Investor Presentation

NASDAQ: ACIU | June 2026

AC Immune

Disclaimer

This presentation contains statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements are statements other than historical fact and may include statements that address future operating, financial or business performance or AC Immune's strategies or expectations. In some cases, you can identify these statements by forward-looking words such as "may," "might," "will," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "outlook" or "continue," and other comparable terminology. Forward-looking statements are based on management's current expectations and beliefs and involve significant risks and uncertainties that could cause actual results, developments and business decisions to differ materially from those contemplated by these statements. These risks and uncertainties include those described under the captions "Item 3. Key Information – Risk Factors" and "Item 5. Operating and Financial Review and Prospects" in AC Immune's Annual Report on Form 20-F and other filings with the Securities and Exchange Commission. These include: the impact of Covid-19 on our business, suppliers, patients and employees and any other impact of Covid-19. Forward-looking statements speak only as of the date they are made, and AC Immune does not undertake any obligation to update them in light of new information, future developments or otherwise, except as may be required under applicable law. All forward-looking statements are qualified in their entirety by this cautionary statement.

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AC Immune – pioneering precision prevention of neurodegeneration

Next generation Precision Medicine for neurodegenerative diseases

Focused pipeline with active immunotherapies and intracellular targeted small molecule programs

Key differentiation: Precision Prevention enabled by leadership in targeting toxic proteins

Differentiated technology platforms validated through multiple clinical candidates and pharma partnering deals

Partnering: strategic, risk-mitigating, timely, monetization with >CHF 4.3 billion in potential milestones

Cash reserves on Balance sheet
Funding into Q4 2027

- Based in Lausanne, Switzerland
- ~120 employees
- Listed on NASDAQ: ACIU
- 102 million shares outstanding[1]
- Cash resources of CHF 74.8 million[2]

Takeda
Janssen
Pharmaceutical Companies of Johnson & Johnson
Lilly
LANTHEUS

(1) As of March 31, 2026; excluding treasury shares; (2) As of March 31, 2026 (~USD 94 million)

AC Immune

Pipeline focused on Precision Prevention for neurodegenerative diseases:

Active Immunotherapies and Intracellular Targeting

Modality	Candidate	Partner	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Active Immunotherapy	ACI-35 (JNJ-2056)	Janssen	Alzheimer's disease (*pTau*[1])				FDA Fast Track	
	ACI-24	Takeda	Alzheimer's disease (*Abeta*[2])				FDA Fast Track	
			Alzheimer's disease: Down Syndrome					
	ACI-7104		Parkinson's disease (*a-syn*[3])					
Intracellular Targeting	ACI-19764		Neuro-inflammation (*NLRP3* [4])					
	Morphomer Tau	Lilly	Alzheimer's disease (*Tau*)					
	Morphomer® a-syn		Parkinson's disease (*a-syn*)					
Tracer	PI-2620	LANTHEUS	Alzheimer's disease, PSP[5] and others (*Tau*)				FDA Fast Track	

(1) Phosphorylated Tau; (2) amyloid beta; (3) alpha-synuclein; (4) (NOD)-like receptor protein 3; (5) Progressive supranuclear palsy

Key milestones 2026

Multiple catalysts across pipeline

● Readouts
○ Other development events

Active immunotherapies		H1 2026	H2 2026	
ACI-24 (Takeda)	Abeta	✓		ABATE Phase 2 trial in AD[1]: first patient dosed in AD4 cohort
		●		**ABATE Phase 2 trial readouts after 12 months of treatment (AD3: Abeta PET)**
ACI-7104	a-syn[3]	✓		Submissions to regulators regarding clinical development plan
			●	**Phase 2 VacSYn trial in PD[2]: end of Part 1 study clinical results**
			○	IND[4]/CTA[5] filing for next clinical trial
Small molecule drugs				
NLRP3 inhibitor (ACI-19764)	NLRP3[6]	✓		Phase 1 clinical trial in healthy volunteers initiated
			●	**Phase 1 clinical trial in healthy volunteers completed**
Morphomer-Tau (Lilly)	Tau	○		Initiation of IND-enabling studies in partnership with Lilly
Morphomer a-syn	a-syn		○	Readiness to initiate IND-enabling studies

(1) Alzheimer's disease; (2) Parkinson's disease; (3) Alpha-synuclein; (4) Investigational new drug; (5) Clinical Trial Application; (6) (NOD)-like receptor protein;

AC Immune's four core value drivers

Combining biomarker-based clinical development, validated targets and strong collaborations

ACI-35 anti-pTau

The only active immunotherapy in a prevention study for pre-symptomatic Alzheimer's disease

ACI-24 anti-Abeta

Biomarker-driven development targeting the hallmark protein in Alzheimer's disease and Alzheimer's in Down syndrome

ACI-7104 anti-a-syn

Active immunotherapy targeting pathological a-syn in early-stage Parkinson's disease

Intracellular targeting

Small molecule programs targeting intracellular pathologies:

- Tau (Lilly)
- a-syn
- NLRP3 inflammasome

Parkinson’s disease

Pathological deposition of alpha-synuclein

Most common neurodegenerative movement disorder
Affects ~1% of the population over 65 years

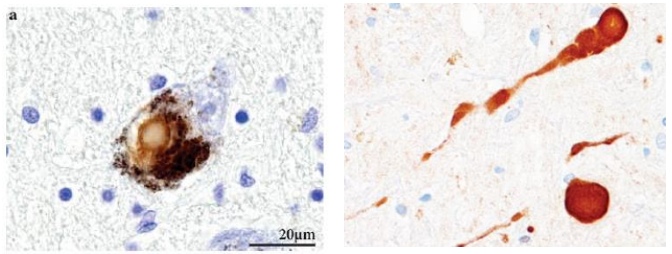
Etiology
5-10% genetic, 90-95% idiopathic, unknown cause

Cardinal motor symptoms
Tremor, rigidity, bradykinesia

Common non-motor symptoms
Sleep disorder, depression, cognitive impairment

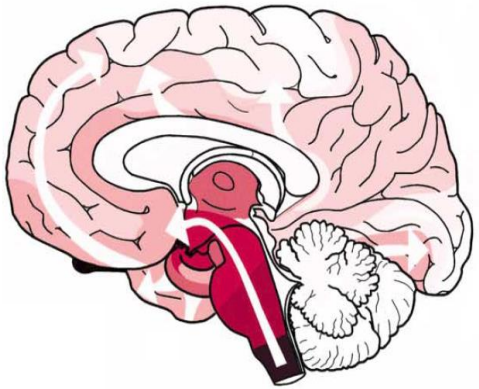
Pathological hallmarks
Neuron loss, alpha-synuclein aggregates – Lewy bodies

Main component of Lewy bodies: Alpha-synuclein



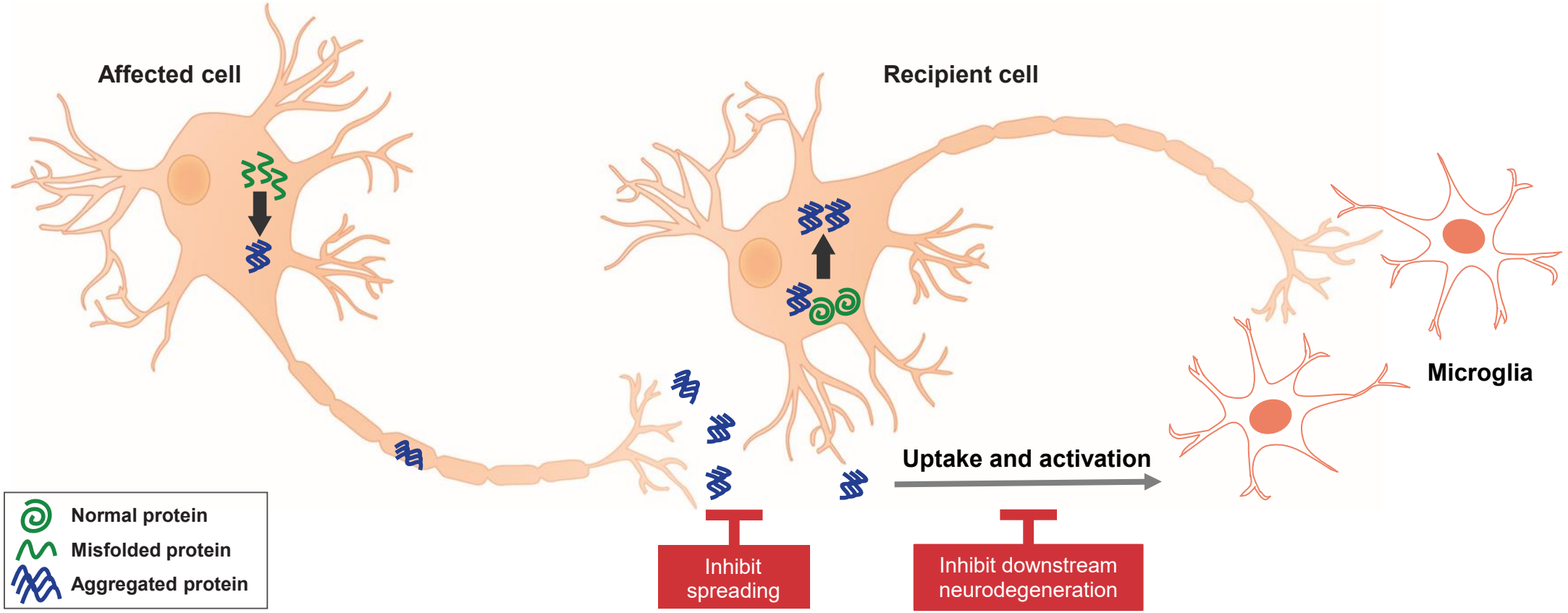
Halliday *et al.* 2011

Progression of pathology



Braak *et al.* 2003

Pathological oligomeric a-syn[1] is causally linked to PD[2] and other NDD[3]



- A-syn misfolding and aggregation are the molecular basis for a-synucleinopathies, e.g. PD, DLB[4] and MSA[5]
- Seeding and spreading of a-syn are potential drivers of disease progression

(1) Alpha-synuclein; (2) Parkinson's disease; (3) Neurodegenerative diseases; (4) Dementia with Lewy bodies; (5) Multiple system atrophy

VacSYn: Adaptive biomarker-based Phase 2 study of ACI-7104 in early PD

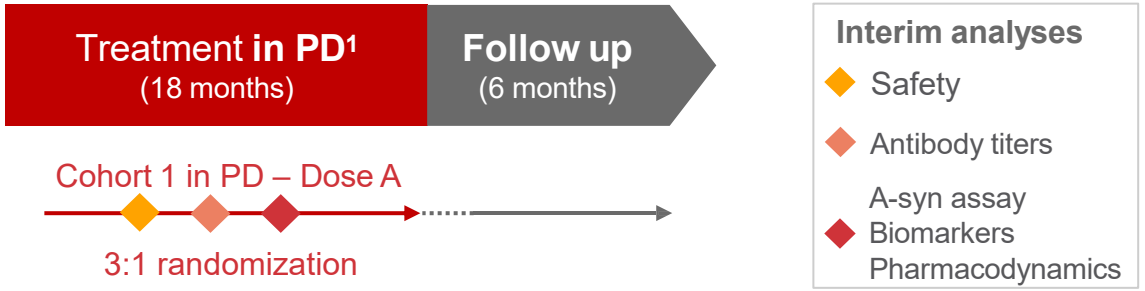
Placebo-controlled Phase 2 Study Overview (clinicaltrials.gov identifier: NCT06015841)

All participants from Part 1 will contribute to final analysis

Biomarker based interim analyses
- Early immunogenicity to tailor dose and/or dose regimen
- Apply disease-relevant biomarkers for early transition to filing

Part 1: Safety & PK/PD

- Key immunogenicity measures
- Measures of pathological a-syn (a-syn oligomers and aggregates)



Part 2: Proof of Concept in Early PD

- Motor and Non-Motor Functioning (UPDRS[2] based)
- Degeneration of dopaminergic terminals (DaT SPECT[3] imaging)
- Advanced MRI (including ASL[4] and DTI[5])
- Digital biomarkers of motor and non-motor function
- Functional and patient reported outcomes

(1) Participants must have idiopathic PD and be stable on up to 300 mg of L-Dopa treatment and dopaminergic deficit determined by Dopamine Transporter Single Photon Emission Computed Tomography; (2) Unified Parkinson's disease rating scale; (3) Dopamine Transporter Single Photon Emission Computed Tomography; (4) Arterial spin labeling; (5) Diffusion tensor imaging

VacSYn an adaptive biomarker-based Phase 2 study of ACI-7104 in early PD[1]

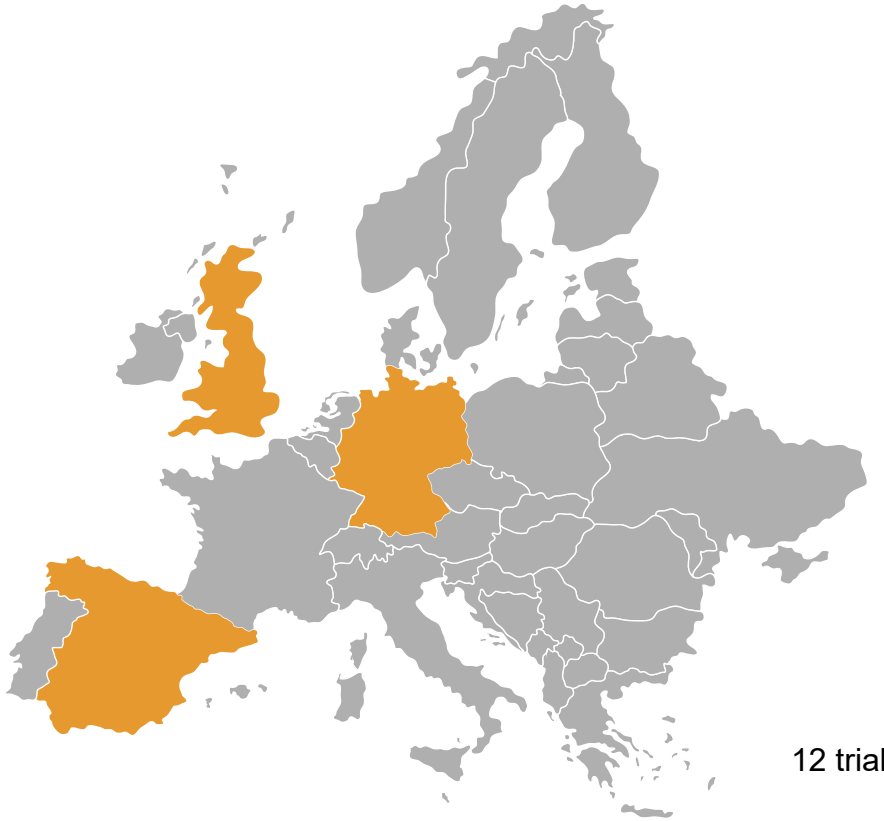
Key Inclusion and Exclusion Criteria

Key Inclusion Criteria

- Aged ≥40 to ≤75 years
- Diagnosis of clinically established early PD[1] (confirmed by DaT-SPECT[2])
- ≤ 2 years from time of onset motor symptoms
- H&Y[3] Stage I to II
- Monotherapy treatment with L-Dopa[4] at 300 mg per day or treatment naïve

Key Exclusion Criteria

- Carriers of certain familial PD[1] gene mutations
- Parkinsonian syndrome other than idiopathic PD[1]
- Significant CNS[5] disease[6]



12 trial sites

- Total enrolment: 34 patients
- In the following analyses, the number of subjects beyond week 50 are expected to increase as participants reach later timepoints

(1) Parkinson's disease; (2) Dopamine Transporter Single Photon Emission Computed Tomography; (3) Hoehn & Yahr scale; (4) Levodopa; (5) Central Nervous System; (6) Parkinsonian syndrome other than idiopathic PD, including but not limited to, progressive supranuclear palsy, multiple system atrophy, drug induced parkinsonism, essential tremor, vascular parkinsonism, primary dystonia.

VacSYn: Patient baseline characteristics and interim safety/tolerability findings

Placebo-controlled Ph 2 Study: No safety concerns raised by DSMB[1,5]

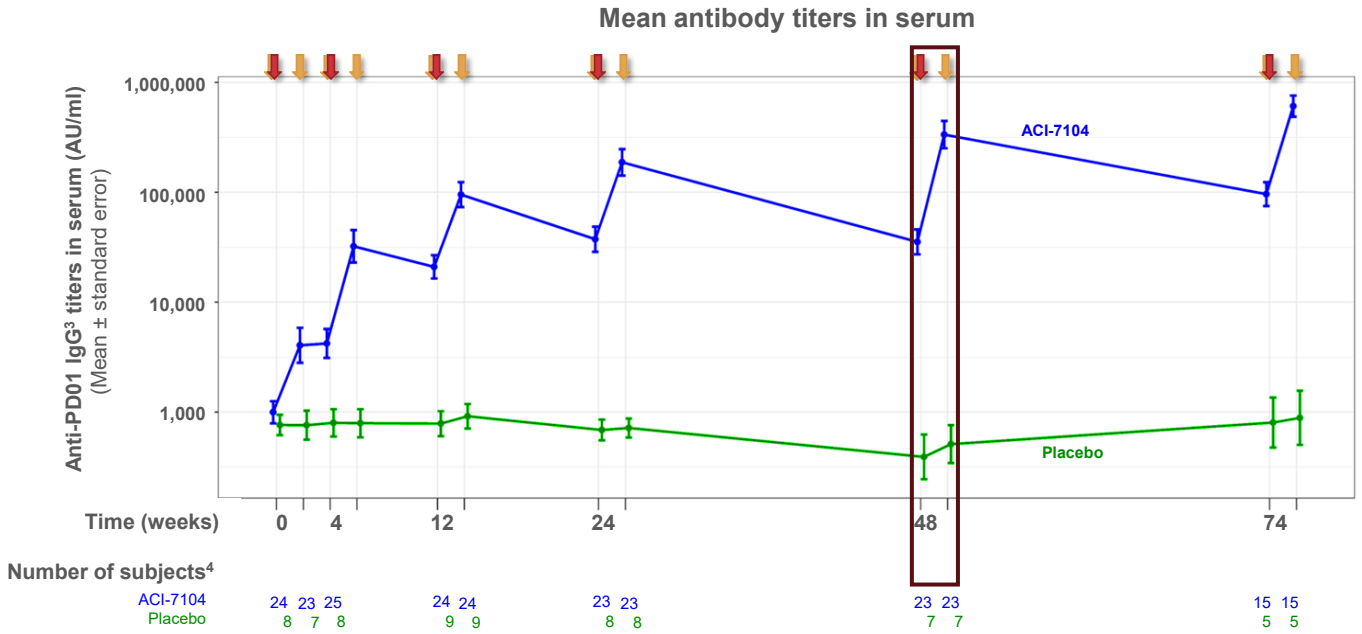
Baseline profile	Unit	Total
Total number of patients	n	34
Age	Years mean (std)	62.1 (6.7)
Sex		
Male	n (%)	22 (65%)
Female	n (%)	12 (35%)
Hoehn and Yahr stage		
Stage I	n (%)	16 (47%)
Stage II	n (%)	18 (53%)
MDS-UPDRS scores		
Part 1: Non-motor experiences of daily living	mean (std)	4.09 (3.1)
Part 2: Non-motor experiences of daily living	mean (std)	4.09 (3.2)
Part 3: Motor examination	mean (std)	21.09 (9.8)
Time since initial PD Diagnosis	Months mean (std)	10.3 (7.5)
PD Treatment		
treatment-naïve	n (%)	11 (32%)
L-Dopa 300mg/day	n (%)	23 (68%)

1. **Overall good safety/tolerability to date**[1]
2. **No SAE**[2] **considered related to the study drug, incl. 1 subject who died during participation in the study (unlikely related to the study drug)**
3. **Two AE leading to discontinuation from the study**[3] **unrelated or unlikely related to study drug**
4. **Most common AEs are transient and generally of mild severity: Injection Site Reactions (55.9%) and headaches (14.7%) and fatigue (11.8%)** [4]
5. **No significant MRI**[6]**, lab, ECG**[7] **abnormalities reported to date**

(1) Data Safety Monitoring Board; (2) Serious Adverse Events: Upper limb fracture, osteoarthritis, perforated appendicitis and intraabdominal sepsis (in the same subject), radical prostatectomy are considered unrelated to study drug, death of unknown cause is considered unlikely related to study drug; (3) One worsening of preexisting generalized anxiety disorder unrelated to study drug and one SAE of death of unknow cause post extraction date; (4) incidence in the pooled active and placebo subjects; (5) Extraction date September 5, 2025; (6) Magnetic Resonance Imaging; (7) Electrocardiogram

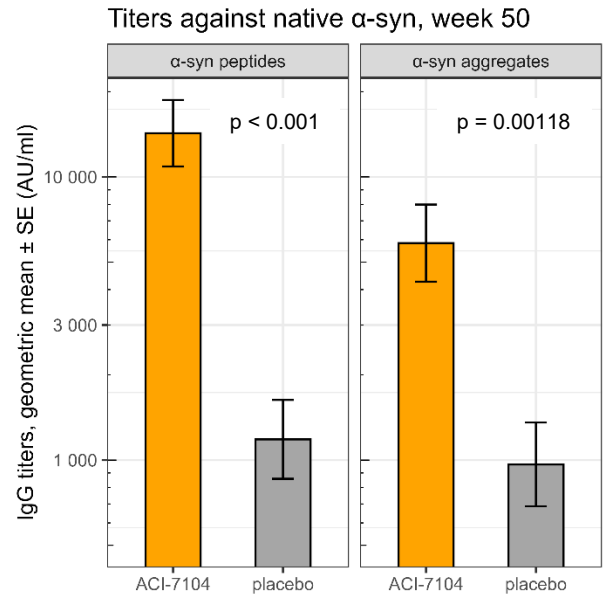
Repeated ACI-7104 immunizations boost anti-a-syn[1] antibody responses

100% responder rate observed for modified a-syn antigen antibody titers in serum



Immunizations at:
0, 4, 12, 24, 48 and 74 weeks

Serum sampling at:
0, 2, 4, 6, 12, 14, 24, 26, 48, 50, 74 and 76 weeks

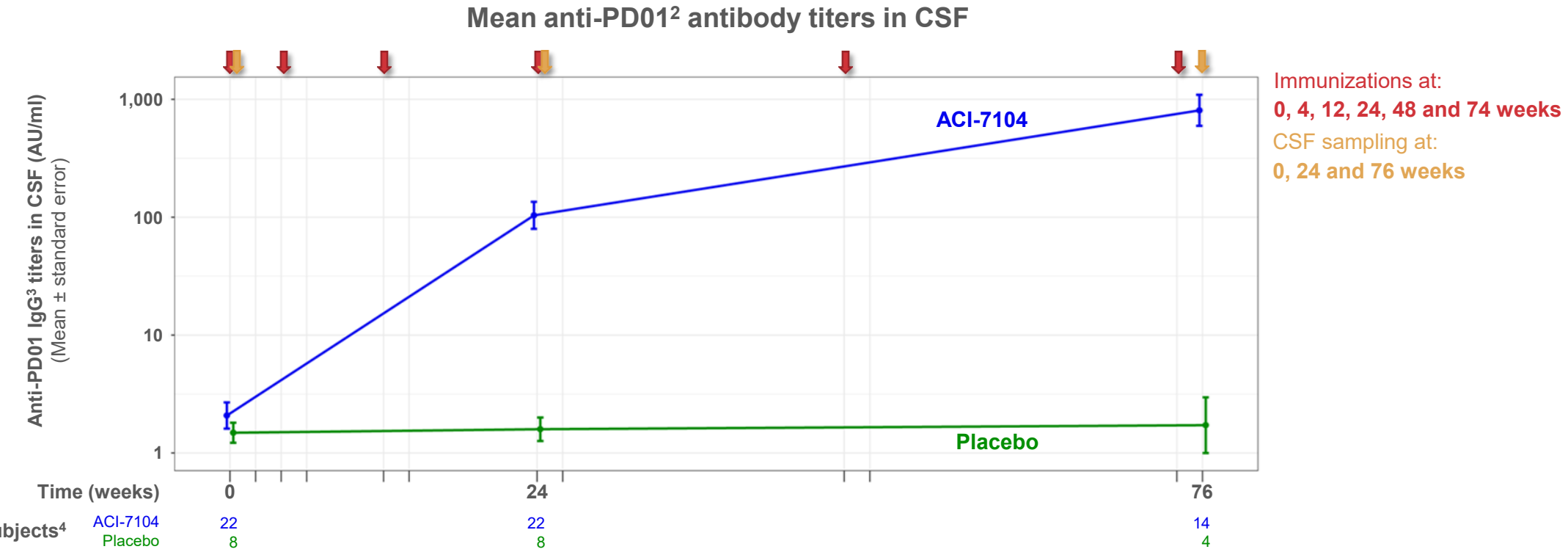


- Antibody responses were boosted after each dose
- ACI-7104-induced antibodies show high reactivity against a-syn peptide and a-syn-aggregates
- The placebo group did not show any detectable change from baseline

(1) Alpha-synuclein; (2) Modified a-syn peptide antigen; (3) Immunoglobulin; (4) Number of subjects beyond week 50 is expected to increase as subjects reach later timepoints.

Antibody titers in CSF[1] increase with successive immunizations

ACI-7104 generates antibodies against modified a-syn that cross the blood-brain barrier

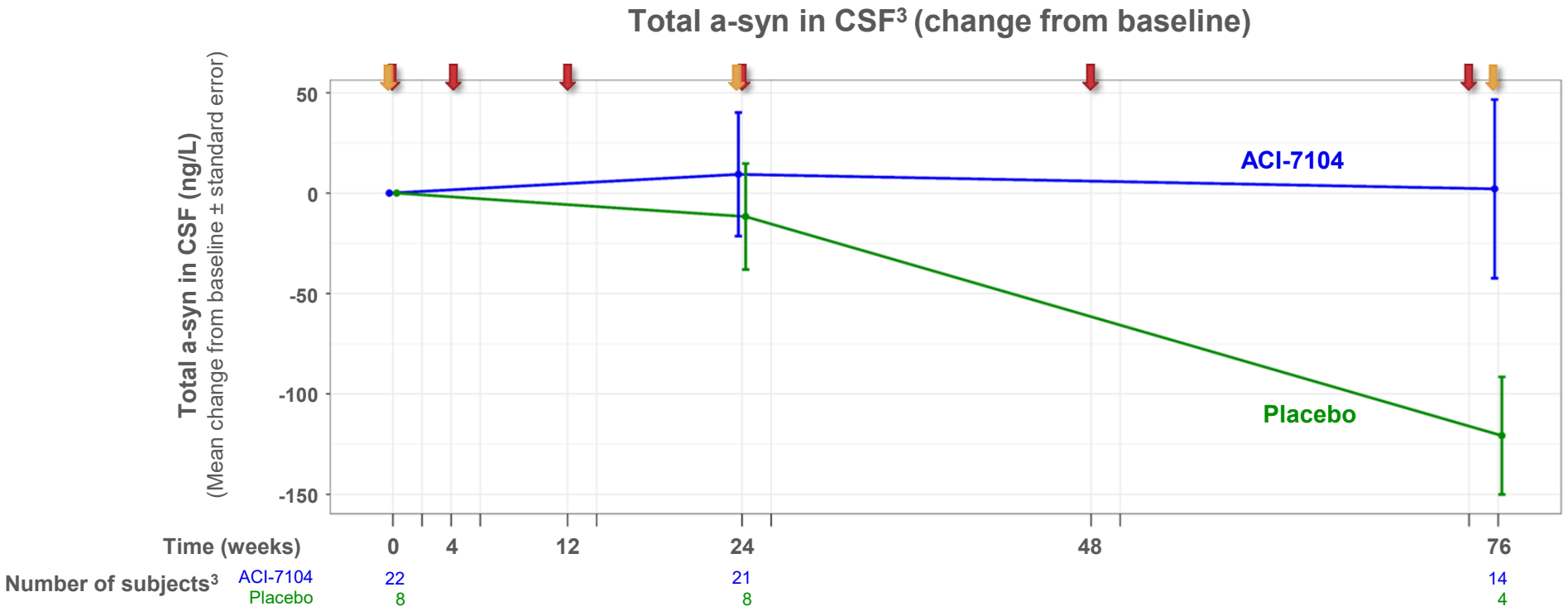


- On average, IgG antibody levels in CSF were an order of magnitude higher after the 6th immunization (week 76) compared to the 3rd immunization (week 24)
- Antibody exposure in the CNS is enhanced with increasing number of doses

(1) Cerebrospinal fluid; (2) Modified a-syn peptide antigen; (3) Immunoglobulin; (3) Number of subjects beyond week 50 is expected to increase as subjects reach later timepoints.

Immunization with ACI-7104 stabilizes total a-syn[1] levels in CSF[2]

ACI-7104-induced anti-a-syn antibodies demonstrate target engagement in CSF



Immunizations at:
0, 4, 12, 24, 48 and 74 weeks
Serum sampling at:
0, 24 and 76 weeks

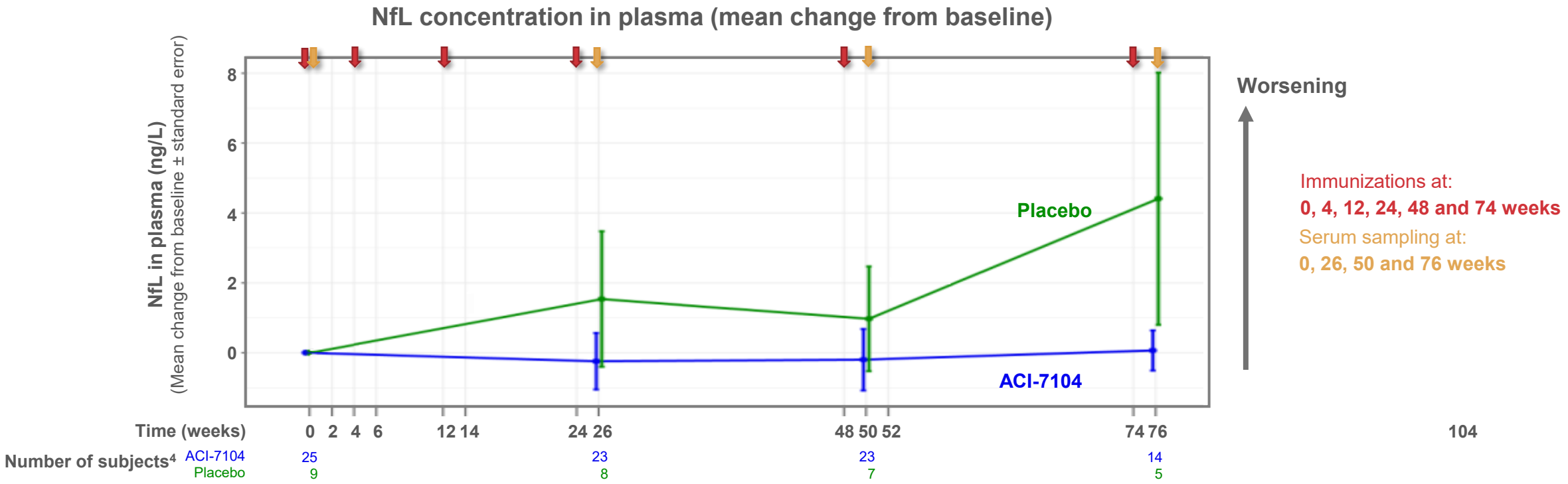
Post-hoc analysis showed a statistically significant difference (p = 0.018, one-sided Welch t-test) at week 76 between active and placebo groups.

- Stabilization of total CSF a-syn levels in treatment arm suggest target engagement
- In the placebo group, a decrease in total CSF a-syn was observed over time

(1) Alpha-synuclein; (2) Cerebrospinal fluid; (3) Number of subjects beyond week 50 is expected to increase as subjects reach later timepoints. One patient with very high a-syn levels at only week 24, likely an outlier value, needs further technical investigation and was removed here.

Stabilization of NfL[1] levels suggests potential slowing of neurodegeneration

Neurofilament light chain in plasma remains at baseline levels after treatment with ACI-7104



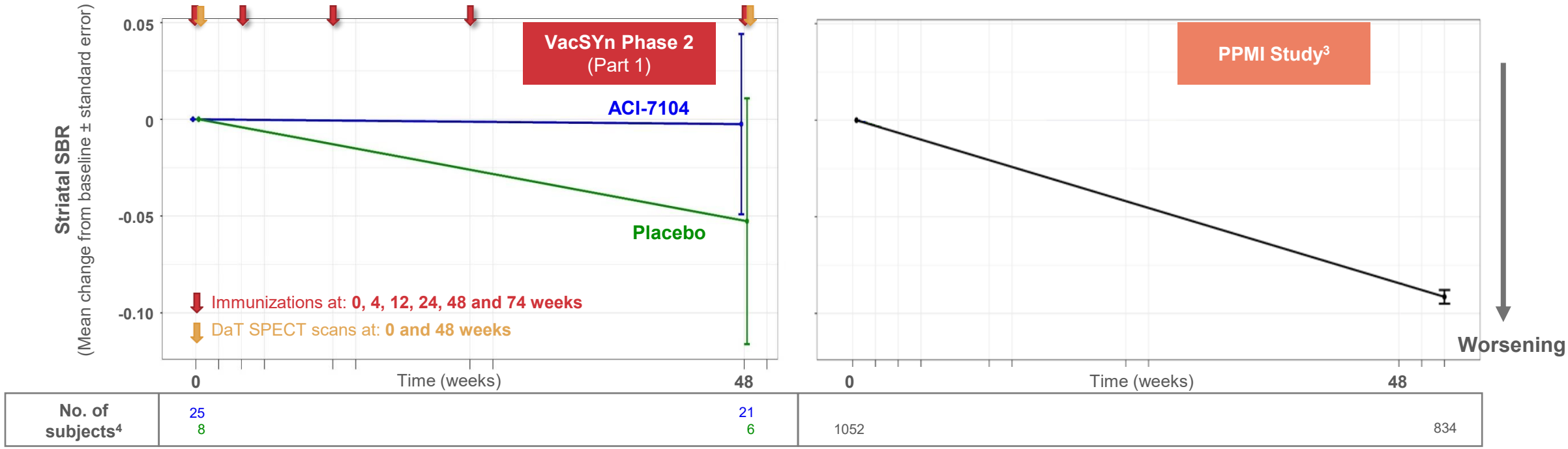
- ACI-7104 group: NfL in plasma and CSF remained stable indicating potential slowing of disease
- Placebo group: NfL in plasma and CSF increases over time, as previously reported in PD[3]

(1) Neurofilament light chain; (2) Cerebrospinal fluid; (3) Parkinson's disease; Mollenhauer *et al.*, Movement Disorders, 2021; (4) Number of subjects beyond week 50 is expected to increase as more subjects reach later timepoints.

Dopamine transporter imaging suggests stabilization of PD[1] pathology

DaT-SPECT[2] scans show degeneration of midbrain dopaminergic neurons

Striatal specific binding ratio (SBR) from DaT-SPECT scans

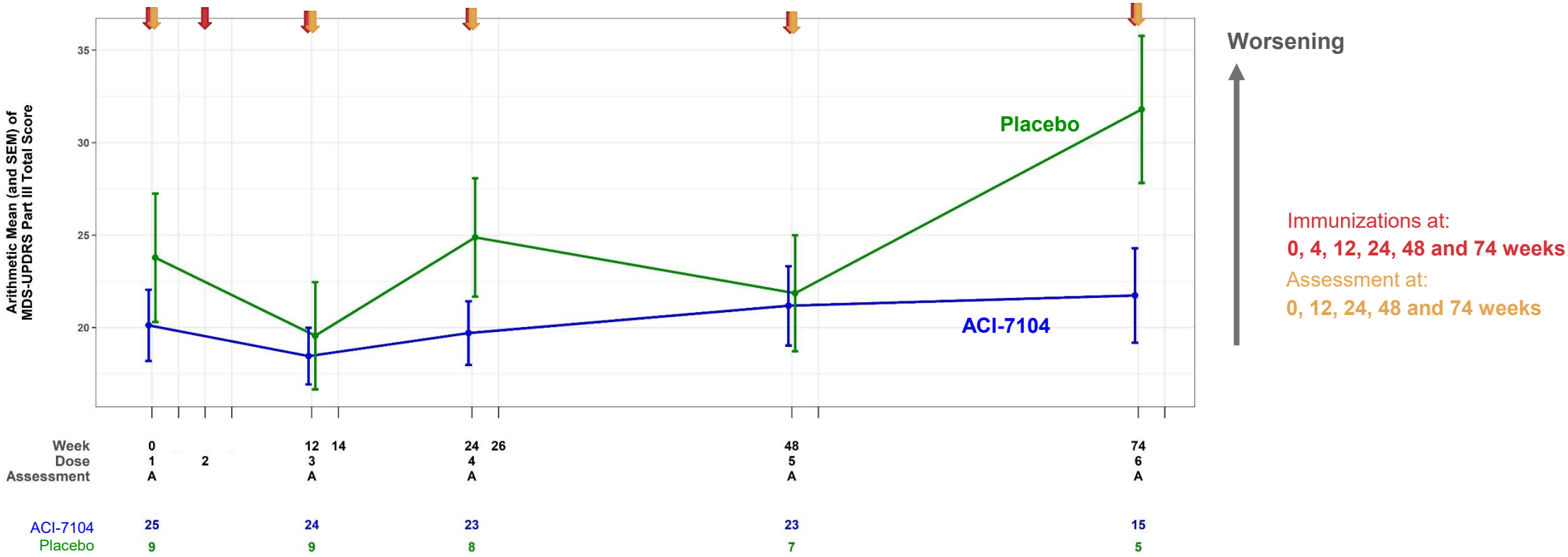


- Lower SBR values in striatum indicate reduced dopaminergic input from the midbrain to the striatum, and are linked to disease progression and motor symptoms
- In the ACI-7104 arm, minimal progression after 48 weeks suggests stabilized pathology

(1) Parkinson's disease; (2) Dopamine transporter single-photon emission computed tomography; (3) Parkinson's Progression Markers Initiative "to identify biological markers of Parkinson's risk, onset and progression"; (4) Number of subjects in VacSYn beyond week 50 is expected to increase as subjects reach later timepoints. One outlier was removed from the placebo group.

Treatment with ACI-7104 limits progression of motor symptoms

MDS-UPDRS[1] Part III examination of motor symptoms suggests faster decline in the placebo group



- The MDS-UPDRS Part III score is expected to increase by 2–3 points per year in early PD[2]
- At week 74, the ACI-7104 group did not show signs of meaningful progression, while the placebo arm trends towards an increase in mean MDS-UPDRS Part III total score

(1) Movement Disorder Society - Unified Parkinson's Disease Rating Scale; (2) Parkinson's disease; Holden *et al.*, Movement Disorders, 2018; (3) Trundell *et al.*, J. of Parkinson's disease, 2025; Horvath *et al.*, Parkinsonism and related disorders, 2015; (4) Number of subjects beyond week 50 is expected to increase as subjects reach later timepoints.

AC Immune

Figure 14.2.4.1.1

Summary – next steps

ACI-7104 to advance

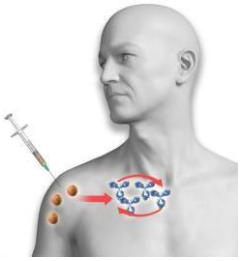
- ACI-7104 modifies disease pathology and appears to delay disease progression
- Suggests potential to slow motor deterioration in patients with early-stage Parkinson's Disease, and to shift from symptomatic treatment to disease modification
- Results support further development of the program and discussion with regulators to establish a clinical development plan towards registration

ACTIVE Immune Therapy

targeting neurodegenerative diseases

Major advantages

- Long-lasting specific immunity for pathological target, consistent, boostable
- Limited annual dosing (once or twice) after priming year
- No observed ARIA-E[1] to date (safety profile well suited to long-term use)
- Ease of administration and simple logistics for global access
- Cost-effective (attractive healthcare economics across global populations)

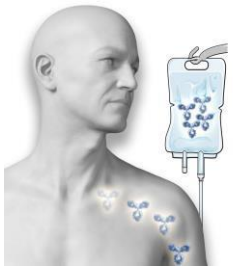


Active immunotherapy

Stimulates the patient's immune system to produce their own polyclonal antibodies

Passive immunotherapy

Externally generated monoclonal antibody requires administration every two to four weeks



(1) Amyloid-related imaging abnormalities-edema

AC Immune's four core value drivers

Combining biomarker-based clinical development, validated targets and strong collaborations

ACI-35 anti-pTau

The only active immunotherapy in a prevention study for pre-symptomatic Alzheimer's disease

ACI-24 anti-Abeta

Biomarker-driven development targeting the hallmark protein in Alzheimer's disease and Alzheimer's in Down syndrome

ACI-7104 anti-a-syn

Active immunotherapy targeting pathological a-syn in early-stage Parkinson's disease

Intracellular targeting

Small molecule programs targeting intracellular pathologies:

- Tau
- a-syn
- NLRP3 inflammasome

Intracellular Targeting for earliest pathology intervention in NDD[1]

Brain penetrant small molecules as a key differentiator

1. Optimal delivery into the central nervous system
2. Cell-penetrant with proven engagement of their specific intracellular target
3. Conformation-specific and highly selective for misfolded forms of target proteins in NDD, i.e. Tau, a-syn[2] and TDP-43 [3]
4. Potential application across all pathological and disease stages
5. Oral, cost-effective and convenient administration

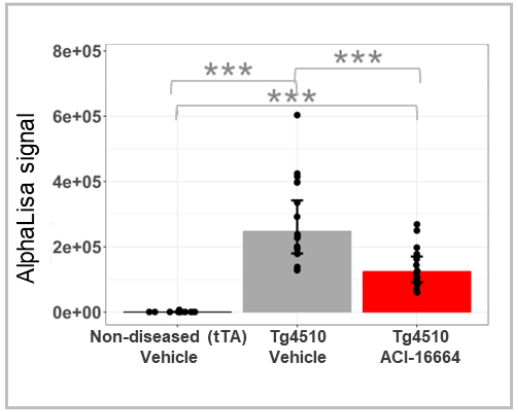
■ Unique product and commercial opportunities over other modalities

(1) Neurodegenerative diseases; (2) Alpha-synuclein; (3) TAR DNA binding protein-43

Tau-targeting Morphomers® halt pathology at multiple points

In vivo efficacy in an aggressive model of Tau pathology[1]

Total Tau aggregates



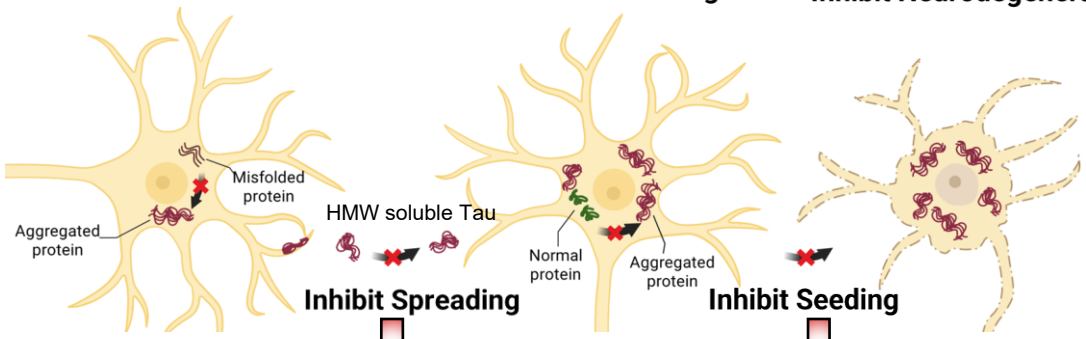
↓ 51% decrease

p=0.001

Inhibit Agregation

Inhibit Seeding

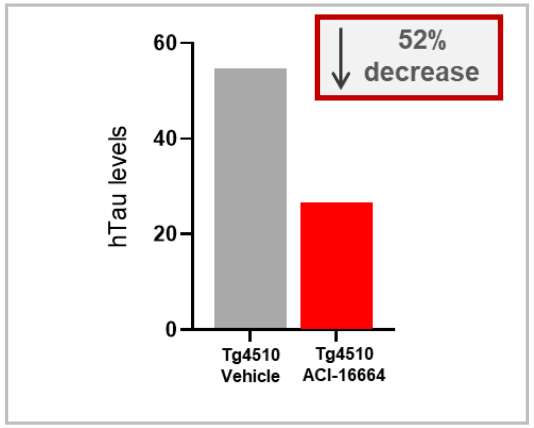
Inhibit Neurodegeneration



Inhibit Spreading

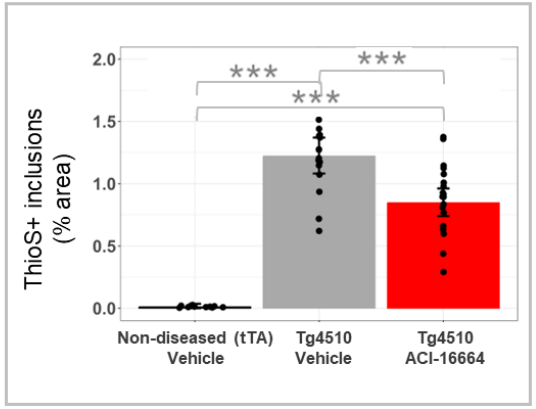
Inhibit Seeding

Soluble HMW Tau aggregates



↓ 52% decrease

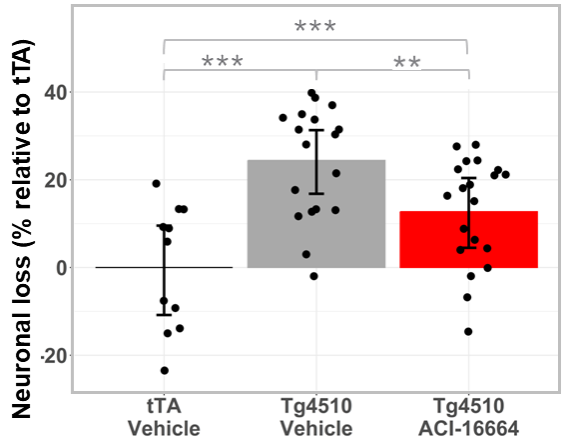
Insoluble Tau tangles



↓ 31% decrease

p=0.001

Reduced neuron loss



↓ 48% decrease

p=0.002

- Potential to reduce Tau pathology in patients to slow or even halt disease progression

(1)Tg4510 model

AC Immune

a-syn[1] targeted small molecules to address Parkinson's disease

Unique small molecule assets including therapeutics and diagnostics

Mor-a-syn

- **Small molecule Morphomer®** targets intracellular pathological a-syn aggregates to treat and prevent Parkinson's disease
- **Lead candidate decision** anticipated in H1 2026

ACI-12589
ACI-15916

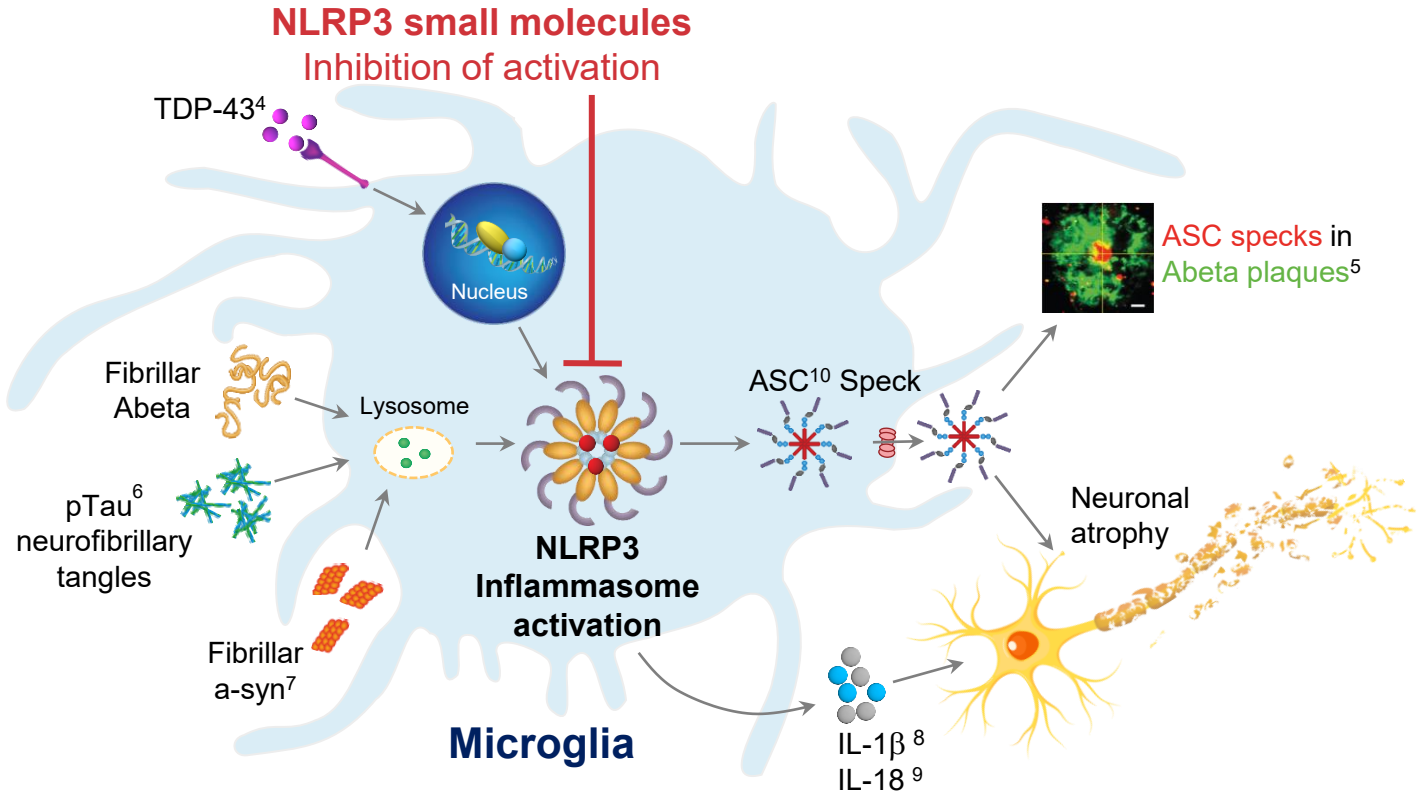
- **Morphomer® diagnostic PET[2] tracers** for pathological a-syn aggregates to detect and differentiate a-synucleinopathies
- ACI-12589 demonstrated excellent clinical results in **M**ultiple **S**ystem **A**trophy
- ACI-15916 in **Phase 1 clinical study** with results anticipated in late 2026

- Parkinson's disease affects over 6 million people worldwide
- Challenges remain in diagnosis and there are substantial unmet needs for effective therapeutic interventions

(1) alpha-synuclein; (2) Positron emission tomography

NLRP3[1] Inflammasome is a promising therapeutic target

Intracellular NLRP3 inhibitors



AC Immune's NLRP3i positioning

- Potential best-in-class CNS[2]-penetrant small molecule drug candidate ACI-19764
- Peripheral candidate (lead stage)

CNS
- Alzheimer's disease
- Parkinson's disease
- Multiple sclerosis
- Other NDDs

Peripheral
- Metabolic diseases
- Rheumatoid arthritis
- Inflam. Bowel Disease
- Neuropathic pain
- Dermatologic diseases

- Mechanism of action can be applied across a broad range of neuroinflammatory and other diseases
- ACI-19764 Phase 1 initiated in Q1 2026

(1) Nod-Like Receptor protein containing Pyrin 3; (2) Central nervous system; (3) Clinical Trial Authorization; (4) TAR DNA binding protein-43; (5) Venegas *et al.*, 2017; (6) phosphorylated Tau; (7) alpha-synuclein; (8) Interleukin-1 beta; (9) Interleukin-18; (10) Apoptosis-associated speck-like protein containing a CARD, also called PYCARD; (11) Neurodegenerative diseases

ACI-19764: Differentiated small molecule targeting NLRP3

Excellent brain penetrance, safety and efficacy (preclinical tox / PK data)

Optimal brain PK

Model	Kp,uu [1]
Mouse brain	0.3
Rat brain	0.71
Dog CSF[2]	1

Optimal developability

- BCS[3] class 1
- **Predicted human oral dose of 40mg/day**

High potency

IL-1β [4] inhibition	IC_{50}
Human macrophages	2nM
Human whole blood	**20.5 nM**

***In vivo* (EAE[5]) inhibits inflammation**	IL-1β caspase-1 GFAP [6] CD4 [7]

Weight loss DIO[9] mice (24d) vs vehicle	
ACI-19764	-9%
semaglutide	-10.9%
ACI-19764 + sema	-15.5%

High selectivity

- No action on other inflammasomes[8]

Excellent safety & tolerability

- No adverse findings up to 400 mg/kg in short toxicology rat study
- No adverse effects upon chronic treatment in several *in vivo* models
  - Tg83 mice (3 months)
  - EAE mice (30 days)
  - DIO mice (28 days)

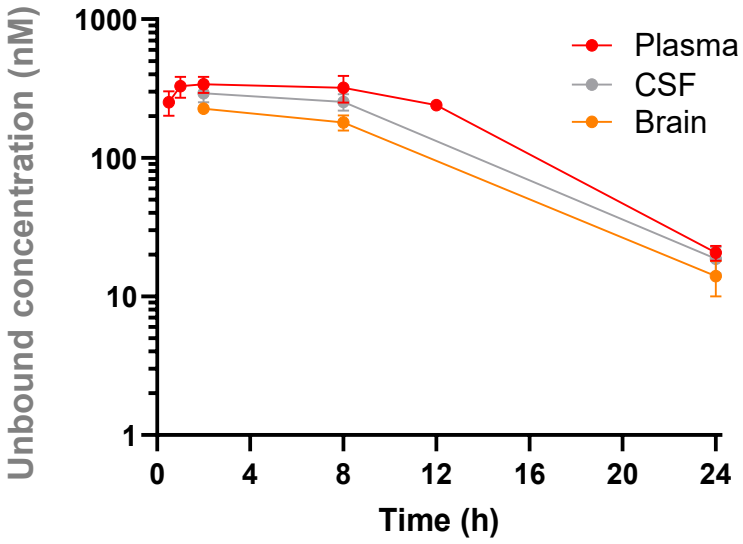
ACI-19764 Phase 1 SAD/MAD in healthy volunteers is ongoing, results expected H2 2026

(1) Optimal brain to plasma ration (Kp,uu) = 1.0; (2) cerebrospinal fluid; (3) Biopharmaceutics Classification System; class 1 defines high soluble and high permeable drugs (4) interleukin-1 beta; (5) Experimental autoimmune encephalomyelitis; (6) Glial fibrillary acidic protein; (7) cluster of differentiation 4, marker of T helper cells; (8) AIM2, NLRP1, NLRC4; (9) Diet-induced obesity model

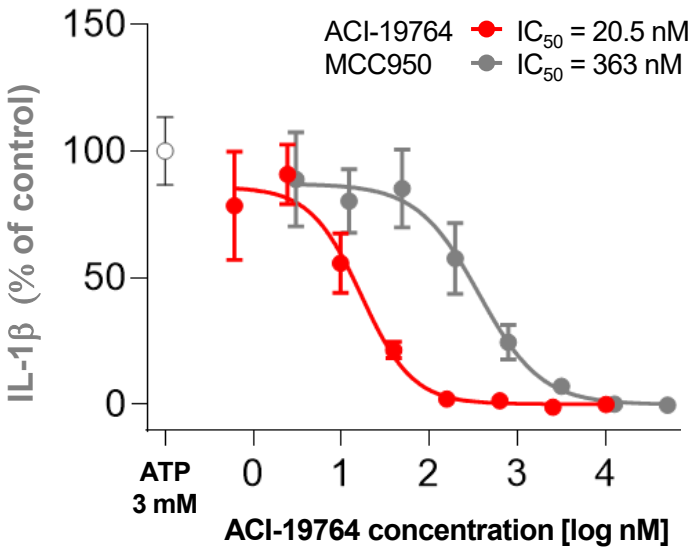
ACI-19764: Differentiated small molecule targeting NLRP3 [1]

Preclinical efficacy demonstrated in mouse models of neuroinflammation

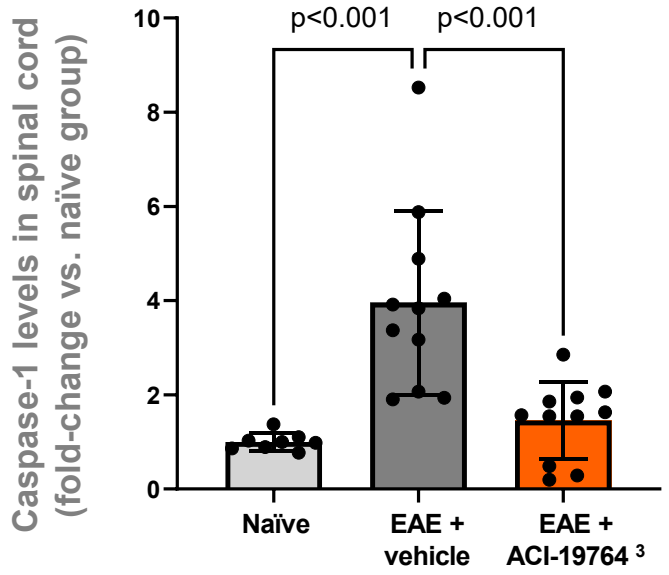
Brain penetration



Human whole blood IL-1β



Multiple sclerosis model (EAE[2])



Highly brain penetrant molecule with a brain/plasma[4] ratio of 0.7 after a single oral dose in rats (5 mg/kg)

ACI-19764 exhibits low nM efficacy in translationally relevant *in vitro* assays

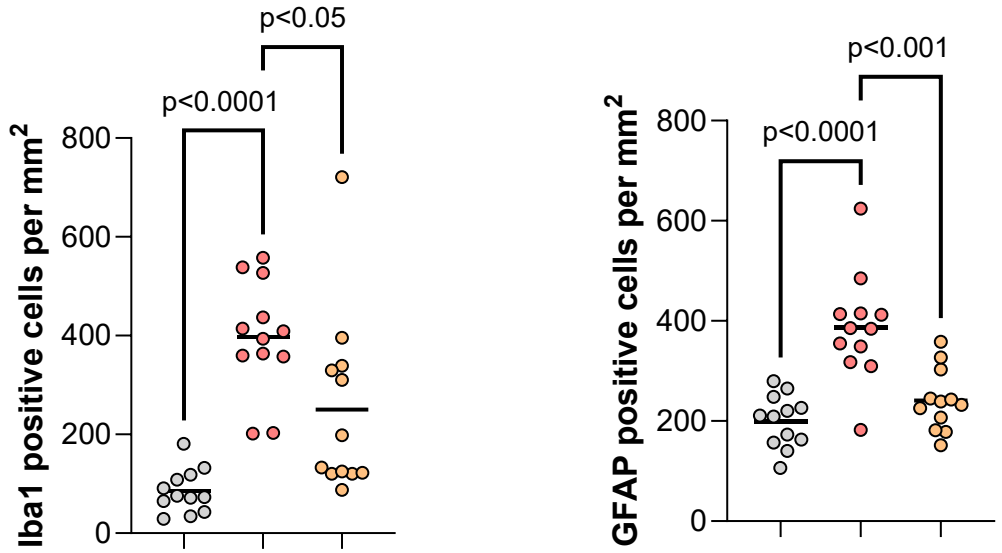
Potent NLRP3 inhibition leads to reduction in pro-pyroptotic caspase-1

(1) (NOD)-like receptor protein 3; (2) Experimental autoimmune encephalomyelitis; (3) Dosed at 5mg/kg in medicated chow; (4) Kp,uu – unbound partition coefficient; (5) Alzheimer's disease; (6) Parkinson's disease; (7) Amyotrophic lateral sclerosis; (8) Frontotemporal dementia; (9) Multiple sclerosis

ACI-19764 inhibits key disease mechanisms relevant to Alzheimer's disease

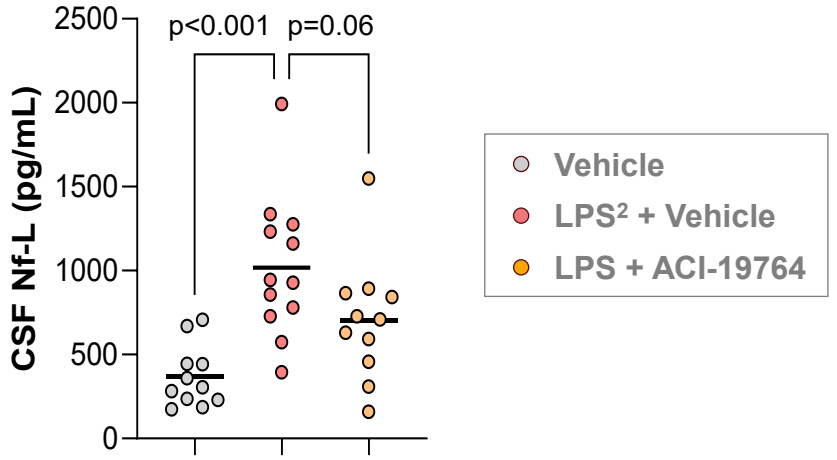
Efficacy in a mouse model of neuroinflammation[1]

Neuroinflammation



Reduced microglial (Iba1[3]) and astrocytic (GFAP[4]) activation, demonstrates attenuation of neuroinflammation

Neurodegeneration



Lower NfL[5] levels in CSF[6] reflects reduced axonal injury and neurodegeneration

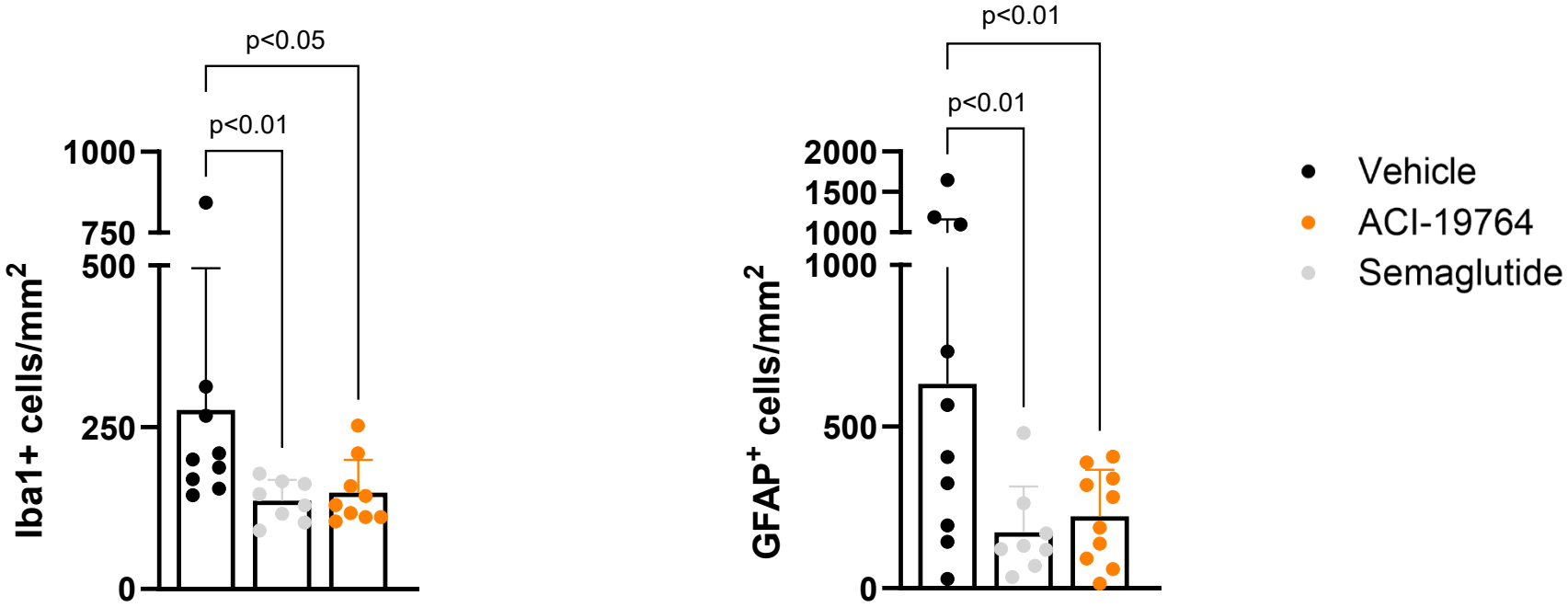
- Reduction of translationally relevant neuroinflammation and neurodegeneration markers demonstrates in vivo efficacy consistent with a potential disease-modifying effect in AD[7]

(1) Chronic LPS-mediated CNS inflammation - 5 days of 1mg/kg/day intraperitoneally, Micheli *et al.,* Int. J. of Mol. Sci., 2022; (2) Lipopolysaccharide; (3) Ionized calcium-binding adapter molecule 1, (4) Glial fibrillary acidic protein; (5) Neurofilament light; (6) Cerebrospinal fluid; (7) Alzheimer's disease

ACI-19764 reduced neuroinflammation in the DIO model

NLRP3 inhibition is leveraging a different mechanism of action as compared to semaglutide

IHC[1] analysis in DIO[2] mouse brains



AC Immune, unpublished data

Reduced microglial (Iba1[2]) and astrocytic (GFAP[3]) activation shows mitigation of neuroinflammation

- ACI-19764 significantly reduced neuroinflammation in the brain by a mechanism different from semaglutide

(1) Immunohistochemistry; (2) Diet-Induced Obesity; (3) Arcuate Nucleus of the Hypothalamus; (4) Ionized calcium-binding adapter molecule 1; (5) Glial fibrillary acidic protein; p values vs vehicle (one-way ANOVA)

AC Immune's four core value drivers

Combining biomarker-based clinical development, validated targets and strong collaborations

ACI-35 anti-pTau

The only active immunotherapy in a prevention study for pre-symptomatic Alzheimer's disease

ACI-24 anti-Abeta

Biomarker-driven development targeting the hallmark protein in Alzheimer's disease and Alzheimer's in Down syndrome

ACI-7104 anti-a-syn

Active immunotherapy targeting pathological a-syn in early-stage Parkinson's disease

Intracellular targeting

Small molecule programs targeting intracellular pathologies:

- Tau (Lilly)
- a-syn
- NLRP3 inflammasome

Retain 2* : Phase 2 study of ACI-35 (JNJ-2056) in preclinical AD[1]

A randomized, multicenter, double-blind, placebo-controlled Phase 2 study

Study population

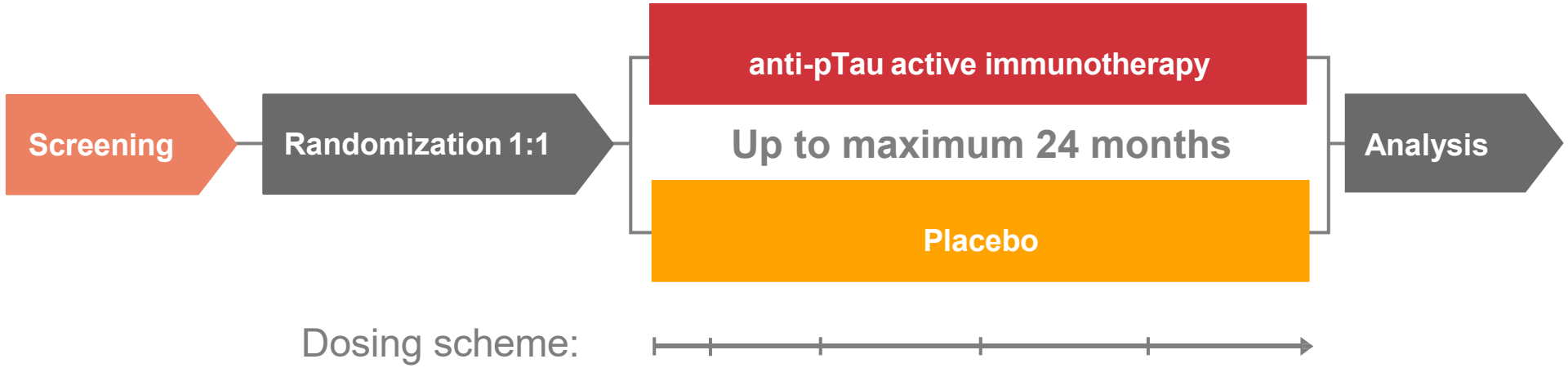
- ~60 participants with **preclinical AD**:
  - Cognitively normal
  - Tau PET positive
  - Amyloid positive[2]
- Prior to appearance of clinical symptoms

Biomarker readouts

- Tau pathology compared with placebo:
  - Tau-PET imaging[3]
  - Baseline, 12-months, and up to 24-months

Cognitive endpoints

- Preclinical AD Cognitive Composite-5 [4]
  - Episodic memory; timed executive function; global cognition
- Clinical Dementia Rating scale
- Speech biomarker (ki:elements)



* Protocol Version: Amendment 5, HA submissions in progress (last updated 05-May-2025)

(1) Alzheimer's disease; (2) Abeta positivity (A+) based on plasma pTau217; (3) Tau-PET SUVR measured in multiple brain regions of interest; (4) PACC-5

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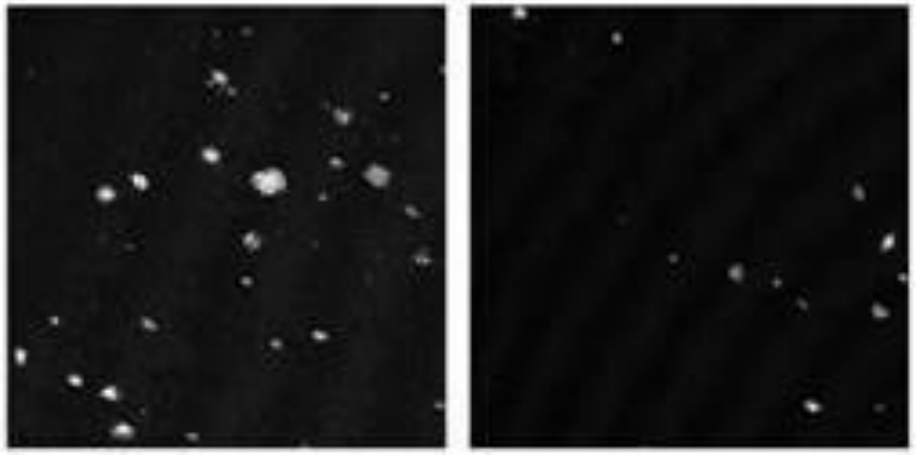
ACI-24 active immunotherapy reduces Abeta plaque burden

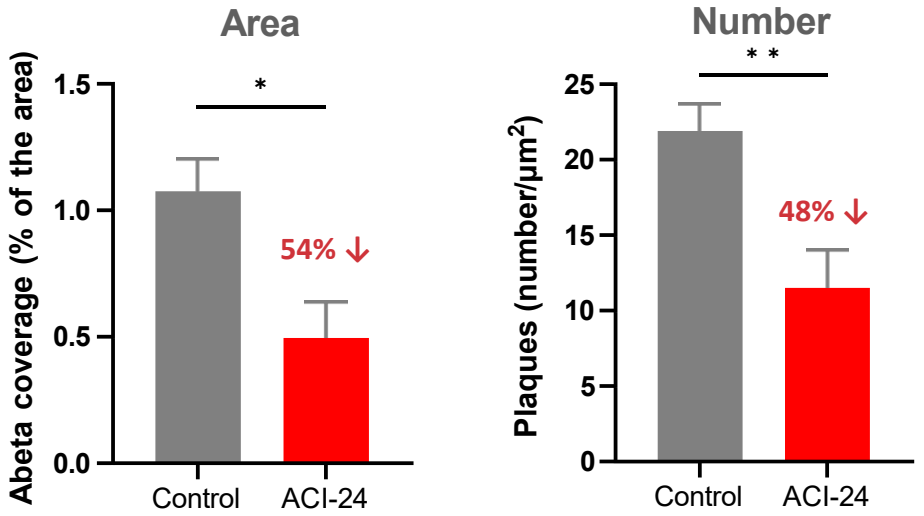
Significant Abeta plaque reduction *in vivo* in preclinical APPxPS1 model[1]

Abeta Plaque Staining in Control and ACI-24-treated Mice



Control ACI-24

Quantification of Abeta Plaques



* p<0.05 ** p<0.01

Ref: Njavro, *et al.*, Cells 2023

- ACI-24 treatment significantly reduces Abeta plaque burden in aggressive APPxPS1 model
- Similar plaque reductions seen with lecanemab and donanemab in less aggressive APP models

(1) Alzheimer's disease mouse model: APPxPS-1 double transgenic mice

ABATE: Biomarker-based Phase 1b/2 study of ACI-24 in AD[1] and DS[2]

Placebo-controlled Phase 1b/2 Study Overview

Adaptive Study Design

Both
- Interim analyses of safety/tolerability & immunogenicity
- Biomarker analyses including Abeta PET[3] and others

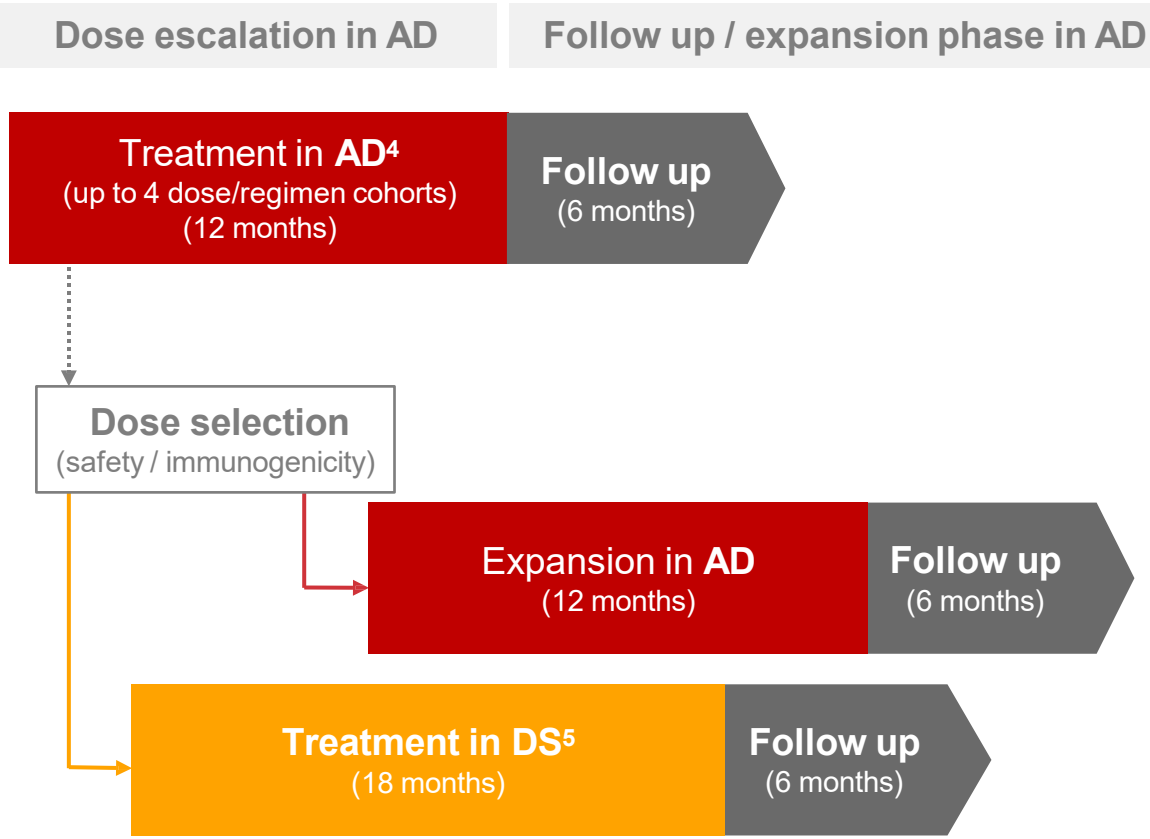
AD
- Up to 4 different doses and/or dose regimens
- Expansion of one cohort to assess effect on Abeta PET

DS
- Initiation using selected dose identified in AD (based on safety/tolerability and immunogenicity)

Outcome measures

Both
- Safety/tolerability
- Pharmacodynamics: Serum anti-Abeta antibody titers
- **Abeta-PET imaging**
- Exploratory biomarkers and clinical endpoints

Trial Schematic



(1) Alzheimer's disease; (2) Down syndrome-related AD; (3) Positron emission tomography; (4) AD participants must between 50 – 85 years of age and have prodromal AD with Clinical Dementia Rating Global Score of 0.5 and Abeta pathology confirmed by PET scan; (5) Cohort comprised of non-demented people living with DS (age 35 – 50 years) and Abeta pathology confirmed by PET scan

Patient baseline characteristics and interim safety/tolerability findings

Placebo-controlled Phase 1b/2 study: interim blinded data

Baseline profile[1]	Unit	Part 1: AD	Part 2: DS
Number of patients	n	74	20
Age			
Years	mean	70.7	45.6
	std	6.14	3.73
Sex			
Male	n (%)	34 (45.9%)	10 (50.0%)
Female	n (%)	40 (54.1%)	10 (50.0%)
Race			
White	n (%)	71 (95.9%)	20 (100%)
Black / African American	n (%)	2 (2.7%)	0
Asian	n (%)	1 (1.4%)	0
Cognitive performance			
MMSE [3]	mean (std)	24.5 (3.6)	-
ADAS-Cog-13 [4]	mean (std)	25.3 (9.0)	-
KBIT-2 [5]	mean (std)	-	52.7 (11.2)

1. **Generally well tolerated in both AD and DS study populations**
2. **To date[2], no death; two serious adverse events considered possibly related to study treatment in subjects with AD**
3. **Most frequent TEAEs[6] are injection site reactions and headaches of mild or moderate intensity**
4. **No ARIA-E observed in study participants to date**
5. **Occasional ARIA-H events were asymptomatic and their frequency in line with expected placebo incidence**

(1) Data cut-off date: 12 May 2025 for interim blinded baseline demographics data; (2) Data cut-off date: 20 June 2025 for interim blinded safety data (3) Mini-mental state examination, interim blinded data; (4) Alzheimer's Disease Assessment Scale, Cognitive part, interim blinded data; (5) Kaufman Brief Intelligence Test Second Edition, interim blinded data; (6) Treatment Emergent Adverse Events

Preliminary insights from blinded cohorts AD1, AD2 and AD3

ACI-24 exhibits a dose-dependent immune response against toxic species of Abeta

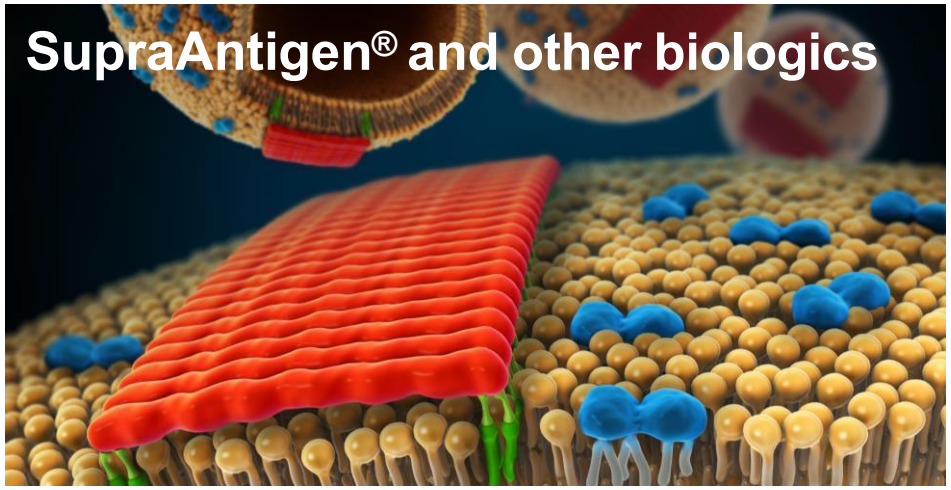
1. **Immunogenicity observed in AD subjects at all tested doses**
2. **Trend towards increase in the magnitude of anti-Abeta$_{1-42}$ IgG titers with increasing dose**
3. **Increase in the responder rate with increasing dose and repeated immunizations**
4. **Boosting effect for all dose levels observed after repeated immunizations with ACI-24**
5. **More durable and sustained immune response were observed in cohorts AD2 and AD3**

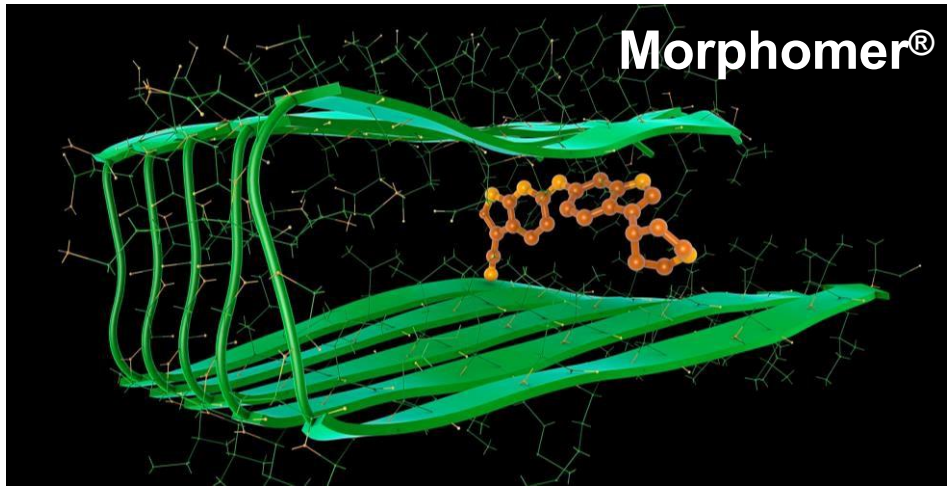
- 12-month treatment time point for AD1, AD2 and AD3 reached in late 2025

Business development opportunities driven by our technology platforms

Strategy: optimize value to risk ratio and retain significant upside

Platform	SupraAntigen® and other biologics	Morphomer®
Wholly-owned Programs	■ Active immunotherapy (a-syn) ■ Antibodies (TDP-43; a-syn; ASC)[1] ■ AAV intrabodies	■ Therapeutic Morphomers / small molecules (a-syn; NLRP3 inhibitors) ■ PET Tracers (a-syn for MSA and PD; TDP-43)[1]





- Over CHF 400 million in upfront payments from deals; further >CHF 4.3 billion possible
- Considerable additional potential value in our unpartnered clinical and preclinical programs

(1) Deprioritized assets not for further development without a partner;

Pioneering Precision Prevention

Shifting the treatment paradigm for neurodegenerative disease towards precision medicine and disease prevention

Supplementary information

AC Immune's strong track record in deals[1] with leading pharma companies

Strategy: optimize value to risk ratio and retain significant upside

Program	Phase	Total value[2]	Upfront[2]	Milestones received[2]	Royalties	Partner
ACI-24 (anti-Abeta active immunotherapy)	Phase 1b/2	>USD 2,100	USD 100	USD 12	Mid-to-high teens	Takeda
ACI-35 (anti-pTau active immunotherapy)	Phase 2b	CHF 500	CHF 26	CHF 45	Low-double digits to mid-teens	Janssen
Tau Morphomer® drugs	Phase 1 [6]	CHF 1,860	CHF 80 +USD 50 [7]	CHF 40	Low-double digits to mid-teens	Lilly
PI-2620 (Tau PET[4] tracer)	Phase 3 [5]	EUR 160	EUR 0.5	EUR 7	Mid-single digits to low-teens	LANTHEUS
Crenezumab (anti-Abeta antibody)	Phase 2	USD 65 [3]	USD 25	USD 40		*
Semorinemab (anti-Tau antibody)	Phase 2	CHF 59 [3]	CHF 17	CHF 42		*
Total (millions)[8]		**CHF ~4,750**	**CHF 255.2 [9]**	**CHF 182**		

- Outstanding potential milestone payments exceed ~CHF 4.3 billion

(1) Disclosure limited due to confidentiality agreements with collaboration partners; (2) In millions; (3) Total payments received from partner until termination of agreement; (4) Positron emission tomography; (5) In Alzheimer's disease; (6) Phase 1 completed; (7) Equity investment; (8) Converted to CHF on date of receipt; (9) Excludes convertible note agreement of USD 50 million ; * previously licensed to Genentech (a member of the Roche Group)