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): March 19, 2024

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 2.02 Results of Operations and Financial Condition.

On March 19, 2024, Acumen Pharmaceuticals, Inc. (the "Company") posted an updated corporate presentation (the "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. The Corporate Presentation was updated to reflect that, as of December 31, 2023, the Company's cash, cash equivalents and marketable securities balance was approximately $306 million (which amount includes proceeds received to date under the Company's Loan and Security Agreement with K2 HealthVentures LLC), based upon which the Company projects that its cash, cash equivalents and marketable securities will be sufficient to support the Company's operations into the first half of 2027. A copy of the Corporate Presentation containing this announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K (the "Current Report").

The cash, cash equivalents and marketable securities information above is based on preliminary unaudited information and management estimates for the year ended December 31, 2023, is not a comprehensive statement of the Company's financial results as of and for the fiscal year ended December 31, 2023, and is subject to completion of the Company's financial closing procedures. The Company's independent registered public accounting firm has not conducted an audit or review of, and does not express an opinion or any other form of assurance with respect to, this preliminary estimate.

Item 7.01 Regulation FD Disclosure.

The information in Item 2.02 of this Current Report is incorporated into this Item 7.01 by reference. The Corporate Presentation was also updated to reflect the Company's anticipation that it will amend its ALTITUDE-AD Phase 2/3 study protocol to become a Phase 2 standalone study.

The information contained in Items 2.02 and 7.01 of this Current 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 March 19, 2024.
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: March 19, 2024

By: /s/ Derek Meisner
Derek Meisner
Chief Legal Officer

Corporate Presentation

March 2024

Forward-Looking Statements

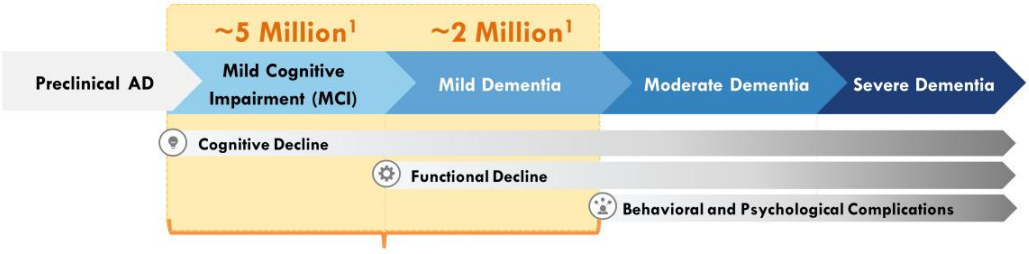
This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Any statement describing Acumen's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Words such as "believes," "expects," "anticipates," "could," "would," "seeks," "aims," "plans," "potential," "will" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements concerning Acumen's business, and Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the expected sufficiency of its cash resources into the first half of 2027, the therapeutic potential of Acumen's product candidate, sabirnetug (ACU193), including against other antibodies, and the anticipated timeline for initiating a Phase 2 clinical trial of sabirnetug and a Phase 1 trial to support a subcutaneous dosing option of ACU 193. 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 Targeting Toxic Amyloid Beta Oligomers (AβOs) for Early Alzheimer's Disease (AD)

- Large market in need of additional treatment options
- Sabirnetug (ACU193): monoclonal antibody (mAb) highly selective for toxic AβOs
- Positive Phase 1 clinical trial results presented in 2H 2023
- Experienced leadership team with extensive AD drug development experience
- Strong balance sheet supporting clinical development plans for sabirnetug
- Expect to initiate Phase 2 (IV) and Phase 1 (subcutaneous) studies in 2024

Early AD Patient Population Represents Significant Market Opportunity

STAGES AND CHARACTERISTICS OF AD PROGRESSION



Early Alzheimer's Disease in the U.S.

Acumen's commercial priority

Uptake of first-generation, disease modifying, anti-amyloid beta treatment options is expected to increase, while significant unmet need and room for improvement will persist

1. 2021 Alzheimer's Association

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AD, Amyloid & Abeta Oligomers

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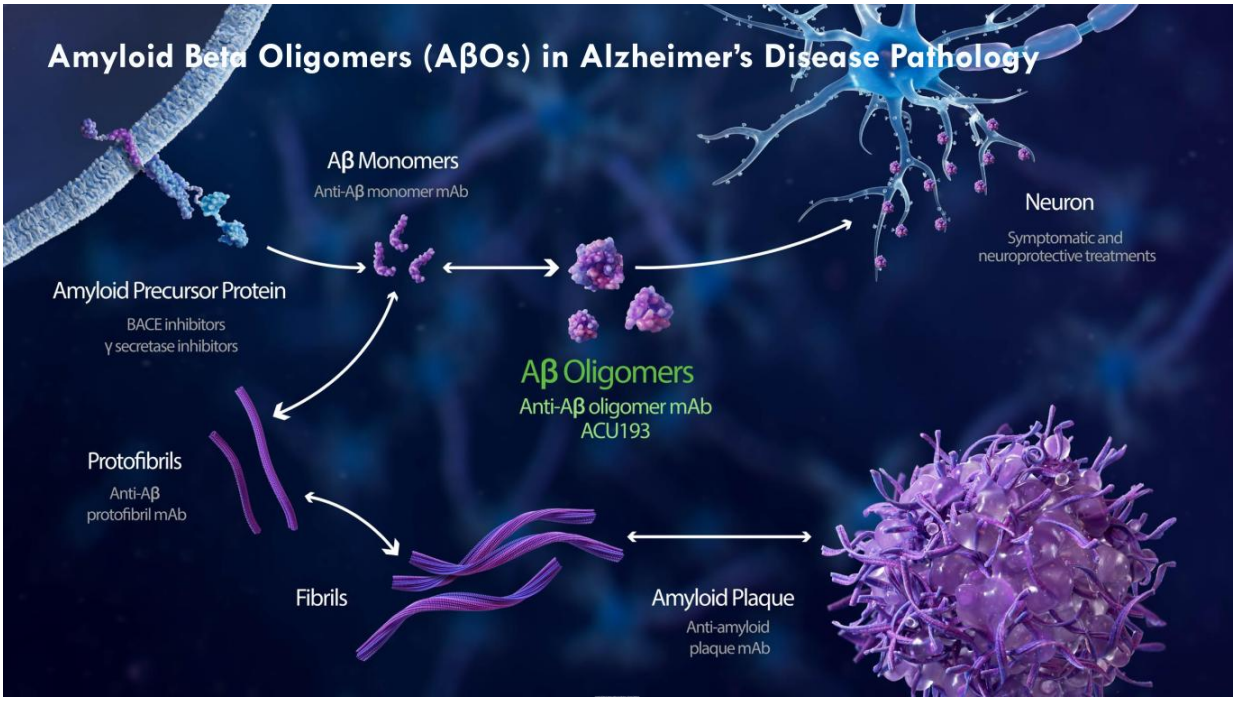
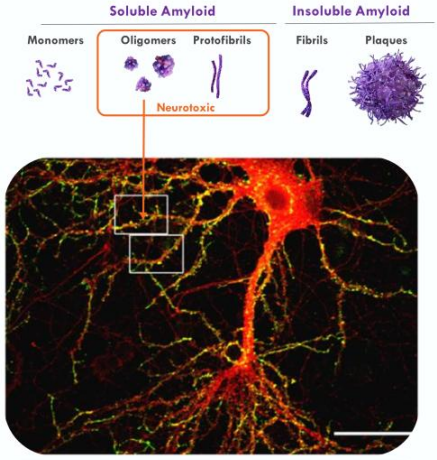

Amyloid Beta Oligomers (AβOs) in Alzheimer's Disease Pathology
Aβ Monomers
Anti-Aβ monomer mAb
Neuron
Symptomatic and neuroprotective treatments
Amyloid Precursor Protein
BACE inhibitors
γ secretase inhibitors
Aβ Oligomers
Anti-Aβ oligomer mAb
ACU193
Protofibrils
Anti-Aβ protofibril mAb
Fibrils
Amyloid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

Amyloid Beta Oligomers (AβOs) are Widely Recognized as Highly Toxic Agents in AD Pathophysiology

- Impair synaptic function[1]
- Contribute to impairment of memory and cognition[2]
- Induce tau hyperphosphorylation[3]



Mature hippocampal neuron and toxic AβOs bound to dendritic spines

Image Lacor et al., 2004.

1. Lacor et al., 2004 & 2007; Townsend et al., 2006; Batista et al., 2018
2. Cleary et al., 2005; Poling et al., 2008; Cline et al., 2019
3. De Felice et al., 2008; Zempel et al., 2010

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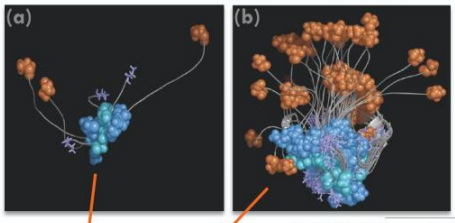
What is an Aβ Oligomer? AβOs May Consist of 2 to >200 Aβ Peptides

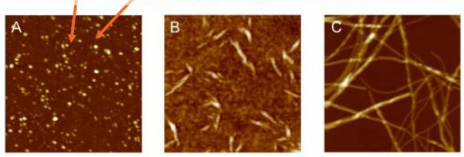
Figure 1. AβOs composed of 3 (a) and 18 (b) Aβ peptides are depicted below.



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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Sabirnetug: Potential Best-in-Class Immunotherapy for Early AD

Sabirnetug's High Selectivity for Toxic AβOs May Provide Meaningful Cognitive Efficacy and Improved Safety

Rationally Designed for Improved Efficacy & Safety

Humanized, affinity matured mAb developed to target toxic Aβ oligomers

> 500-fold greater selectivity for AβOs over Aβ monomers

> 85-fold greater selectivity for AβOs over Aβ fibrils

IgG2 subclass mAb with reduced effector function

Large Pharma Discovery

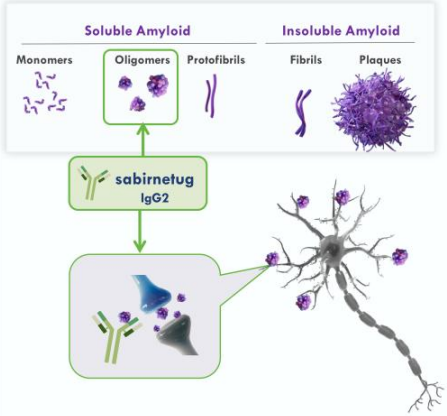
Sabirnetug discovered in collaboration with Merck & Co.

Acumen holds exclusive program rights with no future financial or other obligations due to Merck

Encouraging FDA Interactions

FDA Fast Track designation for the treatment of early Alzheimer's disease

FDA End of Phase 2 meeting in 4Q 2023



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Sabirnetug: 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 **sabirnetug** 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, sabirnetug 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 Sabirnetug

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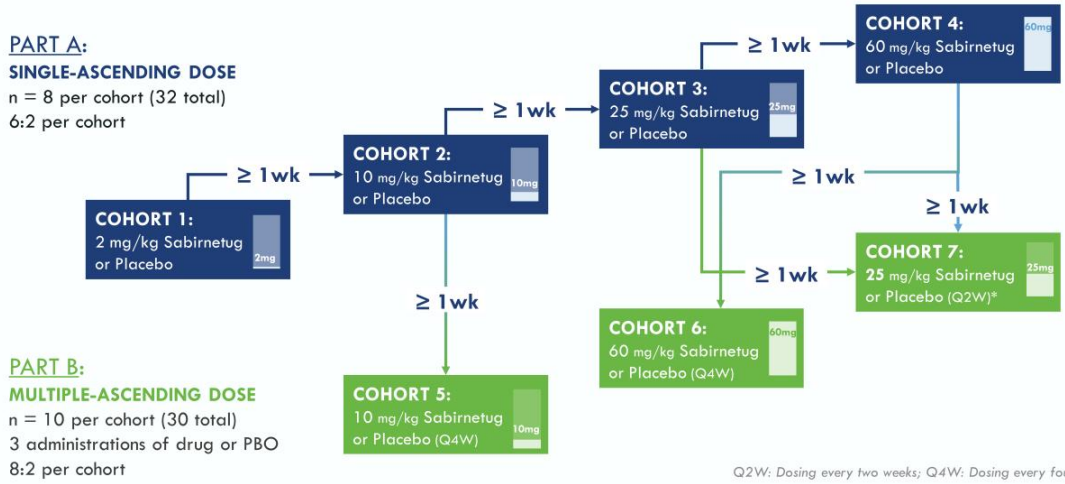
INTERCEPT-AD: A Randomized Placebo Controlled Phase 1 in Early AD Patients



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

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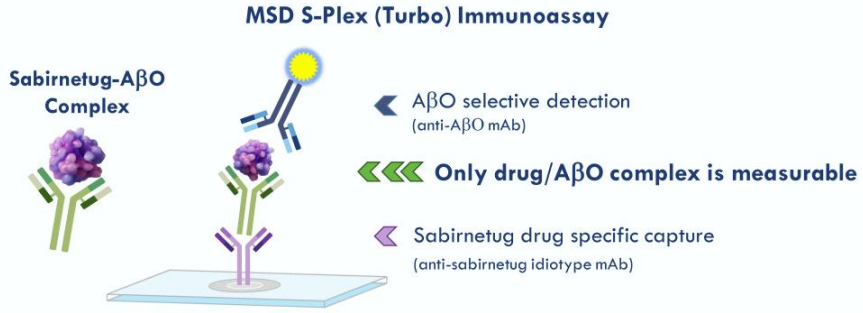
Target Engagement Assessed by Measuring Sabirnetug-AβO Complex in CSF



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

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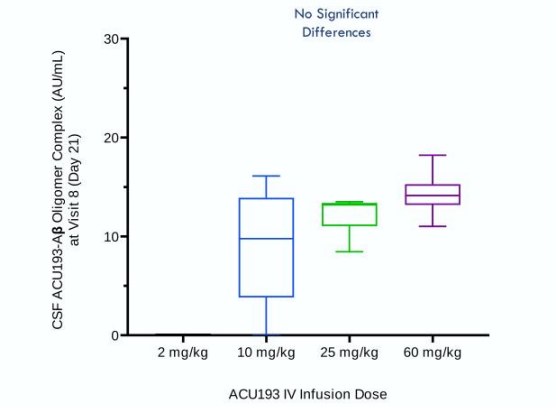
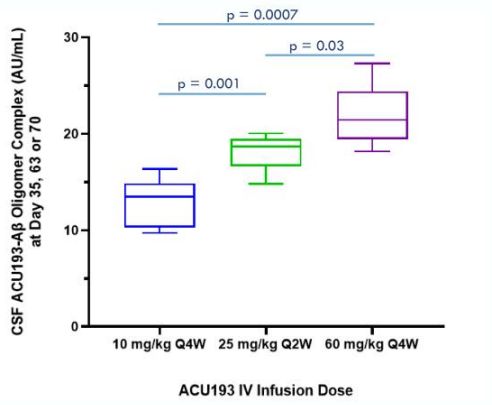
TARGET ENGAGEMENT

Target Engagement of Sabirnetug with AβOs is Dose Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



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

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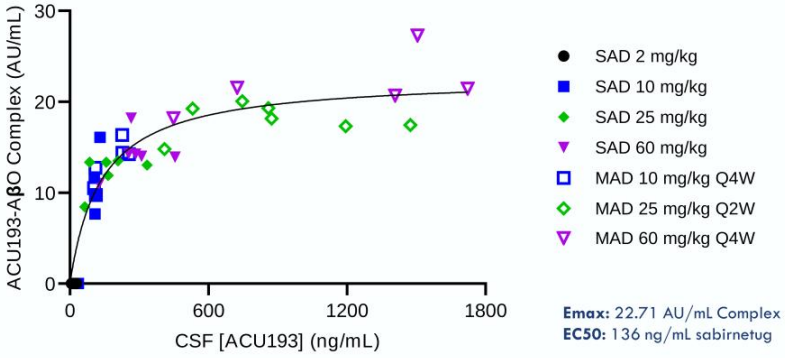
Doses Approaching Maximal Target Engagement Support Sabirnetug AβO Mechanism and Helped Guide Dose Selection for Next Study Phase

Target Engagement

Sabirnetug-AβO Complex

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



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

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

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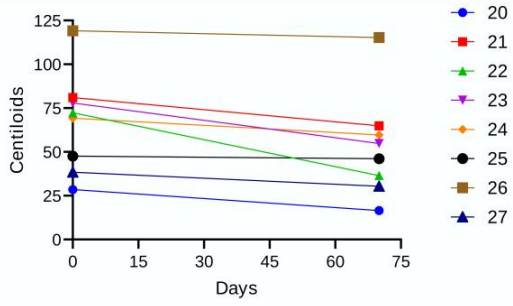
Nearly All Sabirnetug-Treated Patients in High Dose MAD Cohorts Showed Reductions in Plaque Load After Three Doses at 63 or 70 days

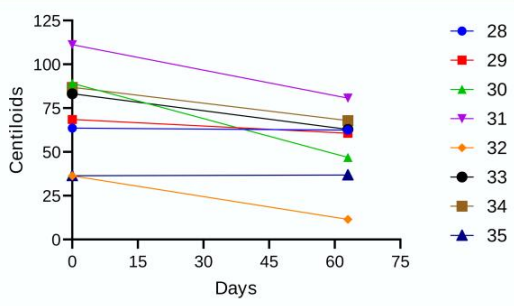
25 mg/kg Q2W MAD



Mean reduction in amyloid plaque

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

60 mg/kg Q4W MAD



Mean reduction in amyloid plaque

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

Plaque load based on florbetapir PET

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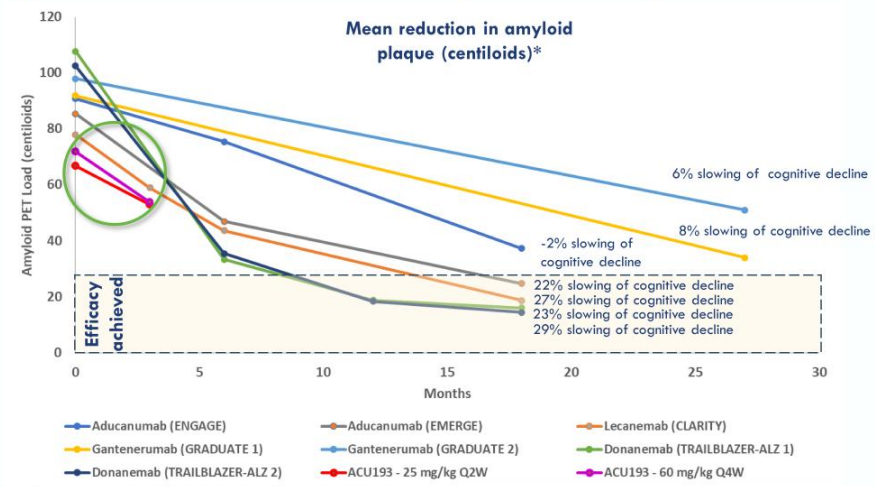
Highest Doses of INTERCEPT-AD Reduced Amyloid Plaque at Similar Rate and Magnitude to Lecanemab at Comparable Timepoints



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

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

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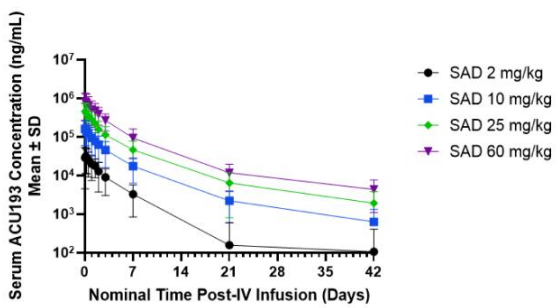
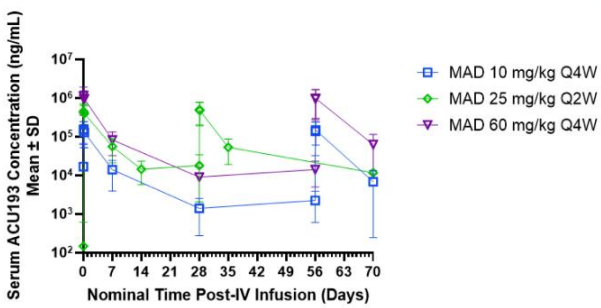
PHARMACOKINETICS

Sabirnetug Serum Exposure is Dose Proportional Without Accumulation

Single Dose Cohorts



Multiple Dose Cohorts



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

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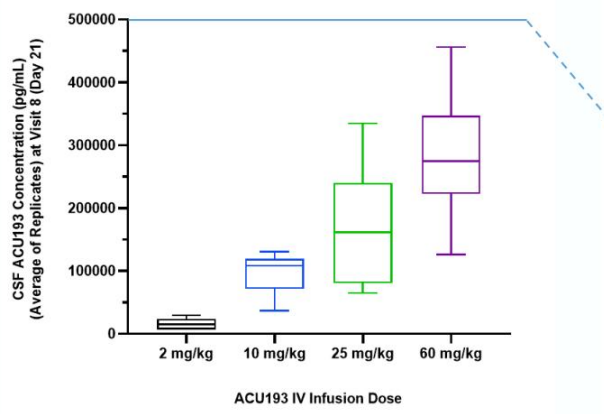
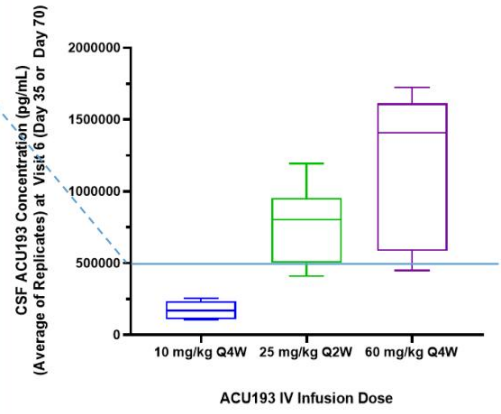
PHARMACOKINETICS

Sabirnetug CSF Exposure is Dose and Dose-Regimen Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



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

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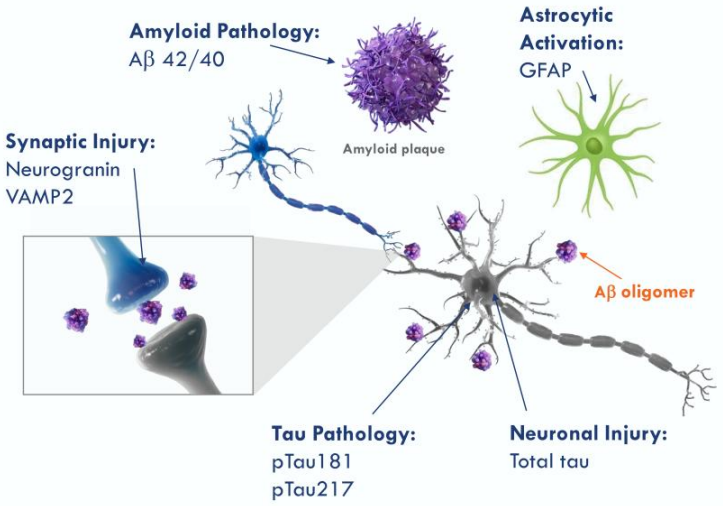
Importance of Key Fluid Biomarkers Associated with AD Pathology

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



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

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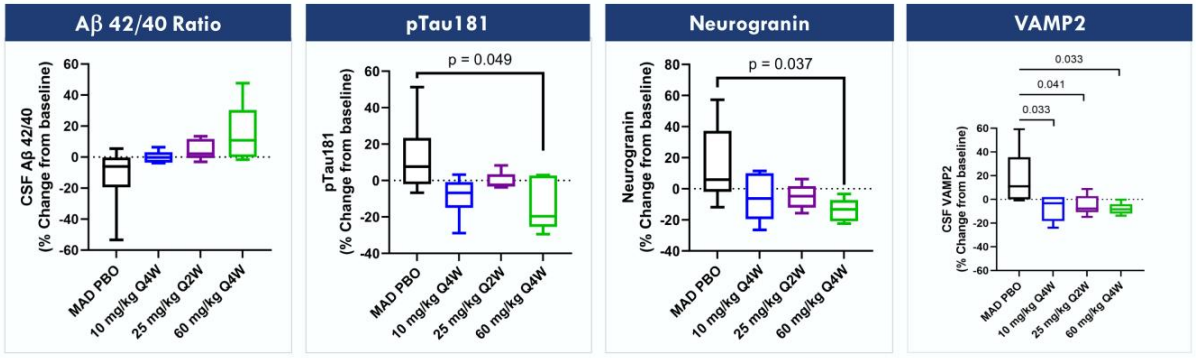
Consistent Improvement in CSF Amyloid, Tau and Synaptic Biomarkers Indicate Downstream Pharmacology of Sabirnetug After Only Three Doses



Amyloid pathology *Tau pathology* *Synaptic injury*

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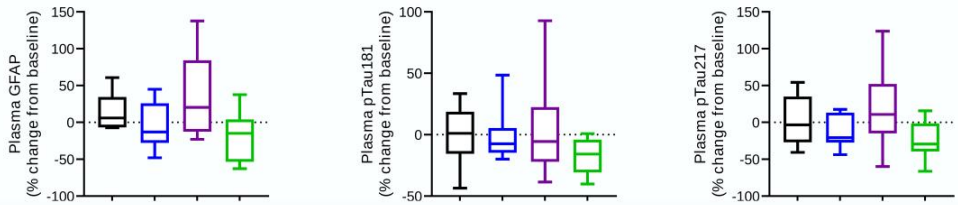
PLASMA BIOMARKERS

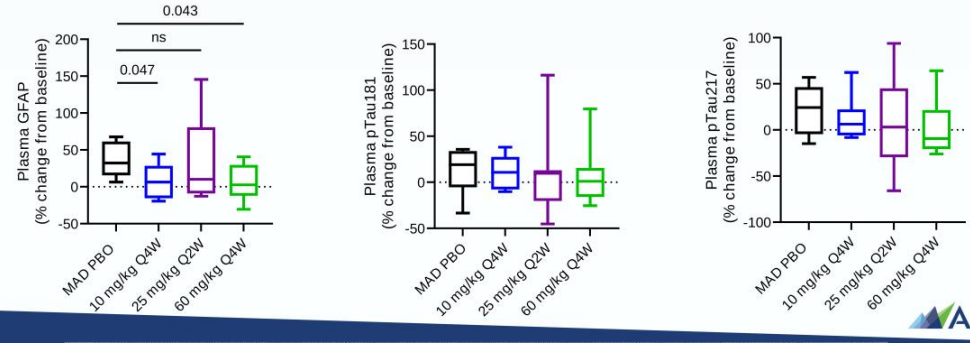
Trend Toward Normalizing Plasma Biomarkers with 10 mg/kg and 60 mg/kg Q4W

- *After longer drug wash-out (10-20 weeks) placebo-treated patients showed an increase in GFAP, pTau181, and pTau 217*
- *For 10 mg/kg and 60 mg/kg dose groups sabirnetug-treated patients directionally remained lower than placebo*

1-6 wk post-dosing



10-20 wk post-dosing



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Sabirnetug Demonstrates Potential for Best-in-Class Safety

Compelling Overall Safety Profile, with Low Incidence of ARIA-E

INTERCEPT-AD Phase 1 Safety Data

5 Total ARIA-E cases, or ~10%

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

0 Deaths, SAEs Related to Study Drug

✓ **Limited incidence of ARIA-E**
- 10 mg/kg Q4W: 1 asymptomatic case
- 25 mg/kg Q2W: 1 asymptomatic case
- 60 mg/kg Q4W: 2 asymptomatic cases; 1 symptomatic case

✓ **No ARIA-E observed in ApoE4 homozygotes (n=6), despite comprising 13% of study**
- Differentiated from other antibodies that have ARIA-E rates ~30% to ~40% in participants who are E4-homozygotes

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

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

Key Takeaways from INTERCEPT-AD

Potential for Differentiated Efficacy	✓ First mAb to demonstrate selective target engagement of AβOs (most toxic form of Aβ) ✓ Rapid, significant plaque reduction comparable to the current market front-runners at similar timepoints ✓ Improvement of AD biomarkers in CSF and plasma are a strong indication of downstream effects
Potential for Differentiated Safety	✓ Compelling safety profile with low incidence of ARIA-E ✓ Absence of ARIA-E observed in ApoE4 homozygotes ✓ Broad therapeutic index with convenient monthly dosing

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Preclinical Data

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Sabirnetug: Extensive Data Package Supporting Development

SELECTIVITY

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

PHARMACOLOGY

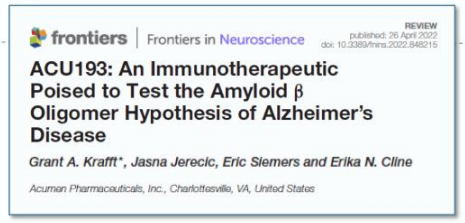
- Dose-dependent effects in multiple in vitro neuroprotection assays
- Positive memory and behavioral effects in multiple in vivo transgenic mouse models for AD

PK/PD

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

SAFETY

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


frontiers | Frontiers in Neuroscience

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

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

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

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

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

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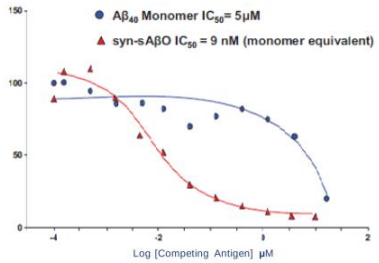
SELECTIVITY

Sabirnetug is the First mAb Developed to Selectively Target AβOs

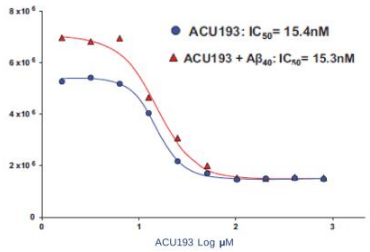
Highly selective for Aβ oligomers versus Aβ monomers

Sabirnetug Selectivity



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

Sabirnetug Selectivity in presence of 5µM monomeric Aβ



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

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

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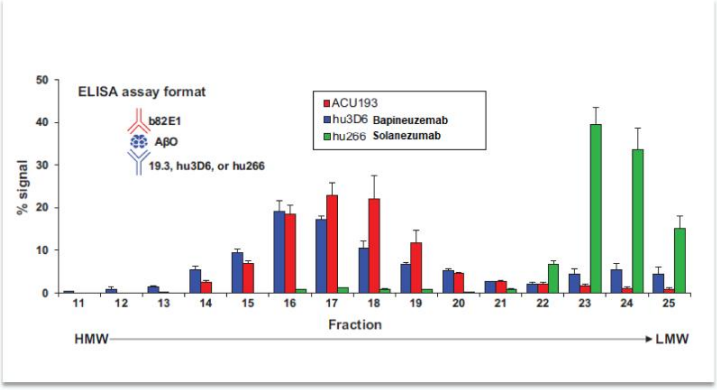
Sabirnetug Binds to a Wide Range of Oligomeric Species of Aβ

Comparison of Aβ species-mAb complex signals across SEC fractions



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

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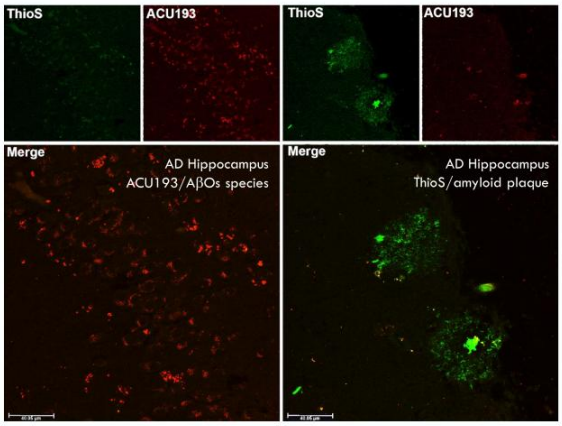
SELECTIVITY

Sabirnetug is Highly Selective for AβOs Versus Aβ Plaques

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



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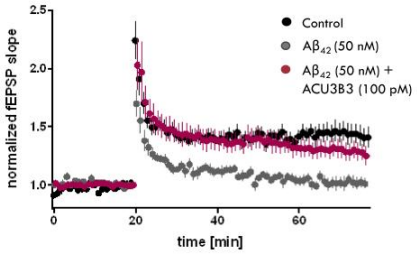
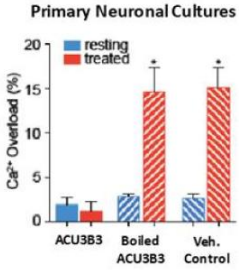
AβOs Bind to Neurons and are Toxic; Mouse Analogue of Sabirnetug Prevents Toxicity

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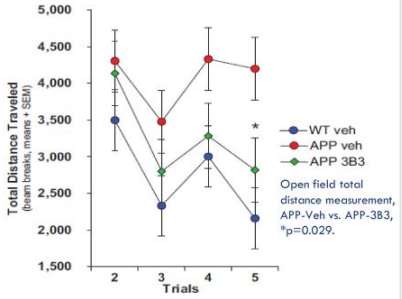
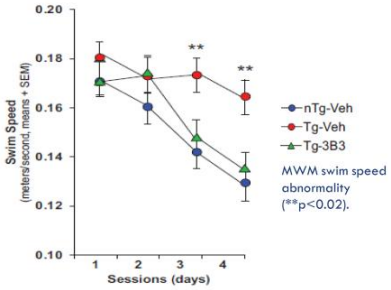
Treatment of a Transgenic Mouse Model of AD Results in Behavioral Improvements

Murine parent version of sabirnetug (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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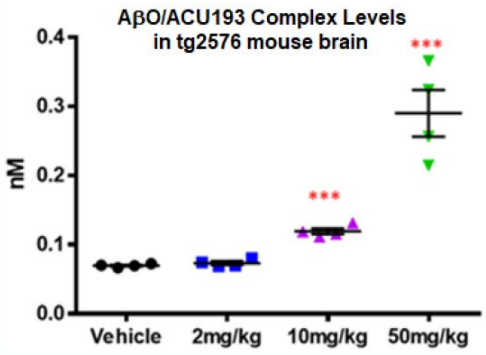
Sabirnetug Enters the CNS and Binds to AβOs in Transgenic Mice in Dose Dependent Manner



Sabirnetug 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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Significant Milestones Achieved in 2023

MILESTONES	STATUS/ EXPECTED TIMING
Proof-of-mechanism topline results	✓
Biomarker results from Phase 1 study	✓
End of Phase 2 meeting with FDA	✓
Anticipated initiation of ALTITUDE-AD trial	1H 2024
Anticipated initiation of Phase 1 subcutaneous trial	Mid-2024

~$306M

Cash, cash equivalents and marketable securities as of Dec. 31, 2023

We believe that Acumen has the expertise and resources to advance sabirnetug into the first half of 2027

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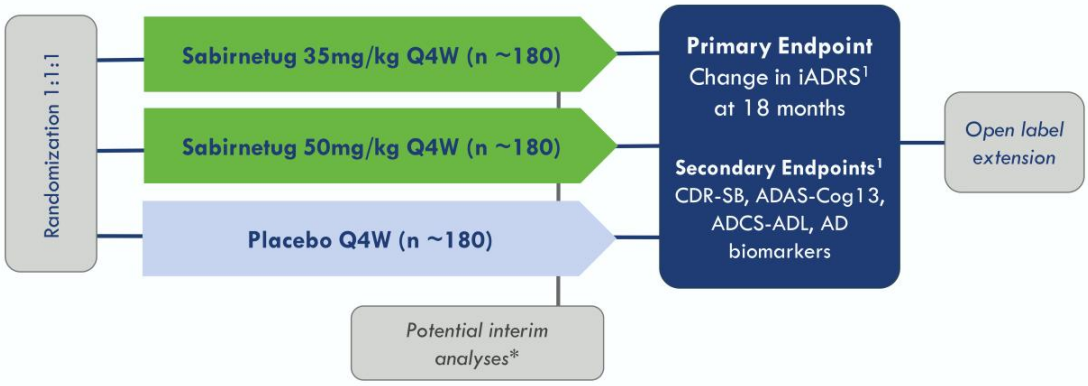
ALTITUDE-AD Study Design

Objective: To evaluate the clinical efficacy, safety and tolerability of sabirnetug
Patient population: Patients with early AD (MCI or mild dementia due to early AD)



*Based on regulatory feedback from the European Medicines Agency (EMA) and to enhance the probability that the EMA will consider our Phase 2 a registration-eligible study for sabirnetug, we anticipate amending the protocol later this year to change the current Phase 2/3 study to a Phase 2 standalone study. If this occurs, any interim analysis may then lead to an initiation of a confirmatory Phase 3 study.

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

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Sabirnetug Subcutaneous Formulation Under Development in Collaboration with Halozyme

Potential to Broaden Patient Access and Increase Treatment Convenience

- Announced partnership with Halozyme in November 2023 to develop subcutaneous dosing option for sabirnetug
- Halozyme's drug delivery technology, ENHANZE®, is commercially validated in seven approved therapies, with global collaborations covering more than 60 therapeutic targets
- Current sabirnetug potential target product profile inclusive of no more than single weekly injection

Plan to initiate Phase 1 bioavailability study in mid-2024 comparing the pharmacokinetics of subcutaneous forms of sabirnetug to the IV form

Acumen Leadership Team

Experienced in AD/Neuro Drug Development

DANIEL O'CONNELL
Chief Executive Officer
ACUMEN
neuroventures

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

ERIC SIEMERS, MD
Chief Medical Officer
ACUMEN
Lilly

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

RUSSELL BARTON
Chief Operating Officer
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JANICE HITCHCOCK, PHD
VP, Regulatory Affairs
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LIEAN SCHENK
VP, Head of CMC
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JASNA JERECIC, PHD
Analytical Methods
Leader, Research Scientist
ACUMEN

DEREK MEISNER, JD
Chief Legal Officer
ACUMEN
X4

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

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

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Sabirnetug IP & Market Exclusivity

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

Summary

Key Takeaways

- ✓ Significant and growing Alzheimer's population in need of additional treatment options
- ✓ Sabirnetug demonstrates high selectivity for toxic AβOs in AD patients
- ✓ Highly experienced clinical, regulatory and development leaders driving sabirnetug 's development
- ✓ **Positive Phase 1 data strengthen potential for sabirnetug to offer best-in-class efficacy and safety**

Next Steps

- ➡ Anticipate initiation of ALTITUDE-AD clinical study in 1H 2024

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

- ➡ Anticipate initiation of Phase 1 subcutaneous clinical study in mid-2024

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Appendix

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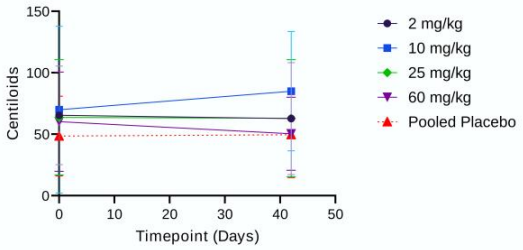
Aβ PET: Mean Changes in Amyloid Plaque in SAD and MAD Cohorts

Single Dose Cohorts

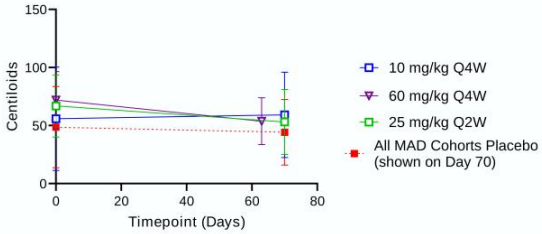
PET Centiloids at Baseline and Endpoint
SAD



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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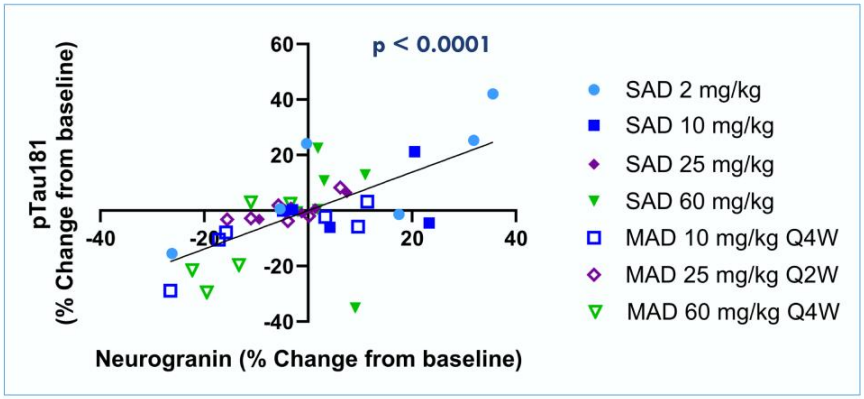
Significant Correlation Between Change in CSF Neurogranin and pTau181

- 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 sabirnetug.



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.

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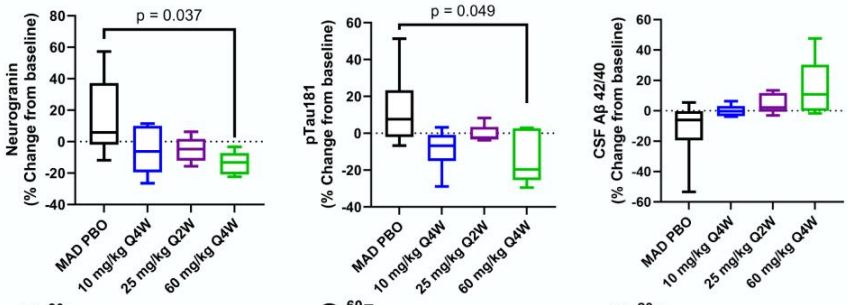
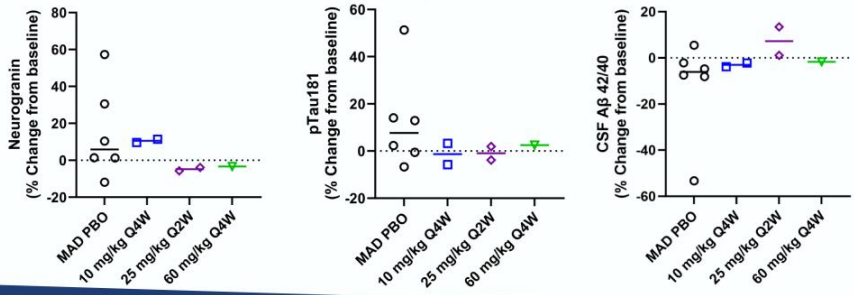
CSF BIOMARKERS

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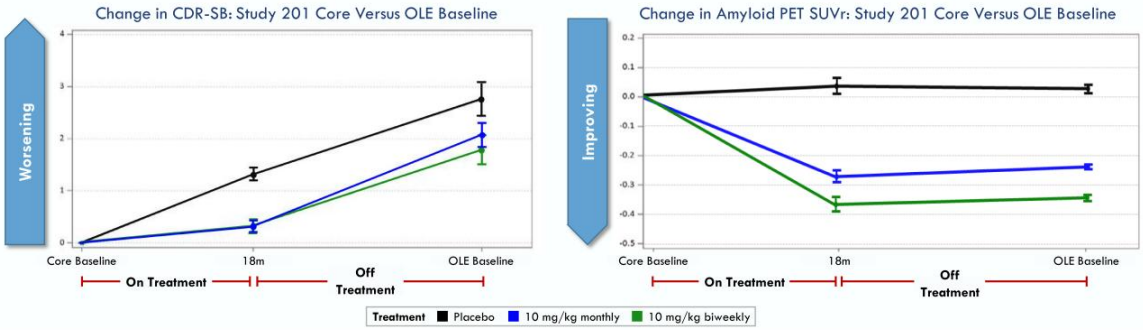
Lecanemab Phase 2 Suggests Amyloid Plaque Reduction Alone is Insufficient to Optimize Alzheimer's Disease Slowing*

- 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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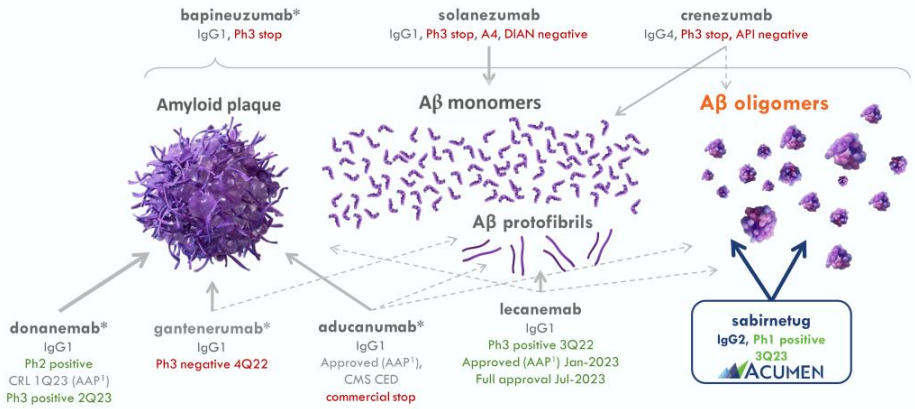
Sabirnetug Targeting Relative to Late-Stage and Approved Anti-Aβ/Plaque mAbs



* 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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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	**sabirnetug**	**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.

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Efficacy Results 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.

Safety Results From Recent Anti-Amyloid mAb AD Studies

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.