



# **Q3 2023 Financial Results & Business Update**

November 13, 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, and 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 into the second half of 2026, the therapeutic potential of Acumen's product candidate, ACU193, including against other antibodies, the anticipated timeline for initiating a Phase 2 clinical trial of ACU193 and a Phase 1 trial to support a subcutaneous dosing option of ACU 193, and the expected use of proceeds from a credit facility. 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.

# Agenda

- **Q3 2023 Business Update**

Dan O'Connell, Chief Executive Officer

- **ACU193 Clinical Development Update**

Dr. Eric Siemers, Chief Medical Officer

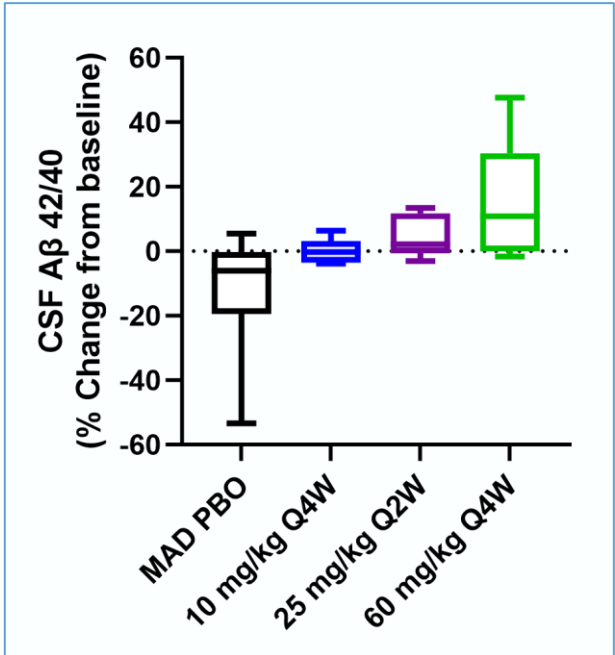
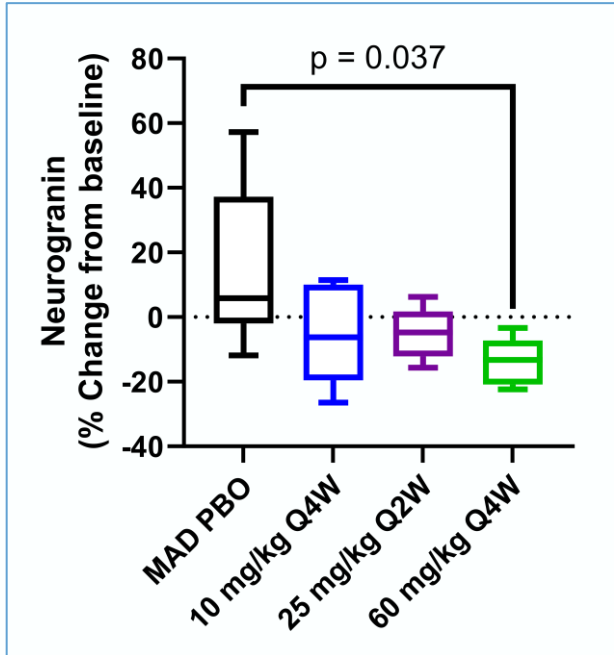
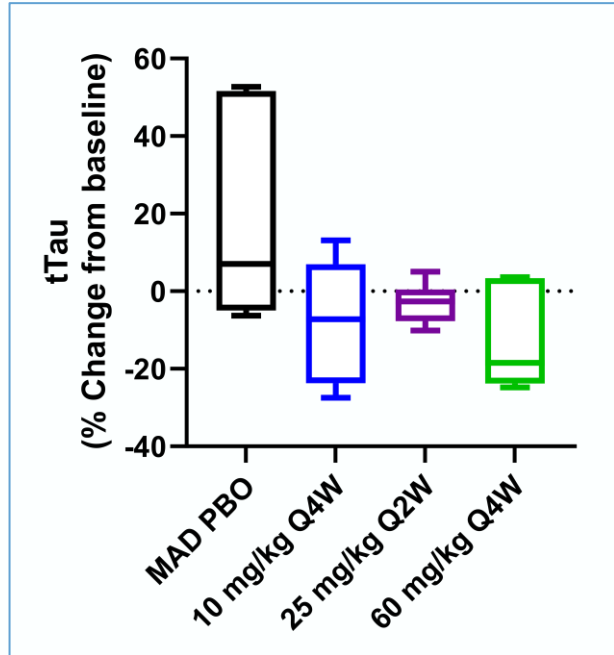
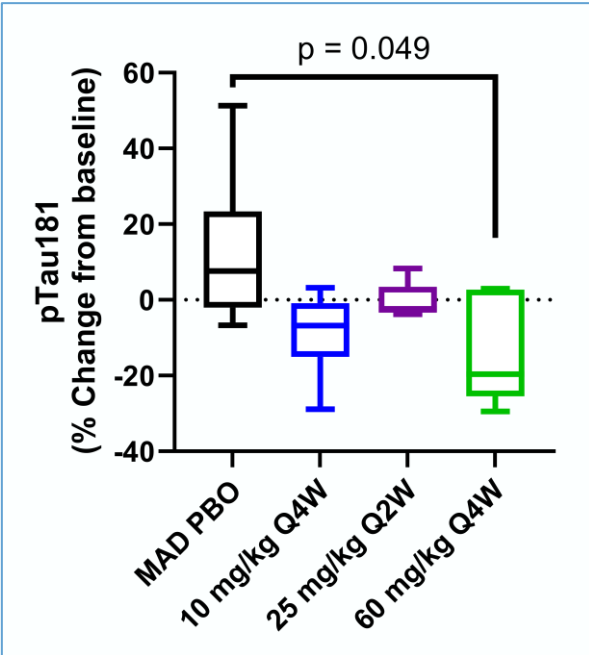
- **Q3 2023 Financial Results**

Matt Zuga, Chief Business Officer & Chief Financial Officer

# Recent Significant Operational and Strategic Progress in ACU193 Clinical Development Program

- Today, presented positive data from CSF biomarkers that is highly supportive of ACU193's downstream pharmacological effects in the brain
  - Observed dose dependent trend in the multiple ascending dose cohorts on CSF levels of p-tau181, total tau, neurogranin and A $\beta$  42/40 ratio
  - P-tau181 (p=0.049) and neurogranin (p=0.037) showed statistically significant improvement at 60 mg/kg Q4W as compared to the placebo group after three administrations of ACU193
  - Nominally significant correlation between target engagement of A $\beta$ O<sub>s</sub> and change in neurogranin across all doses
  - Trend between target engagement of A $\beta$ O<sub>s</sub> and change in p-tau181 across all doses
- Presented deeper dive into our Phase 1 results at the Clinical Trials for Alzheimer's Disease meeting (CTAD) in October that was well-received by the medical community
  - Announced Phase 2 doses in the two treatment arms versus placebo: 50 mg/kg Q4W and 35 mg/kg Q4W
- Met with the FDA in an End of Phase 2 meeting to discuss our next clinical study, ACU193-201 (ALTITUDE-AD)
  - Expect to initiate ALTITUDE-AD in 1H 2024
- Announced license and collaboration agreement with Halozyme
  - Plan to initiate a Phase 1 study to compare the pharmacokinetics of a subcutaneous form of ACU193 to the IV form in mid-2024
- Announced a credit facility for up to \$50 million with K2 HealthVentures
  - Provides additional capital to pursue the development of a subcutaneous administration dosage form of ACU193 and for general corporate purposes

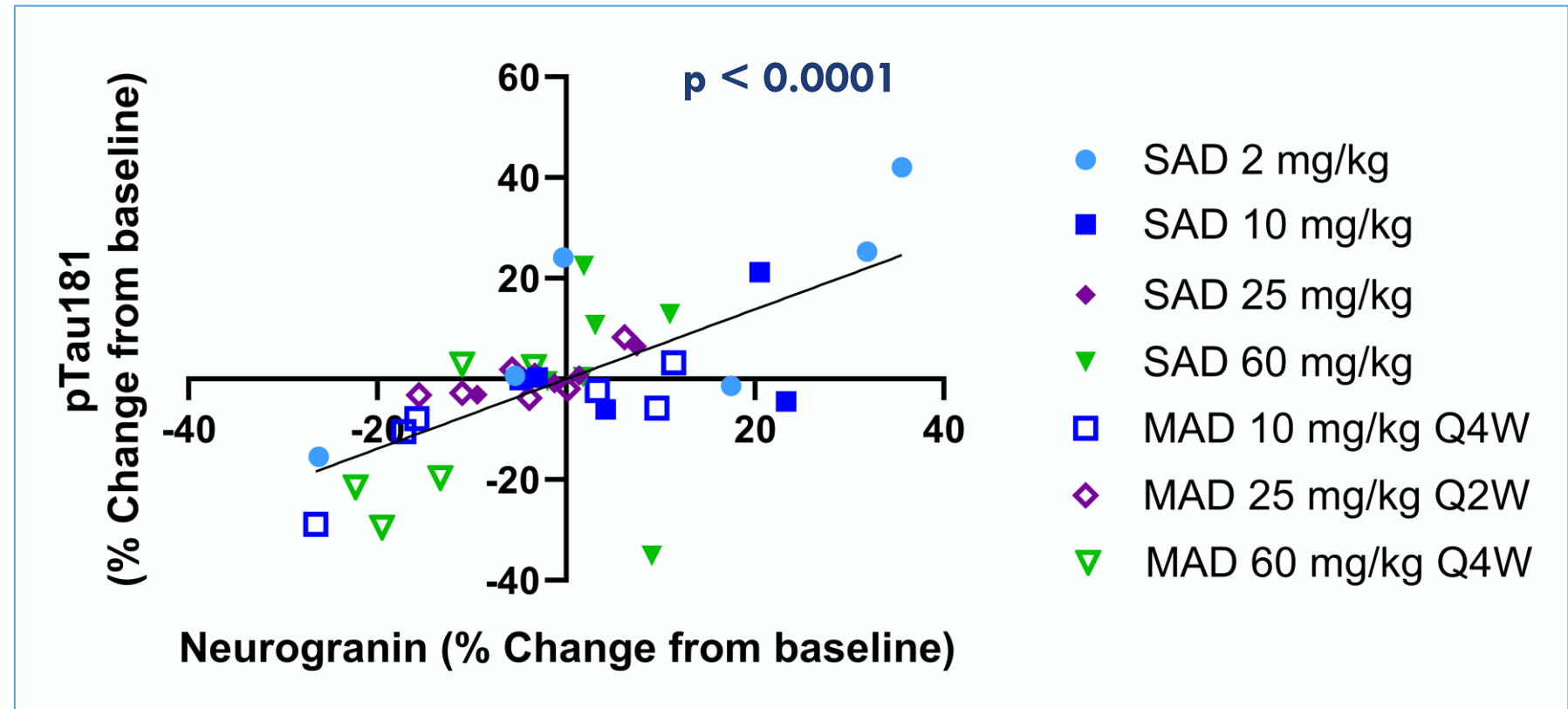
# INTERCEPT-AD: Consistent Drug Effects Observed in the Multiple Ascending Dose Cohorts in the INTERCEPT-AD Trial for CSF Phospho-tau181, Total Tau, Neurogranin and the A $\beta$ 42/40 Ratio



CSF biomarker changes reinforce downstream pharmacology of ACU193 in addition to the previously presented target engagement and amyloid PET data

# INTERCEPT-AD: Significant Correlation Between Change in CSF Neurogranin and pTau181

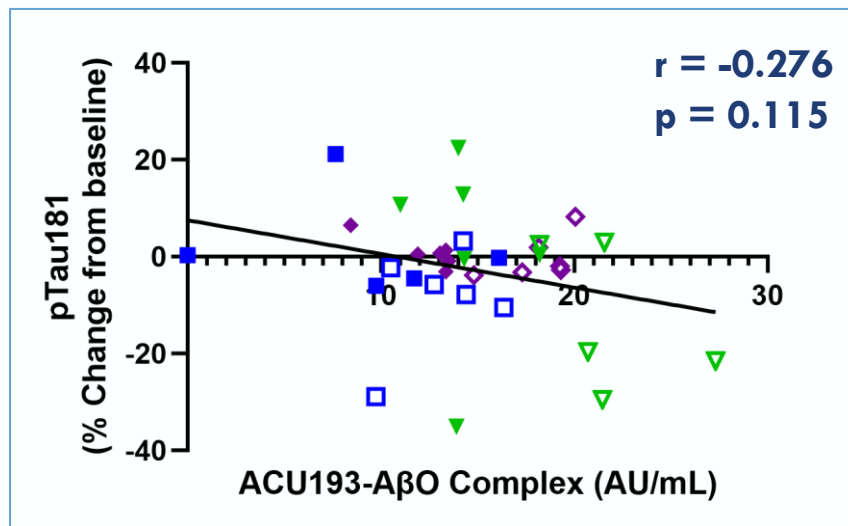
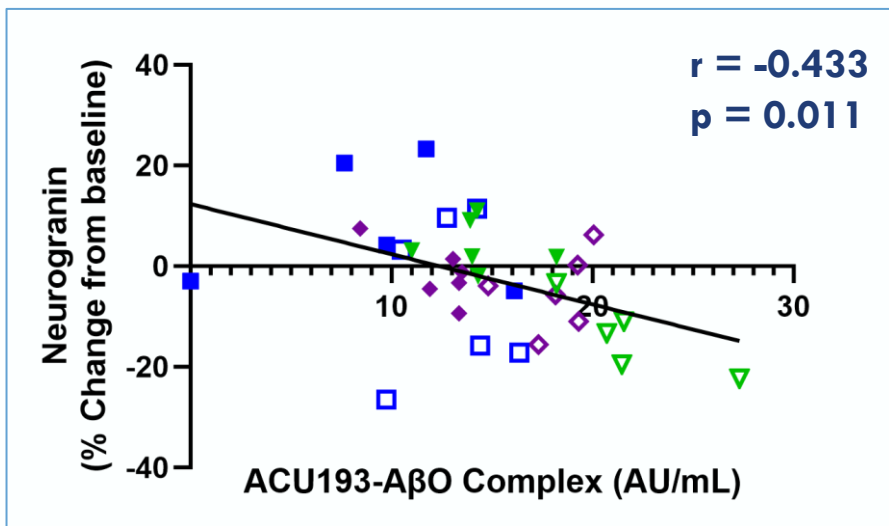
- Researchers in the field, such as Agnello et al and others,<sup>1,2,3</sup> have found correlations between CSF neurogranin and pTau.
- This suggests a biological link between these two biomarkers and provides further confidence in our biomarker observations with ACU193.



1. Agnello L, et al. Neurogranin as a Reliable Biomarker for Synaptic Dysfunction in Alzheimer's Disease. *e. Diagnostics* 2021, 11, 2339. DOI: 10.3390/diagnostics11122339; 2. Thorsell A, Bjerke M, Gobom J, et al. Neurogranin in cerebrospinal fluid as a marker of synaptic degeneration in Alzheimer's disease. *Brain Res* 2010;1362:13-22. DOI: 10.1016/j.brainres.2010.09.073; 3. Hellwig K, Kvaratsberg H, Portelius E, et al. Neurogranin and YKL-40: independent markers of synaptic degeneration and neuroinflammation in Alzheimer's disease. *Alzheimers Res Ther* 2015;7:74. DOI: 10.1186/s13195-015-0161-y.

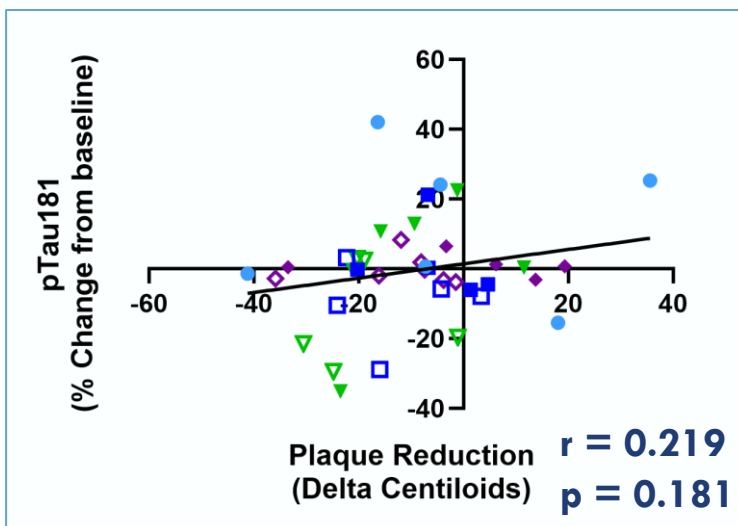
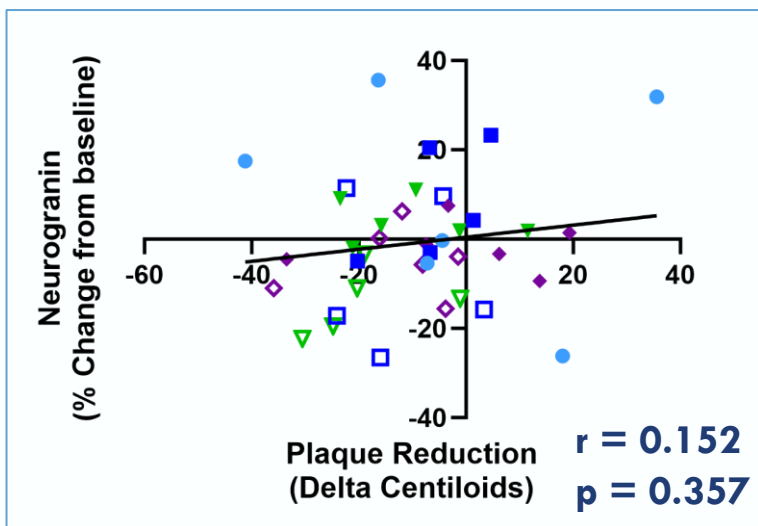
# Changes in CSF Neurogranin and pTau181 are More Closely Related to Target Engagement (Binding to A $\beta$ Oligomers) Than Plaque Reduction

Target Engagement



- SAD 2 mg/kg
- SAD 10 mg/kg
- ◆ SAD 25 mg/kg
- ▼ SAD 60 mg/kg
- MAD 10 mg/kg Q4W
- ◇ MAD 25 mg/kg Q2W
- ▽ MAD 60 mg/kg Q4W

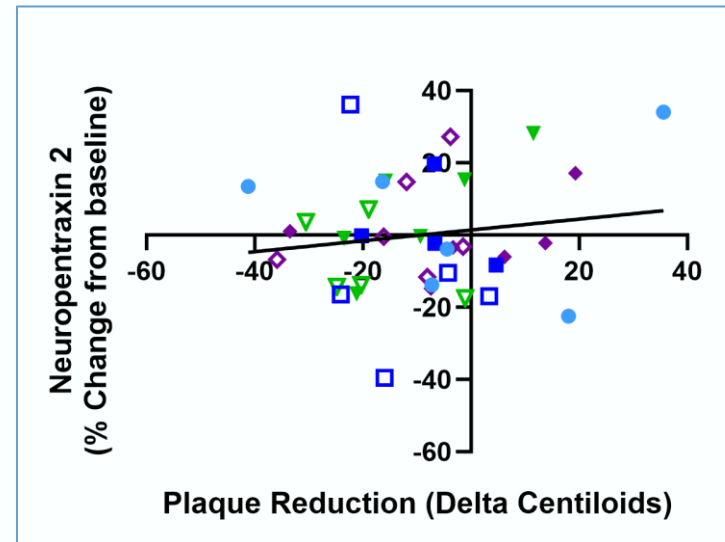
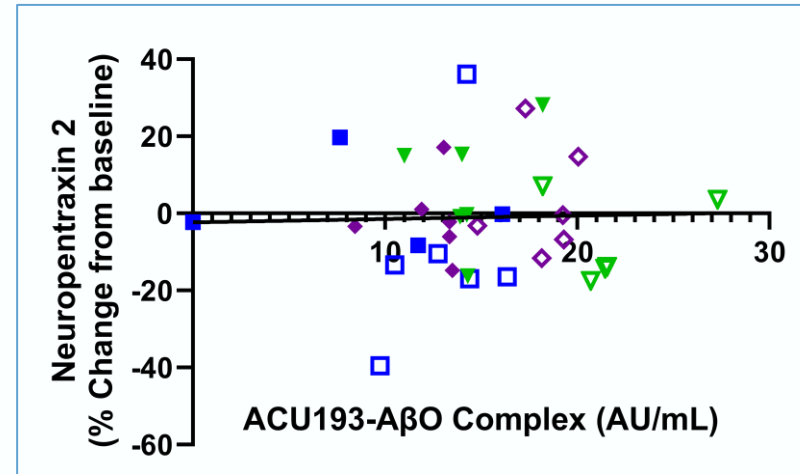
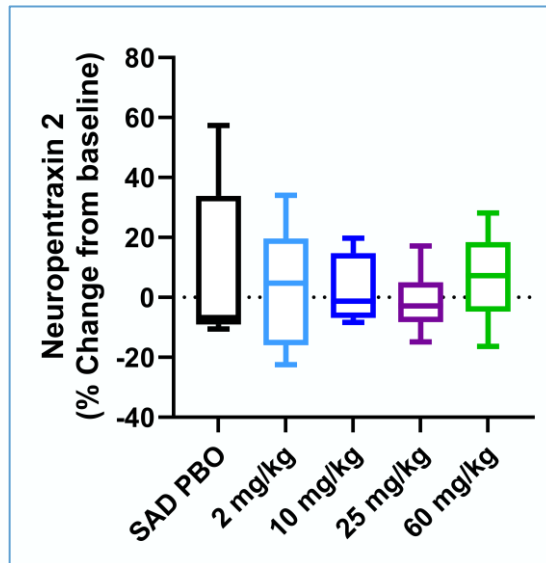
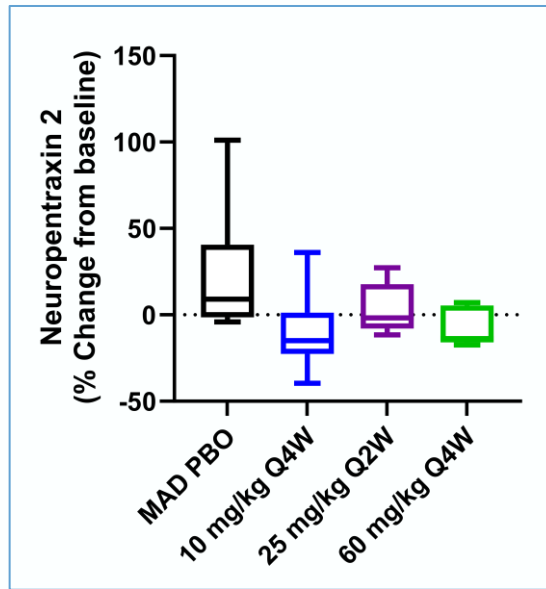
Plaque Reduction



- These data are consistent with the MOA and target engagement of ACU193
- Provide evidence beyond target engagement of downstream pharmacological effects of ACU193

# No Significant Drug Effect Observed on CSF Levels of Neuropentraxin 2

Additional study will be required to understand more about this relatively new biomarker



- SAD 2 mg/kg
- SAD 10 mg/kg
- ◆ SAD 25 mg/kg
- ▼ SAD 60 mg/kg
- MAD 10 mg/kg Q4W
- ◇ MAD 25 mg/kg Q2W
- ▽ MAD 60 mg/kg Q4W



# Significant Milestones Achieved in 2023

MILESTONES	STATUS/ EXPECTED TIMING
Proof-of-mechanism topline results	✓
Biomarker results from Phase 1 study	✓
Anticipated interaction with FDA	✓
Anticipated initiation of ALTITUDE-AD trial	1H 2024
Anticipated initiation of Phase 1 subcutaneous trial	Mid-2024

**~\$283M**  
Cash, cash equivalents and marketable securities as of Sept 30, 2023

**Up to \$50M**  
Debt financing secured from K2 HealthVentures in November 2023

We believe that Acumen has the expertise and resources to advance ACU193 as a potential best-in-class antibody product for early AD