

Sabirnetug (ACU193) Lowers CSF Neurogranin & pTau181 Levels in INTERCEPT-AD Study in Early AD

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AD/PD
Lisbon, Portugal
March 8, 2024

Disclosures

Dr. Cline is an employee and shareholder at Acumen Pharmaceuticals.

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Acknowledgements

Participants and their Study Partners

- We acknowledge with gratitude the individuals who enrolled in the INTERCEPT-AD trial as well as their family, study partners, and friends who supported them.

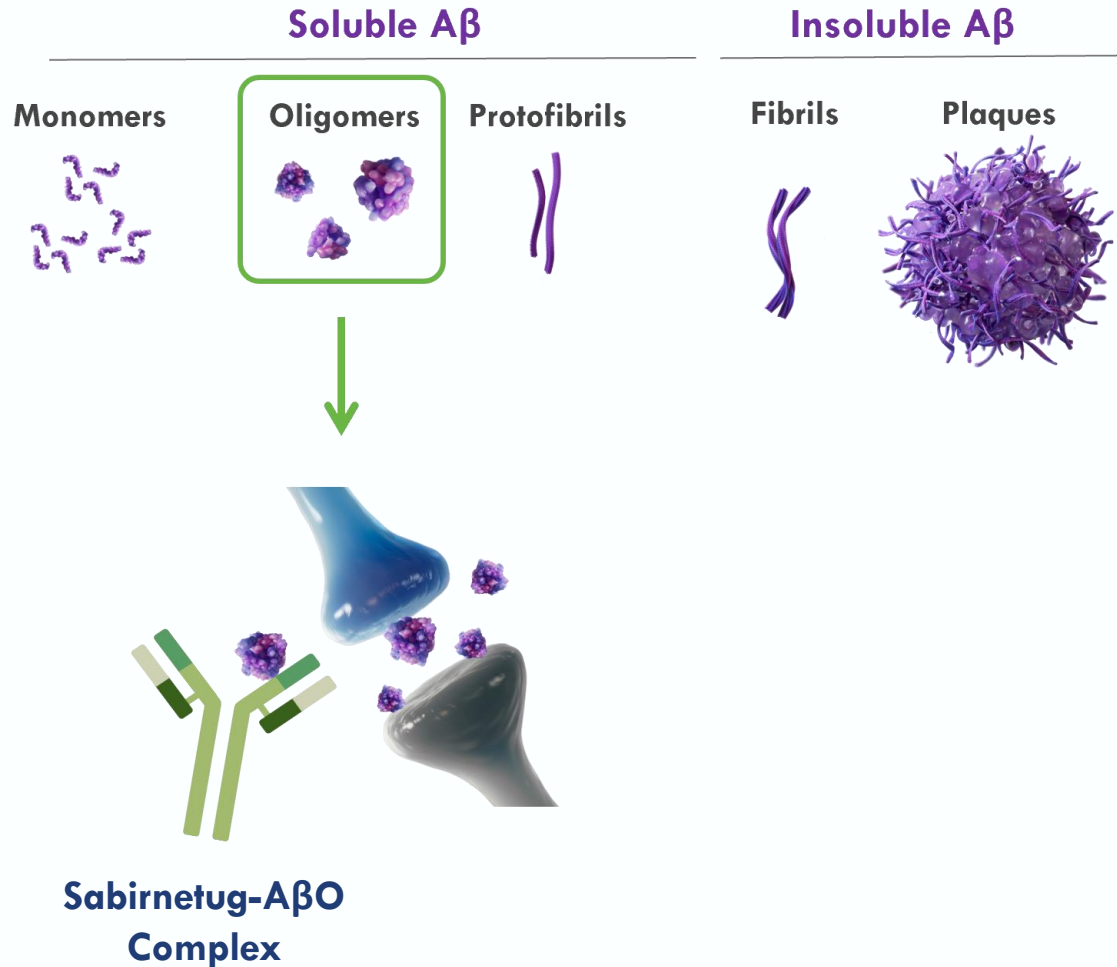
Site Staff and Study Team Members

- We would also like to acknowledge the site staff, CRO, and all study team members who were vital to the successful completion of this trial.

Site Investigators

- Kimball Johnson (iResearch Atlanta), Diana Kerwin (Kerwin Research Center), Jeffrey Norton (Charter Research), Mohammad Reza Bolouri (Alzheimer's Memory Center), Alida Reinoso (Columbus Clinical Services), Shirley Valdez-Arroyo (Santos Research Center), Eric Carbonell (Combined Research), David Weisman (Abington Neurological), Alexander White (Progressive Medical Research), Beth Safirstein (MD Clinical), Lawrence Honig (Columbia University Hospital), Nelson Berrios (Clinical Trial Network), Steve Sitar (Orange County Research Institute), Nida Laurin (Clinical Endpoints), Sanjiv Sharma (CenExel), Gustavo Alva (Hoag Memorial Hospital Presbyterian) and Maria Johnson (ACMR)

Sabirnetug (ACU193) is a Monoclonal Antibody that is Highly Selective for Soluble Amyloid β Oligomers, a Synaptotoxic Form of Amyloid β



Amyloid β oligomers (A β O_s):

- Impair synaptic function¹
- Induce tau hyperphosphorylation²
- Contribute to impairment of memory & cognition³

1. Lacor et al., 2004 & 2007; Townsend et al., 2006; Batista et al., 2018

2. De Felice et al., 2008; Zempel et al., 2010

3. Clearly et al., 2005; Poling et al., 2008; Cline et al., 2019

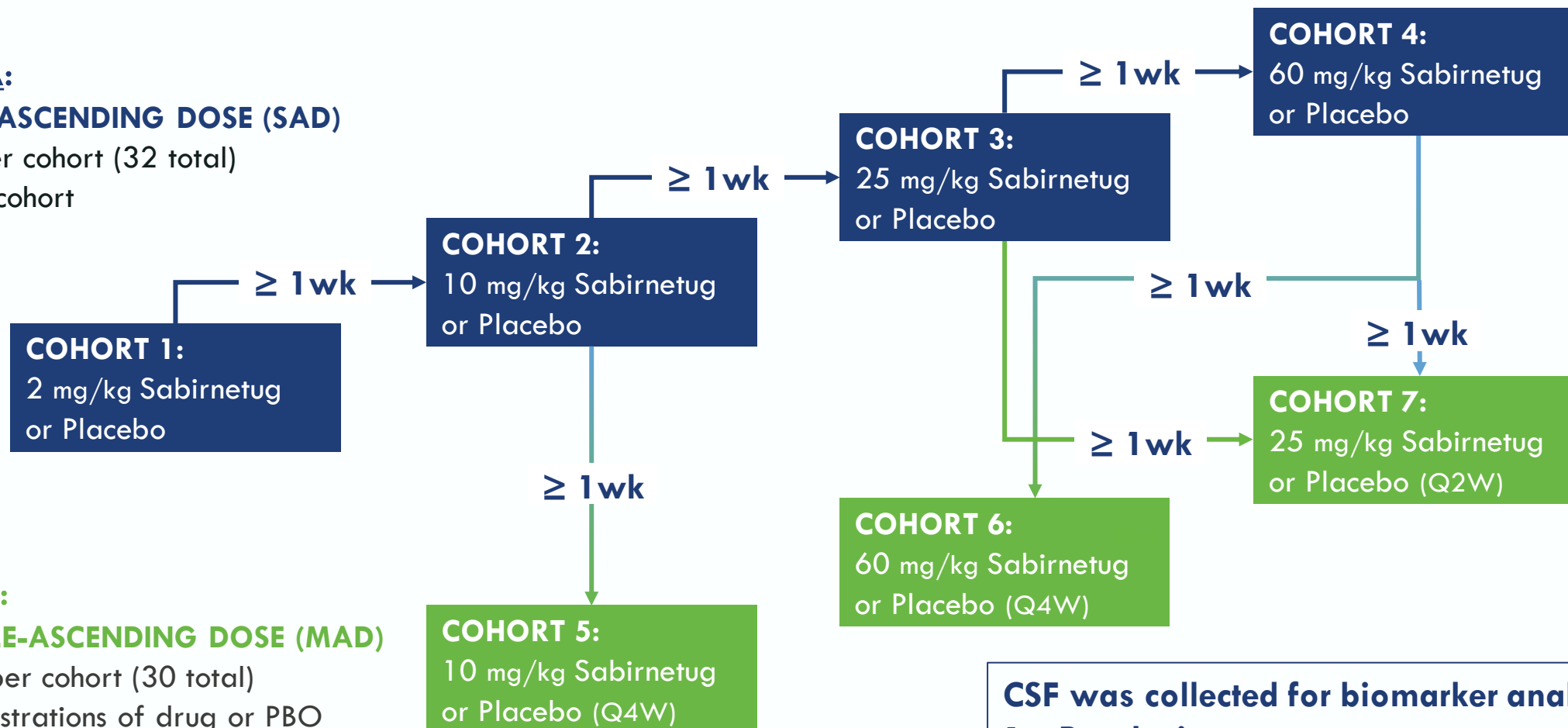
INTERCEPT-AD: A Randomized Placebo Controlled Phase 1 Study in Early AD Patients

PART A:

SINGLE-ASCENDING DOSE (SAD)

n = 8 per cohort (32 total)

6:2 per cohort



PART B:

MULTIPLE-ASCENDING DOSE (MAD)

n = 10 per cohort (30 total)

3 administrations of drug or PBO

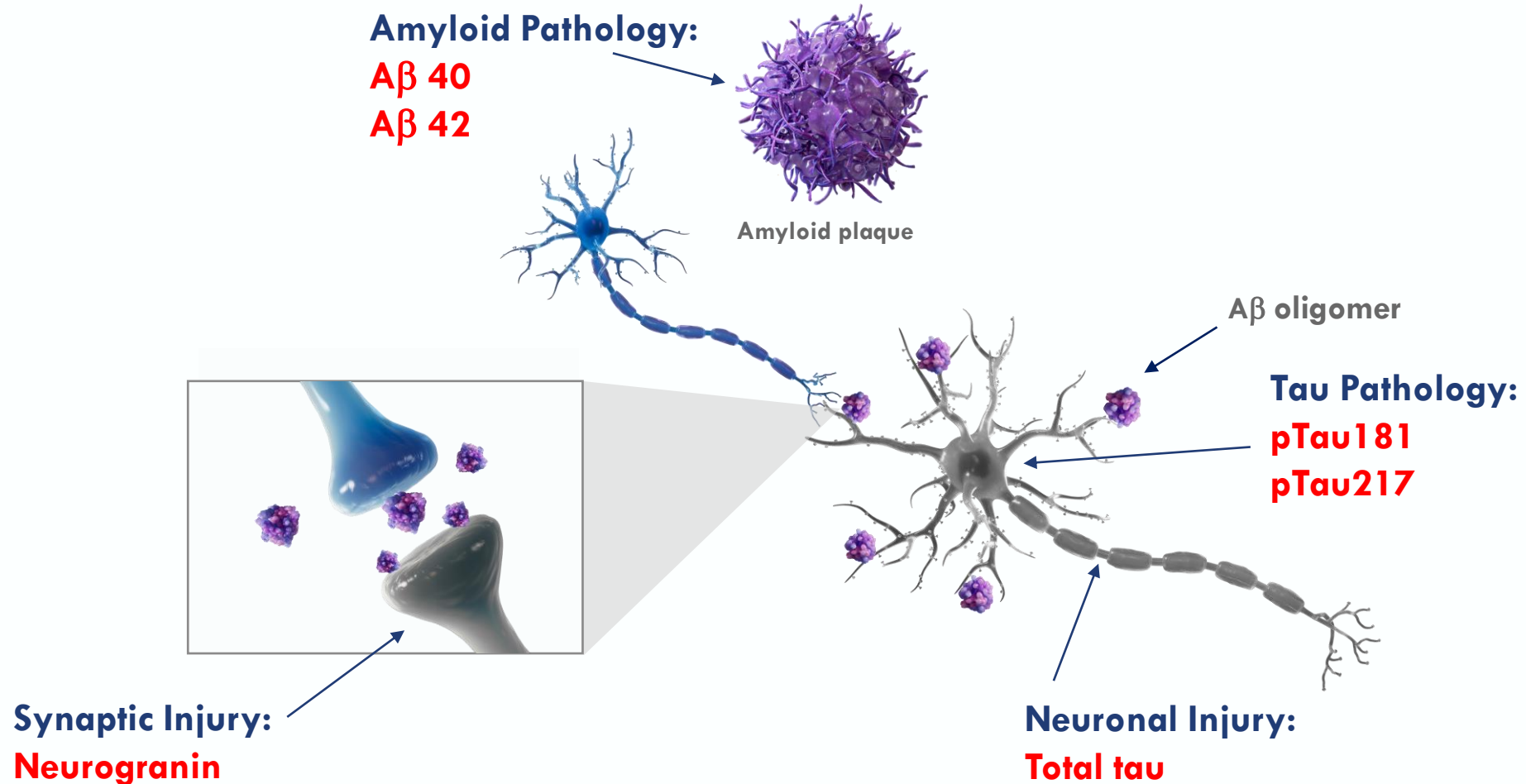
8:2 per cohort

Q2W: Dosing every two weeks; Q4W: Dosing every four weeks.
PBO: placebo

CSF was collected for biomarker analysis:

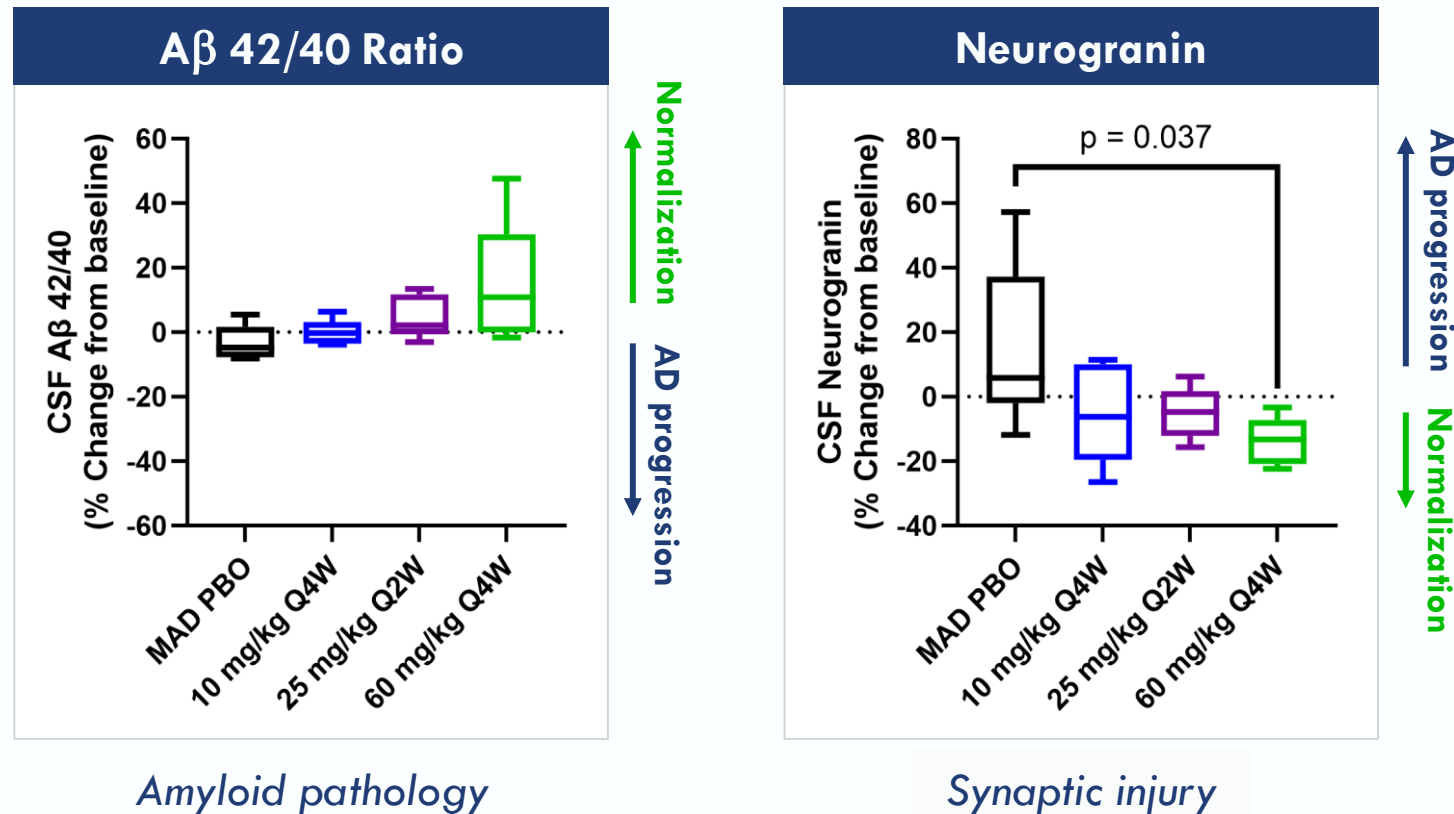
1. Pre-dosing
2. Post-dosing (7-21 days after last dose)

Key CSF Biomarkers Associated with AD Pathology were Assessed



1. Tarawneh, R. Biomarkers: Our Path Towards a Cure for Alzheimer Disease. Biomarker Insights Volume 15: 1–15. 2020; 2. Blennow K, Zetterberg H. The Past and the Future of Alzheimer's Disease Fluid Biomarkers. J Alzheimers Dis. 2018;62(3):1125-1140.

Sabirnetug-Associated Changes in CSF A β and Synaptic Biomarkers Indicate Downstream Pharmacology After 3 Doses



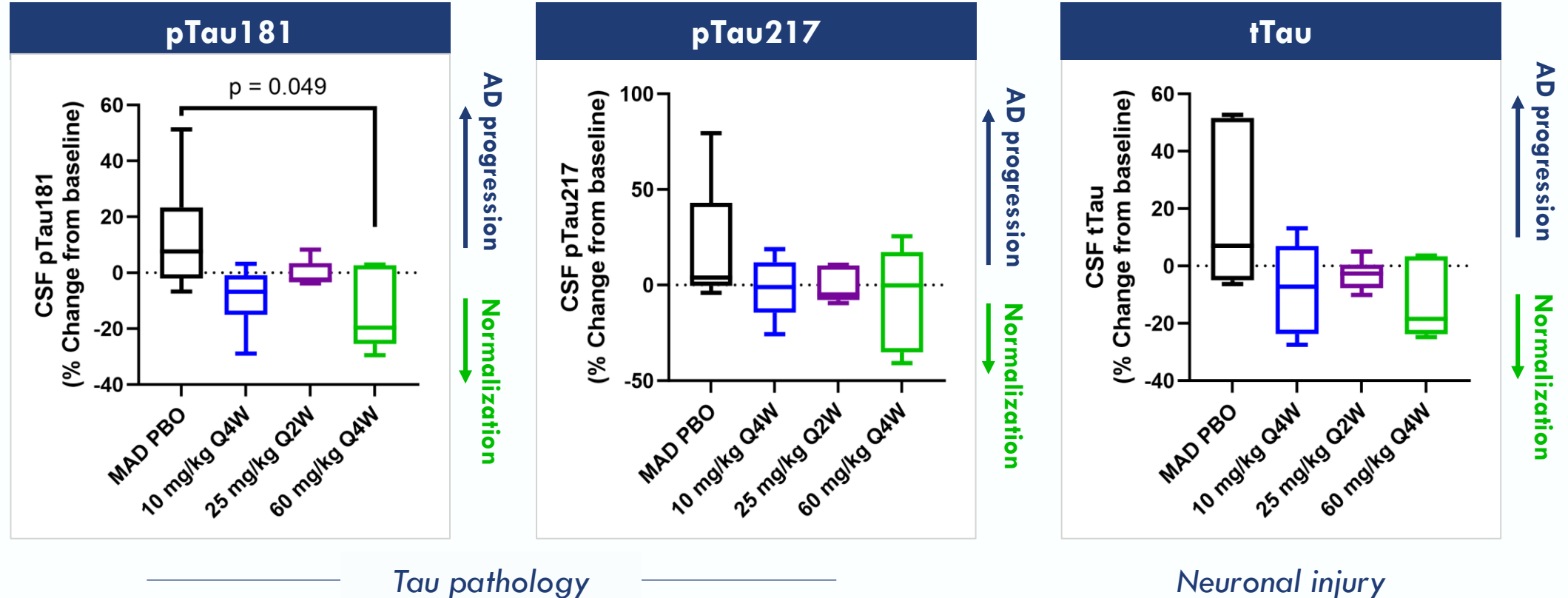
Amyloid pathology

Synaptic injury

- $n = 8$ subjects/treated group; 6 subjects in pooled placebo (PBO)
- p -values from unpaired, 2-sided Student's t test

- A β assays: Lumipulse
- Neurogranin: ELISA

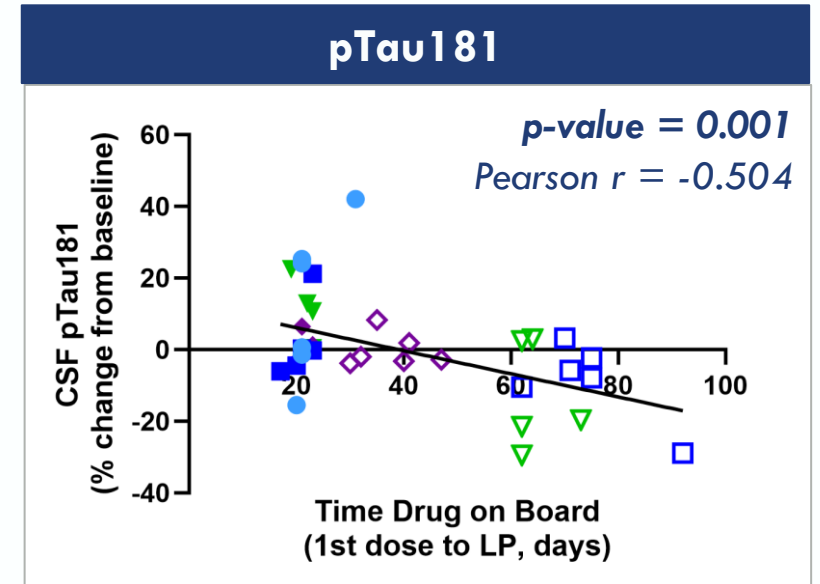
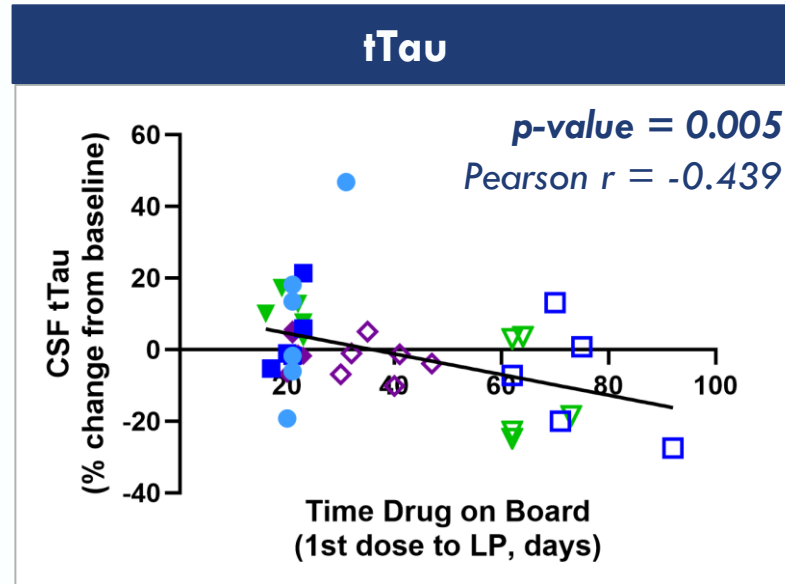
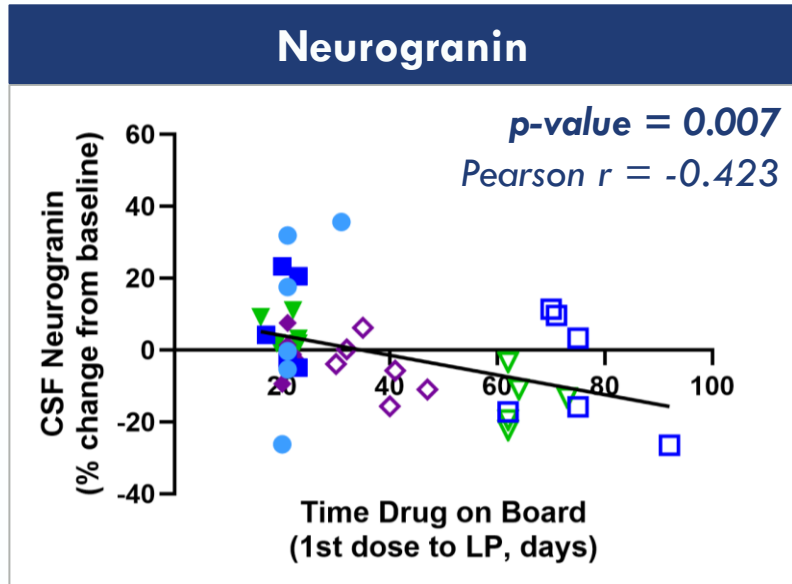
Sabirnetug-Associated Changes in CSF Tau Proteoforms are Consistent with Downstream Pharmacology After 3 Doses



- $n = 8$ subjects/treated group; 6 subjects in pooled placebo (PBO)
- p -values from unpaired, 2-sided Student's t test

- All assays: Lumipulse
- pTau217: ADx prototype

CSF Biomarker Responses to Sabirnetug Are Dose & Duration Dependent



AD progression ↑
Normalization ↓

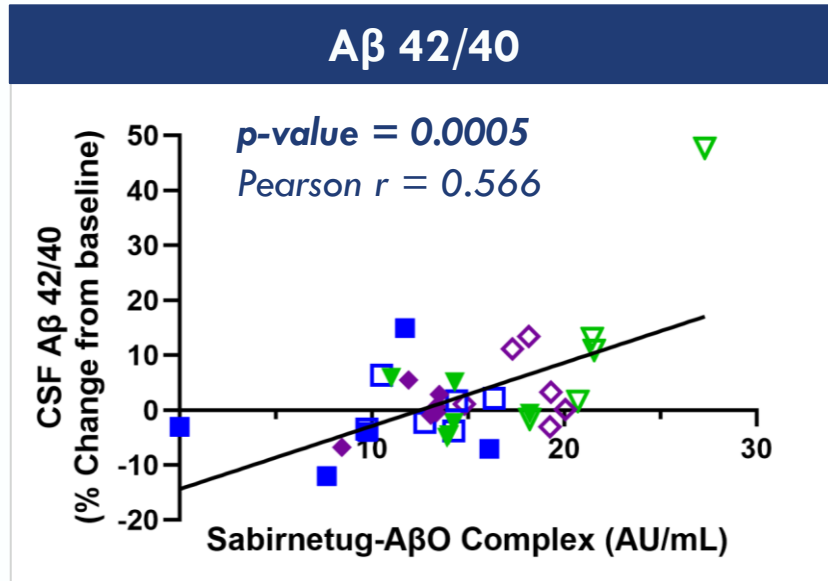
- SAD 2 mg/kg
- SAD 10 mg/kg
- ◆ SAD 25 mg/kg
- ▼ SAD 60 mg/kg
- MAD 10 mg/kg Q4W
- ▼ MAD 60 mg/kg Q4W
- ◇ MAD 25 mg/kg Q2W

- LP = lumbar puncture
- $n = 40$ subjects
- p -values from Pearson's correlation test

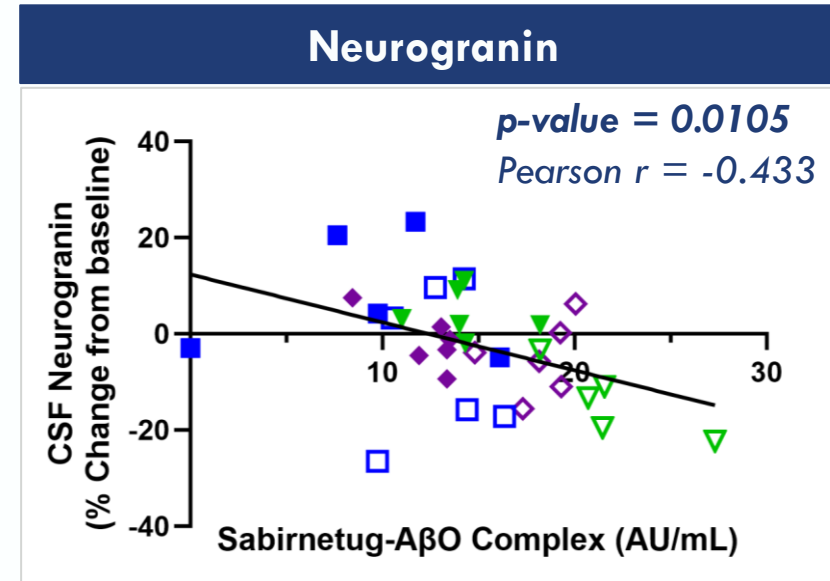
- Neurogranin: ELISA
- Tau assays: Lumipulse



Changes in CSF Neurogranin & A β 42/40 Correlate with Target Engagement (Defined as Sabirnetug Binding to CSF A β Oligomers 🌱)



↑ Normalization
↓ AD progression



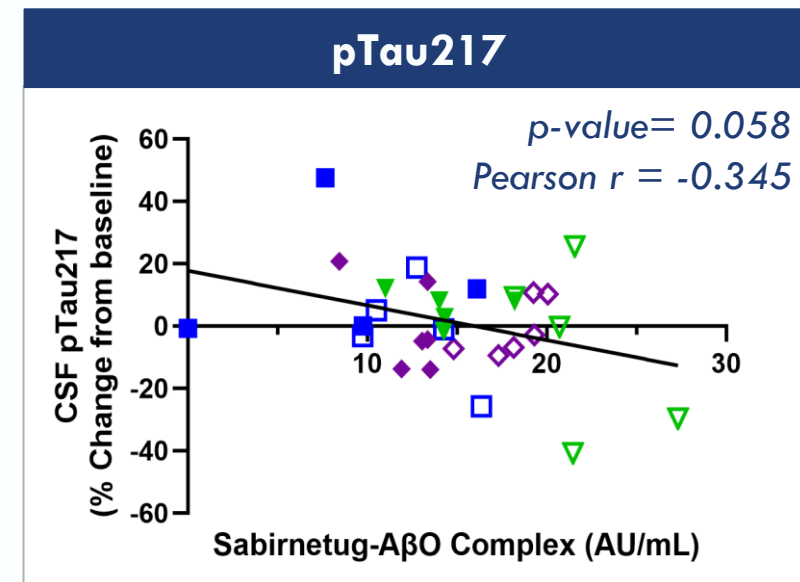
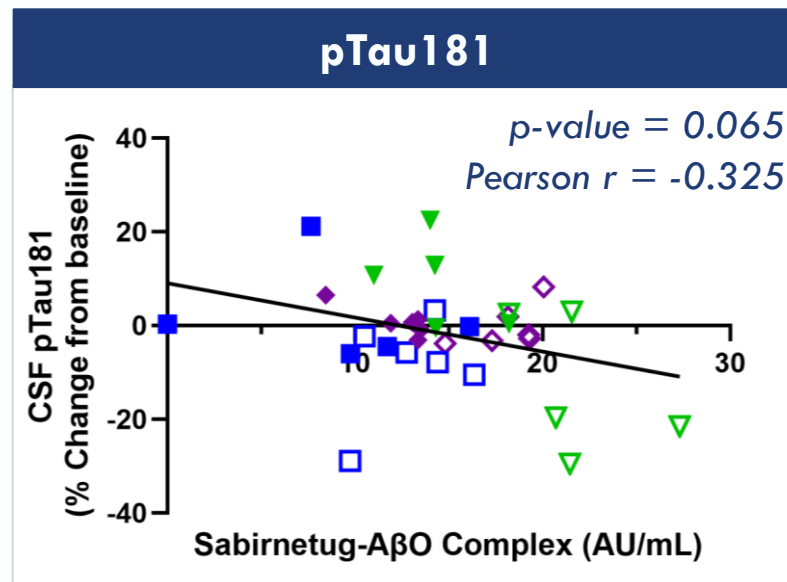
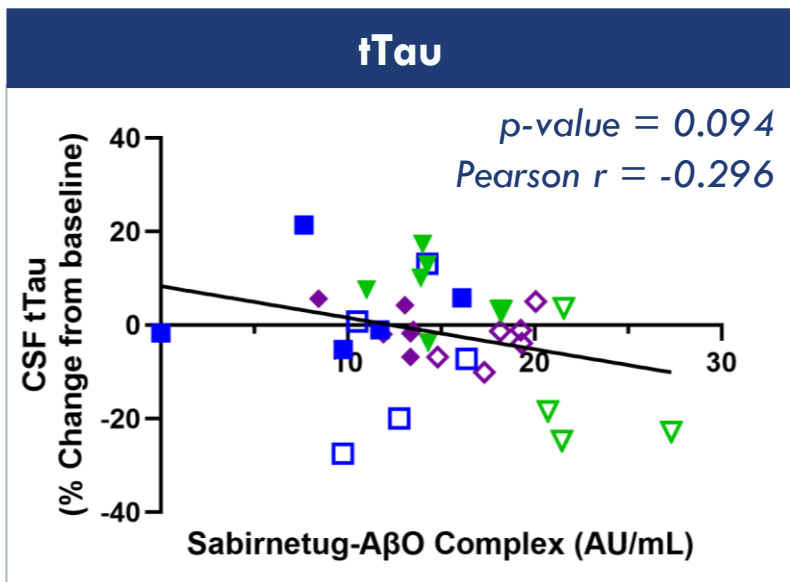
↑ AD progression
↓ Normalization

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

- *n = 34 subjects*
- *p-values from Pearson's correlation test*

- *A β assays: Lumipulse*
- *Neurogranin: ELISA*

Changes in CSF Total & Hyperphosphorylated Tau Do Not Significantly Correlate with Target Engagement (Defined as Sabirnetug Binding to A β Oligomers in CSF)



- 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

- $n = 33$ subjects for tTau & pTau181; 31 for pTau 217
- $p\text{-values}$ from Pearson's correlation test

- All assays: Lumipulse
- pTau217: ADx prototype

Conclusions

- Sabirnetug (ACU193) significantly lowers CSF neurogranin (-13.9 %) and pTau181 (-13.0 %) after only three administrations of 60 mg/kg Q4W
- Reduction of the synaptic marker neurogranin correlated significantly with sabirnetug engagement with A β O target
- Long term changes in biomarkers and their relationship with clinical outcomes will be evaluated in a planned phase 2 study over 18 months

Thank you!

CSF Biomarker Measurements

**Department of Laboratory Medicine, Neurochemistry Lab,
Amsterdam UMC**

Daniel Antwi-Berko

Marleen JA Koel-Simmelink

Charlotte Teunissen

CSF pTau217 Measurements

ADx NeuroSciences

Erik Stoops

Eugeen Vanmechelen

And to colleagues at Acumen Pharmaceuticals

Data Analysis & QC

Karen Sundell

Elizabeth Johnson

Gopalan Sethuraman

Biomarker Study Design & Data Interpretation

Hao Zhang

Hugo Vanderstichele

June Kaplow

Robert A. Dean

Jasna Jerecic

Eric Siemers