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): May 9, 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 May 9, 2023, Acumen Pharmaceuticals, Inc. (the "**Company**") reported financial results and business highlights for the three months ended March 31, 2023. 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 May 9, 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 recent Alzheimer's data in the field and the Company's cash position. 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 May 9, 2023.
99.2	Corporate Presentation, dated May 9, 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: May 9, 2023

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

Exhibit 99.1

Acumen Pharmaceuticals Reports First Quarter 2023 Financial Results and Business Highlights

- Expect to report topline results from INTERCEPT-AD, a Phase 1 clinical trial of ACU193 in patients with early Alzheimer's disease, in the third quarter of 2023
- Cash, cash equivalents and marketable securities of $183.8 million as of March 31, 2023 expected to be sufficient to support clinical and operational activities through 2025
- Company to host conference call and webcast today at 8:00 a.m. ET

Charlottesville, Va. and Carmel, In., May 9, 2023 – Acumen Pharmaceuticals, Inc. (NASDAQ: ABOS), 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), today reported financial results for the first quarter of 2023 and provided a business update.

"In the first quarter, we remained focused on executing the Phase I INTERCEPT-AD trial of ACU193, our novel therapeutic for the treatment of early Alzheimer's disease. We are pleased to confirm our expectation that we will share the first clinical data in the field from a monoclonal antibody with high selectivity for toxic amyloid beta oligomers in the upcoming third quarter," said Daniel O'Connell, President and Chief Executive Officer of Acumen. "Amid a dynamic and evolving Alzheimer's landscape, we look forward to reporting clinical evidence of the overall safety profile, pharmacokinetic data, including the potential for monthly dosing, as well as target engagement. We expect that these topline data will serve as the basis for an anticipated interaction with the FDA in the fourth quarter to inform our next phase of development for ACU193."

Recent Business Highlights and Anticipated Milestones

- **In February 2023, enrollment was completed in our Phase 1 INTERCEPT-AD trial, investigating the safety, tolerability, pharmacokinetics and target engagement of ACU193 in patients with early AD.**
  - Acumen continues to anticipate reporting topline results from this trial in the third quarter of 2023.
- **In March 2023, the Company presented research at the International Conference on Alzheimer's and Parkinson's Diseases (ADPD)**.
  - The research demonstrated the utility of a human in vitro model of induced pluripotent stem cell (iPSC)-derived excitatory neurons for a better understanding of which forms of amyloid beta oligomers contribute to the pathogenesis of AD in the human brain. Utilizing human iPSC-derived excitatory neurons as a model, a panel of Aβ detection antibodies, and a panel of globular soluble AβOs plus monomers, the current study found that soluble Aβ size may influence synaptic binding. Read more here.

First Quarter 2023 Financial Results

- **Cash Balance.** As of March 31, 2023, cash, cash equivalents and marketable securities totaled $183.8 million, compared to cash, cash equivalents and marketable securities of $193.4 million as of December 31, 2022. The decrease in cash is related to funding ongoing operations.
- **Research and Development (R&D) Expenses.** R&D expenses were $8.7 million for the three-month period ended March 31, 2023, compared to $6.0 million for the three-month period ended March 31, 2022. The increase in R&D expenses was primarily due to increased costs related to our ongoing clinical trial, as well as nonclinical research and development activity.
- **General and Administrative (G&A) Expenses.** G&A expenses were $4.4 million for the three-month period ended March 31, 2023, compared to $3.2 million for the three-month period ended March 31, 2022. The increase in G&A expenses was primarily due to increased costs related to personnel, consulting and travel expenses.
- **Loss from Operations.** Losses from operations were $13.1 million for the three-month period ended March 31, 2023, compared to $9.2 million for the three-month period ended March 31, 2022. This increase was due to the increased R&D and G&A expenses over the prior year period.
- **Net Loss.** Net loss was $11.3 million for the three-month period ended March 31, 2023, compared to $9.1 million for the three-month period ended March 31, 2022.

Conference Call Details

Acumen will host a conference call and live audio webcast today, May 9, 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.

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 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 a growing body of evidence indicating that soluble AβOs are a primary underlying cause of the neurodegenerative process in Alzheimer's disease. 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 all sites. 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 early and persistent 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, Acumen's ability to achieve its strategic and financial goals, including its projected use of cash, cash equivalents and marketable securities and the expected sufficiency of its cash resources through 2025, and the therapeutic potential of Acumen's product candidate, ACU193, including against other antibodies, and the anticipated timeline for reporting topline safety and proof of mechanism data and results and for further engagement 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 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.

Investors:
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Media:
AcumenPR@westwicke.com

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

	March 31, 2023	December 31, 2022
	(unaudited)	
ASSETS		
Current assets		
Cash and cash equivalents	$ 77,999	$ 130,101
Marketable securities, short-term	62,410	47,504
Prepaid expenses and other current assets	3,623	2,724
Total current assets	144,032	180,329
Marketable securities, long-term	43,419	15,837
Property and equipment, net	151	165
Right-of-use asset	67	105
Other assets	195	151
Total assets	$ 187,864	$ 196,587
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 762	$ 1,640
Accrued clinical trial expenses	5,203	2,717
Accrued expenses and other current liabilities	2,747	3,350
Operating lease liability	67	105
Total current liabilities	8,779	7,812
Total liabilities	8,779	7,812
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued and outstanding as of March 31, 2023 and December 31, 2022	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized and 41,025,062 shares issued and outstanding as of March 31, 2023 and December 31, 2022	4	4
Additional paid-in capital	361,339	359,949
Accumulated deficit	(181,734)	(170,427)
Accumulated other comprehensive loss	(524)	(751)
Total stockholders' equity	179,085	188,775
Total liabilities and stockholders' equity	$ 187,864	$ 196,587

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

	Three Months Ended March 31,	
	2023	2022
Operating expenses		
Research and development	$ 8,713	$ 5,985
General and administrative	4,422	3,221
Total operating expenses	13,135	9,206
Loss from operations	(13,135)	(9,206)
Other income (expense)		
Interest income, net	1,832	76
Other income (expense), net	(4)	1
Total other income	1,828	77
Net loss	(11,307)	(9,129)
Other comprehensive gain (loss)		
Unrealized gain (loss) on marketable securities	227	(583)
Comprehensive loss	$ (11,080)	$ (9,712)
Net loss per common share, basic and diluted	$ (0.28)	$ (0.23)
Weighted-average shares outstanding, basic and diluted	41,025,062	40,473,270

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

	Three Months Ended March 31,	
	2023	2022
Cash flows from operating activities		
Net loss	$ (11,307)	$ (9,129)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	14	4
Stock-based compensation expense	1,390	618
Amortization of premiums and accretion of discounts on marketable securities, net	(334)	216
Amortization of right-of-use asset	38	33
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(899)	1,416
Other assets	(44)	(65)
Accounts payable	(878)	121
Accrued clinical trial expenses	2,486	281
Operating lease liability	(38)	(32)
Accrued expenses and other current liabilities	(603)	(1,762)
Net cash used in operating activities	(10,175)	(8,299)
Cash flows from investing activities		
Purchases of marketable securities	(52,131)	(9,090)
Proceeds from maturities and sales of marketable securities	10,204	4,000
Purchases of property and equipment	—	(9)
Net cash used in investing activities	(41,927)	(5,099)
Net change in cash and cash equivalents	(52,102)	(13,398)
Cash and cash equivalents at the beginning of the period	130,101	122,162
Cash and cash equivalents at the end of the period	$ 77,999	$ 108,764

Corporate Presentation

May 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.

ACUMEN

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: ~$184M in cash at 31-Mar-23
- 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.

AD, Amyloid & Abeta Oligomers

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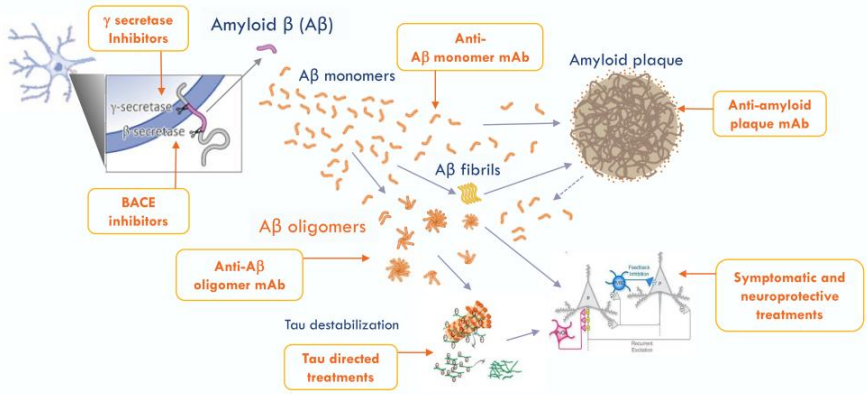
Alzheimer's Pathophysiology

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

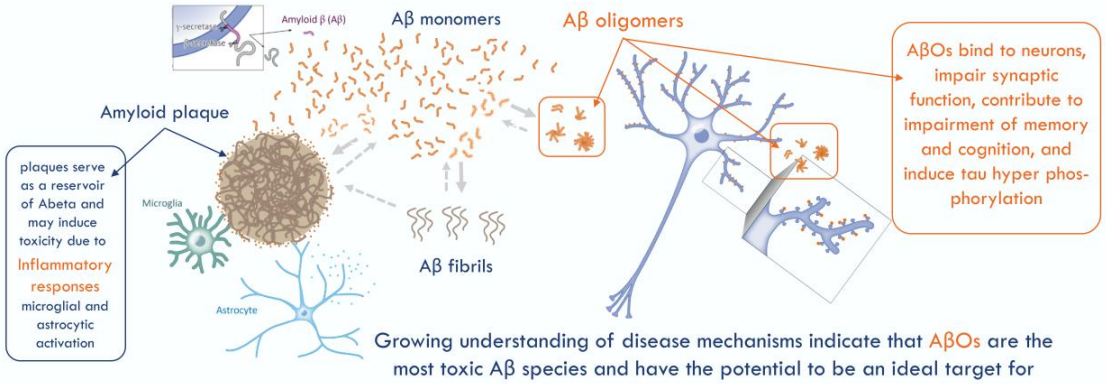
Previous and current anti-amyloid and related drug targets have attempted to intervene



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 majority of peer monoclonal antibodies target amyloid plaques with only limited effects on AβOs; Acumen's drug candidate ACU193 targets AβOs

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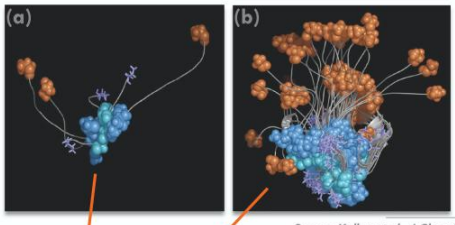
What is an Aβ Oligomer? AβOs May Consist of 2 to >200 Aβ Peptides

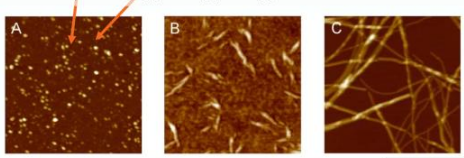
Figure 1. AβOs composed of 3 (a) and 18 (b) Aβ peptides are depicted below.



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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Toxic AβOs Represent an Ideal Alzheimer's Disease Drug Target

AβOs are widely recognized as key pathogenic structures in AD:

1. ***Impair synaptic function[1]***

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

2. ***Contribute to impairment of memory and cognition[3]***

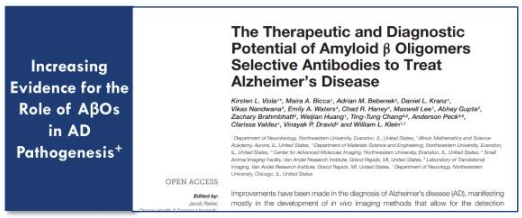
   Soluble AβOs (but not monomers) have been found to block hippocampal long-term potentiation (LTP), a synaptic correlate of memory and learning[4]

3. ***Induce tau hyperphosphorylation[5]***

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

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

Increasing Evidence for the Role of AβOs in AD Pathogenesis+

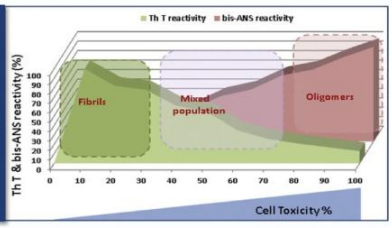


The Therapeutic and Diagnostic Potential of Amyloid β Oligomers Selective Antibodies to Treat Alzheimer's Disease

OPEN ACCESS

Improvements have been made in the diagnosis of Alzheimer's disease (AD), manifesting mostly in the development of *in vivo* imaging methods that allow for the detection

Relationship Between the Aβ Assemblies and Their Toxicity++



Targeting the right form of amyloid may be a key to slowing disease progression in early AD

+ Viola, et al. The Therapeutic and Diagnostic Potential of Amyloid ß Oligomers Selective Antibodies to Treat Alzheimer's Disease, 2022.
++ Sengupta, U. et al. The Role of Amyloid-ß Oligomers in Toxicity, Propagation, and Immunotherapy, 2016

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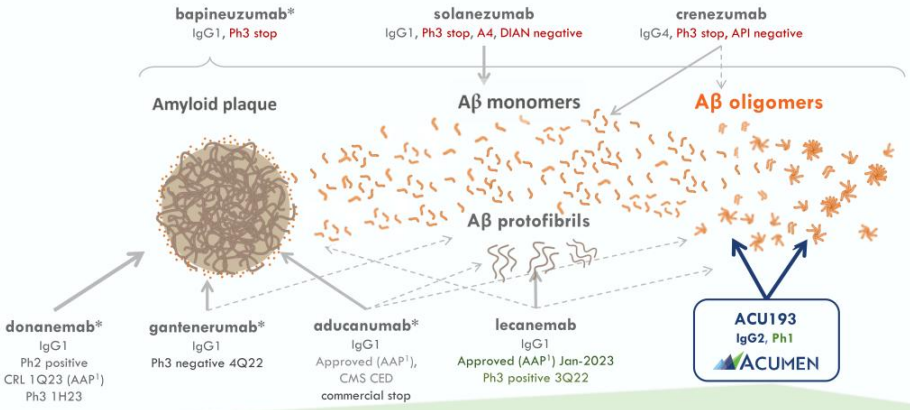
ACU193 Positioning Relative to Late-Stage and Approved Anti-Aβ/Plaque mAbs



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

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

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

ACU193's high selectivity for toxic AβOs, combined with its expected lower rate of ARIA, is anticipated to provide superior efficacy and safety compared to peers

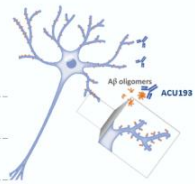
ACUMEN

ACU193:
Our Differentiated Approach

ACUMEN

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 Aβ, from dimers to high molecular weight AβOs

PHARMACOLOGY

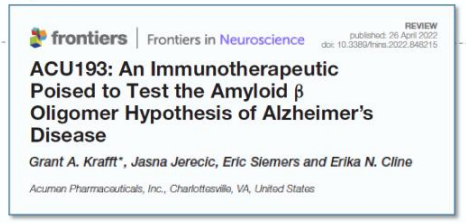
- Dose-dependent effects in multiple in vitro neuroprotection assays
- Positive memory and behavioral effects in multiple in vivo transgenic mouse models for AD

PK/PD

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

SAFETY

- IgG2 subclass lacks inflammatory effector function signaling (FcγR binding)
- Nonclinical microhemorrhage studies show no increased risk of microhemorrhage
- GLP studies demonstrated acceptable safety 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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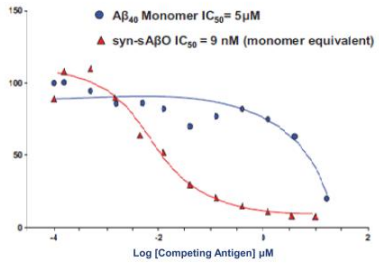
SELECTIVITY

ACU193 is the First mAb Developed to Selectively Target AβOs

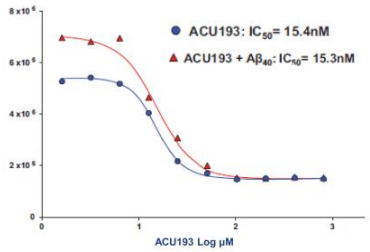
Highly selective for Aβ oligomers versus Aβ monomers

ACU193 Selectivity



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

ACU193 Selectivity in presence of 5μM monomeric Aβ



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

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

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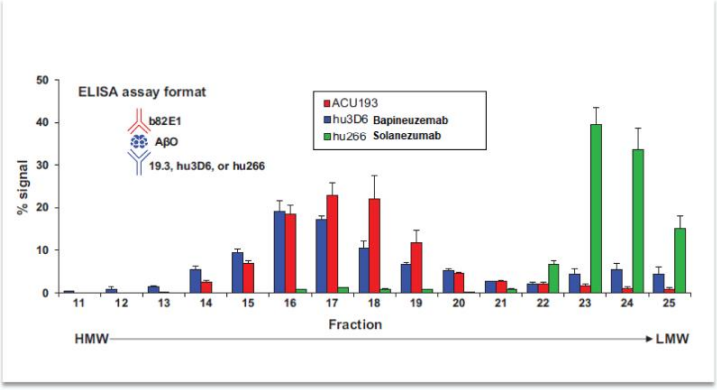
ACU193 Binds to a Wide Range of Oligomeric Species of Aβ

Comparison of Aβ species-mAb complex signals across SEC fractions



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

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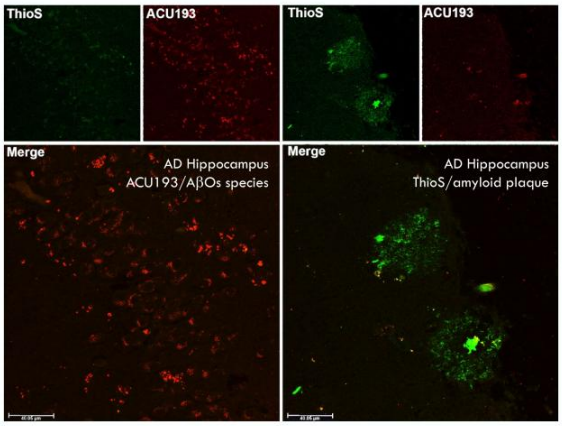
SELECTIVITY

ACU193 is Highly Selective for AβOs Versus Aβ Plaques

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



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

Sources: E. Cline et al. CTAD 2019.

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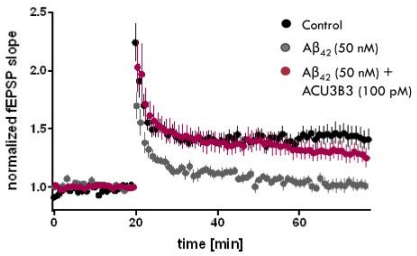
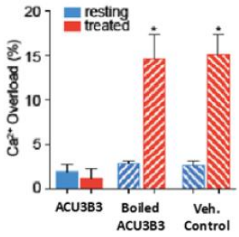
AβOs Bind to Neurons and are Toxic; Mouse Analogue of ACU193 Prevents Toxicity

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

ACU3B3 prevents AβO inhibition of hippocampal LTP *ex vivo*



ACU3B3 prevents AβO mediated Ca2+ elevation in cell cultures



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

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

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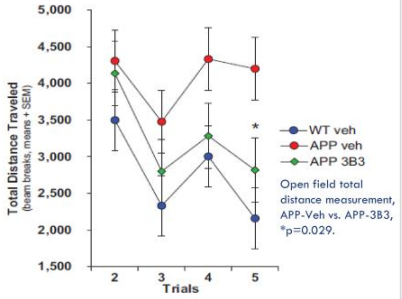
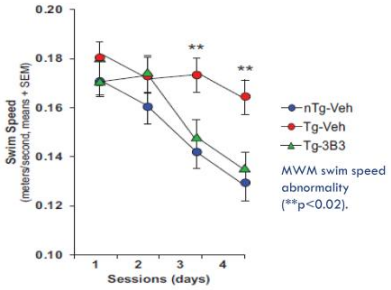
Treatment of a Transgenic Mouse Model of AD Results in Behavioral Improvements

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



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



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

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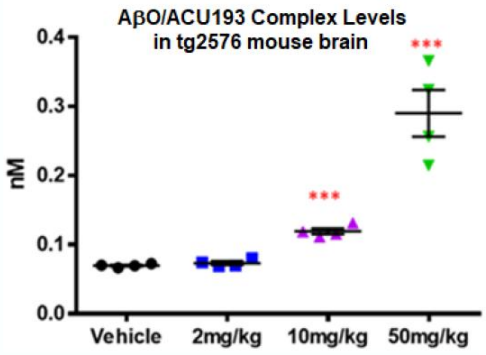
ACU193 Enters the CNS and Binds to AβOs in Transgenic Mice in Dose Dependent Manner



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

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Clinical Development Plans

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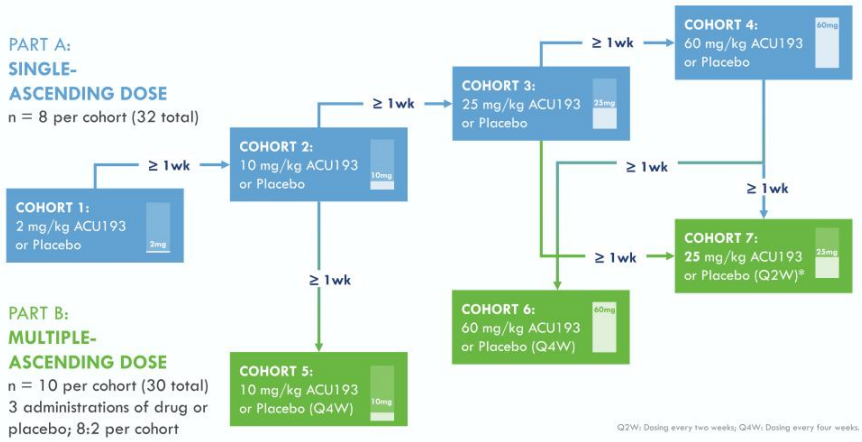
INTERCEPT-AD a Randomized Placebo Controlled Phase 1 in Early AD patients



*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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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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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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CSF Target Engagement Assay (CSF-TE) Expected to Show Presence of ACU193-AβO Complex

Unique assay configuration tailored to detect ACU193-AβO complex in CSF
MSD S-PLEX (Turbo) Immunoassay

AβO selective detection
(anti-AβO mAb)

Only drug/oligomer complex is measurable

ACU193 drug specific capture
(anti-ACU193 idiotype mAb)

AβO concentration in CSF is very low (≤10pg/ml; 2pM)
Preliminary data in 25 mg/kg cohort shows ACU193 in excess of reported endogenous AβOs

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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

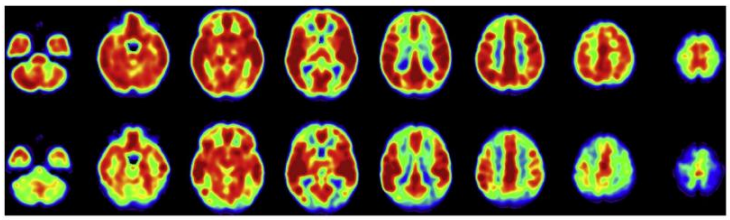

Fig. 1. Processed CBF images measured with ASL of a young and an old healthy control from our database. The top row images are from a 32 year-old woman, and the bottom row images are from an 80 year-old man. The reduction of CBF can be readily observed in widespread brain areas of the older subject compared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

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ACU193 IP & Market Exclusivity

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

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

~$184M

Cash, cash equivalents and marketable securities as of March 31, 2023

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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Appendix

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

Percent Slowing of Cognitive/Functional Decline*

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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