ALTITUDE-AD: Use of a Validated Plasma pTau217 Assay to Screen Potential Participants in an Ongoing Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Sabirnetug for Early Symptomatic Alzheimer's Disease

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Disclosure

- Dr. Siemers is an employee and shareholder at Acumen Pharmaceuticals

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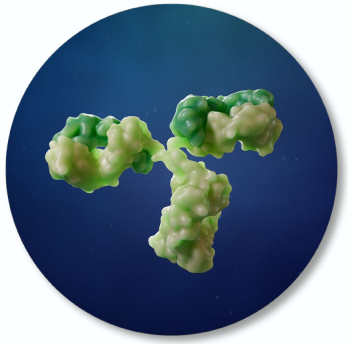
Sabirnetug (ACU193) Overview



- **Sabirnetug**
  - Humanized monoclonal IgG2 antibody
  - Highly selective for globular amyloid beta oligomers (AβOs)
  - Clinical effect on synaptic biomarkers consistent with proposed mechanism of targeting AβOs[2]

- **INTERCEPT-AD Phase 1 clinical trial (NCT04931459, completed)[1,2]**
  - US-only study in early symptomatic AD (MCI or mild dementia with amyloid positivity based on PET)
  - SAD and MAD study design
  - Objectives: safety, pharmacokinetics, and target engagement

INTERCEPT-AD STUDY

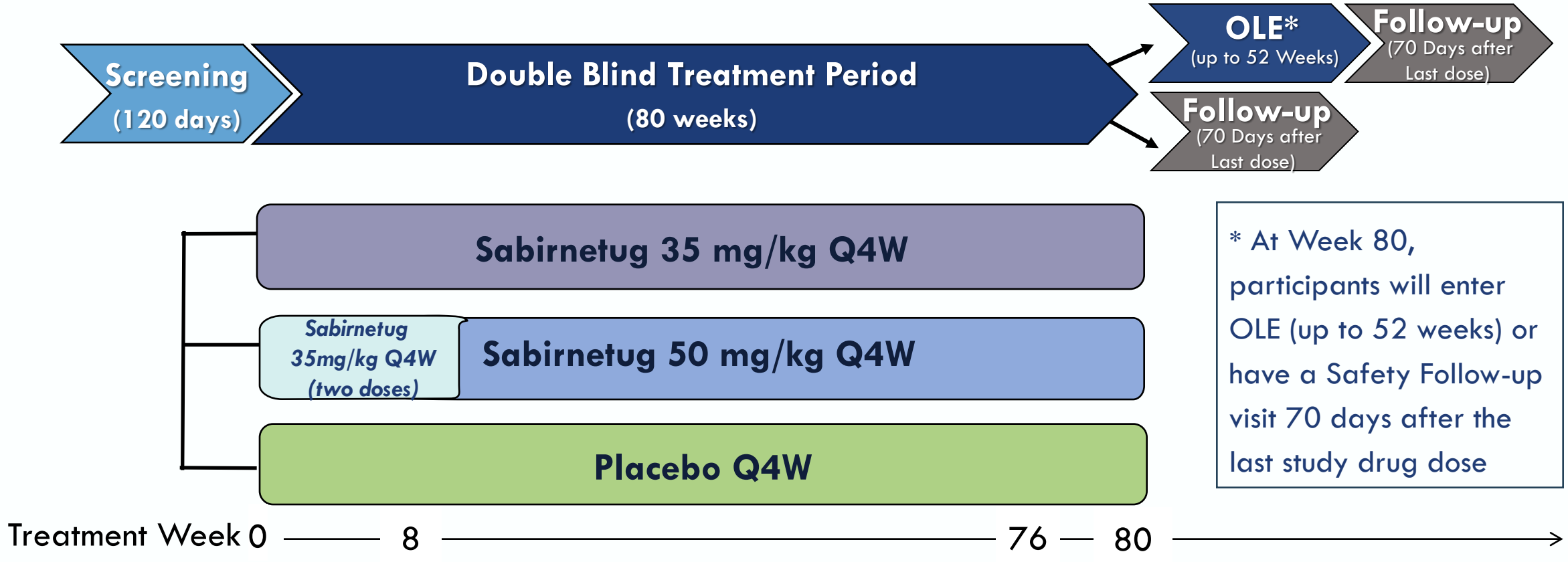
- **ALTITUDE-AD Phase 2 clinical trial (NCT06335173, ongoing)**
  - Global study in MCI or mild AD participants
  - US, Canada, UK, Germany and Spain
  - MMSE: 22-30
  - CDR-GS: 0.5 or 1 and CDR Memory Box ≥0.5
  - Primary objective: evaluate efficacy in slowing cognitive and functional decline
  - iADRS change from baseline to Week 80

ALTITUDE-AD
CLINICAL RESEARCH STUDY

1. Siemers et al. (2025) JPAD 12(1):100005
2. Cline et al. (2025) JPAD 12(4):100082

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

542 participants randomized 1:1:1



* At Week 80, participants will enter OLE (up to 52 weeks) or have a Safety Follow-up visit 70 days after the last study drug dose

In ALTITUDE-AD, Screening with Plasma pTau217 was Introduced to Reduce PET/LP Burden

- Plasma concentrations of pTau217 are highly predictive for amyloid pathology[1]
  - 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 stand-alone diagnostic

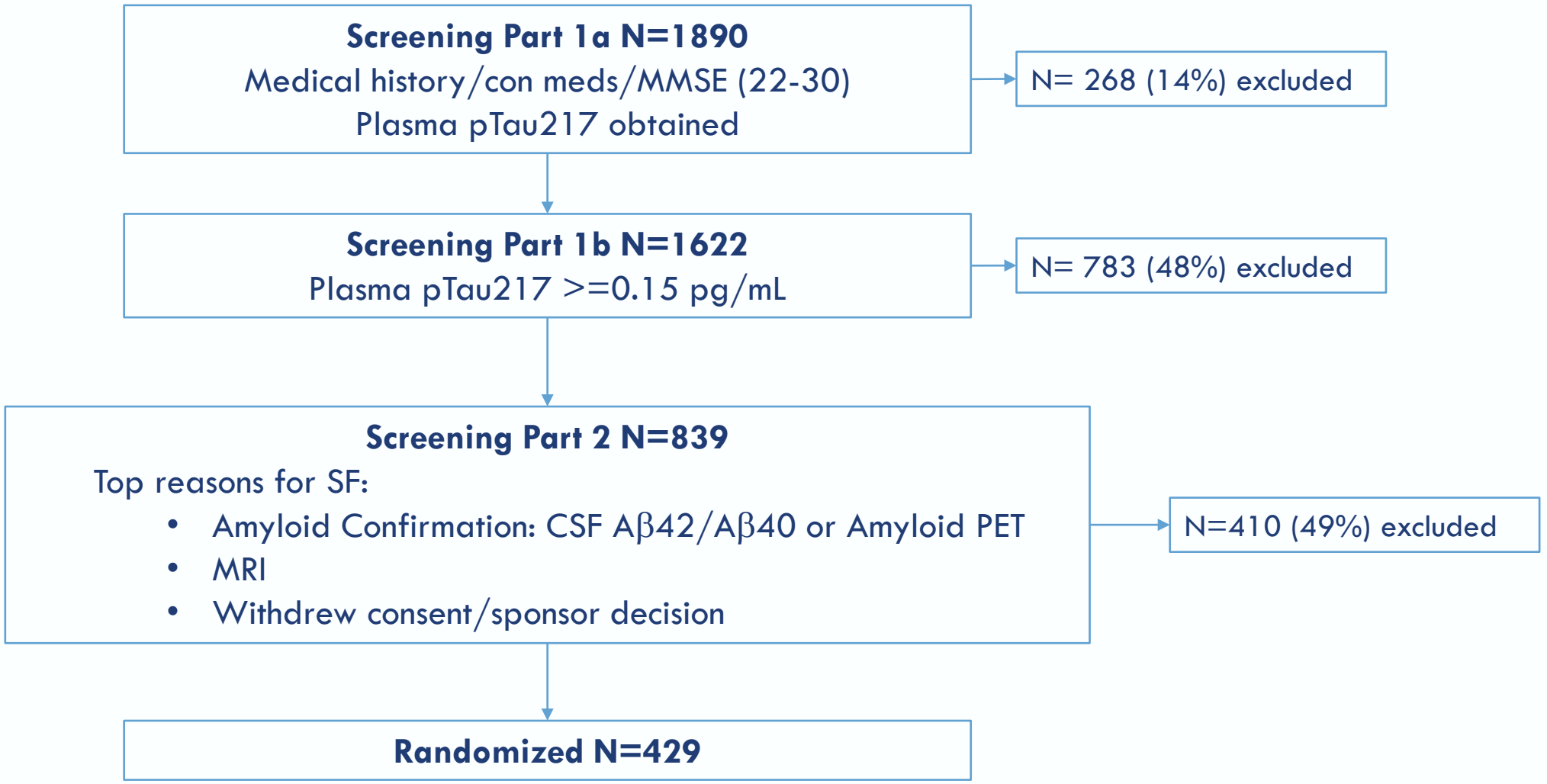
- The Fujirebio plasma pTau217 assay is a Lumipulse platform-based research use only assay that has been analytically and clinically validated as a Lab-Developed Test consistent with CLIA regulations

- Plasma pTau217 testing was not used in UK, Spain, and Germany due to lack of "CE marking" and additional hurdles related to GDPR regulations

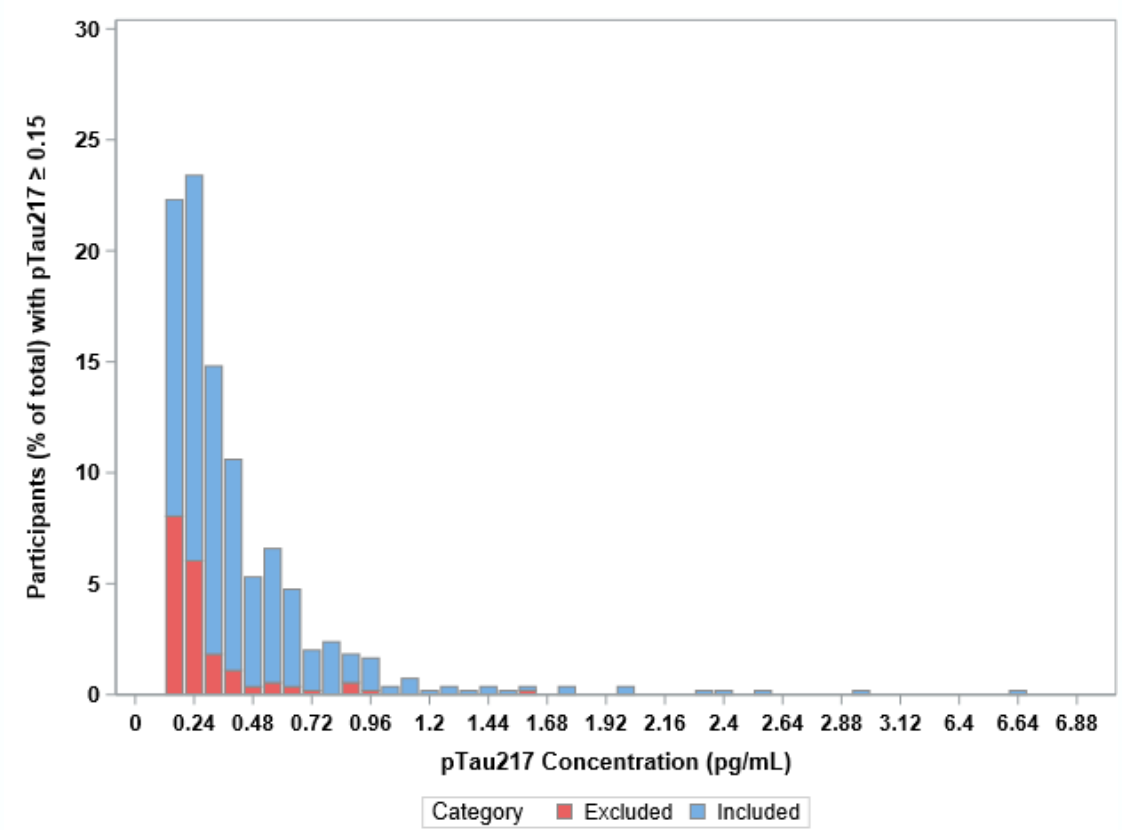
- For screening, we selected the pTau217 cut-point of 0.15 pg/mL because of its the high sensitivity (0.992) in this assay

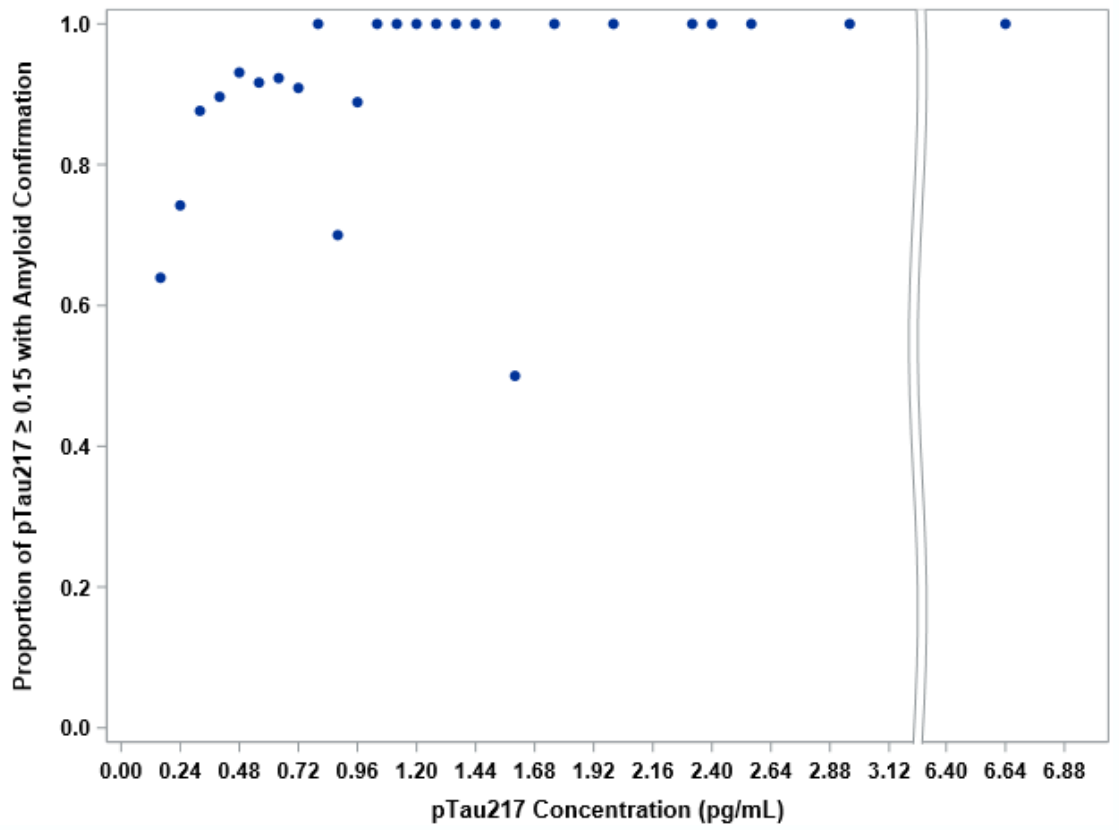
1. Ashton NJ, et al. (2024) *JAMA Neurol,* 81(3):255–263.

ALTITUDE-AD: Two-Part Screening Process
(preliminary data shown for US and Canada only)



Amyloid Status for Participants with Plasma pTau217 ≥ 0.15 pg/mL

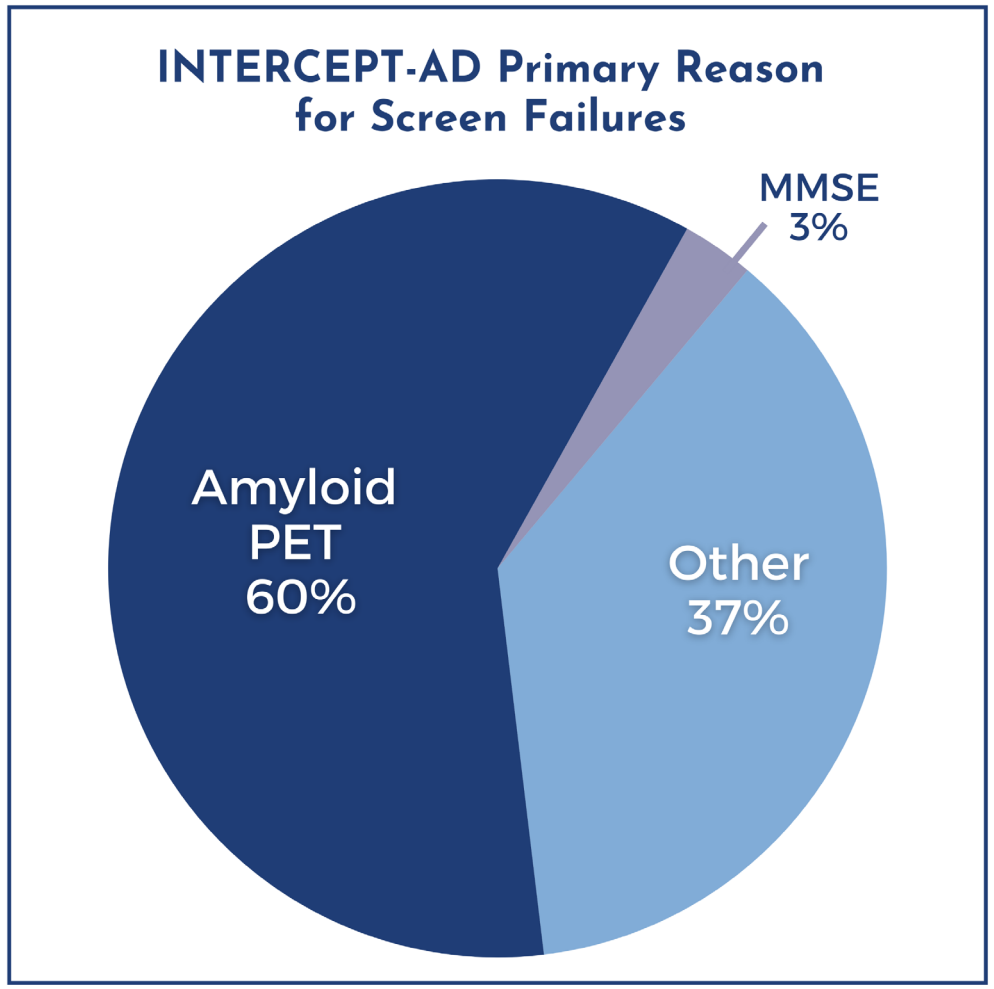




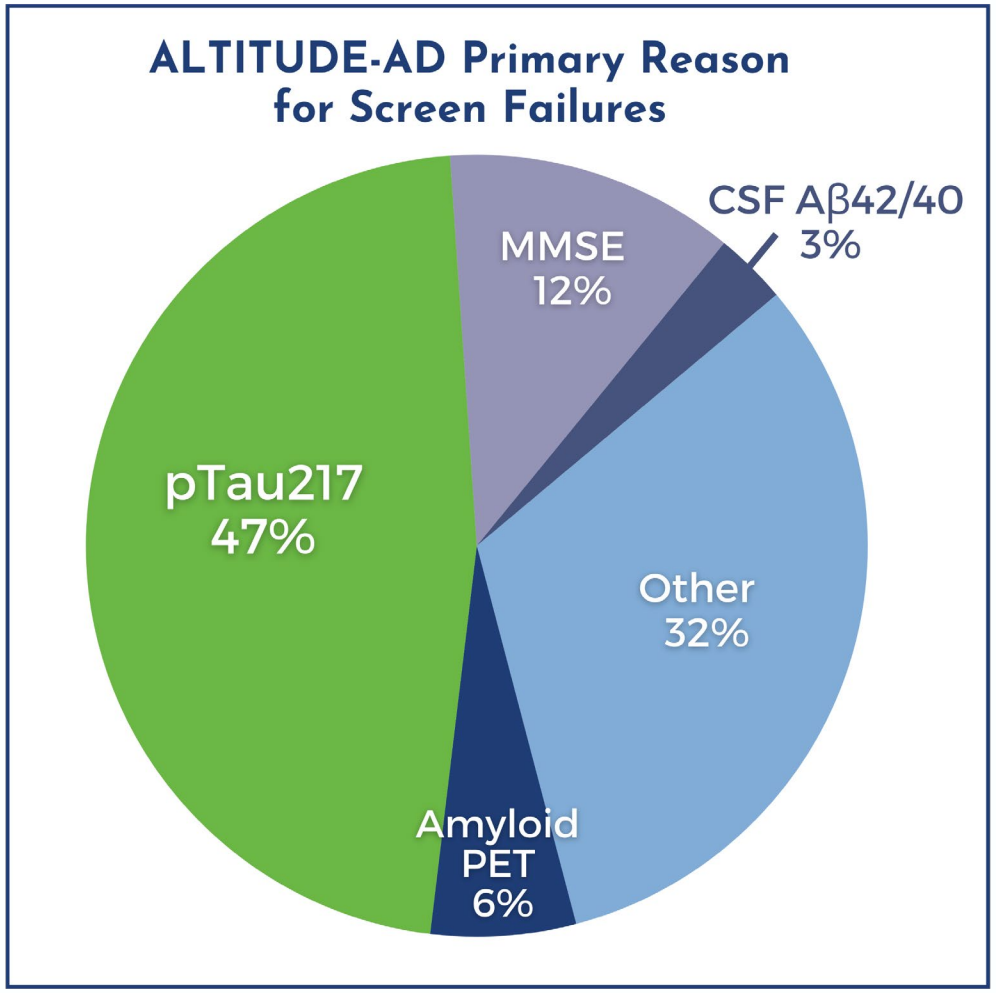
- Graph shows the percentage of participants included or excluded from the study based on amyloid status after a positive pTau217 result
- Bin width represents a pTau217 range of 0.08 pg/mL

- Graph shows the proportion of participants with positive PET or CSF after a positive pTau217 result
- Bin width represents a pTau217 range of 0.08 pg/mL

Screening with Plasma pTau217 Greatly Reduced Screen Failure due to Amyloid PET



Final US data



Preliminary global data

Summary

The pTau217 enrichment strategy performed as intended

- Improved amyloid positive screen rates
  - 81% of the participants who proceed to PET or CSF are positive for meeting amyloid-based inclusion criteria
  - Significant improvement from INTERCEPT-AD where only 40% of participants were amyloid positive using PET

- Reduced participant burden and sponsor costs
  - Almost half of potential study participants excluded because of a plasma pTau217 test result <0.15 pg/mL
    - Reduced burden for patients, clinical trial investigators/staff, and sponsor
    - Amount of radiation exposure with an amyloid PET or burden of LP was reduced
    - Savings in time and resources

Acknowledgments

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Thank you!