# Acumen Pharmaceuticals Presents Sabirnetug (ACU193) Fluid Biomarker and Target Engagement Analyses from Phase 1 INTERCEPT-AD Study in Early Alzheimer's at the AD/PD™ 2024 Annual Meeting

March 8, 2024

*- Cerebrospinal fluid (CSF) biomarker results are highly supportive of sabirnetug's downstream pharmacological effects in the brain in early AD*

*- Poster presentation showcases method used to develop a first-of-its-kind assay to assess sabirnetug's binding to amyloid beta oligomers (AβOs) in Alzheimer's disease*

*- Company on track to initiate Phase 2 trial evaluating sabirnetug in the first half of 2024 and Phase 1 subcutaneous study in mid-2024*

CHARLOTTESVILLE, Va., March 08, 2024 (GLOBE NEWSWIRE) -- Acumen Pharmaceuticals, Inc. (NASDAQ: ABOS), a clinical-stage biopharmaceutical company developing a novel therapeutic that targets soluble amyloid beta oligomers (AβOs) for the treatment of Alzheimer's disease (AD), today presented cerebrospinal fluid (CSF) biomarker data from the sabirnetug (ACU193) Phase 1 INTERCEPT-AD trial in an oral presentation at the International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders (AD/PD) in Lisbon, Portugal, and online. Acumen also presented a poster showcasing the method used to develop a first-of-its-kind assay to measure target engagement of an AβO-selective antibody.

Acumen's sabirnetug is the first humanized monoclonal antibody to clinically demonstrate selective target engagement of AβOs, a soluble and highly toxic form of Aβ that accumulates early in AD and triggers synaptic dysfunction and neurodegeneration. Positive topline results from 62 participants dosed in the Phase 1 INTERCEPT-AD trial (NCT04931459) were reported in July 2023, and additional insights from exploratory analyses have further confirmed sabirnetug's proof-of-mechanism and broad therapeutic potential as a next-generation treatment for early AD.

**Sabirnetug (ACU193) Lowers CSF Neurogranin & pTau181 Levels in INTERCEPT-AD Study in Early AD**

Several key CSF biomarkers are associated with the pathological changes that occur in AD, and evidence suggests these biomarkers may better reflect the underlying pathology of AD than imaging alone.[i,ii] Results from CSF samples collected before and after drug exposure in the INTERCEPT-AD study were presented and assessed for biomarkers indicative of amyloid pathology (Aβ42/40 ratio), tau pathology (pTau181, pTau217), neuronal injury (total tau) and synaptic injury (neurogranin).

Sabirnetug had an observed dose-dependent trend in the multiple ascending dose cohorts on CSF levels of pTau181, pTau217 total tau, neurogranin and the Aβ42/Aβ40 ratio, consistent with the downstream pharmacologic effects after just three administrations of the drug. Key findings include:

- Improvements in biomarkers associated with AD pathology, including significantly lowered CSF levels of neurogranin (-13.9%) and pTau181 (-13.0%) and trending toward an increasing Aβ42/40 ratio using 60 mg/kg Q4W as compared to the placebo group;
- A nominally significant correlation between target engagement of AβOs and change in neurogranin across all doses, supportive of drug effect; and
- A trend in correlation between target engagement of AβOs and change in p-tau181 across all doses, also supportive of drug effect.

These findings support a biological link between sabirnetug and neurogranin and pTau181 and are consistent with sabirnetug's proposed mechanism of action and intended target engagement of AβOs, as sabirnetug's effects on these two biomarkers are more closely related to binding of AβOs than plaque reduction.

"We're thrilled to return to AD/PD this year since completing the Phase 1 INTERCEPT-AD trial with results from our biomarker assessment, which further validate our confidence in sabirnetug's proposed mechanism of action," said Daniel O'Connell, Chief Executive Officer of Acumen. "As the Alzheimer's treatment landscape continues to evolve, we're seeing just how important biomarkers are to better characterize and understand the underlying pathology of disease, and we look forward to exploring the relationship between these biomarkers and clinical outcomes in a longer-term Phase 2 study."

**Target Engagement in INTERCEPT-AD: Development of a Novel Assay Measuring Sabirnetug (ACU193)-Amyloid Beta Oligomer Complexes in Human CSF**

Additionally, Acumen presented a poster detailing its method to develop the first assay to directly measure target engagement of AβOs by an immunotherapy (as measured by sabirnetug-AβO complex in CSF) in the INTERCEPT-AD trial. The novel assay configuration was tailored to selectively detect sabirnetug-AβO complex in CSF as a direct measure of target engagement, showing clear dose-related increases in target engagement across all cohorts. This data also informed development of a pharmacokinetic-pharmacodynamic (PK/PD) model, which ultimately demonstrated that the highest doses used in INTERCEPT-AD (60 mg/kg Q4W and 25mg/kg Q2W) approached maximal target engagement, as was presented in October 2023.

"Despite longstanding evidence implicating soluble AβOs as a significant driver of AD pathology, historically it's been difficult to measure and characterize this form of Aβ," said Erika Cline, Ph.D., lead author and Manager of Bioanalytical Methods at Acumen Pharmaceuticals. "As Acumen progresses the clinical study of the first-in-clinic antibody with high selectivity for AβOs, the development of the first assay to detect direct target

engagement of AβOs is crucial to deepen our understanding of how sabirnetug acts *in vivo."*

Acumen is on track to initiate a Phase 2 trial evaluating sabirnetug in the first half of 2024 and a Phase 1 subcutaneous study in mid-2024.

**About Sabirnetug (ACU193)**
Sabirnetug (ACU193) is a humanized monoclonal antibody (mAb) discovered and developed based on its selectivity for soluble AβOs, which are a highly toxic and pathogenic form of Aβ, relative to Aβ monomers and amyloid plaques. Soluble AβOs have been observed to be potent neurotoxins that bind to neurons, inhibit synaptic function and induce neurodegeneration. By selectively targeting toxic soluble AβOs, sabirnetug aims to directly address a growing body of evidence indicating that soluble AβOs are a primary underlying cause of the neurodegenerative process in Alzheimer's disease. Sabirnetug 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 was 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 sabirnetug 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 sabirnetug. The INTERCEPT-AD study consisted of single-ascending-dose (SAD) and multiple-ascending-dose (MAD) cohorts and was designed to evaluate the safety, tolerability, pharmacokinetics (PK), and target engagement of intravenous doses of sabirnetug. More information can be found on www.clinicaltrials.gov, NCT identifier NCT04931459.

**About Acumen Pharmaceuticals, Inc.**
Acumen, headquartered in Charlottesville, VA, with additional offices in Indianapolis, IN and Newton, MA, 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, sabirnetug (ACU193), a humanized monoclonal antibody that selectively targets toxic soluble AβOs, following positive results 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 "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 therapeutic potential of Acumen's product candidate, sabirnetug (ACU193), Acumen's preparations with respect to its plans to initiate a Phase 2 study and subcutaneous study, and Acumen's potential to receive regulatory approval for and bring sabirnetug to patients living with AD. These statements are based upon the current beliefs and expectations of Acumen's 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.

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