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): November 14, 2022

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 November 14, 2022, Acumen Pharmaceuticals, Inc. (the "**Company**") reported financial results and business highlights for the quarter ended September 30, 2022. 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 November 14, 2022, 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. 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 November 14, 2022.
99.2	Corporate Presentation, dated November 2022.
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: November 14, 2022

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

Exhibit 99.1

Acumen Pharmaceuticals Reports Third Quarter 2022
Financial Results and Business Highlights

- INTERCEPT-AD, a Phase 1 clinical trial of ACU193 in patients with early Alzheimer's disease continues to progress
  - Acumen anticipates completing enrollment in the first quarter of 2023 and reporting topline data from this trial in the second half of 2023
- ACU193 was granted Fast Track designation from the U.S. FDA for the treatment of early Alzheimer's disease
- Cash, cash equivalents and marketable securities of $200.2 million as of Sept. 30, 2022 expected to be sufficient to support clinical and operational goals through 2025
- Company to host conference call and webcast today at 4:30 p.m. ET

Charlottesville, Va. and Carmel, In., Nov. 14, 2022 – Acumen Pharmaceuticals, Inc. (NASDAQ: ABOS), a clinical-stage biopharmaceutical company focused on the development of novel targeted therapeutics for Alzheimer's disease (AD), today reported financial results for the third quarter of 2022 and provided a business update.

"During the third quarter, we remained focused on executing INTERCEPT-AD, our Phase 1 clinical trial of ACU193 in patients with early AD. We are pleased with the rate of progress in the study in the quarter, which is a testament to our team's efforts and the therapeutic promise of ACU193. We believe that our recent receipt of Fast Track designation from the FDA also reflects the clinical potential of ACU193 and underscores the high unmet need for additional disease-modifying treatments in the Alzheimer's patient community," said Daniel O'Connell, President and Chief Executive Officer of Acumen. "We remain well capitalized through 2025 based on our current business plans and anticipate achieving the completion of study enrollment in INTERCEPT-AD in the first quarter of 2023 and topline results in the second half of 2023."

Dr. Eric Siemers, M.D., Chief Medical Officer of Acumen said, "ACU193 is the first clinical-stage monoclonal antibody designed to selectively target toxic soluble amyloid beta oligomers. Many studies have shown these soluble species disrupt neuronal function and initiate the process of neurodegeneration leading to AD. Underscoring our goal to expeditiously advance ACU193, the recent publication of our clinical development plan in the *Journal for Prevention of Alzheimer's Disease* details incorporation of several advancements in AD research methodology, including an adaptive Phase 2/3 trial design. Our recent Fast Track designation should also allow for close engagement with the FDA as we seek the most efficient path to develop ACU193 as a potential better and differentiated therapeutic option for patients living with AD."

Recent Business Highlights and Anticipated Milestones

ACU193 Clinical Development

- **INTERCEPT-AD enrollment remains ongoing.** Patient screening and enrollment is continuing for INTERCEPT-AD, with 17 active clinical trial sites currently recruiting patients.
  - The study has progressed as planned in the protocol and blinded safety data for ACU193 are consistent with our expectations.
  - Acumen anticipates completing enrollment in the first quarter of 2023 and reporting topline data from this trial in the second half of 2023.
- **In October 2022, Fast Track designation was granted by the U.S. Food and Drug Administration (FDA) for ACU193 for the treatment of early Alzheimer's disease.** Fast Track Designation is granted to drugs being developed for the treatment of serious or life-threatening conditions where there is an unmet medical need. A drug candidate that receives Fast Track designation is eligible for more frequent communication with the FDA throughout the drug development process for the purpose of expediting the drug's development, review, and potential approval.
- **In October 2022, the development rationale and clinical development plan for ACU193 was published in the *Journal for Prevention of Alzheimer's Disease* (JPAD).** It outlines the design of the ongoing Phase 1 INTERCEPT-AD trial for ACU193 and planned criteria for advancing to a Phase 2/3 clinical trial based on recent advancements in clinical research on Alzheimer's disease.

Corporate

- **In September 2022, Derek Meisner joined Acumen as Chief Legal Officer.** Mr. Meisner brings more than two decades of experience providing counsel to public and private companies across key legal and operational functions, including regulatory compliance, debt and equity financings, mergers and acquisitions, strategic partnerships, and corporate governance. Mr. Meisner previously served in a similar capacity at two other publicly-traded biotechnology companies. He also served as the General Counsel of RA Capital Management and as a Branch Chief in the Division of Enforcement of the U.S. Securities and Exchange Commission.

Third Quarter 2022 Financial Results

- **Cash Balance.** As of September 30, 2022, cash, cash equivalents and marketable securities totaled $200.2 million, compared to cash, cash equivalents and marketable securities of $225.9 million as of December 31, 2021. The decrease in cash is related to funding ongoing operations.
- **Research and Development (R&D) Expenses.** R&D expenses were $8.3 million for the three-month period ended September 30, 2022, compared to $1.8 million for the three-month period ended September 30, 2021. The increase in research and development expenses was primarily due to increased costs related to our ongoing clinical trial, which was initiated in 2021 and started enrolling patients in the second half of 2021, as well as nonclinical research and development activity.

- **General and Administrative (G&A) Expenses.** G&A expenses were $3.1 million for the three-month period ended September 30, 2022, compared to $2.1 million for the three-month period ended September 30, 2021. The increase in general and administrative expenses was primarily due to increased costs related to personnel, accounting, marketing, recruiting and travel expenses.
- **Loss from Operations.** Losses from operations were $11.4 million for the three-month period ended September 30, 2022, compared to $3.9 million for the three-month period ended September 30, 2021. This increase was due to the increased R&D and G&A expenses over the prior year period.
- **Net Loss.** Net loss was $10.7 million for the three-month period ended September 30, 2022, compared to $3.9 million for the three-month period ended September 30, 2021. The increase was due to the increased R&D and G&A expenses over the prior year period.

Conference Call Details

Acumen will host a conference call and live audio webcast today, Nov. 14, 2022, at 4:30 p.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 ACU193

ACU193 is a humanized monoclonal antibody (mAb) discovered and developed based on its selectivity for soluble AßOs, which Acumen believes are the most toxic and pathogenic form of Aß, relative to Aß monomers and amyloid plaques. Soluble AßOs have been observed to be potent neurotoxins that bind to neurons, inhibit synaptic function and induce neurodegeneration. By selectively targeting toxic soluble AßOs, ACU193 aims to directly address what a growing body of evidence indicates is a primary underlying cause of the neurodegenerative process in AD. ACU193 has been granted Fast Track designation for the treatment of early Alzheimer's disease by the U.S. Food and Drug Administration.

About INTERCEPT-AD

Approximately 62 individuals with early AD (mild cognitive impairment or mild dementia due to AD) are expected to be randomized into this double-blind, placebo-controlled, first-in-human study of ACU193.

INTERCEPT-AD is designed to establish safety and proof of mechanism. It consists of single-ascending-dose (SAD) and multiple-ascending-dose (MAD) cohorts and is designed to evaluate the safety, tolerability, pharmacokinetics (PK), and target engagement of intravenous doses of ACU193. The study is enrolling at multiple investigative sites located in the United States. More information can be found on www.clinicaltrials.gov, NCT identifier NCT04931459.

About Acumen Pharmaceuticals, Inc.

Acumen, headquartered in Charlottesville, VA, with clinical operations based in Carmel, IN, is a clinical stage biopharmaceutical company developing a novel disease-modifying approach to treat Alzheimer's disease. Acumen's scientific founders pioneered research on AßOs, which a growing body of evidence indicates are primary triggers of Alzheimer's disease pathology. Acumen is currently focused on advancing its investigational product candidate, ACU193, a humanized monoclonal antibody that selectively targets toxic soluble AßOs in INTERCEPT-AD, a Phase 1 clinical trial involving early Alzheimer's disease patients. For more information, visit www.acumenpharm.com.

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, Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the sufficiency of its cash resources, and the therapeutic potential of Acumen's product candidate, ACU193, including its potential for improved safety and efficacy as compared to other monoclonal antibodies in development and expectations with respect to blinded safety data and the potential of soluble amyloid beta (Aß) species to be more effective or safer disease-modifying therapeutic targets, as well as the expectations concerning the INTERCEPT-AD trial and criteria for Acumen's planned Phase 2/3 clinical trial, and the potential benefits of receiving Fast Track designation from the FDA. 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, 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 Annual Report on Form 10-K for the fiscal year ended December 31, 2021, and future filings with the SEC, including Acumen's Quarterly Report on Form 10-Q for the quarter ended and September 30, 2022. 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.

Investors:
Alex Braun
abraun@acumenpharm.com

Media:

AcumenPR@westwicke.com

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

	September 30, 2022 (unaudited)	December 31, 2021
ASSETS		
Current assets		
Cash and cash equivalents	$ 157,540	$ 122,162
Marketable securities, short-term	42,654	72,075
Prepaid expenses and other current assets	2,366	4,424
Total current assets	202,560	198,661
Marketable securities, long-term	—	31,619
Property and equipment, net	142	36
Deferred offering costs	337	—
Right-of-use asset	133	—
Other assets	92	14
Total assets	$ 203,264	$ 230,330
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 2,084	$ 1,088
Accrued expenses and other current liabilities	4,396	4,059
Operating lease liability, current portion	133	—
Total current liabilities	6,613	5,147
Total liabilities	6,613	5,147
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued and outstanding as of September 30, 2022 and December 31, 2021	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized and 40,503,124 and 40,473,270 shares issued and outstanding as of September 30, 2022 and December 31, 2021, respectively	4	4
Additional paid-in capital	355,173	352,981
Accumulated deficit	(157,561)	(127,571)
Accumulated other comprehensive loss	(965)	(231)
Total stockholders' equity	196,651	225,183
Total liabilities and stockholders' equity	$ 203,264	$ 230,330

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses				
Research and development	$ 8,309	$ 1,800	$ 21,615	$ 6,632
General and administrative	3,062	2,135	9,374	4,537
Total operating expenses	11,371	3,935	30,989	11,169
Loss from operations	(11,371)	(3,935)	(30,989)	(11,169)
Other income (expense)				
Change in fair value of preferred stock tranche rights liability and preferred stock warrant Liability	—	—	—	(81,157)
Interest income, net	663	14	1,000	22
Other income, net	(2)	19	(1)	47
Total other income (expense)	661	33	999	(81,088)
Net loss	(10,710)	(3,902)	(29,990)	(92,257)
Other comprehensive loss				
Unrealized loss on marketable securities	—	(28)	(734)	(28)
Comprehensive loss	$ (10,710)	$ (3,930)	$ (30,724)	$ (92,285)
Net loss per common share, basic and diluted	$ (0.26)	$ (0.10)	$ (0.74)	$ (7.00)
Weighted-average shares outstanding, basic and diluted	40,502,860	38,266,593	40,491,181	13,177,983

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

	Nine Months Ended September 30,	
	2022	2021
Cash flows from operating activities		
Net loss	$ (29,990)	$ (92,257)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	20	1
Change in fair value of preferred stock tranche rights liability and preferred stock warrant liability	—	81,157
Stock-based compensation expense	2,173	557
Amortization of premiums and accretion of discounts on marketable securities, net	575	(6)
Amortization of right-of-use asset	100	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	2,058	(4,297)
Other assets	(78)	(13)
Accounts payable	996	(149)
Operating lease liability	(100)	—
Accrued expenses and other current liabilities	296	685
Net cash used in operating activities	(23,950)	(14,322)
Cash flows from investing activities		
Purchases of marketable securities	(12,129)	(94,095)
Proceeds from maturities and sales of marketable securities	71,860	—
Purchases of property and equipment	(126)	(14)
Net cash provided by (used in) investing activities	59,605	(94,109)
Cash flows from financing activities		
Proceeds from issuance of Series B milestone shares, net of issuance costs	—	30,031
Proceeds from exercise of Series A-1 warrant	—	1,250
Proceeds from exercise of common stock warrants	—	614
Payments for deferred offering costs	(296)	168,559
Proceeds from the exercise of stock options	19	2
Net cash provided by (used in) financing activities	(277)	200,456
Net change in cash and cash equivalents	35,378	92,025
Cash and cash equivalents at the beginning of the period	122,162	43,777
Cash and cash equivalents at the end of the period	$ 157,540	$ 135,802
Supplemental disclosure of noncash investing and financing activities		
Right-of-use asset obtained in exchange for operating lease liabilities	$ 233	$ —
Deferred offering costs in accrued expenses and other current liabilities	$ 41	$ —
Conversion of convertible preferred stock into common stock upon initial public offering	$ —	$ 174,504
Reclassification of preferred stock tranche rights liability upon share issuance	$ —	$ 81,190
Reclassification of warrant liability upon exercise of preferred stock warrant	$ —	$ 5,380

Exhibit 99.2

Corporate Presentation

November 2022

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, Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the sufficiency of its cash resources, and the therapeutic potential of Acumen's product candidate, ACU193, including its potential for improved safety and efficacy as compared to other monoclonal antibodies in development, as well as the expectations concerning the INTERCEPT-AD trial and Acumen's planned Phase 2/3 clinical trial, including the expected timing of initiation, enrollment and reporting data, and risks and uncertainties relating to the progression and duration of the COVID-19 pandemic and responsive measures thereto and related effects on Acumen. 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 Form 10-K for the year ended December 31, 2021, Acumen's Form 10-Q for the quarter ended September 30, 2022, 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-/First-In-Class Antibody Product for Early Alzheimer's disease (AD)

Alzheimer's Represents an Enormous Market Driven by **High Unmet Need** and **Recent Scientific and Regulatory Momentum**

Scientific Consensus Supports **Amyloid-Beta Oligomers (AβOs)** as the **Most Toxic Form of Aβ** and a Novel Target for **Effective AD Treatment**

ACU193: First, Clinical-Stage Monoclonal Antibody (mAb) to **Selectively Target AβOs** with Promising Pre-Clinical Evidence Supporting its Differentiation

Experienced Leadership Team Comprised of Industry Leaders and several with AD clinical Drug, Development, and Regulatory Expertise from **Eli Lilly & Co.**

Strong Balance Sheet: ~$200M in cash at 30-Sep-22

July 2021 IPO ~$184M Gross

RA Capital
Deep Track
Sands Capital
PBM Capital

Phase 1 Clinical Trial in Early AD Patients Ongoing

Proof of Mechanism
Target Engagement
Safety Data

Topline Results Expected 2H 2023

We believe that Acumen has the organizational expertise and fiscal resources to advance ACU193 through 2025.

Acumen Business Strategy: 2022-2025

→ Rapidly advance ACU193 through clinical development in patients with early AD;

→ Evaluate combination approaches to complement our core ACU193 monotherapy strategy;

→ Selectively explore potential of ACU193 for other diseases;

→ Expand our product portfolio by in-licensing and/or developing additional candidates and/or alternative formulations for, or derivatives of, ACU193; and

→ Optimize value of ACU193 and future drug candidates in major markets.

INTERCEPT-AD Trial Update – 3Q 2022

- **INTERCEPT-AD: Phase 1 clinical trial of ACU193 in patients with early Alzheimer's disease (AD) (RCT)**
  - → Trial enrollment ongoing at 17 active sites
    - Enrollment completion expected in 1Q 2023
  - → Topline results (proof-of-mechanism) following full database lock expected in 2H 2023
    - Safety / ARIA-E
    - PK
    - Target engagement

- **Phase 2/3 'Ready' Activities**
  - → Chronic GLP toxicity study in-life phase completed; final study report expected in 1Q 2023
  - → Well-positioned to efficiently scale manufacturing to have sufficient drug supply to meet the requirements of our current development plan
  - → Confirmation of ACU193's IgG2 antibody subclass; maintain expectation that reduced effector function should favorably influence ACU193 safety outcomes

AD, Amyloid & Abeta Oligomers

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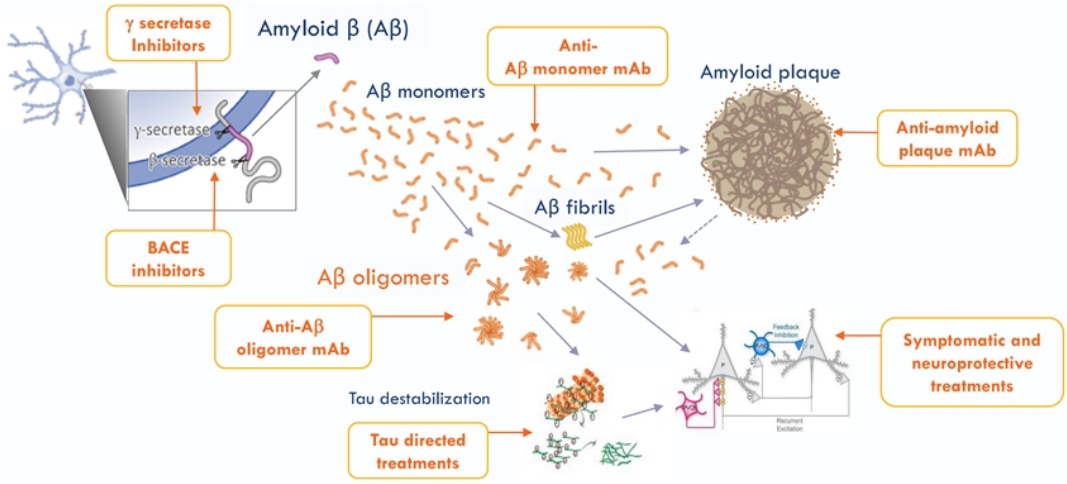
Alzheimer's Pathophysiology

Build-up of amyloid-beta (Aβ) is believed to lead to neurodegeneration and dementia

Previous and current anti-amyloid and related drug targets have attempted to intervene



Data indicate that soluble amyloid β oligomers (AβOs) are the most toxic species and should be preferentially targeted for removal.

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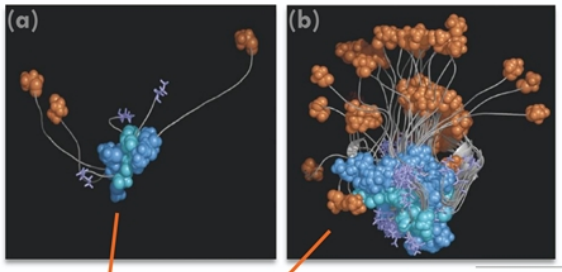
What is an Aβ Oligomer? AβOs May Consist of 2 to >200 Aβ Peptides

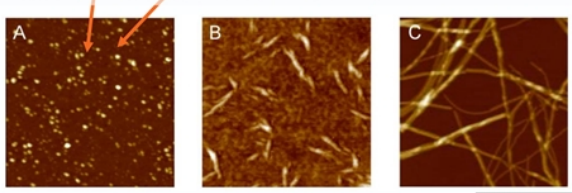
Figure 1. AβOs composed of 3 (a) and 18 (b) Aβ peptides are depicted below.



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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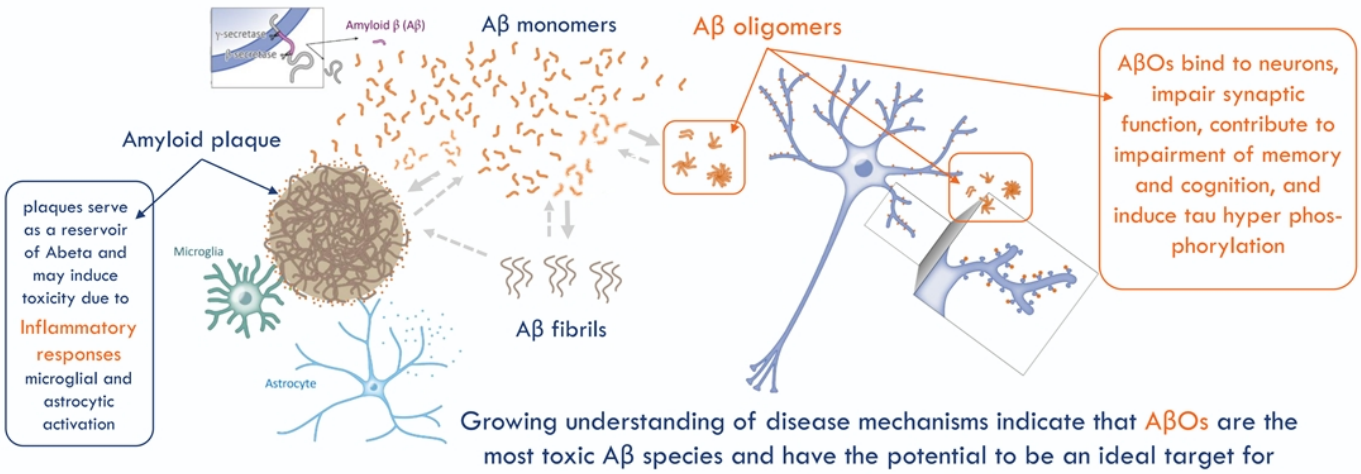
Scientific Evidence Supports AβO Hypothesis

Predominant forms of Aβ in AD: Aβ monomers (non-toxic), AβOs, Aβ fibrils, and amyloid plaques



Growing understanding of disease mechanisms indicate that AβOs are the most toxic Aβ species and have the potential to be an ideal target for effective AD therapy

Sources: Adopted From: Selkoe, Hardy EMBO Molecular Medicine, 2016
Cline, Journal of Alzheimer's Disease, 2018

The only approved antibody product for AD and several late stage products preferentially target amyloid plaques with only limited effects on AβOs. Acumen's drug candidate ACU193 targets AβOs.

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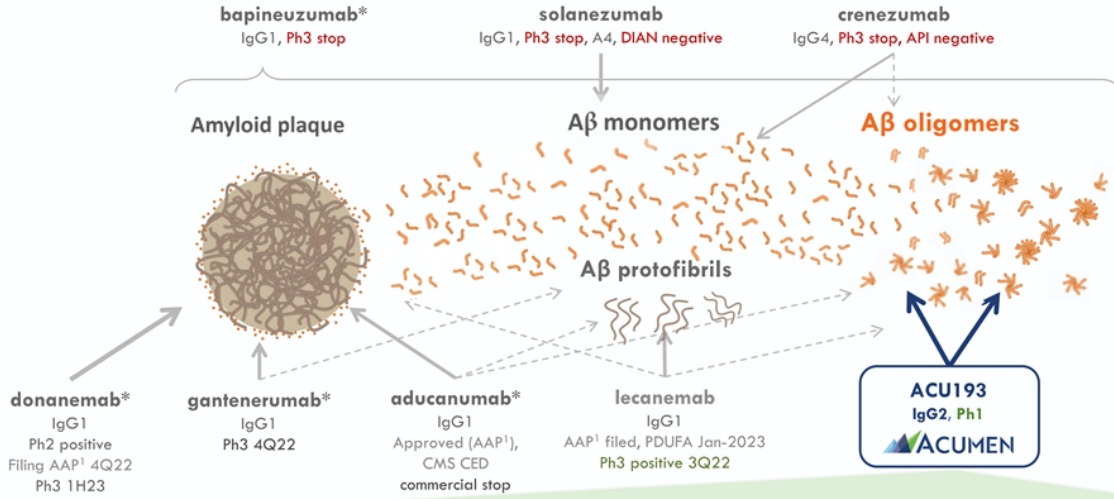
ACU193 Positioning Relative to Late-Stage and Approved Anti-Aβ/Plaque mAbs



ACU193's high selectivity for AβOs combined with an expected lack of ARIA-related safety concerns is anticipated to provide better safety and efficacy compared to anti-plaque mAbs

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

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

[1] AAP: Accelerated approval

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Positive Signals and Proof of Concept From Recent Phase 2-3 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)	donanemab (Phase 2)	lecanemab BAN2401 (Phase 2)	lecanemab Clarity-AD (Phase 3)+
ADAS-cog	-11%	-27%	-12%	-39%	-47%	(p<0.01)
ADCS-ADL	-15%	-40%	-18%	-23%	N.A.	(p<0.01)
CDR-SB	-15%	-23%	2%	-23%	-26%	-27%
MMSE	-13%	-15%	3%	-21%	N.A.	(p<0.01)
iADRS	-11%	N.A.	N.A.	-32%	N.A.	(p<0.01)

* 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: 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.

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

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

	TARGETING AB MONOMERS		TARGETING AMYLOID PLAQUES								TARGETING PROTOFIBRILS			
	solanezumab EXPEDITION 3 (Phase 3)		aducanumab EMERGE (Phase 3)			aducanumab ENGAGE (Phase 3)			donanemab (Phase 2)		lecanemab BAN2401 (Phase 2)		lecanemab BAN2401 (Phase 3)+	
	PC	Treated	PC	Low	High	PC	Low	High	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%	0.8%	9.9%	1.7%	12.5%
ApoE ε4 carriers			1.9%	29.8%	42.5%	2.4%	28.7%	41.8%	3.6%	44.0%	1.2%	14.6%	N.A.	N.A.
ApoE ε4 non-carriers			2.9%	18.1%	17.9%	4.3%	17.5%	27.7%			0.0%	8.0%	N.A.	N.A.
Any ARIA E or H			10.3%	32.8%	41.2%	9.8%	30.7%	40.3%	8.0%	38.9%		N.A.	9.3%	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 avoid ARIA 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

ACUMEN

ACU193's High Selectivity for Toxic AβOs, Combined With its Expected Lack of ARIA-Related Safety Concerns, is Anticipated to Provide Superior Efficacy Compared to Peers

		TARGET SELECTIVITY+				SAFETY PROFILE
Company	Asset	Amyloid plaque	Aβ fibrils	Aβ monomers	Aβ oligomers	Lack of ARIA-related safety concerns
ACUMEN	ACU193	×	untested	×	✓	Expected
Biogen	Aduhelm™	✓	✓	×	✓	✘
Eisai / Biogen	lecanemab	✓	✓	×	✓	×
Roche	gantenerumab	✓	✓	×	✓	✘
Lilly	donanemab	✓	untested	×	×	✘
Lilly	solanezumab*	✘	×	✓	×	✓
Roche / Genentech	crenezumab*	✓	✓	✓	✓	✓
Pfizer / Janssen	bapineuzumab*	✓	✓	✓	✓	×

Phase 3 discontinued for primary AD indication.

+ 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..

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ACU193:
Our Differentiated Approach

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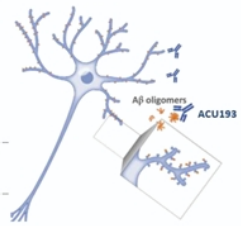
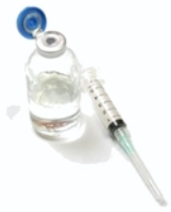
ACU193 Target Product Profile: Best-in-Class, 1st Line, Anti-AβO, Disease-Modifying Immunotherapy for Early AD

DRUG:	ACU193 is a humanized, affinity-matured, mAb with high selectivity for toxic **AβOs vs. Aβ monomers (>500x)** and limited to no binding to amyloid plaques. **ACU193 is an IgG2 subclass** mAb which lacks inflammatory effector functions of other IgG subclasses.
POPULATION:	Early AD - Mild Cognitive Impairment and Mild Dementia due to AD (amyloid positive by PET)
DOSING:	IV infusion every 4 weeks
DURATION:	Chronic therapy for duration of Early AD
VALUE PROPOSITION:	**Selectivity for toxic AβOs is expected to provide superior cognitive efficacy** and **improved safety and tolerability** relative to non-selective anti-Aβ/plaque mAbs, including: • Slowing the decline of memory and cognition in Early AD • Decreasing AβO induced synaptic and neuronal network toxicity • Slowing disease progression and downstream effects on tau, neurodegeneration, and neuro-inflammation • With expected low rate of ARIA • **Potentially effective as stand-alone therapy or in combination with other symptomatic, anti-inflammatory, and/or tau directed therapies**





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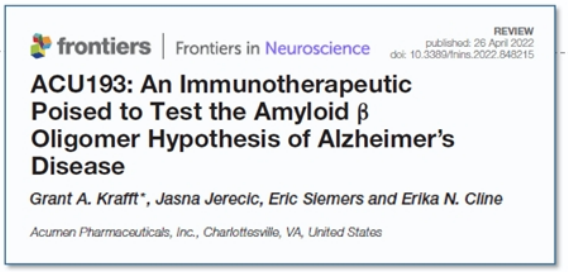
ACU193: Extensive Data Package Supporting Development

SELECTIVITY
- Nanomolar affinity for AβOs, >500-fold greater selectivity for AβOs over Aβ monomer, with limited or no discernable binding to vascular amyloid or dense core amyloid plaques
- Binds broad range of endogenous AβOs present in transgenic mice and human AD samples (binds dimers to mid-sized 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 margin for clinical dosing plans


frontiers | Frontiers in Neuroscience

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

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

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

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

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

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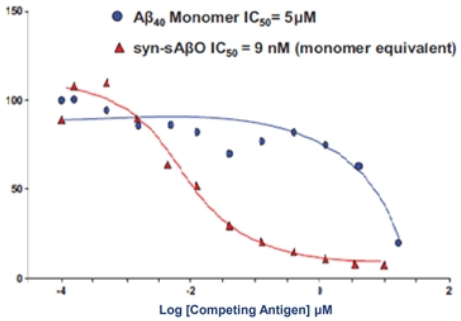
ACU193 is the First mAb Developed to Selectively Target AβOs

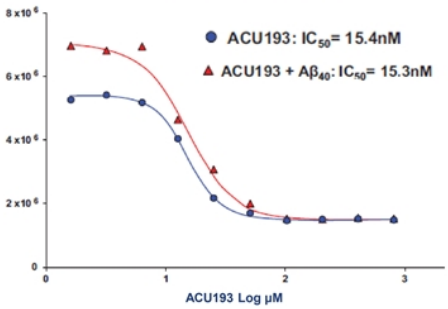
Highly selective for Aβ oligomers versus Aβ monomers

ACU193 Selectivity



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

ACU193 Selectivity in presence of 5μM monomeric Aβ



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

ACU193 selective for binding to AβOs is preserved even in the presence of a large excess of Aβ monomers – such as what is present in the brain, thus limiting 'target distraction.'

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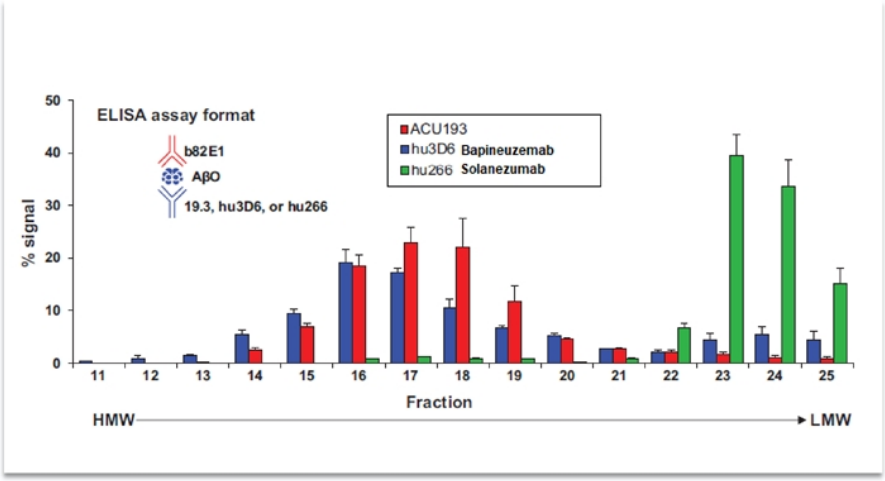
ACU193 Has a Greater Preference for AβOs Than Other mAbs

Comparison of Aβ species-mAb complex signals across SEC fractions



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

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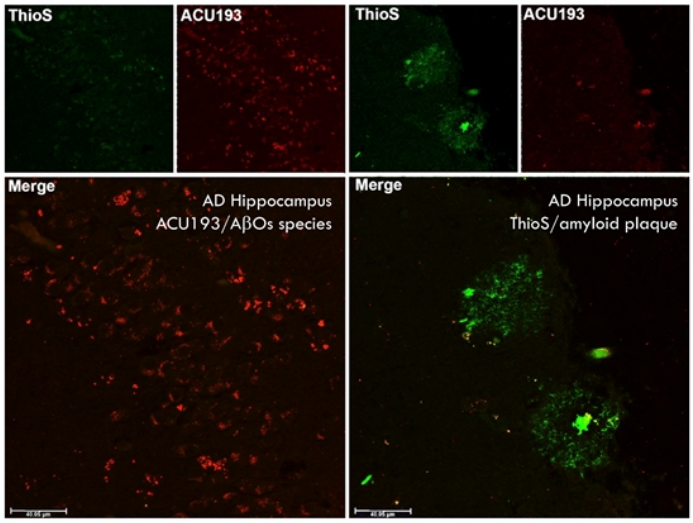
ACU193 is Highly Selective for AβOs Versus Aβ Plaques

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



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

Sources: E. Cline et al. CTAD 2019.

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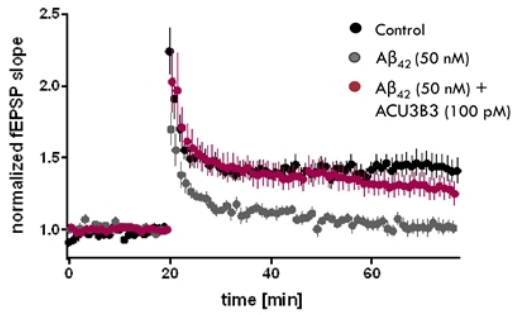
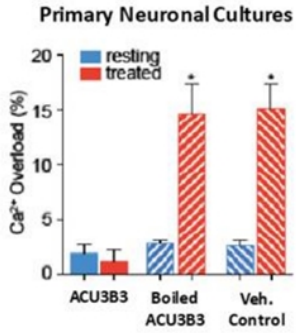
AβOs Bind to Neurons and are Toxic; Mouse Analogue of ACU193 Prevents Toxicity

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

ACU3B3 prevents AβO inhibition of hippocampal LTP *ex vivo*



ACU3B3 prevents AβO mediated Ca2+ elevation in cell cultures



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

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

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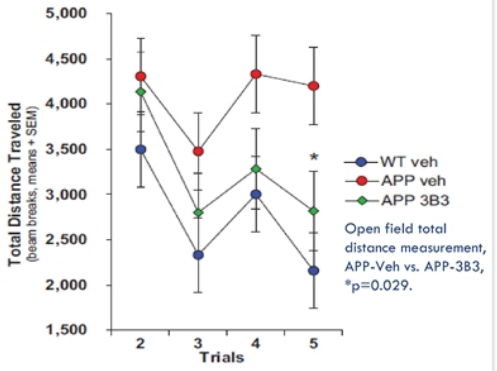
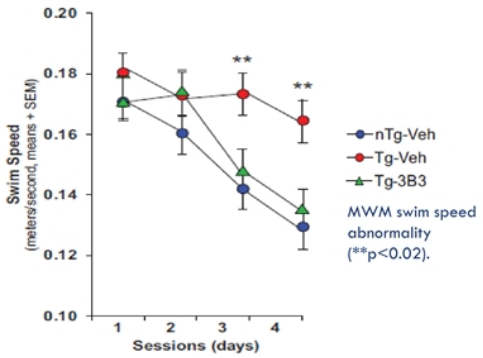
Treatment of a Transgenic Mouse Model of AD Results in Behavioral Improvements

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



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



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

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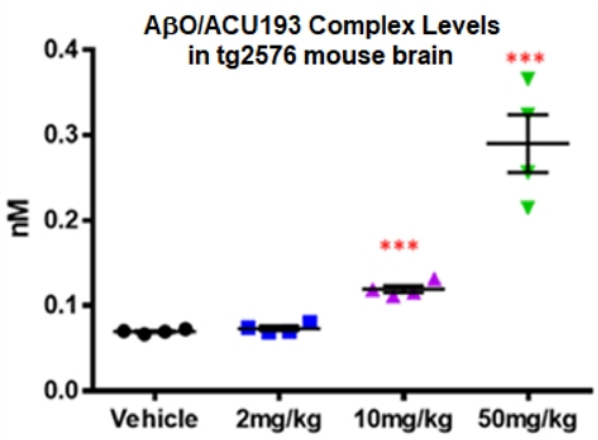
ACU193 Enters the CNS and Binds to AβOs in Transgenic Mice in Dose Dependent Manner



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

Clinical Development Plans

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(ACU-001) INTERCEPT-AD Trial: Phase 1 Overview

TRIAL DESIGN:

Randomized Placebo Controlled Phase 1

- Part A : Single-Ascending Doses
- Part B : Multiple-Ascending Doses

ENROLLMENT CRITERIA:

Early AD

- Mild Cognitive Impairment and Mild Dementia due to AD (amyloid positive by PET)

TRIAL OBJECTIVES:

Proof of Mechanism (PoM)

- Safety and tolerability
- Pharmacokinetics
- Target engagement
- Biomarkers; cognition (exploratory)

For more information on the INTERCEPT-AD trial, see https://clinicaltrials.gov/ct2/show/NCT04931459.

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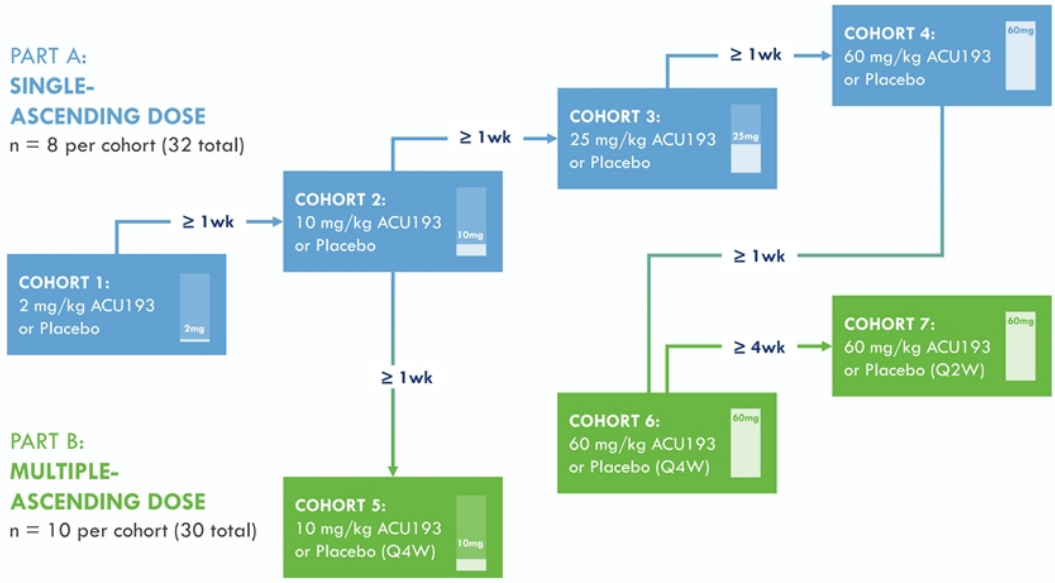
INTERCEPT-AD a Randomized Placebo Controlled Phase 1 in Early AD patients



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

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Phase 1 Objectives: Proof of Mechanism – Ability to Move to Phase 2/3

1. SAFETY AND TOLERABILITY
- Assessment of ARIA-E
- Absence of problematic immunogenicity

2. PHARMACOKINETICS
- Peripheral and Central

3. EVIDENCE OF TARGET ENGAGEMENT
- CSF level of ACU193: AβO complexes (bound)

4. FLUID BIOMARKER EFFECTS
- Phospho-tau, Neurofilament light, et. al.

5. CLINICAL MEASURES (exploratory)
- Assessment of clinical cognitive measures, computerized tests (Cogstate Ltd.)

6. MRI EFFECTS (exploratory)
- Potential improvements in cerebral blood flow shown with MRI ASL pulse sequence

PROOF OF MECHANISM

Requirements for Phase 2/3

- ✓ Acceptable safety and tolerability
- ✓ Show ACU193 gets across the blood brain barrier and into central compartment
- ✓ Target engagement

Topline results anticipated in 2H 2023: primary outcomes safety/ARIA-E, PK and target engagement. Detailed study results anticipated to be presented at an Alzheimer's medical meeting.

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Cogstate

Cogstate computerized test battery (exploratory)

Test	Domains tested	Time (minutes)
International shopping list test (immediate)	Immediate recall	5
Cogstate brief battery	Attention, working memory, learning	15
International shopping list test (delayed)	Delayed recall	1
Groton maze learning test	Executive function	7
International digit-symbol substitution test	Processing speed	3
		Total = 31

Frequency of administration and sensitivity of battery offers improved possibility to observe effects.

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Arterial Spin Labelling (ASL) as an MRI Measure of Cerebral Blood Flow

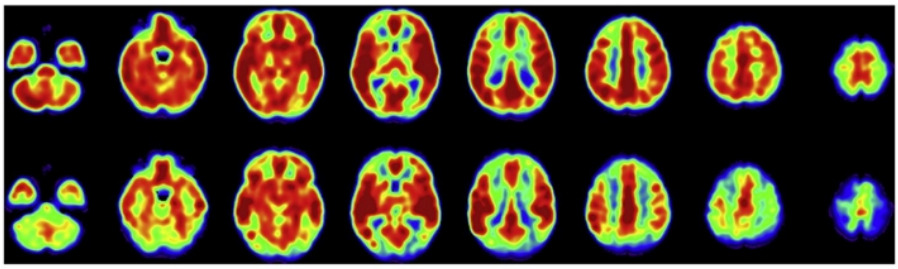

Fig. 1. Processed CBF images measured with ASL of a young and an old healthy control from our database. The top row images are from a 32 year-old woman, and the bottom row images are from an 80 year-old man. The reduction of CBF can be readily observed in widespread brain areas of the older subject compared with the younger subject.

- Mild cognitive impairment patients show hypoperfusion in parietal cortex, precuneus, posterior cingulate cortex and medial temporal lobe
- AD patients show global hypoperfusion, but especially cingulate, precuneus, parietal lobes and inferior frontal regions
- Perfusion correlates with several neuropsychological tests
- Hypoperfusion can be improved in middle and posterior cingulate cortex with cholinesterase inhibitors and was associated with improvement in ADAS-cog scores

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ACU193 Development Summary

- ⇒ Differentiated profile: Nonclinical data consistent with toxicity of Aβ oligomers and selective binding of ACU193 to Aβ oligomers
- ⇒ Enrollment in a Phase1 study assessing safety, PK, and target engagement is ongoing
- ⇒ Although unlikely with this small sample size, the possibility of improvement in cognitive scales, computerized cognitive testing, and cerebral blood flow will also be assessed as exploratory outcomes in the Phase 1 study
- ⇒ Anticipate next clinical study, with success in Phase 1, starting as Phase 2 study with potential to expand to Phase 3 registration study based on interim expansion analysis

Business Considerations

ACUMEN

Acumen Leadership Team

Experienced in AD/Neuro Drug Development

DANIEL O'CONNELL
President & CEO
ACUMEN
neuroVentures

ERIC SIEMERS, MD
Chief Medical Officer
ACUMEN
Lilly

JANICE HITCHCOCK, PHD
VP, Regulatory Affairs
ACUMEN
Lilly

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

RUSSELL BARTON
Chief Operating Officer
ACUMEN
Lilly

ROBERT DEAN, MD, PHD
Sr. Development Advisor
ACUMEN
Lilly

LIEAN SCHENK
VP, Head of CMC
ACUMEN
Lilly Lonza
NOVAVAX

SIEW TIN GAN
Head of Clinical
Operations
ACUMEN
Landsteiner
Takeda

JASNA JERECIC, PHD
Analytical Methods
Leader, Research Scientist
ACUMEN

DEREK MEISNER, JD
Chief Legal Officer
ACUMEN
X4

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

ACU193 IP & Market Exclusivity

- Exclusive, perpetual, irrevocable, worldwide, royalty-free license from Merck to its Amyloid Derived Diffusible Ligand (ADDL) IP including, issued ACU193 patents
- ACU193 Global IP estate:
  - ✓ Issued patents in 19 countries
  - ✓ Composition of matter patents and methods of use run into July 2031
  - ✓ Patent term extensions may be available, 3-5 years depending on jurisdiction
- Biologics market exclusivity is expected for ACU193 as a novel biologic drug
  - ✓ US provides 12 years market exclusivity for novel biologics
  - ✓ Europe provides 10 years of market exclusivity for novel biologics

Acumen is Well Capitalized, With Expected Cash Runway Through 2025

MILESTONES	STATUS/ EXPECTED TIMING
Initiated Ph1 clinical trial INTERCEPT-AD	✓
INTERCEPT-AD enrollment complete	1Q 2023
Proof-of-mechanism topline results	2H 2023

~$200M

Cash, cash equivalents and marketable securities as of September 30, 2022

We believe that Acumen has the organizational expertise and cash and marketable securities on hand to advance ACU193 through 2025.

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ABOS: Key Takeaways

- Massive unmet need in AD, recent favorable trends and cumulative learnings position field for future successes
- Upcoming sector catalysts 2H22 - 1H23
- Differentiated product candidate targeting toxic AβOs
- Experienced AD drug development team
- Blue chip investors, very strong balance sheet and cash runway with multiple milestones through 2025
- Value-inflection clinical data 2H 2023

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Thank you!

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