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 26, 2026**

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.)

1210-1220 Washington Street, Suite 210 **Newton, Massachusetts**	**02465**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's Telephone Number, Including Area Code: **(617) 344-4190**

(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 26, 2026, Acumen Pharmaceuticals, Inc. (the "**Company**") reported financial results and business highlights for the year ended December 31, 2025. A copy of this press release (the "**Earnings Press Release**") is furnished as Exhibit 99.1 to this Current Report on Form 8-K (this "**Report**") and is incorporated by reference.

The information in this Item 2.02 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 (the "**Securities Act**"), or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

On March 26, 2026, 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. The corporate presentation was updated to reflect the Company's cash, cash equivalents and marketable securities balance as of December 31, 2025 and to include the private placement completed by the Company on March 16, 2026. A copy of the corporate presentation is attached as Exhibit 99.2 to this Report.

The information in this Item 7.01 of this Report (including Exhibit 99.2), is being furnished and shall not be deemed "filed" for purposes of Section 18 of 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 or the Exchange Act, except as expressly set forth by specific reference in such filing. The Company's submission of this Report shall not be deemed an admission as to the materiality of any information required to be disclosed solely to satisfy the requirements of Regulation FD.

Item 9.01 Financial Statements and Exhibits.

(d). Exhibits

Exhibit No.	Description
99.1	Earnings Press Release, dated March 26, 2026
99.2	Corporate Presentation, dated March 26, 2026
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 26, 2026

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

Acumen Pharmaceuticals Reports Financial Results for the Year Ended December 31, 2025 and Business Highlights

- Expect to report topline results for ALTITUDE-AD, a Phase 2 study to investigate sabirnetug (ACU193) for the treatment of early Alzheimer's disease, in late 2026
- Lead clinical candidate IND filing in Acumen's Enhanced Brain Delivery (EBD™) program targeted for mid-2027, following strong preclinical data and $35.75 million private placement to advance candidates in AβO-selective EBD portfolio
- Cash, cash equivalents and marketable securities of $116.9 million as of Dec. 31, 2025, expected to support current clinical and operational activities into early 2027
- Company to host conference call and webcast today at 8:00 a.m. ET

NEWTON, Mass., Mar. 26, 2026 – Acumen Pharmaceuticals, Inc. (NASDAQ: ABOS) ("Acumen" or the "Company"), a clinical-stage biopharmaceutical company developing novel therapeutics that target toxic soluble amyloid beta oligomers (AβOs) for the treatment of Alzheimer's disease (AD), today reported financial results for the full year ended December 31, 2025 and provided a business update.

"2025 was defined by significant clinical progress supporting our Phase 2 ALTITUDE-AD study investigating our lead therapeutic candidate, sabirnetug, and the expansion of our pipeline via a notable Enhanced Brain Delivery (EBD™) partnership to develop a transferrin-receptor-targeting blood-brain barrier-penetrating therapy," said Daniel O'Connell, Chief Executive Officer of Acumen. "2026 is poised to be transformative for Acumen. Topline results for ALTITUDE-AD are expected late in the year and are anticipated to provide important insights into the role of AβOs in Alzheimer's disease. Supported by our recent financing, we are also advancing toward clinical candidate nomination in our EBD program, with an IND filing targeted for mid-2027. Pairing a commitment to scientific innovation with a track record of strong execution, we believe that we are well-positioned to deliver differentiated treatment options for Alzheimer's patients."

Recent Highlights

- **In March 2026, the Company announced a $35.75 million private placement to advance candidates in its AβO-selective EBD portfolio, following strong preclinical data, including *in vitro*, *in vivo* and non-human primate study results.**
  - Candidates exceeded key preclinical criteria, demonstrating elevated brain exposure in non-human primates up to 40-fold over native antibodies, low risk of anemia, and robust stability profiles to enable subcutaneous administration
  - Lead clinical candidate Investigational New Drug (IND) filing targeted for mid-2027

- **In March 2026 and in November 2025, the Company presented one oral and four poster presentations at the International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD) and the 18th Annual Clinical Trials on Alzheimer's Disease (CTAD) conference.**
  - At AD/PD, the presentations highlighted new data regarding the EBD program, sabirnetug biomarker treatment responses, and the development of new AβO-targeting antibodies.
  - At CTAD, results presented from a collaborative study with JCR Pharmaceuticals demonstrated that bispecific antibodies that target transferrin (TfR) as well as the AβO-targeting antibody sabirnetug achieved increased brain penetration in mice while preserving target binding. Results presented on clinical trial recruitment from the Phase 2 ALTITUDE-AD clinical trial showed that site databases and physician referrals were the most reliable recruitment methods overall.
  - Presentations are available on the Company's website here.

- **In November 2025, the Company dosed the first patient in the open-label extension (OLE) portion of its Phase 2 ALTITUDE-AD clinical trial evaluating sabirnetug (ACU193) in patients with early Alzheimer's disease.**
  - The OLE provides all participants who completed the 18-month placebo-controlled double-blind portion of ALTITUDE-AD, including patients previously treated with placebo, with the opportunity to receive sabirnetug at 35 mg/kg administered intravenously once every four weeks for up to 52 weeks.

Anticipated Milestones

- The Company expects topline results from ALTITUDE-AD, a Phase 2 study to investigate sabirnetug for the treatment of early Alzheimer's disease, in late 2026.

- The Company is targeting the submission of an IND filing with respect to a lead clinical candidate in its EBD program in mid-2027.

2025 Financial Results

- **Cash Balance.** As of Dec. 31, 2025, cash, cash equivalents and marketable securities totaled $116.9 million compared to cash, cash equivalents and marketable securities of $136.1 million as of Sept. 30, 2025. The decrease in cash is related to funding ongoing operations. Cash is expected to support current clinical and operational activities into early 2027.

- **Research and Development (R&D) Expenses.** R&D expenses were $104.9 million for the year ended Dec. 31, 2025, compared to $93.8 million for the year ended Dec. 31, 2024. The increase was primarily due to an increase in manufacturing and materials mainly associated with our ALTITUDE-AD clinical trial, as well as personnel-related costs and research expenses, including EBD research.

- **General and Administrative (G&A) Expenses.** G&A expenses were $18.9 million for the year ended Dec. 31, 2025, compared to $20.2 million for the year ended Dec. 31, 2024. The decrease was primarily due to reductions in recruiting expenses, corporate insurance expenses and consulting costs.
- **Loss from Operations.** Loss from operations was $123.8 million for the year ended Dec. 31, 2025, compared to $114.0 million for the year ended Dec. 31, 2024. This increase was due to the increased R&D expenses over the prior year period.
- **Net Loss.** Net loss was $121.3 million for the year ended Dec. 31, 2025, compared to $102.3 million for the year ended Dec. 31, 2024.

Conference Call Details

Acumen will host a conference call and live audio webcast today, Mar. 26, 2026, at 8:00 a.m. ET.

To participate in the live conference call, please register using this link. After registration, you will be informed of the dial-in numbers including PIN. Please register at least one day in advance.

The webcast audio will be available via this link.

An archived version of the webcast will be available for at least 30 days in the Investors section of the Company's website at www.acumenpharm.com.

About Sabirnetug (ACU193)

Sabirnetug (ACU193) is a humanized monoclonal antibody (mAb) discovered and developed based on its selectivity for soluble amyloid beta oligomers (AβOs), which are a highly toxic and pathogenic form of Aβ, relative to Aβ monomers and amyloid plaques. Soluble AβOs have been observed to be potent neurotoxins that bind to neurons, inhibit synaptic function and induce neurodegeneration. By selectively targeting toxic soluble AβOs, sabirnetug aims to address the hypothesis that soluble AβOs are an early and persistent underlying cause of the neurodegenerative process in Alzheimer’s disease (AD). Sabirnetug has been granted Fast Track designation for the treatment of early AD by the U.S. Food and Drug Administration and is currently being evaluated in a Phase 2 study in patients with early AD.

About ALTITUDE-AD (Phase 2)

Initiated in 2024, ALTITUDE-AD is a Phase 2, multi-center, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the efficacy and safety of sabirnetug (ACU193) infusions administered once every four weeks in slowing cognitive and functional decline as compared to placebo in participants with early Alzheimer's disease. The study has enrolled 542 individuals with early Alzheimer’s disease (mild cognitive impairment or mild dementia due to AD) at multiple investigative sites located in the United States, Canada, the European Union and

the United Kingdom. Topline results are expected in late 2026. More information can be found on www.clinicaltrials.gov, NCT identifier NCT06335173.

About Acumen Pharmaceuticals, Inc.

Acumen Pharmaceuticals is a clinical-stage biopharmaceutical company developing a novel therapeutic that targets toxic soluble amyloid beta oligomers (AβOs) for the treatment of Alzheimer's disease (AD). Acumen's scientific founders pioneered research on AβOs, which a growing body of evidence indicates are early and persistent triggers of Alzheimer's disease pathology. Acumen is currently focused on advancing its lead investigational product candidate, sabirnetug (ACU193), a humanized monoclonal antibody that selectively targets toxic soluble AβOs, in its ongoing Phase 2 clinical trial ALTITUDE-AD (NCT06335173) in early symptomatic Alzheimer's disease patients, following positive results in its Phase 1 trial INTERCEPT-AD. Acumen is also investigating a subcutaneous formulation of sabirnetug using Halozyme's proprietary ENHANZE® drug delivery technology. Acumen is also collaborating with JCR Pharmaceuticals to develop an Enhanced Brain Delivery (EBD™) therapy for Alzheimer's disease utilizing a transferrin-receptor-targeting blood-brain barrier-penetrating technology. The company is headquartered in Newton, Mass. For more information, visit www.acumenpharm.com.

About JCR Pharmaceuticals Co., Ltd.

JCR Pharmaceuticals Co., Ltd. is a global specialty pharmaceutical company that develops treatments that go beyond rare diseases to solve the world's most complex healthcare challenges. JCR continues to build upon our 50-year legacy in Japan while expanding our global footprint into the US, Europe, and Latin America. JCR's innovative therapies address conditions like growth disorder, MPS II, Fabry disease, acute graft-versus-host disease, and renal anemia. JCR is also developing treatments for rare diseases like MPS I, MPS II, MPS IIIA and B, and more.

Forward-Looking Statements

This press release 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," "should," "would," "seeks," "aims," "plans," "potential," "will," "milestone" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements concerning Acumen's business, and Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the expected sufficiency of its cash resources into early 2027, the therapeutic potential of Acumen's product candidate, sabirnetug (ACU193), including against other antibodies, the timing of anticipated topline results of ALTITUDE-AD, the potential for additional development to support a subcutaneous dosing option of sabirnetug, Acumen's plans to develop a candidate to treat Alzheimer's Disease utilizing EBD technology, including its expectations with respect to timing for the submission of an IND, as well as its potential for developing a best-in-class therapeutic candidate for people living with Alzheimer's Disease. 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 geopolitical events and macroeconomic conditions, such as rising inflation and interest rates, supply disruptions and uncertainty of credit and financial markets. 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 on Form 10-K, and in subsequent filings with the SEC. 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.

CONTACTS:

Investors:
Alex Braun
abraun@acumenpharm.com

Media:
ICR Healthcare
AcumenPR@icrhealthcare.com

Acumen Pharmaceuticals, Inc.
Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2025	**2024**
ASSETS		
Current assets		
Cash and cash equivalents	$ 53,989	$ 35,627
Marketable securities, short-term	62,876	135,930
Prepaid expenses and other current assets	5,387	6,749
Total current assets	122,252	178,306
Marketable securities, long-term	—	59,968
Restricted cash	231	232
Other assets, long-term	350	486
Total assets	$ 122,833	$ 238,992
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 554	$ 5,648
Accrued clinical trial expenses	10,616	15,344
Accrued expenses and other current liabilities	10,072	6,615
Debt, short-term	8,765	—
Total current liabilities	30,007	27,607
Debt, long-term	22,396	29,419
Other liabilities, long-term	—	150
Total liabilities	52,403	57,176
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued and outstanding as of December 31, 2025 and 2024	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized as of December 31, 2025 and 2024; 60,575,369 and 60,094,083 shares issued and outstanding as of December 31, 2025 and 2024, respectively	6	6
Additional paid-in capital	516,803	506,985
Accumulated deficit	(446,462)	(325,127)
Accumulated other comprehensive income (loss)	83	(48)
Total stockholders' equity	70,430	181,816
Total liabilities and stockholders' equity	$ 122,833	$ 238,992

Acumen Pharmaceuticals, Inc.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2025	**2024**
Operating expenses		
Research and development	$ 104,885	$ 93,798
General and administrative	18,947	20,219
Total operating expenses	123,832	114,017
Loss from operations	(123,832)	(114,017)
Other income (expense)		
Interest income	7,447	14,317
Interest expense	(4,224)	(4,068)
Change in fair value of embedded derivatives	(460)	1,590
Other expense, net	(266)	(151)
Total other income	2,497	11,688
Net loss	(121,335)	(102,329)
Other comprehensive gain (loss)		
Unrealized gain (loss) on marketable securities	131	(360)
Comprehensive loss	$ (121,204)	$ (102,689)
Net loss per common share, basic and diluted	$ (2.00)	$ (1.71)
Weighted-average shares outstanding, basic and diluted	60,561,836	60,013,277

Acumen Pharmaceuticals, Inc.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2025	**2024**
Cash flows from operating activities		
Net loss	$ (121,335)	$ (102,329)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	58	63
Stock-based compensation expense	9,852	9,635
Amortization of premiums and accretion of discounts on marketable securities, net	(809)	(5,015)
Change in fair value of embedded derivatives	460	(1,590)
Amortization of right-of-use asset	126	115
Realized gain on marketable securities	(59)	(97)
Noncash interest expense	1,288	1,118
Other noncash expense	—	232
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,362	(3,656)
Other long-term assets	40	74
Accounts payable	(5,094)	4,269
Accrued clinical trial expenses	(4,728)	10,957
Accrued expenses and other liabilities	3,301	32
Finance lease liability	—	(23)
Net cash used in operating activities	(115,538)	(86,215)
Cash flows from investing activities		
Purchases of marketable securities	(38,056)	(170,731)
Proceeds from maturities and sales of marketable securities	172,077	218,774
Purchases of property and equipment	(88)	(16)
Net cash provided by investing activities	133,933	48,027
Cash flows from financing activities		
Proceeds from issuance of common stock, net of issuance costs	—	7,938
Proceeds from exercise of stock options	39	—
Payment for financing lease	—	(739)
Payments for deferred offering costs	—	(230)
Repurchase of common shares to pay employee withholding taxes	(73)	(41)
Net cash (used in) provided by financing activities	(34)	6,928
Net change in cash and cash equivalents and restricted cash	18,361	(31,260)
Cash and cash equivalents and restricted cash at the beginning of the period	35,859	67,119
Cash and cash equivalents and restricted cash at the end of the period	$ 54,220	$ 35,859

Corporate Presentation

March 2026

Forward-Looking Statements

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

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

Targeting Toxic Amyloid Beta Oligomers (AβOs)

With passion, expertise, and perseverance, we are forging a path toward innovative treatments that preserve quality time for all people impacted by Alzheimer's and other neurodegenerative diseases.

Large and growing market in need of additional treatment options

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

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

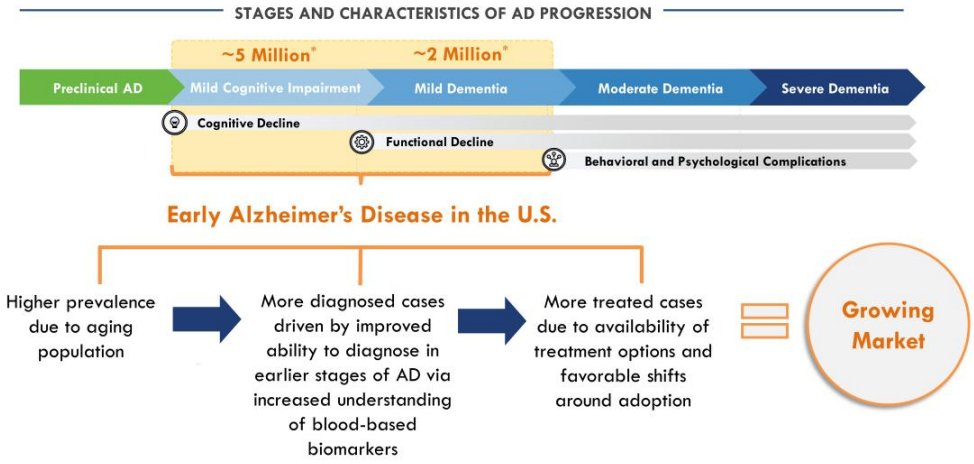
Experienced leadership team with extensive AD drug development experience

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

BBB: blood-brain-barrier

ACUMEN

Early AD Patient Population Represents Significant and Growing Market



*Alzheimer's Association

ACUMEN

AD Treatment Landscape Continues to Evolve

Approved Therapies Establish Momentum and Next-generation Approaches Expand Impact

Current AD Treatments
Offer Hope for People Living with AD

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

Opportunities for New Anti-amyloid Therapies
to Strengthen Risk-Benefit Tradeoff

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

Future of AD Landscape
Broadens Growth Prospects

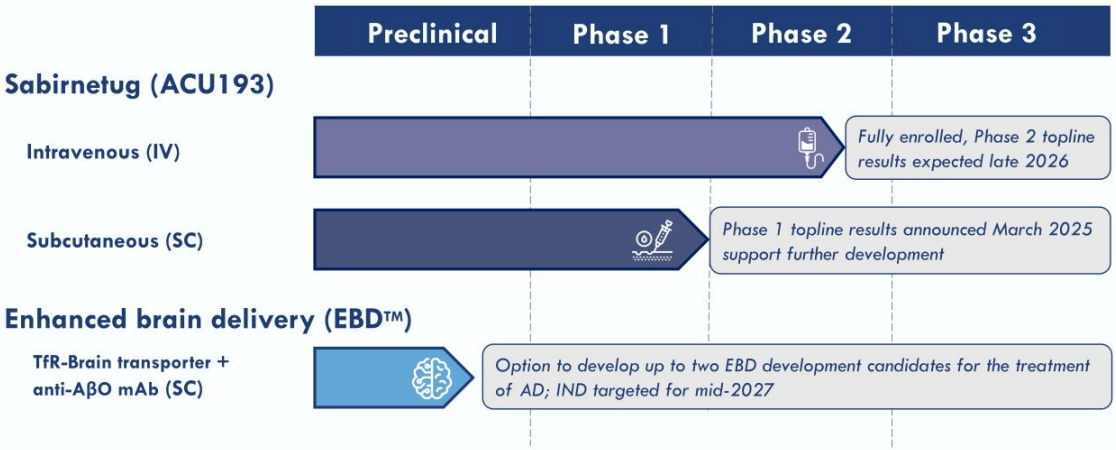
- New blood-based biomarkers and imaging tools will improve diagnostic and monitoring capabilities
- Expansion into preclinical AD will significantly increase the addressable population
- Combinations with other targets, such as tau, hold promise

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

ACUMEN

2026 a Pivotal Year for Acumen's Pipeline

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



ACUMEN

Acumen Leadership Team

Experienced in AD/Neuro Drug Development

DANIEL O'CONNELL
Chief Executive Officer
ACUMEN
neuroventures

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

ERIC SIEMERS, MD
Chief Medical Officer
ACUMEN
Lilly

MATT ZUGA
Chief Financial Officer &
Chief Business Officer
ACUMEN
HighCape Partners

RUSSELL BARTON
Chief Operating Officer
ACUMEN
Lilly

LIEAN SCHENK
SVP, Head of CMC
ACUMEN
Lilly · Lonza · NOVAVAX

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

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

SIEW TIN GAN
Head of Clinical
Operations
ACUMEN
Landsdowne · Takeda

JASNA JERECIC, PHD
Disease Area Strategy Lead
ACUMEN

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

DEREK MEISNER, JD
Chief Legal Officer
ACUMEN
X4

JULIE BOCKENSTETTE
Chief People Officer
ACUMEN
Roche · Lilly

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

Milestones Achieved and Upcoming

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

~$117M

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

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

Acumen expects its cash runway to extend into early 2027

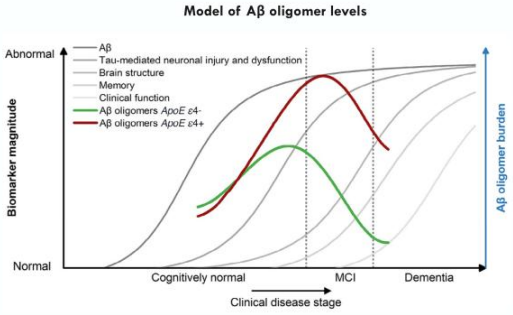
ACUMEN

Amyloid Beta Oligomers in AD

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

ACUMEN

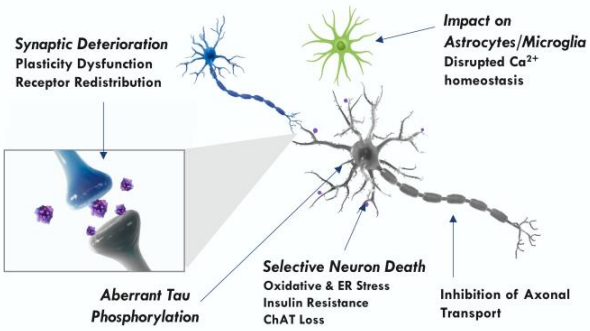
Soluble AβOs Contribute to Pathophysiological Processes Associated with Alzheimer's Disease



Adapted from Blomeke et al. 2024

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

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



Sabirnetug: Potential Next Generation Immunotherapy for Early AD

Designed for Improved Efficacy & Safety

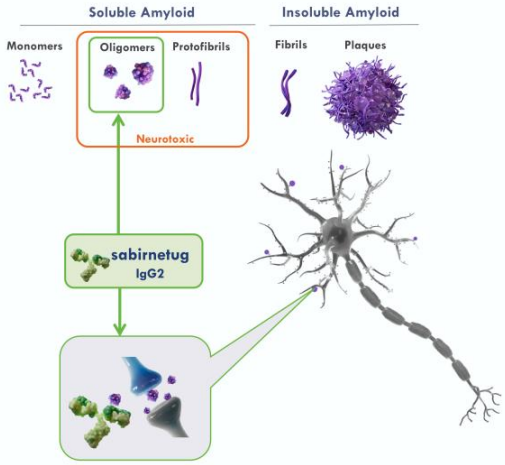
- Humanized, affinity matured mAb developed to target toxic Aβ oligomers
- IgG2 subclass mAb with reduced effector function

Encouraging Regulatory Interactions

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

Positive Ph1 in AD Patients & Encouraging Ph2 Enrollment

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

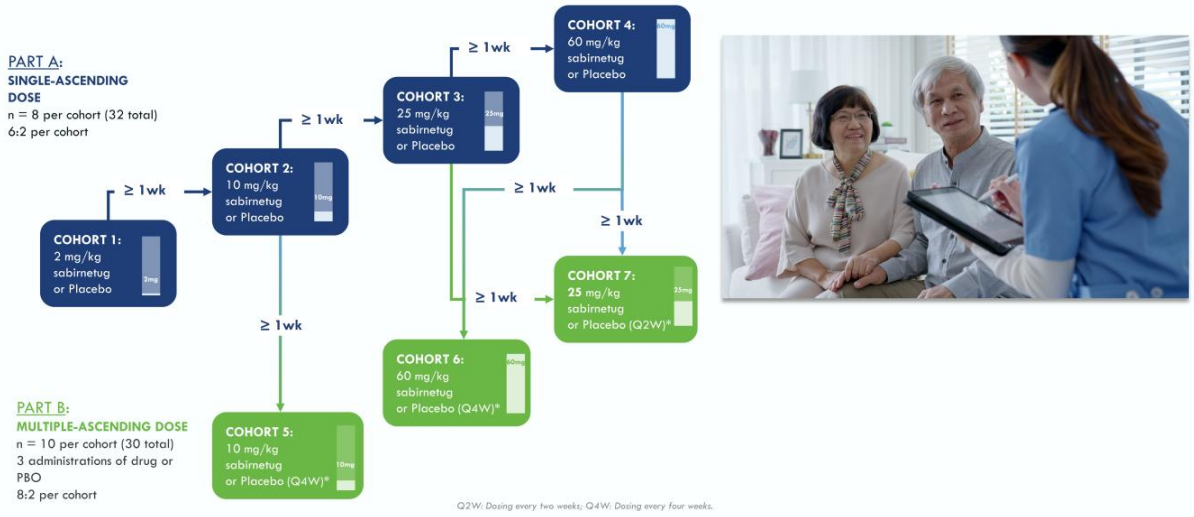


ACUMEN

Sabirnetug

ACUMEN

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

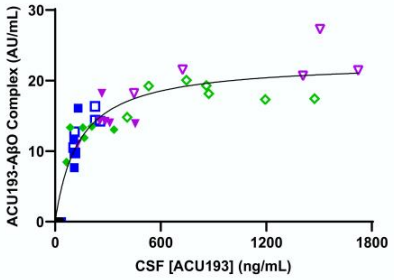


ACUMEN

TARGET ENGAGEMENT

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

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



- 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

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

Sabirnetug-AβO Complex

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

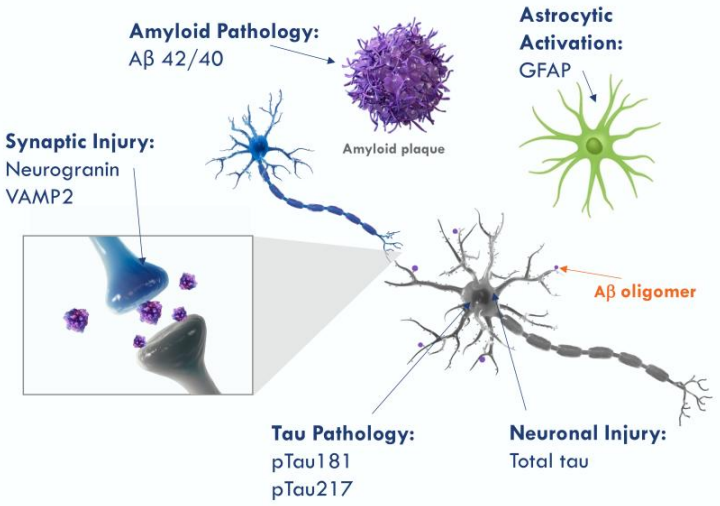
*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

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

ACUMEN

Importance of Key Fluid Biomarkers Associated with AD Pathology

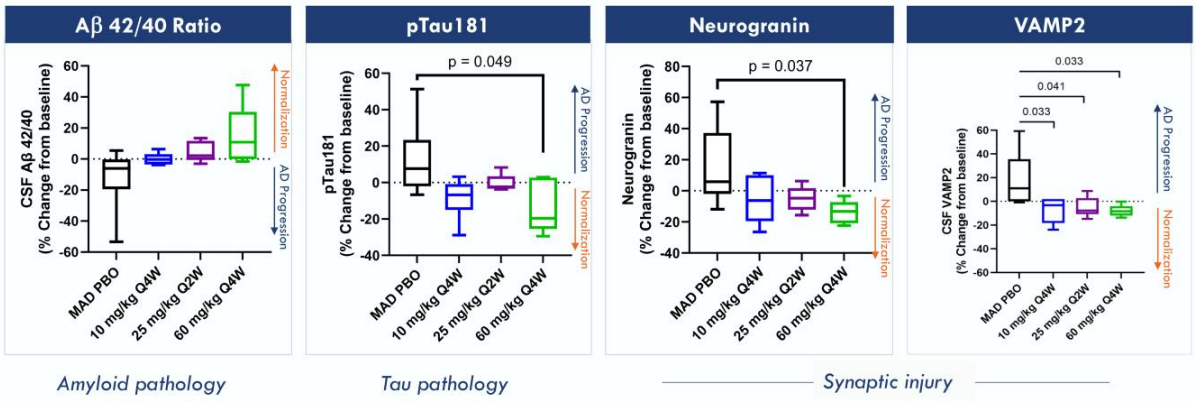
- Biomarkers from cerebrospinal fluid and plasma capture neuronal, synaptic, and axonal injury and reflect the cumulative outcome of different pathological substrates in AD[1]
- Evidence suggests that biomarkers are likely to be better predictors of the underlying pathology of AD than imaging alone[2]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



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

ACUMEN

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



Amyloid pathology *Tau pathology* *Synaptic injury*

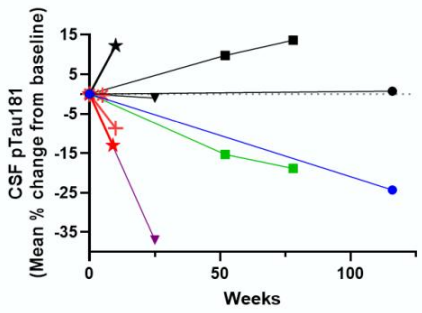
E. Cline, et al, Biofluid biomarker changes following treatment with sabirnetug (ACU193) in INTERCEPT-AD, a phase 1 trial in early Alzheimer's disease. JPAD 2025.

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

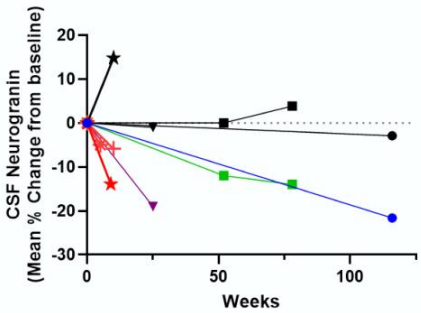
ACUMEN

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

CSF pTau181



CSF Neurogranin



- ACU193 (60 mg/kg Q4W)
- ACU193 (25 mg/kg Q2W)
- ACU193 (10 mg/kg Q4W)
- Pooled Placebo ACU193
- Gantenerumab (510 mg Q2W)
- Gantenerumab Placebo
- Lecanemab (10 mg/kg Q2W)
- Lecanemab Placebo
- Trontinemab (3.6 mg/kg Q4W)
- Trontinemab Placebo

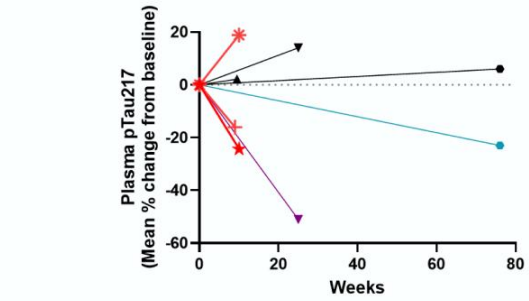
Acumen Pharmaceuticals, data on file; AAIC 2023; Bateman et al 2023 NEJM; ADPD 2025.

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

ACUMEN

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

Plasma pTau217



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

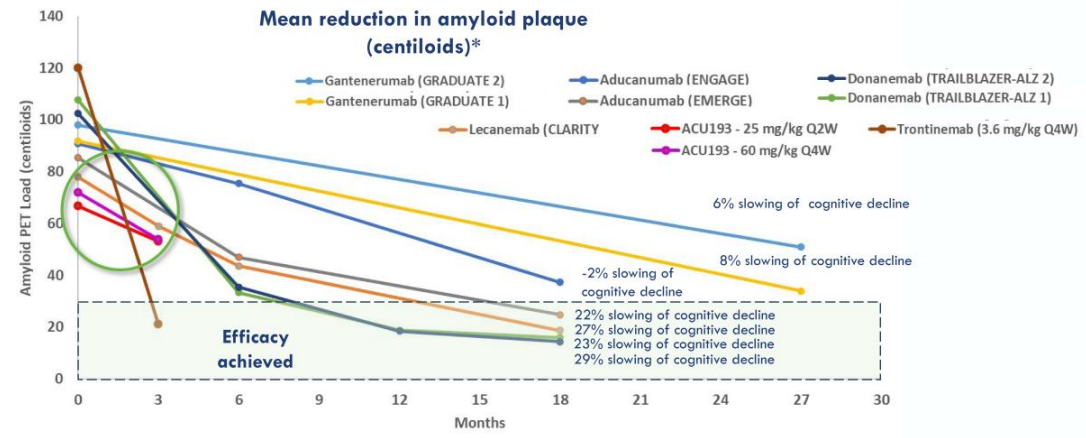
Acumen Pharmaceuticals, data on file; AAIC 2023; Sims et al 2023 JAMA; ADPD 2025.

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

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

ACUMEN

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.

ACUMEN

SAFETY

Sabirnetug Demonstrates Potential for Best-in-Class Safety Profile

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

INTERCEPT-AD Phase 1 Safety Data

5 Total ARIA-E cases, or ~10%

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

0 Deaths, SAEs Related to Study Drug

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

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

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

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

ApoE4: ε4 allele of Apolipoprotein E

ACUMEN

INTERCEPT-AD Phase 1 Data Support Potential for Sabirnetug to Offer Next Generation Efficacy and Safety

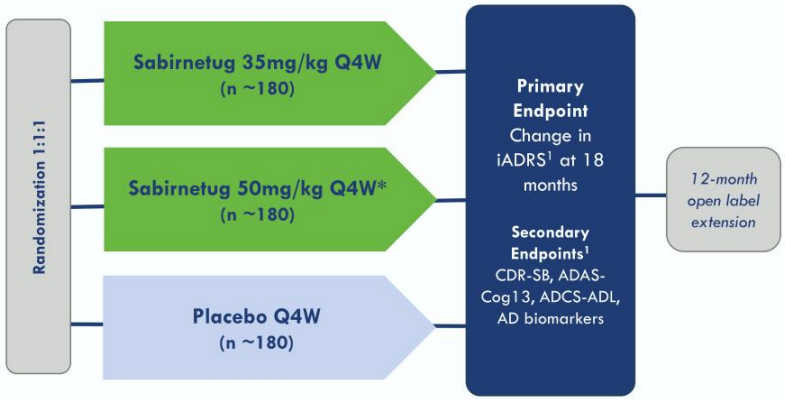
Key Takeaways from INTERCEPT-AD

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

ACUMEN

ALTITUDE-AD Phase 2 Study Results Expected in Late 2026

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



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

Key Highlights

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

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

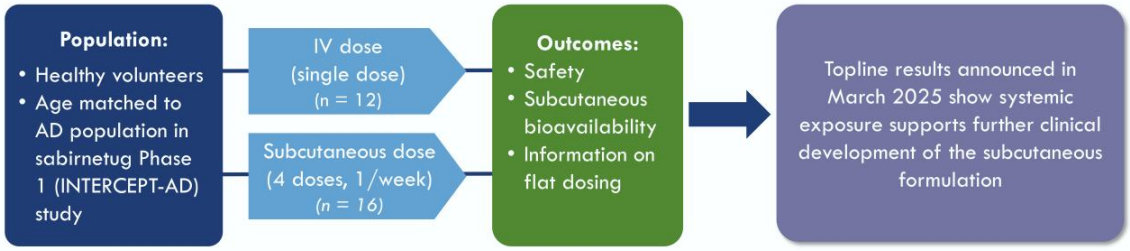
ACUMEN

Subcutaneous Formulation Well-Tolerated in Phase 1 Healthy Volunteer Study

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

Phase 1 Subcutaneous Healthy Volunteer Study

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



Halozyme

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

ACUMEN

Sabirnetug IP & Market Exclusivity

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

Enhanced Brain Delivery (EBD™)

ACUMEN

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

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

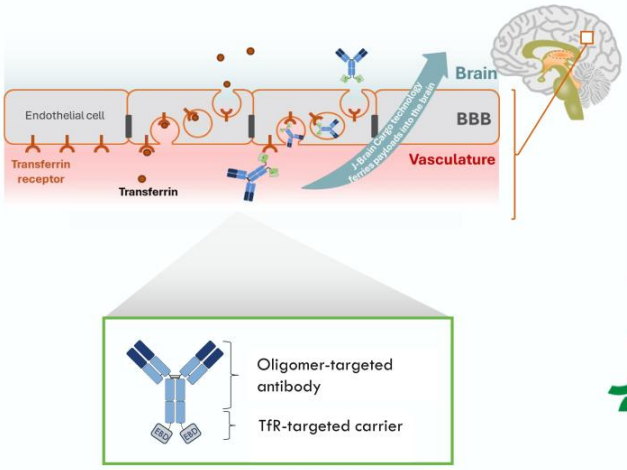


Image courtesy of JCR Pharmaceuticals

Enhanced Brain Delivery (EBD) Opportunities:

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

JCR Pharmaceuticals

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

ACUMEN

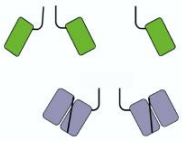
Acumen's EBD May Improve Efficacy, Safety and Delivery Compared to Non-AβO Selective Antibodies

Differentiated Cargo (AβO-selective mAb)

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

+

Validated BBB Carrier Technology (TfR-targeting)



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

=

Acumen EBD Candidates

Differentiated Aβ targeting

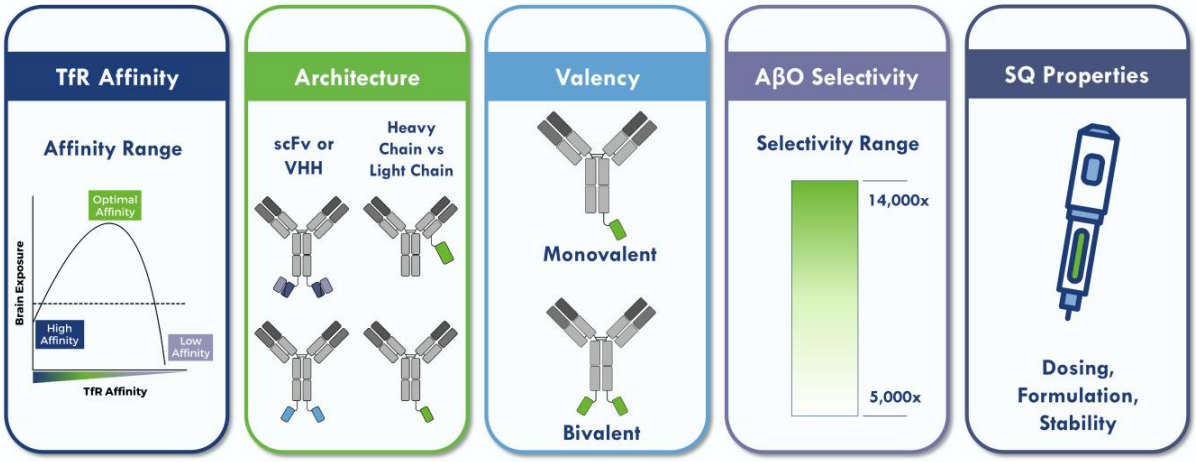
Validated TfR-binding

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

ApoE4: ε4 allele of Apolipoprotein E

ACUMEN

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



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

ACUMEN

Phase 1 Results Provide Foundation for EBD™ Program

Half-life/Dosing Interval

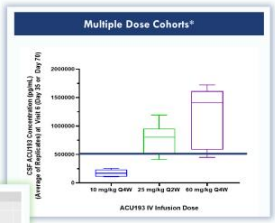
Once monthly dosing

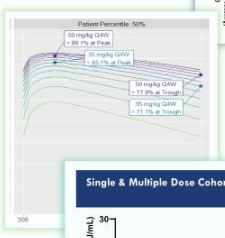
Dosing Exposure

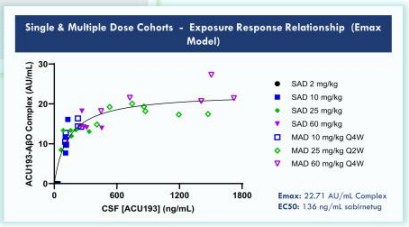
35 mg/kg and 50 mg/kg in Phase 2 IV

Target Engagement

Maximal TE of AβOs observed





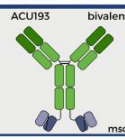
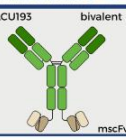
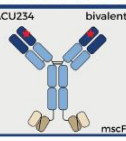


*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

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

ACUMEN

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

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

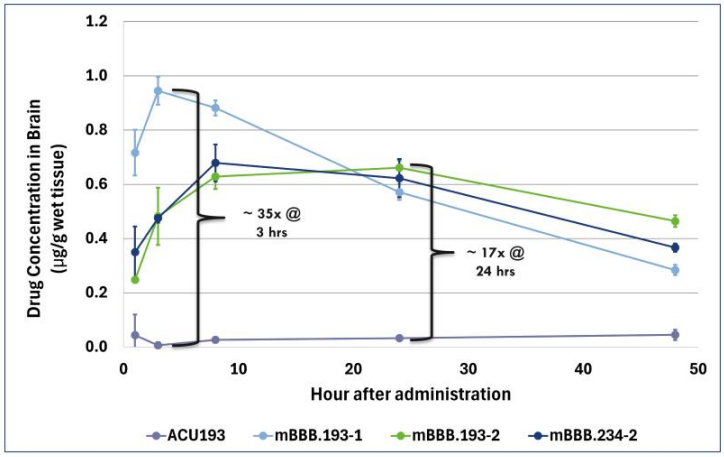
Cline et al., CTAD, 2025
*Cline et al., AAIC, 2025

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

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

ACUMEN

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



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

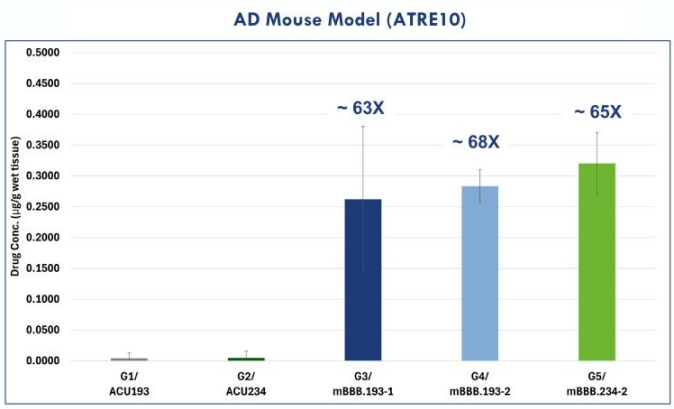
Animals dosed IV at 2 mpk

Cline et al., CTAD, 2025

ACUMEN

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

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



Animals dosed at IV 2 mpk

Cline et al., CTAD, 2025

ACUMEN

Robust Data Package Supporting EBD™ Construct Selection

Inclusive of NHP Primate Data

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

ACUMEN

Key Takeaways from NHP Study Results

✓ **Enhanced Brain Penetration**

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

✓ **Low Anemia Risk**

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

✓ **Subcutaneous Dosing Capability**

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

Lead clinical candidate IND targeted for 2027

ACUMEN

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

Key Takeaways

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

Next Steps

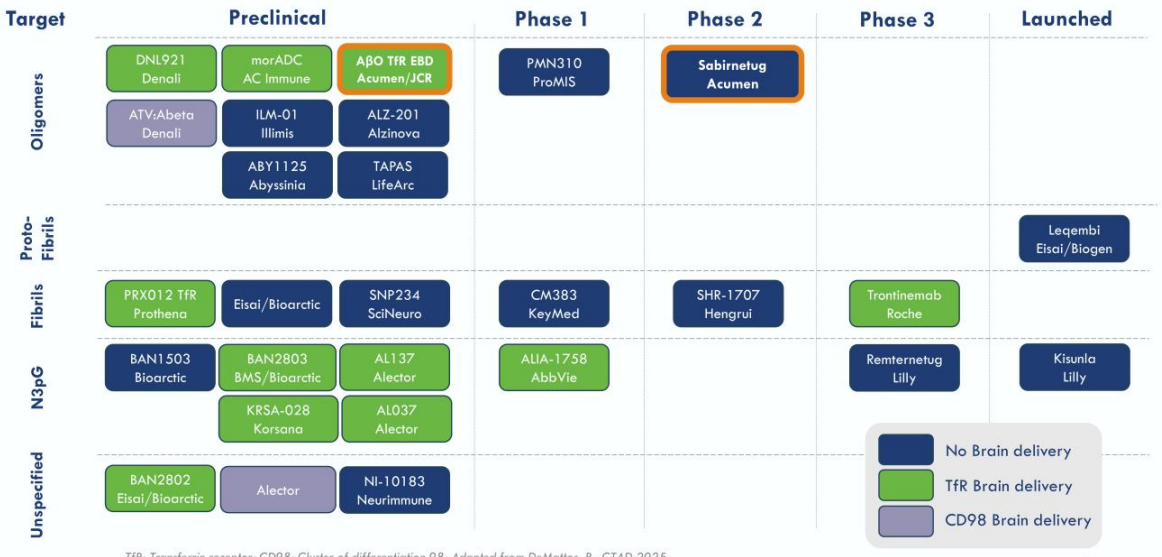
- ✓ EBD™ program pre-clinical candidate (PCC) data announced in **early 2026**
- ❑ Topline results from ALTITUDE-AD Phase 2 IV study evaluating the clinical efficacy and safety of sabirnetug in patients with MCI or mild dementia due to Alzheimer's expected in **late 2026**
- ❑ IND for EBD program targeted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

ACUMEN

Appendix

www.acumenpharm.com

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

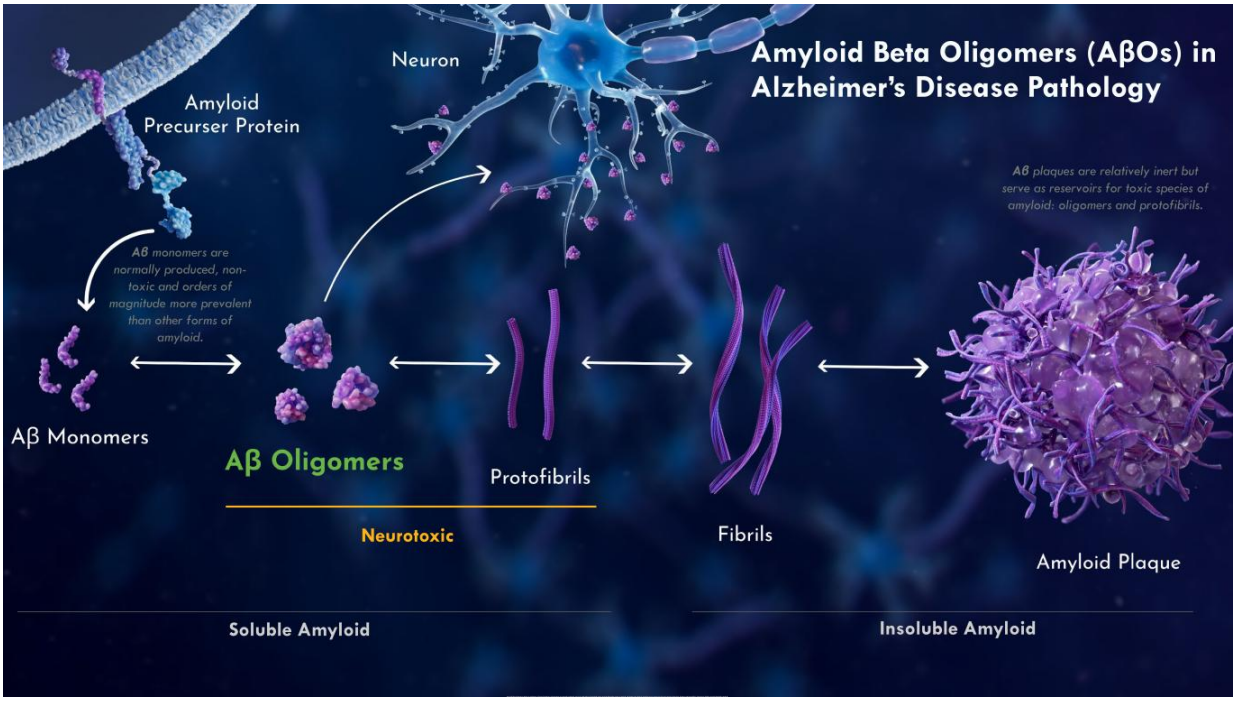


TfR: Transferrin receptor; CD98: Cluster of differentiation 98; Adapted from DeMattos, R., CTAD 2025.

ACUMEN

Non-clinical Sabirnetug Data

ACUMEN


Amyloid Beta Oligomers (AβOs) in Alzheimer's Disease Pathology
Neuron
Amyloid Precurser Protein
Aβ monomers are normally produced, non-toxic and orders of magnitude more prevalent than other forms of amyloid.
Aβ plaques are relatively inert but serve as reservoirs for toxic species of amyloid: oligomers and protofibrils.
Aβ Monomers
Aβ Oligomers
Protofibrils
Fibrils
Amyloid Plaque
Neurotoxic
Soluble Amyloid
Insoluble Amyloid

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

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

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

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

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

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

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

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

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

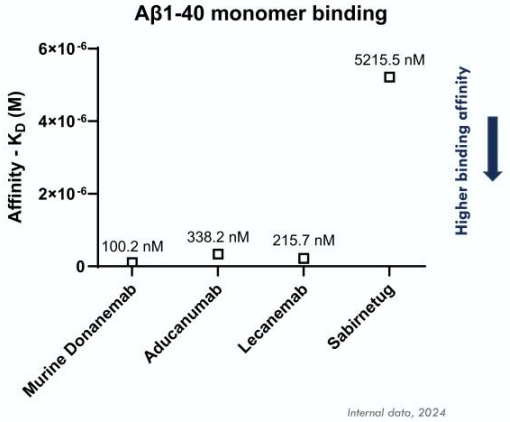
Disrupted Ca^{2+} homeostasis
Demuro et al, 2005
De Felice et al, 2007
Alberdi et al, 2010
Wang et al, 2018

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

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

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

Sabirnetug Demonstrates Low Affinity for Monomeric Aβ



Internal data, 2024

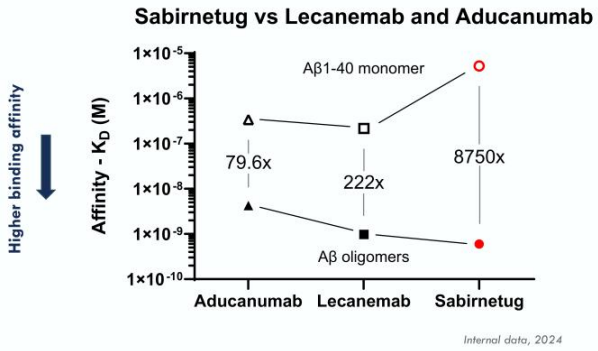
Note: Calculated K_D value for sabirnetug was above the highest analyzed concentration.

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

Sabirnetug is Highly Selective for Aβ Oligomers Versus Aβ Monomers

Relative Selectivity for AβO versus Monomeric Aβ Measured with SPR

Sabirnetug is more selective for AβOs than aducanumab or lecanemab

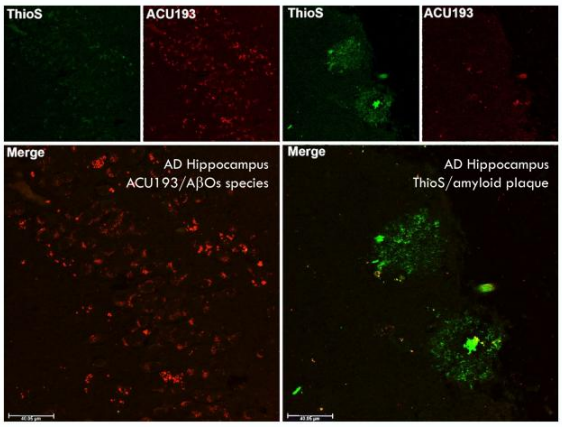


Internal data, 2024

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

Sabirnetug is Selective for AβOs Versus Aβ Plaques

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

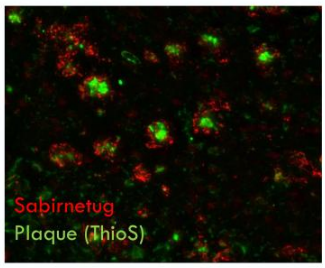


Sabirnetug
Thioflavin S

Adapted from Krafft et al. 2022

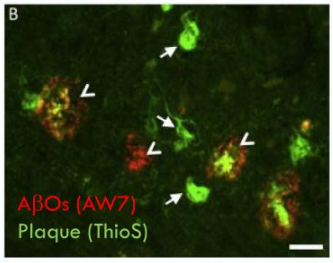
Amyloid Plaques are Surrounded by a Halo of AβOs

Transgenic mouse model of AD



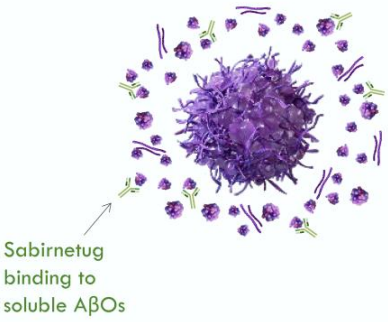
Lab of William Klein, NU, 2017

AD human brain tissue



Spires-Jones et al. 2014

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



Sabirnetug binding to soluble AβOs

ACUMEN

Sabirnetug: Extensive Data Package Supporting Development

SELECTIVITY

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

PHARMACOLOGY

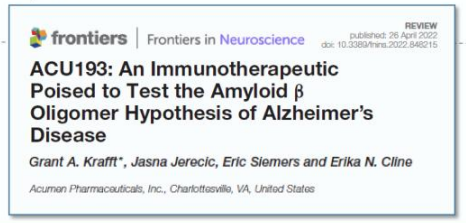
- Dose-dependent effects in multiple in vitro neuroprotection assays
- Positive memory and behavioral effects in multiple in vivo transgenic mouse models for AD

PK/PD

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

SAFETY

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


frontiers | Frontiers in Neuroscience

REVIEW
published: 26 April 2022
doi: 10.3389/fnins.2022.846215

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

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

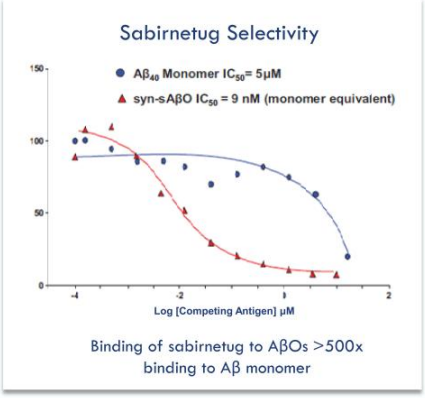
Acumen Pharmaceuticals, Inc., Charlottesville, VA, United States

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

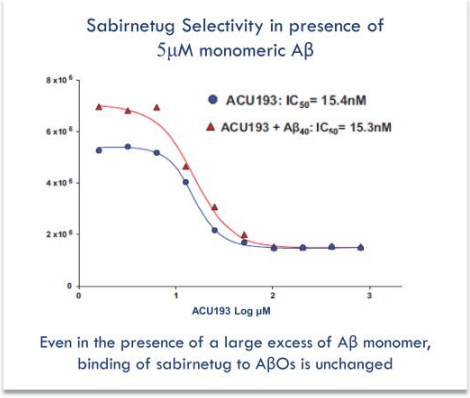
ACUMEN

Sabirnetug is the First mAb Developed to Selectively Target AβOs

Highly selective for Aβ oligomers versus Aβ monomers



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



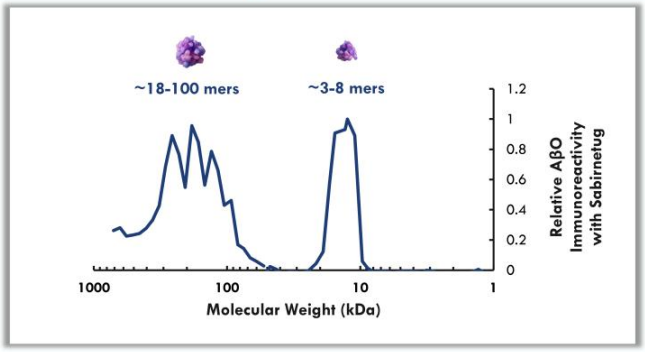
Even in the presence of a large excess of Aβ monomer, binding of sabirnetug to AβOs is unchanged

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'

ACUMEN

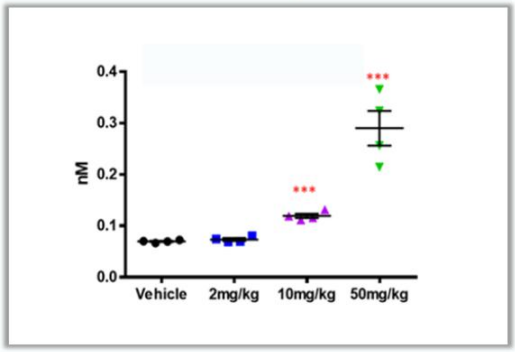
Sabirnetug Recognizes a Wide Range of Oligomeric Species of Aβ

Broad AβO size distribution recognized by sabirnetug in human AD brain



Data from lab of William Klein, NU, 2018

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

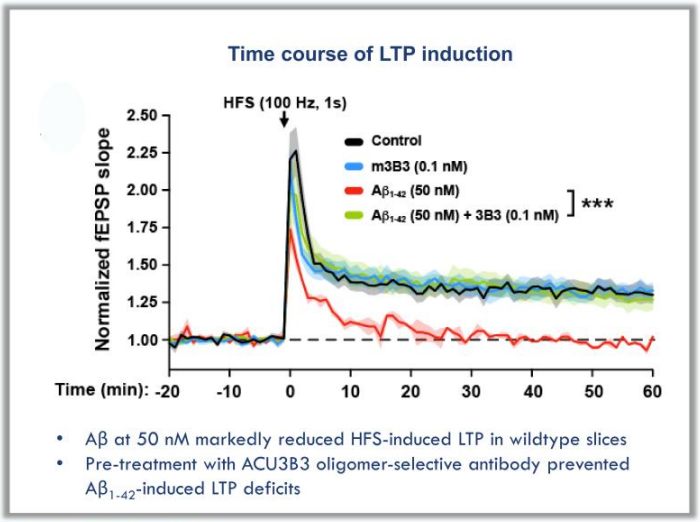


Merck internal data, 2011

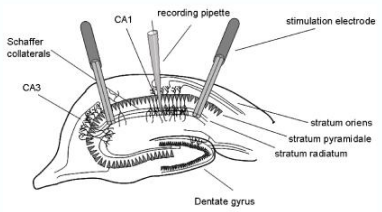
ACUMEN

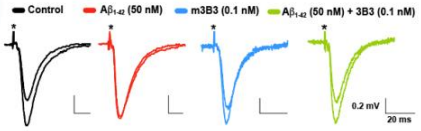
Functional Consequences of AβO Clearance: Restoring Plasticity

1. Prevention of hippocampal LTP impairment



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



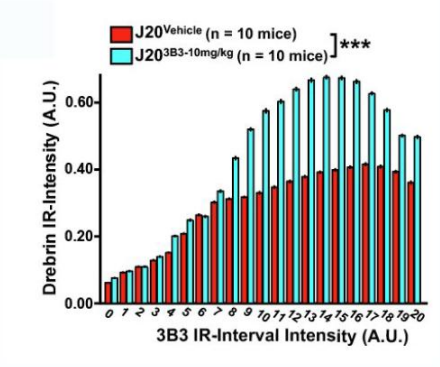


From manuscript in prep; data collected by lab of Gerhard Rammes, University of Regensburg, Max-Planck Institute of Psychiatry, Germany

ACUMEN

Functional Consequences Following ACU3B3 Treatment

2. Reduced amyloid deposition and increased spine density



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

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

ACUMEN

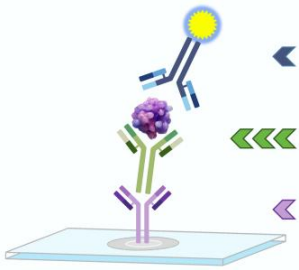
Phase 1 INTERCEPT-AD

ACUMEN

Target Engagement Assessed by Measuring Sabirnetug-AβO Complex in CSF

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

MSD S-Plex (Turbo) Immunoassay



AβO selective detection
(anti-AβO mAb)

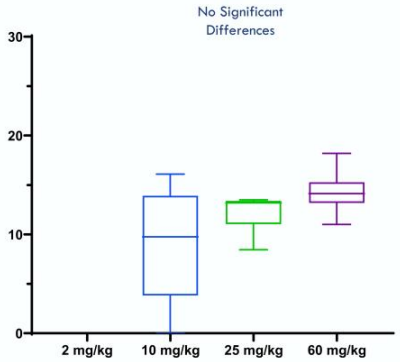
Only Sabirnetug-AβO complex is measurable

Sabirnetug drug specific capture
(anti-sabirnetug idiotype mAb)

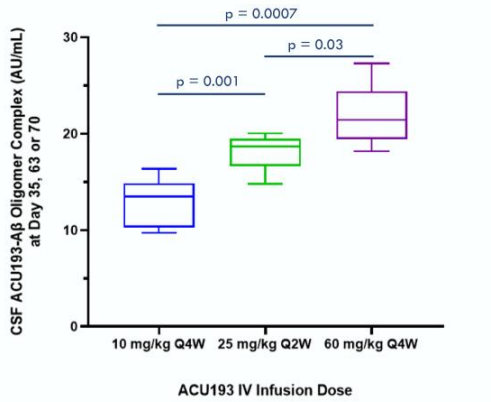
ACUMEN

Target Engagement of Sabirnetug with AβOs is Dose Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



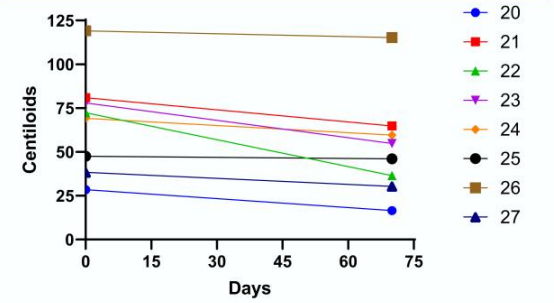
*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

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

ACUMEN

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

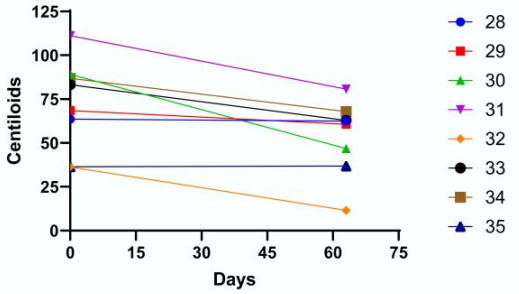
25 mg/kg Q2W MAD



Mean reduction in amyloid plaque

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

60 mg/kg Q4W MAD



Mean reduction in amyloid plaque

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

Plaque load based on florbetapir PET

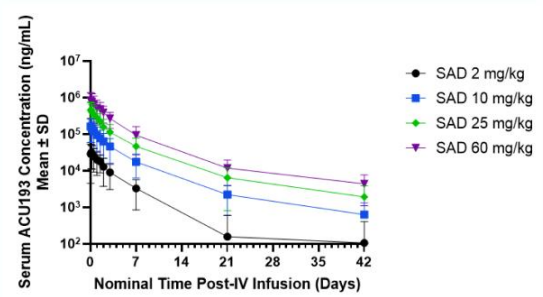
E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

ACUMEN

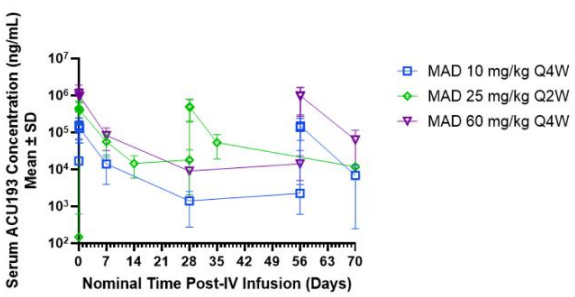
PHARMACOKINETICS

Sabirnetug Serum Exposure is Dose Proportional Without Accumulation

Single Dose Cohorts



Multiple Dose Cohorts



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

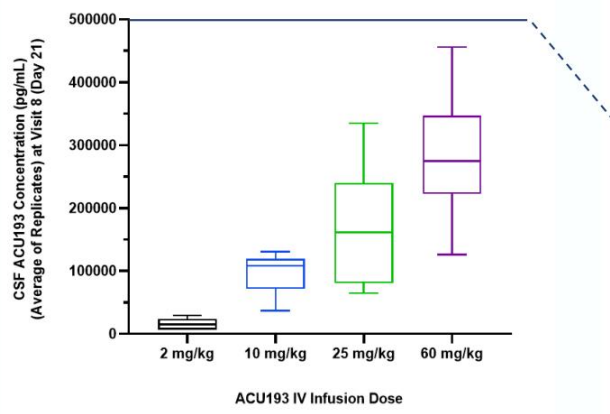
E. Siemers, et al. INTERCEPT-AD, a phase 1 study of intravenous sabirnetug in participants with mild cognitive impairment or mild dementia due to Alzheimer's disease. JPAD 2025.

ACUMEN

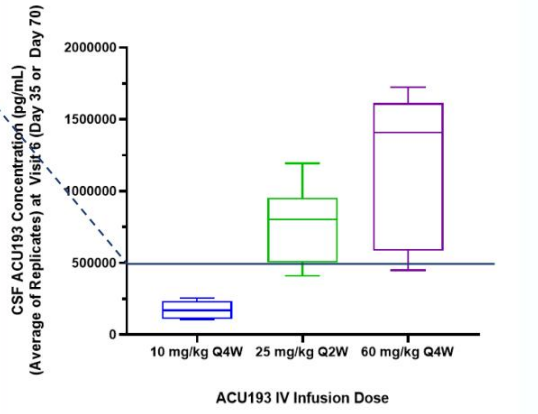
PHARMACOKINETICS

Sabirnetug CSF Exposure is Dose and Dose-Regimen Proportional

Single Dose Cohorts



Multiple Dose Cohorts*



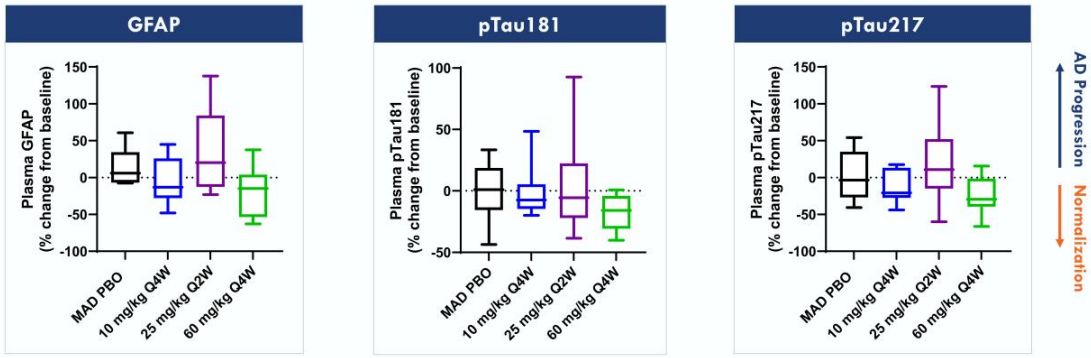
*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

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

ACUMEN

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

1-6 wk post-dosing



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

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

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

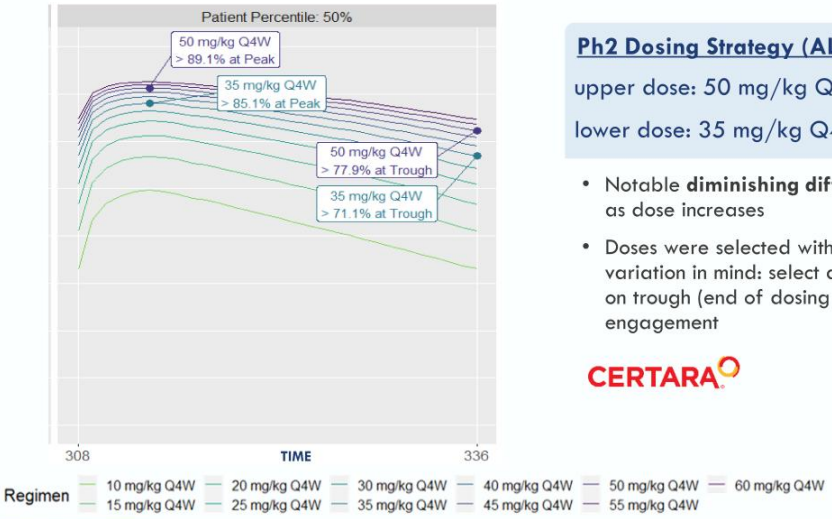
ACUMEN

Phase 2 ALTITUDE-AD

ACUMEN

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

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



Ph2 Dosing Strategy (ALTITUDE-AD)

upper dose: 50 mg/kg Q4W

lower dose: 35 mg/kg Q4W

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

CERTARA

ACUMEN