A phase 1 study, INTERCEPT-AD, of ACU193: safety, target engagement, and biomarker changes

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Denver, Colorado
April 16, 2024

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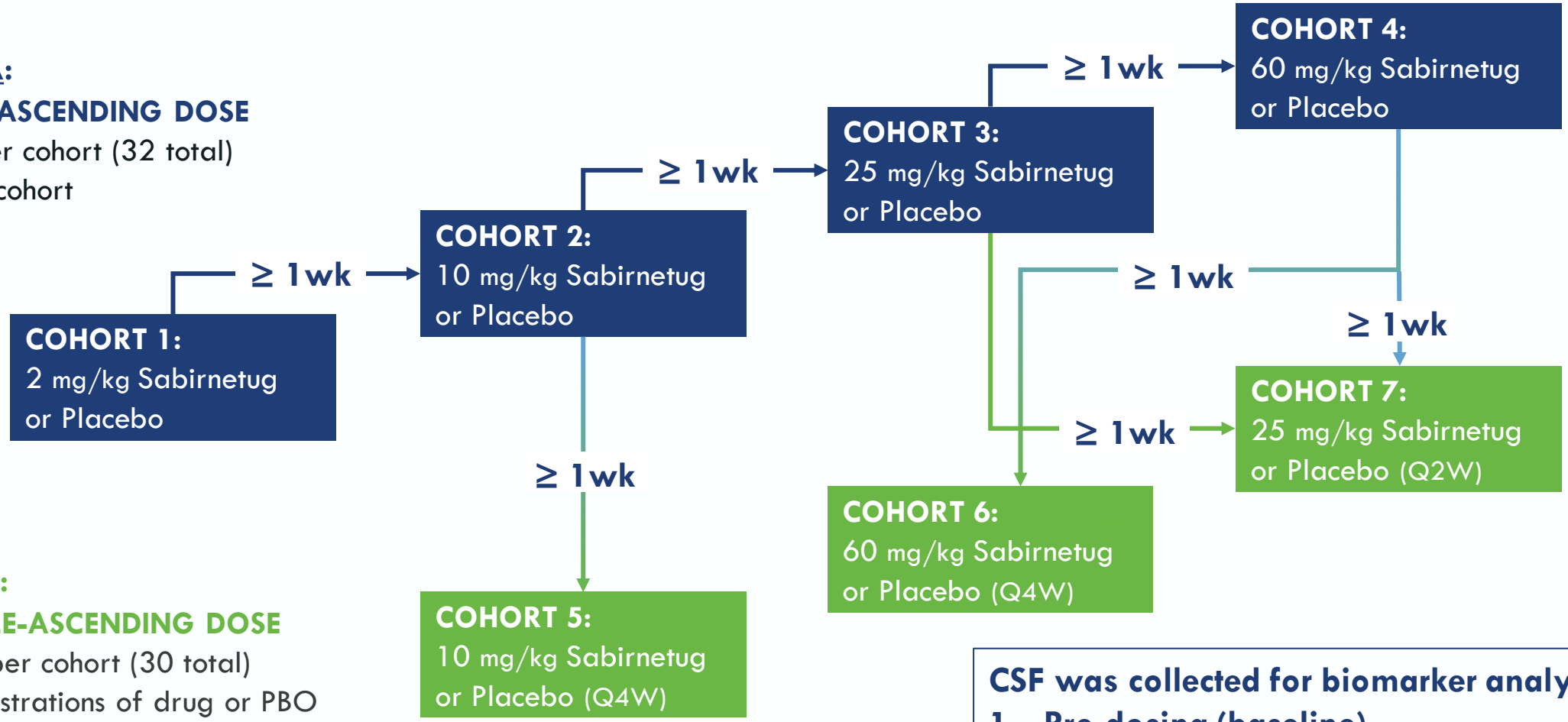
INTERCEPT-AD: A Randomized Placebo Controlled Phase 1 Study in Early AD Patients



CSF was collected for biomarker analysis:

1. **Pre-dosing (baseline)**
2. **Post-dosing (7-21 days; endpoint)**

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

NCT04931459

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INTERCEPT-AD: ARIA-E summary

SAD

2 mg/kg
Cohort 1

ApoE	D21	D140
3,4		
3,3	PBO	PBO
3,4		
2,3		
3,4	PBO	PBO
3,3		
3,3		
3,3		

10 mg/kg
Cohorts 2, 5

ApoE	D21	D140
3,4	PBO	PBO
3,3		
3,3		
3,4		
3,4	PBO	PBO
3,4		
3,4		
3,4		

25 mg/kg
Cohorts 3, 7

ApoE	D21	D140
3,3		
3,3	PBO	PBO
4,4		
3,3		
2,4		
3,3	PBO	PBO
3,4		
3,3		

60 mg/kg
Cohorts 4, 6

ApoE	D21	D140
4,4	PBO	PBO
3,4		
3,4	PBO	PBO
3,3		
3,3		
3,4		
2,4		
3,4		

MAD

ApoE	D28	D70	D196
2,3			
3,3			
3,3			
4,4			
3,3	PBO	PBO	PBO
3,4			
4,4			
3,4			
3,3			
3,4	PBO	PBO	PBO

ApoE	D28	D70	D98
3,3			
3,4			
3,4			
3,4			
3,4			
3,4	PBO	PBO	PBO
3,3			
3,4	PBO	PBO	PBO
4,4			
4,4			

ApoE	D28	D63	D126
3,4			
3,3			
3,3			
4,4			
4,4	PBO	PBO	PBO
3,3			
3,4			
3,4			
3,4	PBO	PBO	PBO
3,3			

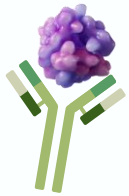
NO ARIA-E
Asymptomatic ARIA-E
Symptomatic ARIA-E
Discontinued

PBO: Patient on placebo

No ε4 homozygotes developed ARIA-E despite comprising 6 individuals (13%) in study; 4/5 ARIA-E cases are ε4 heterozygotes and 1/5 (at 60 mg/kg) was a non-carrier.

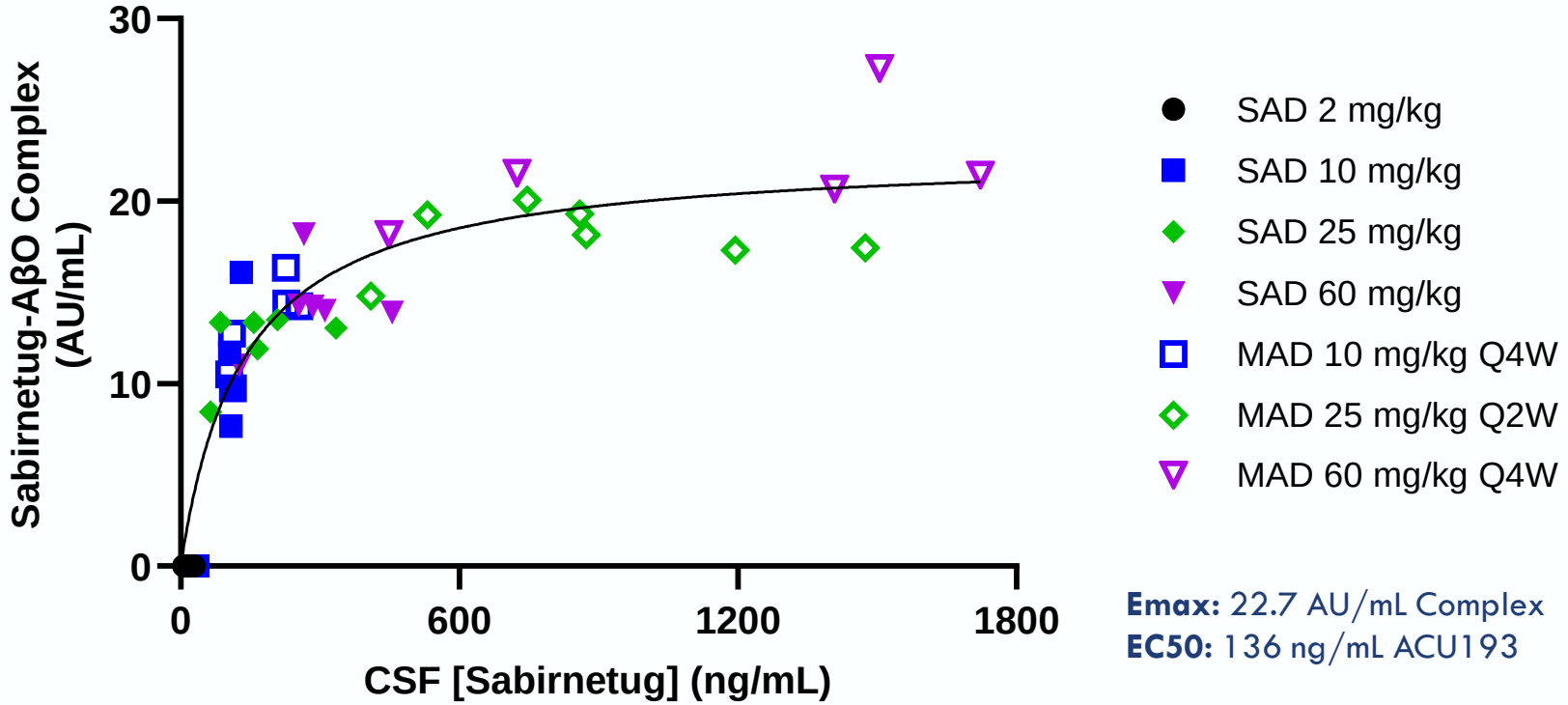
Central Target Engagement (Sabirnetug-AβO Complex) Approaches Maximum at Highest Sabirnetug Doses Administered in INTERCEPT-AD

Target Engagement



Sabirnetug-AβO Complex

Single & Multiple Dose Cohorts - Exposure Response Relationship (Emax Model)



Emax: 22.7 AU/mL Complex
EC50: 136 ng/mL ACU193

*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

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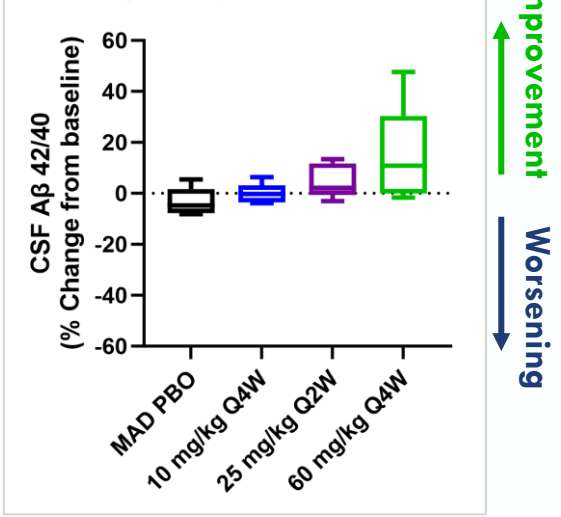
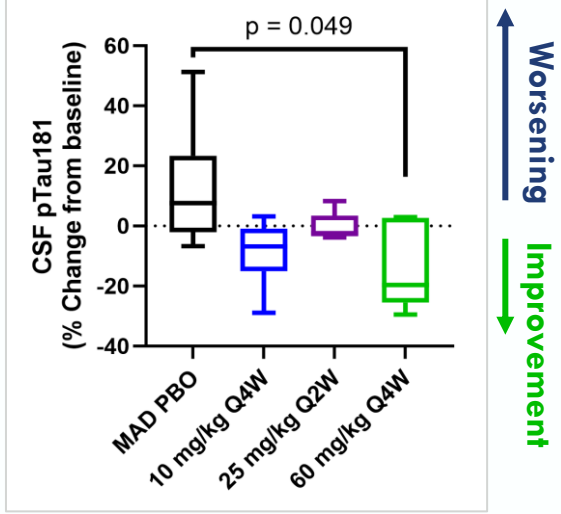
Sabirnetug-Associated Changes in CSF Biomarkers Indicate Downstream Pharmacology for Amyloid, pTau Species, and Synaptic Markers After 3 Administrations

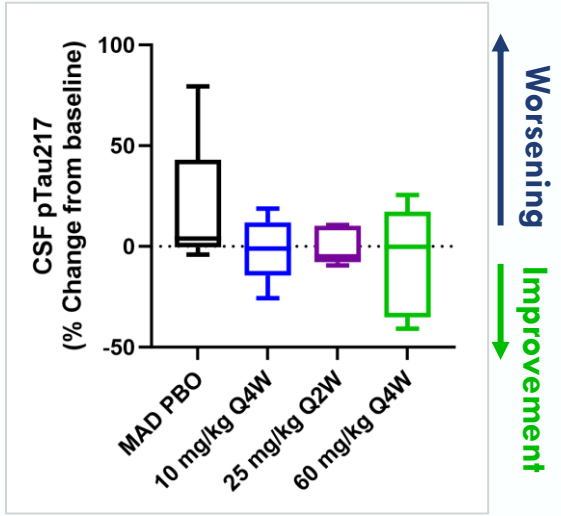
Aβ 42/40 Ratio



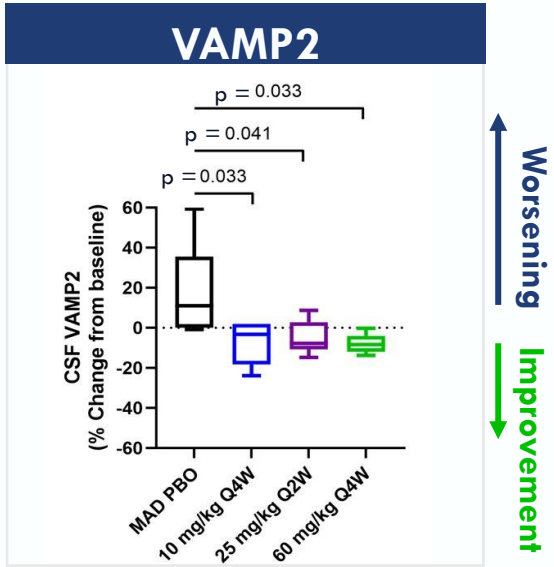
pTau181



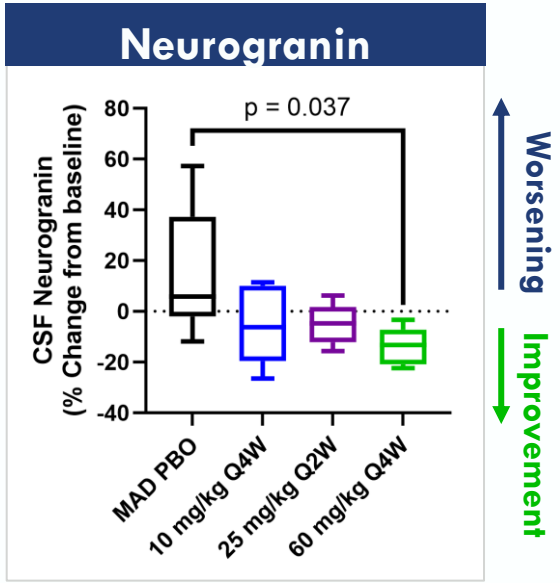
pTau217



VAMP2



Neurogranin



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