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 27, 2023

Acumen Pharmaceuticals, Inc.

(Exact name of Registrant as Specified in Its Charter)

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

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

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 2.02 Results of Operations and Financial Condition.

On March 27, 2023, Acumen Pharmaceuticals, Inc. (the "**Company**") reported financial results and business highlights for the year ended December 31, 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 March 27, 2023, the Company posted an updated corporate presentation to its website at https://investors.acumenpharm.com/news-events/presentations, which the Company may use from time to time in communications or conferences. This corporate presentation was updated to include additional info on the Company's cash runway requirements.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 27, 2023.
99.2	Corporate Presentation, dated March 27, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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

Acumen Pharmaceuticals, Inc.

Dated: March 27, 2023

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

Exhibit 99.1

Acumen Pharmaceuticals Reports Financial Results for Full Year Ended December 31, 2022 and Business Highlights

- INTERCEPT-AD, a Phase 1 clinical trial of ACU193 in patients with early Alzheimer's disease completed enrollment in February 2023
    - Topline data expected in the third quarter of 2023
- Cash, cash equivalents and marketable securities of $193.4 million as of Dec. 31, 2022 expected to be sufficient to support clinical and operational goals through 2025
- Company to host conference call and webcast today at 8:00 a.m. ET

Charlottesville, Va. and Carmel, In., March 27, 2023 – Acumen Pharmaceuticals, Inc. (NASDAQ: ABOS), a clinical-stage biopharmaceutical company focused on developing a novel therapeutic that targets toxic soluble amyloid beta oligomers (AβOs) and is designed for the treatment of Alzheimer's disease (AD), today reported financial results for the full year ended December 31, 2022 and provided a business update.

"2022 was a year of significant accomplishment as we advanced the clinical development of ACU193, our novel therapeutic targeting toxic amyloid beta oligomers for the treatment of Alzheimer's Disease. We recently completed enrollment in our Phase I INTERCEPT-AD trial and are encouraged by preliminary pharmacokinetic and safety data that support ACU193's differentiated product profile," said Daniel O'Connell, President and Chief Executive Officer of Acumen. "We believe that our continued execution will drive Acumen's momentum during 2023. Our Phase 1 topline results expected in the third quarter and anticipated interaction with FDA in the fourth quarter of 2023 will help inform our next phase of clinical development. With cash runway expected through 2025, a strong scientific foundation, and an increasingly attractive market environment, we believe we are well positioned to achieve our near-term milestones and to advance our mission of delivering a novel treatment option for patients with Alzheimer's Disease."

Recent Business Highlights and Anticipated Milestones

ACU193 Clinical Development

- **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. Fast Track designation does not change the standard for approval, but 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 January 2023, a protocol amendment was submitted to the FDA with respect to Cohort 7 of the Company's Phase 1 INTERCEPT-AD clinical trial to reduce the dose to 25 mg/kg every two weeks (updated from 60 mg/kg every two weeks).** The change was based in part on a blinded review of preliminary pharmacokinetic data in the trial, inclusive of levels of ACU193 in plasma and cerebrospinal fluid, which indicated a dose of 60 mg/kg every two weeks should not be needed to attain central target engagement, and preliminary safety data, including two asymptomatic cases of ARIA-E (one in Cohort 4 after a single 60 mg/kg dose and one in Cohort 5 after the third 10 mg/kg dose).

- **In February 2023, enrollment was completed in the Company's Phase 1 INTERCEPT-AD trial of ACU193 in patients with early Alzheimer's disease.**
  - Acumen anticipates reporting topline results from this trial, including safety and proof-of-mechanism data, in the third quarter of 2023.

Corporate

- **In 2022, we continued to expand our team with talent necessary to advance our mission to develop a novel treatment for AD.** These appointments included Liean Schenck, MS as our VP, Head of Chemistry, Manufacturing and Controls (CMC) and Derek Meisner, JD as our Chief Legal Officer.

- **In January 2023, Derrell Porter, M.D. joined Acumen's Board of Directors.** Dr. Porter is a physician-entrepreneur with more than 20 years of experience in drug development. He is currently the Founder and CEO of Cellevolve, a development and commercialization company focused on cell therapy, and previously served in commercial and corporate development roles at Atara Biotherapeutics, Inc., Gilead, AbbVie and Amgen.

2022 Financial Results

- **Cash Balance.** As of December 31, 2022, cash, cash equivalents and marketable securities totaled $193.4 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 for 2022 were $32.4 million, compared to $12.3 million in 2021. The increase in R&D expenses in 2022 compared to 2021 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 for 2022 were $12.9 million, compared to $7.3 million in 2021. The increase in G&A expenses in 2022 compared to 2021 was primarily due to increased expenses as a public company and additions to its financial and administrative infrastructure, such as costs related to personnel, accounting, marketing, recruiting and travel and entertainment expenses.

- **Loss from Operations.** Losses from operations for 2022 were $45.2 million, compared with $19.6 million in 2021. This increase was due to the increased R&D and G&A expenses over the prior year period.

- **Net Loss.** Net loss for the year ended December 31, 2022 was $42.9 million, compared to a net loss of $100.6 million for the year ended December 31, 2021. Net loss in 2021 includes a $81.2 million non-cash expense that represents the changes in fair value of Acumen's Series B tranche liability and Series A-1 warrant liability.

Conference Call Details

Acumen will host a conference call and live audio webcast today, March 27, 2023, 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 ACU193

ACU193 is a recombinant humanized immunoglobin gamma 2 (IgG2) monoclonal antibody (mAb) discovered and developed based on its selectivity for soluble AβOs, which Acumen believes are the most 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, 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

INTERCEPT-AD is a Phase 1, U.S.-based, multi-center, randomized, double-blind, placebo-controlled clinical trial evaluating the safety and tolerability, and establishing clinical proof of mechanism, of ACU193 in patients with early Alzheimer's disease (AD). Sixty-five individuals with early AD (mild cognitive impairment or mild dementia due to AD) enrolled in this first-in-human study of ACU193. The INTERCEPT-AD study 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 has completed enrollment across 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 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 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 AβOs 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 and continued momentum, 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 through 2025, and the therapeutic potential of Acumen's product candidate, ACU193, including the anticipated timeline for reporting topline safety and proof-of-mechanism data and results, ACU193's differentiated product profile, as supported by preliminary pharmacokinetic and safety data, and the potential benefits and outcomes of receiving Fast Track designation and anticipated upcoming interactions with 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 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.

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

	December 31, 2022	December 31, 2021
ASSETS		
Current assets		
Cash and cash equivalents	$ 130,101	$ 122,162
Marketable securities, short-term	47,504	72,075
Prepaid expenses and other current assets	2,724	4,424
Total current assets	180,329	198,661
Marketable securities, long-term	15,837	31,619
Property and equipment, net	165	36
Right-of-use asset	105	—
Other assets	151	14
Total assets	$ 196,587	$ 230,330
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 1,640	$ 1,088
Accrued clinical trial expenses	2,717	147
Accrued expenses and other current liabilities	3,350	3,912
Operating lease liability, current portion	105	—
Total current liabilities	7,812	5,147
Total liabilities	7,812	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 December 31, 2022 and 2021	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized and 41,025,062 and 40,473,270 shares issued and outstanding as of December 31, 2022 and 2021; respectively	4	4
Additional paid-in capital	359,949	352,981
Accumulated deficit	(170,427)	(127,571)
Accumulated other comprehensive loss	(751)	(231)
Total stockholders' equity	188,775	225,183
Total liabilities and stockholders' equity	$ 196,587	$ 230,330

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

	Year Ended December 31,	
	2022	2021
Operating expenses		
Research and development	32,361	12,305
General and administrative	12,876	7,279
Total operating expenses	45,237	19,584
Loss from operations	(45,237)	(19,584)
Other income (expense)		
Interest income, net	2,392	84
Other income (expense), net	(11)	51
Change in fair value of preferred stock tranche rights liability and preferred stock warrant liability	—	(81,157)
Total other income (expense)	2,381	(81,022)
Net loss	(42,856)	(100,606)
Other comprehensive loss		
Unrealized loss on marketable securities	(520)	(231)
Comprehensive loss	$ (43,376)	$ (100,837)
Net loss per common share, basic and diluted	$ (1.06)	$ (5.02)
Weighted-average shares outstanding, basic and diluted	40,601,936	20,057,534

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

	Year Ended December 31,	
	2022	2021
Cash flows from operating activities		
Net loss	$ (42,856)	$ (100,606)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	32	4
Change in fair value of preferred stock tranche rights liability and preferred stock warrant liability	—	81,157
Stock-based compensation expense	3,061	922
Amortization of premiums and accretion of discounts on marketable securities, net	487	155
Amortization of right-of-use asset	137	—
Other non-cash expense	—	109
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,700	(3,881)
Other assets	(137)	(14)
Accounts payable	552	557
Accrued clinical trial expenses	2,570	147
Operating lease liability	(137)	—
Accrued expenses and other current liabilities	(562)	3,489
Net cash used in operating activities	(35,153)	(17,961)
Cash flows from investing activities		
Purchases of marketable securities	(41,514)	(104,080)
Proceeds from maturities and sales of marketable securities	80,860	—
Purchases of property and equipment	(161)	(40)
Net cash provided by (used in) investing activities	39,185	(104,120)
Cash flows from financing activities		
Proceeds from issuance of common stock, net of issuance costs	3,792	168,556
Proceeds from exercise of stock options	115	15
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
Net cash provided by financing activities	3,907	200,466
Net change in cash and cash equivalents	7,939	78,385
Cash and cash equivalents at the beginning of the period	122,162	43,777
Cash and cash equivalents at the end of the period	$ 130,101	$ 122,162

Corporate Presentation

March 2023

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Any statement describing Acumen's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Words such as "believes," "expects," "anticipates," "could," "would," "seeks," "aims," "plans," "potential," "will" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements concerning Acumen's business, 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 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.

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Advancing a Potential Best-/First-In-Class Antibody Product for Early Alzheimer's disease (AD)

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

- Amyloid-beta oligomers (AβOs) accepted as most toxic form of Aβ
- Novel target for effective AD treatment

ACU193: First, clinical-stage monoclonal antibody (mAb) to selectively target AβOs

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

- Strong balance sheet: ~$193M in cash at 31-Dec-22
- July 2021 IPO ~$184M gross

- Phase 1 clinical trial in early AD patients ongoing
- Topline results expected Q3 2023

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

Acumen Business Strategy: 2023 - 2025

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

INTERCEPT-AD Trial Update – February 2023

- **INTERCEPT-AD: Phase 1 clinical trial of ACU193 in patients with early Alzheimer's disease (AD) (RCT)**
  - → Topline results, safety and clinical proof-of-mechanism following full database lock expected in Q3 2023
  - → Enrollment completed in February 2023
  - → Cohort 7 dose level amended to 25 mg/kg every two weeks (Q2W) from 60 mg/kg Q2W prior to start
    - Preliminary, blinded plasma pharmacokinetic (PK) data demonstrated higher-than-expected ACU193 exposures at all dose levels
    - Preliminary Cohort 3 (SAD 25 mg/kg) dose results in Day 21 cerebrospinal fluid (CSF) ACU193 levels in excess of reported soluble amyloid beta oligomer (AβO) levels
    - Two blinded observations of asymptomatic ARIA-E factored into decision to amend Cohort 7 dose; one in Cohort 4 (after single 60 mg/kg dose) and one in Cohort 5 (after third 10 mg/kg dose)
    - Cohort 6 is fully enrolled with planned dose (60 mg/kg every four weeks (Q4W))

Safety profile to date remains supportive of targeting soluble amyloid beta oligomers and, combined with the selectivity of ACU193, is expected to offer a favorable benefit-to-risk ratio for patients with early AD.

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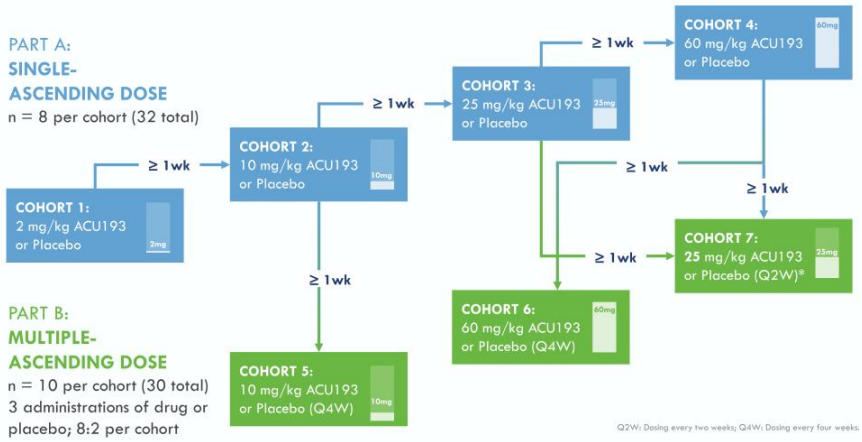
INTERCEPT-AD a Randomized Placebo Controlled Phase 1 in Early AD patients



*On January 30, 2023, Acumen submitted a protocol amendment to FDA to reduce the dose in Cohort 7 to 25 mg/kg Q2W from 60 mg/kg Q2W. This was based on a blinded review of preliminary pharmacokinetic data, inclusive of plasma and CSF levels, that indicate a dose of 60 mg/kg Q2W should not be needed to attain central target engagement, and preliminary safety data, inclusive of two asymptomatic cases of ARIA-E. While ACU193 is early in clinical development, the incidence of ARIA-E to date is consistent with our previous expectations regarding the safety profile of ACU193. The dose of ACU193 in Cohort 6 (60 mg/kg Q4W) has been maintained as planned.

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AD, Amyloid & Abeta Oligomers

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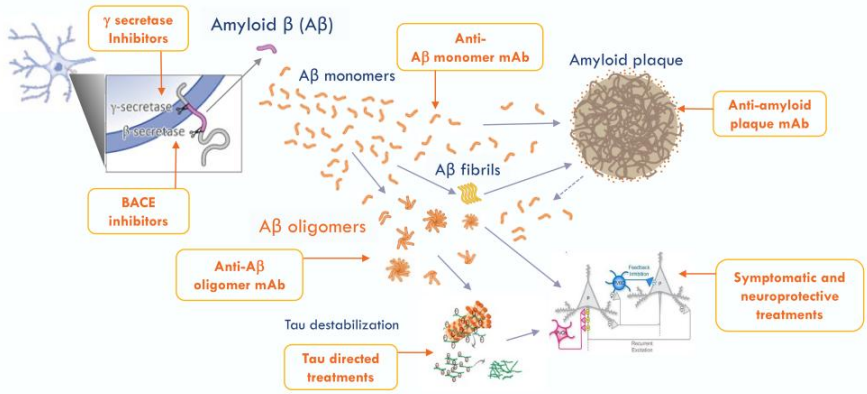
Alzheimer's Pathophysiology

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

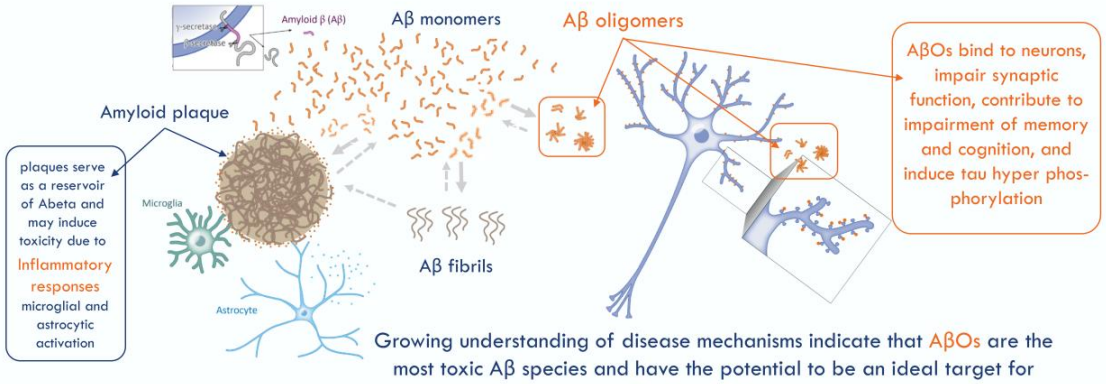
Previous and current anti-amyloid and related drug targets have attempted to intervene



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

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

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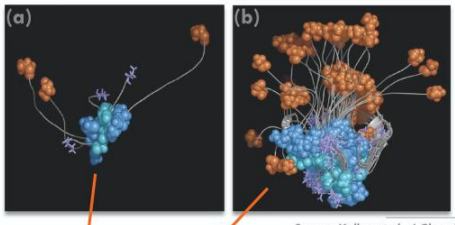
What is an Aβ Oligomer? AβOs May Consist of 2 to >200 Aβ Peptides

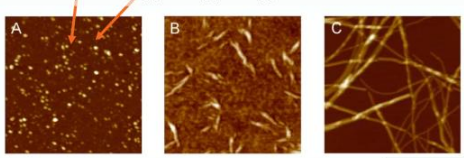
Figure 1. AβOs composed of 3 (a) and 18 (b) Aβ peptides are depicted below.



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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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%	-26%
ADCS-ADL	-15%	-40%	-18%	-23%	N.A.	-37%
CDR-SB	-15%	-23%	2%	-23%	-26%	-27%
MMSE	-13%	-15%	3%	-21%	N.A.	N.A.
iADRS	-11%	N.A.	N.A.	-32%	N.A.	N.A.

* 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 (Phase 2)		lecanemab (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%	12.6%
ApoE ε4 carriers			1.9%	29.8%	42.5%	2.4%	28.7%	41.8%	3.6%	44.0%	1.2%	14.6%	2.3%	15.8%
ApoE ε4 non-carriers			2.9%	18.1%	17.9%	4.3%	17.5%	27.7%			0.0%	8.0%	0.3%	5.4%
Any ARIA E or H			10.3%	32.8%	41.2%	9.8%	30.7%	40.3%	8.0%	38.9%		N.A.	9.5%	21.5%

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

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

ARIA-E represents a dose limiting adverse effect for mAbs with amyloid plaque binding. We believe antibodies that 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

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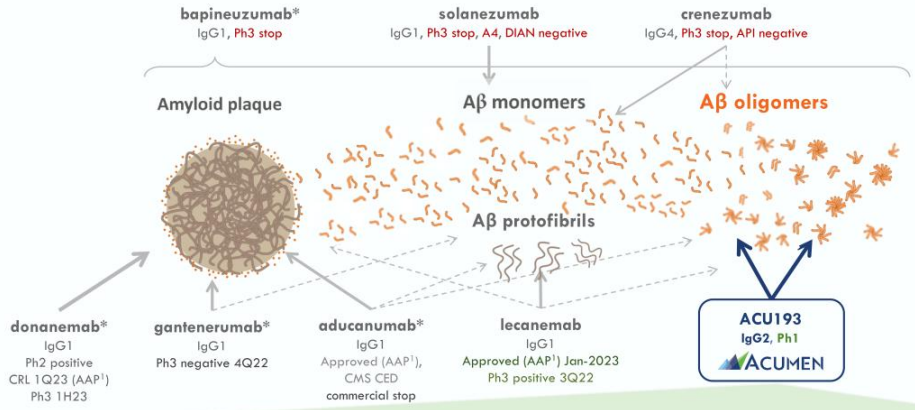
ACU193 Positioning Relative to Late-Stage and Approved Anti-Aβ/Plaque mAbs



ACU193's high selectivity for AβOs combined with an expected lower rate of ARIA 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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ACU193's High Selectivity for Toxic AβOs, Combined With its Expected Lower Rate of ARIA, is Anticipated to Provide Superior Efficacy Compared to Peers

		TARGET SELECTIVITY+				SAFETY PROFILE
Company	Asset	Amyloid plaque	Aβ fibrils	Aβ monomers	Aβ oligomers	Lower rate of ARIA
ACUMEN	ACU193	✗	untested	✗	✓	✓ Expected
Eisai / Biogen	lecanemab	✓	✓	✗	✓	No
Lilly	donanemab	✓	untested	✗	✗	No
Biogen	Aduhelm™	✓	✓	✗	✓	No
Lilly	solanezumab*	✗	✗	✓	✗	✓
Roche	gantenerumab*	✓	✓	✗	✓	No
Roche / Genentech	crenezumab*	✓	✓	✓	✓	✓
Pfizer / Janssen	bapineuzumab*	✓	✓	✓	✓	No

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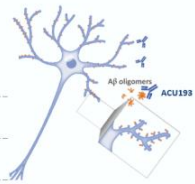
ACU193 Target Product Profile: Best-in-Class, 1st Line, Anti-AβO, Disease-Modifying Immunotherapy for Early AD

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 has a reduced effector function.
POPULATION:	Early AD - Mild Cognitive Impairment and Mild Dementia due to AD (amyloid positive by PET)
DOSING:	IV infusion every 4 weeks
DURATION:	Chronic therapy for duration of Early AD
VALUE PROPOSITION:	**Selectivity for toxic AβOs 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

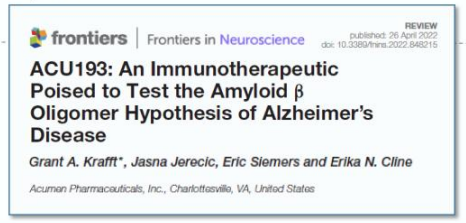
- Dose-dependent effects in multiple in vitro neuroprotection assays
- Positive memory and behavioral effects in multiple in vivo transgenic mouse models for AD

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 including Ph 2/3


frontiers | Frontiers in Neuroscience

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

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

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

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

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

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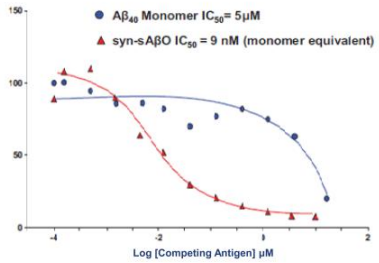
ACU193 is the First mAb Developed to Selectively Target AβOs

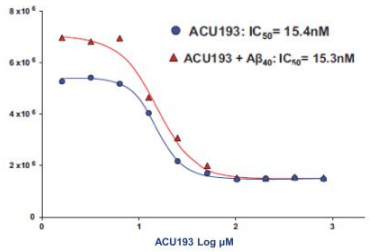
Highly selective for Aβ oligomers versus Aβ monomers

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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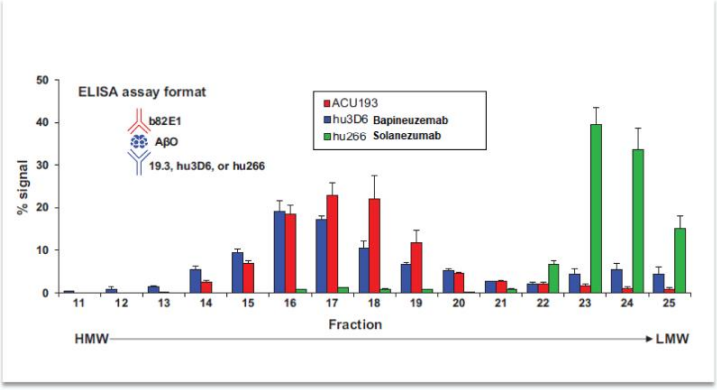
ACU193 Has a Greater Preference for AβOs Than Other mAbs

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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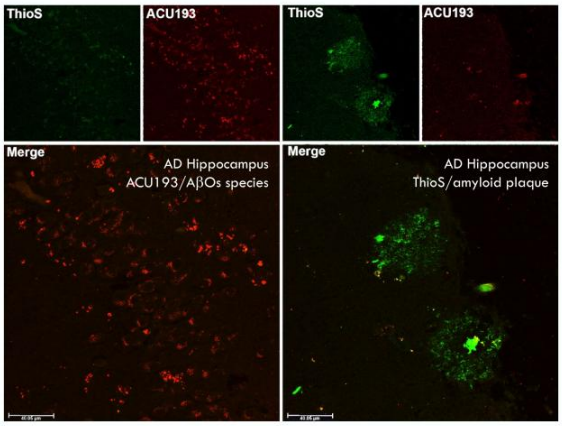
SELECTIVITY

ACU193 is Highly Selective for AβOs Versus Aβ Plaques

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



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

Sources: E. Cline et al. CTAD 2019.

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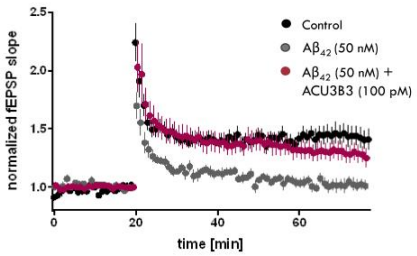
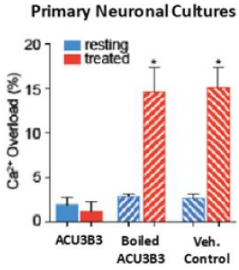
AβOs Bind to Neurons and are Toxic; Mouse Analogue of ACU193 Prevents Toxicity

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

ACU3B3 prevents AβO inhibition of hippocampal LTP *ex vivo*



ACU3B3 prevents AβO mediated Ca2+ elevation in cell cultures



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

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

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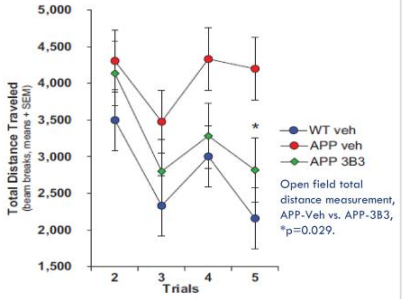
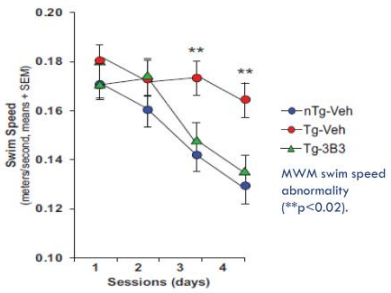
Treatment of a Transgenic Mouse Model of AD Results in Behavioral Improvements

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



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



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

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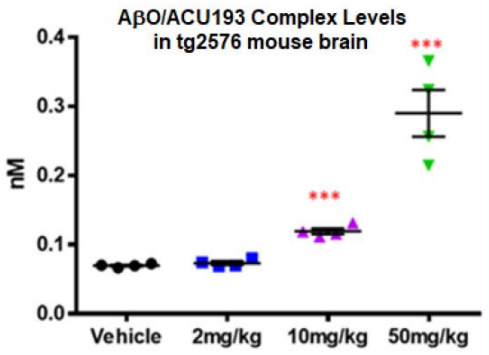
ACU193 Enters the CNS and Binds to AβOs in Transgenic Mice in Dose Dependent Manner



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

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Clinical Development Plans

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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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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 Q3 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

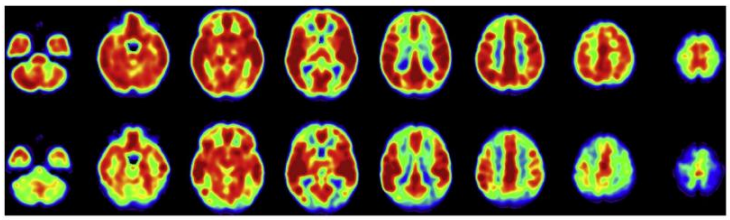

Fig. 1. Processed CBF images measured with ASL of a young and an old healthy control from our database. The top row images are from a 32 year-old woman, and the bottom row images are from an 80 year-old man. The reduction of CBF can be readily observed in widespread brain areas of the older subject compared 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
- ⇒ Topline results from Phase1 study assessing safety, PK, and target engagement expected in Q3 2023
- ⇒ 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[1]

[1]Completion of a Phase 2 trial, with or without an expansion to Phase 3, will likely require us to raise capital in an amount sufficient to extend our cash runway into the second half of 2026.

Business Considerations

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Acumen Leadership Team

Experienced in AD/Neuro Drug Development

DANIEL O'CONNELL
President & CEO
ACUMEN
neuroventures

ERIC SIEMERS, MD
Chief Medical Officer
ACUMEN
Lilly

JANICE HITCHCOCK, PHD
VP, Regulatory Affairs
ACUMEN
Lilly

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

RUSSELL BARTON
Chief Operating Officer
ACUMEN
Lilly

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

LIEAN SCHENK
VP, Head of CMC
ACUMEN
Lilly Lonza
NOVAVAX

SIEW TIN GAN
Head of Clinical Operations
ACUMEN
Takeda

JASNA JERECIC, PHD
Analytical Methods Leader, Research Scientist
ACUMEN

DEREK MEISNER, JD
Chief Legal Officer
ACUMEN

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

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

ACU193 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	✓
Proof-of-mechanism topline results	Q3 2023

~$193M

Cash, cash equivalents and marketable securities as of December 31, 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 throughout 2023
- 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 Q3 2023

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Thank You !

www.acumenpharm.com

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