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 Alzheimer's Disease

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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[1]

Presentation Alert
Wed. 11:45-12:45; P12, #3-003
INTERCEPT-AD Biomarker Results: Early effect of sabirnetug treatment on synaptic biomarkers in Alzheimer's disease

- **INTERCEPT-AD Phase 1 clinical trial (completed)**
  - US study in MCI or mild AD participants
  - SAD and MAD study design
  - Objectives: safety and pharmacokinetics

INTERCEPT-AD STUDY

- **ALTITUDE-AD Phase 2 clinical trial (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

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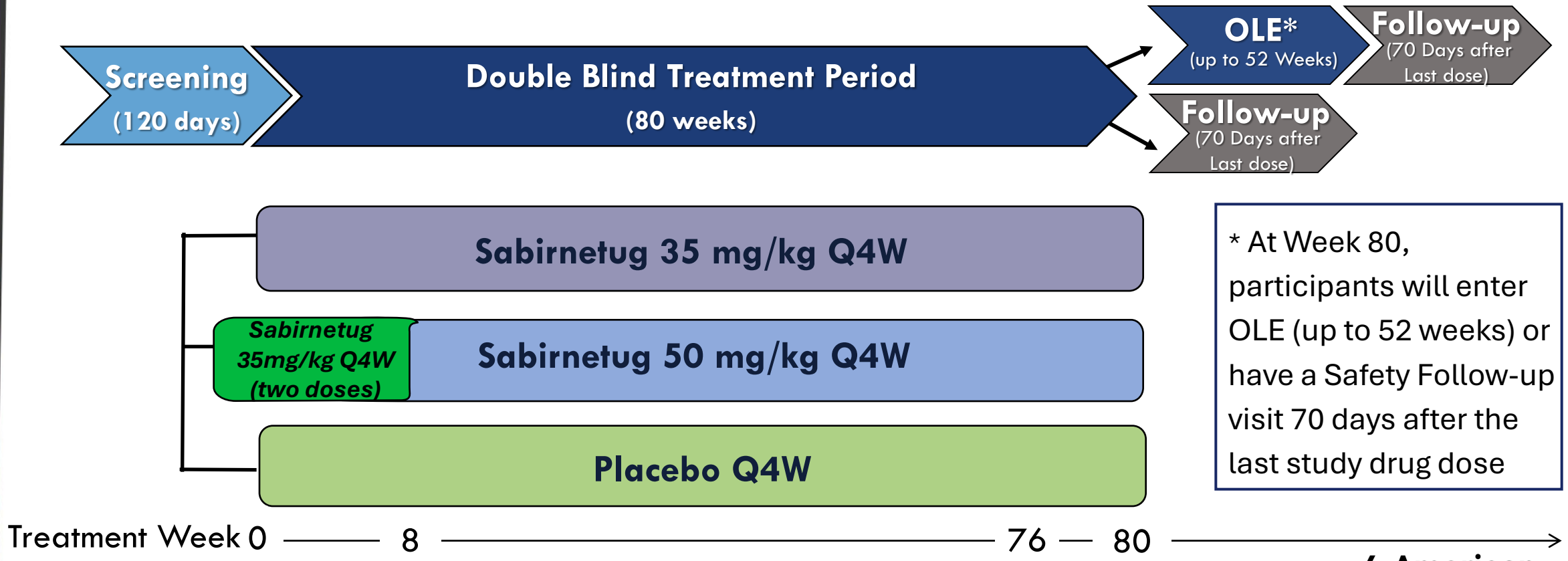
1. Cline et al. AAIC 2024

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

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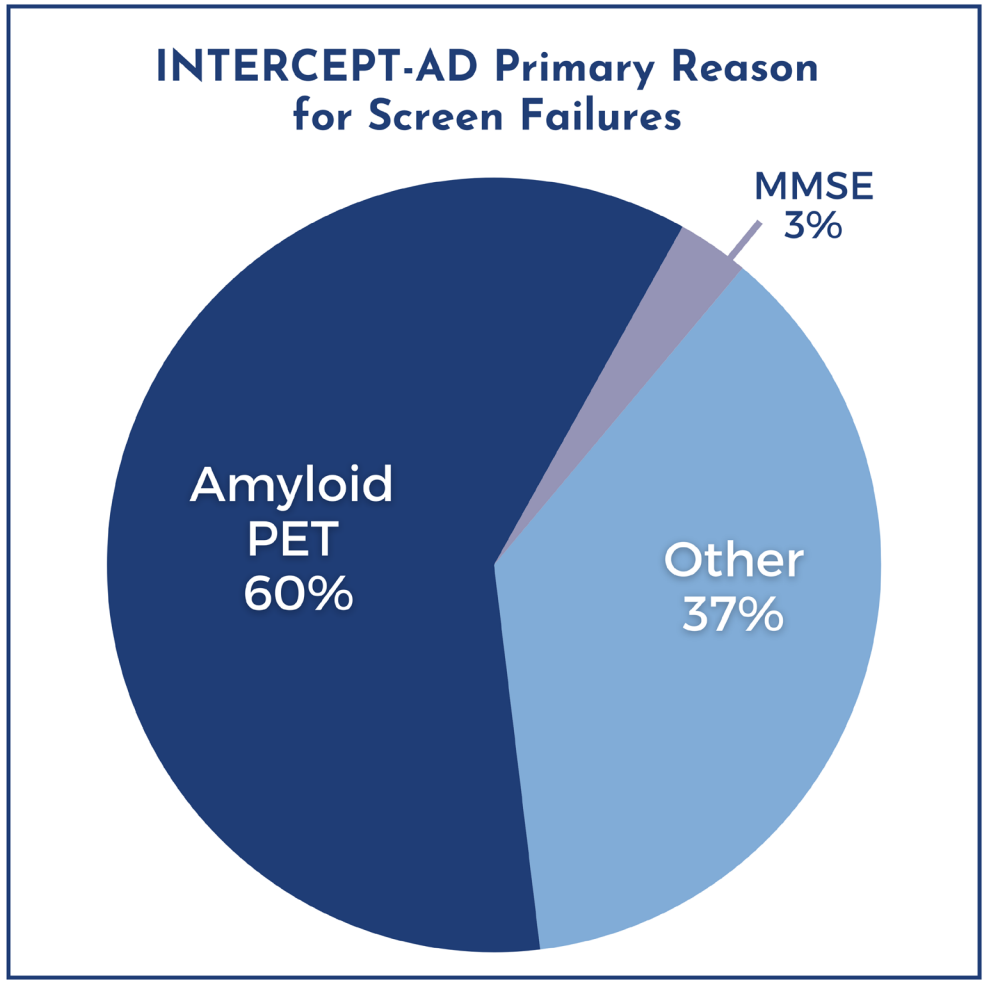
AD Trials Often Have High Percentages of Negative Amyloid PET During Screening



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

- Plasma concentrations of pTau217 are highly predictive for AD[1]
  - pTau217 is being used in North America 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 performed in the United States 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 the high sensitivity (0.992) using this cut-point (unpublished data)

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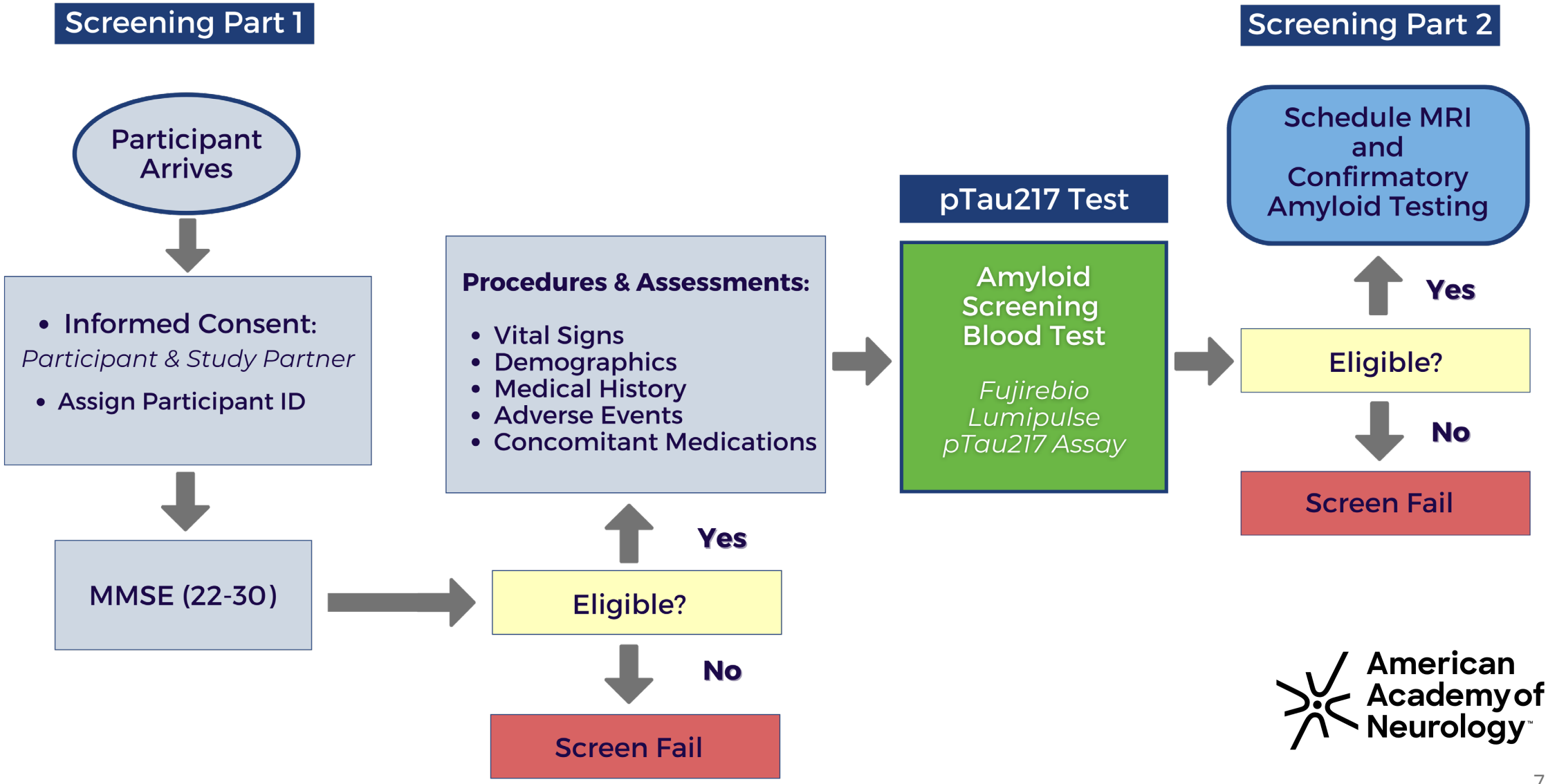
[1]Ashton NJ, et al. (2024) *JAMA Neurol,* 81(3):255–263.

ALTITUDE-AD: Two-Part Screening Process



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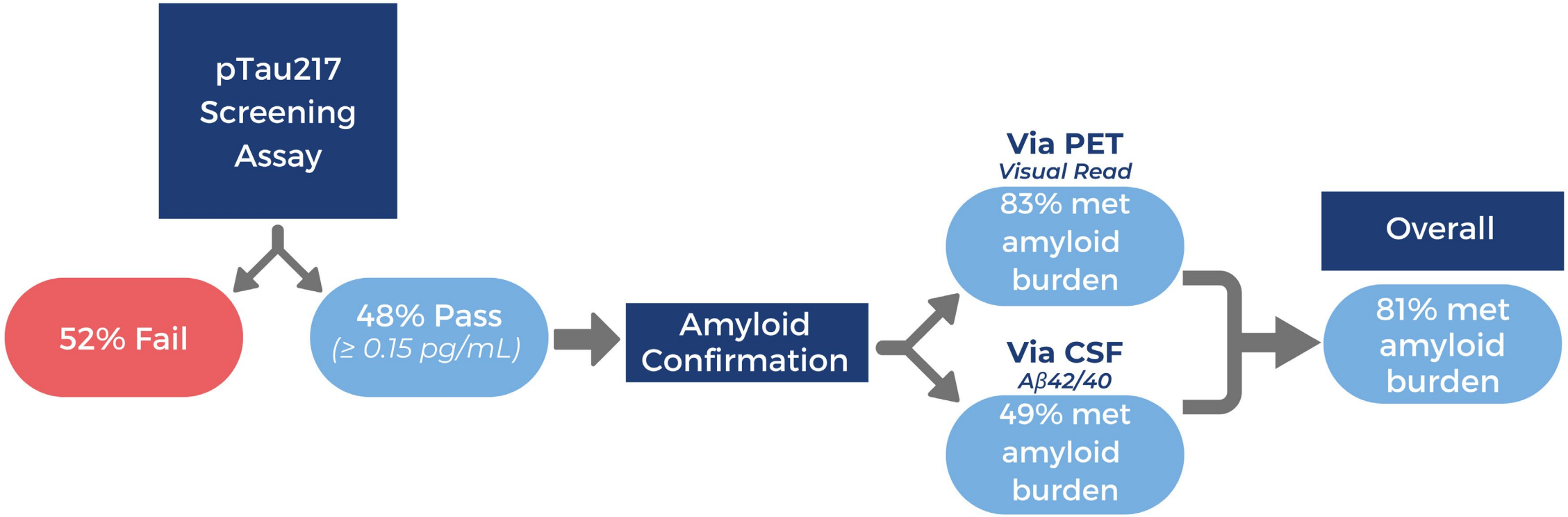
pTau217 Screening Results

North America (US and Canada) Study Data

- UK and EU sites did not use pTau217 as a screening enrichment strategy



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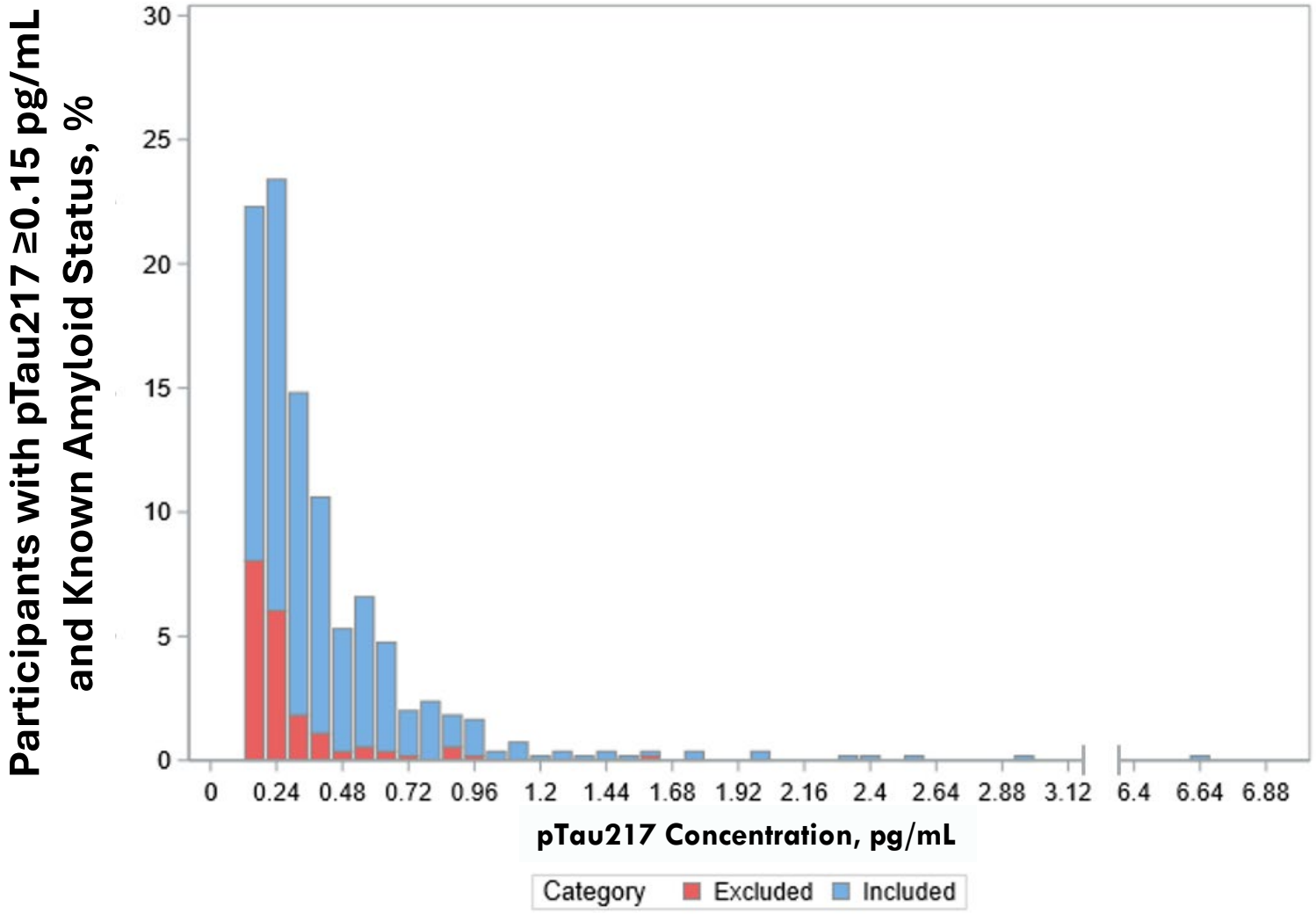
Amyloid Status for Participants With pTau217 ≥0.15 pg/mL



- 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

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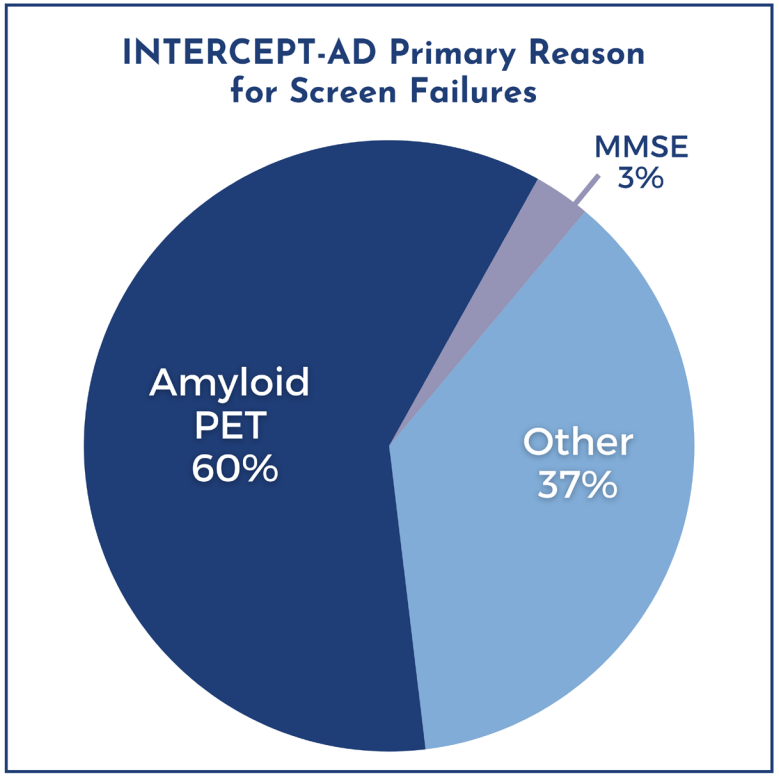
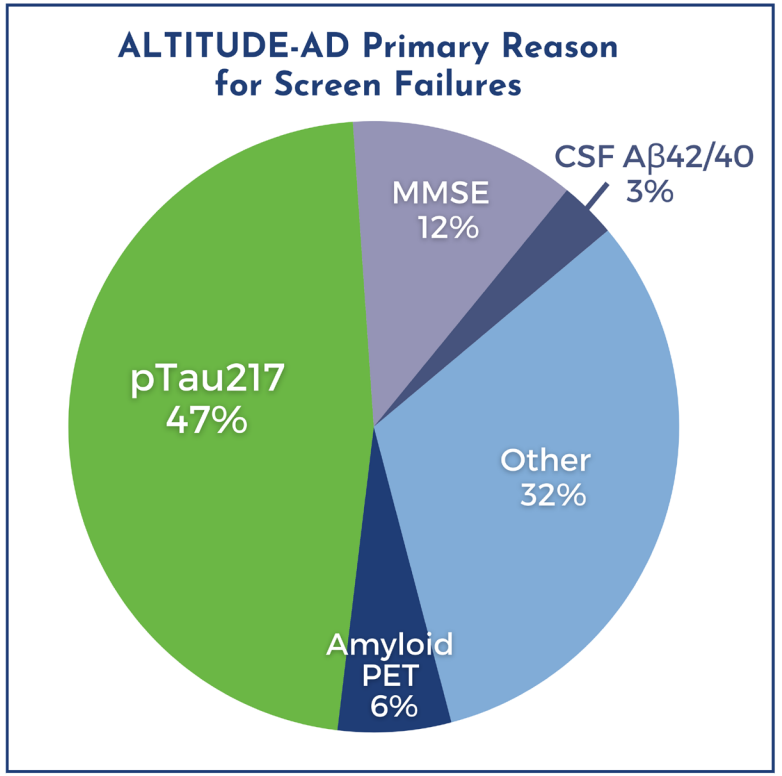
pTau217 Enrichment Strategy Reduced Amyloid PET Screen Failure Rates



Final Data (US study)



Preliminary Global Data

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Summary

The pTau217 enrichment strategy in North America performed as intended

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

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

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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!

Scan for additional publications

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