UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 4, 2023

Acumen Pharmaceuticals, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40551**	**36-4108129**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

427 Park St., Charlottesville, Virginia	**22902**
(Address of Principal Executive Offices)	**(Zip Code)**

(434) 297-1000
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value	**ABOS**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On December 4, 2023, Acumen Pharmaceuticals, Inc. (the "**Company**") posted an updated corporate presentation to its website at https://investors.acumenpharm.com/news-events/presentations, which the Company may use from time to time in communications or conferences. This corporate presentation was updated to include plasma biomarker data from the Company's Phase 1 INTERCEPT-AD trial. A copy of the corporate presentation is attached as Exhibit 99.1 to this Report.

The information in this Item 7.01 of this Report (including Exhibit 99.1) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d). Exhibits

Exhibit No.	Description
99.1	Corporate Presentation, dated December 4, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Company has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Acumen Pharmaceuticals, Inc.

Dated: December 4, 2023

By: /s/ Matthew Zuga
Matthew Zuga
Chief Financial Officer and Chief Business Officer

Corporate Presentation

December 2023

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Any statement describing Acumen's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Words such as "believes," "expects," "anticipates," "could," "would," "seeks," "aims," "plans," "potential," "will" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements concerning Acumen's business, and Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the expected sufficiency of its cash resources into the second half of 2026, the therapeutic potential of Acumen's product candidate, ACU193, including against other antibodies, the anticipated timeline for initiating a Phase 2 clinical trial of ACU193 and a Phase 1 trial to support a subcutaneous dosing option of ACU 193, and the expected use of proceeds from a credit facility. 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 a Potential Best-In-Class Antibody Product for Early Alzheimer's disease (AD)

- Large market
- High unmet need
- Recent scientific & regulatory momentum

- Amyloid-beta oligomers (AβOs) accepted as most toxic form of Aβ
- ACU193: First, clinical-stage monoclonal antibody (mAb) to selectively target AβOs

- Experienced leadership team
- AD clinical, drug development, & regulatory leaders from Eli Lilly & Co.

- Strong balance sheet: ~$283M in cash at 30-Sep-23
- Up to $50M credit facility announced in Nov-23

- Positive topline results from Phase 1 clinical trial in early AD patients presented in July 2023

- Expect initiation of Phase 2 ALTITUDE-AD trial in 1H 2024
- Expect initiation of Phase 1 subcutaneous trial in mid-2024

We believe that Acumen has the organizational expertise and financial resources to advance ACU193 as a potential best-in-class antibody product for early AD

Acumen Business Strategy: 2023 - 2026

- → Rapidly advance ACU193 through clinical development in patients with early AD;
- → Evaluate combination approaches to complement our core ACU193 monotherapy strategy;
- → Expand our product portfolio by in-licensing and/or developing additional candidates and/or alternative formulations for, or derivatives of, ACU193; and
- → Optimize value of ACU193 and future drug candidates in major markets.

AD, Amyloid & Abeta Oligomers

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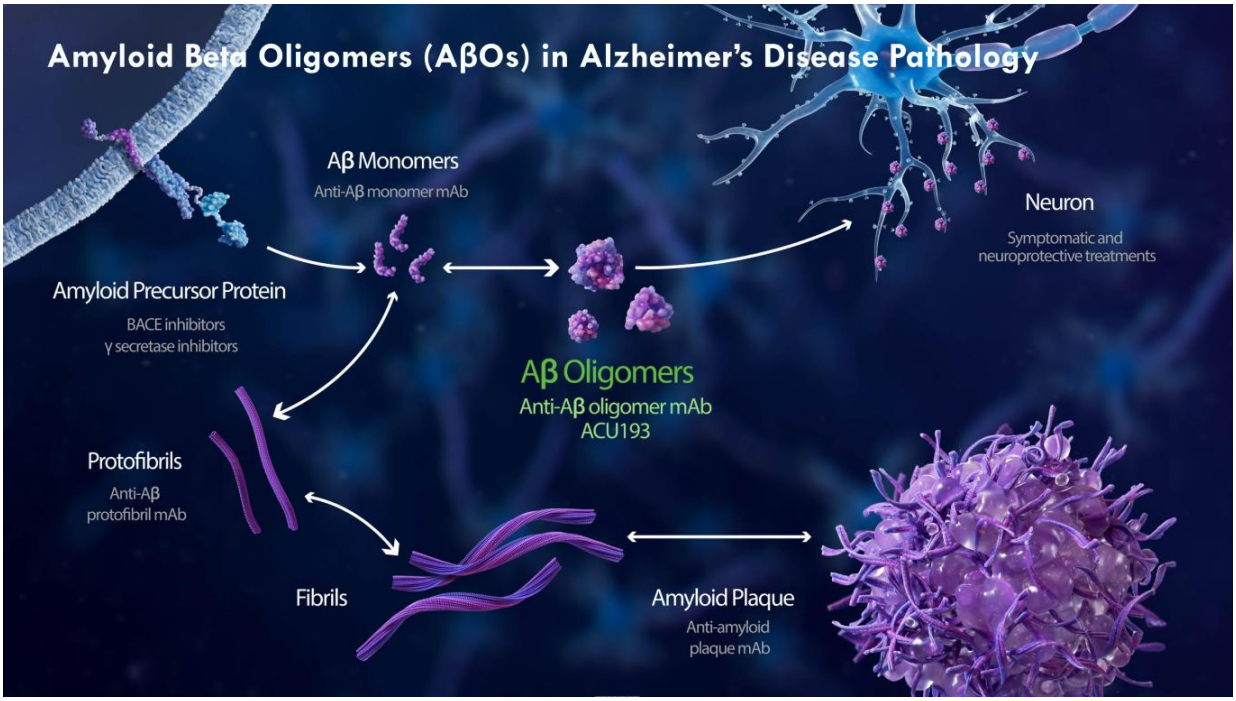

Amyloid Beta Oligomers (AβOs) in Alzheimer's Disease Pathology
Aβ Monomers
Anti-Aβ monomer mAb
Neuron
Symptomatic and
neuroprotective treatments
Amyloid Precursor Protein
BACE inhibitors
γ secretase inhibitors
Aβ Oligomers
Anti-Aβ oligomer mAb
ACU193
Protofibrils
Anti-Aβ
protofibril mAb
Fibrils
Amyloid Plaque
Anti-amyloid
plaque mAb

Toxic AβOs Represent an Ideal Alzheimer's Disease Drug Target

AβOs are widely recognized as key pathogenic structures in AD

1 Impair synaptic function[1]

Pyramidal neurons in rat organotypic slices had markedly decreased density of dendritic spines and numbers of electro-physiologically active synapses after exposure to picomolar levels of soluble oligomers[2]

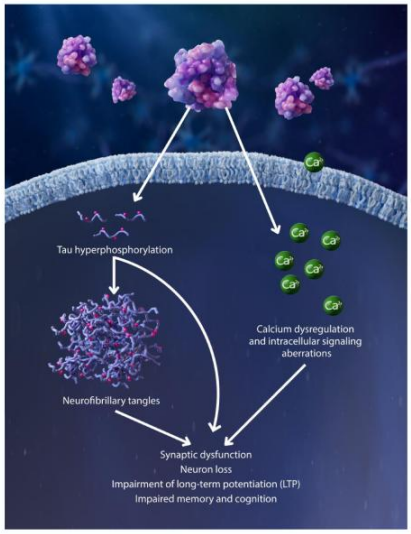
2 Contribute to impairment of memory and cognition[3]

Soluble AβOs (but not monomers) have been found to block hippocampal long-term potentiation (LTP), a synaptic correlate of memory and learning[4]

3 Induce tau hyperphosphorylation[5]

It was demonstrated in 2008 that AβOs were capable of inducing tau hyperphosphorylation in cultured neurons in the absence of fibrils[5]

[1]Cleary et al., 2005; Townsend et al., 2006; Poling et al., 2008; Reed et al., 2011; Batista et al., 2018.
[2]Shankar et al., 2007.
[3]Ferreira, S. T., and Klein, W. L., 2011.
[4]Lambert et al., 1998; Walsh et al., 2002; Wang et al., 2002; Klyubin et al., 2005; Townsend et al., 2006; Shankar et al., 2007, 2008.
[5]De Felice et al., 2008; Zempel et al., 2010; Ochalek et al., 2017.



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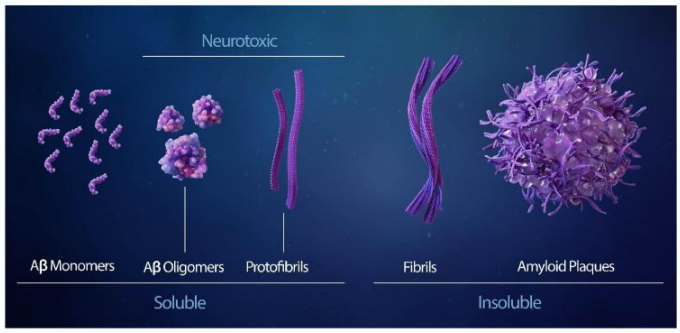
ACU193: A Monoclonal Antibody that Selectively Binds Toxic AβOs

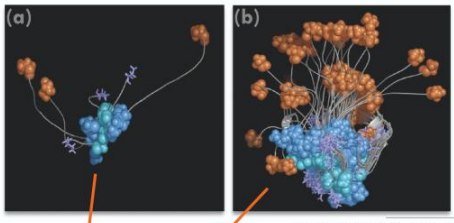
- Humanized, affinity matured mAb developed to target toxic Aβ oligomers
  - >500-fold greater selectivity for AβOs over Aβ monomers
  - >85-fold selectivity for AβOs over Aβ fibrils
- IgG2 subclass mAb with reduced effector function
  - Potential for more selective targeting of AβOs and lower ARIA-E relative to Aβ plaque directed mAbs
- ACU193 discovered as part of research collaboration between Acumen and Merck & Co.
  - Currently developed by several former senior members of Eli Lilly's global Alzheimer's development team
- ACU193 has been granted Fast Track designation for the treatment of early Alzheimer's disease by the U.S. FDA



ACU193's high selectivity for toxic AβOs may provide meaningful cognitive efficacy and improved safety and tolerability

What is an Aβ Oligomer? AβOs May Consist of 2 to >200 Aβ Peptides

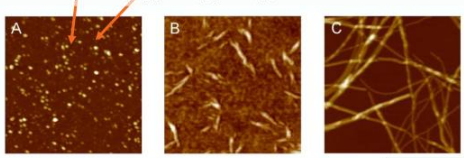
Figure 1. AβOs composed of 3 (a) and 18 (b) Aβ peptides are depicted below.



Source: Kelley et al. J Chem Physics 2008.

Quaternary structures of Aβ oligomers, protofibrils, and fibrils

Figure 2. Atomic force microscopy images of representative steps of amyloid aggregation: (A) oligomers; (B) protofibrils; (C) mature fibrils. Scan size 1.0 μm. Z range (A) 8.0 nm; (B) 15 nm; (C) 20 nm.



Source: Relini et al. Biomolecules 2014.

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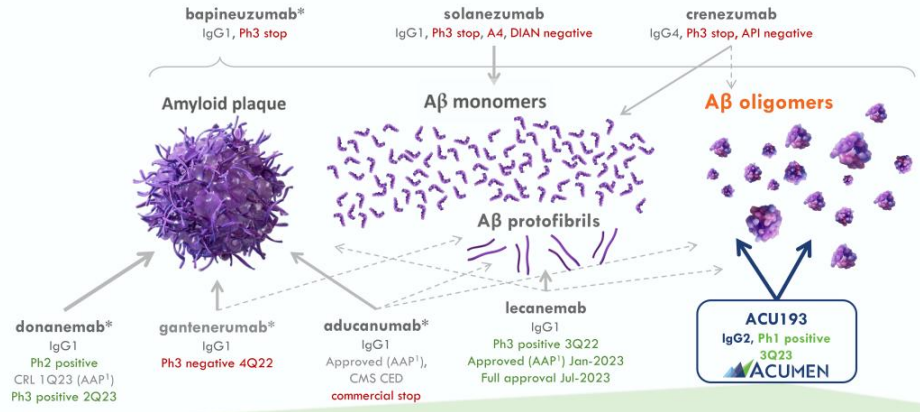
ACU193 Positioning Relative to Late-Stage and Approved Anti-Aβ/Plaque mAbs



ACU193's high selectivity for AβOs combined with an expected low rate of ARIA in subsequent studies is anticipated to provide a better safety and efficacy profile compared to anti-plaque mAbs

* IgG1 monoclonal antibodies that bind amyloid plaque are associated with high rates of ARIA-E. See e.g., *Plotkin, Neurobiology of Disease*, 2020.

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

[1] AAP: Accelerated approval

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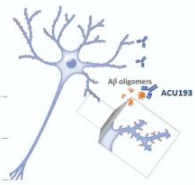
ACU193 Target Product Profile: Best-in-Class, 1st Line, Anti-AβO, Disease-Modifying Immunotherapy for Early AD

DRUG:	ACU193 is a humanized, affinity-matured, mAb with high selectivity for toxic **AβOs vs. Aβ monomers (>500x)**, >85-fold selectivity for AβOs over Aβ fibrils **ACU193 is an IgG2 subclass** mAb which has a reduced effector function.
POPULATION:	Early AD - Mild Cognitive Impairment and Mild Dementia due to AD (amyloid positive by PET)
DOSING:	IV infusion every 4 weeks
DURATION:	Chronic therapy for duration of Early AD
VALUE PROPOSITION:	**Selectivity for toxic AβOs may provide meaningful cognitive efficacy** and an **improved safety and tolerability** profile relative to non-selective anti-Aβ/plaque mAbs, including: • Slowing the decline of memory and cognition in Early AD • Decreasing AβO induced synaptic and neuronal network toxicity • Slowing disease progression and downstream effects on tau, neurodegeneration, and neuro-inflammation • With expected low rate of ARIA in subsequent studies • Potentially effective as stand-alone therapy or in combination with other symptomatic, anti-inflammatory, and/or tau directed therapies



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Comparative Profiles of Recent and Current Anti-Aβ Antibodies in Development

Company	Asset	mAb epitope / isotype[4]	Aβ Target Selectivity[1][2]				Safety Profile	Efficacy Profile
			monomers	plaque	fibrils	oligomers	ARIA-E[4]	
ACUMEN	**ACU193**	**N-term, Confirmational IgG2**	-	-	+	+++++	Expected Low in Phase 2	TBD
Eisai / Biogen	Leqembi™	N-term, Confirmational IgG1	-	+++	++++ Protofibrils	+++	Low	Positive Ph2 and Ph3 CLARITY-AD
Lilly	donanemab	N3pG IgG1	-	+++++	+++	-	High	Positive Ph2 and Ph.3 TRAILBLAZER
Biogen	Aduhelm™	N-term IgG1	-	+++++	++ Protofibrils	++	High	Ph3 Emerge Positive, Engage Negative
Roche	gantenerumab[3]	N-term + Mid domain IgG1	-	+++++	+++	++	High	Ph3 Negative
Lilly	solanezumab[3]	Mid domain / IgG1	+++++	-	-	-	None	Ph3 Negative, trends; A4 negative
Roche / Genentech	crenezumab[3]	Mid domain / IgG4	++++	-	++	+++	None	Ph3 Negative, no trends
Pfizer / Janssen	bapineuzumab[3]	N-term IgG1	++	+++	++	++	High	Ph3 Negative

(1) There have been no head-to-head trials between any of the product candidates listed above. Study designs and protocols for each product candidate were different, and results may not be comparable between product candidates.
(2) Goure et al. (2014). Targeting the proper amyloid-beta neuronal toxins: a path forward for Alzheimer's disease immunotherapeutics. Alzheimer's Research & Therapy. 6:42. DOI: http://alzres.com/content/6/4/42.
(3) Phase 3 discontinued for primary AD indication.
(4) van Dyck, C. (2017). Anti-Amyloid-b Monoclonal Antibodies for Alzheimer's Disease: Pitfalls and Promise. Biological Psychiatry. 83:4, 311-319. DOI: https://doi.org/10.1016/j.biopsych.2017.08.010.

ACU193: Value Proposition

The Alzheimer's disease market is at a **key inflection point** with **recent and expected approvals** paving a new path for the treatment of AD …

… and **ACU193** is well-positioned to emerge as a potential **treatment of choice.**

Market will likely remain consolidated with Aβ therapies emerging as the primary treatment option over the next few years

Stakeholders are encouraged about the advancements in the AD treatment landscape and are working together to enable broader patient access

With potential clinical and safety benefits conferred by AβO selectivity, ACU193 has the opportunity to be a treatment of choice in the broader early AD population

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Positive INTERCEPT-AD Phase 1 Results for ACU193

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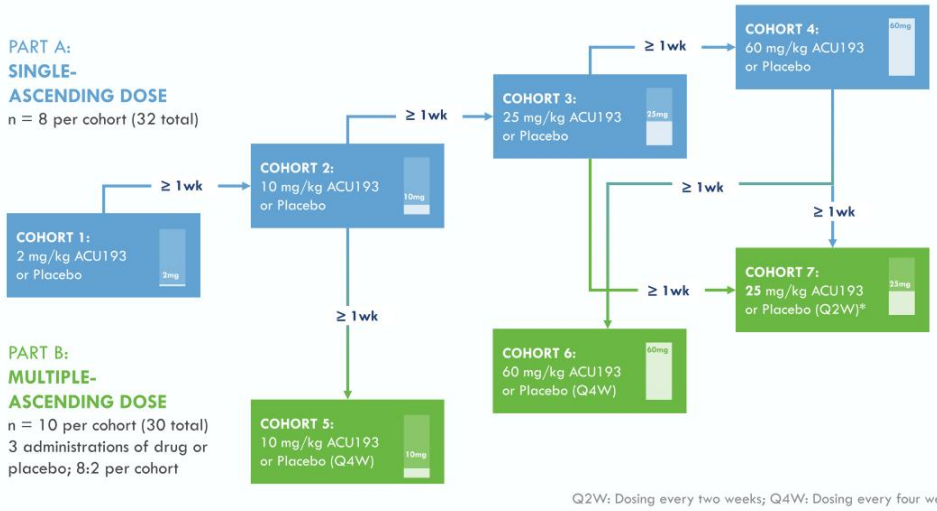
INTERCEPT-AD: A Randomized Placebo Controlled Phase 1 in Early AD patients



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

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INTERCEPT-AD Results Confirm Proof of Mechanism for ACU193 and Demonstrate Reduction in Amyloid Plaques at Higher Doses Studied

1. **Rapid, dose-related, statistically significant amyloid plaque reduction observed at higher doses studied (60 mg/kg Q4W and 25 mg/kg Q2W cohorts)***
   - Comparable to currently approved Aβ monoclonal antibodies at similar time points in their clinical development
2. **First antibody to demonstrate target engagement of Aβ oligomers, the most toxic form of amyloid beta, in a dose-related manner**
   - Serum and CSF exposure are dose proportional; antibody concentrations significantly exceeded levels of endogenous oligomers in the CSF
   - Highest doses studied (25 mg/kg Q2W and 60 mg/kg Q4W) approached maximal target engagement (23.2 AU/mL Emax)
3. **Compelling overall safety profile, with low rate of ARIA-E**
   - No known drug-related SAEs; treatment emergent ADAs consistently low titer
   - No cases of symptomatic ARIA-E at 10 mg/kg Q4W and 25 mg/kg Q2W doses
   - No ARIA-E observed in ApoE4 homozygotes (n=6)
4. **Broad therapeutic index; clear path to more convenient monthly dosing regimen**

*Statistically significant reduction from baseline to endpoint within cohorts (p = 0.01)

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Proof of Mechanism Demonstrated

Low Levels of ARIA-E, Dose-Related Target Engagement, CSF ACU193 Levels Exceeding AβO Levels, Supporting Q4W Dosing

		Potentially Therapeutic Doses		
Endpoint	**Critical Success Factors**	**10mg/kg**	**25mg/kg**	**60mg/kg**
Safety & Tolerability	• Deaths, SAEs Related to Study Drug	**None**	**None**	**None**
	• Any ARIA-E	1/14 (7.1%)	1/14 (7.1%)	3/14 (21.4%)
	• Symptomatic ARIA-E	0/14 (0.0%)	0/14 (0.0%)	1/14 (7.1%)
PK	• Consistent Dose-Related PK • CSF Exposure Above Endogenous CSF Oligomer Levels	**Achieved** *(**Significantly Higher** than Reported Aβ Oligomer Levels)*	**Achieved** *(**Orders of Magnitude Higher** than Reported Aβ Oligomer Levels)*	**Achieved** *(**Orders of Magnitude Higher** than Reported Aβ Oligomer Levels)*
Target Engagement	• Measurement of ACU193-Aβ Oligomer Complex in CSF	**Measurement Achieved**	**Dose-Related; Nearing Max Target Engagement**	**Dose-Related; Nearing Max Target Engagement**
Amyloid PET	• Reduction in Amyloid PET in Centiloids	**No Reduction Observed**	**Reduction within MAD Cohort** *($p = 0.01$)*	**Reduction within MAD Cohort** *($p = 0.01$)*

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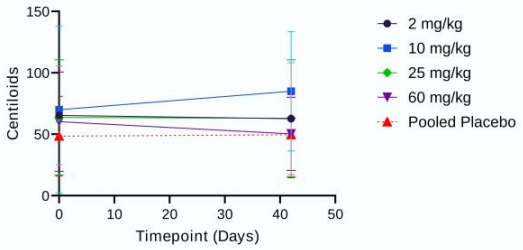
Aβ PET: Mean Changes in Amyloid Plaque in SAD and MAD Cohorts

Single Dose Cohorts

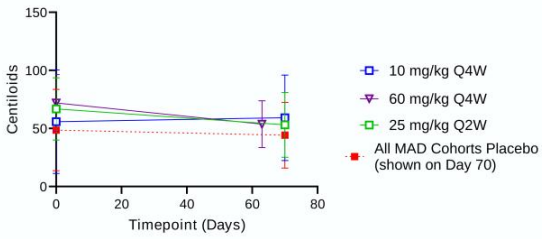
PET Centiloids at Baseline and Endpoint
SAD



Means ± SD.

Multiple Dose Cohorts+

PET Centiloids at Baseline and Endpoint
MAD



Means ± SD.

Rapid, dose-related, statistically significant reduction of plaque load based on florbetapir PET present in 60 mg/kg Q4W and 25 mg/kg Q2W cohorts

+p=0.01 from baseline to endpoint within cohorts 6 (60mg/kg Q4W) and 7 (25mg/kg Q2W); n=6 on placebo, and change observed in placebo cohort was not statistically significant

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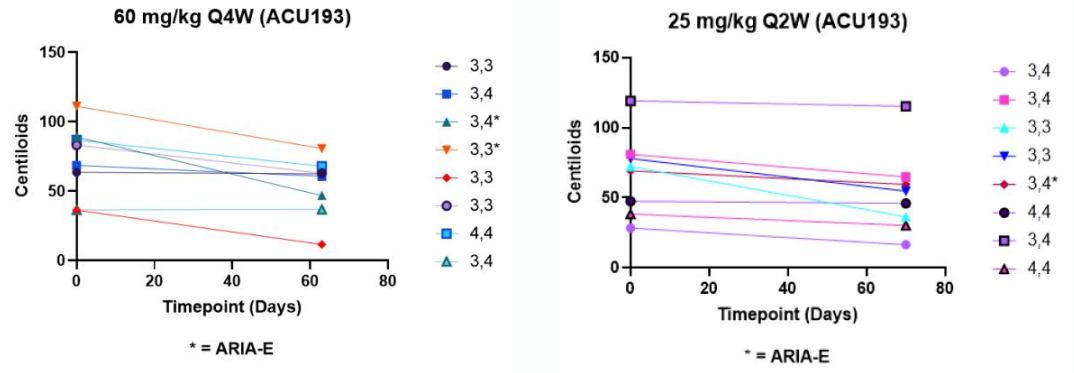
Aβ PET: Individual Patient Changes in Amyloid Plaque in Cohort 6 at 60 mg/kg Q4W and Cohort 7 at 25 mg/kg Q2W



Majority of patients in 60 mg/kg Q4W and 25 mg/kg Q2W cohorts showed reductions in plaque load after 63 or 70 days

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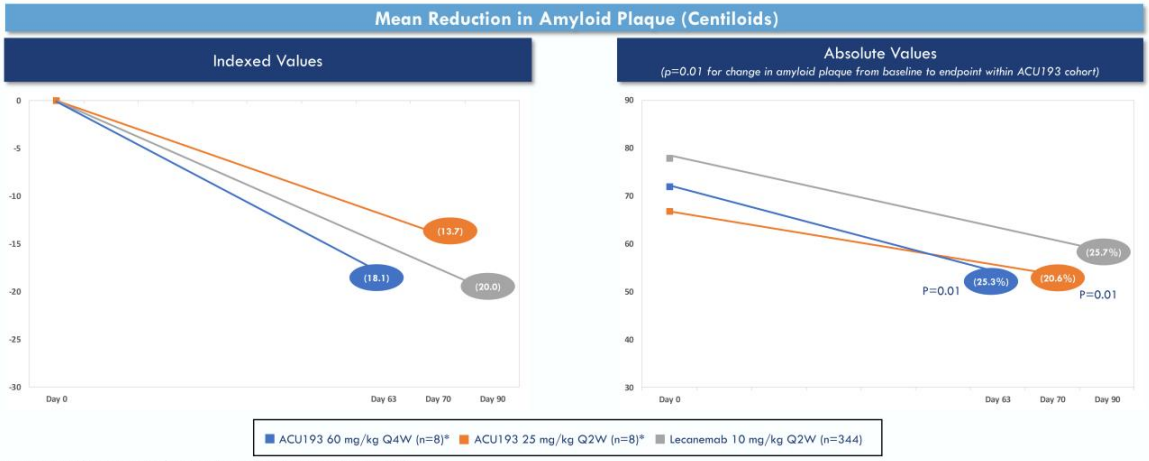
EXPLORATORY MEASURES

Highest Doses of ACU193 Demonstrate Rapid Reduction in Amyloid Plaque Reduction Comparable to Lecanemab (in Phase 3) at Similar Timeframe



*Statistically significant reduction from baseline to endpoint within cohort (p = 0.01).

Source: Acumen Pharmaceuticals, data on file; van Dyck (2023), NEJM (amyloid PET reduction estimated from graphs); Cumulative drug administered: ACU193 60mg/kg = 180 mg/kg (three doses administered); ACU193 25mg/kg = 75mg/kg (three doses administered)

Note: 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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ARIA-E Summary for INTERCEPT-AD

SAD

2 mg/kg *Cohort 1*

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

10 mg/kg *Cohorts 2, 5*

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

25 mg/kg *Cohorts 3, 7*

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

60 mg/kg *Cohorts 4, 6*

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

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

MAD

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

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

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

PBO: Patient on placebo

No ε4 homozygotes developed ARIA-E despite comprising 13% in study;
4/5 ARIA-E cases are ε4 heterozygotes which comprise 47% of our study population

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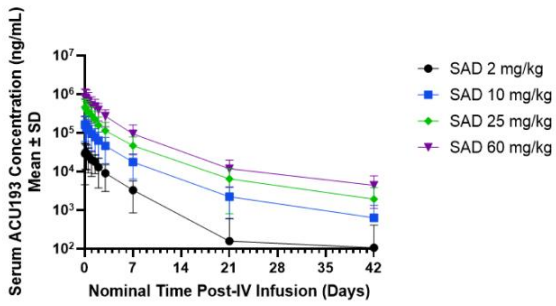
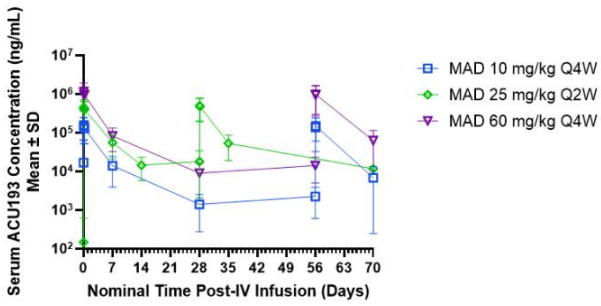
PHARMACOKINETICS

ACU193 Serum PK

Single Dose Cohorts



Multiple Dose Cohorts



Serum exposure is dose proportional without accumulation

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

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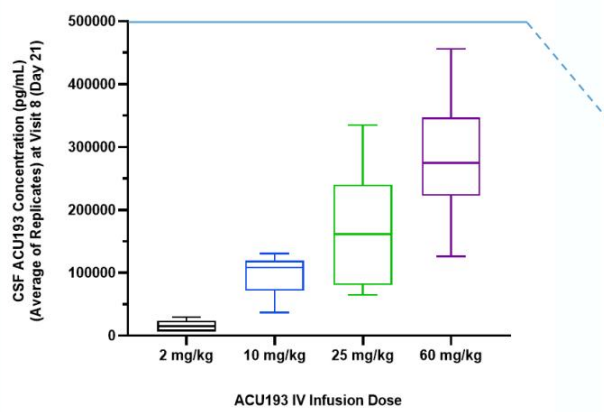
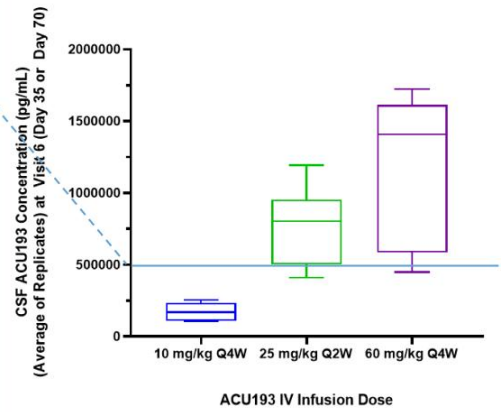
PHARMACOKINETICS

Dose-Related CSF ACU193 Exposure: Above Endogenous CSF AβO Levels

Single Dose Cohorts



Multiple Dose Cohorts*



CSF exposure is dose & dose-regimen proportional

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

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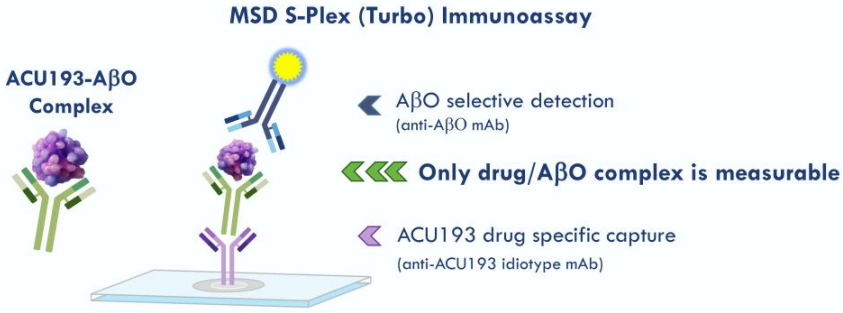
Target Engagement Assessed by Measuring ACU193-AβO Complex in CSF



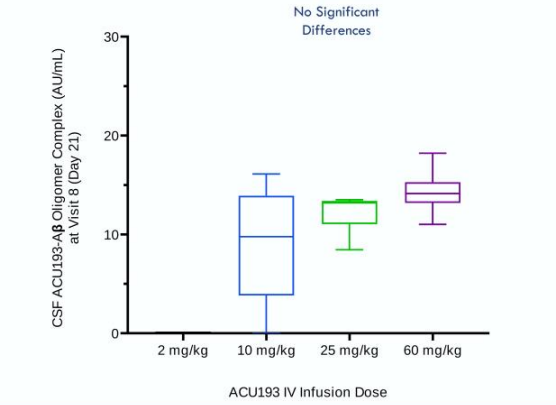
Novel assay configuration tailored to selectively detect ACU193-AβO complex in CSF as direct measure of target engagement

ACUMEN

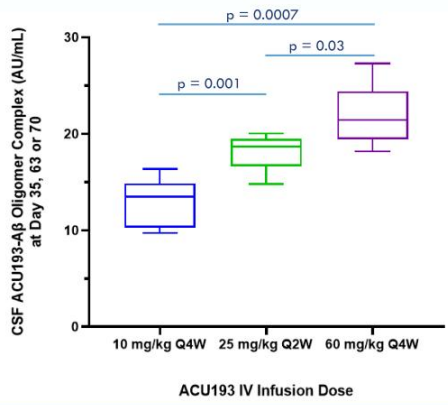
TARGET ENGAGEMENT

Target Engagement of ACU193 with AβOs is Dose Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



Dose-related target engagement

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

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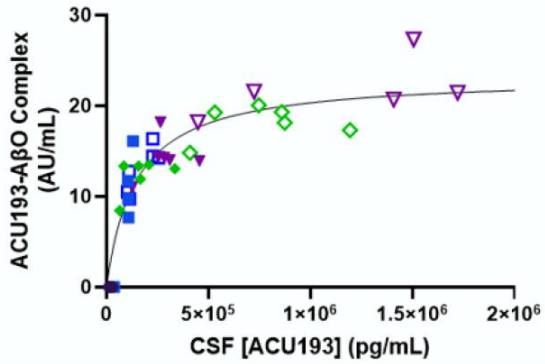
Maximal TE Response Observed at Doses of 25 mg/kg Q2W and 60 mg/kg Q4W

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



Emax: 23.2 AU/mL ACU193-AβO complex
EC50: 1.43 x 10^5 pg/mL ACU193

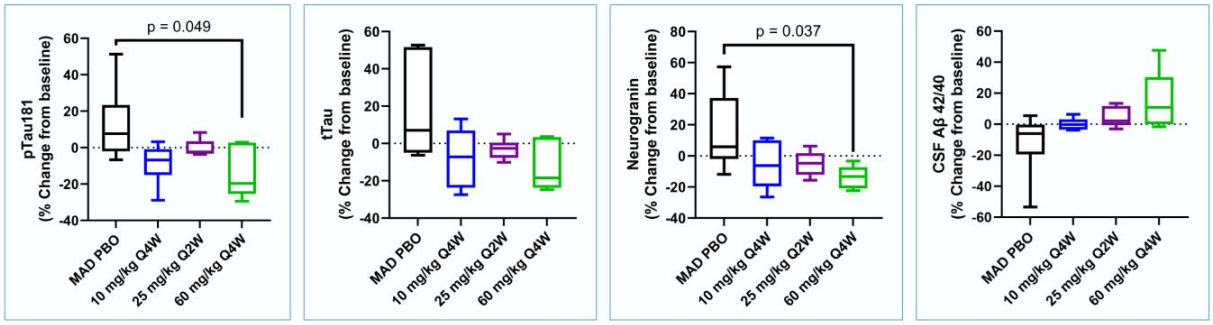
- SAD 2 mg/kg
- SAD 10 mg/kg
- SAD 25 mg/kg
- SAD 60 mg/kg
- MAD 10 mg/kg Q4W
- MAD 60 mg/kg Q4W
- MAD 25 mg/kg Q2W

Taken together with compelling safety profile and rapid plaque reduction, doses approaching maximal TE helped to guide dose selection for next study phase

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

ACUMEN

Consistent Drug Effects Observed in the Multiple Ascending Dose Cohorts in the INTERCEPT-AD Trial for CSF Phospho-tau181, Total Tau, Neurogranin and the Aβ 42/40 Ratio

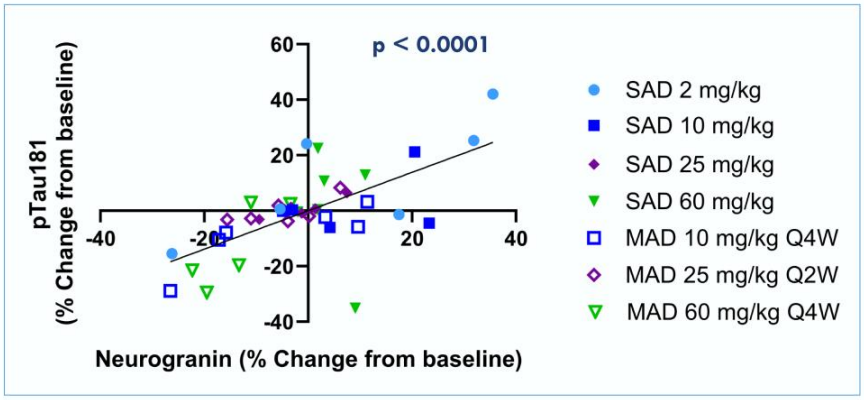


CSF biomarker changes reinforce downstream pharmacology of ACU193 in addition to the previously presented target engagement and amyloid PET data

ACUMEN

Significant Correlation Between Change in CSF Neurogranin and pTau181

- Neurogranin is a synaptic protein that has been shown to modulate glutamatergic neuronal activity and may be linked to enhancement in synaptic plasticity and cognitive function.[1,2]
- Researchers in the field, such as Agnello et al and others,[3,4,5] have found correlations between CSF neurogranin and p-tau.
- This suggests a biological link between these two biomarkers and provides further confidence in our biomarker observations with ACU193.

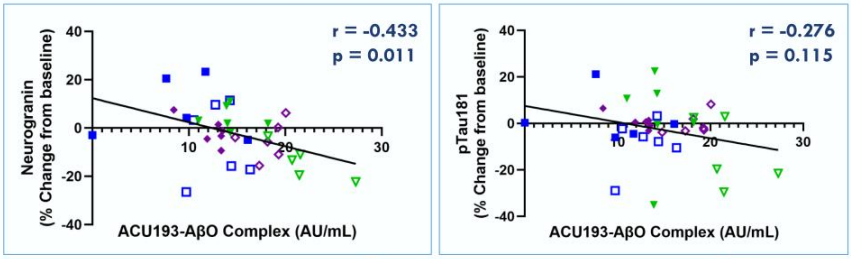


1. Xiang, Yang, et al. Neurogranin: A Potential Biomarker of Neurological and Mental Diseases. Front. Aging Neurosci. 2020 Volume 12 DOI: 10.3389/fnagi.2020.584743; 2. Saunder, Tyler, et al. Neurogranin in Alzheimer's disease and ageing: A human post-mortem study. Neurobiology of Disease 2023. DOI:10.1016/j.nbd.2023.10599. 3. Agnello L, et al. Neurogranin as a Reliable Biomarker for Synaptic Dysfunction in Alzheimer's Disease. Diagnostics 2021, 11, 2339. DOI: 10.3390/diagnostics11122339; 4. Thorsell A, Bjerke M, Gobom J, et al. Neurogranin in cerebrospinal fluid as a marker of synaptic degeneration in Alzheimer's disease. Brain Res 2010;1362:13-22. DOI: 10.1016/j.brainres.2010.09.073; 5. Hellwig K, Kvartsberg H, Portelius E, et al. Neurogranin and YKL-40: independent markers of synaptic degeneration and neuroinflammation in Alzheimer's disease. Alzheimers Res Ther 2015;7:74. DOI: 10.1186/s13195-015-0161-y.

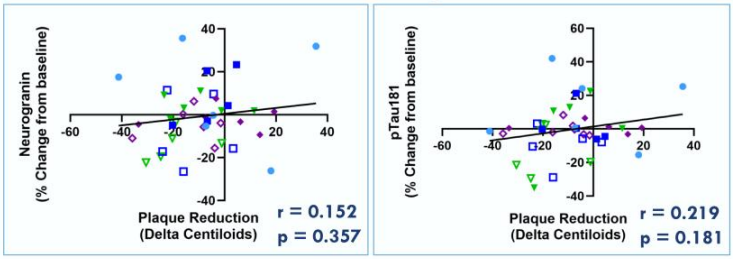
ACUMEN

Changes in CSF Neurogranin and pTau181 are More Closely Related to Target Engagement (Binding to Aβ Oligomers) Than Plaque Reduction

Target Engagement



Plaque Reduction



- These data are consistent with the MOA and target engagement of ACU193
- Provide evidence beyond target engagement of downstream pharmacological effects of ACU193

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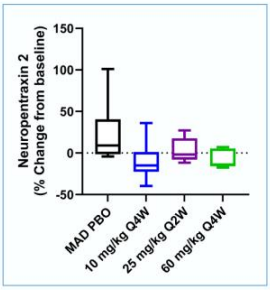
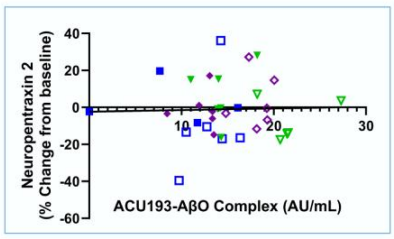
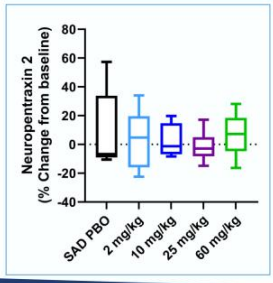
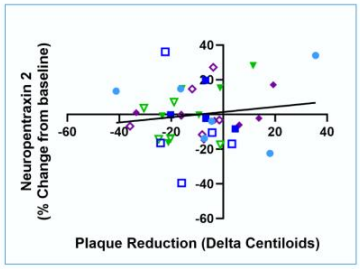
No Significant Drug Effect Observed on CSF Levels of Neuropentraxin 2

Additional study will be required to understand more about this relatively new biomarker





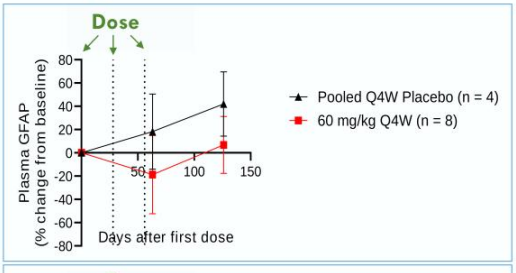


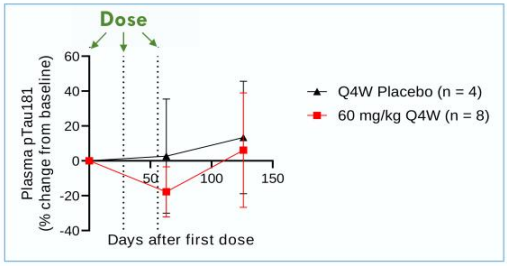


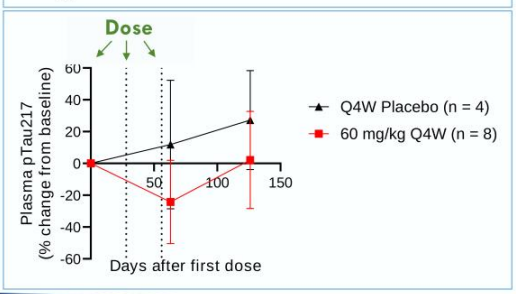
- SAD 2 mg/kg
- SAD 10 mg/kg
- SAD 25 mg/kg
- SAD 60 mg/kg
- MAD 10 mg/kg Q4W
- MAD 25 mg/kg Q2W
- MAD 60 mg/kg Q4W

ACUMEN

Consistent Drug Effects Observed in Plasma Biomarkers in the 60 mg/kg Multiple Ascending Dose Cohort







- Consistent drug effects observed in plasma GFAP, pTau217 and pTau181 in the 60 mg/kg MAD cohort
- Following last dose, plasma biomarkers rebound quickly to baseline, supportive of a drug effect of ACU193

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Phase 1 Data Supports Advancing to Phase 2

- Rapid, dose-related, statistically significant amyloid plaque reduction observed within higher dose cohorts
- Topline results from INTERCEPT-AD trial demonstrated proof-of-mechanism for ACU193, the first clinical stage AβO-targeting antibody
- ACU193 was well-tolerated in patients with early AD; resulted in no drug-related SAEs; low rate of ARIA-E
- ACU193 approached maximal central target engagement of toxic AβOs, establishing broad therapeutic index and path to convenient monthly dosing
- Positive biomarker data is highly supportive of ACU193's downstream pharmacological effects in the brain
- Recent meeting with FDA indicated alignment with the study design of ALTITUDE-AD

Exploratory measures:

- As expected, no effects observed with clinical cognitive measures in this small study of short duration
- As expected, no effects observed with MRI ASL pulse sequence in this small study of short duration

COMPELLING PROOF OF MECHANISM DEMONSTRATED

Next Steps: Expected Phase 2 Initiation 1H 2024

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ACU193: Preclinical Data

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ACU193: 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

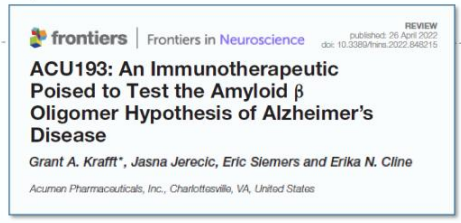
- Dose-dependent effects in multiple in vitro neuroprotection assays
- Positive memory and behavioral effects in multiple in vivo transgenic mouse models for AD

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)
- Nonclinical microhemorrhage studies show no increased risk of microhemorrhage
- GLP studies demonstrated acceptable safety supporting clinical dosing plans including Ph 2/3


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

ACU193 is a promising immunotherapy for early AD expected to provide meaningful cognitive and functional benefits, slow disease progression, and offer an attractive safety profile.

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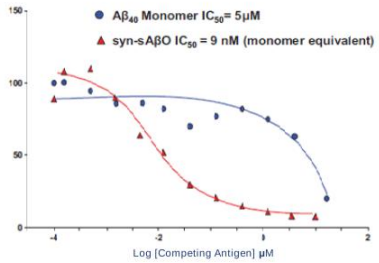
SELECTIVITY

ACU193 is the First mAb Developed to Selectively Target AβOs

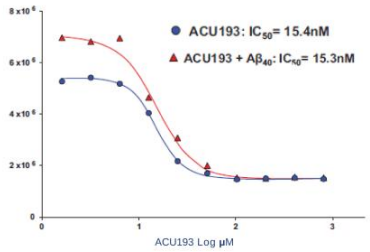
Highly selective for Aβ oligomers versus Aβ monomers

ACU193 Selectivity



Binding of ACU193 to AβOs >500x binding to Aβ monomer

ACU193 Selectivity in presence of 5µM monomeric Aβ



Even in the presence of a large excess of Aβ monomer, binding of ACU193 to AβOs is unchanged

ACU193 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'

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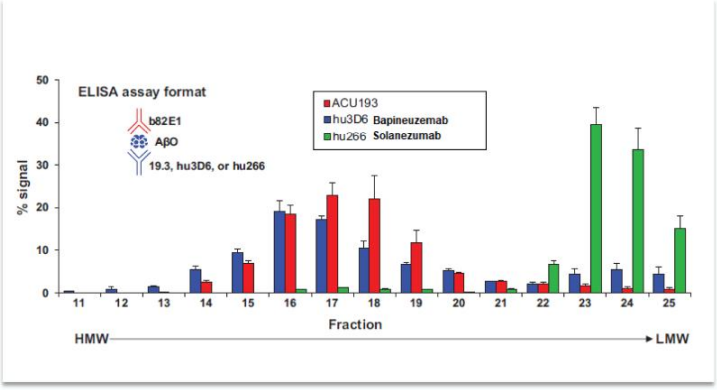
ACU193 Binds to a Wide Range of Oligomeric Species of Aβ

Comparison of Aβ species-mAb complex signals across SEC fractions



ACU193 binds to oligomeric species of Aβ that are differentiated from those bound by hu266 (solanezumab) or hu3D6 (bapineuzumab)

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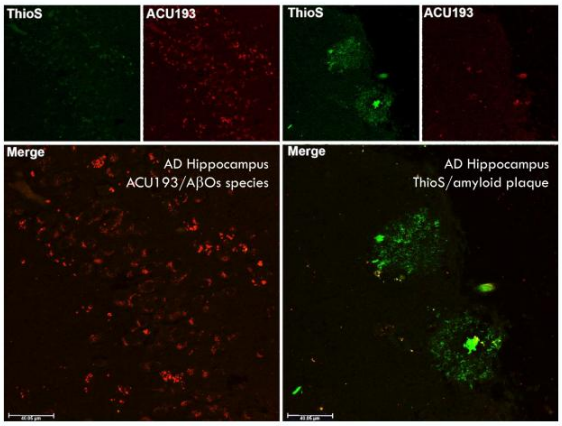
SELECTIVITY

ACU193 is Highly Selective for AβOs Versus Aβ Plaques

ACU193 staining in human AD brain slices ACU193 (red) binds non-Thioflavin S positive Aβ (green)



ACU193 has little or no binding to thioflavin S positive fibrillar Aβ plaque in human AD brain tissue

Sources: E. Cline et al. CTAD 2019.

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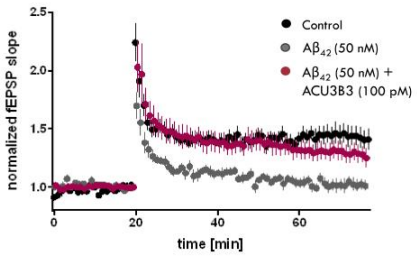
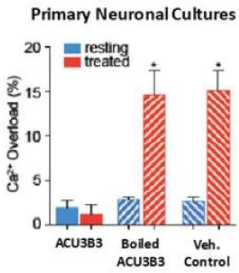
AβOs Bind to Neurons and are Toxic; Mouse Analogue of ACU193 Prevents Toxicity

After binding to neurons, AβOs disrupt Long Term Potentiation (LTP) and cause pathologic increases in intracellular calcium that is destructive to cells.

ACU3B3 prevents AβO inhibition of hippocampal LTP *ex vivo*



ACU3B3 prevents AβO mediated Ca2+ elevation in cell cultures



Note: (1) ACU3B3 is the mouse monoclonal antibody precursor to and equivalent of humanized ACU193

ACU3B3 prevents changes in aberrant neuronal activity thought to underlie memory loss in AD and prevents AβO mediated disruption of calcium homeostasis in neuronal cultures

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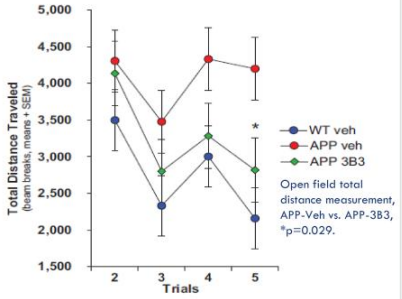
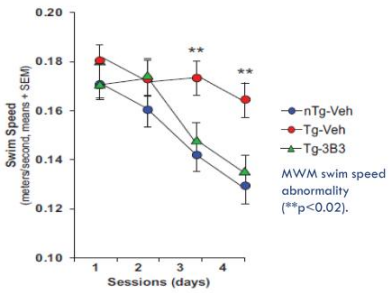
Treatment of a Transgenic Mouse Model of AD Results in Behavioral Improvements

Murine parent version of ACU193 (ACU3B3) was used to treat younger mice with depositing plaque or older mice with abundant plaque



Deficits in younger (5-7 months) transgenic mice are markedly reduced with treatment



Deficits in older (9-10 months) transgenic mice are markedly reduced with treatment

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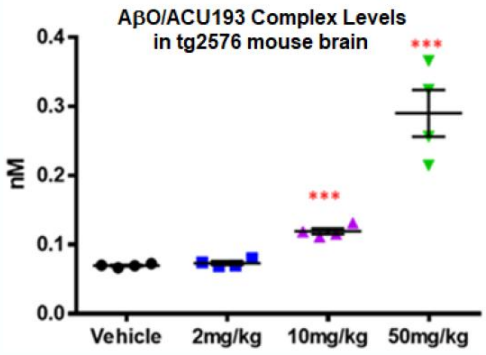
ACU193 Enters the CNS and Binds to AβOs in Transgenic Mice in Dose Dependent Manner



ACU193 engages target AβOs in transgenic mouse brain (tg2576) in dose dependent manner; Ability to administer higher doses in patient clinical trials may provide increased target coverage

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Clinical Development Plans & Strategic Considerations

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Acumen Leadership Team

Experienced in AD/Neuro Drug Development

DANIEL O'CONNELL
President & CEO
ACUMEN
neuroventures

ERIC SIEMERS, MD
Chief Medical Officer
ACUMEN
Lilly

JANICE HITCHCOCK, PHD
VP, Regulatory Affairs
ACUMEN
Lilly

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

RUSSELL BARTON
Chief Operating Officer
ACUMEN
Lilly

ROBERT DEAN, MD, PHD
Sr. Development Advisor, Biomarkers and Analytical Methods
ACUMEN
Lilly

LIEAN SCHENK
VP, Head of CMC
ACUMEN
Lilly Lonza
NOVAVAX

SIEW TIN GAN
Head of Clinical Operations
ACUMEN
Takeda

JASNA JERECIC, PHD
Analytical Methods Leader, Research Scientist
ACUMEN

DEREK MEISNER, JD
Chief Legal Officer
ACUMEN
Xᵢ

JULIE BOCKENSTETTE
Executive Vice President, Head of HR
ACUMEN
Roche Lilly

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

ACU193 Development Summary

⇒ Differentiated profile: Nonclinical and Phase 1 data consistent with toxicity of Aβ oligomers and selective binding of ACU193 to Aβ oligomers

⇒ Positive topline results from Phase1 study assessing safety, PK, and target engagement

⇒ Anticipate Phase 2 clinical study, ALTITUDE-AD, to initiate in 1H 2024

- Two treatment arms versus placebo: 50 mg/kg Q4W and 35 mg/kg Q4W

⇒ Anticipate Phase 1 subcutaneous clinical study to initiate in mid-2024, to compare the pharmacokinetics of a subcutaneous form of ACU193 to the IV form

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ACU193 IP & Market Exclusivity

- Exclusive, perpetual, irrevocable, worldwide, royalty-free license from Merck to its Amyloid Derived Diffusible Ligand (ADDL) IP including issued ACU193 patents
- ACU193 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 ACU193 as a novel biologic drug
  - ✓ US provides 12 years market exclusivity for novel biologics
  - ✓ Europe provides 10 years of market exclusivity for novel biologics

Significant Milestones Achieved in 2023

MILESTONES	STATUS/ EXPECTED TIMING
Proof-of-mechanism topline results	✓
Biomarker results from Phase 1 study	✓
Anticipated interaction with FDA	✓
Anticipated initiation of ALTITUDE-AD trial	1H 2024
Anticipated initiation of Phase 1 subcutaneous trial	Mid-2024

~$283M
Cash, cash equivalents and marketable securities as of Sept 30, 2023

Up to $50M
Debt financing secured from K2 HealthVentures in November 2023

We believe that Acumen has the expertise and resources to advance ACU193 into the second half of 2026

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ABOS: Key Takeaways

- Massive unmet need in AD, recent favorable trends and cumulative learnings position field for future successes
- Positive Phase 1 clinical data presented in July 2023
- Differentiated product candidate targeting toxic AβOs
- Experienced AD drug development team
- Blue chip investors and strong balance sheet
- Phase 2 study, ALTITUDE-AD, expected to initiate in 1H 2024; subcutaneous Phase 1 expected to initiate in mid-2024

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Appendix

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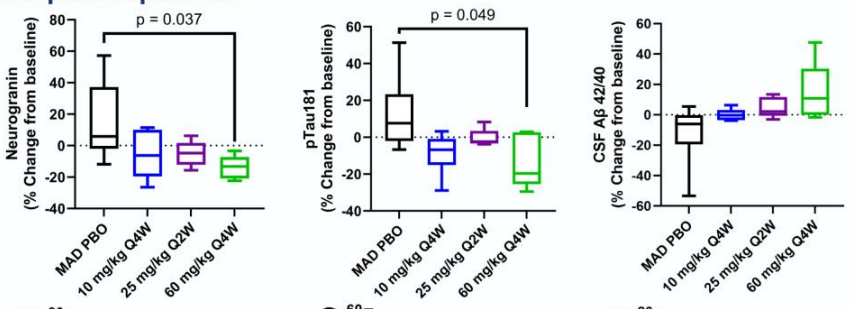
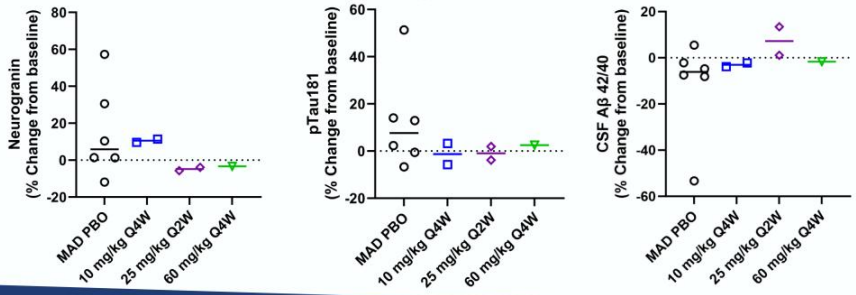
Observed Apparent Drug Effect on CSF Biomarkers in the ApoE4 Homozygotes in Line With the Total Participant Population

All Participants



Individual ApoE4 homozygotes (all patients for PBO)



*A larger sample size is needed to know if ApoE4 carrier status has a quantitative effect on response.

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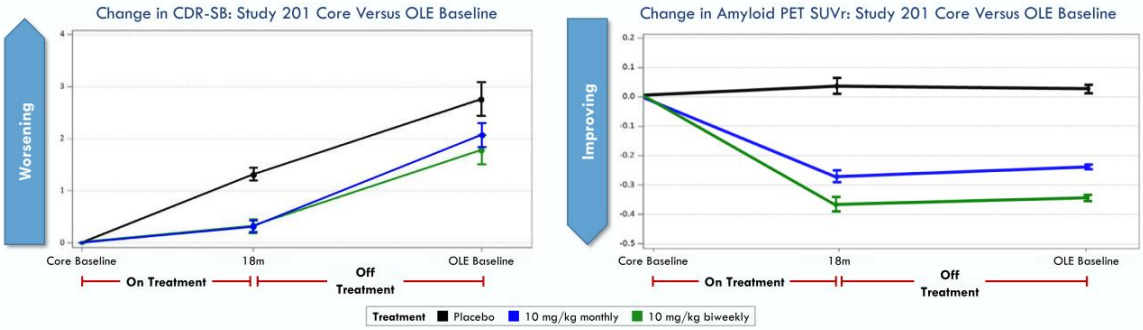
Lecanemab Phase 2 Suggests Amyloid Plaque Reduction Alone is Insufficient to Optimize Alzheimer's Disease Slowing*

- Lecanemab (BAN2401) Study 201 – Off treatment "gap" period prior to start of Open Label Extension (OLE) study confirmed cognitive outcomes (CDR-SB) worsened upon discontinuation of Lecanemab despite sustained reduced amyloid plaque (Aβ PET SUVr). Aβ PET measures amyloid plaque in the brain, **but does not measure soluble Aβ species, such as oligomers or protofibrils**



Suggests soluble Aβ aggregate species (e.g. protofibrils, oligomers) play a role in clinical decline

*Persistence Of BAN2401-Mediated Amyloid Reductions Post-treatment: A Preliminary Comparison of Amyloid Status Between the Core Phase of BAN2401-G000-201 and Baseline of the Open-Label Extension Phase in Subjects with Early Alzheimer's Disease (1330); Chad J. Swanson, et al. Neurology Apr 2020, 94 (15 Supplement) 1330; *Presented at the American Academy of Neurology (AAN) conference in April 2020.

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Positive Signals and Proof of Concept From Recent Phase 3 Anti-Amyloid mAb AD Studies

Percent Slowing of Cognitive/Functional Decline*

Measured Outcome**	solanezumab EXPEDITION 3 (Phase 3)	aducanumab EMERGE (Phase 3)	aducanumab ENGAGE (Phase 3)	lecanemab Clarity-AD (Phase 3)+	donanemab TRAILBLAZER-2 (Phase 3)++ *(Intermediate & High Tau)*	donanemab TRAILBLAZER-2 (Phase 3)++ *(Intermediate Tau)*
ADAS-cog	-11%	-27%	-12%	-26%	-20%	-32%
ADCS-ADL	-15%	-40%	-18%	-37%	-28%	-40%
CDR-SB	-15%	-23%	2%	-27%	-29%	-36%
MMSE	-13%	-15%	3%	N.A.	N.A.	N.A.
iADRS	-11%	N.A.	N.A.	N.A.	-22%	-35%

* Percent Slowing = P[1- [(endpoint score-baseline score)active/(endpoint score-baseline score)placebo]]*100%*(-1)

** ADAS-cog: Alzheimer's Disease Assessment Scale – Cognitive Subscale
ADCS-ADL: Alzheimer's Disease Cooperative Study – Activities of Daily Living
CDR-SB: Clinical Dementia Rating – Sum of Boxes
MMSE: Mini-Mental State Examination
iADRS: Integrated Alzheimer's Disease Rating Scale

Note: ENGAGE Post-Protocol Version 4 – at least 14 doses of 10 mg/kg, High Dose cohort achieved 27% improvement on CDR-SB compared to placebo

"We're looking for a biological foothold against Alzheimer's that we can build on. And so, these effects are small, but I think they are meaningful, and I hope they're the beginning of a process that we can add to." - ***Stephen Salloway, MD*** *of Brown University*++

+ Source: Eisai/Biogen press release September 28, 2022.
++ Source: Eli Lilly press release May 3, 2023.
++Source: Wall Street Journal, Biogen Details Case for Controversial Alzheimer's Drug, published December 5, 2019. See e.g., Plotkin, Neurobiology of Disease, 2020.
There have been no head-to-head clinical trials between any of the product candidates listed above. Study designs and protocols for each product candidate were different, and results may not be comparable between product candidates.

Anti-Plaque mAbs Demonstrate Dose-Related ARIAs That Will Likely Limit Their Use

Percent of ARIA Events for Anti-Aβ/plaque mAbs*

	TARGETING AB MONOMERS		TARGETING AMYLOID PLAQUES										TARGETING PROTOFIBRILS			
	solanezumab EXPEDITION 3 (Phase 3)		aducanumab EMERGE (Phase 3)			aducanumab ENGAGE (Phase 3)			donanemab (Phase 2)		donanemab (Phase 3)++ *(Intermediate & High Tau)*		lecanemab (Phase 2)		lecanemab (Phase 3)+	
	PC	Treated	PC	Low	High	PC	Low	High	PC	Treated	PC	Treated	PC	High	PC	Treated
ARIA-E	0.2%	0.1%	2.2%	26.1%	34.4%	3.0%	25.6%	35.7%	0.8%	27.5%		24%	0.8%	9.9%	1.7%	12.6%
Symptomatic												6%				3%
ApoE ε4 carriers			1.9%	29.8%	42.5%	2.4%	28.7%	41.8%	3.6%	44.0%			1.2%	14.6%	2.3%	15.8%
ApoE ε4 non-carriers			2.9%	18.1%	17.9%	4.3%	17.5%	27.7%					0.0%	8.0%	0.3%	5.4%
Any ARIA E or H			10.3%	32.8%	41.2%	9.8%	30.7%	40.3%	8.0%	38.9%		31%			9.5%	21.5%

* PC = Placebo, Low = Low Dose; High = High Dose

Shows the absence of ARIA after treatment with antibodies targeting Aβ monomers (solanezumab) in comparison to the increasing presence of ARIA after treatment at increasing dose levels with antibodies targeting amyloid plaques (aducanumab, BAN2401, and donanemab), indicate that ARIA results from the removal of amyloid plaques around blood vessels and likely does not result from treatment with antibodies that target other species of Aβ, i.e. Aβ monomers and AβOs.

ARIA-E represents a dose limiting adverse effect for mAbs with amyloid plaque binding; We believe antibodies that exhibit lower ARIA-E should be safer and more feasible to administer, possibly at higher doses

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

+ Source: Eisai/Biogen press release September 28, 2022.

++ Source: Eli Lilly press release May 3, 2023.