

ALTITUDE-AD: Use of a pTau217 Assay as a Marker of Amyloid Burden for Screening Participants in an Ongoing Phase 2 Study of Sabirnetug in Early Alzheimer's Disease

Todd Feaster, PsyD

Acumen Pharmaceuticals

## **Disclosure**

• Dr. Feaster is an employee shareholder at Acumen Pharmaceuticals

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## Sabirnetug in Early AD Clinical Trials

#### Sabirnetug

- Humanized monoclonal IgG2 antibody
- Highly selective for amyloid beta oligomers (AβOs)
- Clinical effect on synaptic biomarkers consistent with proposed mechanism of targeting AβOs<sup>1</sup>

#### INTERCEPT-AD Phase 1 clinical trial (completed)

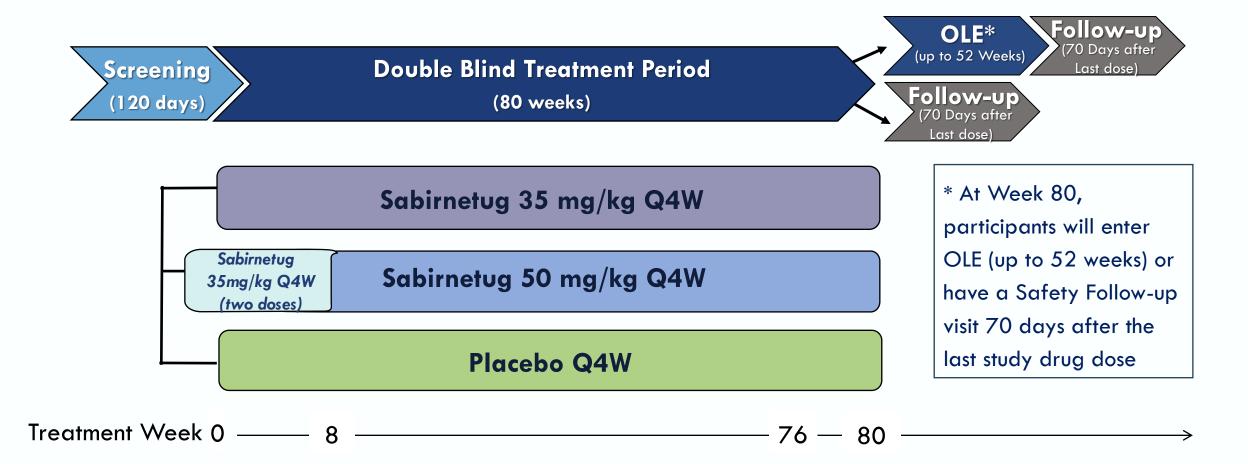
- US study in MCI or mild AD participants
- SAD and MAD study design
- Objectives: safety and pharmacokinetics

#### ALTITUDE-AD Phase 2 clinical trial (ongoing)

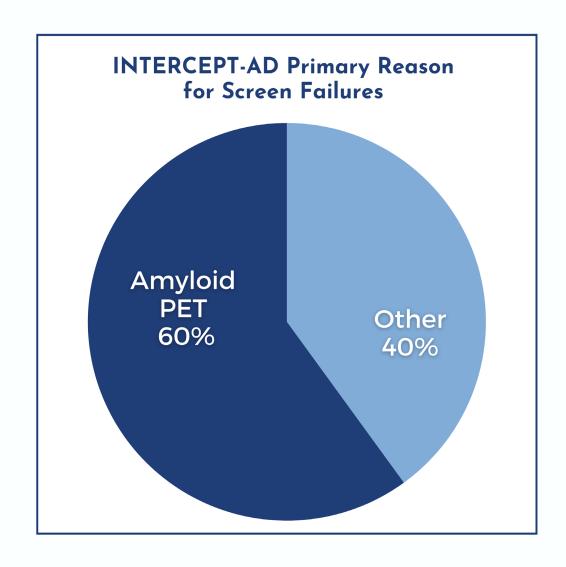
- Global study in MCI or mild AD participants
  - o US, Canada, UK, Germany and Spain
- Primary objective: evaluate efficacy in slowing cognitive and functional decline
  - o iADRS change from baseline to Week 80

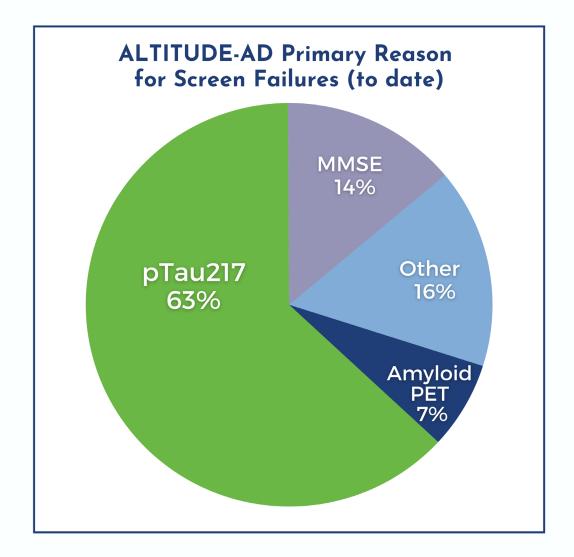
#### **ALTITUDE-AD: Phase 2 Study Design of Sabirnetug for Early AD**

540 participants randomized 1:1:1



#### AD Trials Often Have High Percentages of Negative PET During Screening

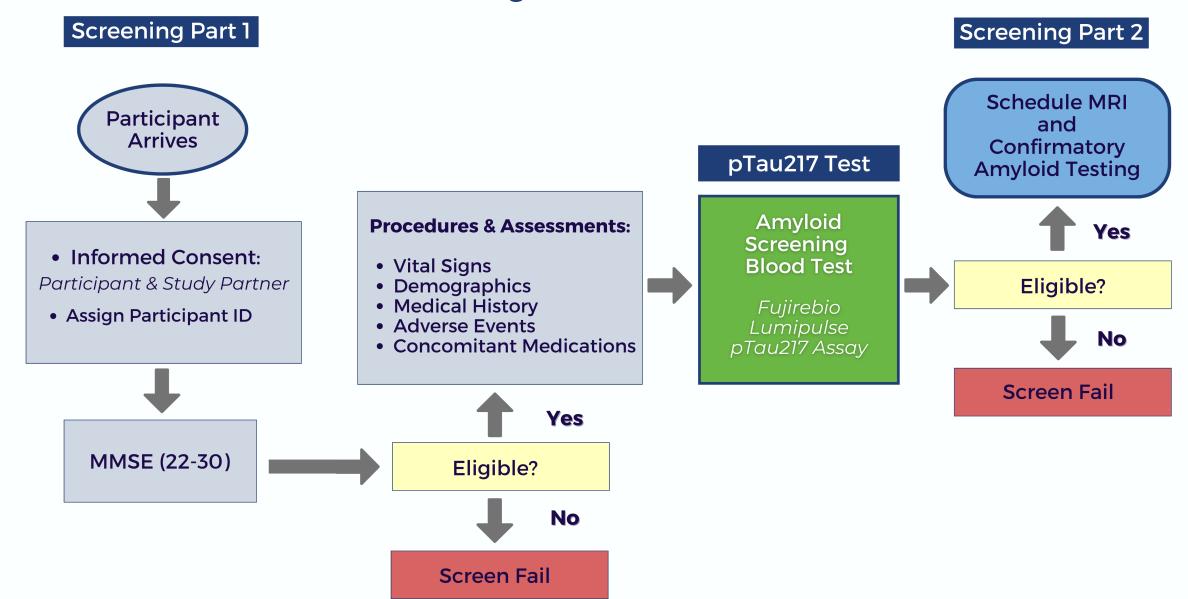




# In ALTITUDE-AD, We Aim to Reduce PET/LP Burden by Screening for pTau217

- Plasma concentrations of pTau217 are highly predictive for AD1
  - pTau217 is being used as an enrichment strategy to help identify potential participants with a high likelihood of meeting amyloid inclusion criteria on PET or CSF
  - The assay is not being used as a diagnostic
- The Fujirebio plasma pTau217 assay is a Lumipulse platform-based research use only assay that has been analytically and clinically validated as a Lab-Developed Test consistent with CLIA regulations
- For screening, we selected the pTau217 cut-point of 0.15 pg/mL because of its the high sensitivity (0.992) in this assay

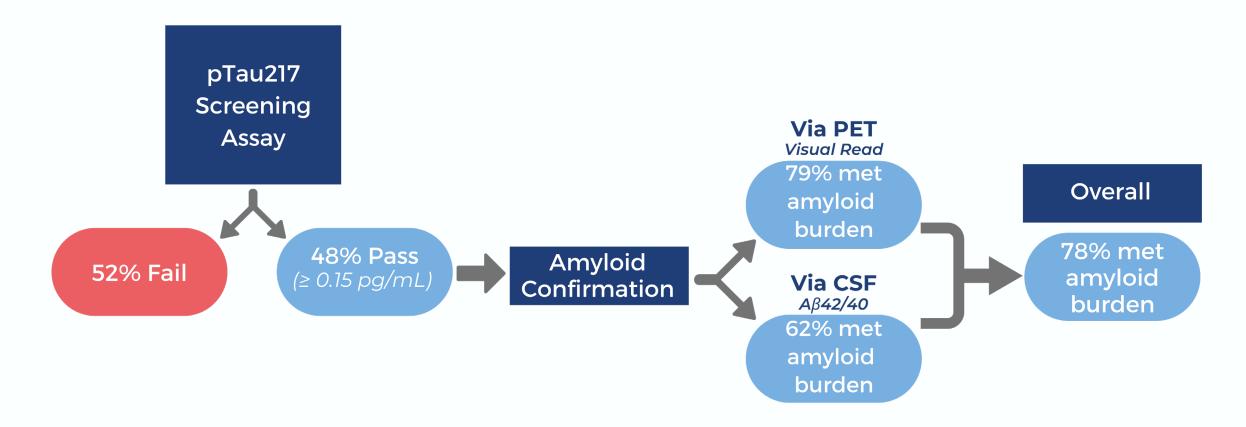
#### **ALTITUDE-AD: Two-Part Screening Process**



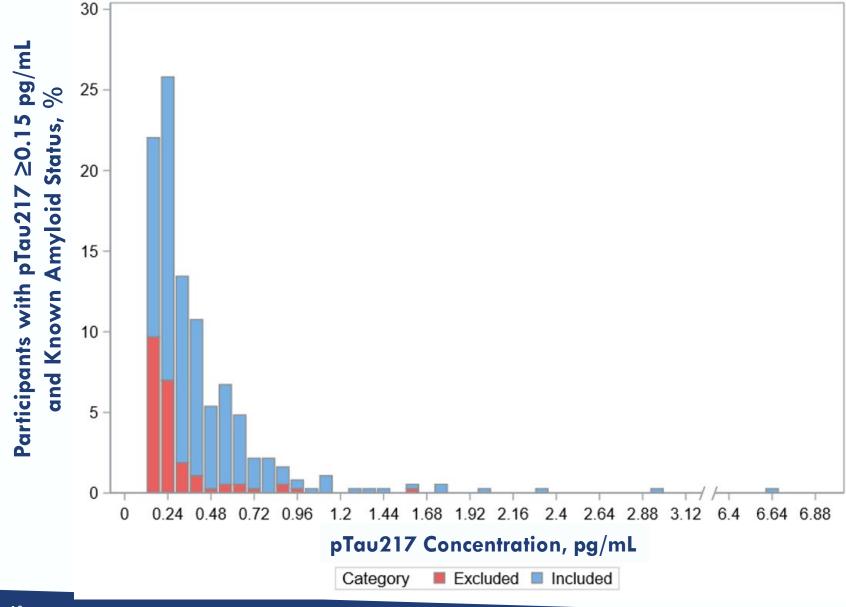
## pTau217 Screening Results

#### North America (US and Canada) Study Data

• UK and EU sites are not using pTau217 as a screening enrichment strategy (not CE marked)



# Amyloid Status for Participants With pTau217 ≥0.15 pg/mL



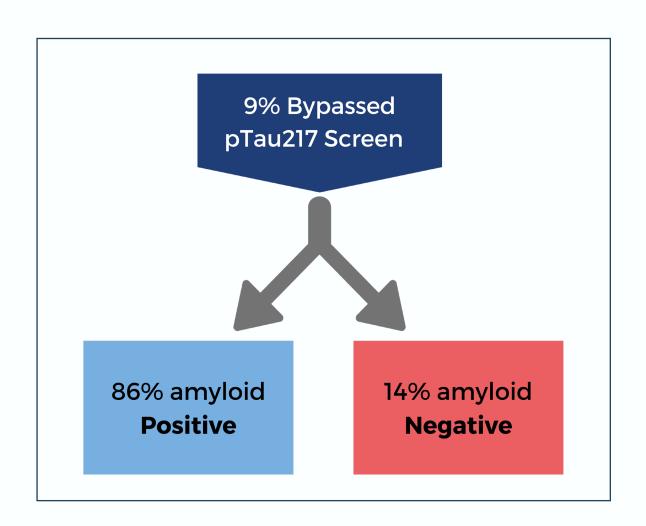
- of participants included or excluded from the study based on amyloid status after a positive pTau217 result
- Bin width represents a pTau217 range of 0.08 pg/mL

## History of Amyloid Can be Used to Bypass Screening pTau217

 May use outside evidence of amyloid positivity in place of pTau217

• Examples include historical PET or CSF  $A\beta_{42/40}$  ratio and must be approved by medical monitor

 Upon approval, the participant will skip the blood draw for pTau217 and move directly to Screening 2 Amyloid confirmation (PET or CSF)



# Summary

#### The pTau217 enrichment strategy is performing as intended

- Improving amyloid positive screen rates
  - 78% of the participants who proceed to PET or CSF are enriched for meeting amyloid-based inclusion criteria
  - Significant improvement from INTERCEPT-AD where 40% of participants were amyloid positive via PET

- Reducing burden and fostering sustainability
  - More than half of potential study participants excluded because of a plasma pTau217 test result <0.15 pg/mL</li>
    - Reduced burden for patients, clinical trial investigators/staff, and sponsor
    - Participants were spared LP and unnecessary radiation exposure with an amyloid PET
    - Savings in time and resources

## **Acknowledgments**

• The authors are grateful to the study participants and their study partners, as well as the study investigators and staff, all of whom make the ALTITUDE-AD clinical trial possible

# Thank you!