Acumen Pharmaceuticals Presents in vitro Human Neuron Model for Evaluating Binding of Amyloid Beta Oligomers in Alzheimer's Disease

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- *Data describe induced pluripotent stem cell (iPSC)-derived excitatory neurons as a human model for assessing selectivity of drug binding to soluble amyloid beta oligomers in Alzheimer's disease*
- *Results provide evidence that oligomer size may influence neuronal binding and detection, and substantiate the importance of oligomer preparation and antibody selection in assay results*
- *Poster presented at AD/PD 2023, the International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders*

CHARLOTTESVILLE, Va. and CARMEL, Ind., March 28, 2023 (GLOBE NEWSWIRE) -- Acumen Pharmaceuticals, Inc. (NASDAQ: ABOS) ("Acumen" or the "Company"), a clinical-stage biopharmaceutical company developing a novel therapeutic that targets toxic globular soluble amyloid beta oligomers (sAβOs) for the treatment of Alzheimer's disease (AD), has demonstrated the utility of a human *in vitro* model of 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. This research will be presented in a poster at the International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders (AD/PD), held in-person in Gothenburg, Sweden, and virtually March 28 – April 1, 2023.

There is considerable scientific evidence that supports the role of toxic forms of soluble aggregates of Aβ, such as oligomers and protofibrils, in the pathogenesis of AD. Soluble AβOs have been found to bind at synapses, which leads to altered neuronal function, and can initiate and perpetuate the process of neurodegeneration. However, soluble AβOs exist in many forms – including globular and linear conformations, a wide range of size distributions, and diverse epitope displays – and it remains unclear which of these species are most relevant to AD pathogenesis. Soluble AβOs have been challenging to model in the laboratory even though they have been identified in the cerebrospinal fluid (CSF) of AD patients; their concentrations are low in CSF, and an understanding of their diversity, especially with regard to molecular weights in the human brain, needs additional refinement.

Utilizing human iPSC-derived excitatory neurons as a model, a panel of Aβ detection antibodies, and a panel of globular sAβOs plus monomers, the current study found that sAβ size may influence synaptic binding. Regardless of sAβ preparation or detection antibody, low-molecular weight sAβ species (monomers-trimers) demonstrated the lowest levels of detectable synaptic binding, compared with those of mid- and high-molecular weight (> 150 kDa).

This research complements Acumen's ongoing clinical development of ACU193, a humanized monoclonal antibody candidate that selectively targets toxic globular sAβOs. Acumen recently completed patient enrollment in INTERCEPT-AD, 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 AD. The Company plans to initiate a Phase 2 trial of ACU193 with the potential to expand into a Phase 3 trial.

"We believe that these research efforts contribute to the development of next-generation therapies with higher selectivity for toxic soluble amyloid species that are most relevant to Alzheimer's pathogenesis," said Erika Cline, Ph.D., lead author and Manager of Bioanalytical Methods at Acumen Pharmaceuticals. "Studies assessing how different soluble AβO species bind to synapses are important for identifying AβO preparations that will help bridge the understanding of how AβO-targeting antibodies behave in biochemical assays and *in vivo*. Furthermore, models utilizing human neurons have the potential to accelerate the identification of prime targets for clinical drug development. Together with Acumen's ongoing Phase 1 clinical trial of ACU193, we aim to provide proof of mechanism data that we believe will shed additional light on the role of toxic oligomeric species in Alzheimer's disease."

The poster, "Binding of Soluble Amyloid Beta Oligomer Species to Human iPSC-Derived Excitatory Neurons Assessed Using a Panel of Aβ Antibodies" (P0007 / #1726), will become available on Tuesday, March 28, 2023 and will be presented throughout the conference beginning on March 29.

About ACU193

ACU193 is a humanized monoclonal antibody (mAb) discovered and developed based on its selectivity for soluble amyloid beta oligomers (sAβOs), which Acumen believes are more toxic forms of Aβ, relative to Aβ monomers and amyloid plaques. Globular sAβOs have been observed to be potent neurotoxins that bind to neurons, inhibit synaptic function and induce neurodegeneration. By selectively targeting toxic globular sAβOs, ACU193 aims to directly address a growing body of evidence indicating that sAβOs 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 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 globular soluble amyloid beta oligomers (sAβOs) 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 globular 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 the therapeutic potential of Acumen's product candidate, ACU193, and amyloid beta oligomers. 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 Annual Report on Form 10-K for the fiscal year ended December 31, 2022, and future 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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