Investor Day

September 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® (Enhanced Brain Delivery) technology, including the ability to make an IND filing in mid-2027. 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.

Speakers & Agenda

The Potential of AβO-Directed Therapies

DANIEL O'CONNELL
Chief Executive Officer

6 min

Sabirnetug's MOA and Potential Differentiation from Other DMTs

JAMES DOHERTY, PHD
President & Chief Development Officer

22 min

ALTITUDE-AD: A Well-Powered Phase 2 Study Designed to Test the AβO Hypothesis

ERIC SIEMERS, MD
Chief Medical Officer

20 min

Enhanced Brain Delivery: A Promising Next-Generation Pipeline Addition

PAUL SHUGHRUE, PHD
VP, Program Lead and Head of Research

18 min

Q&A

The Potential of AβO-Directed Therapies

Daniel O'Connell
Chief Executive Officer

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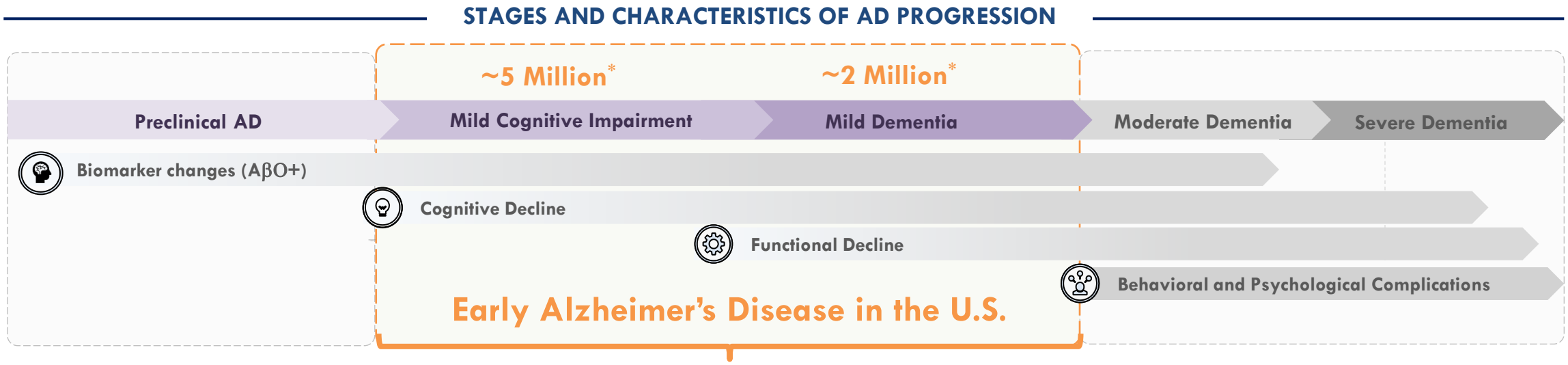
Early Alzheimer's Disease (AD) Patient Population Represents Significant and Growing Market; Preclinical AD a Potential Future Addressable Population



An estimated

7.2 million*

Americans age 65 and older live with Alzheimer's dementia today

~92% growth

This number is projected to grow to

13.8 million*

by 2060

*Alzheimer's Association

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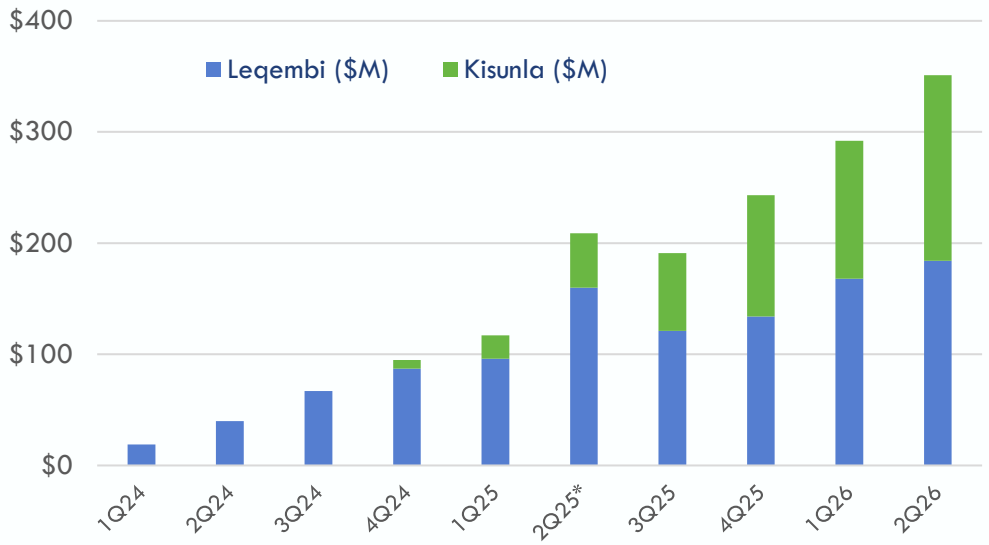
Global Sales of Approved anti-Aβ mAbs Growing and Poised to Accelerate

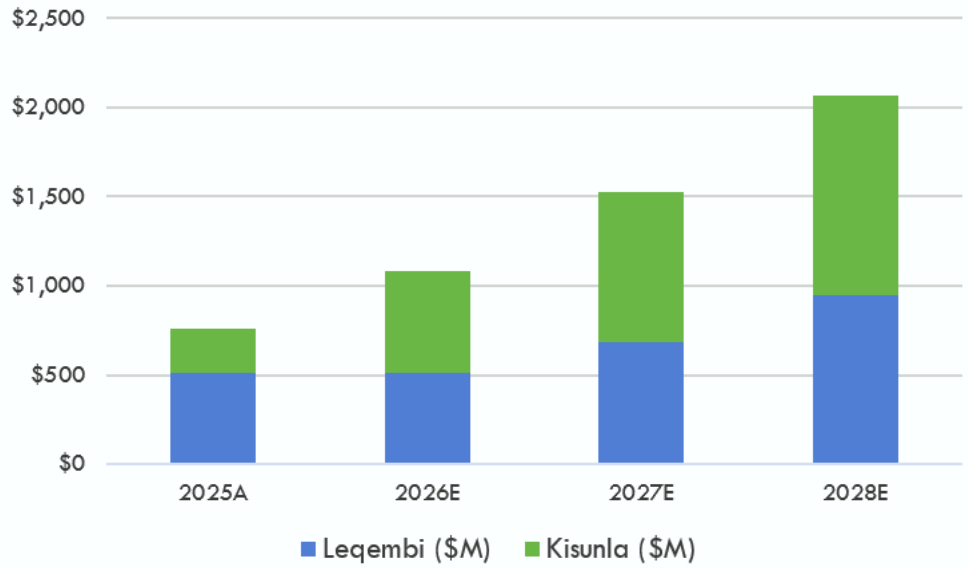
Amyloid beta market surpassing $1B run rate in spite of infrastructure challenges, efficacy & ARIA concerns

Quarterly Global Sales of Approved anti-Aβ mAbs



Source: Company quarterly filings (Biogen, Eli Lilly)

Annual Consensus Estimates of Approved anti-Aβ mAbs



Source: IR Insight sell-side consensus estimates

Global annual sales expected to reach:
$2B+ in 2028 and $3B-$4B by 2030**

*Includes favorable one-time impact of $35M (inventory) in Leqembi's 2Q25 global sales

***Citi, The 2026 Biopharma Outlook, Jan 6 2026; ***Lecanemab in Early Alzheimer's Disease. C. H. van Dyck, et al., NEJM, 2022; Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. J. R. Sims, et al., JAMA, 2023.*

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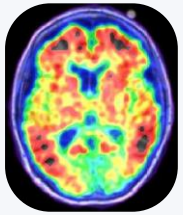
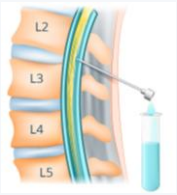
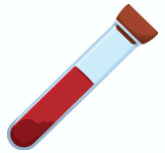
Adoption of BBBs Expected to Accelerate Growth & Potentially Improve Care

Evolution of Alzheimer's diagnosis from tissue to blood

Pre-2005	~2005 – 2025+		2025 →
			
Autopsy	**Amyloid PET**	**CSF Assays**	**Blood-Based Biomarkers**
Post-mortem neuropathology, variable accuracy	*In vivo imaging · PiB 2004; florbetapir FDA 2012*	*Lumbar puncture · Aβ42/40 and p-tau*	*Plasma p-tau217 · routine blood draw*
Only post-mortem	**In vivo — but costly and capacity-limited**	**Accurate — but invasive**	**Scalable — confirmation at the point of care**

- FDA has approved 4 BBBs for AD; increased use of BBBs to triage patients in primary care may lead to higher rates of confirmed cases and shift focus to treatment options
- A recent study noted diagnostic accuracy rate increased from 60-70% to ~90% after utilizing a BBB test; test was most valuable for ruling Alzheimer's out; 1 in 3 diagnoses was changed based on BBB result*

Source: FDA clearance announcements (Fujirebio 2025; C2N 2026; Roche/Lilly 2026); Grand View Research, blood-based biomarker market, 2025; published amyloid PET and CSF assay performance literature.

**Palmqvist et al., interim results presented at the Alzheimer's Association International Conference (AAIC) 2026, London, July 14, 2026; Alzheimer's Association press release.*

BBB: blood-based biomarker; PET: positron emission tomography; CSF: cerebrospinal fluid; PCP: primary care physician

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Growth Drivers in AD Market Expected to Support Increased Adoption of anti-Aβ Treatments

Current Market

Alzheimer's Disease

Anti-amyloid antibodies

LEQEMBI (lecanemab-irmb) 100 mg/mL INJECTION FOR INTRAVENOUS USE

kisunla (donanemab-azbt)

SALES · ANNUALIZED RUN-RATE	~$0.7B	~$0.5B
Efficacy (% slowing)*	27%	29%
ARIA-E*	12%	24%
Dosing	Q2W	Q4W
Dosing	QW	--

Growth Drivers

- ***Continued buildout of infrastructure supporting AD treatment deployment***
- ***Continued adoption of Alzheimer's fluid biomarkers for diagnosis and monitoring capabilities***
- ***Improved delivery / dosing options such as approval of Leqembi IQLIK (induction treatment)***
- ***Improved physician understanding of ARIA risk and management requirements***
- ***Combination strategies that build on Aβ as a cornerstone of treatment***

**Lecanemab in Early Alzheimer's Disease. C. H. van Dyck, et al., NEJM, 2022; Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. J. R. Sims, et al., JAMA, 2023.*

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.

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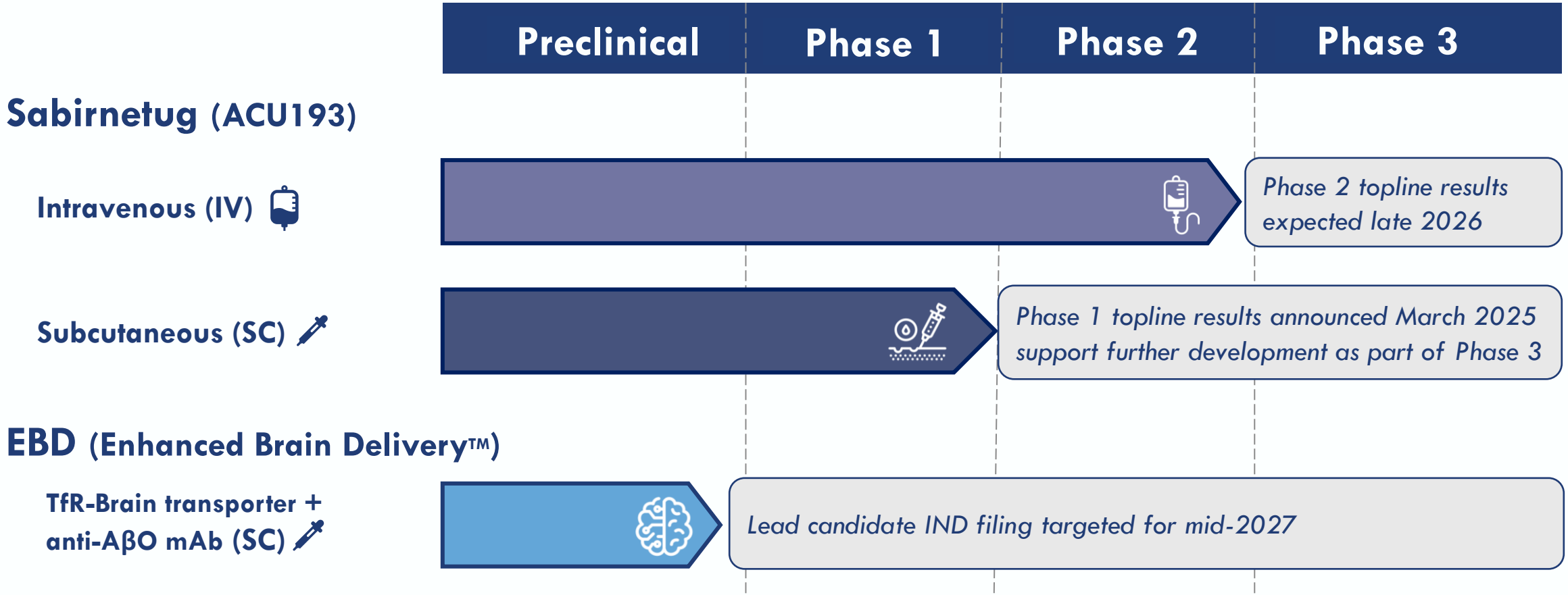
2026 a Pivotal Year for Acumen's Innovative anti-AβO Pipeline

Sabirnetug global Phase 2 study results & next generation EBD® candidate selection



Acumen's Compelling Value Proposition & Strategy

Growing and diverse AD population in need of improved treatment options

Novel AβO-selective MOA in validated amyloid space

Compelling Phase 1 results in AD patients increases POS for AβO-selective therapies

Phase 2 study ongoing and next-generation EBD program expands optionality

Acumen's strategy to expand stakeholder value – based on successful Phase 2 results, expedite sabirnetug development with a partner; rapidly advance EBD candidate through clinical value inflection point

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Sabirnetug's Mechanism of Action and Potential Differentiation from Other Disease Modifying Therapies (DMTs)

James Doherty, PhD
President and Chief Development Officer

ACUMEN

How Does Sabirnetug Differentiate From Approved Anti-Aβ DMTs*?

- Like approved Anti-Aβ DMTs, sabirnetug is an amyloid protein-targeting monoclonal antibody

- Unlike approved Anti-Aβ DMTs, sabirnetug targets soluble Aβ oligomers
  - Potential effects on efficacy: Direct removal of toxic agents that disrupt cortical function
  - Potential effects on safety: Less interaction with CAA plaques

- Unlike approved Anti-Aβ DMTs, sabirnetug is an IgG2 antibody
  - Potential effects on safety: Reduced inflammatory effects; reduced ARIA risk

*Approved Aβ DMTs include Leqembi (lecanemab) and Kisunla (donanemab)
DMT: disease-modifying treatment; CAA: cerebral amyloid angiopathy

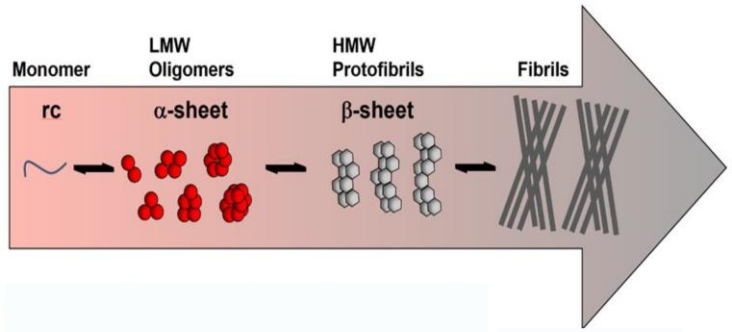
Amyloid Species and Disease Relevance

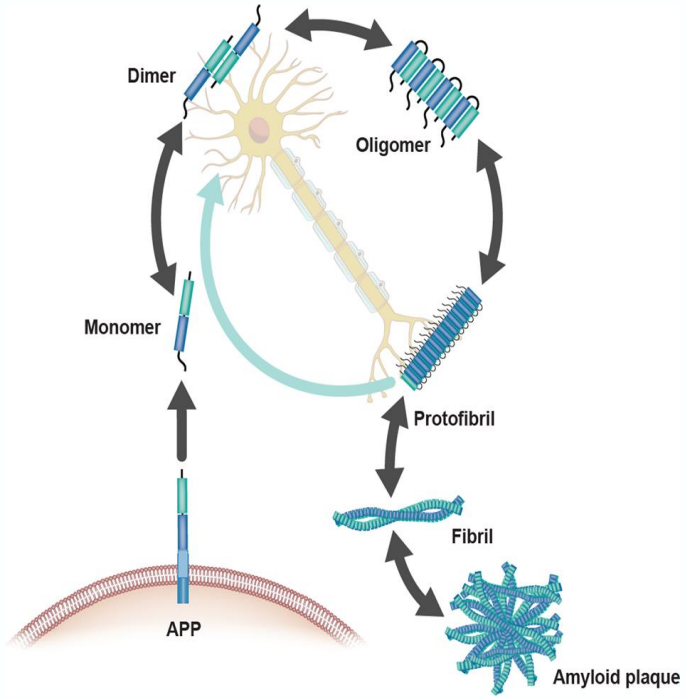
The role of Aβ oligomers

Amyloid-β Species Continuum

Amyloid-β exists in forms from monomers to insoluble plaques along a dynamic continuum.

- The classical idea was that a linear amyloid cascade moved from smaller aggregates to larger aggregates
- This has evolved into a dynamic amyloid-β model characterized by multiple interacting Aβ species with distinct biological and pathological roles

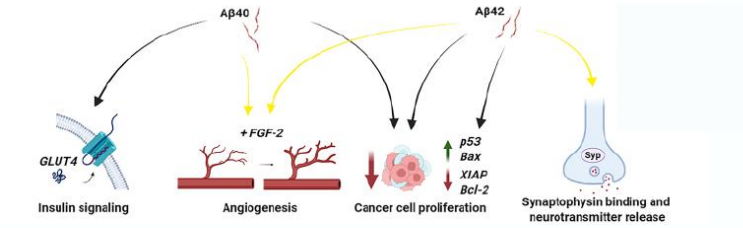




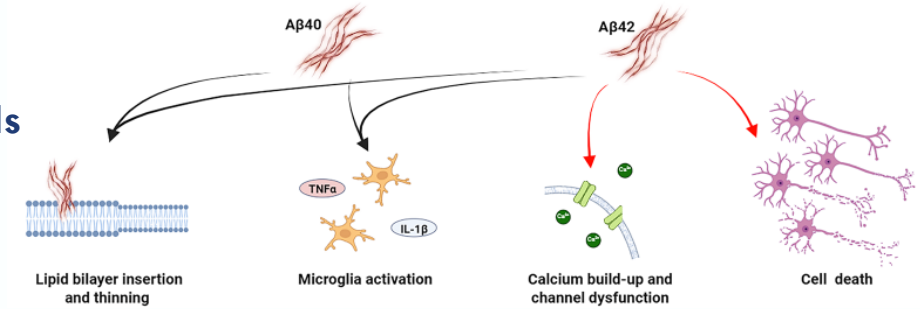
Hampel, H., Hardy, J., Blennow, K. et al. The Amyloid-β Pathway in Alzheimer's Disease. Mol Psychiatry, 2021.
Shea, D.; Daggett, V. Amyloid-β Oligomers: Multiple Moving Targets. Biophysica, 2022.

Aβ Aggregates and Species Have Different Effects on Brain Function

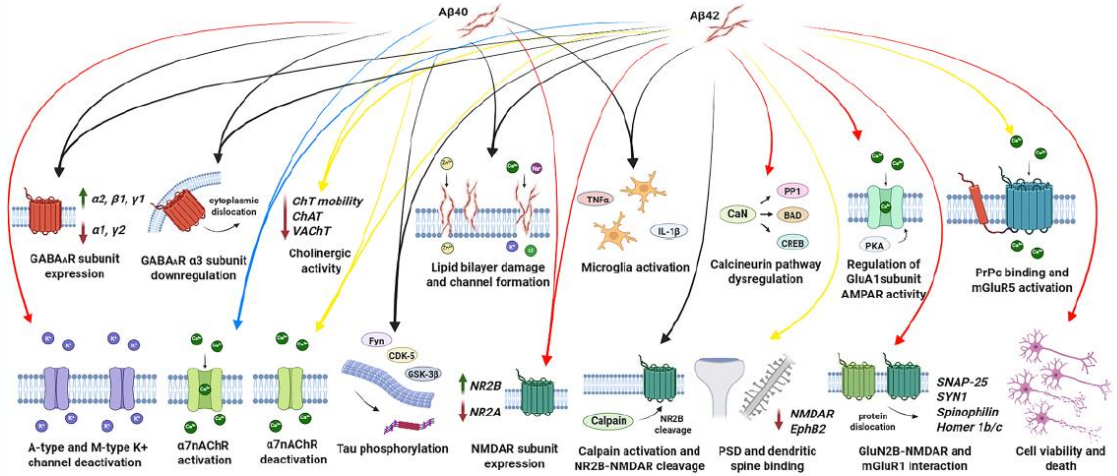
Monomers



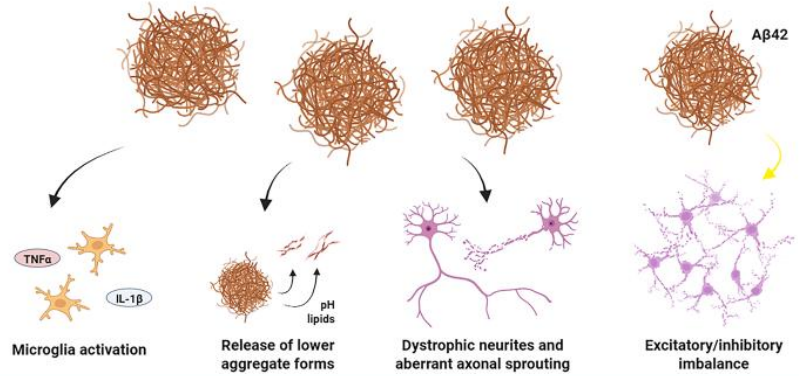
Protofibrils



Oligomers



Fibrils

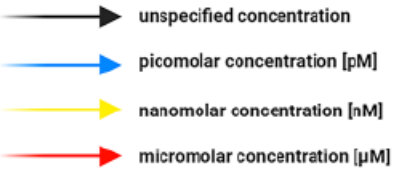


Toruński et al., 2026.

- **Oligomeric Aβ (AβOs)** exert extensive effects on neuronal and glial physiology, including:
  - Engaging neurotransmitter receptors and ion channels
  - Driving cholinergic dysfunction and tau phosphorylation
  - Dysregulating calcium homeostasis
  - Triggering microglial activation
  - Inducing excitotoxicity by disturbing glutamate reuptake
  - Disrupting excitability and synaptic synchronization

- **Aβ protofibrils (PFs)** can insert into membranes, cause lipid bilayer thinning, and foster microglial activation. PFs facilitate calcium influx and partial disassembly into smaller toxic aggregates.

- **Fibrillar Aβ aggregates** induce microglial activation, release lower-order aggregates, and promote dystrophic neurites

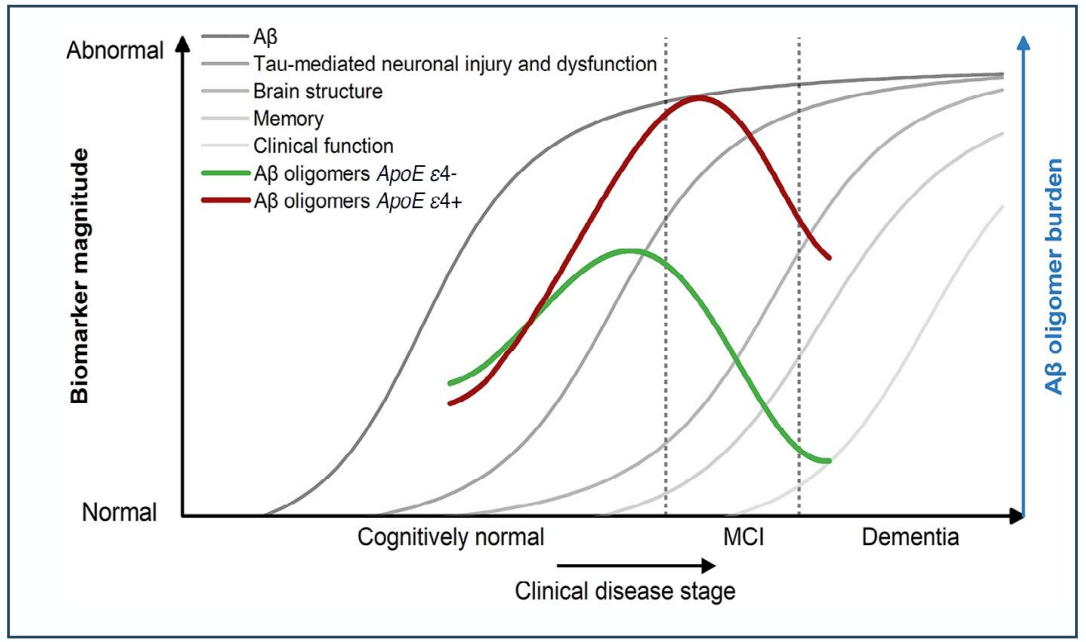


Amyloid Beta Oligomer (AβO) Levels: Clinical Implications in MCI/Mild AD

Soluble oligomers are an early and persistent feature of AD

- Soluble Aβ oligomers appear very early, likely years before plaques are detectable
  - Amyloid PET positivity then develops as fibrillar deposits accumulate
  - Tau biomarkers begin to rise shortly thereafter
- Soluble oligomers likely remain present throughout disease progression and may continue driving synaptic dysfunction even after plaques are established

AβO elevation in early AD and APOE ε4 carriers



Adapted from Blömeke L et al., Aβ oligomers peak in early stages of Alzheimer's disease preceding tau pathology. Alz & Dementia, 2024.

MCI: mild cognitive impairment; PET: positron emission tomography; APOE: apolipoprotein E

AβO Hypothesis

Plaques are the visible pathology, but hard-to-detect oligomers are the most synaptotoxic species

- It has been long-appreciated that amyloid plaque load does not correlate well with progression of cognitive decline in AD, and many cognitively normal elderly have high amyloid plaque loads
- Soluble oligomers of amyloid-β protein (AβO) **do** correlate with cognitive decline, are highly synaptotoxic, and occur earlier in disease

Toxicity of Soluble Oligomers

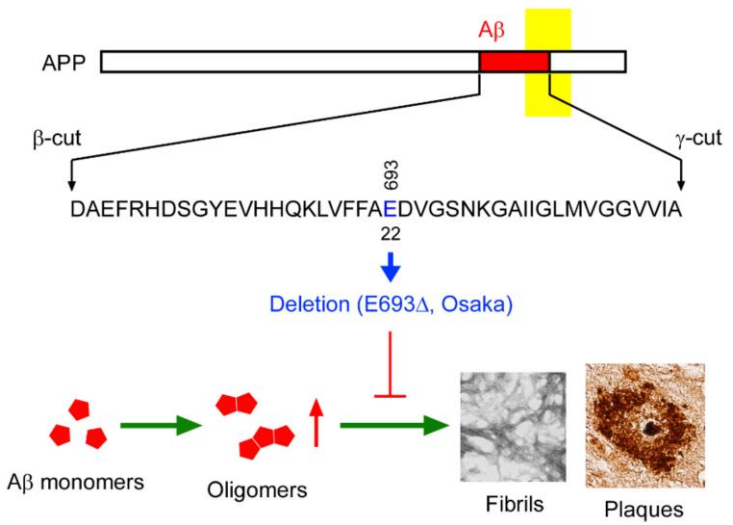
Soluble oligomers are the most synaptotoxic species of Aβ, disrupting receptor trafficking and promoting tau spread.

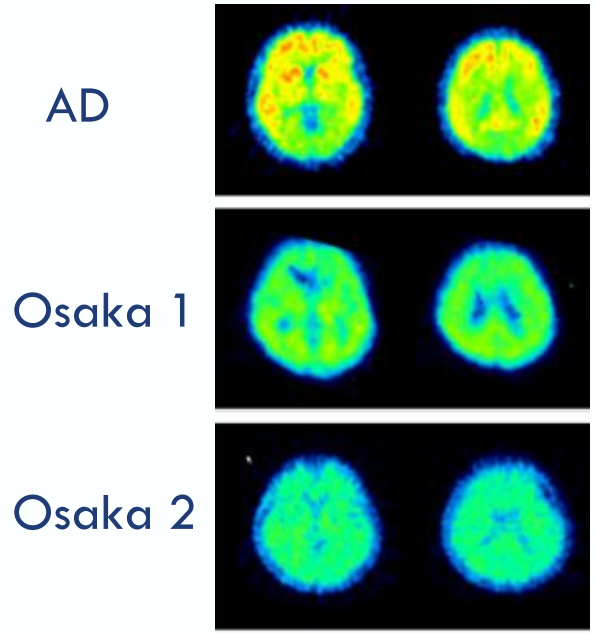
Therapeutic Strategy

Sabirnetug selectively targets toxic oligomers throughout the disease continuum, sparing monomers and plaques for improved safety.

Osaka Mutation: AβOs Are Associated with Cognitive Impairment in AD

A rare human mutation that supports the oligomer hypothesis





Tomiyama & Shimada, Int J Mol Sci., 2020.

- Extremely rare inherited mutation of APP protein first identified in several Japanese families that is linked to early-onset familial Alzheimer's disease
- APP E693Δ produces mutant Aβ lacking 22nd glutamate (E22)
- Osaka mutation accelerates Aβ oligomerization but does not form amyloid fibrils or plaques
- Evidence that soluble Aβ oligomers alone may be sufficient to trigger Alzheimer's disease pathology

Sabirnetug: First Oligomer-Selective Immunotherapy to Reach POC

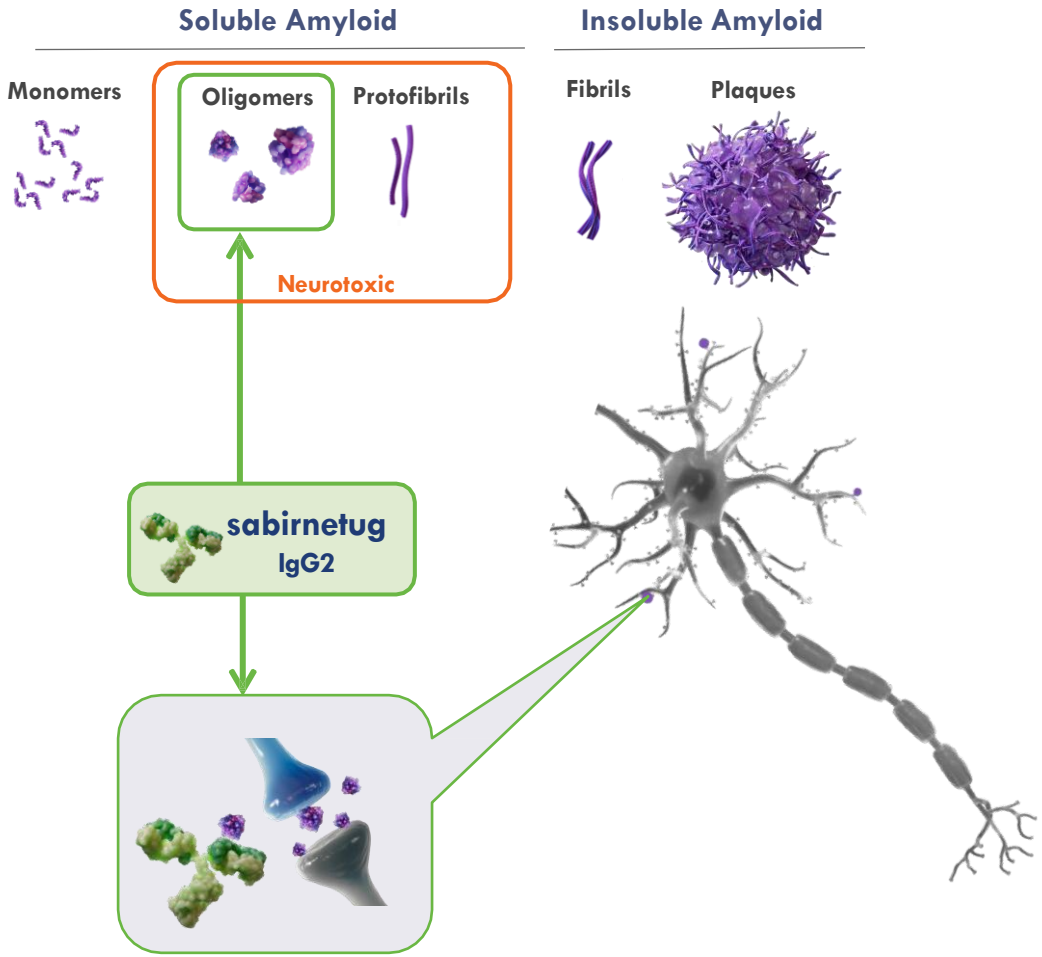
Specifically developed against globular AβOs – amyloid-derived diffusible ligands (ADDLs)

Designed for Improved Efficacy & Safety

- **Humanized, affinity matured mAb developed to target toxic Aβ oligomers**

Positive Ph1 in AD Patients

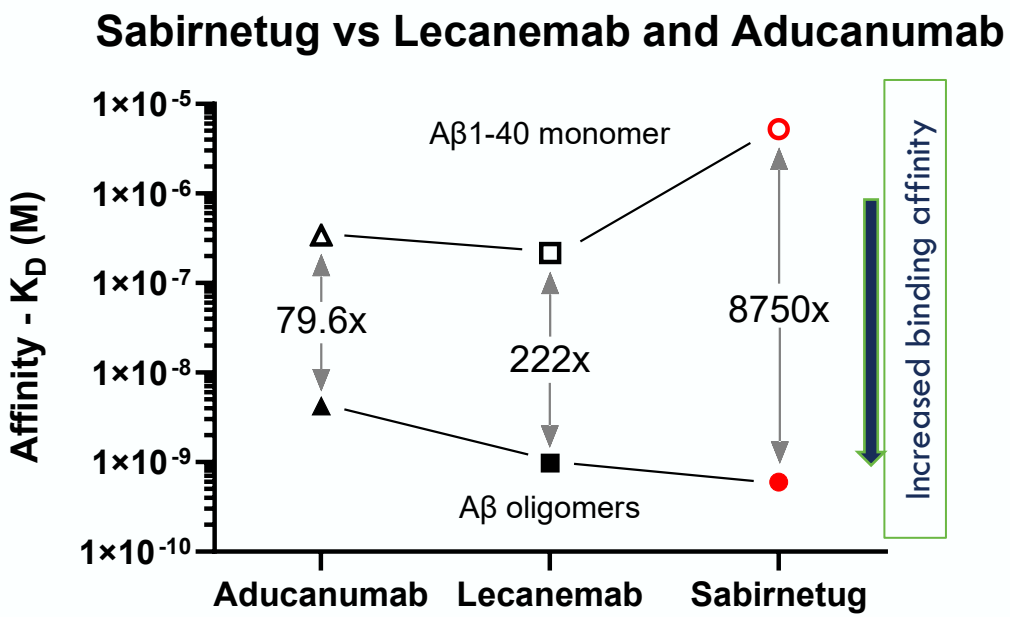
- **Successful Phase 1 exclusively in early AD patients**
  - ✓ Safety, target engagement, biomarker effects



Differences in the Profile of Sabirnetug Relative to Approved anti-Aβ DMTs:

Greater AβO selectivity against Aβ monomers and linear fibrillar species

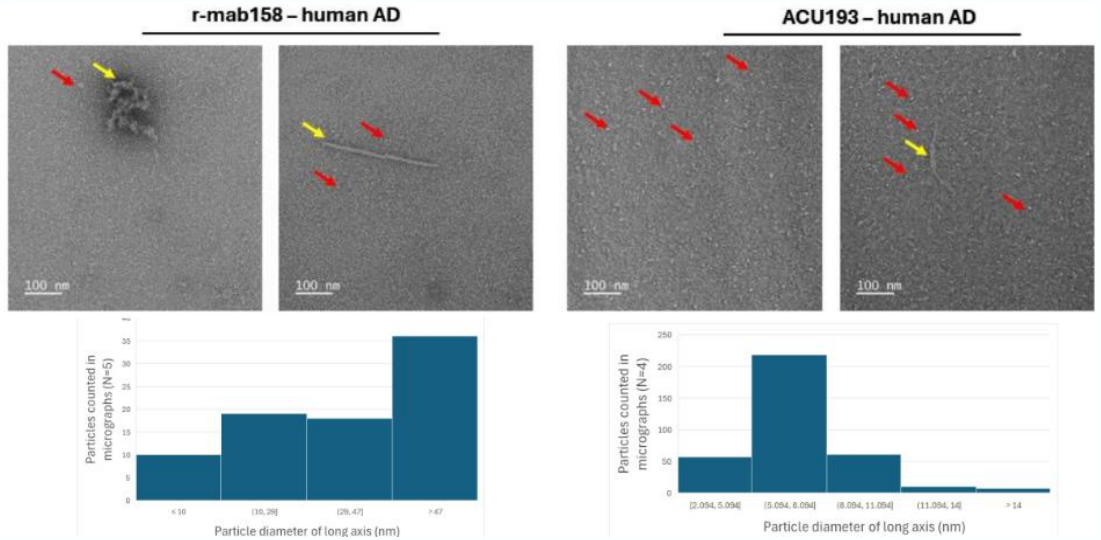
Greater selectivity against monomeric Aβ



Cline et al, AAIC 2025.

- **lecanemab → 222x** higher affinity to AβO than monomer
- **sabirnetug → 8750x** higher affinity to AβO than monomer

Greater selectivity for soluble Aβ species isolated from human AD brain



De Leon et al, AAIC 2025.

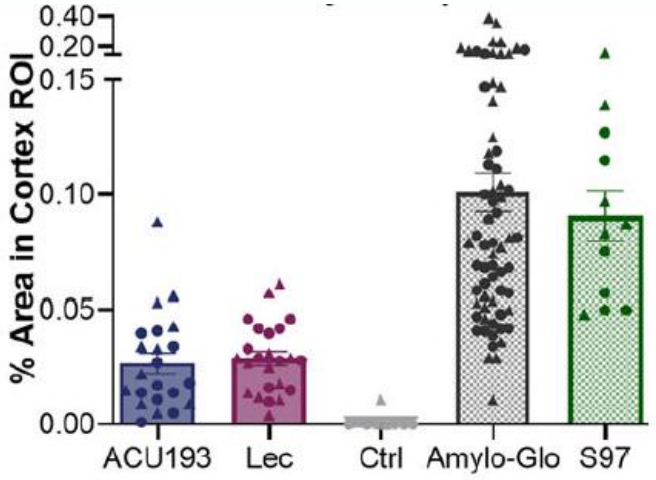
- Eluates from affinity chromatography using:
  - **r-mab158** → 36% globular, **64% fibrillar,** Aβ species
  - **sabirnetug** → 99% globular, **1% fibrillar** Aβ species

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.

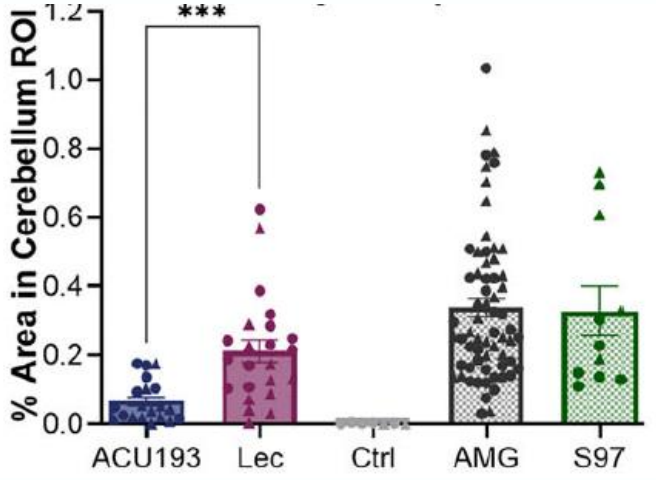
Vascular Aβ Binding Profile in a Murine Model of Vascular CAA

Immunohistochemical comparison of vascular Aβ binding in the APP:hE4 mouse brain

Cortex



Cerebellum



- Sabirnetug (ACU193) and lecanemab showed **qualitatively similar overall staining** in both cortex and cerebellum
- But sabirnetug had **significantly less cerebellar vascular labeling** than lecanemab ($p = 0.0001$)

Grenon, Martine et al., Ex vivo comparison of ACU193 and lecanemab reveals binding differences in mouse brain, Alzheimer's & Dementia, 2026.

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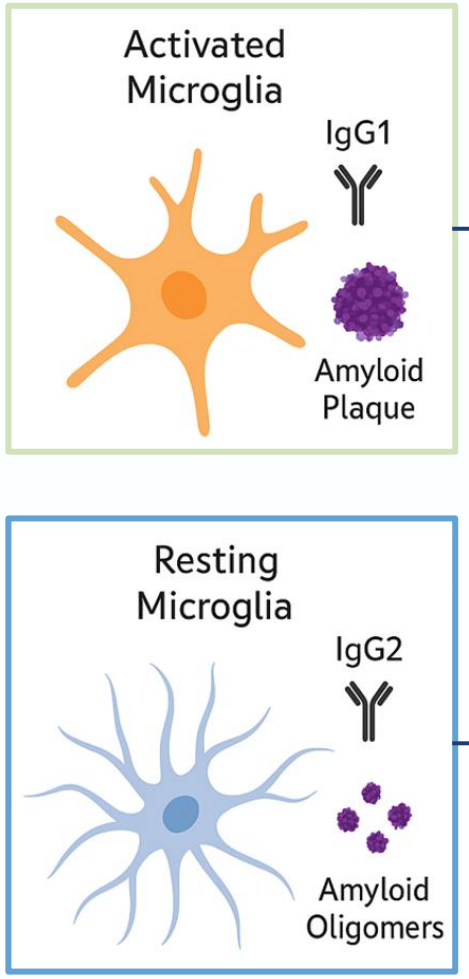
Sabirnetug is an IgG2 Antibody, Which May Lower Risk of ARIA and IRR

Differences in effector coupling may influence inflammatory risk profile

IgG1 antibodies
(lecanemab, donanemab)
strongly bind Fcγ1 receptors and C1q, triggering complement activation and antibody-dependent cellular phagocytosis (ADCP), causing inflammation and triggering strong cytokine release.

IgG2 antibodies,
like sabirnetug, weakly bind Fcγ1 receptors and avoid complement activation, potentially reducing the risk of inflammation and cytokine release.

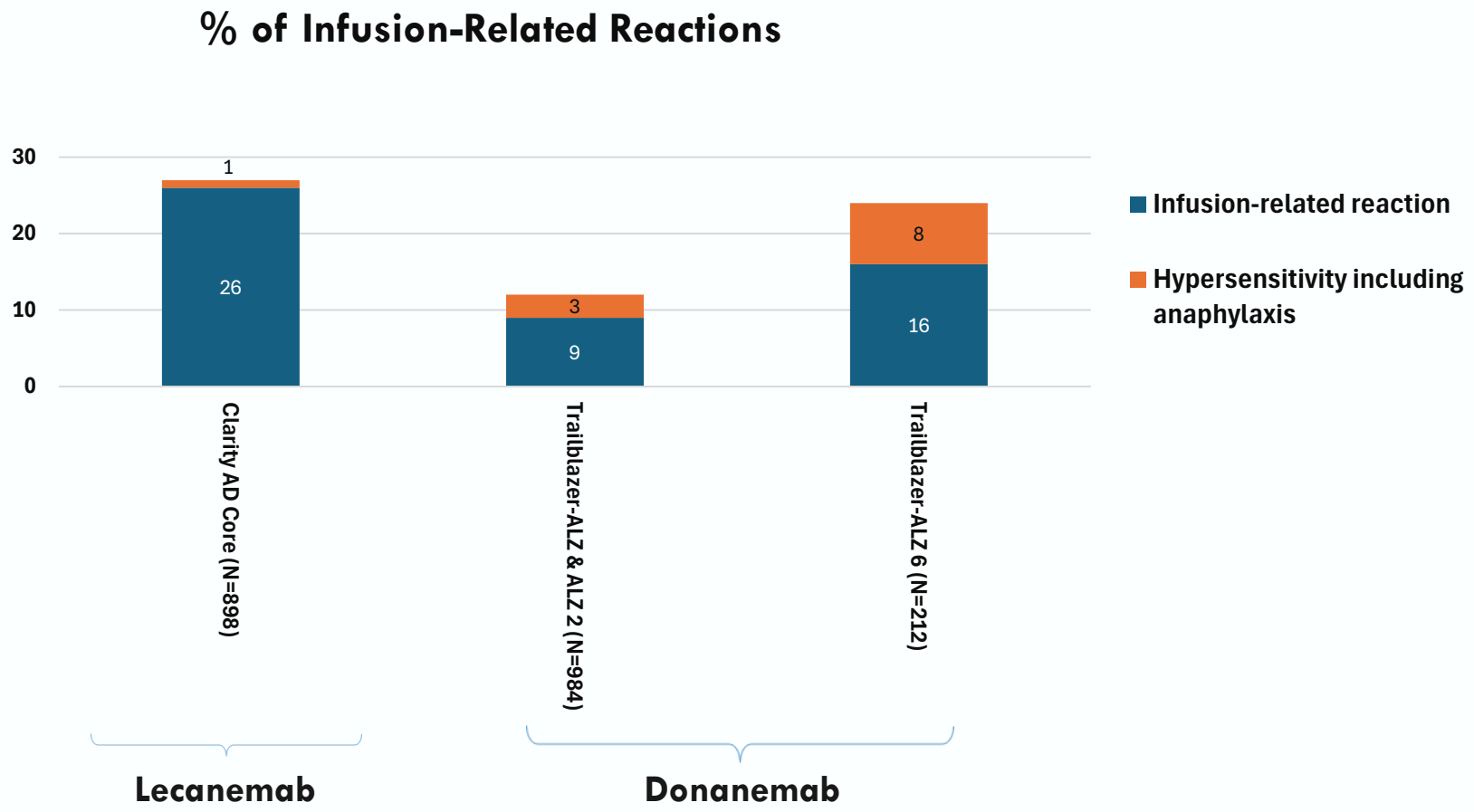


Potential Impact on Safety:

- **IgG1-based anti-Aβ DMTs (lecanemab, donanemab) show substantial inflammatory risk, leading to ARIA and hypersensitivity reactions**
  - Including IRRs and anaphylaxis
  - This may limit the doses that can be used to drive efficacy
- **IgG2-based sabirnetug may enable amyloid clearance with reduced inflammation, cytokine release, and ADCP involvement**
  - IgG2 Fc attenuation may lower the frequency and severity of hypersensitivity reactions or ARIA

Maverakis E et al. Glycans in the immune system and The Altered Glycan Theory of Autoimmunity: a critical review. J Autoimmun., 2015.
Wang, J., et al. A systemic view of Alzheimer disease — Insights from amyloid-β metabolism beyond the brain. Nature Reviews Neurology, 2017.
Shashidharamurthy R, et al. Dynamics of the interaction of human IgG subtype immune complexes with cells expressing R and H allelic forms of a low-affinity Fcγ receptor CD32A, 2009.

Infusion-Related Reactions in Lecanemab and Donanemab Phase 3 Studies



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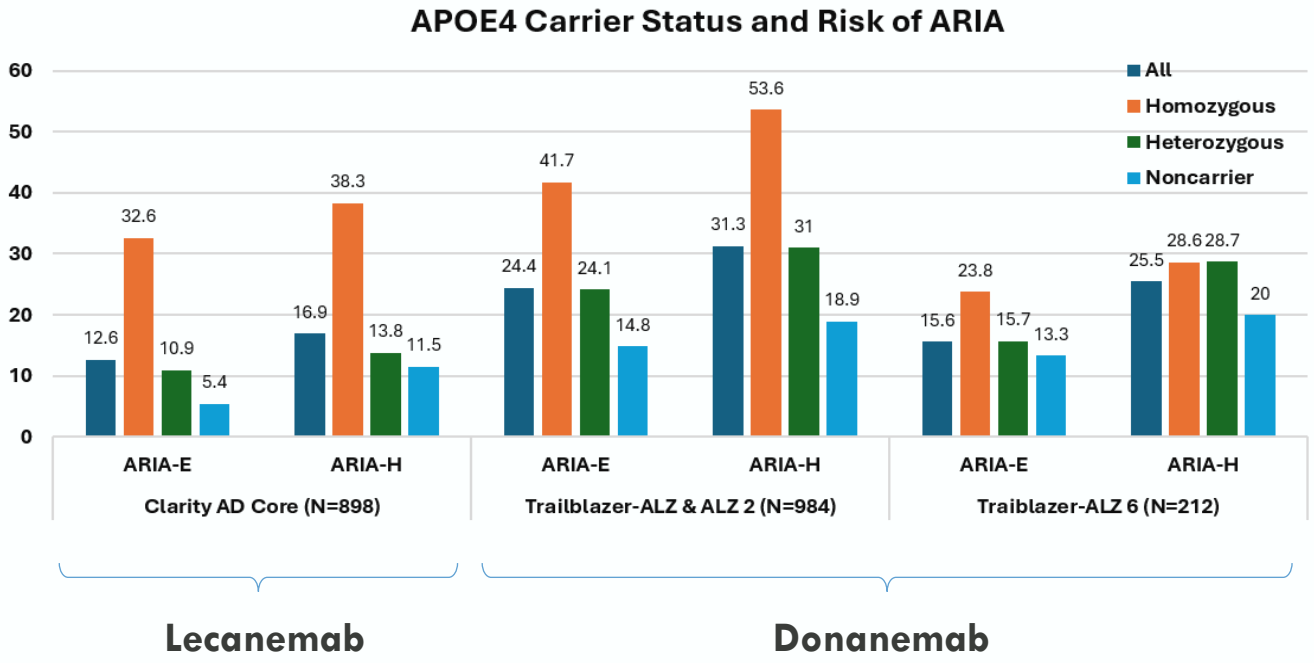
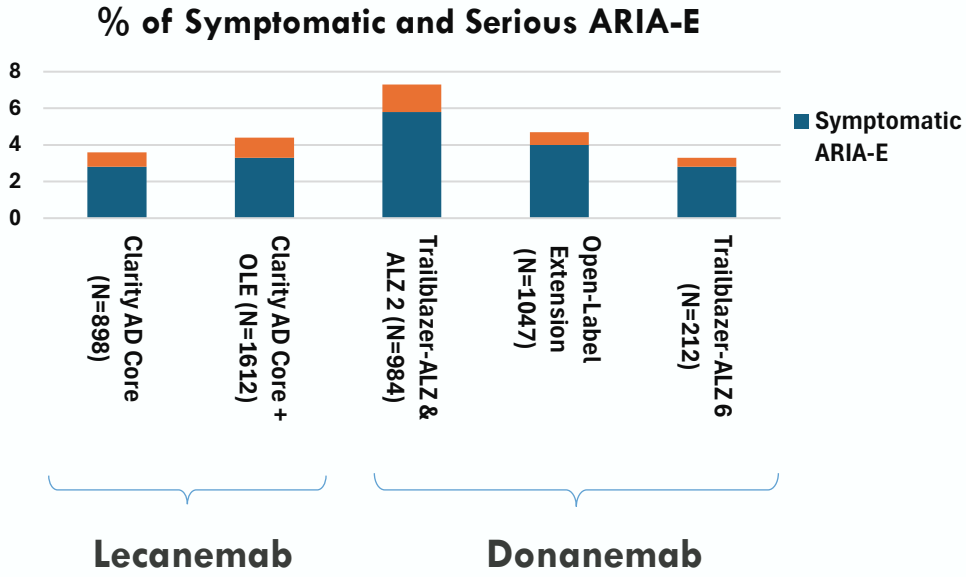
Incidence and Severity of ARIA with Approved anti-Aβ DMTs





Despite improvement with titration, a high rate of ARIA is associated with approved anti-amyloid treatments

Honig et al. Updated safety results from ph3 lecanemab study in early AD. Alzheimers Res Ther., 2024.
Van Dyck et al. Long-term safety and efficacy of lecanemab in early AD. Alzheimers Dement, 2025.
Zimmer et al. ARIA with donanemab in early symptomatic AD. JAMA, 2025.
Wang et al. The effect of modified donanemab titration on ARIA-E and amyloid reduction. JPAD, 2025.

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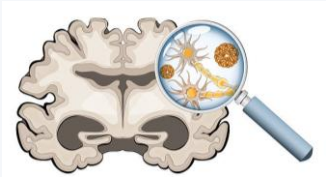
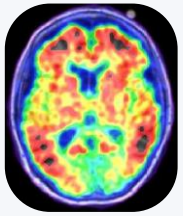
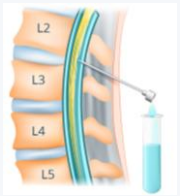
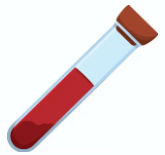
Adoption of BBBs Expected to Accelerate Growth & Potentially Improve Care

Evolution of Alzheimer's diagnosis from tissue to blood

Pre-2005	~2005 – 2025+		2025 →
			
Autopsy	**Amyloid PET**	**CSF Assays**	**Blood-Based Biomarkers**
Post-mortem neuropathology, variable accuracy	*In vivo imaging · PiB 2004; florbetapir FDA 2012*	*Lumbar puncture · Aβ42/40 and p-tau*	*Plasma p-tau217 · routine blood draw*
Only post-mortem	**In vivo — but costly and capacity-limited**	**Accurate — but invasive**	**Scalable — confirmation at the point of care**

Source: FDA clearance announcements (Fujirebio 2025; C2N 2026; Roche/Lilly 2026); Grand View Research, blood-based biomarker market, 2025; published amyloid PET and CSF assay performance literature.

BBB: blood-based biomarker; PET: positron emission tomography; CSF: cerebrospinal fluid; PCP: primary care physician

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Four FDA Clearances in 15 Months Are Unlocking a Fast-Growing Blood-Based Diagnostics Market

SEQUENTIAL REGULATORY APPROVALS

U.S. clearances and EU CE marks, May 2025 to date

MAY 2025

Fujirebio Lumipulse pTau217/Aβ42

First FDA-cleared blood test for Alzheimer's, ages 55+

AUG 2025

Labcorp national launch

Cleared IVD reaches scale; Quest AD-Detect expands access

MAY 2026

Roche Elecsys pTau217 — CE mark

First single-assay rule-in / rule-out test in Europe

JUL 2026

Beckman Coulter Access p-Tau217

CE mark broadens platform coverage across the EU

AUG 20, 2026

C2N PrecivityAD2 — FDA cleared

Third U.S. clearance; first for adults as young as 40

AUG 24, 2026

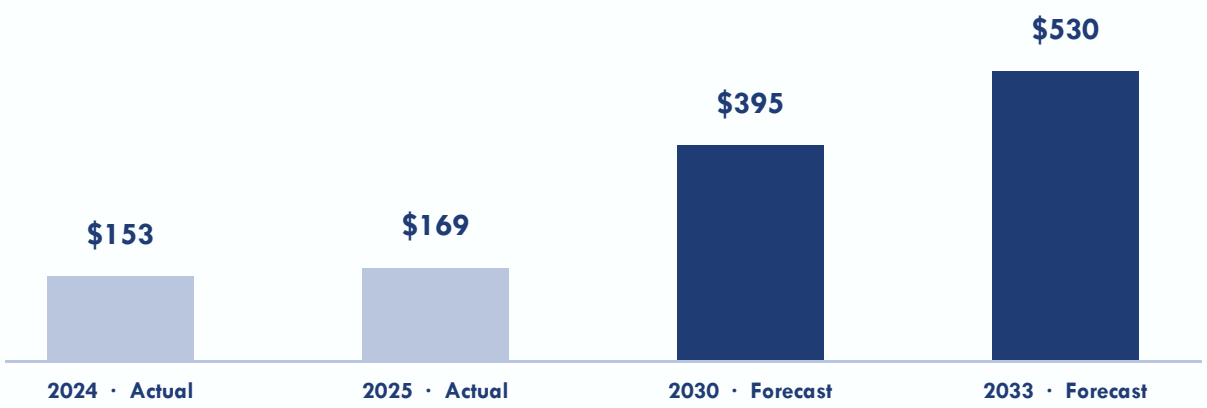
Roche / Lilly Elecsys pTau217 — FDA cleared

Fourth clearance; first cleared for primary care

Diagnostic momentum growing

MODELED MARKET GROWTH

Global blood-based biomarkers for Alzheimer's · USD millions



~17.4% CAGR
sustained through 2033

3.5x expansion
$153M in 2024 to ~$530M by 2033

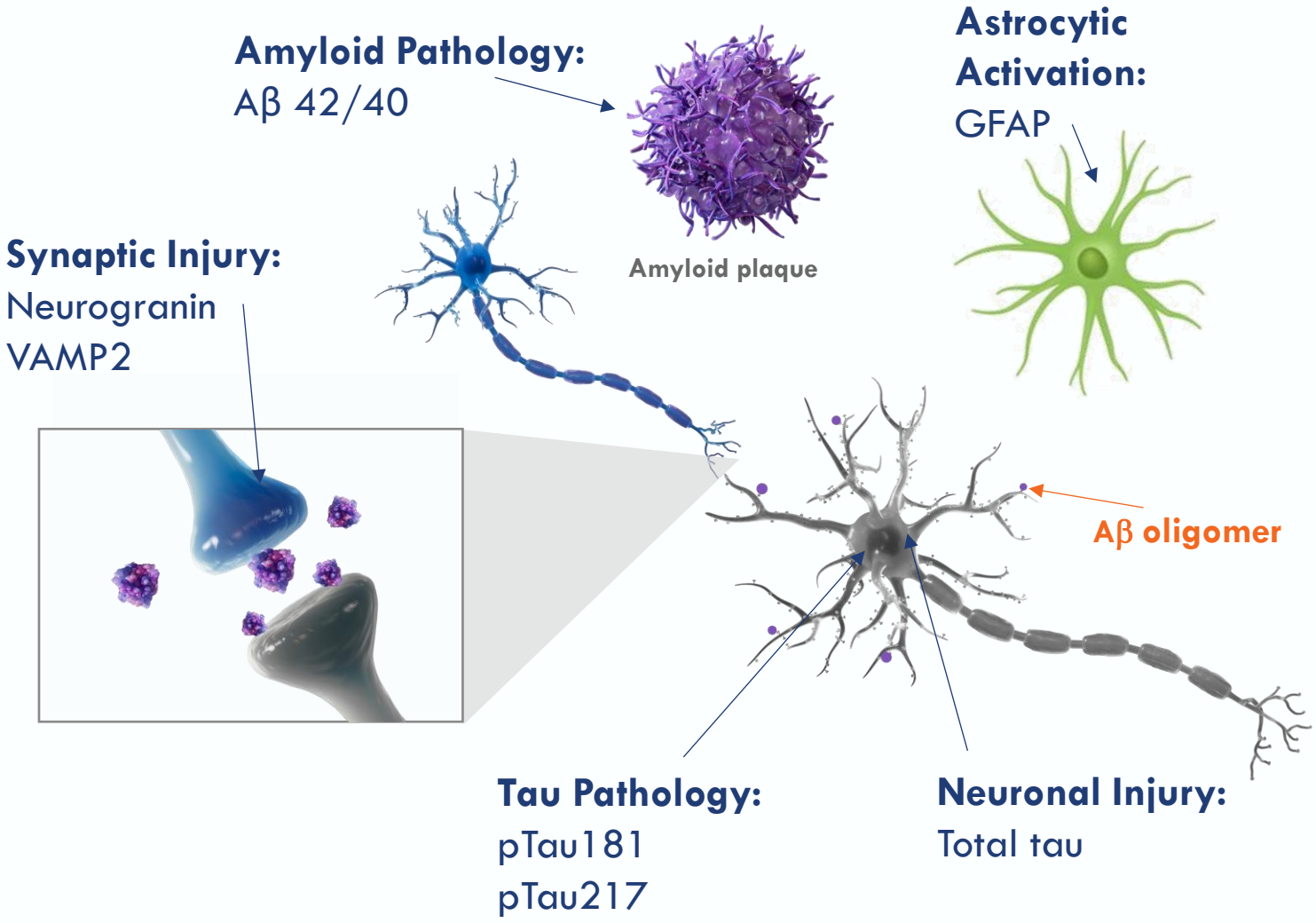
Growth driven by FDA-cleared IVDs replacing PET and CSF testing, and by amyloid-therapy eligibility screening

Source: Grand View Research, Alzheimer's Disease Diagnostics / blood-based biomarker market (2026–2033), 2025. Regulatory milestones: FDA, Fujirebio, Roche, C2N Diagnostics, Beckman Coulter, Labcorp and Quest Diagnostics announcements. 2030 and 2033 values are forecasts.

Measuring Key AD-associated Fluid Biomarkers in INTERCEPT and ALTITUDE

CSF and plasma markers of amyloid pathology, tau pathology, and synaptic injury

- 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**



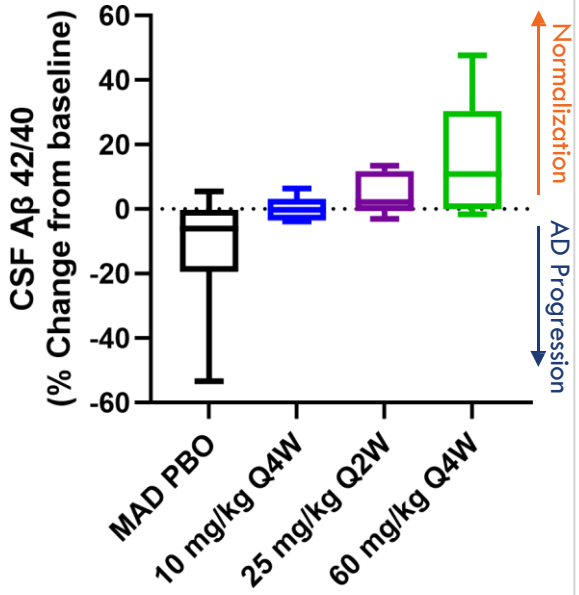
1. *Tarawneh, R. Biomarkers: Our Path Towards a Cure for Alzheimer Disease. Biomarker Insights Volume 15: 1–15. 2020; 2. Blennow K, Zetterberg H. The Past and the Future of Alzheimer's Disease Fluid Biomarkers. J Alzheimer's Dis. 2018;62(3):1125-1140.*

Improvement in Amyloid, Tau and Synaptic Biomarkers in INTERCEPT-AD

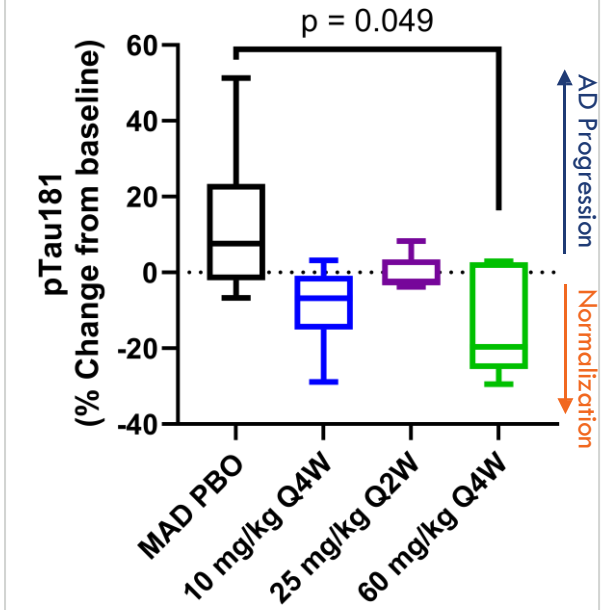
Consistent reduction of elevated CSF biomarkers after only three administrations of sabirnetug

Amyloid pathology | *Tau pathology* | *Synaptic injury*

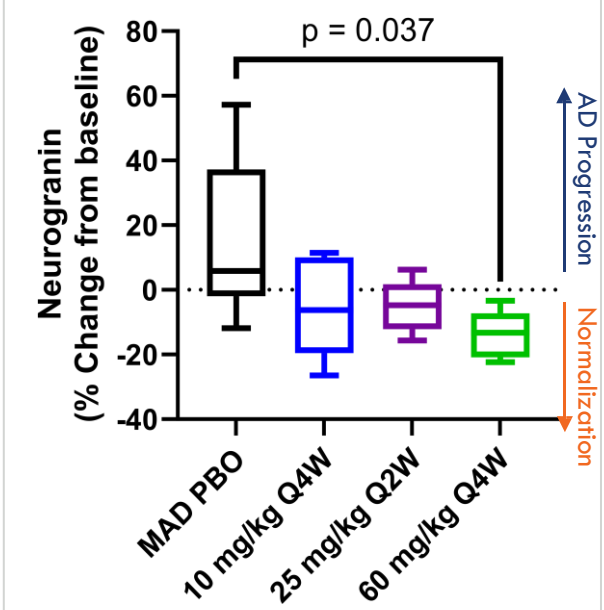
Aβ 42/40 Ratio



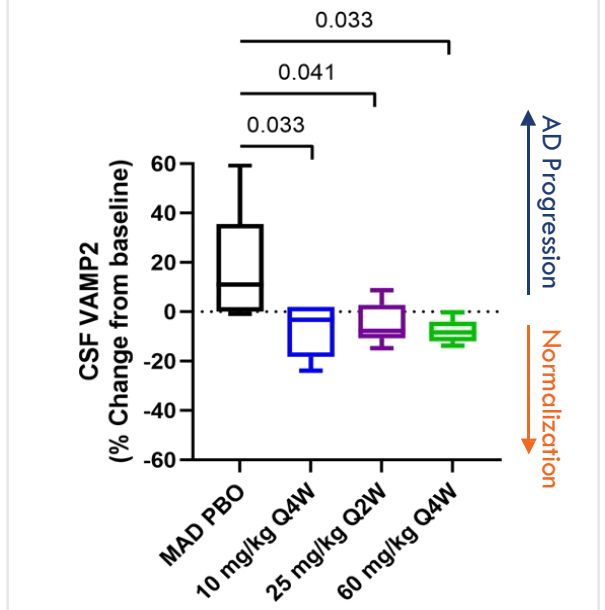
pTau181



Neurogranin



VAMP2



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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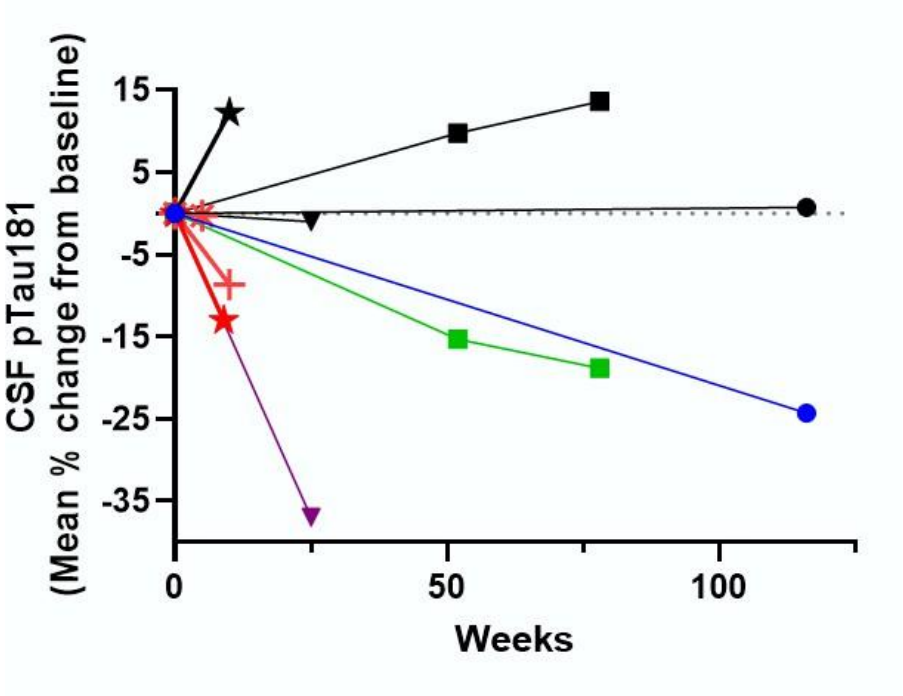
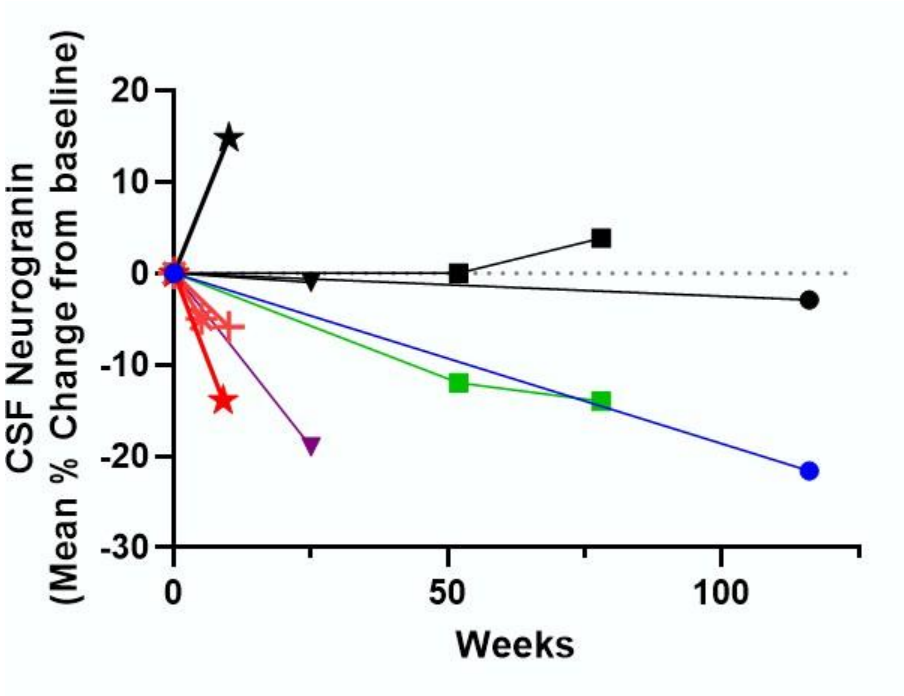
Sabirnetug Rapidly Reduced CSF Biomarkers in INTERCEPT-AD

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.

Summary and Conclusions

- Sabirnetug preferentially binds to soluble oligomers, a low abundance, highly toxic form of Aβ that appears during the early phases of disease; this profile offers the opportunity to differentiate from currently approved anti-Aβ DMTs that target other forms of Aβ

- Sabirnetug has an IgG2 backbone, which connects to immune effector functions differently from the IgG1 signaling with approved anti-Aβ DMTs, potentially impacting both efficacy and tolerability

- Sabirnetug shows rapid and robust effects on multiple fluid biomarkers that may be associated with improvements in cognitive function in studies with approved anti-Aβ DMTs

ALTITUDE-AD: A Well-Powered Phase 2 Study Designed to Test the Oligomer Hypothesis

Eric Siemers, MD
Chief Medical Officer

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ALTITUDE-AD Late 2026 Readout: Efficacy, Safety, and Biomarker Profile

Clinical Endpoints

Primary: iADRS

Key Secondary:
- CDR-SB
- ADCS-iADL
- ADAS-Cog13

Amyloid PET: Centiloid (CL)

Safety

ARIA: *(total and by APOE4 genotype)*
- ARIA-E
- ARIA-H

Adverse Events:
- SAEs
- TEAEs (by SOC)
- Infusion Reactions

Biomarkers

CSF Biomarkers: *(sub-study)*
- Aβ40, Aβ42, Aβ42/40
- pTau181/tTau
- Neurogranin

Plasma Biomarkers:
- Plasma GFAP
- Plasma pTau217

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; SAE: serious adverse event; TEAE: treatment-emergent adverse event; SOC: standard of care; tTau: total tau; GFAP: glial fibrillary acidic protein

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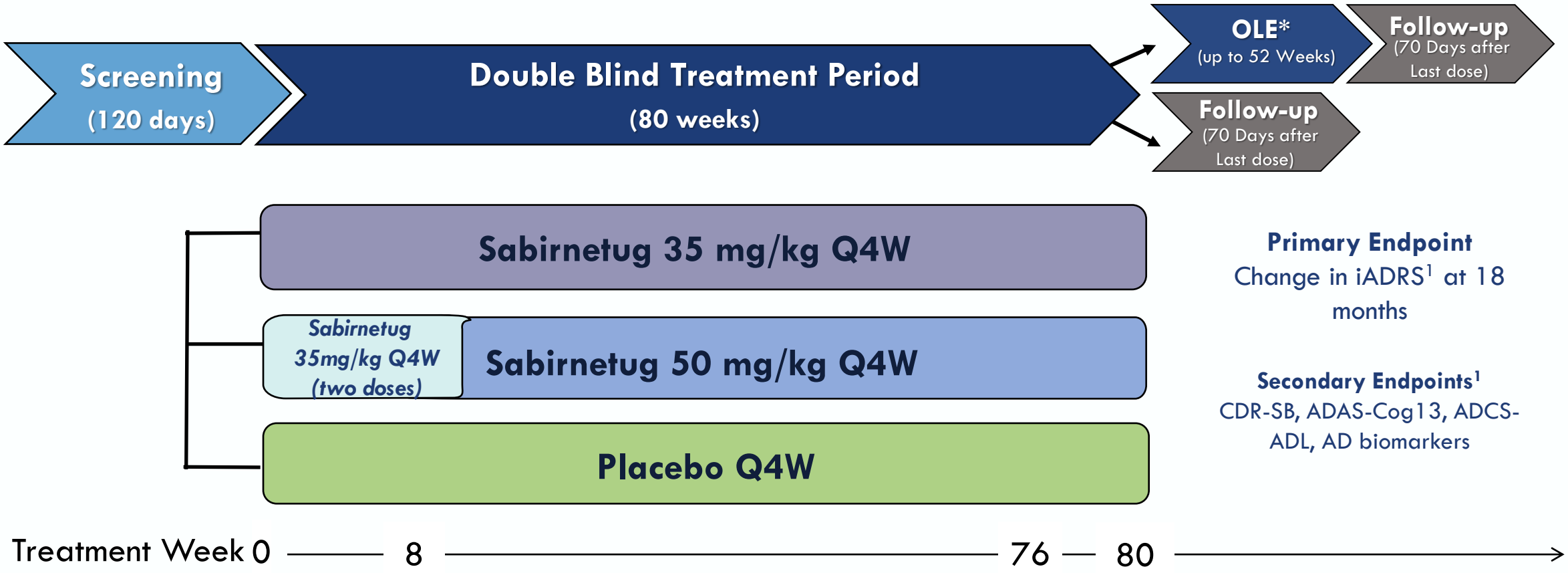
ALTITUDE-AD: Phase 2 Study Design of Sabirnetug for Early AD

542 participants randomized 1:1:1



Primary Endpoint
Change in iADRS[1] at 18 months

Secondary Endpoints[1]
CDR-SB, ADAS-Cog13, ADCS-ADL, AD biomarkers

* At Week 80, participants will enter OLE (up to 52 weeks) or have a Safety Follow-up visit 70 days after the last study drug dose

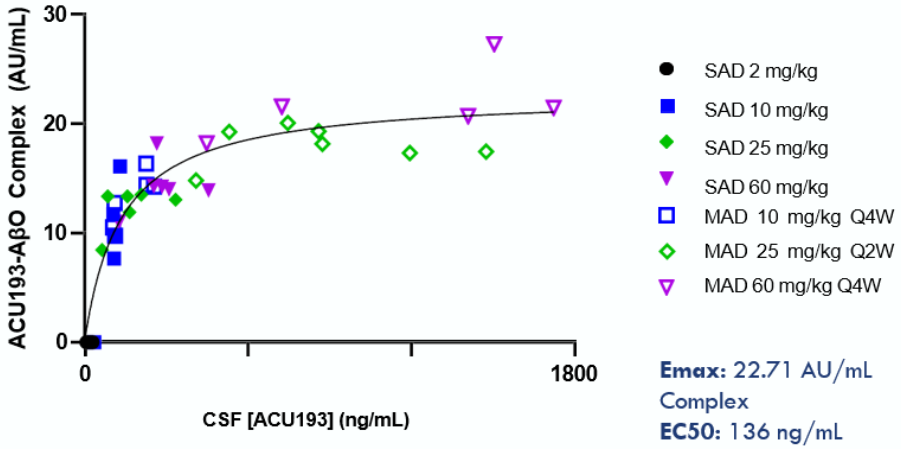
1. iADRS: Integrated Alzheimer's Disease Rating Scale; CDR-SB: Clinical Dementia Rating – Sum of Boxes; ADAS-cog: Alzheimer's Disease Assessment Scale – Cognitive Subscale; ADCS-ADL: Alzheimer's Disease Cooperative Study – Activities of Daily Living

Phase 1 Data Demonstrate Sabirnetug's Potential to Achieve More Optimal Benefit-to-Risk Profile than Existing Options

1. Maximal target engagement of toxic AβOs
2. AD fluid biomarker trend to normalization
3. Wider therapeutic index

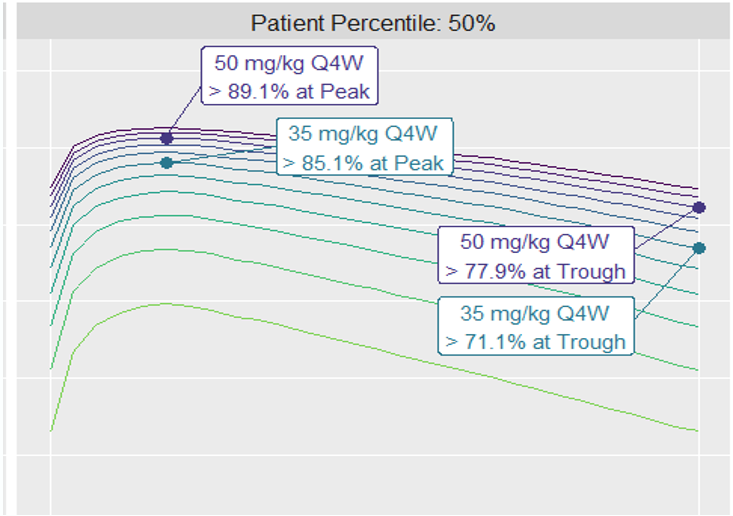
= **Potential for improved benefit-to-risk profile**

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



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

Doses were selected with peak-trough variation in mind: select doses based on trough (end of dosing interval) CSF engagement



Ph2 Dosing Strategy

upper dose: 50 mg/kg Q4W
lower dose: 35 mg/kg Q4W

Phase 1 Data Demonstrate Sabirnetug's Potential to Achieve More Optimal Benefit-to-Risk Profile than Existing Options

1. Maximal target engagement of toxic AβOs
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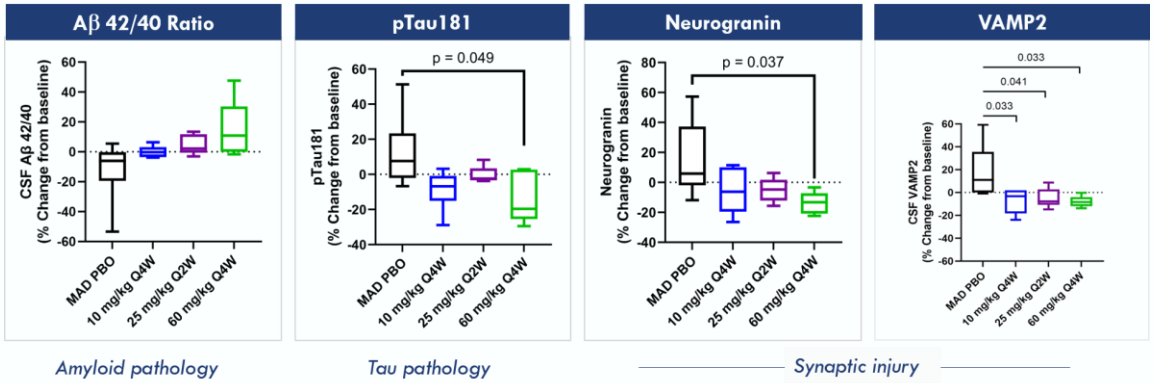
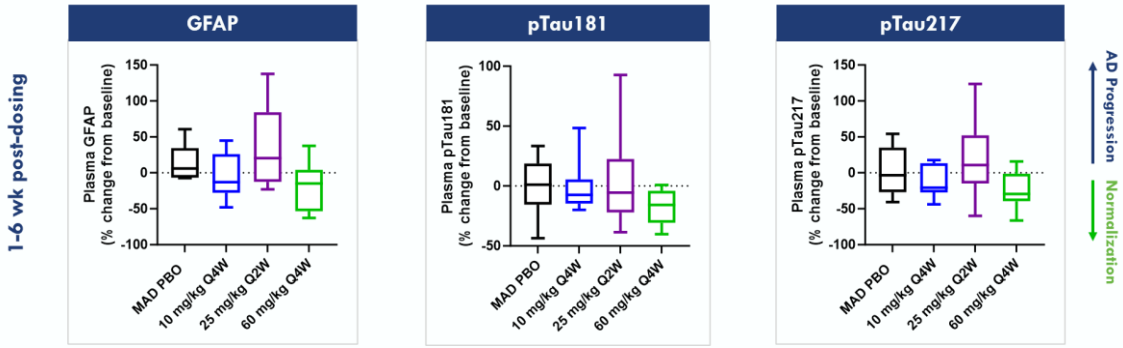
= **Potential for improved benefit-to-risk profile**

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



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



Phase 1 Data Demonstrate Sabirnetug's Potential to Achieve More Optimal Benefit-to-Risk Profile than Existing Options

1. Maximal target engagement of toxic AβOs
2. AD fluid biomarker trend to normalization
3. Wider therapeutic index

= **Potential for improved benefit-to-risk profile**

INTERCEPT-AD Phase 1 Safety Data

5 Total ARIA-E cases, or ~10%

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
- ✓ **Broad therapeutic index** with convenient monthly dosing
  - Safety profile may support attractive benefit/risk option for large portion of patients

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iADRS as Primary Endpoint

- The iADRS was developed to improve sensitivity to treatment effects and disease progression in earlier AD populations

- Measures the two domains most relevant to disease progression — cognitive decline and loss of everyday functioning

- Aligns well with the view that a clinically meaningful treatment benefit should translate beyond test performance into day-to-day functioning

- Better dynamic range may lead to a greater ability to detect subtle changes in an earlier AD population
  - CDR-SB score range is 0-18
  - iADRS score range is 0-144

ALTITUDE-AD Readout Includes the iADRS as the Primary Outcome and the CDR-SB as an Important Secondary Outcome

The iADRS and CDR-SB are both composites of cognitive and functional measures

	iADRS	CDR-SB
Number of cognitive measures	13 items (from ADAS-cog13)	3 items
Number of functional measures	18 items (from ADCS-iADL)	3 items
Method for cognitive measures	Performance based	Performance based + structured interview + rater judgement
Method for functional measures	Structured interview with study partner	Semi-structured interview with study partner + rater judgement
Signal/noise in mild AD[1]	0.74	0.68
Effect size in EXPEDITION, EXPEDITION2, EXPEDITION3 (mild AD only)[2]	0.193, 0.200, 0.112	0.006, 0.110, 0.109
Statistical significance (N) in donanemab Phase 2[3] / donanemab Phase 3[4]	P=0.04 (245)/P<0.001(1093)	P=0.14 (245)/P<0.001(1115)

1. *Wessels et al. JPAD 2015.; 2. Wessels et al. JPAD 2018.; 3. Mintun et al. NEJM, 2021. 4. Sims et al. JAMA 2023 (Low/Med tau group).*

The iADRS is a well-behaved, consistent measure of cognitive and functional decline

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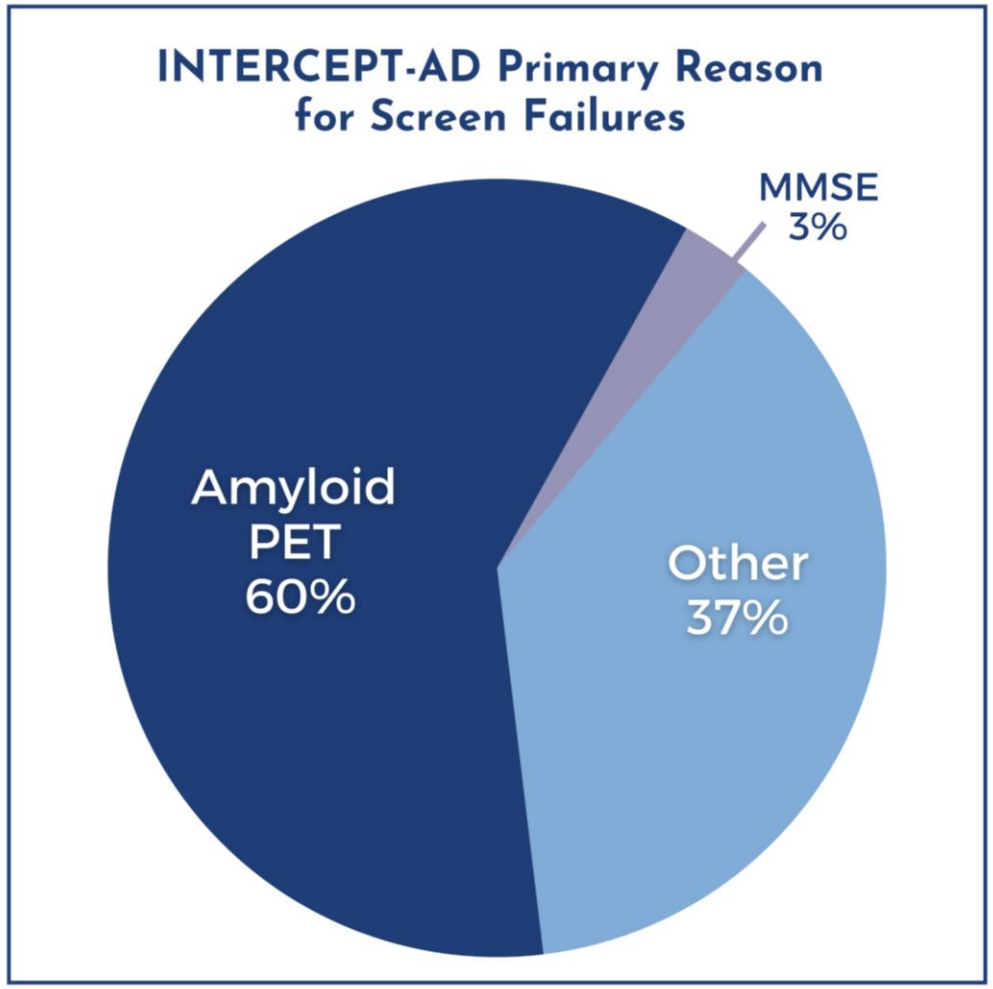
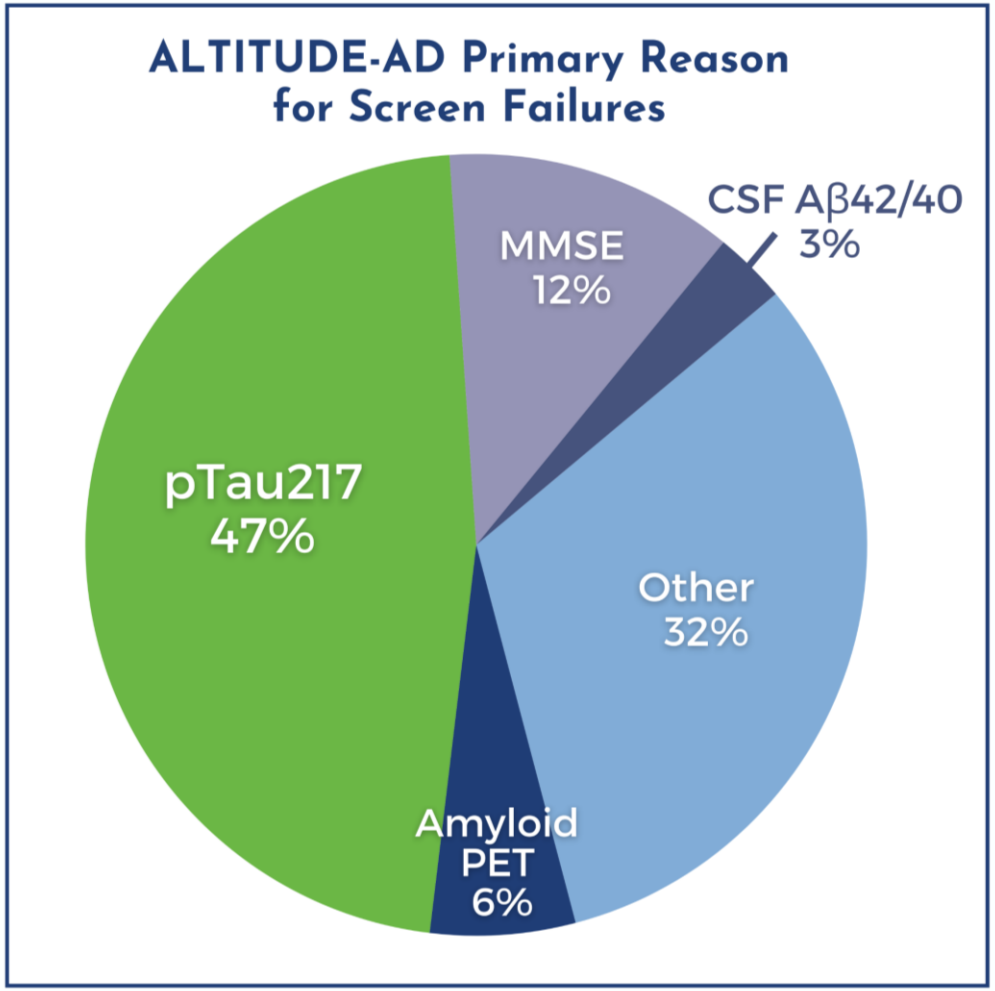
Screening with Plasma pTau217 Greatly Reduced Screen Failure due to Amyloid PET

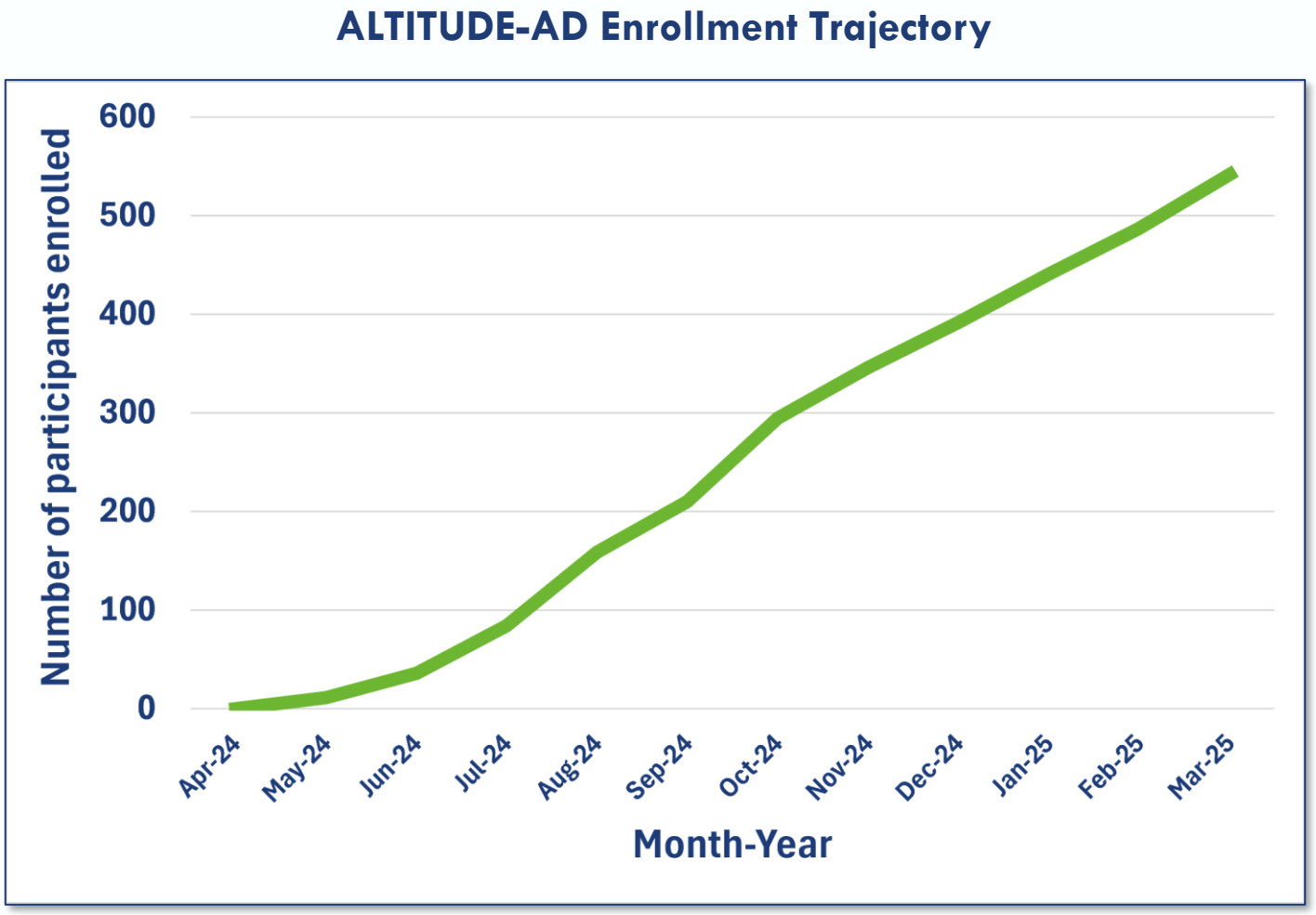


Final US data



Preliminary global data

ALTITUDE-AD Participant Enrollment Completed in 10 Months



- PTau217 screener contributed to the rapid enrollment rate
  - Expect an increase in the use of such blood-based biomarker screeners by clinical practices in the future
- Positive feedback received from site investigators about the study design, patient retention and our team's engagement

Baseline ALTITUDE-AD Characteristics Similar to CLARITY-AD

	ALTITUDE-AD (randomized patients)	CLARITY (active treatment only)*
N	542	859
Age (years) [mean (range) or SD]	73.6 (50-89)	71.4 (+/- 7.9)
Sex (% female)	53.0	51.6
ApoE genotype		
ApoE e4 homozygotes	10.3%	15.8%
ApoE e4 heterozygotes	46.3%	53.1%
ApoE e4 non-carriers	43.3%	31.1%
Global CDR score (screening)		
gCDR = 0.5	83.95%	80.8%
gCDR = 1.0	16.05%	19.2%
CDR-SB mean (SD)	2.91 (1.7)	3.17 (1.34)
MMSE mean (SD)	25.5 (3.2)	25.5 (2.2)
Amyloid PET Centiloids mean (range)	76.7 (-20.4 – 220.3)	77.92 (-16.6 – 213.2)

**Van Dyck et al. Lecanemab in Early Alzheimer's Disease, NEJM, 2022.*

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.

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ALTITUDE-AD Late 2026 Readout: Efficacy, Safety, and Biomarker Profile

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ALTITUDE-AD Takeaways

- Large, well-powered, registration-quality ALTITUDE-AD Phase 2 study currently ongoing
  - Baseline demographics as expected and similar to CLARITY-AD baseline population
  - Two doses studied that have potential to both prove efficacious
- Phase 1 study results demonstrating target engagement of AβOs, normalization of AD biomarkers and low ARIA-E increases potential probability-of-success in Phase 2 study
- PTau217 screener employed in ALTITUDE-AD recruitment contributed to rapid enrollment rate by improving amyloid positivity rate while reducing patient burden and sponsor expenses
- ALTITUDE-AD topline results expected in late 2026, inclusive of efficacy, safety and biomarker data
  - iADRS as primary endpoint established as a sensitive measure incorporating cognitive and functional elements
  - iADRS was successfully used in TRAILBLAZER-ALZ studies

Enhanced Brain Delivery (EBD®) a Promising Next-Generation Pipeline Addition

Paul Shughrue, PhD
VP, Program Lead and Head of Research

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Inherent Challenges with Therapeutic Monoclonal Antibodies and Neurodegenerative Diseases

Blood-Brain Barrier Challenge

Monoclonal antibodies show poor penetration of the blood-brain barrier (BBB), limiting drug delivery to the intended target

High Systemic Dosing Issues

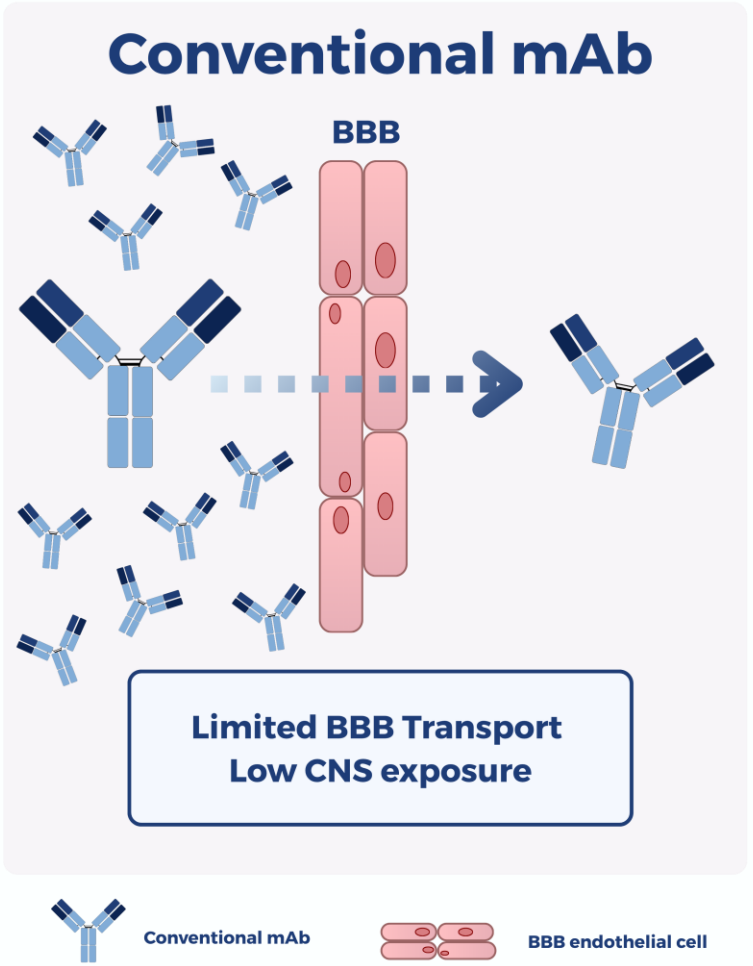
High systemic doses are required to get drug into the brain, doses that may have associated safety and tolerability risks

Amyloid-Related Imaging Abnormalities (ARIA)

ARIA (vasogenic edema and microhemorrhage) arise from conventional antibody interactions with amyloid deposits in the walls of large vessel

Limitations in Brain Distribution

Uneven antibody distribution throughout the brain leads to underdosing in deep brain regions, potentially affecting treatment outcomes



The Use of TfR-Mediated Transcytosis to Shuttle Large Molecules, such as Monoclonal Antibodies, May Help Overcome the BBB Challenge

Active Transport Mechanism

The transferrin receptor (TfR) is expressed in the fine capillary beds on the BBB and is used to transport transferrin/iron into the brain

Enhanced Brain Delivery

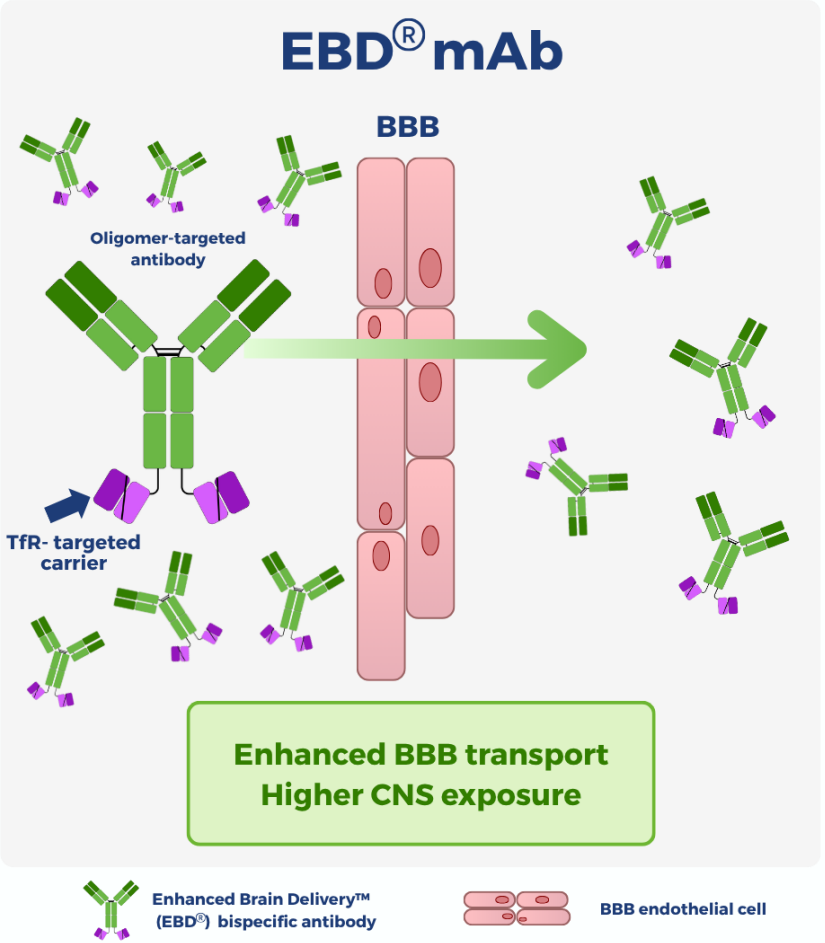
Anti-TfR antibodies and fragments (scFv and VHH) are actively transported across the BBB and can be used to shuttle large molecules into brain

Improved Therapeutic Index

Enhanced delivery of therapeutic antibodies lowers dose, increases amyloid targeting, reduces side effects, and may enable safe and effective treatments

Modular Next-Generation Platforms

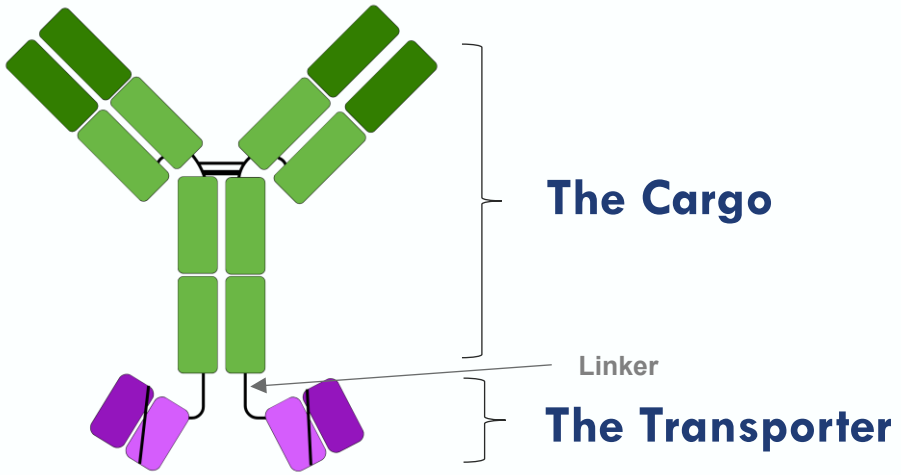
Bispecific antibodies combining anti-amyloid and TfR-binding fragments enable the development of next generation treatments for Alzheimer's disease



Program Concept: Building a Bispecific Antibody

- The Cargo determines the Aβ species (oligomer, monomer, plaque, pyroglutamate) targeted by the bispecific antibody
- Efficacy is dependent on the Cargo

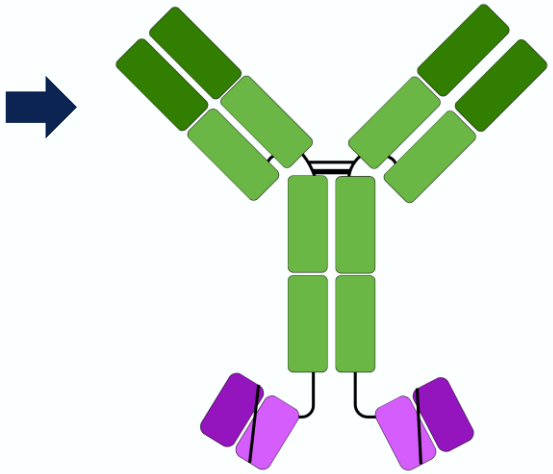
- The Transporter determines the mechanism used to cross the BBB as well as brain PK
- The binding site of the Transporter may have associated safety risks (e.g. anemia)



In building two-sided antibodies, careful consideration was given to both the Cargo and the Transporter since they are both essential for success

Use of anti-Aβ Oligomer Antibodies as the Cargo Differentiates Acumen from Competitors

- Clinical candidate ACU193 and a newly developed anti-AβO antibody ACU234 were both used as "Cargo" in the program
- The use of anti-AβO antibodies as Cargo sets us apart from our competitors



The Cargo

- **ACU193 and ACU234 are highly selective anti-Aβ oligomer antibodies, with ~7,000-20,000x selectivity over Aβ monomers**
- **Selectivity against Aβ monomer binding increases the drug available to bind toxic Aβ species**

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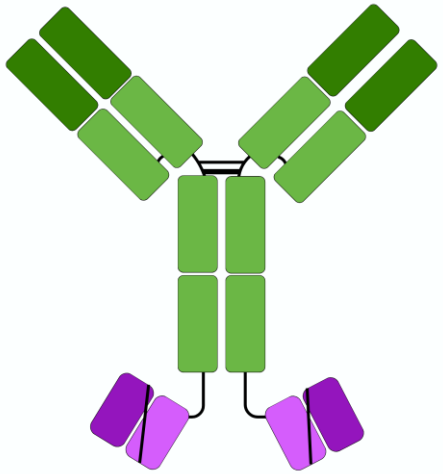
Use of a Proven TfR Transporter Increases the Chance of Success and Reduces the Risk of Anemia

- The Anti-TfR scFv and VHH "Transporter" used is a fragment of JCR's approved drug IZCARGO
- IZCARGO binds TfR efficiently, low nM range, and is readily transported into brain



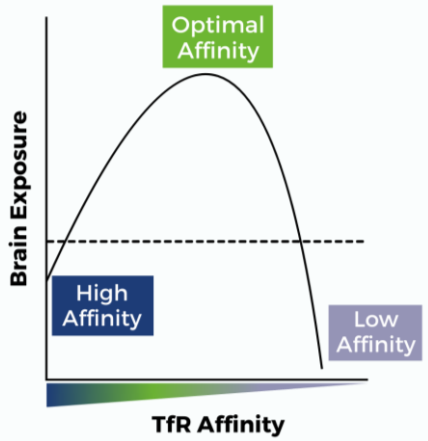
The Transporter

- **The little to no anemia seen in patients treated with IZCARGO may be associated with the unique binding site on TfR**
- **Anemia in Alzheimer's patients could lead to unwanted safety concerns**

Identification of Program Leads from a Diverse anti-TfR Fragment Library

TfR Affinity

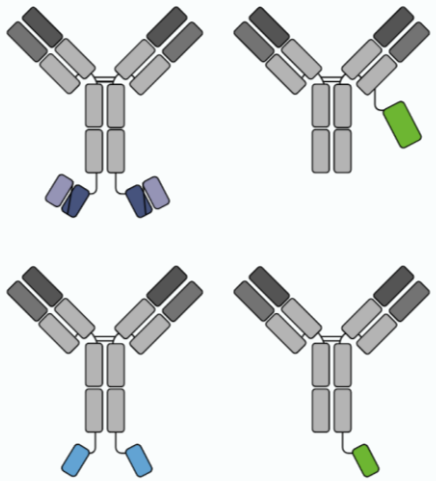
Affinity Range



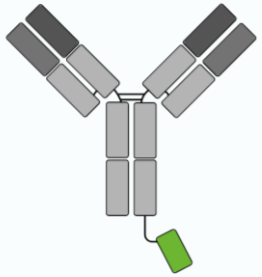
Architecture

scFv or VHH

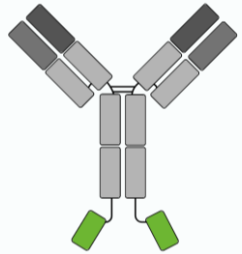
Heavy Chain vs Light Chain



Valency



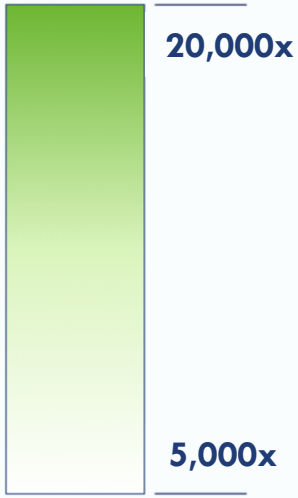
Monovalent



Bivalent

AβO Selectivity

Selectivity Range



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

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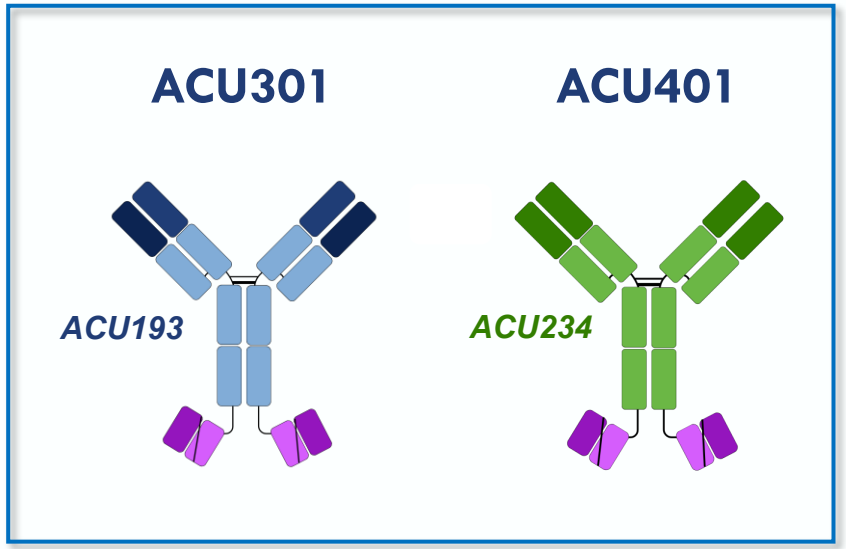
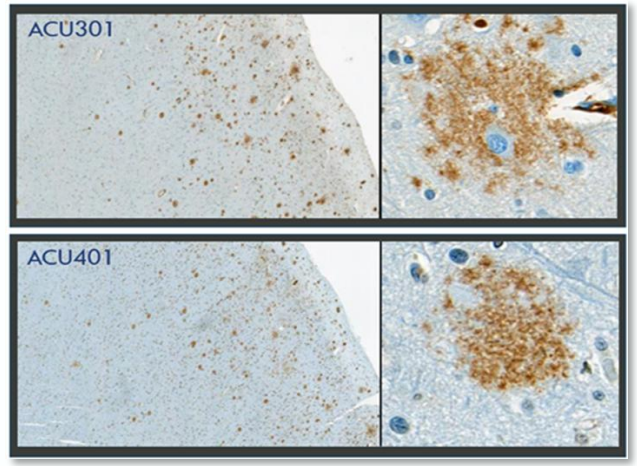
Program Leads: ACU301 and ACU401

- ACU301 and ACU401 have high affinity for hTfR, 2.81 nM and 2.35 nM, and release into the parenchyma after dosing
  - The high affinity binding to TfR enables the use of small doses of antibody to deliver meaningful drug levels into the brain
- ACU401 uses a novel anti-AβO antibody ACU234 as cargo
  - ACU234 has pM affinity for oligomers and ~ 20,000x specificity versus Aβ monomers*
  - ACU401 has excellent stability and is well-suited for an autoinjector and 4°C storage
- Studies in rodents and primates have shown ACU301 and ACU401 are rapidly taken up after SC dosing and widely distributed throughout brain parenchyma
- Histochemical studies with AD samples demonstrated ACU301 and ACU401 bind native Aβ species of interest in the cerebral cortex

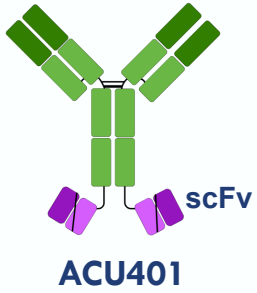




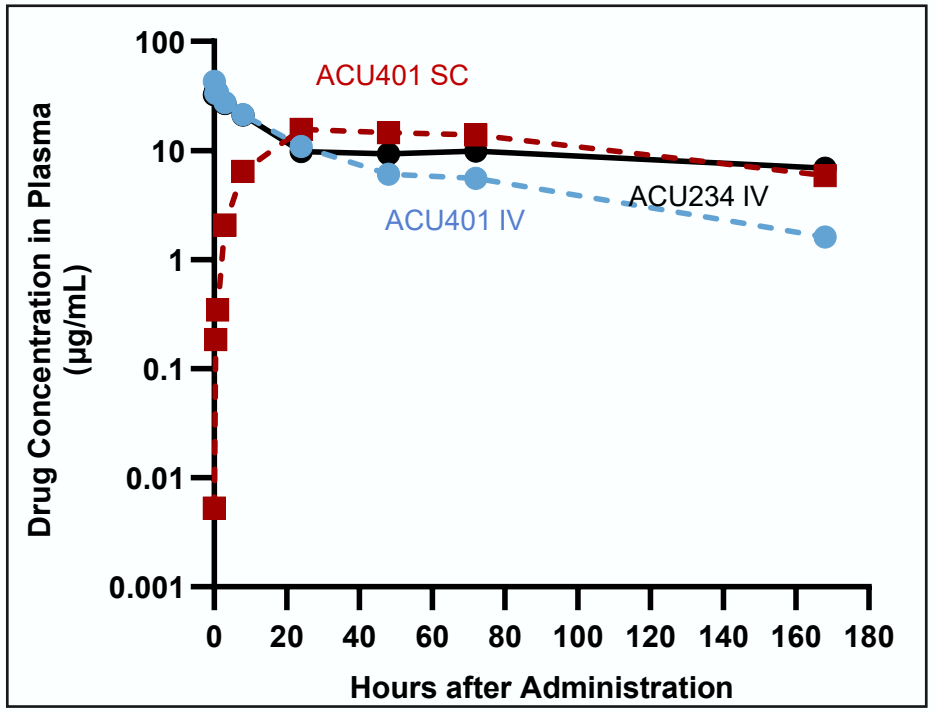
SC: subcutaneous

**Cline et al., AAIC 2026.*

Program Leads Had Excellent Plasma PK and High Brain Exposure After SC Dosing of hTfR Transgenic mice

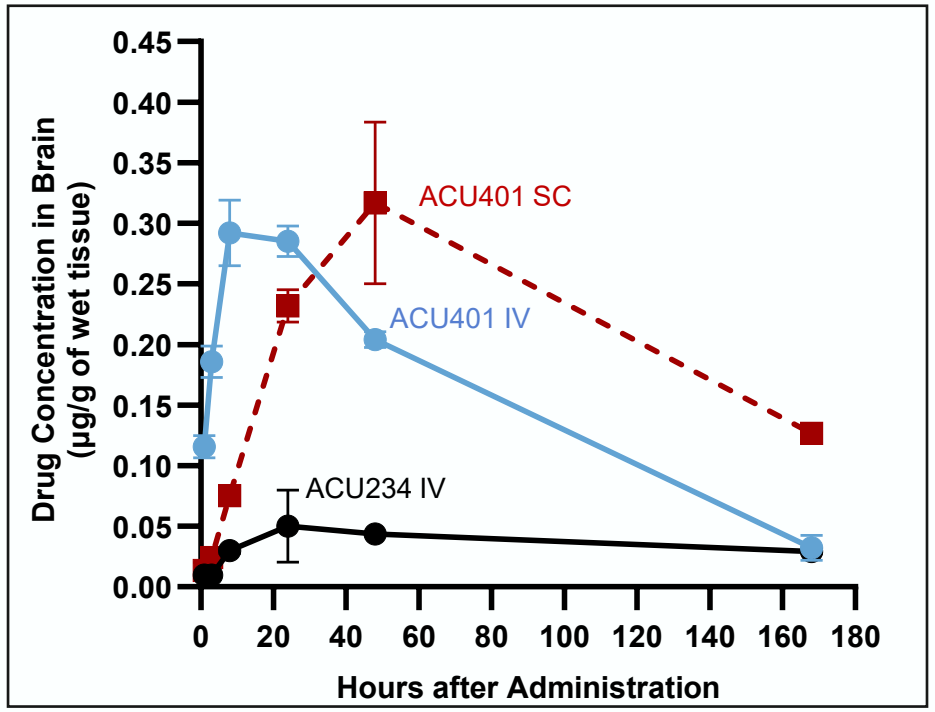


Plasma PK



Human (+/-) TfR mice dosed 2 mpk (IV) or 5 mpk (SC)

Brain PK

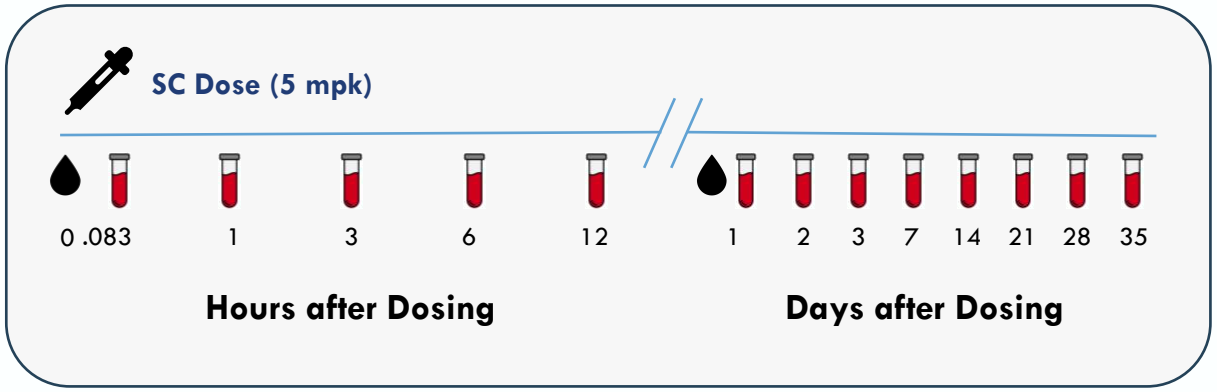


Cline et al., AAIC 2026.

- After SC dosing, antibodies had excellent PK profiles in plasma, with high C_{MAX} and slow clearance
- Comparison of plasma and brain PK suggests a direct relationship between the two compartments

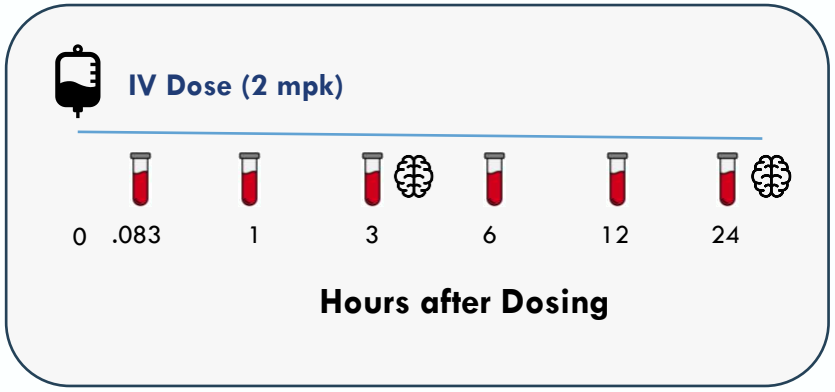
Cross-Over Study to Investigate the Plasma and Brain PK Profile after SC vs. IV Dosing in Cynomolgus Monkeys

SC Dosing Arm



All NHPs Crossed Over to IV Arm

IV Dosing Arm

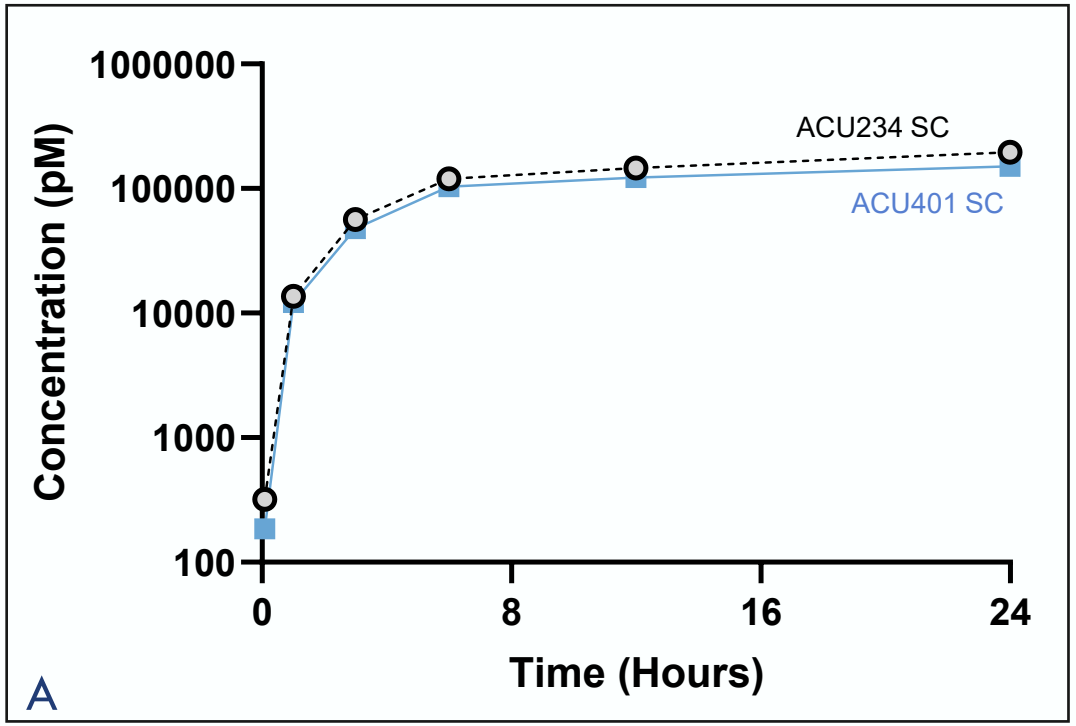


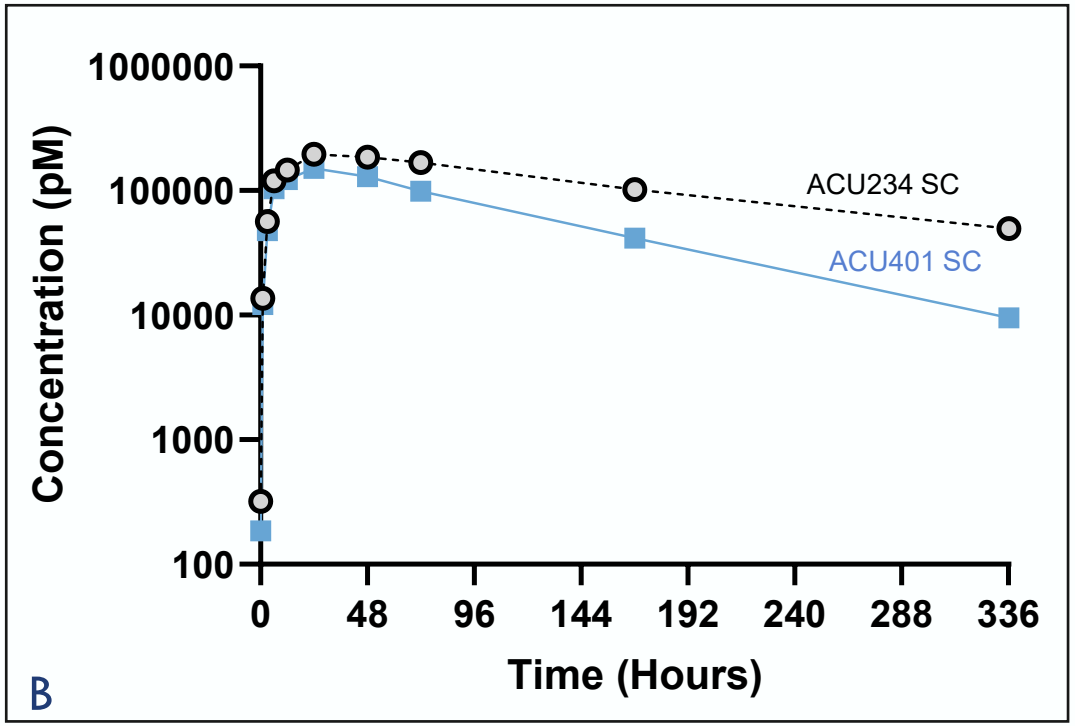
Hematology | Collect Plasma | Collect brain / CSF

Groups (n=3/ group)

- 3 hours post IV dose:
  - ACU234 mAb
  - ACU401 EBD
- 24 hours post IV dose:
  - ACU234 mAb
  - ACU401 EBD

Robust and Rapid Uptake of ACU401 in Plasma after SC Dosing



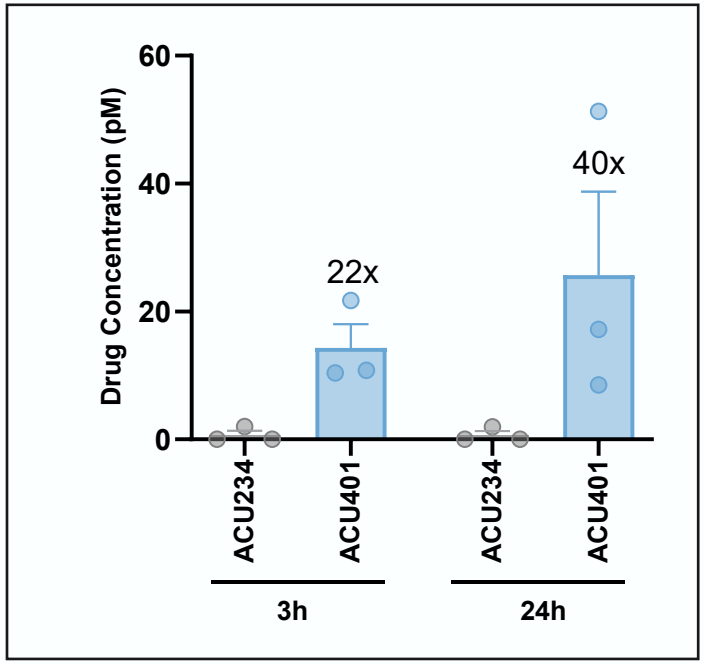


Shughrue et al., AAIC 2026

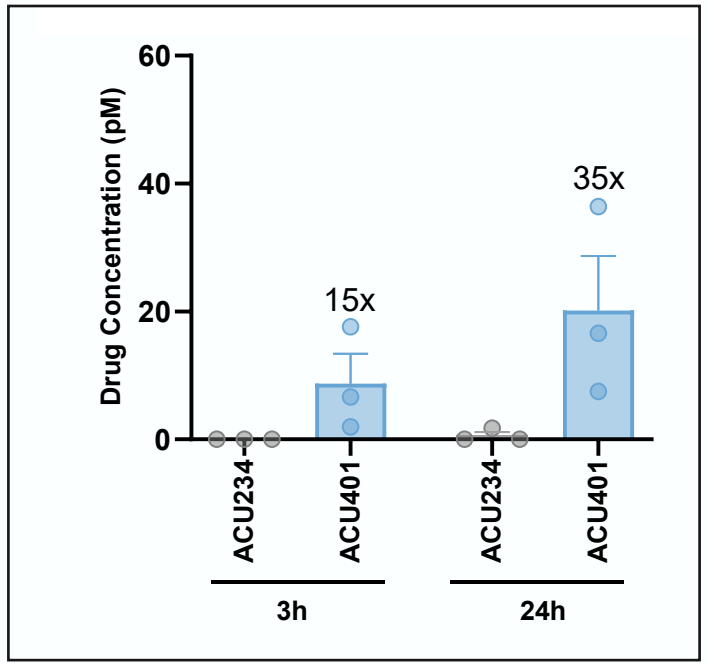
- After SC dosing, ACU401 was rapidly taken up in plasma and had a good PK profile
- The rapid uptake of ACU401 into brain after SC dosing reduces the need for an extended half-life as is typical for molecules that have poor BBB penetration
- The plasma levels of ACU401 14 days after dosing suggests optionality for human dosing

Analysis of Three Brain Regions Showed a 35 – 40x Enhancement of ACU401 Delivery Compared to Monoclonal Antibody ACU234

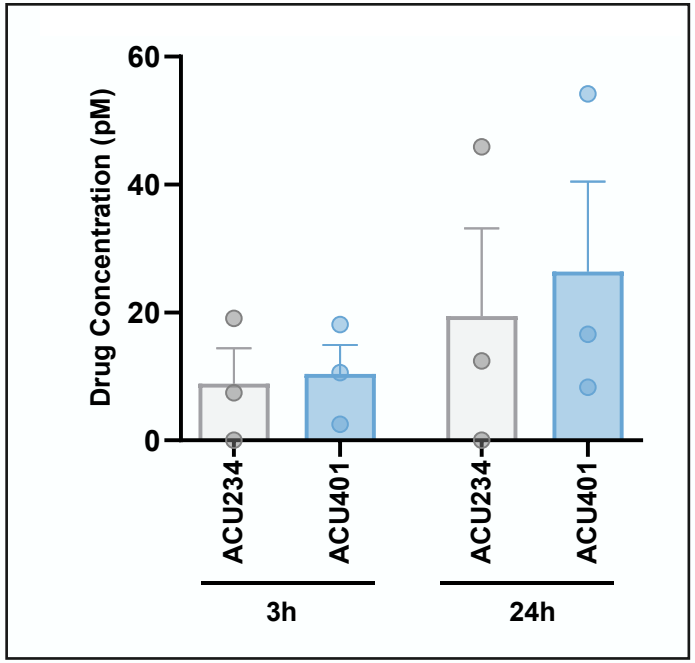
Prefrontal Cortex



Putamen



Hippocampus*



** Observed unexpectedly high levels of ACU234 in hippocampal samples (perhaps caused by contamination or sampling error). Currently running a confirmatory NHP study.*

Shughrue et al., AAIC 2026

- Antibody is rapidly delivered throughout the brain including deep brain regions
- CSF levels were not different among groups (not shown), reinforcing the selective delivery to brain

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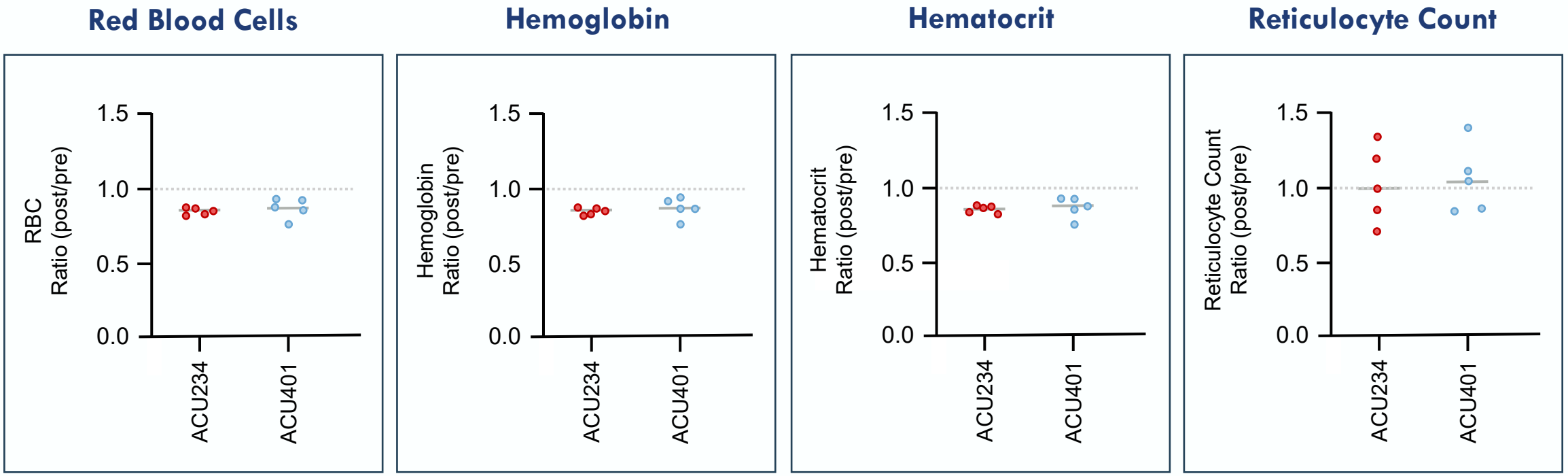
Analysis of a Panel of Hematology Endpoints after SC Dosing of Monkeys Suggest a Low Risk for Anemia



Shughrue et al., AAIC 2026

- Analysis of a panel of hematological endpoints showed no impact on any measure assessed 24 hours after ACU401 dosing
- The present results suggest that ACU401 has a low risk of anemia

Key Takeaways from the NHP Study

✓ Robust Brain Delivery of ACU401

The EBD candidate achieved up to 40x higher brain exposure and extensive brain distribution compared to the monoclonal antibody ACU234

✓ Low Anemia Risk

A hematology panel showed no meaningful changes after SC dosing with ACU401 and suggests a low risk for anemia

✓ Subcutaneous Dosing Capability

Favorable stability data, PK profile and enhanced brain delivery support SC administration with a low-volume device

Lead Candidates Achieved Requirements to Move Forward with Development

	EBD Program: *Lead Candidate Profile*	
BBB Penetration	Up to 40x monoclonal antibody levels	✓
Oligomer Binding	High selectivity versus monomer	✓
TfR Binding	High affinity binding to TfR & release into parenchyma	✓
Anemia	None observed; differentiation from competition	✓
Stability	Good stability, amenable to use with an autoinjector	✓
SC Dosing	Data supports a standard, low volume SC device	✓

Profile ideally suited for early AD and pre-clinical AD

BBB: blood-brain barrier

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Next Steps

- Complete a follow-on PK study in cynomolgus monkeys with ACU301 and ACU401 to assess the uptake of bispecific antibody after SC dosing
  - The results will be used to select doses for the planned Phase 1 EBD clinical study for the lead candidate
- Additional IND enabling studies, including supportive CMC work
- Develop bioanalytical assays needed for clinical trials (PK, ADA, etc.)
- Continue interactions with the agency

Lead clinical candidate IND filing targeted for mid-2027

Q&A

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