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

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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]

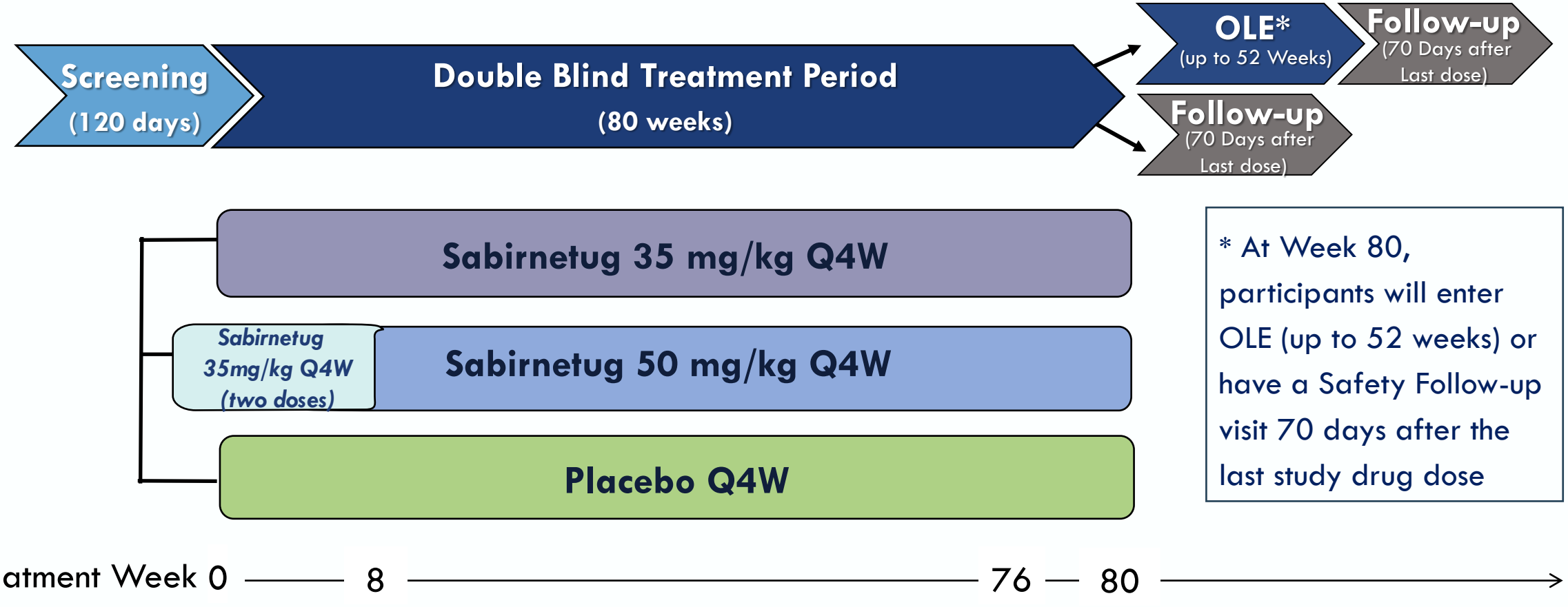
- **INTERCEPT-AD Phase 1 clinical trial (completed)**
  - US study in MCI or mild AD participants
  - SAD and MAD study design
  - Objectives: safety and pharmacokinetics

- **ALTITUDE-AD Phase 2 clinical trial (ongoing)**
  - Global study in MCI or mild AD participants
    - US, Canada, UK, Germany and Spain
  - Primary objective: evaluate efficacy in slowing cognitive and functional decline
    - iADRS change from baseline to Week 80

1. Cline et al. AAIC 2024

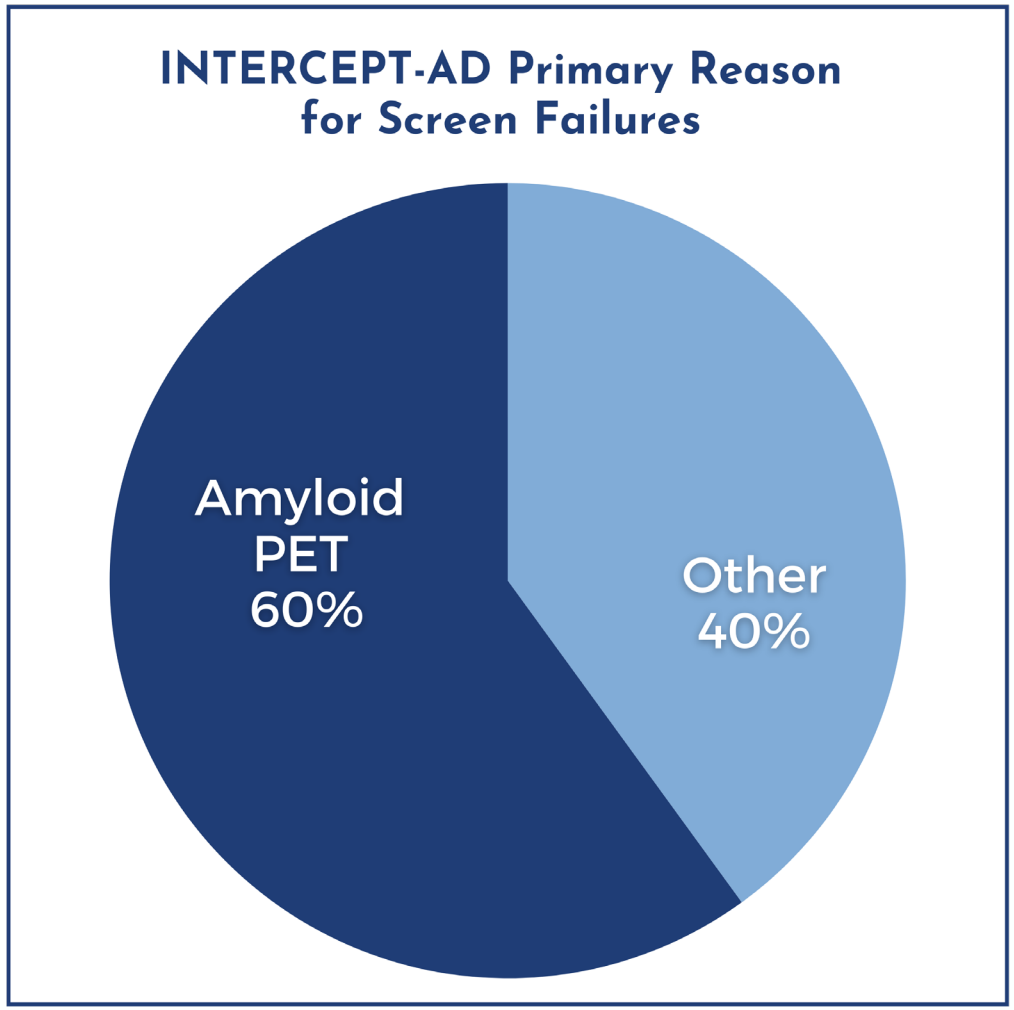
ALTITUDE-AD: Phase 2 Study Design of Sabirnetug for Early AD

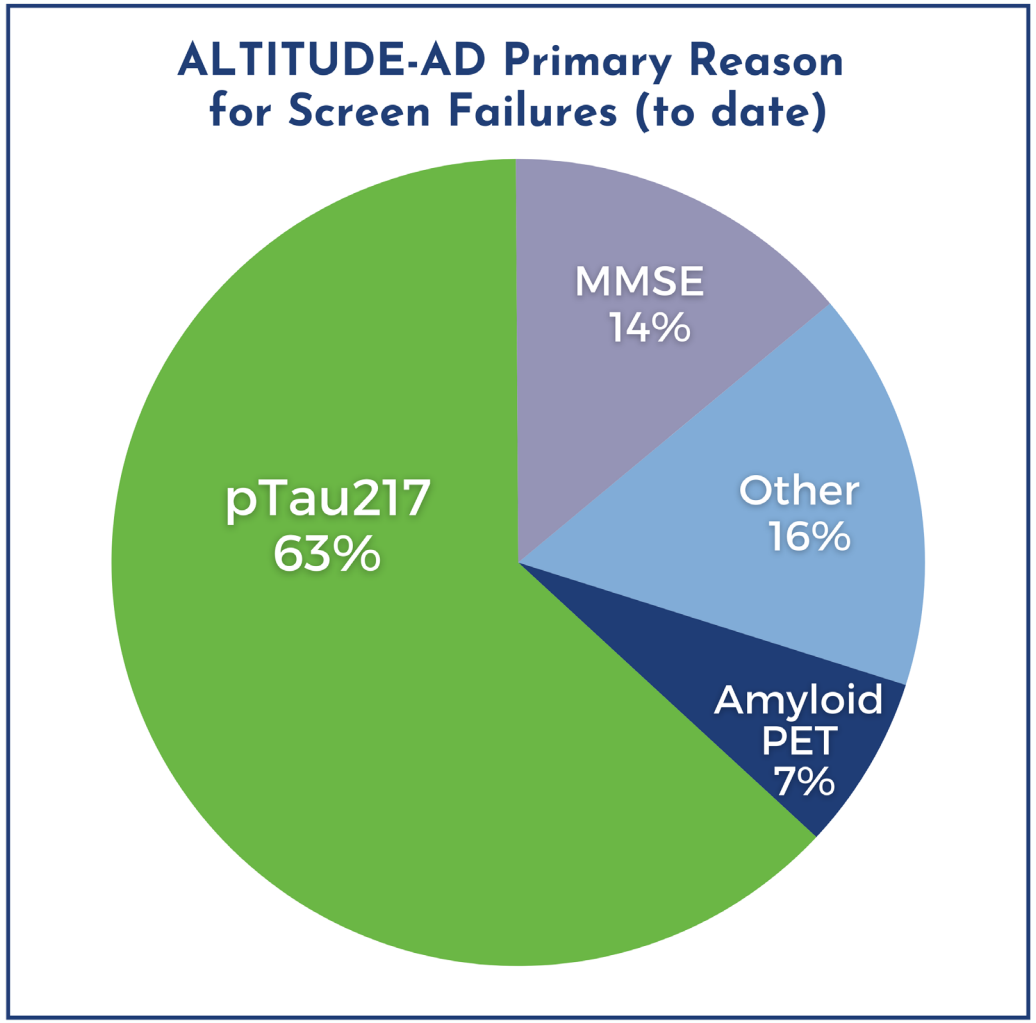
540 participants randomized 1:1:1



* 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

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

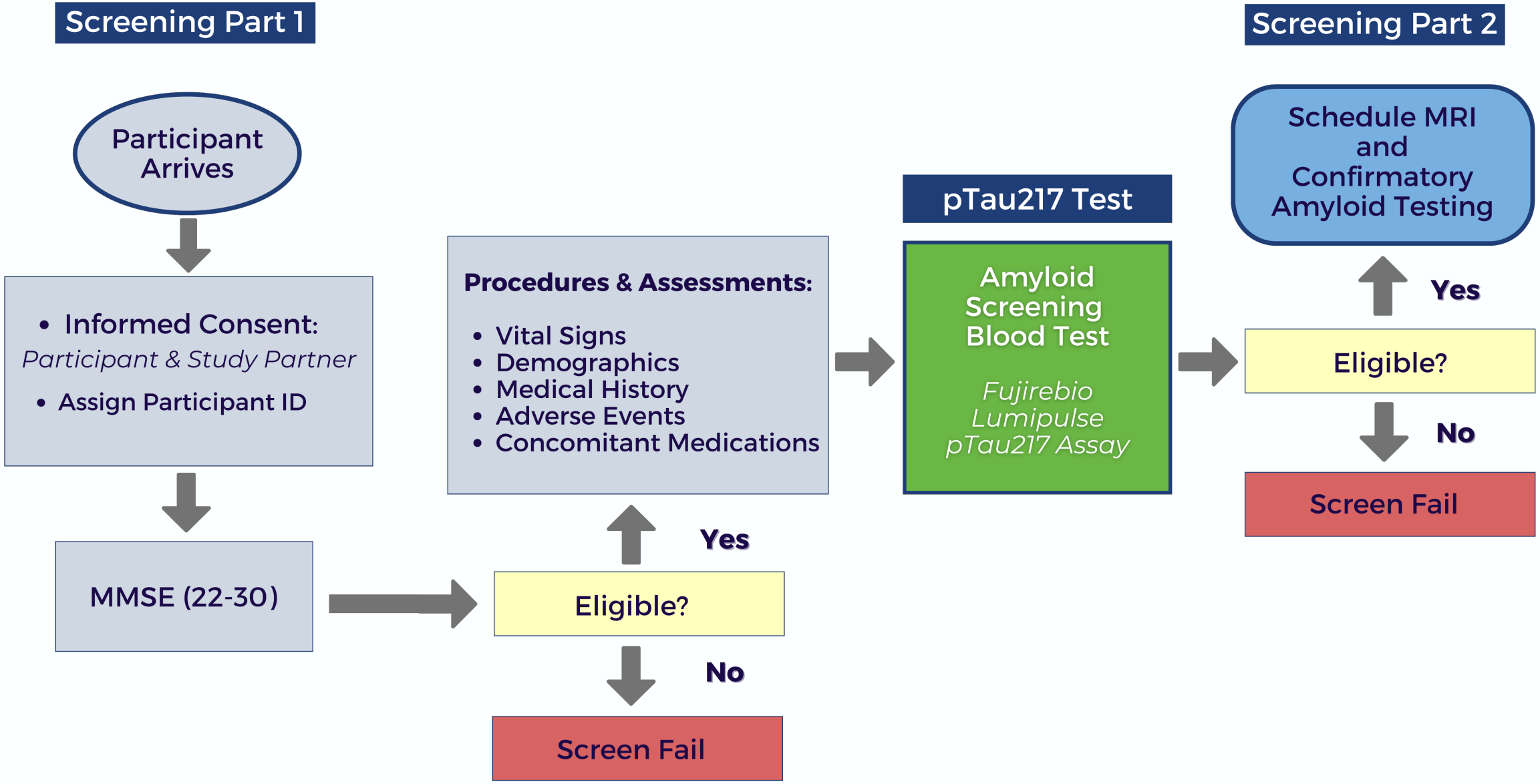
- Plasma concentrations of pTau217 are highly predictive for AD[1]
  - pTau217 is being used as an enrichment strategy to help identify potential participants with a high likelihood of meeting amyloid inclusion criteria on PET or CSF
  - The assay is not being used as a diagnostic

- 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

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

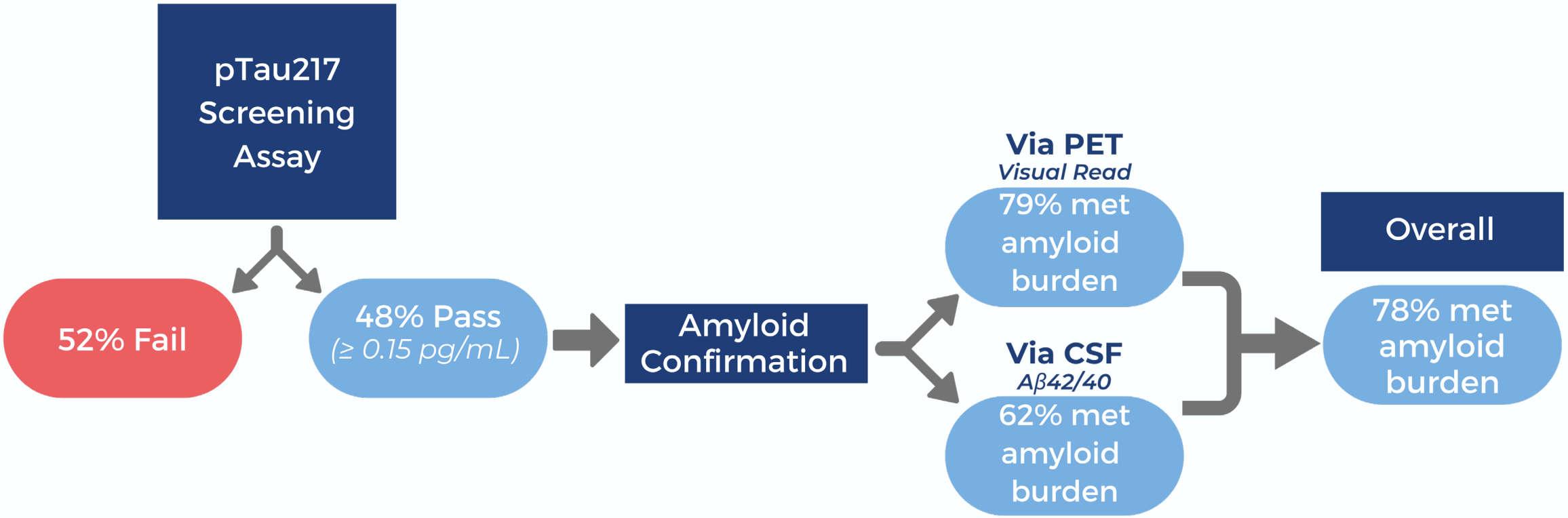
ALTITUDE-AD: Two-Part Screening Process



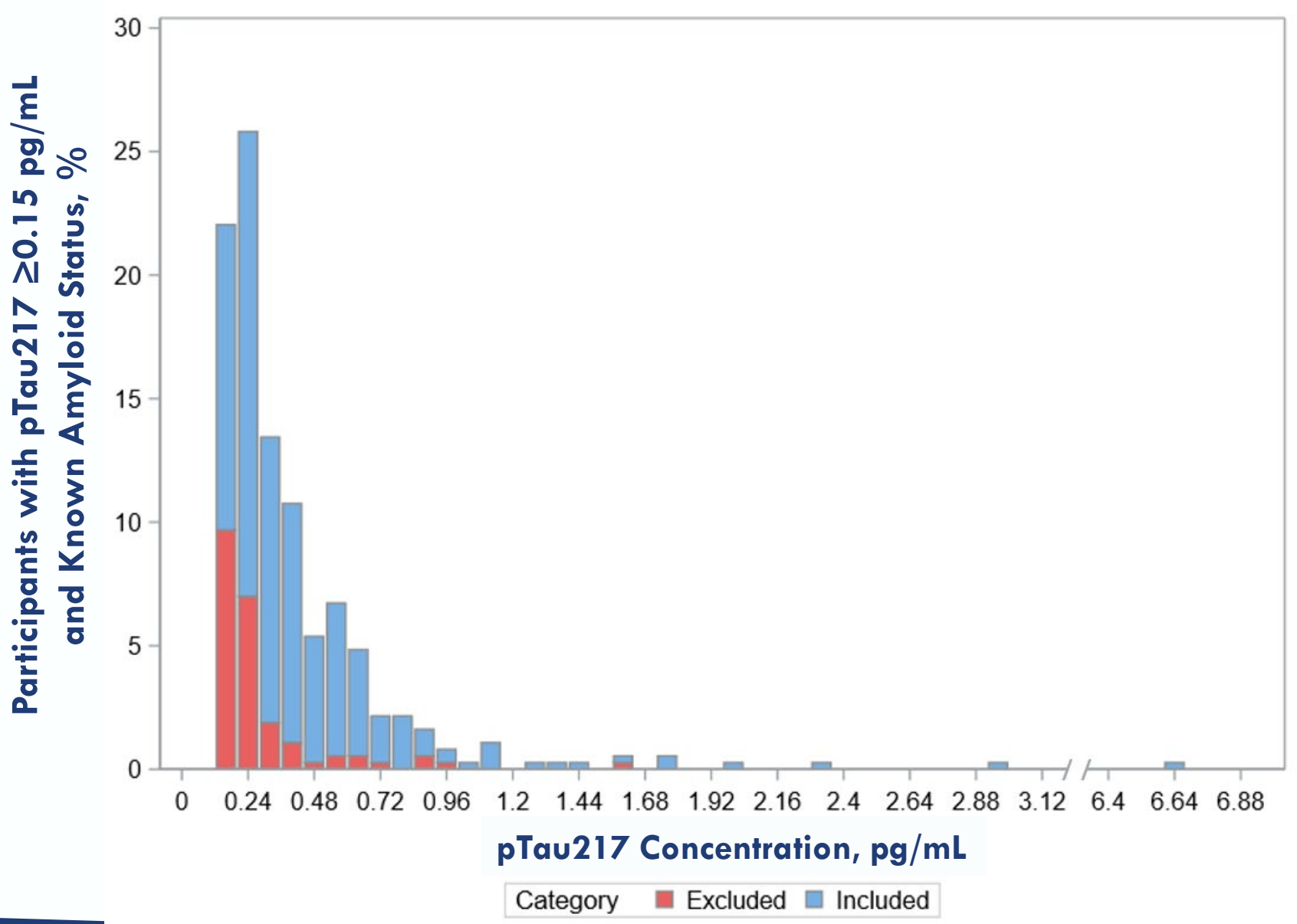
pTau217 Screening Results

North America (US and Canada) Study Data

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



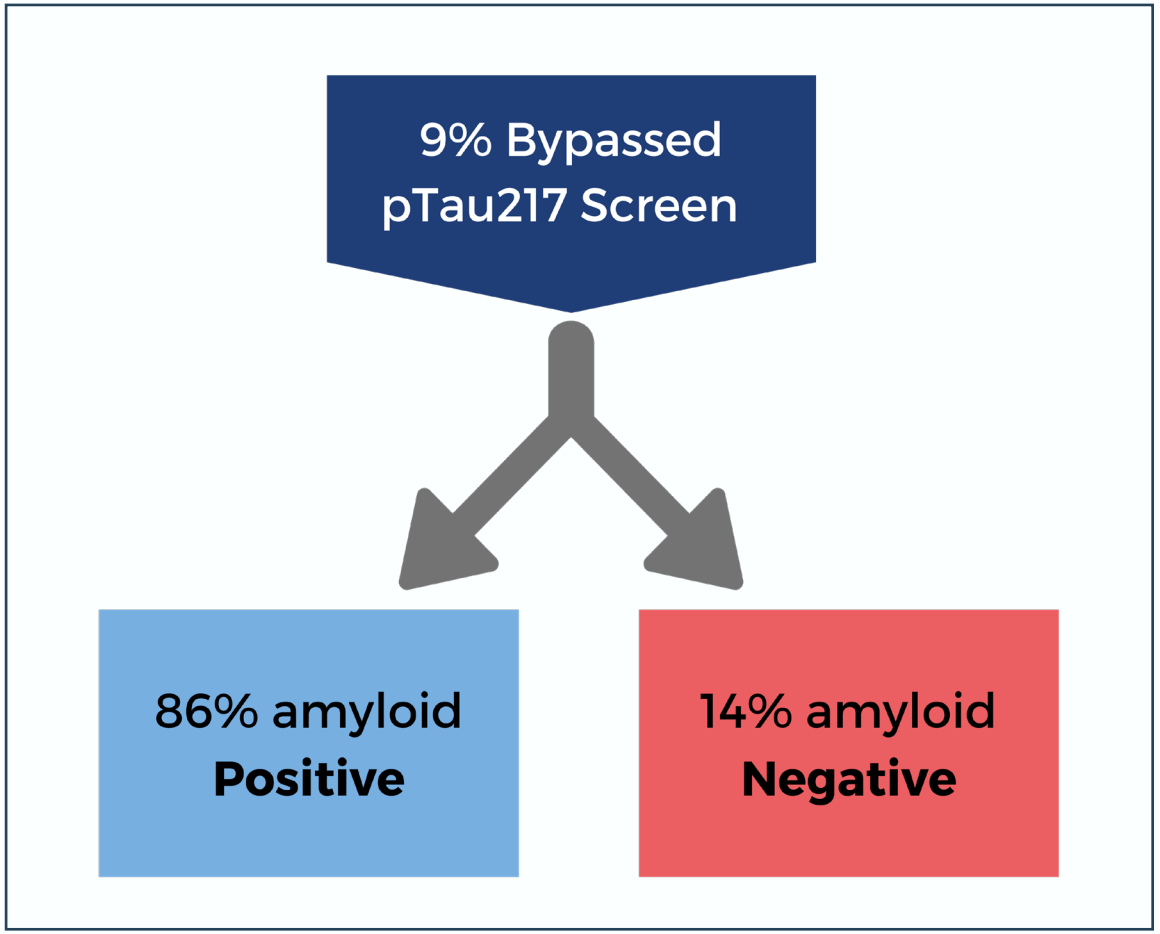
Amyloid Status for Participants With pTau217 ≥0.15 pg/mL



- 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

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
    - 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

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Thank you!