



Acumen Pharmaceuticals Presents Positive Topline Results from First-in-Human Phase 1 Study of ACU193 for Early Alzheimer's Disease at the Alzheimer's Association International Conference (AAIC) 2023

July 16, 2023

- *Topline results from INTERCEPT-AD trial met primary and secondary objectives, demonstrating proof-of-mechanism for ACU193, the first clinical-stage amyloid beta oligomer (A β O)-targeting antibody*
- *Rapid, dose-related, statistically significant ($p=0.01$) amyloid plaque reduction observed within higher dose cohorts (25% reduction in 60 mg/kg Q4W cohort at day 63 and 20% reduction in 25 mg/kg Q2W cohort at day 70)*
- *ACU193 approached maximal central target engagement of toxic A β Os beyond expected levels, establishing broad therapeutic index and path to convenient monthly dosing*
- *ACU193 was well-tolerated in patients with early Alzheimer's disease and resulted in no drug-related serious adverse events, with a low rate of ARIA-E across all cohorts*
- *Company to host conference call and webcast for investors and analysts July 17 at 8 a.m. ET*

CHARLOTTESVILLE, Va. and CARMEL, Ind., July 16, 2023 (GLOBE NEWSWIRE) -- [Acumen Pharmaceuticals, Inc.](#) (NASDAQ: ABOS), a clinical-stage biopharmaceutical company developing a novel therapeutic that targets soluble amyloid beta oligomers (A β Os) for the treatment of Alzheimer's disease (AD), today presented positive topline results from the Phase 1 INTERCEPT-AD trial of ACU193, the first clinical-stage A β O targeting antibody therapy in early AD, at the Alzheimer's Association International Conference (AAIC[®]) 2023, taking place in Amsterdam and online from July 16-20, 2023.

Topline results demonstrated that ACU193 was generally well-tolerated with a compelling overall safety profile, meeting the primary objective of this Phase 1, first-in-human, randomized, double-blind, placebo-controlled study in both single and multiple doses in 60 participants with early AD. Dose levels were 2, 10, 25 and 60 mg/kg for one to three doses administered intravenously. An analysis of change in amyloid plaque load, as measured by positron emission tomography (PET) SUVR, demonstrated a rapid, dose-related mean decrease at the higher dose levels studied (60 mg/kg every 4 weeks [Q4W] and 25 mg/kg every 2 weeks [Q2W]). This finding is comparable to mean amyloid plaque decreases of approved A β monoclonal antibodies at similar time points in their clinical development. The overall rate of amyloid related imaging abnormalities – edema (ARIA-E) was 10.4%, which included one case of symptomatic ARIA-E (2.1%). Pharmacokinetic results in serum and cerebrospinal fluid (CSF) demonstrated statistically significant dose proportionality and support monthly dosing of ACU193. Statistically significant, dose-related central target engagement was observed as measured by ACU193-A β O complex, establishing the first target engagement assay developed that is specific to an A β O-targeting antibody. An exposure response relationship (Emax) model revealed near maximal target engagement with repeated dosing at 25 mg/kg and 60 mg/kg.

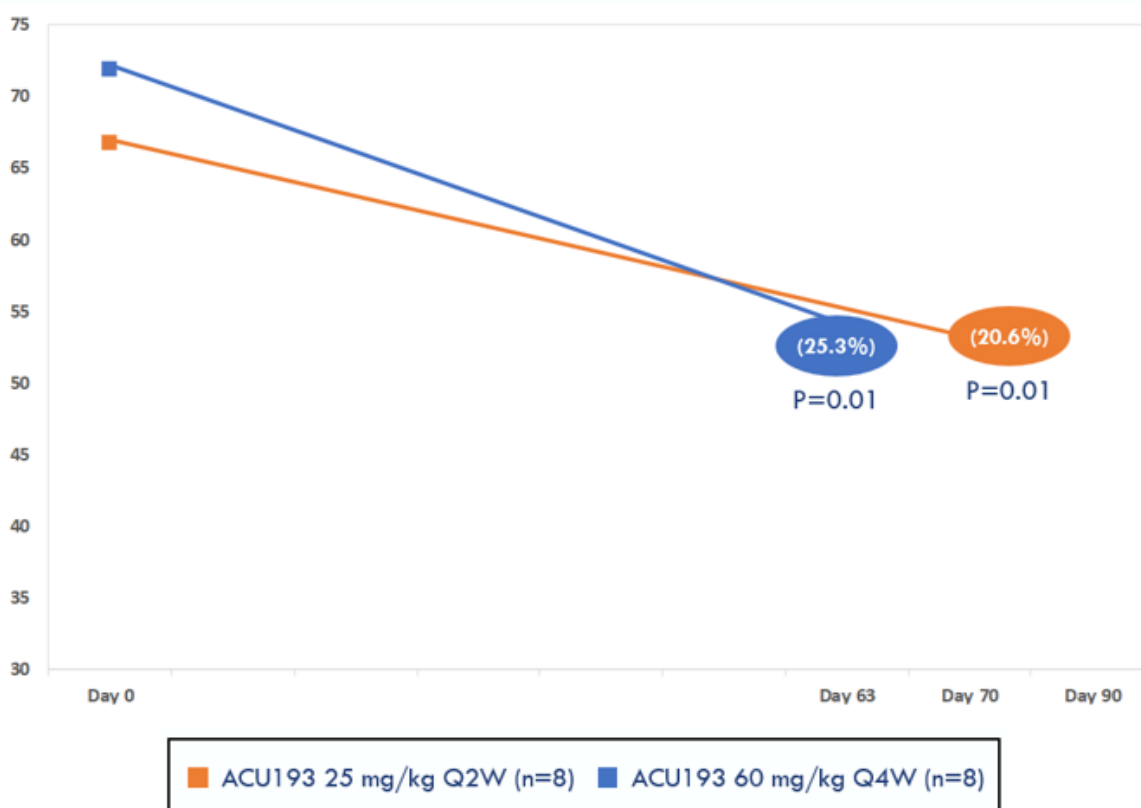
"We are very pleased to present the first clinical data from our Phase 1 INTERCEPT-AD study at AAIC. ACU193's observed dose-related central target engagement, rapid reduction of amyloid plaque and compelling safety profile validate our confidence in ACU193's differentiated mechanism of action: selectively targeting amyloid beta oligomers," said Daniel O'Connell, President and Chief Executive Officer of Acumen. "We believe that the robust data package generated by this comprehensive Phase 1 study establishes ACU193's broad therapeutic index and guides a future clinical dosing rationale. We look forward to an anticipated interaction with the FDA in the fourth quarter to inform our next phase of development for ACU193."

ACU193 Demonstrated Rapid, Dose-Related, Statistically Significant Amyloid Plaque Reduction

Higher doses of ACU193 (60 mg/kg Q4W and 25 mg/kg Q2W) showed a statistically significant reduction in amyloid plaque load as determined by amyloid PET after 6-12 weeks (from baseline to endpoint within cohorts ($p = 0.01$)). This finding provides evidence that ACU193 is active in the brain.

Mean Reduction in Amyloid Plaque (Centiloids)

Absolute Values



Source: Acumen Pharmaceuticals, data on file; Cumulative drug administered: ACU193 60 mg/kg = 180 mg/kg (three doses administered); ACU193 25 mg/kg = 75 mg/kg (three doses administered)

ACU193 was Well-Tolerated Across Dose Cohorts

ACU193 was well-tolerated throughout the single-ascending (SAD) and multiple-ascending (MAD) dose cohorts. Three treatment-emergent serious adverse events (SAEs) were observed after administration of ACU193; all were deemed not related or unlikely related to ACU193. The most common treatment-emergent adverse events (AEs) from all dose groups combined were ARIA-E (10.4%), ARIA-H (hemorrhage) (8.3%), COVID-19 (6.3%), hypersensitivity (6.3%), bronchitis (4.2%), headache (4.2%), fall (4.2%) and post LP syndrome (4.2%). Of the five individuals who developed ARIA-E, only one had associated clinical symptoms, representing an overall symptomatic ARIA-E rate of 2.1% in the study. Of note, no APOE4 homozygote patients exhibited ARIA-E (n=6 treated).

INTERCEPT-AD ARIA-E Results*

	10 mg/kg	25 mg/kg	60 mg/kg	Overall Study
Any ARIA-E	1/14 (7.1%)	1/14 (7.1%)	3/14 (21.4%)	5/48 (10.4%)
Symptomatic ARIA-E	0/14 (0.0%)	0/14 (0.0%)	1/14 (7.1%)	1/48 (2.1%)

*2 mg/kg cohort is omitted due to lack of ARIA-E cases. Denominator of 14 participants in 10 mg/kg, 25 mg/kg and 60 mg/kg inclusive of single-ascending dose and multiple-ascending dose cohorts. Overall study denominator of 48 participants includes all participants on ACU193.

ACU193 Demonstrated Consistent Dose-Related Pharmacokinetics (PK)

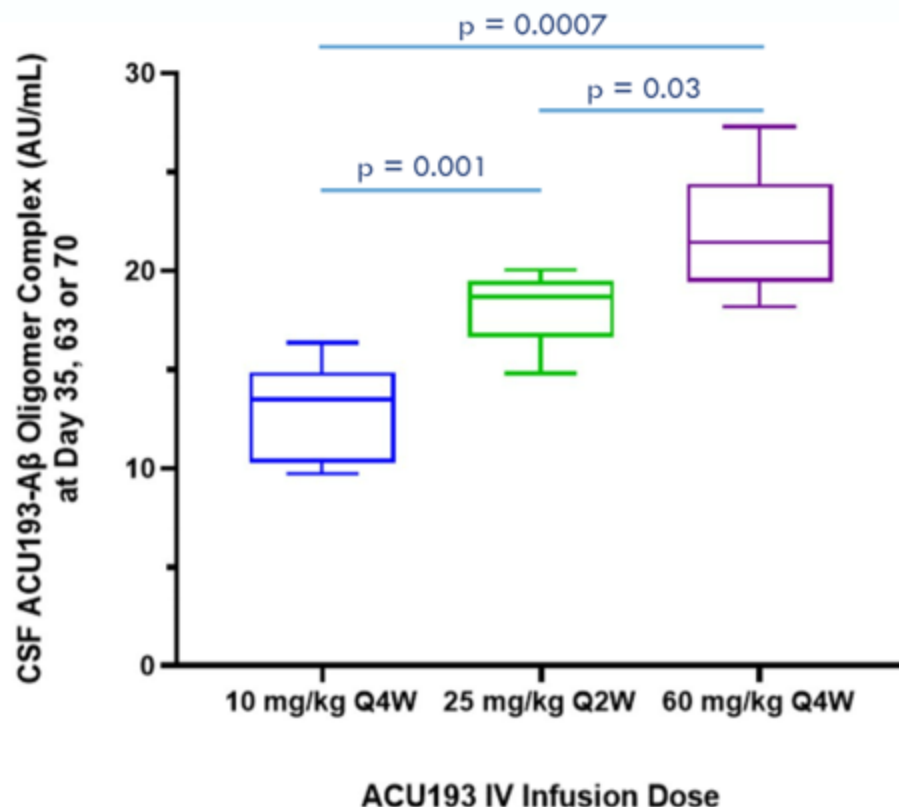
In both the SAD and MAD cohorts of the study, clear evidence of a dose relationship was observed for ACU193 exposure. Serum PK was dose-related without drug accumulation, and CSF PK was dose- and dose-regimen proportional. Levels of ACU193 detected in CSF in all cohorts were in excess of endogenous levels of AβOs reported in CSF. Evidence of treatment emergent immunogenicity was observed; anti-drug antibodies were consistently low titer and preliminary assessment revealed no apparent effect on serum PK. These data support monthly dosing of ACU193.

ACU193 Demonstrated Dose-Related Target Engagement of Toxic AβOs

In both the SAD and the MAD portions of the study, a statistically significant, dose-related increase in target engagement of toxic AβOs was observed starting at 10 mg/kg and was related to concentrations of drug in CSF. This was evaluated by a novel assay of target engagement that assessed the concentration of the ACU193-AβO complex in CSF. Notably, maximal target engagement response was approached at the highest doses studied (25 mg/kg Q2W and 60 mg/kg Q4W), as assessed in an exposure-response relationship (Emax) model. This implies that at these dose levels, ACU193 concentrations approached saturation of AβOs, and suggests active removal of target from the brain.

Target Engagement of ACU193 with AβOs is Statistically Significant and Dose Proportional

Multiple Dose Cohorts*



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

"I am thrilled to announce that ACU193 bound to toxic AβOs in patients and did so in a dose-proportional manner with evidence of near-maximal target engagement. I'm also proud that our team has made significant progress developing the first target engagement assay for an Aβ oligomer-targeted antibody," said Eric Siemers, M.D., Chief Medical Officer of Acumen. "Taken together with the compelling safety profile at doses that engage the target, and pharmacokinetic data that supports monthly dosing, ACU193 has the distinct potential to be a differentiated antibody for the treatment of early Alzheimer's disease."

Exploratory measures of potential acute drug effects including assessment of cognition, as determined by a computerized cognitive battery, and changes in cerebral blood flow, as determined by arterial spin labelling (ASL) with magnetic resonance imaging (Siemens MRI), did not show discernible effects from the immediate administration of ACU193. This was not unexpected due to the short duration and small sample size of INTERCEPT-AD. Additional biofluids for assessment of biomarkers of downstream neurodegeneration were collected during the study and analyses are in progress. These results will be presented at a later date and are not expected to show significant changes due to the short duration and small sample size of the trial.

In addition to the topline readout, Acumen also presented data during the Featured Research Session at AAIC describing the baseline characteristics for INTERCEPT-AD patients as well as study recruitment techniques that were used to help Acumen recruit a diverse population for the trial.

The full results of the INTERCEPT-AD study will be presented at a future medical congress and submitted for publication in a peer-reviewed clinical journal. Acumen plans to discuss these results with regulators to assess next steps for the clinical development of ACU193 and determine a timeline for progressing to a Phase 2/3 clinical study.

Conference Call Details

Acumen will host a webcast presentation and conference call for analysts and investors on Monday, July 17, 2023, at 8:00 a.m. ET to discuss the topline data from the INTERCEPT-AD clinical trial. The webcast will feature members of Acumen's leadership team as well as Steven DeKosky, M.D., Deputy Director of the McKnight Brain Institute at the University of Florida and member of Acumen's scientific advisory board, and Lawrence Honig, M.D., Ph.D., Director of the New York State Center of Excellence for Alzheimer's Disease at Columbia University and an INTERCEPT-AD trial investigator.

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 A β , relative to A β monomers and amyloid plaques. Soluble A β Os have been observed to be potent neurotoxins that bind to neurons, inhibit synaptic function and induce neurodegeneration. By selectively targeting toxic soluble A β Os, ACU193 aims to directly address a growing body of evidence indicating that soluble A β Os 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. 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 (A β Os) for the treatment of Alzheimer's disease (AD). Acumen's scientific founders pioneered research on A β Os, 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 A β Os. 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. Words such as "believes," "expects," "anticipates," "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 the safety profile and mechanism of action of Acumen's product candidate, ACU193, the regulatory path and clinical development of ACU193, including a possible Phase 2/3 study, and the timing of the presentation of additional data on ACU193. 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, including Acumen's most recent Quarterly Report on Form 10-Q. 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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Photos accompanying this announcement are available at:

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