Investor Presentation – Part 1 of VacSYn Phase 2 trial

NASDAQ: ACIU | September 23, 2026

AC Immune

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AC Immune – targeting the key pathologic misfolded proteins and pathways that drive neurodegenerative diseases

Focused pipeline: extensively validated neurodegenerative disease pipeline

Deep expertise based on two decades of research and clinical development in the field of misfolded proteins for the treatment of neurodegenerative diseases

Clinical leadership validated through multiple clinical candidates and pharma partnering deals

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

Lead program – ACI-7104 targets one of the largest unmet opportunities in neuroscience with a differentiated approach

- Based in Lausanne, Switzerland
- ~120 employees
- Listed on NASDAQ: ACIU
- 102.5 million shares outstanding[1]
- Cash resources of CHF 75.4 million[2]

(1) As of June 3, 2026; excluding treasury shares; (2) As of June 30, 2026 (~USD 93 million)

Validation from multiple pharmaceutical partners across proprietary platforms and modalities

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])			FDA Fast Track		
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

Positive Safety & Immunogenicity in Part 1 of VacSYn Phase 2 Trial

Randomized, double-blind, placebo-controlled Phase 2 trial of ACI-7104 in patients with early-stage Parkinson's disease. 34 patients (25 receiving ACI-7104 and nine receiving placebo).

ACI-7104 anti-a-syn

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

ACTIVE Immune Therapy

Met primary endpoints

Primary endpoints of safety, tolerability and immunogenicity, all met

100% of patients developed antibodies against the target antigen, PD01, after three immunizations

Robust antibody penetration

Robust antibody penetration into the cerebrospinal fluid was observed in all subjects

Exploratory correlations

Exploratory correlation analysis identified trends suggesting an association between antibody levels and disease activity measures

Parkinson’s disease

Pathological deposition of alpha-synuclein

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

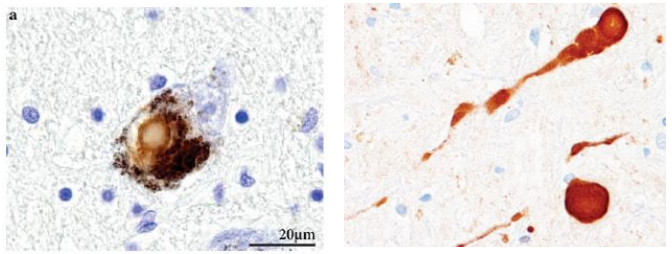
Etiology
5-10% genetic, 90-95% idiopathic, unknown cause

Cardinal motor symptoms
Tremor, rigidity, bradykinesia

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

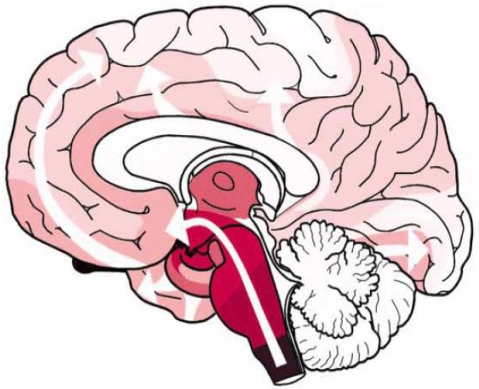
Pathological hallmarks
Neuron loss, alpha-synuclein aggregates – Lewy bodies

Main component of Lewy bodies: Alpha-synuclein



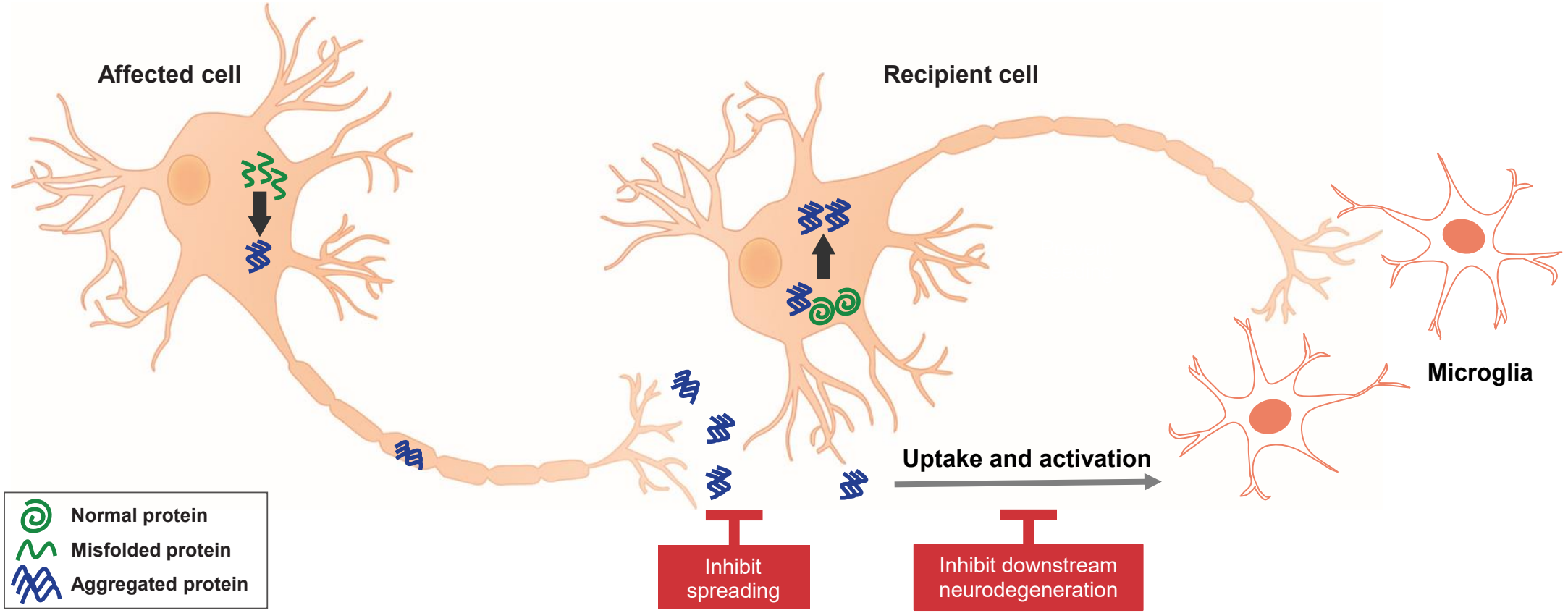
Halliday *et al.* 2011

Progression of pathology



Braak *et al.* 2003

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



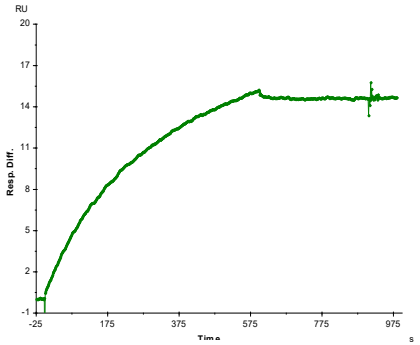
- a-syn misfolding and aggregation are the molecular basis for a-synucleinopathies, e.g. PD, DLB[4] and MSA[5]
- Seeding and spreading of a-syn are potential drivers of disease progression

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

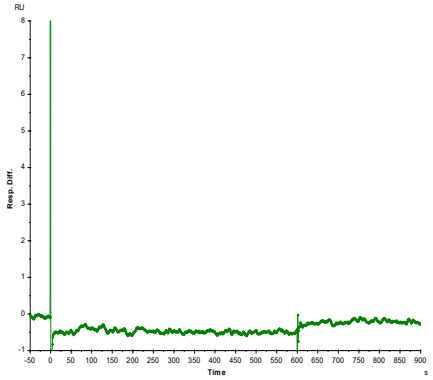
Immunological potential of ACI-7104 active immunotherapy in humans

a-syn reactivity of ACI-7104 peptide-induced human Abs (SPR analysis)

Aggregated a-syn used as substrate

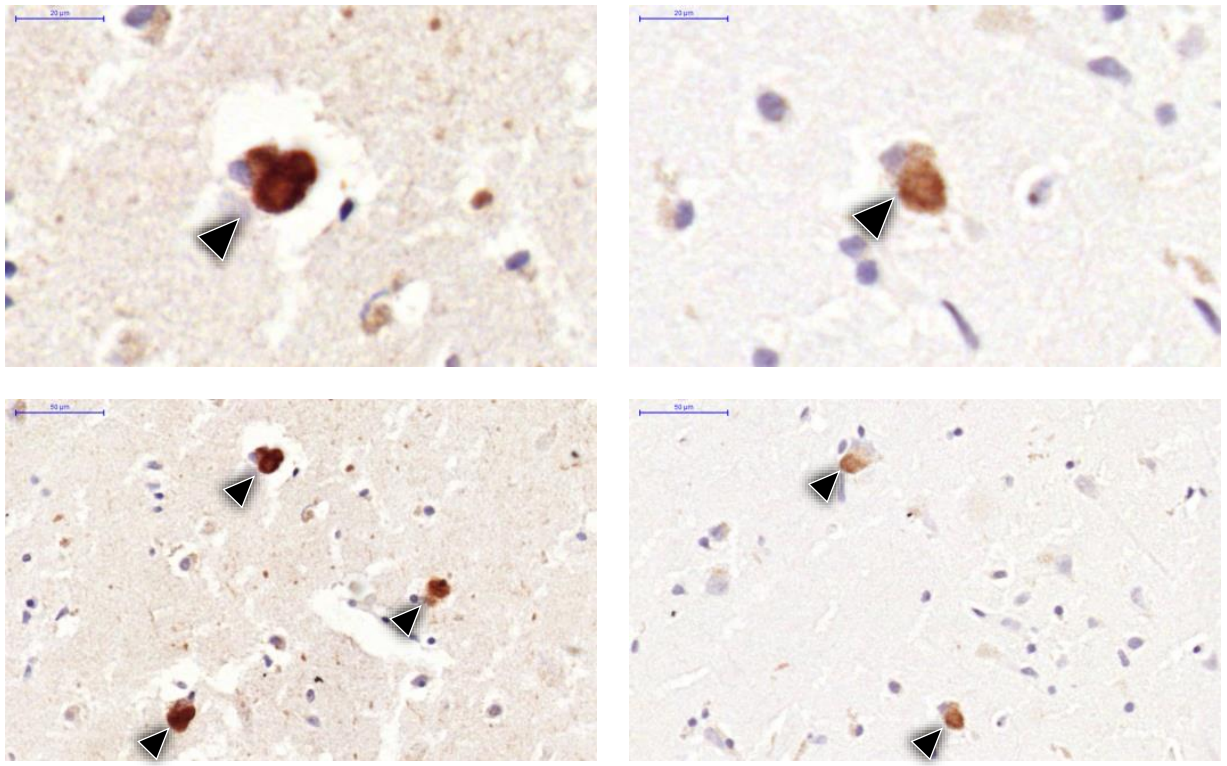


Monomeric a-syn used as substrate



Anti a-syn mAb
Positive Control

ACI-7104 peptide-induced human Abs



Arrow heads: Indicate reactivity to aggregated a-syn in Lewy bodies

- Induced antibodies bind aggregated a-syn with high selectivity and bind to Lewy bodies in post-mortem PD brains

ACI-7104: formulation tested in VacSYn Part 1 based on proven carrier

PD01 – modified a-syn target antigen

Improved design of ACI-7104 formulation

CRM197 [2] selected as new carrier:

- strong immunological performance driven by high T cell helper activation
- extensive regulatory acceptance, with use in multiple approved vaccines
- well established safety profile, supported by extensive clinical and post-marketing experience
- manufacturing advantages, including easier scale-up and analytical testing

Extensive studies showed that CRM197**:**

- did not affect anti-PD01 antibody specificity or quality
- led to a higher antibody response compared with the previous formulation

Development objective for Part 1 with improved formulation with well-established carrier:

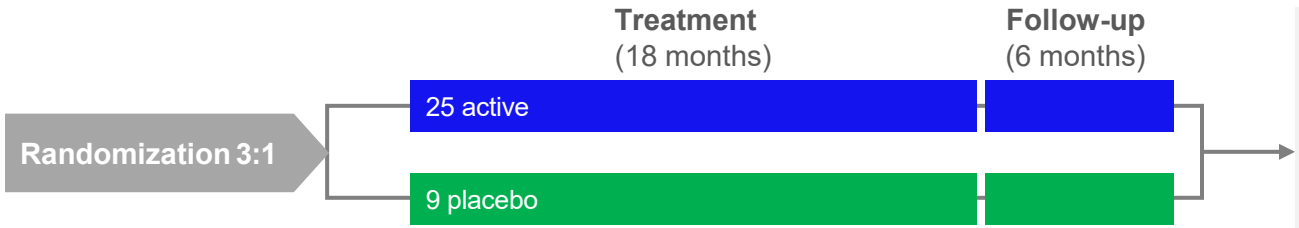
- demonstrate clinical safety and tolerability
- determine immunogenicity of new formulation

(1) CMC - Chemistry, manufacturing, and controls; (2) CRM197 – inactive diphtheria toxin derivative;

VacSYn: Adaptive Phase 2 study of ACI-7104 in early PD[1]

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

Part 1: Safety & Immunogenicity



Analysis

- **Primary outcome measures:**
  - Safety-tolerability / Immunogenicity (antibody titers)
- **Exploratory signals:**
  - a-syn levels / biomarkers / clinical (MDS-UPDRS)

Part 2: Provide evidence of clinical activity as the basis for entry into Phase 3

- Motor and Non-Motor Functioning (MDS-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

Expansion in ~250 patients

Treatment in PD (24 months) → **Follow up** (6 months)

(1) Parkinson's disease (idiopathic); (2) Unified Parkinson's disease rating scale; (3) Dopamine Transporter Single Photon Emission Computed Tomography; (4) Arterial spin labeling; (5) Diffusion tensor imaging

ACI-7104 - Part 1 VacSYn Phase 2: outcome measures

Primary:

- Safety and tolerability
- Immunogenicity

Exploratory:

- Changes in biomarkers
- Disease activity measures

VacSYn: Safety/tolerability findings: No safety concerns raised by DSMB[1]

Baseline profile		Unit	Total[2]
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%)
MOCA total score		mean (std)	26.4 (2.0)
MDS-UPDRS scores			
Part 1: Non-motor experiences of daily living		mean (std)	4.09 (3.1)
Part 2: Motor aspects 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%)

Overall good benefit/risk to date.

DSMB consistently recommended that the trial may continue without modification to date.

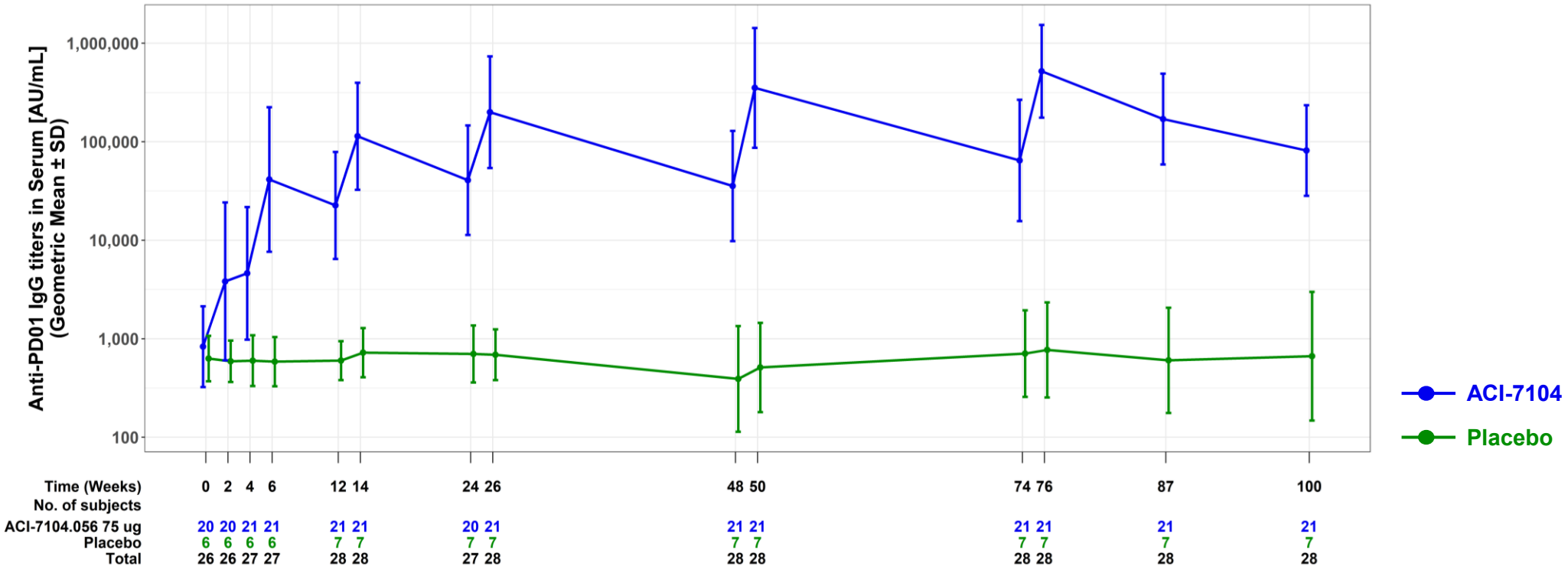
- Most common AEs were transient and generally of mild severity: injection site reactions (55.9%); fatigue, headache and nasopharyngitis (each in 11.8%).[6]
- 6 serious adverse events[3] (including one death of unknown cause in the post-treatment period) have been observed to date in 3 subjects. A second death occurred in another subject after Informed Consent withdrawal[4]
- 2 severe AEs (death and cognitive disorder) have been reported in 2 participants, both considered not related to study drug
- 2 AEs leading to discontinuation from the study[5] unrelated or unlikely related to study drug
- No significant MRI, lab, ECG abnormalities reported to date

(1) Data Safety Monitoring Board; (2) Extraction date April 08, 2026; (3) SAEs: Upper limb fracture, osteoarthritis, perforated appendicitis, intraabdominal sepsis (in the same subject) and radical prostatectomy are considered unrelated to IMP, death of unknown cause is considered unlikely related to IMP; (4) Not counted as an SAE since post-study occurrence; (5) Worsening of preexisting generalized anxiety disorder unrelated to study drug before the extraction date; one SAE of death of unknow cause; (6) interim incidence in the pooled active and placebo subjects.

ACI-7104 induces robust antibody response in early PD[1]

100% responder rate observed for anti-PD01[2] antibody titers in serum

Mean antibody titers in serum[3]

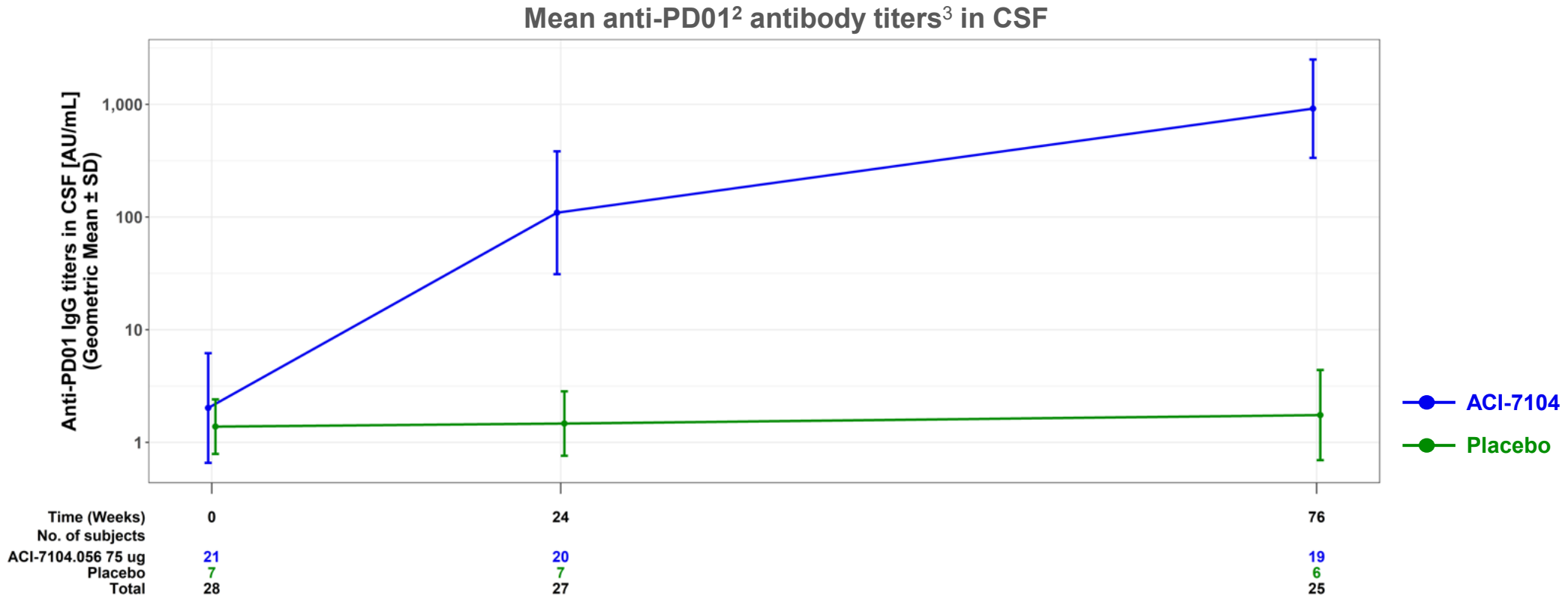


- All participants exhibited anti-PD01 IgG[4] antibodies in serum (from week 14)
- Antibody responses were boosted after each dose (from the 2nd immunization)
- The placebo group did not show a detectable signal

(1) Parkinson's disease; (2) Modified a-syn peptide antigen; (3) per protocol population; (4) Immunoglobulin G isotype.

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[4] 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) per protocol population; (4) Immunoglobulin G isotype.

ACI-7104 - Part 1 VacSYn Phase 2: outcome measures

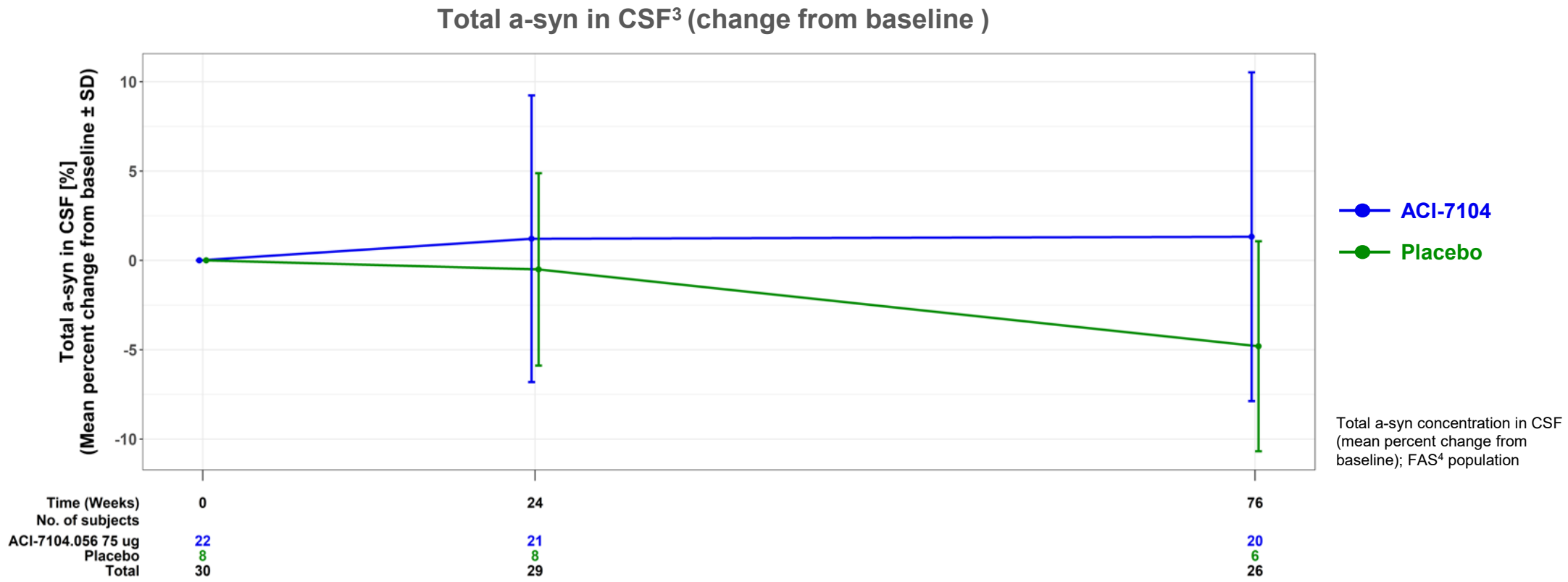
Primary:

- Safety and tolerability
- Immunogenicity

Exploratory:

- Changes in biomarkers
- Disease activity measures

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

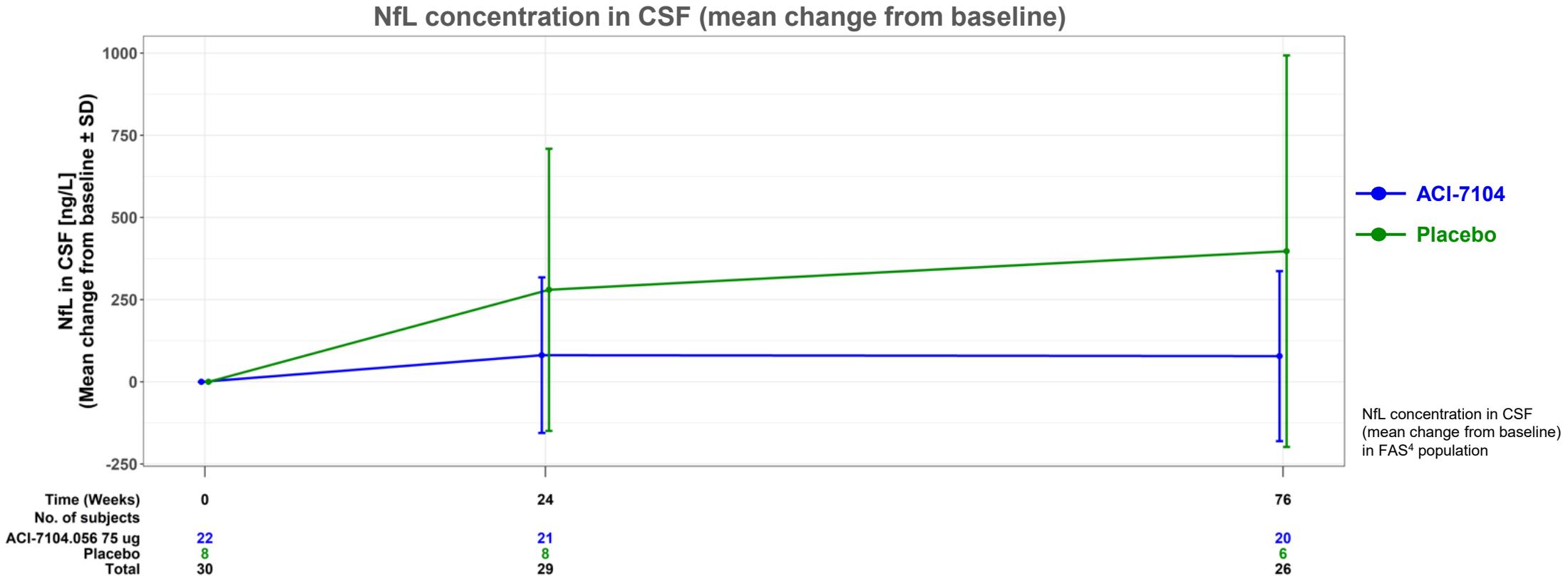


Total a-syn concentration in CSF (mean percent change from baseline); FAS[4] population

- Total CSF a-syn levels in treatment arm suggest possible 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; (4) Full Analysis Set.

Trend in NfL[1] signals



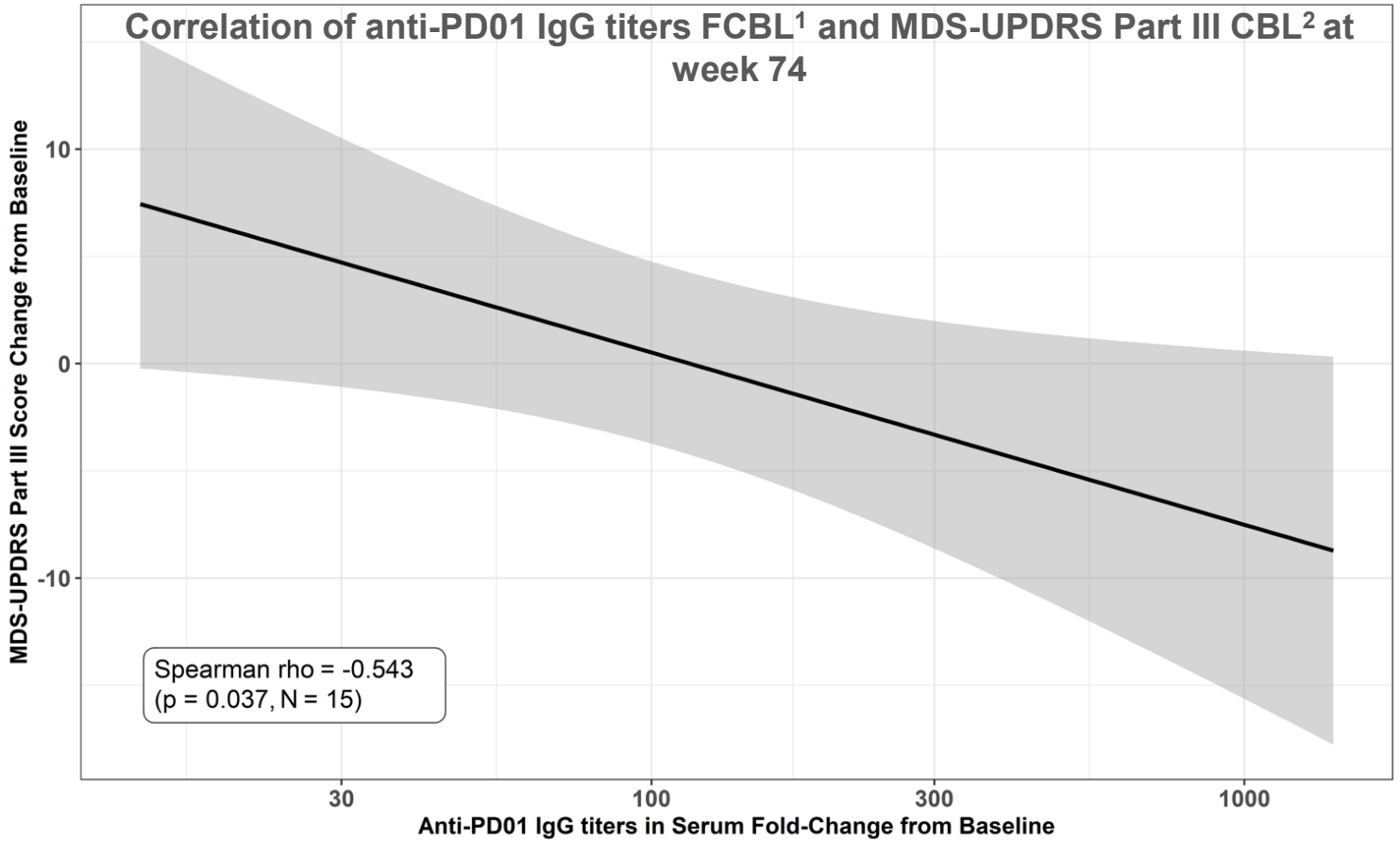
NfL concentration in CSF (mean change from baseline) in FAS[4] population

- NfL in CSF remained stable in the ACI-7104 group
- NfL levels in CSF increase 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) Full Analysis Set.

Figure 14.2.13.2.2

Antibody titers in serum correlate with disease activity measures



Correlation between anti-PD01 IgG titers in serum (Fold Change from Baseline) and MDS-UPDRS III (Change from Baseline) at week 74 (FAS[3] population – OFF state only

- Patients with highest increase of antibodies tend to have less change in their MDS-UPDRS scores over time
- Anti-PD01 IgG, as well as anti-a-syn titers have shown correlation with MDS-UPDRS Part II and Part III

(1) Fold change from baseline; (2) Change from baseline; (3) Full Analysis Set.

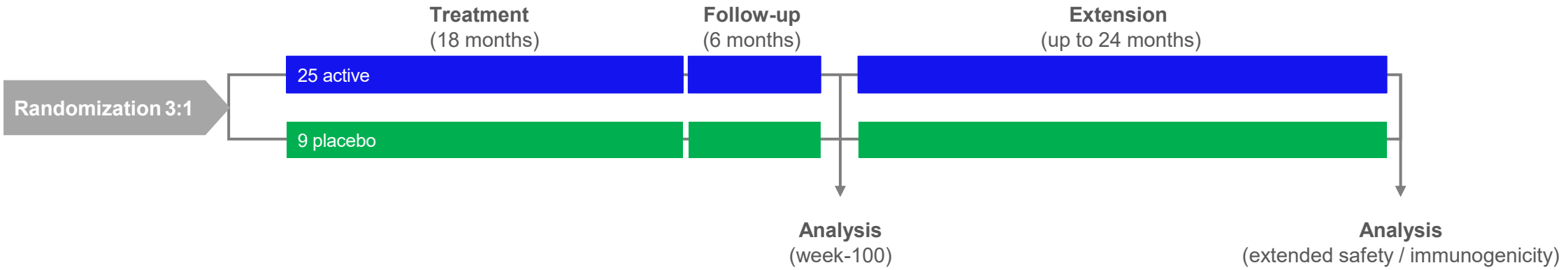
Summary – ACI-7104 Part 1 results support further development

- ACI-7104 was safe and induced significant antibody levels with robust antibody penetration into the cerebrospinal fluid (CSF) observed in all treated participants
- Antibody reactivity against the aggregated species of a-syn was observed
- At least 2-fold improvement in immunogenicity over previous formulation
- Signals observed on exploratory correlations between biological and clinical parameters suggesting potential link between antibody levels and response
- Results continue to support further development of the program and discussion of clinical development plan towards registration with Regulators

VacSYn: Adaptive Phase 2 study of ACI-7104 in early PD[1]

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

Part 1: Safety & Immunogenicity - extension



Part 2: Provide evidence of clinical activity as the basis for entry into Phase 3

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Outlook – ACI-7104 moving into expanded Phase 2

- Objective to demonstrate clinical activity as the basis for Phase 3
- Phase 2 study designed with optimized inclusion criteria (N~250 patients) and enhanced clinical outcome measures:
  - Digital measures of motor function
  - Safety/tolerability and immunogenicity
  - Advanced MRI
- Protocol design to be discussed with FDA under Fast Track designation

VacSYn: Adaptive Phase 2 study of ACI-7104 in early PD[1]

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

Part 1: Safety & Immunogenicity

Part 2: Provide evidence of clinical activity as the basis for entry into Phase 3

- Digital measures of motor function
- Safety and immunogenicity
- Advanced MRI
- Motor and Non-Motor Function (MDS-UPDRS[2] based)
- Functional and patient reported outcomes

Expansion in ~250 patients

Treatment in PD
(24 months)

Follow up
(6 months)

(1) Parkinson's disease (idiopathic); (2) Movement Disorder Society - Unified Parkinson's disease rating scale;

ACI-7104 Summary and outlook

Part 1 VacSYn results summary:

- **Primary endpoints met**: ACI-7104 is generally **safe** and **well tolerated** and **strongly immunogenic**
- ACI-7104 induced robust antibody response against target a-syn antigen with clear CSF penetration
- Exploratory correlation analyses identified trends suggesting an association between immunogenicity antibody titers and disease activity measures

Progress into expanded VacSYn Part 2:

- Objective to demonstrate clinical activity as the basis for entry into Phase 3
- Discussions with FDA under Fast Track designation in early 2027
- IND/CTA filing following FDA meeting

Comments: Prof. Werner Poewe

Q & A

Selectively targeting the key pathologic misfolded proteins and pathways that drive neurodegenerative diseases

Back-up

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 results after 12 months of treatment**
ACI-7104	a-syn[2]	✓		Submissions to regulators regarding clinical development plan
			●	**Phase 2 VacSYn trial in PD[3]: 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 results in healthy volunteers**
			●	**Phase 1b clinical results in patients with elevated hsCRP**
Morphomer a-syn	a-syn		○	Readiness to initiate IND-enabling studies

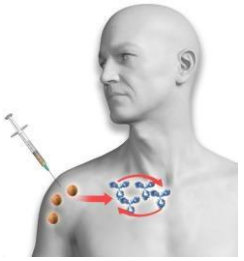
(1) Alzheimer's disease; (2) Alpha-synuclein; (3) Parkinson's disease;(4) Investigational new drug; (5) Clinical Trial Application; (6) (NOD)-like receptor protein;

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)

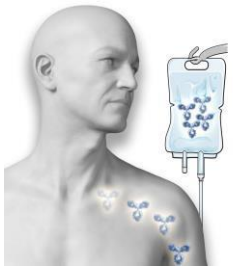


Active immunotherapy

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