# Acumen Pharmaceuticals Presents First Comprehensive Clinical and Biomarker Data for Sabirnetug (ACU193) at American Academy of Neurology 2024 Annual Meeting

April 16, 2024

- *Presentation and poster include deeper data insights on sabirnetug safety profile, target engagement and fluid biomarker changes*
- *Presentation to be featured during AAN Emerging Science Session*
- *Company on track to initiate Phase 2 trial evaluating sabirnetug in first half of 2024*

CHARLOTTESVILLE, Va., April 16, 2024 (GLOBE NEWSWIRE) -- 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), will present the comprehensive clinical and biomarker results from its positive Phase 1 INTERCEPT-AD study of sabirnetug (ACU193) in early AD during an Emerging Science Session at the American Academy of Neurology (AAN) 2024 Annual Meeting in Denver on April 16, 2024. The results build upon Acumen's prior presentations at the AD/PD™ 2024 Annual Meeting and positive topline data first announced in July 2023 and will be presented together for the first time with expanded analysis.

A platform presentation, titled "A phase 1 study, INTERCEPT-AD, of ACU193: safety, target engagement, and biomarker changes," will take place on Tuesday, April 16, from 6:06-6:12 PM MDT within the ES2 – Emerging Science 2 track at the Colorado Convention Center, Bluebird 1A, followed by a poster presentation with more in-depth results from 6:25-7:00 PM MDT.

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 is an early and persistent trigger of synaptic dysfunction and neurodegeneration. Acumen is developing sabirnetug as a potential best-in-class antibody treatment for early AD.

"For the first time, we're presenting a comprehensive set of safety, biomarker and target engagement data from INTERCEPT-AD, which continue to support sabirnetug's mechanism and potential to offer differentiated safety and efficacy as a next-generation treatment for people with early Alzheimer's disease," said Eric Siemers, M.D., Chief Medical Officer of Acumen and presenting author. "The results of this robust Phase 1 trial give us hope that sabirnetug could have a safety and efficacy profile that could make it an attractive option for a large number of patients. We look forward to applying insights learned from INTERCEPT-AD as we embark upon our ALTITUDE-AD Phase 2 trial for sabirnetug."

Sabirnetug Demonstrated Favorable Safety and Tolerability Profile

The poster outlines that sabirnetug demonstrated a favorable safety and tolerability profile in participants with early AD with a relatively low incidence of ARIA-E. There were four cases of asymptomatic ARIA-E and one symptomatic case among 48 participants who were treated with sabirnetug. Notably, none of the six participants who were APOE Ɛ4 homozygotes experienced ARIA-E despite making up 13% of all participants in the study. This contrasts with other studies of amyloid-targeting monoclonal antibodies where approximately 30 to 40 percent of participants who are APOE Ɛ4 homozygotes experienced ARIA-E.

Target Engagement

Sabirnetug target engagement with AβOs in cerebrospinal fluid (CSF) increased in a dose-dependent manner in both single and multiple ascending dose groups. Central target engagement approached the maximum at the highest doses of sabirnetug administered. The results suggest that at these dose levels, ACU193 concentrations approached saturation of AβOs, and suggests active removal of target from the brain.

Sabirnetug Associated with Changes in CSF and Plasma Biomarkers Indicating Downstream Effects on Amyloid, pTau Species, and Synaptic Markers After Three Administrations

Sabirnetug treatment also changed a number of CSF biomarkers in the multiple ascending dose cohorts, which are indicative of amyloid pathology (Aβ42/40 ratio), tau pathology (pTau181, pTau217), and synaptic injury (neurogranin, VAMP2). Sabirnetug significantly lowered CSF neurogranin (-13.9%), VAMP2 (-8.1%) and pTau181 (-13.0%) concentrations and numerically increased Aβ42/40 after three administrations of sabirnetug at 60 mg/kg once every 4 weeks (Q4W). Sabirnetug target engagement with AβOs was significantly correlated with reduction of CSF neurogranin. Additionally, plasma biomarkers for neuroinflammation (GFAP) and tau pathology (pTau181, pTau217) were lower in the 10 mg/kg Q4W and 60 mg/kg Q4W groups compared to placebo. Furthermore, nearly all patients treated with sabirnetug in the high dose multiple-ascending dose cohorts showed reductions in plaque load after three doses at 63 or 70 days. These results support sabirnetug's proposed mechanism of action and intended target engagement of synaptotoxic AβOs.

A copy of the poster and presentation will be available following the conference in the Investors section of the Company's website at www.acumenpharm.com.

**Acumen Remains On Track to Initiate Additional Clinical Studies of Sabirnetug**

Acumen remains on track to initiate the ALTITUDE-AD placebo-controlled Phase 2 trial of sabirnetug in the first half of 2024. Based on safety, target engagement and biomarker data from the INTERCEPT-AD trial, Acumen has determined sabirnetug doses of 35 mg/kg Q4W and 50 mg/kg Q4W in ALTITUDE-AD. This study will also evaluate long-term changes in clinical cognitive outcomes, biomarkers, and safety over 18 months.

Acumen also plans to initiate a Phase 1 bioavailability study to support a subcutaneous dosing option of sabirnetug in mid-2024, as announced in

November 2023.

**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 an early and persistent 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), and Acumen's preparations with respect to its plans to initiate a Phase 2 study. 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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