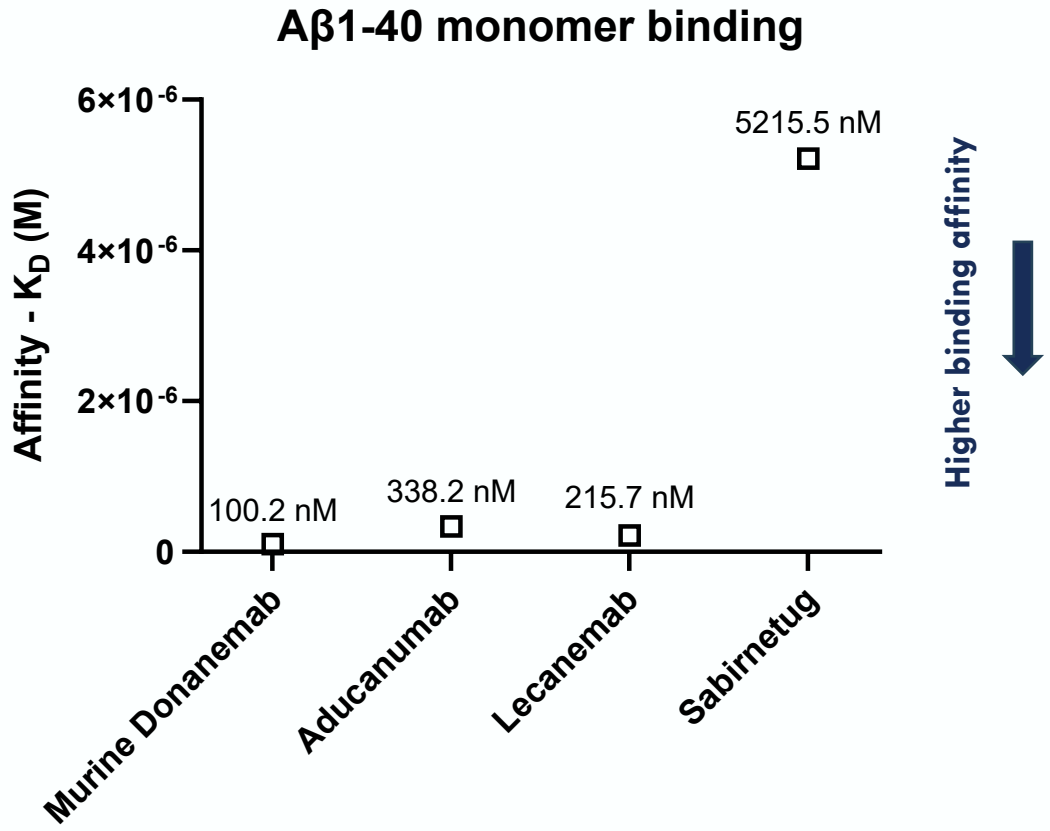
Disrupted Ca^{2+} homeostasis
Demuro et al, 2005
De Felice et al, 2007
Alberdi et al, 2010
Wang et al, 2018

Insulin resistance
Zhao et al, 2008
Zhao et al, 2009
Ma et al, 2009
De Felice et al, 2009

ChAT loss
Heinitz et al, 2006
Nunes-Tavares et al, 2012

Inhibition of axonal transport
Pigino et al, 2009
Poon et al, 2009
Decker et al, 2010

Sabirnetug Demonstrates Low Affinity for Monomeric Aβ



Internal data, 2024

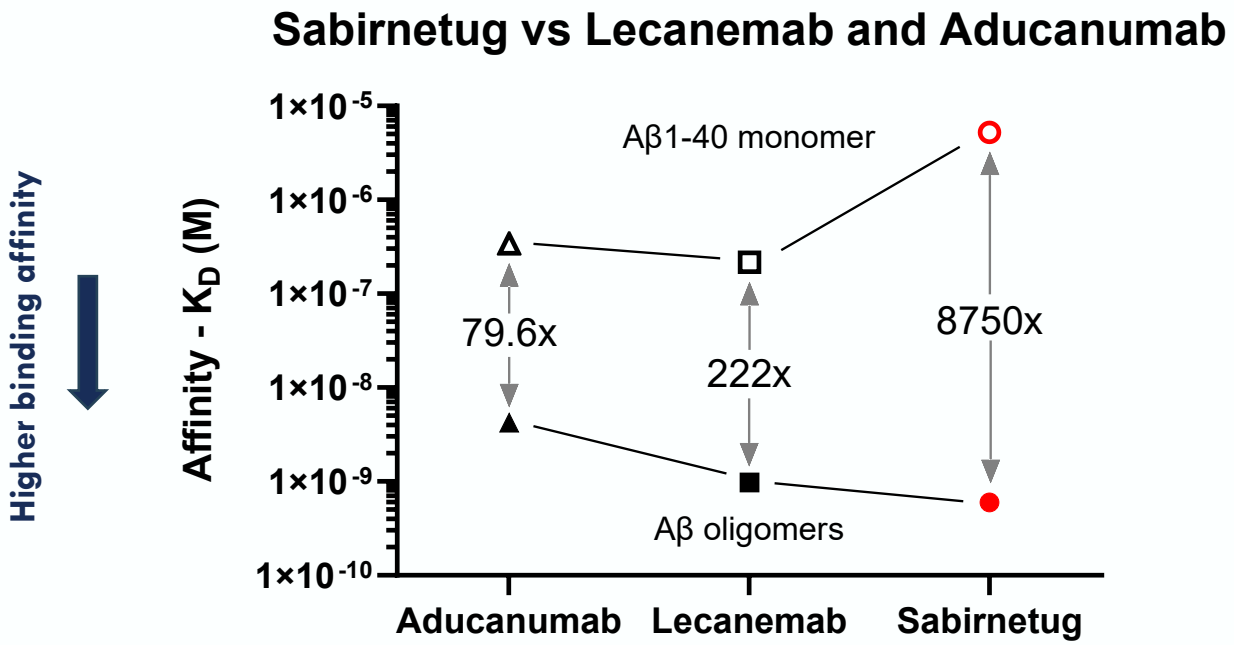
Note: Calculated K_D value for sabirnetug was above the highest analyzed concentration.

- Aβ monomers are ~7000x 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 Versus Aβ Monomers

Relative Selectivity for AβO versus Monomeric Aβ Measured with SPR

Sabirnetug is more selective for AβOs than aducanumab or lecanemab

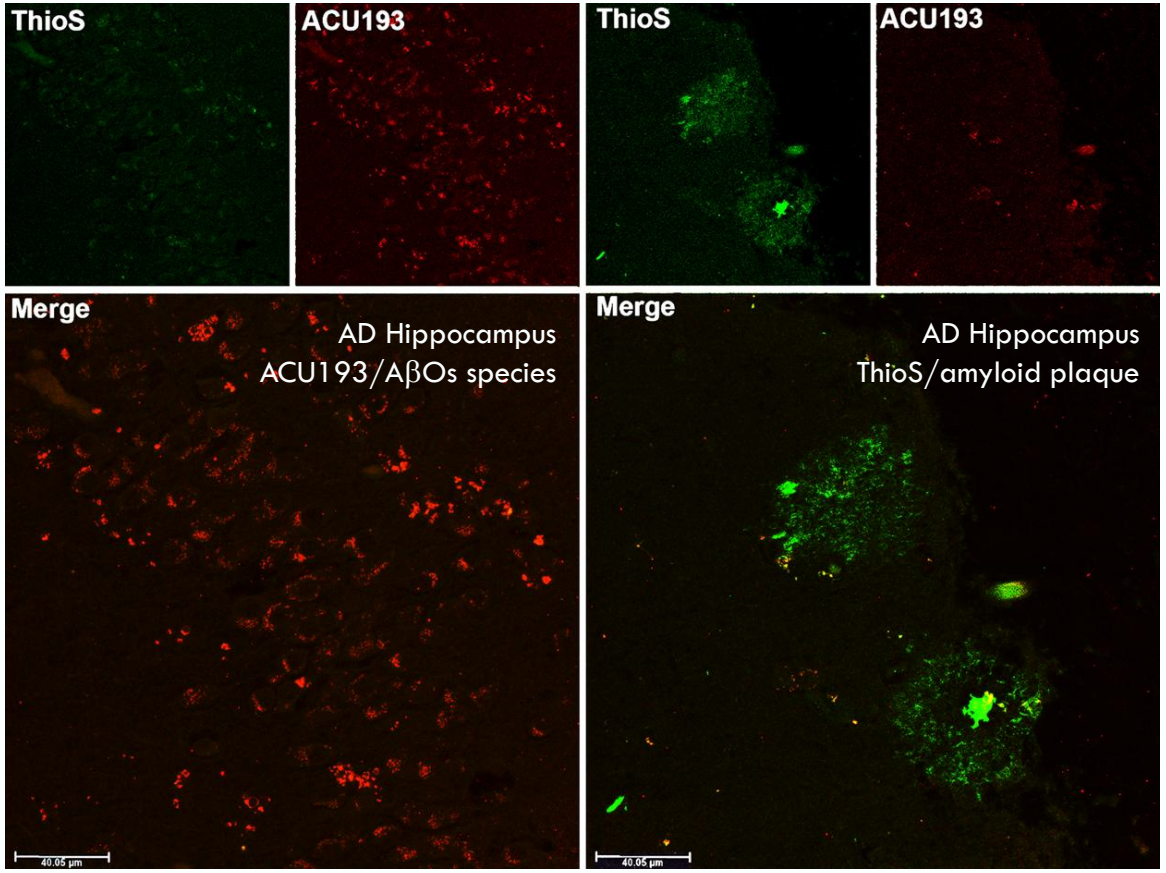


Internal data, 2024

Note: Murine donanemab shows very low signals for Aβ oligomer binding compared to all other antibodies tested; therefore, it was not included in this comparison.

Sabirnetug is Selective for AβOs Versus Aβ Plaques

Sabirnetug Binds AβOs Not Associated with Plaques in Human AD Brain Slices

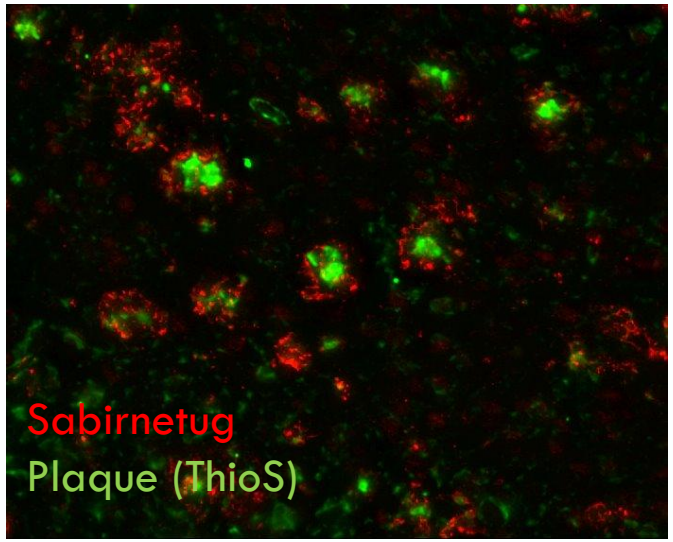


Sabirnetug
Thioflavin S

Adapted from Krafft et al. 2022

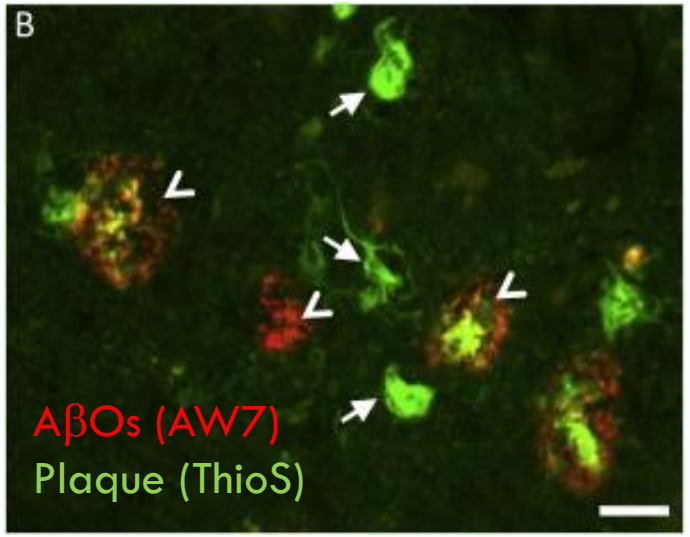
Amyloid Plaques are Surrounded by a Halo of AβOs

Transgenic mouse model of AD



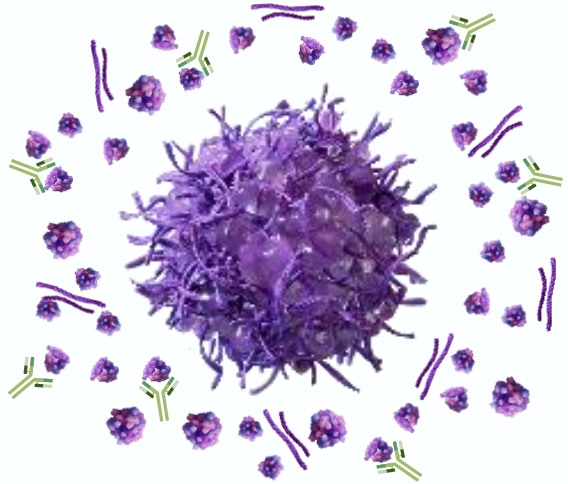
Lab of William Klein, NU, 2017

AD human brain tissue



Spires-Jones et al. 2014

AβOs can form halos of soluble aggregates around dense core of amyloid plaques, to which sabirnetug also binds



Sabirnetug binding to soluble AβOs

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Sabirnetug: Extensive Data Package Supporting Development

SELECTIVITY

- Nanomolar affinity for AβOs, >500-fold greater selectivity for AβOs over Aβ monomer, with limited or no discernable binding to vascular amyloid or dense core amyloid plaques
- Binds broad range of endogenous Aβ, from dimers to high molecular weight AβOs

PHARMACOLOGY

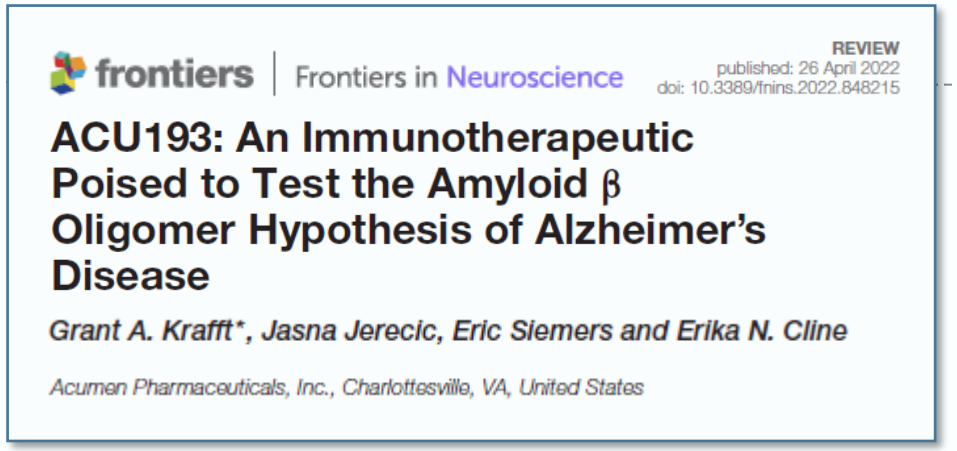
- Dose-dependent effects in multiple in vitro neuroprotection assays
- Positive memory and behavioral effects in multiple in vivo transgenic mouse models for AD

PK/PD

- Brain penetration and biodistribution demonstrated in multiple species
- Performs like other peripherally administered CNS mAbs

SAFETY

- IgG2 subclass lacks inflammatory effector function signaling (FcγR binding)
- Non-clinical microhemorrhage studies show no increased risk of microhemorrhage
- GLP studies demonstrated acceptable safety package supporting clinical dosing plans including Phase 2


frontiers | Frontiers in Neuroscience

REVIEW
published: 26 April 2022
doi: 10.3389/fnins.2022.848215

ACU193: An Immunotherapeutic Poised to Test the Amyloid β Oligomer Hypothesis of Alzheimer's Disease

Grant A. Krafft, Jasna Jerecic, Eric Siemers and Erika N. Cline*

Acumen Pharmaceuticals, Inc., Charlottesville, VA, United States

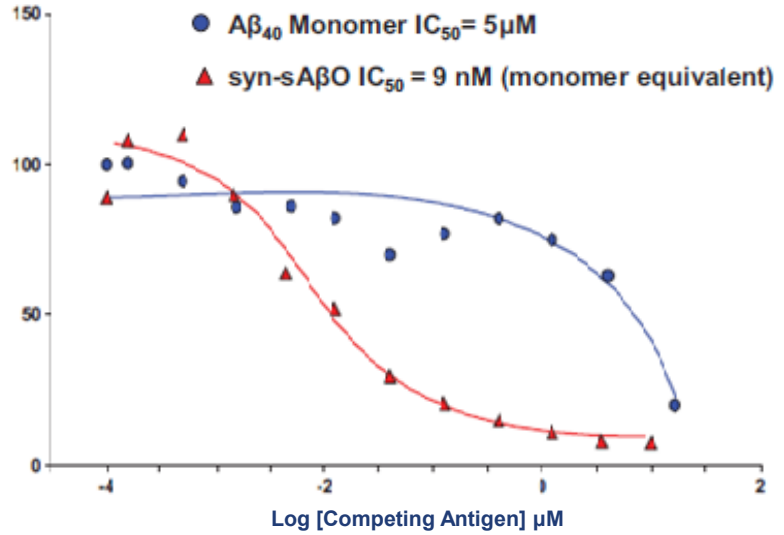
Sabirnetug is a promising immunotherapy for early AD expected to provide meaningful cognitive and functional benefits, slow disease progression, and offer an attractive safety profile

ACUMEN

Sabirnetug is the First mAb Developed to Selectively Target AβOs

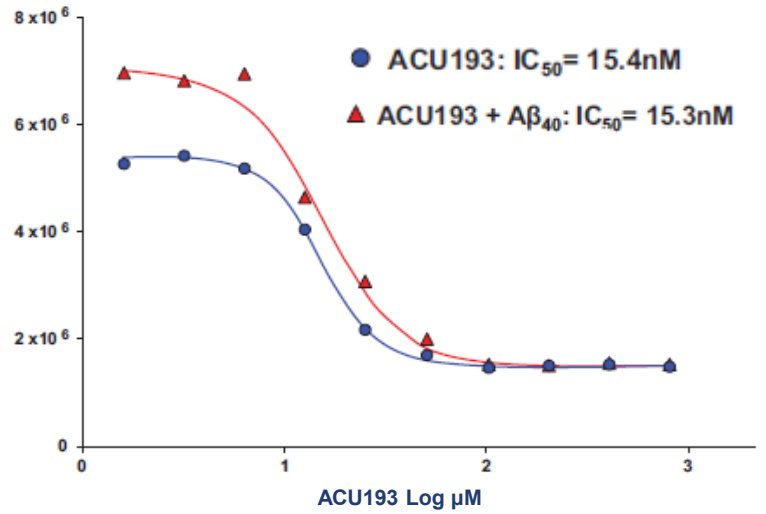
Highly selective for Aβ oligomers versus Aβ monomers

Sabirnetug Selectivity



Binding of sabirnetug to AβOs >500x binding to Aβ monomer

Sabirnetug Selectivity in presence of 5μM monomeric Aβ

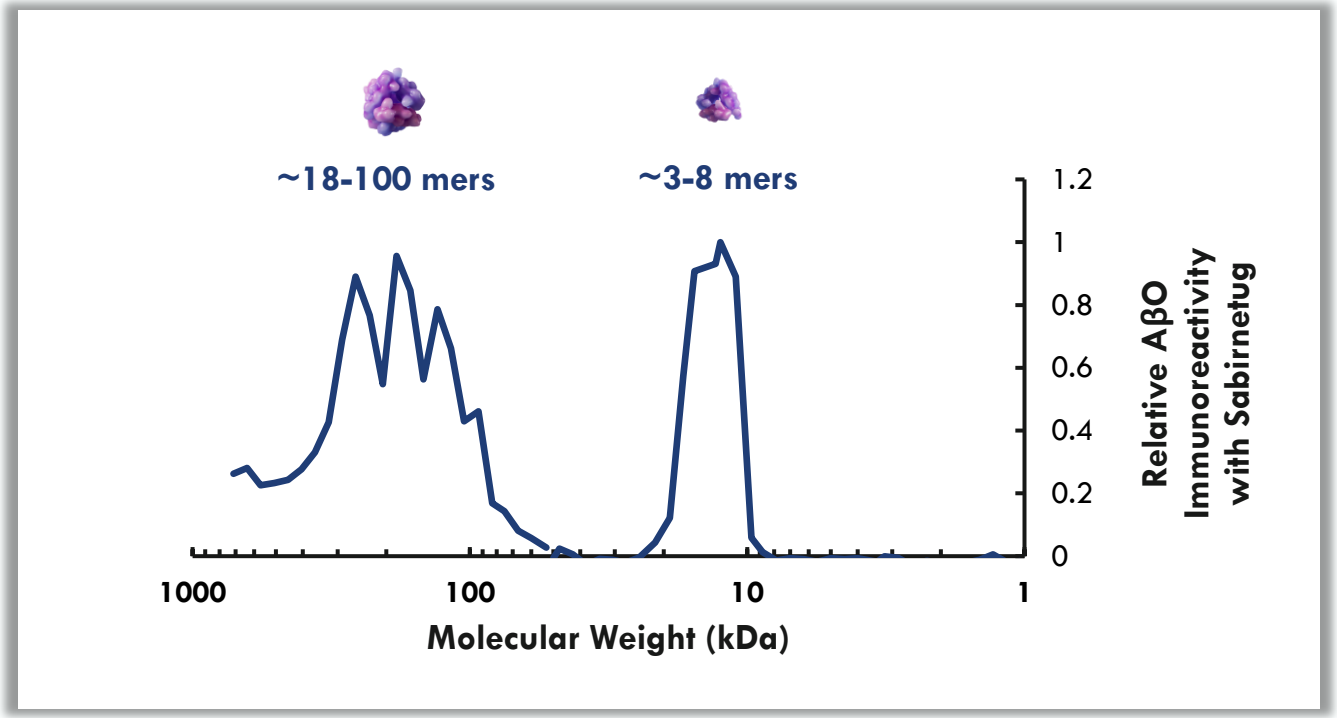


Even in the presence of a large excess of Aβ monomer, binding of sabirnetug to AβOs is unchanged

Sabirnetug selective for binding to AβOs is preserved even in the presence of a large excess of Aβ monomers – such as what is present in the brain, thus limiting 'target distraction'

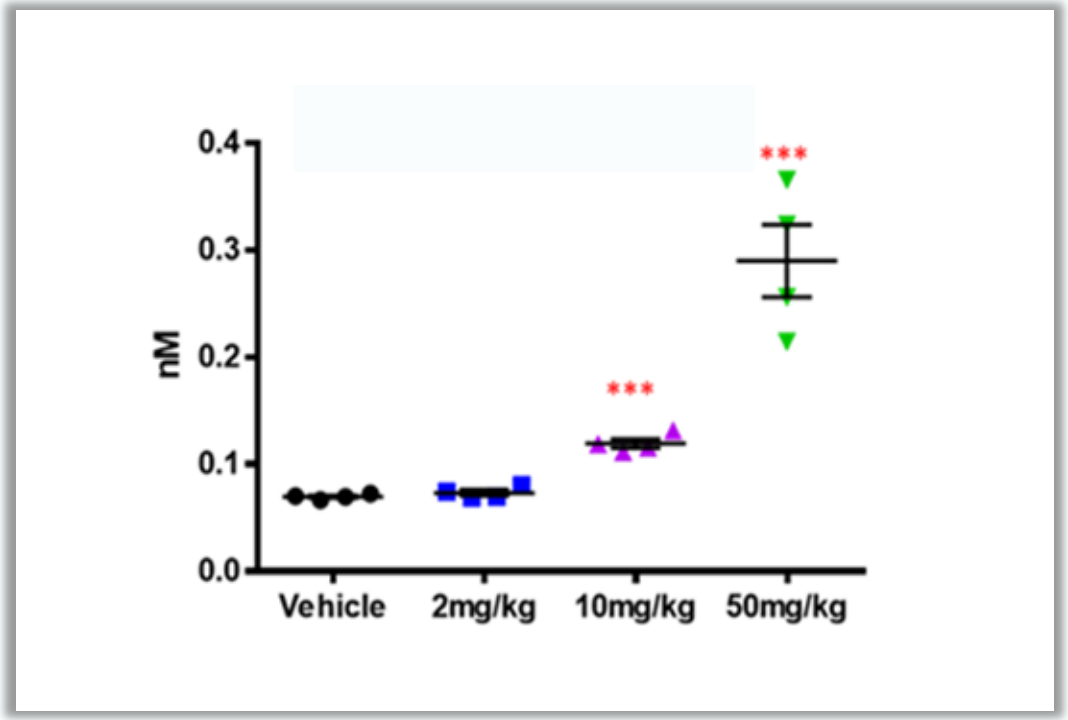
Sabirnetug Recognizes a Wide Range of Oligomeric Species of Aβ

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

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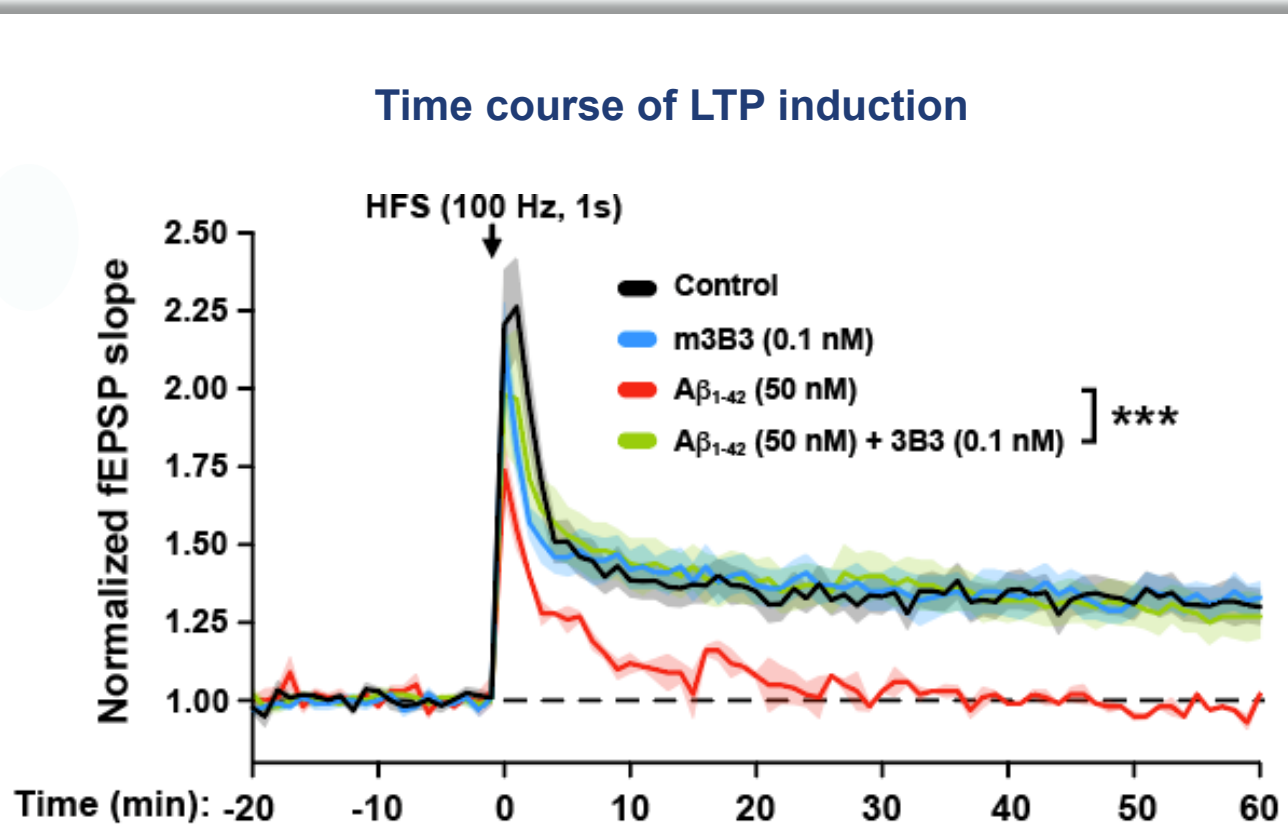
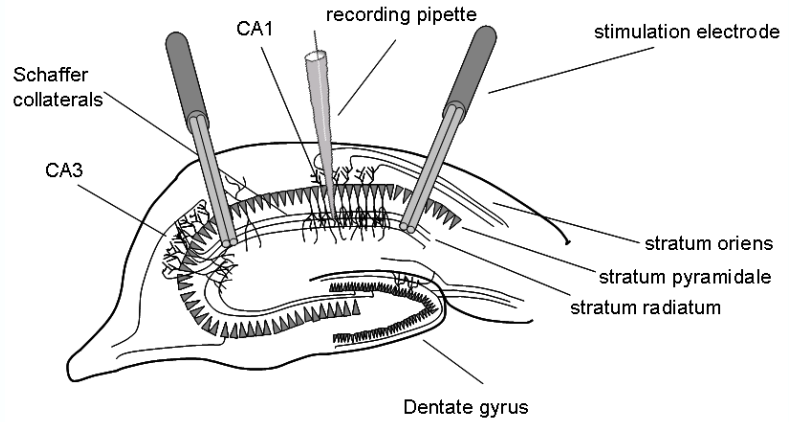
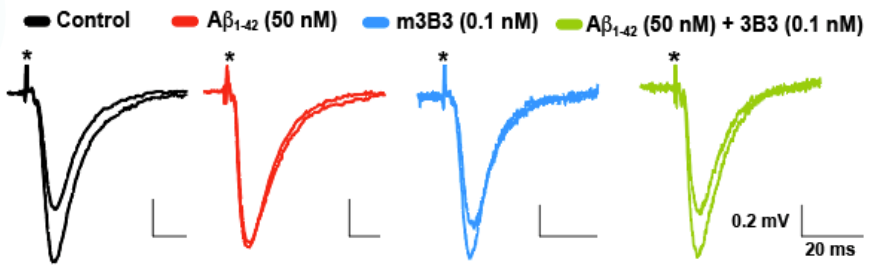
Functional Consequences of AβO Clearance: Restoring Plasticity

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

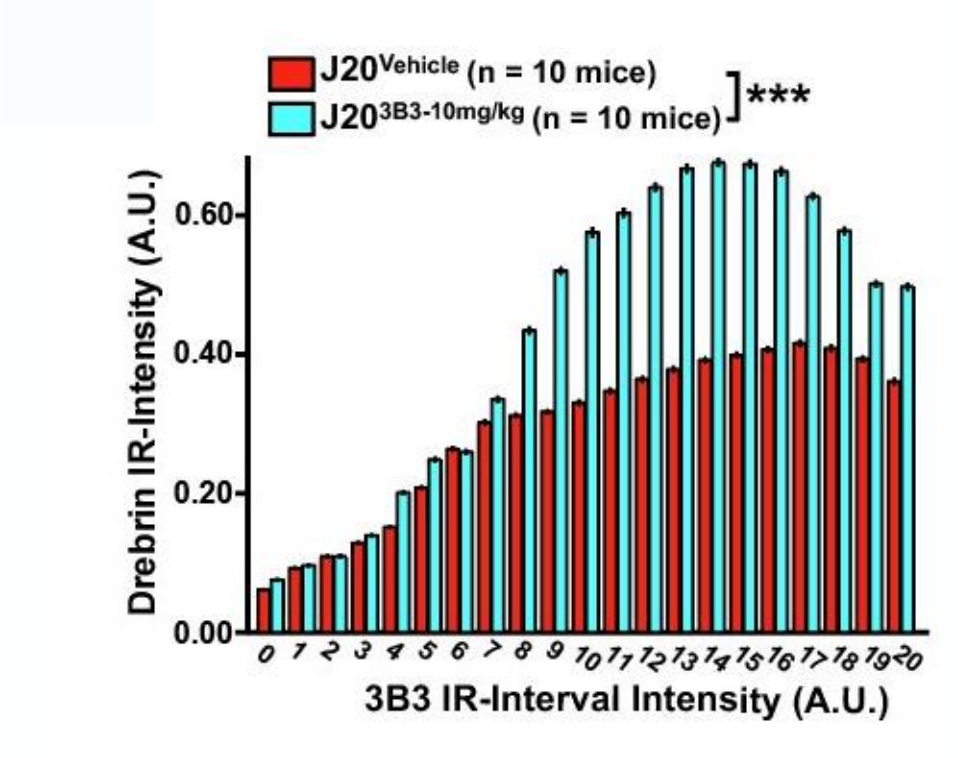




From manuscript in prep; data collected by lab of Gerhard Rammes, University of Regensburg, Max-Planck Institute of Psychiatry, Germany

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

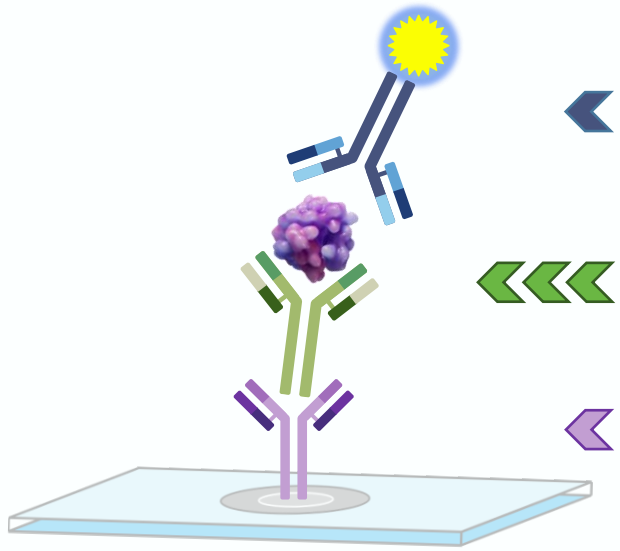
- ACU3B3 (murine oligomer selective antibody) treatment ***prior*** to plaque pathology leads to reduced amyloid deposition in J20 Tg model (5-7 months)
- Treatment effects are less prominent in aged animals (16-23 months)
- Evidence of synaptic recovery in advanced stages of pathology in contrast to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

Phase 1 INTERCEPT-AD

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

MSD S-Plex (Turbo) Immunoassay



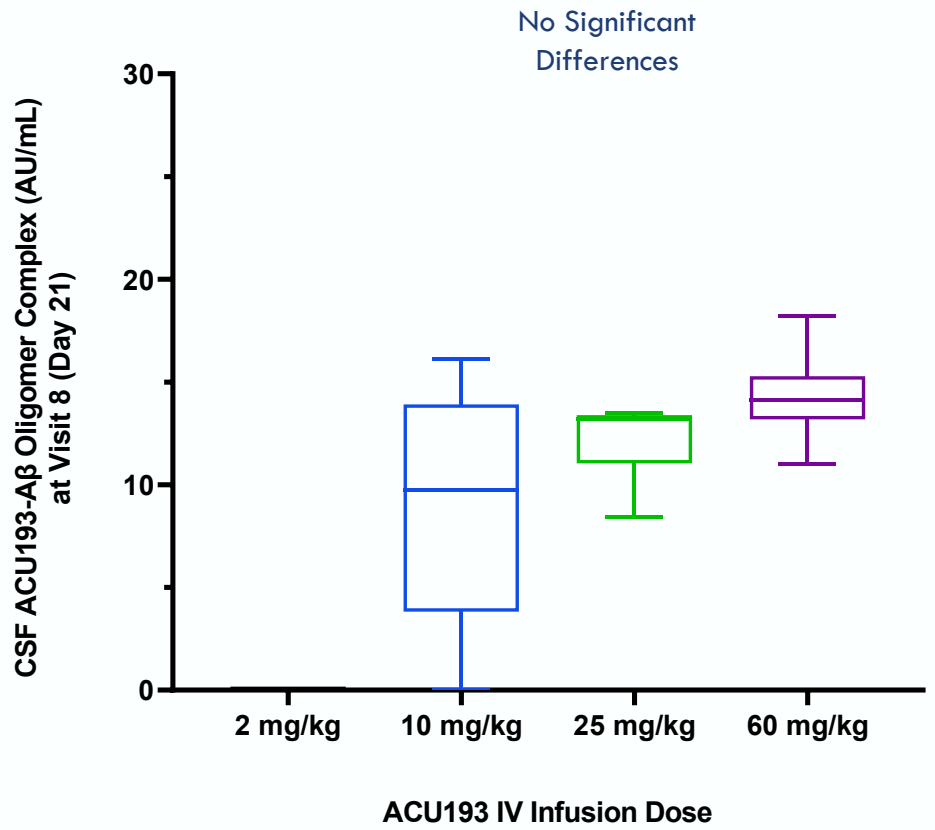
AβO selective detection
(anti-AβO mAb)

Only Sabirnetug-AβO complex is measurable

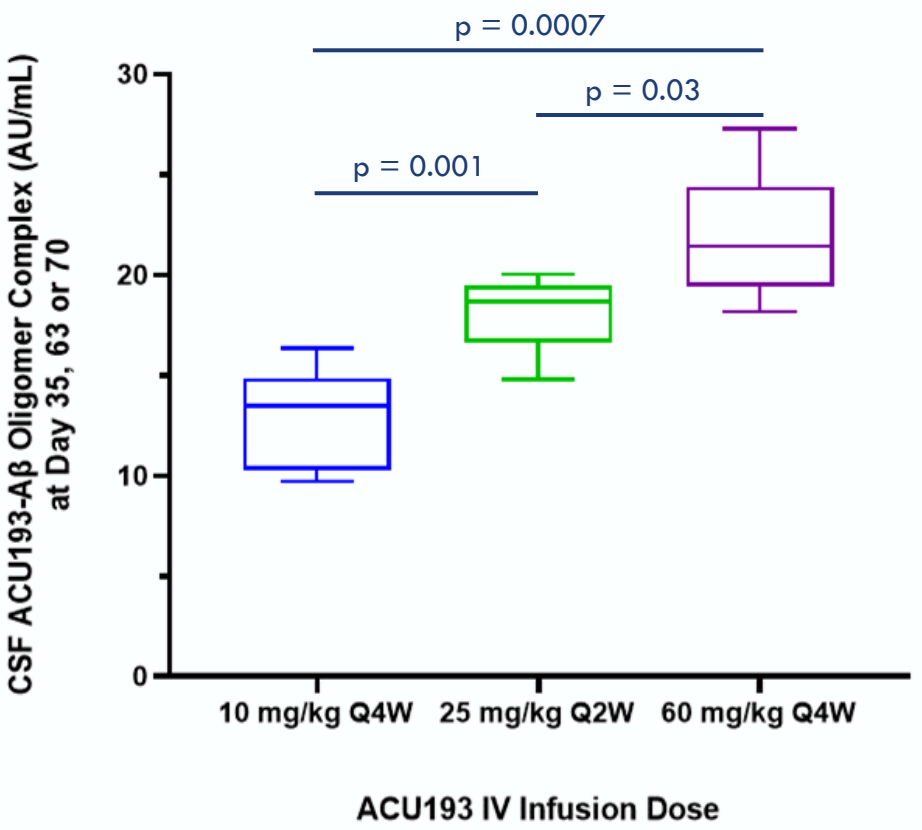
Sabirnetug drug specific capture
(anti-sabirnetug idiotype mAb)

Target Engagement of Sabirnetug with AβOs is Dose Proportional

Single Dose Cohorts



Multiple Dose Cohorts*

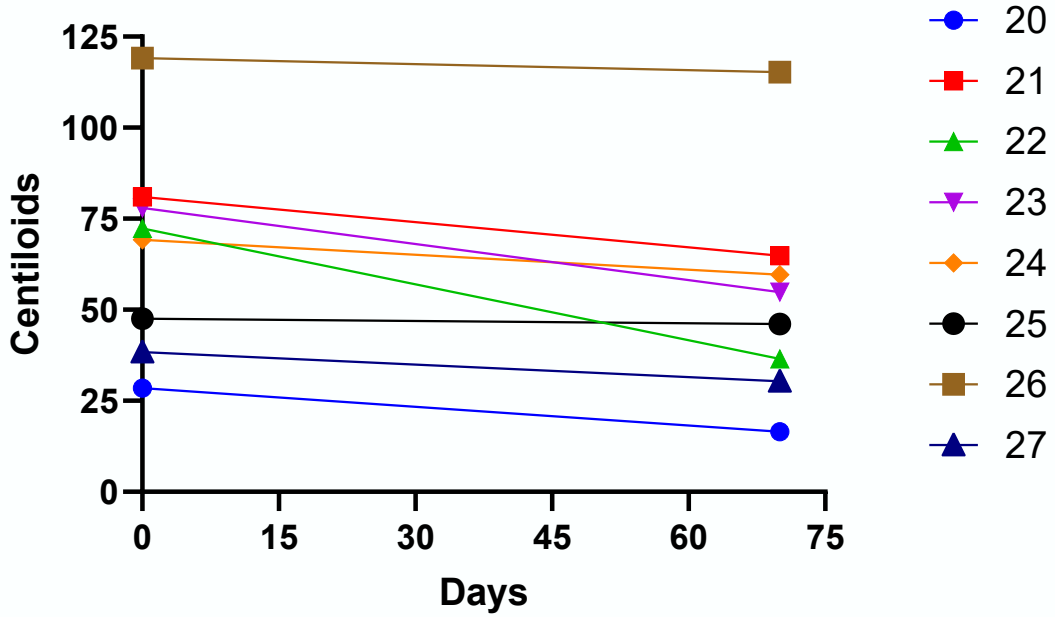


*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

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

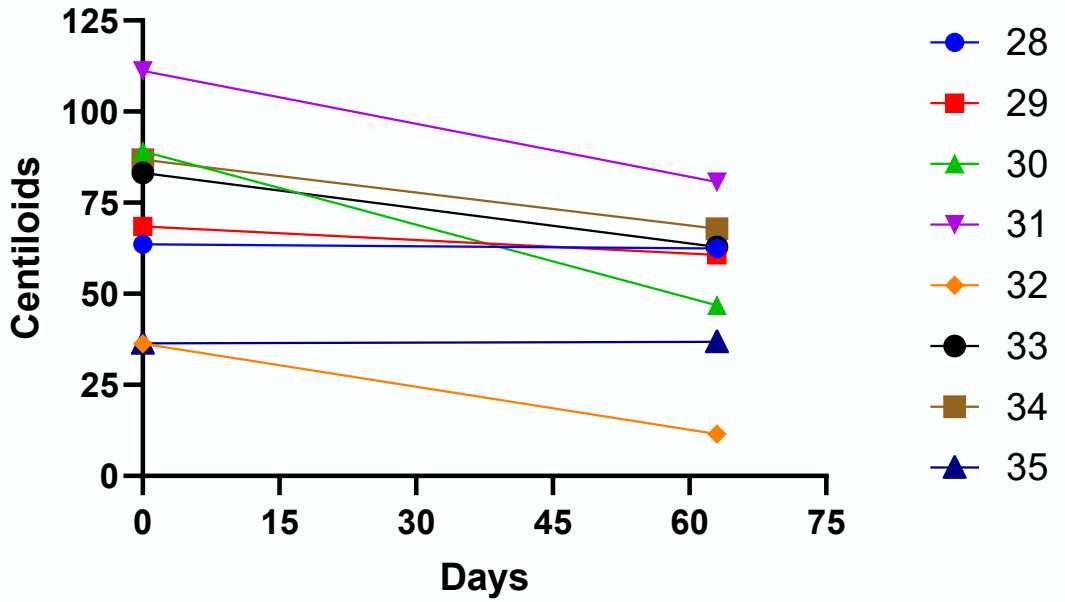
25 mg/kg Q2W MAD



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

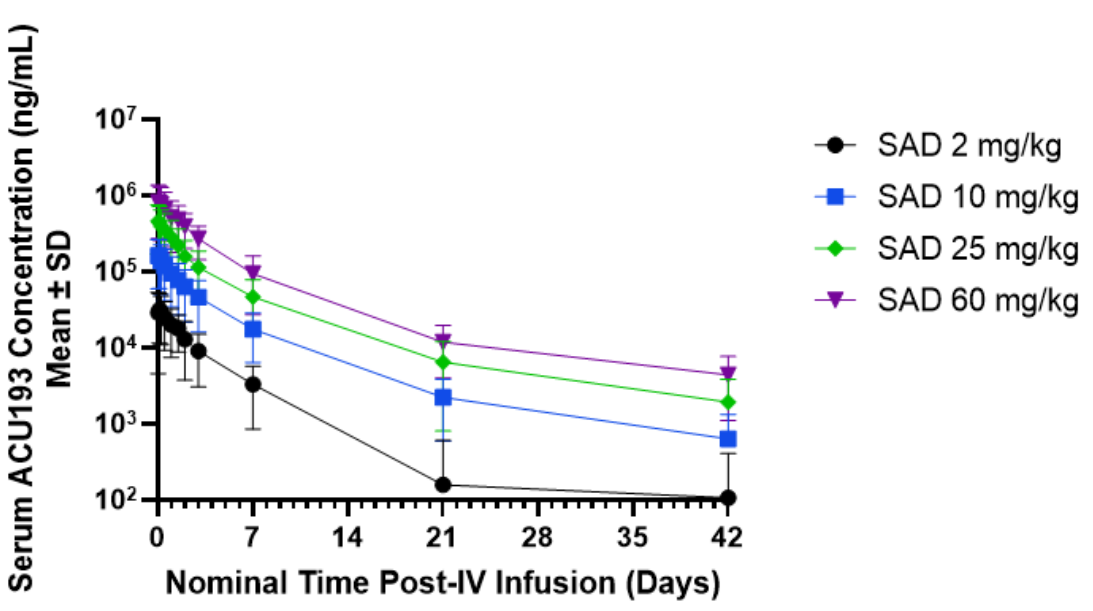
Δ (absolute value, centiloids)	18.1
Δ (%, centiloids)	25.6%

Plaque load based on florbetapir PET

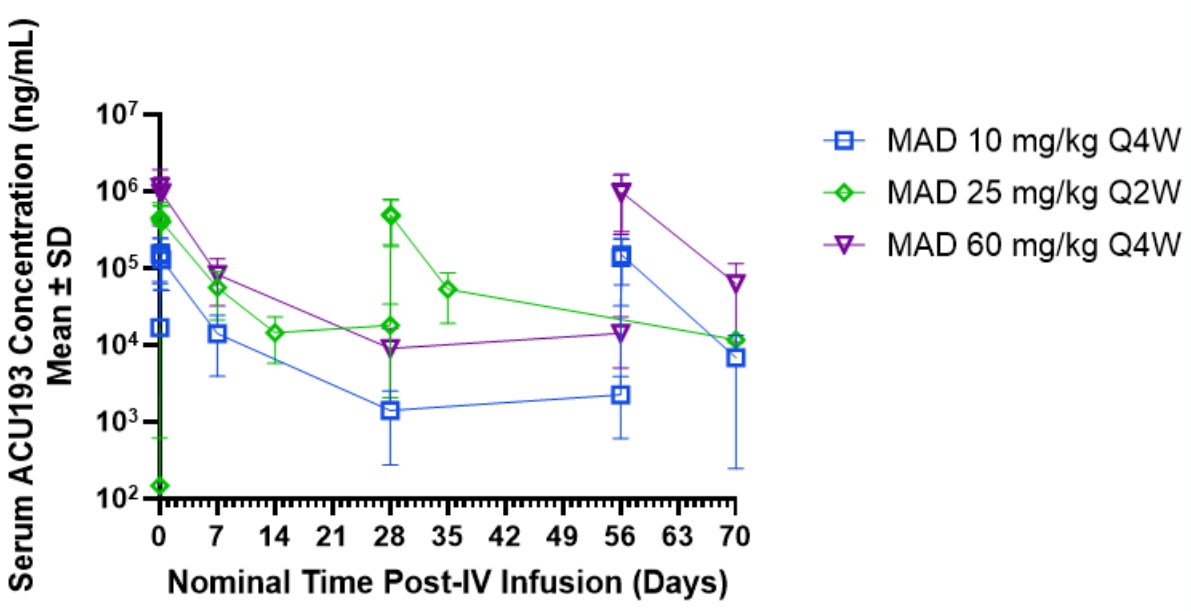
E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

Sabirnetug Serum Exposure is Dose Proportional Without Accumulation

Single Dose Cohorts



Multiple Dose Cohorts

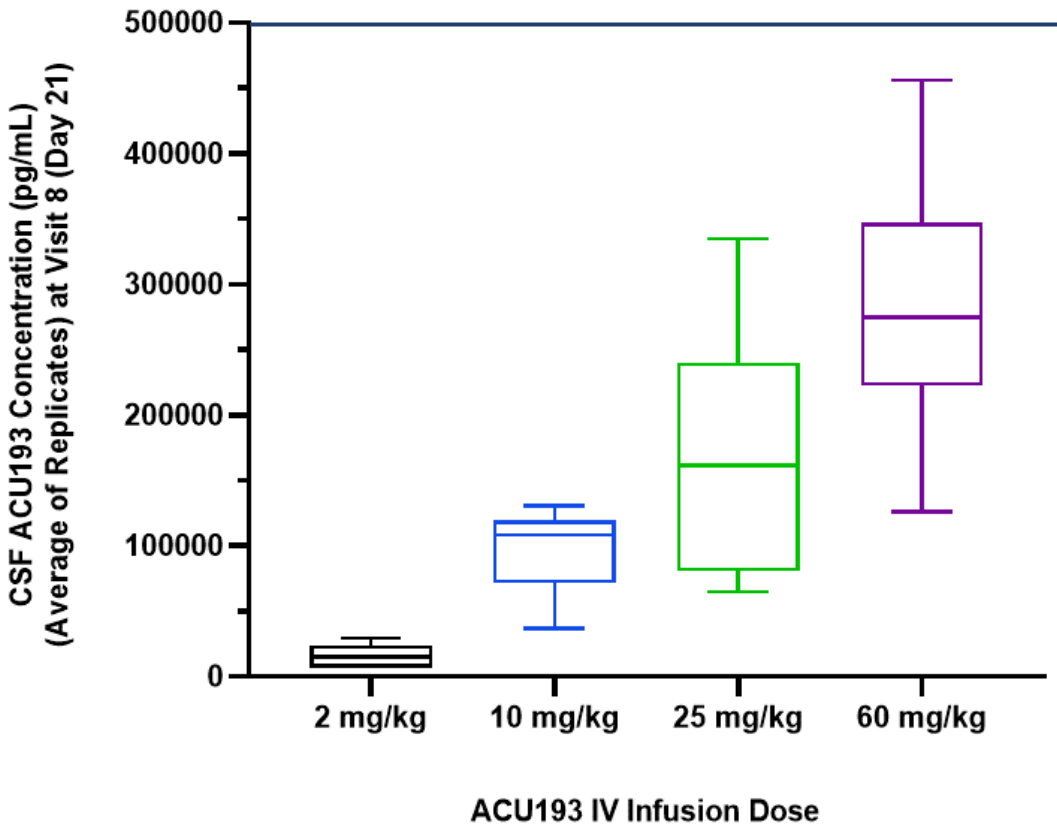


Estimated serum terminal $T_{1/2}$ of 5-7 days

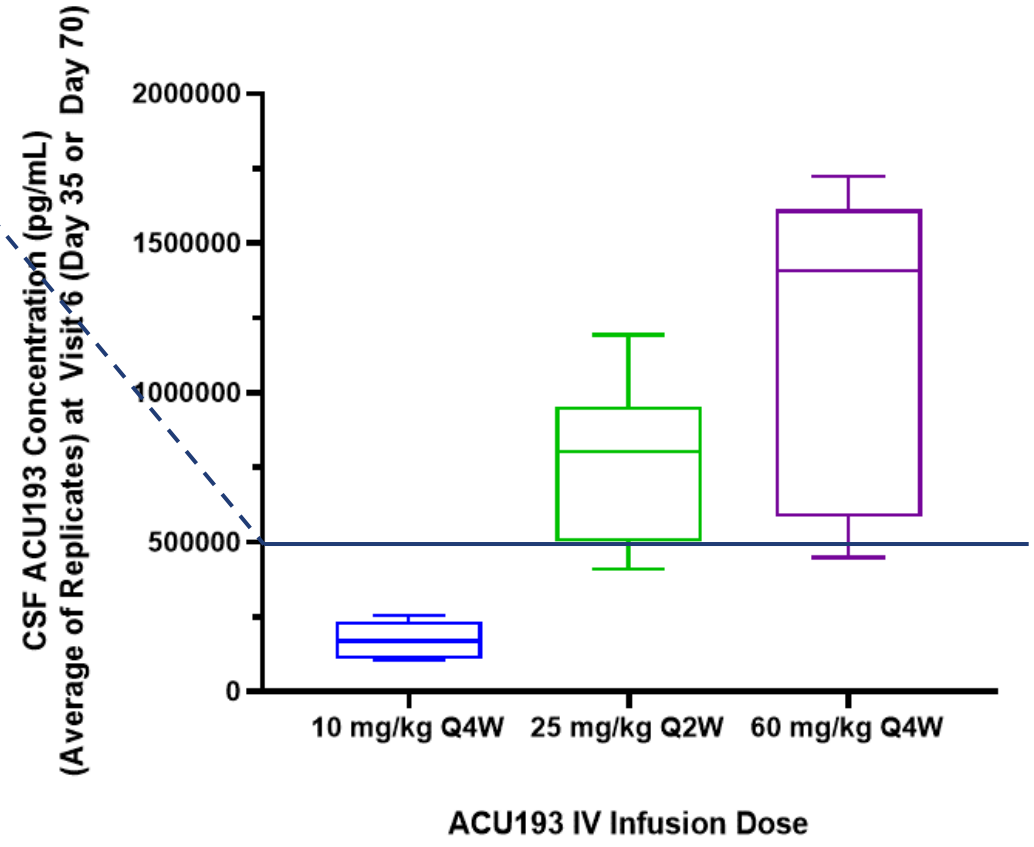
E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

Sabirnetug CSF Exposure is Dose and Dose-Regimen Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



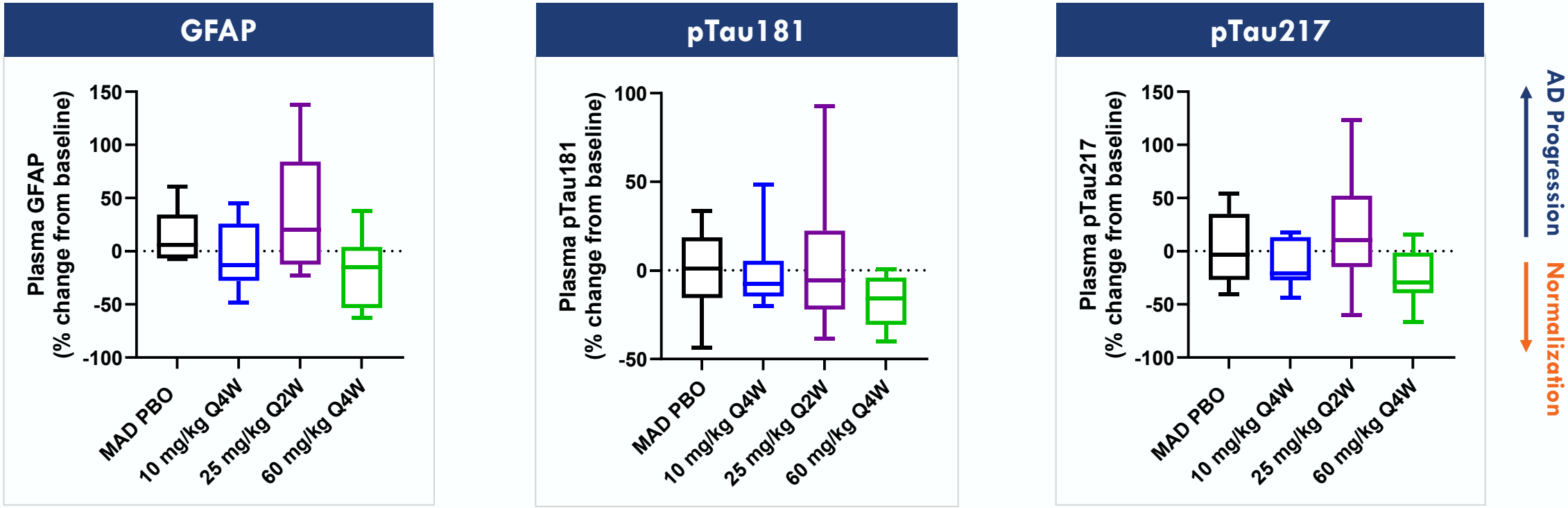
*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

ACUMEN

Trend Toward Normalizing Plasma Biomarkers with 10 mg/kg and 60 mg/kg Q4W

1-6 wk post-dosing



- Plasma measurements of glial fibrillary acidic protein (GFAP), pTau181, and pTau217 in 10 mg/kg Q4W & 60 mg/kg Q4W groups were lower than placebo
- More impact to fluid biomarkers was observed with longer dosing duration
  - The 25 mg/kg Q2W cohort differed in dose and sample timing, with drug on board for less time than the 10 mg/kg & 60 mg/kg Q4W cohorts

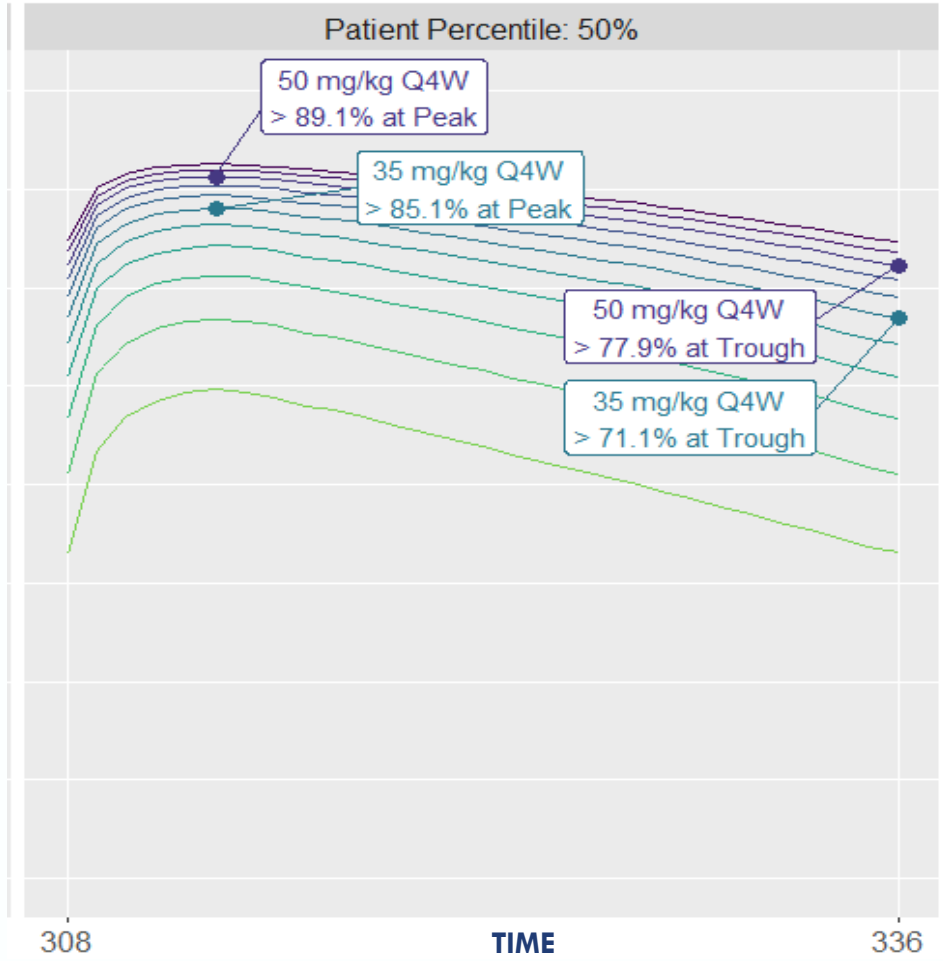
E. Cline, et al, Biofluid biomarker changes following treatment with sabirnetug (ACU193) in INTERCEPT-AD, a phase 1 trial in early Alzheimer's disease. JPAD 2025.

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

Phase 2 ALTITUDE-AD

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)

upper dose: 50 mg/kg Q4W

lower dose: 35 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

CERTARA

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