Investor Conference Call to Discuss INTERCEPT-AD Results

July 17, 2023

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Agenda

- **Introduction**

  Alex Braun, Head of Investor Relations

- **ACU193 & INTERCEPT-AD Topline Results**

  Dan O'Connell, Chief Executive Officer

  Dr. Eric Siemers, Chief Medical Officer

- **Topline Results Q&A**

  Dr. Eric Siemers, Chief Medical Officer

  Dr. Steven DeKosky, *Deputy Director of the McKnight Brain Institute at the University of Florida and member of Acumen's scientific advisory board*

  Dr. Lawrence Honig, *Director of the New York State Center of Excellence for Alzheimer's Disease at Columbia University and INTERCEPT-AD trial investigator*

- **Open Q&A**

  Dan O'Connell, Chief Executive Officer

  Dr. Eric Siemers, Chief Medical Officer

  Matt Zuga, Chief Business Officer & Chief Financial Officer

  Dr. Steven DeKosky

  Dr. Lawrence Honig

ACU193: Novel mAb Targeting Amyloid Beta Oligomers (AβOs), the Most Toxic Form of Aβ

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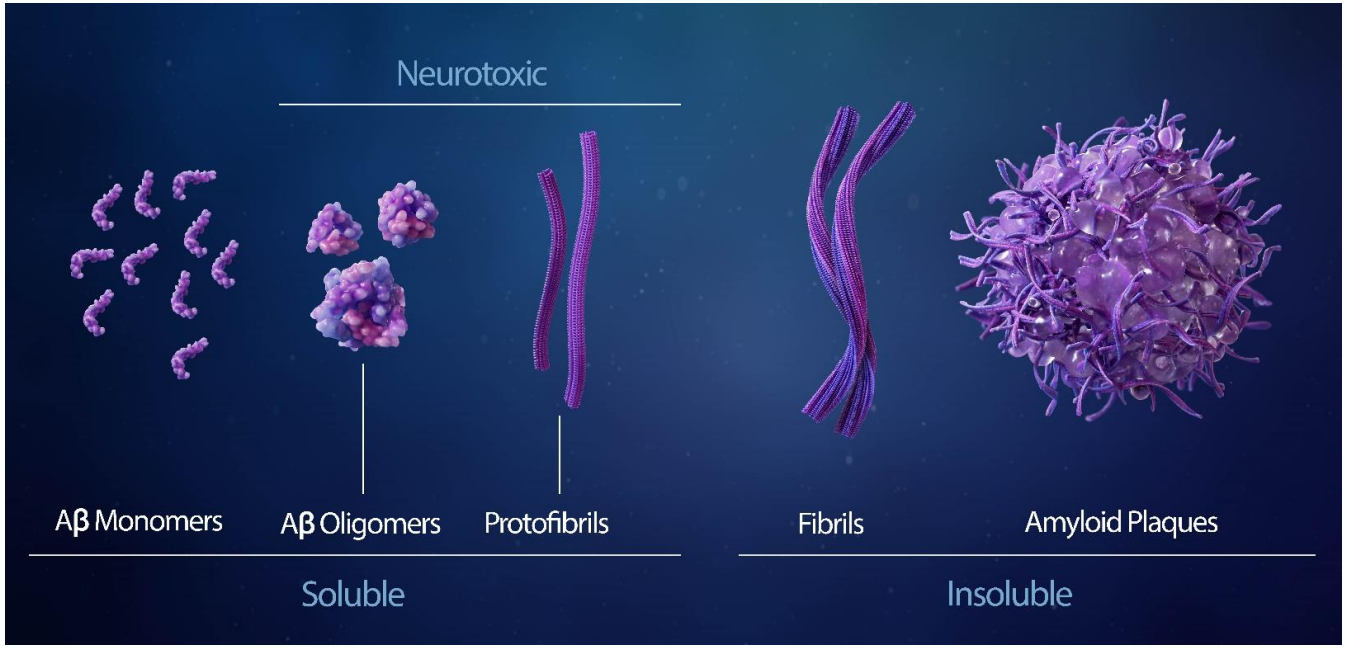
ACU193: A Monoclonal Antibody that Selectively Binds Toxic AβOs

- Humanized, affinity matured mAb developed to target toxic Aβ oligomers
  - >500-fold greater selectivity for AβOs over Aβ monomers
  - >85-fold selectivity for AβOs over Aβ fibrils
- IgG2 subclass mAb with reduced effector function
  - Potential for more selective targeting of AβOs and lower ARIA-E relative to Aβ plaque directed mAbs
- ACU193 discovered as part of research collaboration between Acumen and Merck & Co.
  - Currently developed by several former senior members of Eli Lilly's Global Alzheimer's development team
- ACU193 has been granted Fast Track designation for the treatment of early Alzheimer's disease by the U.S. FDA



ACU193 high selectivity for toxic AβOs may provide superior cognitive efficacy and improved safety and tolerability

INTERCEPT-AD Results Confirm Proof of Mechanism for ACU193 and Demonstrate Reduction in Amyloid Plaques at Higher Doses Studied

1. **Rapid, dose-related, statistically significant amyloid plaque reduction observed at higher doses studied (60 mg/kg Q4W and 25 mg/kg Q2W cohorts)* at 6-12 weeks**
   - Comparable to currently approved Aβ monoclonal antibodies at similar time points in their clinical development
2. **First antibody to demonstrate target engagement of Aβ oligomers, the most toxic form of amyloid beta, in a dose-related manner**
   - Serum and CSF exposure are dose proportional; antibody concentrations significantly exceeded levels of endogenous oligomers
   - Highest doses studied (25 mg/kg Q2W and 60 mg/kg Q4W) approached maximal target engagement (23.2 AU/mL Emax)
3. **Compelling overall safety profile, with low rate of ARIA-E**
   - No known drug-related SAEs; treatment emergent ADAs consistently low titer
   - No cases of symptomatic ARIA-E at 10 mg/kg Q4W and 25 mg/kg Q2W doses
   - No ARIA-E observed in ApoE4 homozygotes (n=6)
4. **Broad therapeutic index; clear path to more convenient monthly dosing regimen**

*Statistically significant reduction from baseline to endpoint within cohorts (p = 0.01)

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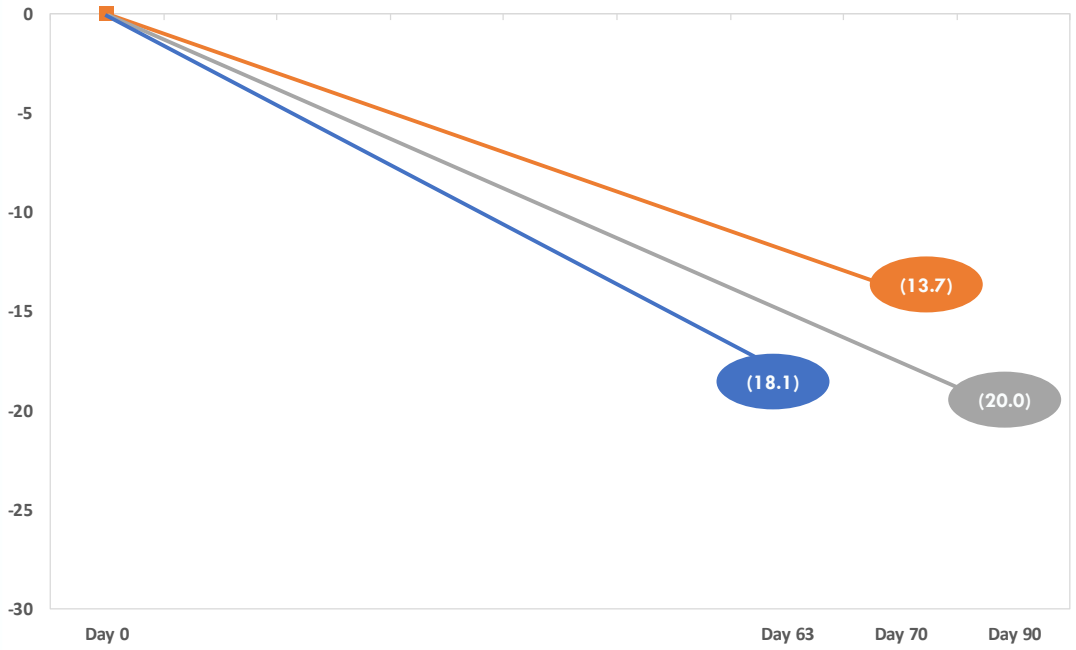
Highest Doses of ACU193 Demonstrate Rapid Reduction in Amyloid Plaque Reduction Comparable to Lecanemab (in Phase 3) at Similar Timeframe

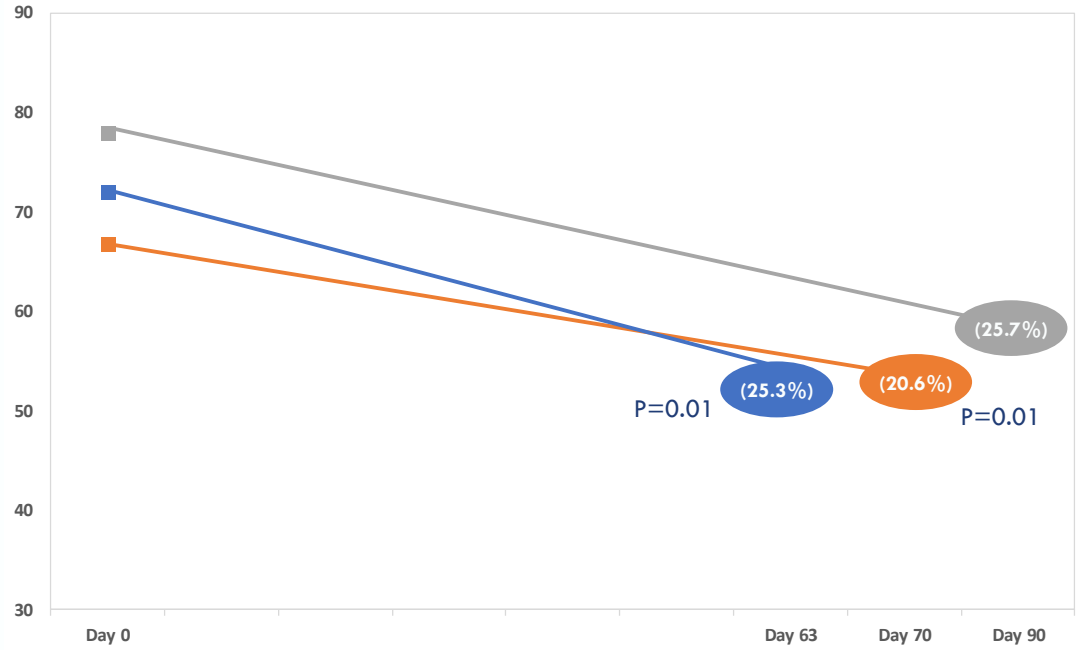
Mean Reduction in Amyloid Plaque (Centiloids)

Indexed Values



Absolute Values

(p=0.01 for change in amyloid plaque from baseline to endpoint within ACU193 cohort)



ACU193 60 mg/kg Q4W (n=8)* ACU193 25 mg/kg Q2W (n=8)* Lecanemab 10 mg/kg Q2W (n=344)

*Statistically significant reduction from baseline to endpoint within cohort (p = 0.01).

Source: Acumen Pharmaceuticals, data on file; van Dyck (2023), NEJM (amyloid PET reduction estimated from graphs); Cumulative drug administered: ACU193 60mg/kg = 180 mg/kg (three doses administered); ACU193 25mg/kg = 75mg/kg (three doses administered)

Note: There have been no head-to-head clinical trials between the product candidates listed above. Study designs and protocols for each product candidate were different, and as a result, results may not be comparable between product candidates.

Low ARIA-E at Elevated Single Doses Enables Broad Therapeutic Index

Lower Doses	Aducanumab[1] (30 mg/kg)	Donanemab[2] (20 mg/kg)	Lecanemab[3] (15 mg/kg)	ACU193[4,5] (25 mg/kg)
ARIA-E rate	0% (0/6)	28.6% (2/7)	0% (0/6)	0% (0/6)
Higher Doses	**Aducanumab[1] (60 mg/kg)**	**Donanemab[2] (40 mg/kg)**	**Lecanemab[3]**	**ACU193[4] (60 mg/kg)**
ARIA-E rate	100% (3/3)	50% (2/4)	Not tested	14.3% (2/14)

1. Ferrero et al. Alzheimer's & Dementia: Translational Research & Clinical Interventions 2 (2016) 169-176 (3 of 3 ARIA-E cases symptomatic).
2. Lowe et al. J Prev Alz Dis 2021; Published online http://dx.doi.org/10.14283/jpad.2021.56 (2 of 12 total ARIA-E cases symptomatic).
3. Logovinsky et al. Alzheimer's Research & Therapy (2016) 8:14 DOI 10.1186/s13195-016-0181-2.
4. Acumen Pharmaceuticals, data on file (1 of 2 ARIA-E cases symptomatic).
5. For 25 mg/kg dosing level, analyzed SAD patient group (6 patients) instead of both SAD and MAD because MRIs were after the *second* dose of MAD (dosing was Q2W and first MRI was on Day 28)

Note: There have been no head-to-head clinical trials between any of the product candidates listed above. Study designs and protocols for each product candidate were different, and as a result, results may not be comparable between product candidates.

Low levels of ARIA-E at elevated single doses compared with aducanumab and donanemab, as was expected, and now is confirmed

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Proof of Mechanism Demonstrated

Low Levels of ARIA-E, Dose-Related Target Engagement, CSF ACU193 Levels Exceeding AβO Levels, Supporting Q4W Dosing

		Potentially Therapeutic Doses		
Endpoint	**Critical Success Factors**	**10mg/kg**	**25mg/kg**	**60mg/kg**
Safety & Tolerability	• Deaths, SAEs Related to Study Drug	**None**	**None**	**None**
	• Any ARIA-E	1/14 (7.1%)	1/14 (7.1%)	3/14 (21.4%)
	• Symptomatic ARIA-E	0/14 (0.0%)	0/14 (0.0%)	1/14 (7.1%)
PK	• Consistent Dose-Related PK • CSF Exposure Above Oligomer Levels	**Achieved** (***Significantly Higher*** *than Reported Aβ Oligomer Levels)*	**Achieved** (***Orders of Magnitude Higher*** *than Reported Aβ Oligomer Levels)*	**Achieved** (***Orders of Magnitude Higher*** *than Reported Aβ Oligomer Levels)*
Target Engagement	• Measurement of ACU193-Aβ Oligomer Complex in CSF	**Measurement Achieved**	**Dose-Related; Nearing Max Target Engagement**	**Dose-Related; Nearing Max Target Engagement**
Amyloid PET	• Reduction in Amyloid PET in Centiloids	**No Reduction Observed**	**Reduction within MAD Cohort** *(p = 0.01)*	**Reduction within MAD Cohort** *(p = 0.01)*

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INTERCEPT-AD Summary

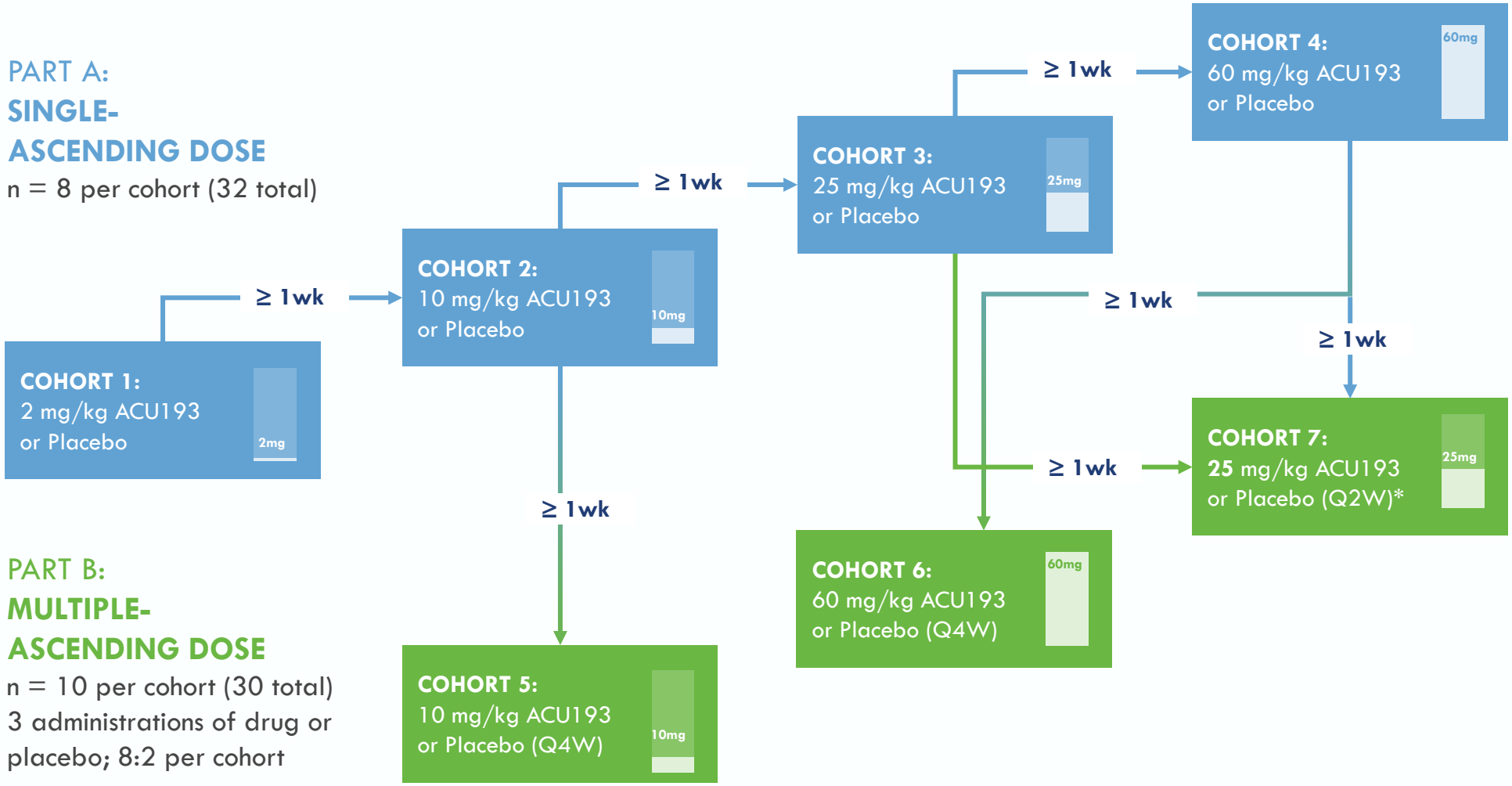
Design	Robust and well-designed study with well established (PK, ARIA) and novel endpoints (AβO target engagement, COGState/ASL)
Execution	60 patients completed the study
Data	Proof-of-Mechanism achieved and new learnings demonstrated through statistically significant plaque reduction shown in highest MAD dose cohorts
Dosing	Optionality for dose in next phase of development (Proof of Concept) – broad therapeutic index due to higher doses nearing maximal target engagement
Team	Former Eli Lilly AD Development Team executing ACU193 trials since initiation of Phase 1 & plans to advance program into next stage of development

INTERCEPT-AD Topline Results

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

PART A:
SINGLE-ASCENDING DOSE
n = 8 per cohort (32 total)

PART B:
MULTIPLE-ASCENDING DOSE
n = 10 per cohort (30 total)
3 administrations of drug or placebo; 8:2 per cohort



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

INTERCEPT-AD Baseline Characteristics

Modified intent to treat

Characteristic	ACU193 N=48	Placebo N=14
Age, mean (SD)	72.3 (7.9)	71.5 (7.5)
Gender Female, n (%)	27 (56.3)	7 (50)
Race Caucasian, n (%)	46 (95.8)	14 (100)
Ethnicity non-Latino, n (%)	41 (85.4)	13 (92.9)
BMI, mean (SD)	28.0 (5.4)	28.9 (5.7)
MMSE, mean (SD)	24.1 (3.7)	24.8 (3.6)
CDR-GS, mean (SD)	0.6 (0.3)	0.6 (0.2)
CDR-SB, mean (SD)	3.6 (1.9)	3.2 (1.8)
APOE4 homozygote, n (%)	6 (12.5)	2 (14.3)
APOE4 heterozygote, n (%)	21 (43.8)	8 (57.1)

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Treatment Emergent SAEs

Treatment Assignment	SAE Verbatim	Severity	Relationship	Action Taken	Outcome
10mg/kg (Cohort 5, MAD)	Ovarian Fibroma	3	**Not Related**	Dose Not Changed	Resolved
10mg/kg (Cohort 5, MAD)	Pneumonia	3	**Unlikely Related**	Dose Not Changed	Resolved
10mg/kg (Cohort 5, MAD)	Altered Mental Status	2	**Not Related**	Dose Not Changed	Resolved

All SAEs for patients taking ACU193 were deemed unrelated or unlikely related by the site Principal Investigator

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TEAEs >3% and ACU193>Placebo

TEAE	ACU193 (N=48) n (%)	Placebo (N=14) n (%)
≥ 1 TEAE	27 (56.3)	6 (42.9)
COVID-19	3 (6.3)	0
Bronchitis	2 (4.2)	0
Headache	2 (4.2)	0
ARIA-H	4 (8.3)	1 (7.1)
ARIA-E	5 (10.4)	0
Hypersensitivity	3 (6.3)	0
Fall	2 (4.2)	0
Post LP syndrome	2 (4.2)	0

ARIA-E Summary for INTERCEPT-AD

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		

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

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			

PBO: Patient on placebo

No ε4 homozygotes developed ARIA-E despite comprising 13% in study;
4/5 ARIA-E cases are ε4 heterozygotes which comprise 47% of our study population

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Safety Update: ARIA-E, Total 5 Cases

Cohort	ApoE4	Gender	Age	Baseline/Endpoint Plaque Load (Centiloids)	Severity by FDA Criteria
C4 SAD 60 mg/kg	**Heterozygote**	**F**	**58**	93.1/83.8	Moderate - Asymptomatic
C5 10 mg/kg Q4W	**Heterozygote**	**F**	**72**	78.2/62.2	Mild - Asymptomatic 3rd/final dose on D56
C6 60 mg/kg Q4W	**Heterozygote**	**F**	**80**	89.1/46.9	Moderate - **Symptomatic** (R leg dysfunction) 1 dose at BL; 2 remaining doses withheld
C6 60 mg/kg Q4W	**NonCarrier**	**F**	**56**	111.2/80.7	Mild - Asymptomatic 3rd/final dose on D56
C7 25 mg/kg Q2W	**Heterozygote**	**F**	**70**	69.3/59.6	Moderate - Asymptomatic 3rd/final dose on D28 D28 ARIA-E (mild) noted in retrospective review

Of 5 total ARIA-E cases, 1 was symptomatic (2.1% overall) and symptoms resolved with resolution of radiographic ARIA-E; All cases showed radiographic resolution or improvement

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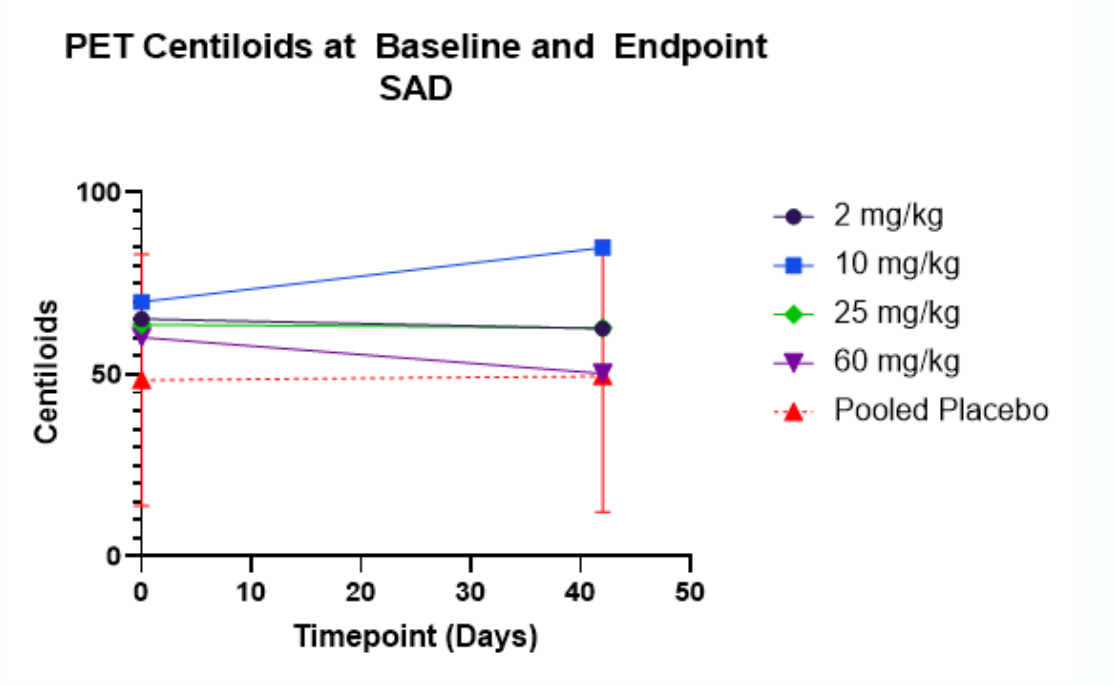
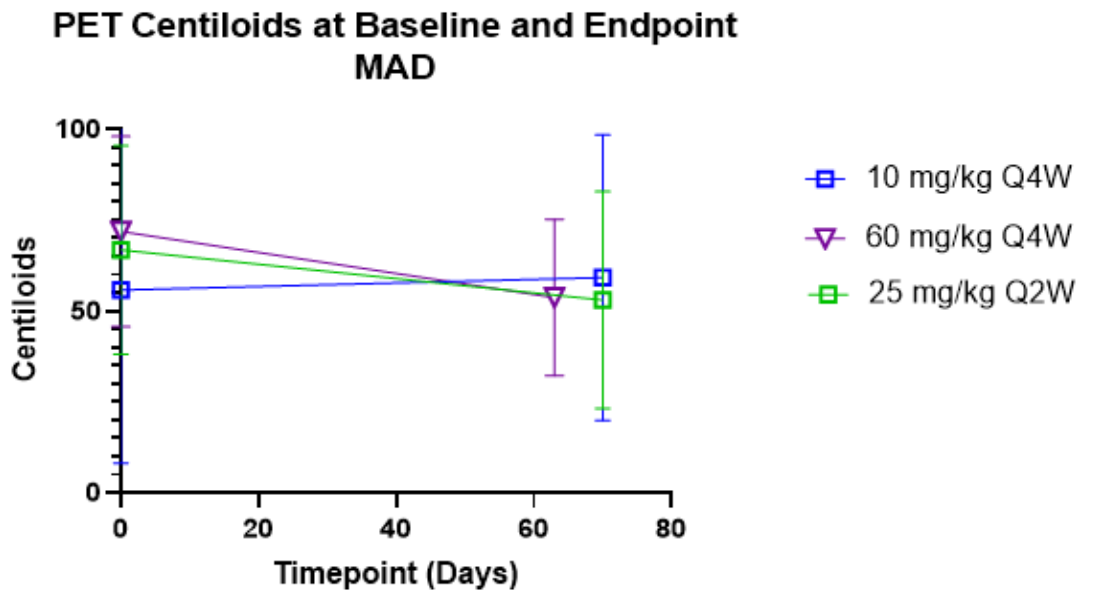
Aβ PET: Mean Changes in Amyloid Plaque in SAD and MAD Cohorts

Single Dose Cohorts



Means ± SD. Error bars shown only for pooled placebo group.

Multiple Dose Cohorts*+



Means ± SD.

Rapid, dose-related, statistically significant reduction of plaque load based on florbetapir PET present in 60 mg/kg Q4W and 25 mg/kg Q2W cohorts

*Placebo patients not included in MAD due to limited patient numbers and varying data collection time points.

+p=0.01 from baseline to endpoint within cohorts 6 (60mg/kg Q4W) and 7 (25mg/kg Q2W)

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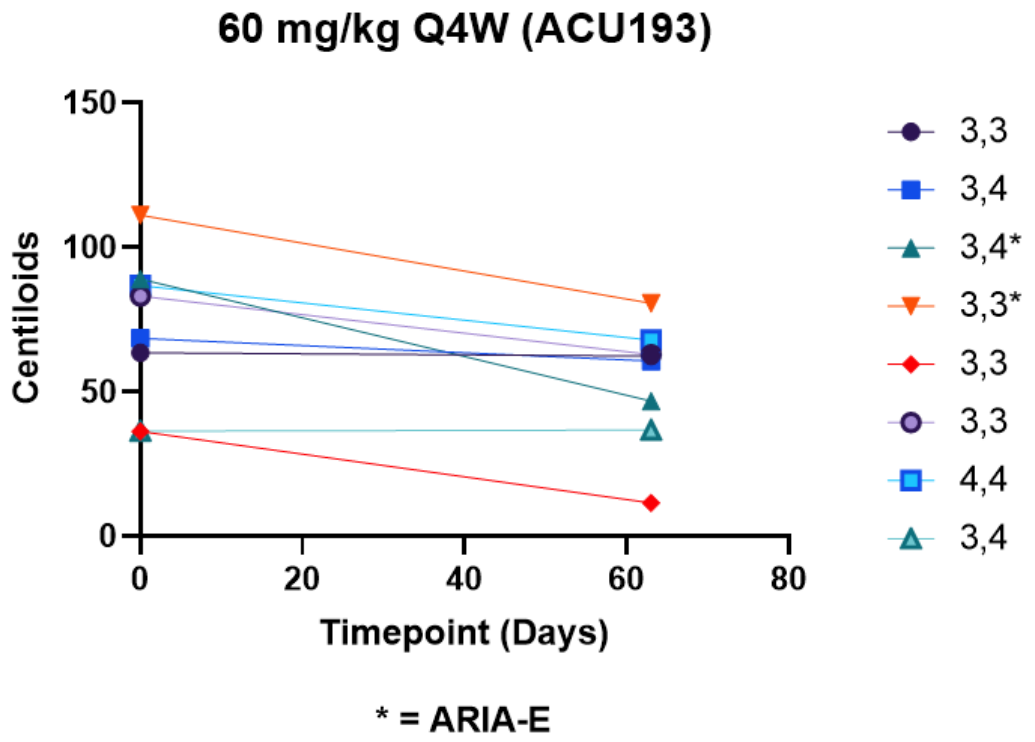
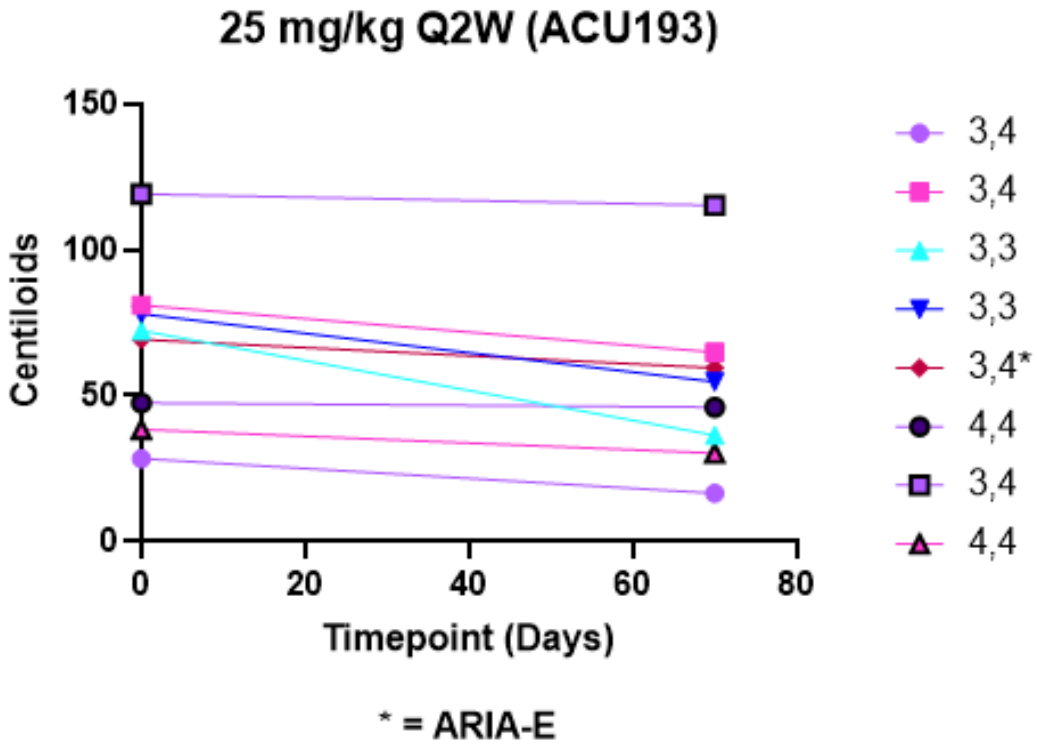
Aβ PET: Individual Patient Changes in Amyloid Plaque in Cohort 6 at 60 mg/kg Q4W and Cohort 7 at 25 mg/kg Q2W

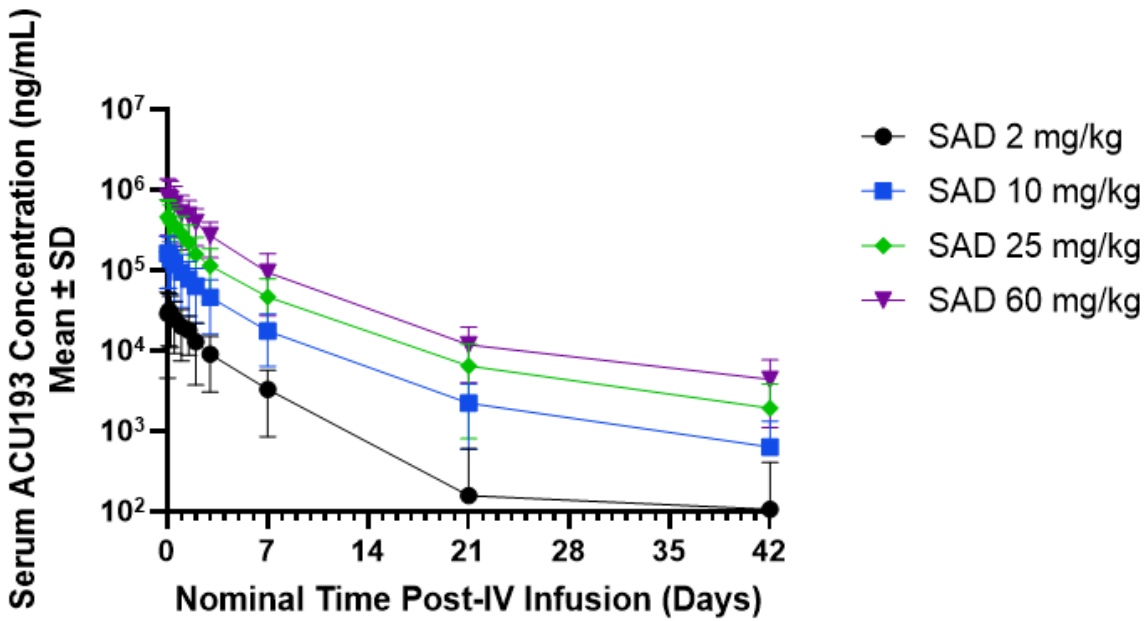




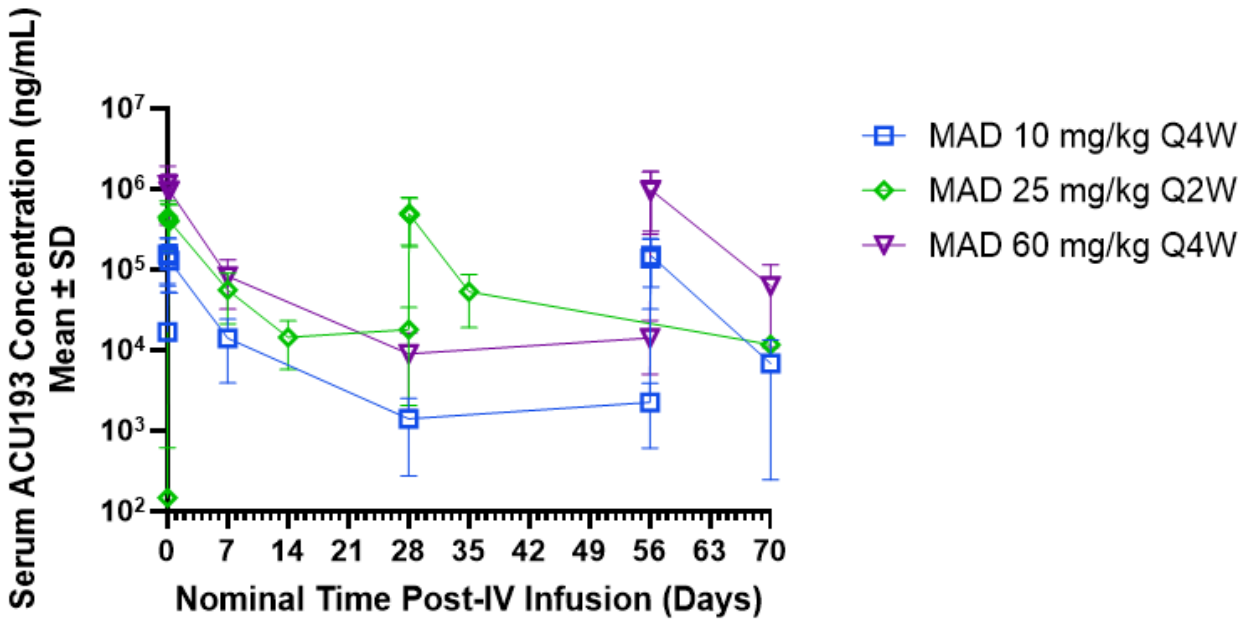
Majority of patients in 60 mg/kg Q4W and 25 mg/kg Q2W cohorts showed reductions in plaque load after 63 or 70 days

ACU193 Serum PK

Single Dose Cohorts



Multiple Dose Cohorts



Serum exposure is dose proportional without accumulation

Estimated serum terminal $T_{1/2}$ of 5-7 days

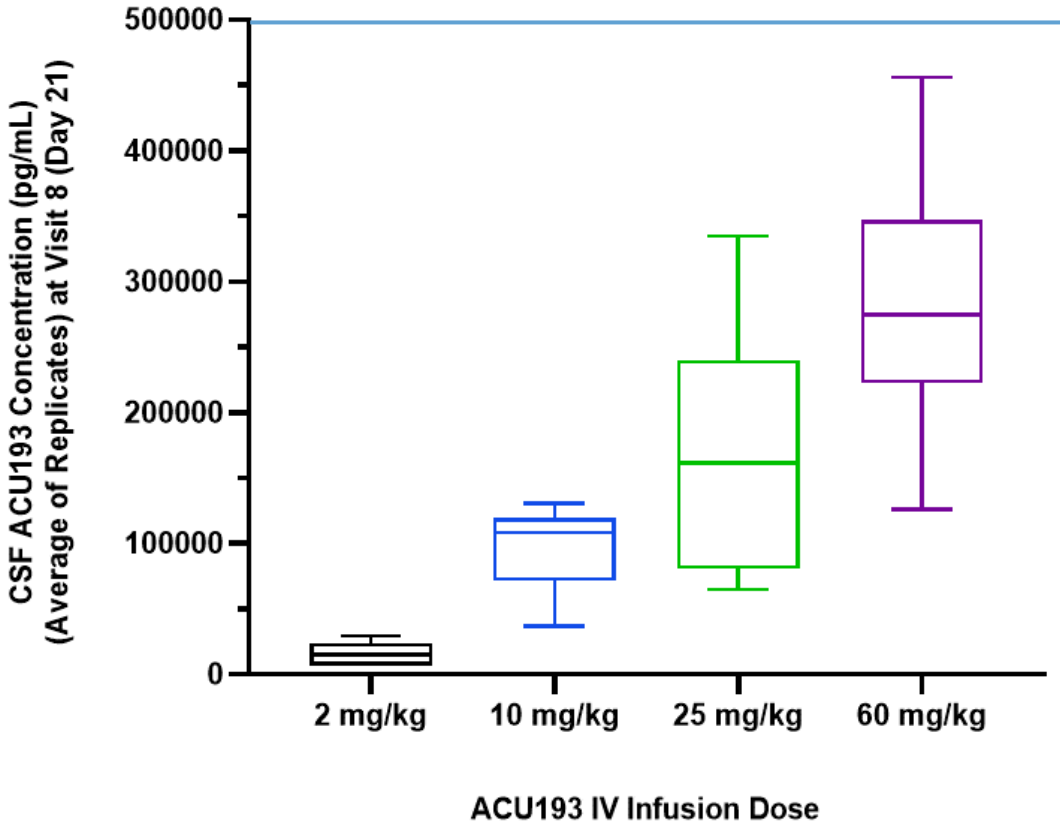
Immunogenicity (preliminary assessment)

- Some evidence of treatment emergent immunogenicity was observed
- Observations more common in the MAD cohorts vs. SAD cohorts
- Treatment emergent ADAs are consistently low titer
- Preliminary assessment reveals no apparent effect on serum PK

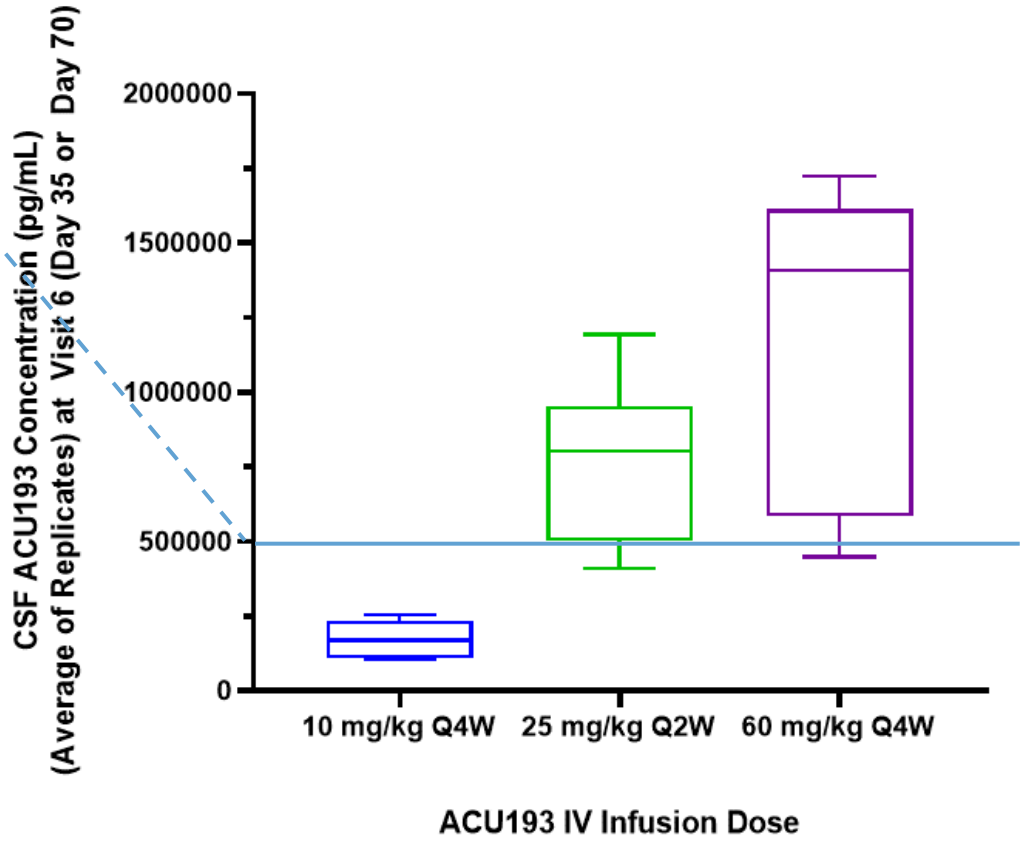
Evidence of low titer treatment emergent immunogenicity

Dose-Related CSF ACU193 Exposure: Above Endogenous CSF AβO Levels

Single Dose Cohorts



Multiple Dose Cohorts*

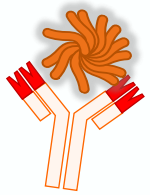


CSF exposure is dose & dose-regimen proportional

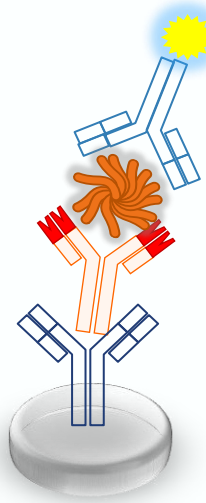
*One patient from Cohort 5 (10 mg/kg Q4W) excluded because only received one administration of drug (study drug discontinued after lacunar infarct).

Target Engagement Assessed by Measuring ACU193-AβO Complex in CSF

ACU193-AβO Complex



MSD S-Plex (Turbo) Immunoassay



AβO selective detection
(anti-AβO mAb)

Only drug/oligomer complex is measurable

ACU193 drug specific capture
(anti-ACU193 idiotype mAb)

Novel assay configuration tailored to selectively detect ACU193-AβO complex in CSF as direct measure of target engagement

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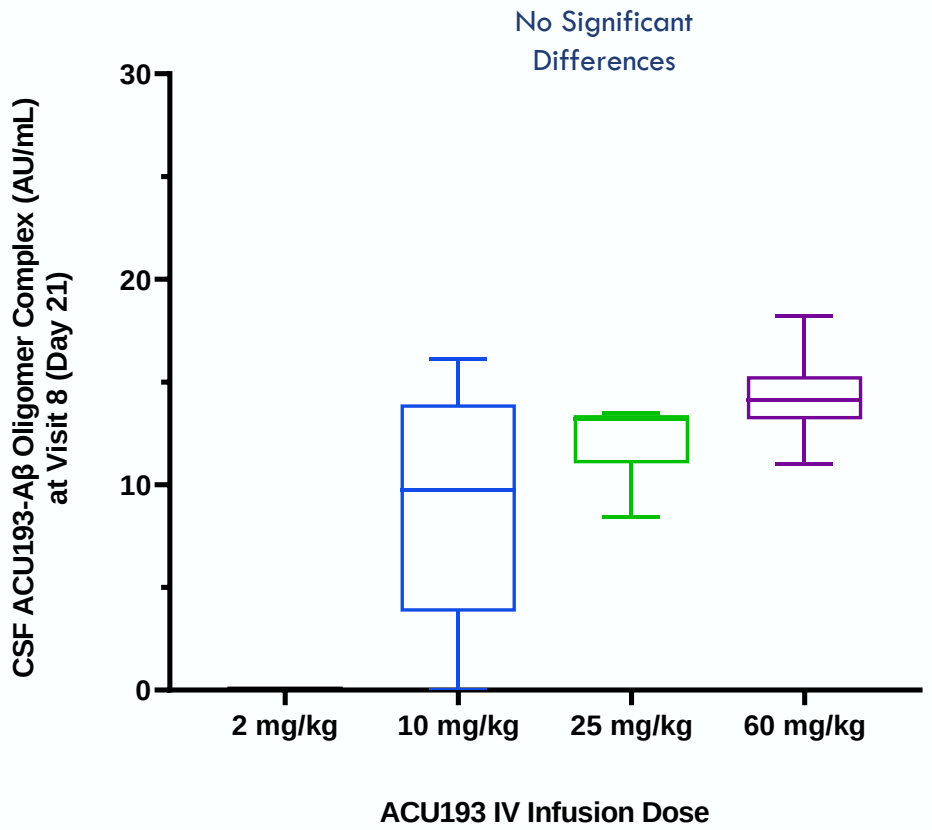
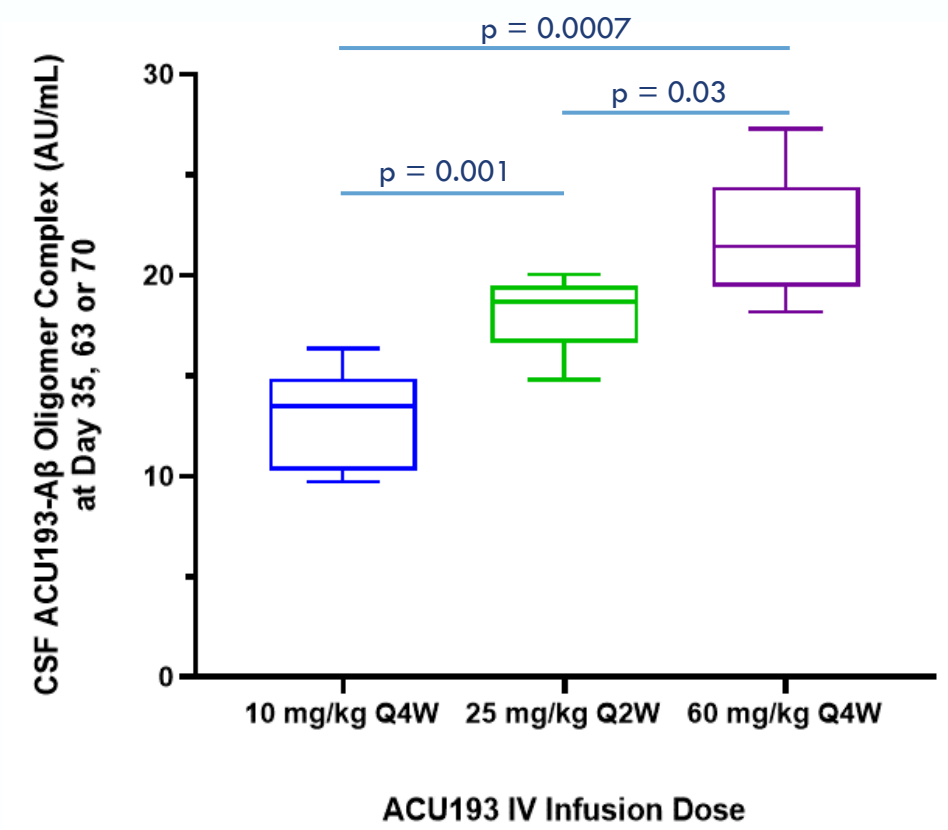
Target Engagement of ACU193 with AβOs is Dose Proportional

Single Dose Cohorts



Multiple Dose Cohorts*

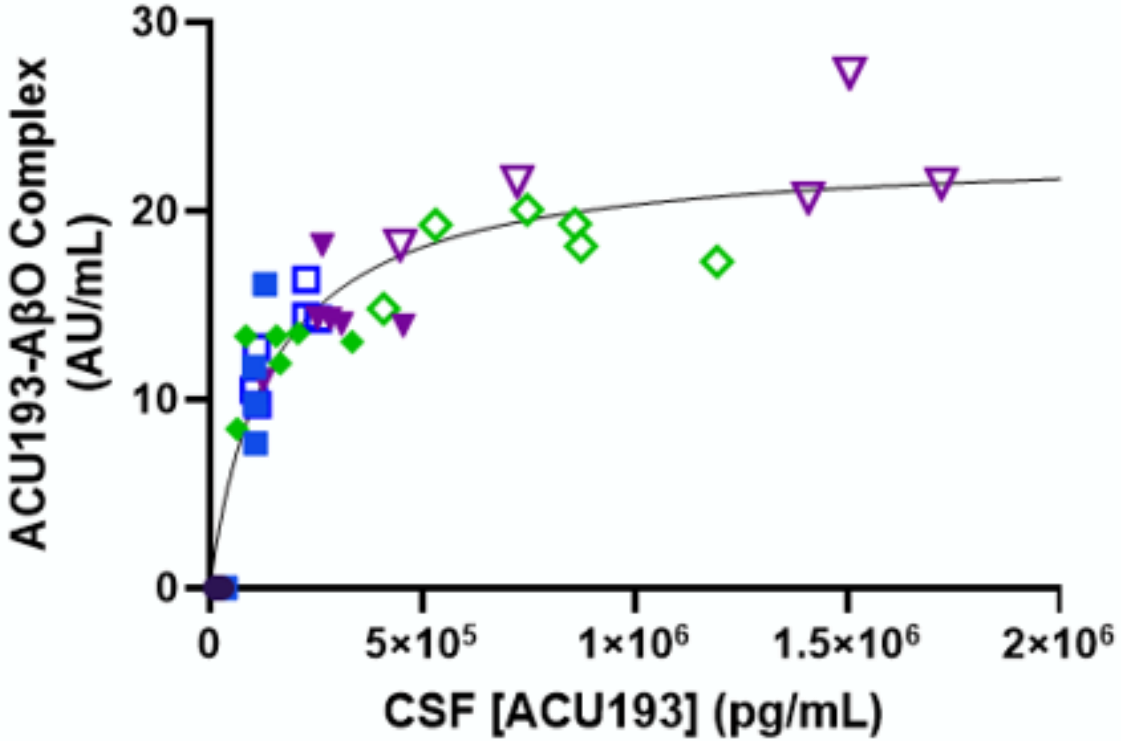


Dose-related target engagement

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

Maximal TE Response Observed at Doses of 25 mg/kg Q2W and 60 mg/kg Q4W

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



Emax: 23.2 AU/mL ACU193-AβO complex
EC50: 1.43 x 10^5 pg/mL ACU193

- 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

Taken together with compelling safety profile and rapid plaque reduction, doses approaching maximal TE should guide dose selection for next study phase

*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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Phase 1 Data Supports Advancing to Phase 2/3

- ☑ Rapid, dose-related, statistically significant amyloid plaque reduction observed within higher dose cohorts
- ☑ Topline results from INTERCEPT-AD trial demonstrated proof-of-mechanism for ACU193, the first clinical stage AβO-targeting antibody
- ☑ ACU193 was well-tolerated in patients with early AD; resulted in no drug-related SAEs; low rate of ARIA-E
- ☑ ACU193 approached maximal central target engagement of toxic AβOs, establishing broad therapeutic index and path to convenient monthly dosing

- Exploratory measures:
  - As expected, no effects observed with clinical cognitive measures
  - As expected, no effects observed with MRI ASL pulse sequence
  - Fluid biomarker data expected late Q3 2023

PROOF OF MECHANISM DEMONSTRATED

RAPID, DOSE-RELATED, STATISTICALLY SIGNIFICANT AMYLOID PLAQUE REDUCTION OBSERVED AT HIGHER DOSES STUDIED

Compelling Safety Profile and CNS Target Engagement;
Monthly Dosing Supported

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Future Strategic Plans

- Anticipated interaction with the FDA in Q4 2023 to inform our proposed Phase 2/3 study
- Further investigate the development of a subcutaneous administration of ACU193
- Evaluate potential next generation product opportunities
- Explore partnership opportunities that have the potential to enhance shareholder value

Q&A

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