



PIONEERING PRECISION MEDICINE

TARGETED THERAPEUTICS
FOR NEURODEGENERATIVE DISEASES

Investor Update

NASDAQ: ACIU | Investor Presentation - August 2024



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 at a glance

Pioneering new ways to treat neurodegenerative diseases



Broad, diverse pipeline – 16 programs

1 Phase 3 program and 5 in Phase 2



Key differentiation: Precision Medicine

Enables leadership in targeted therapies



Multiple global partnerships

>CHF 4.3 billion in potential milestones



Clinically validated technology platforms

Best-in-class small molecules and biologics



Cash reserves on Balance sheet

Funding into 2027³

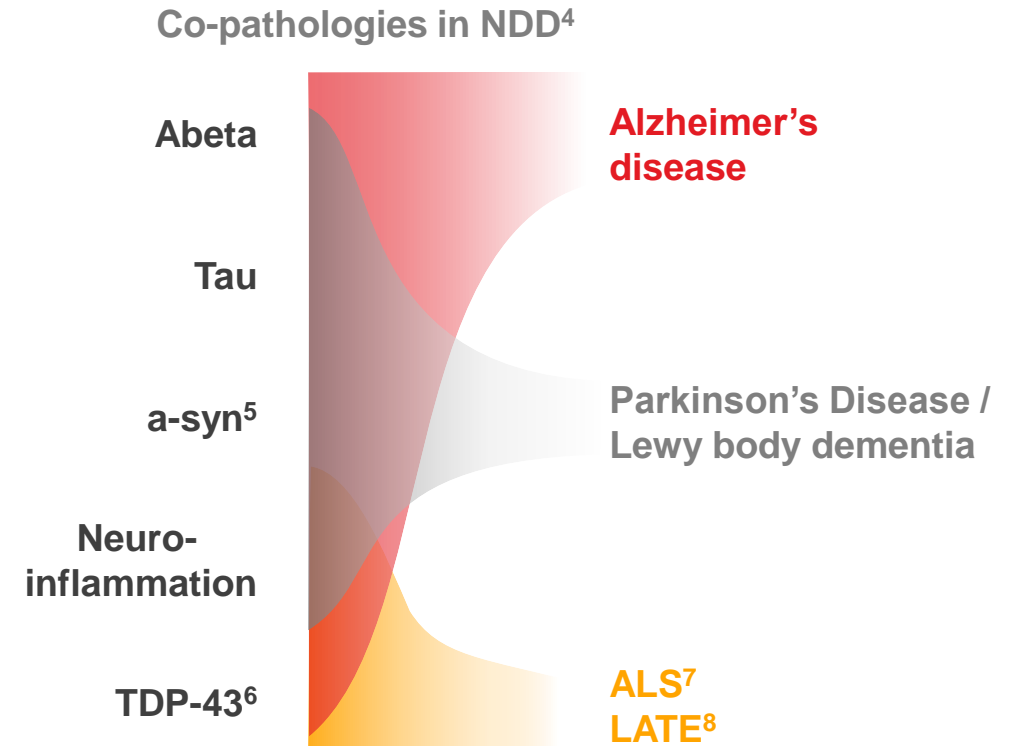
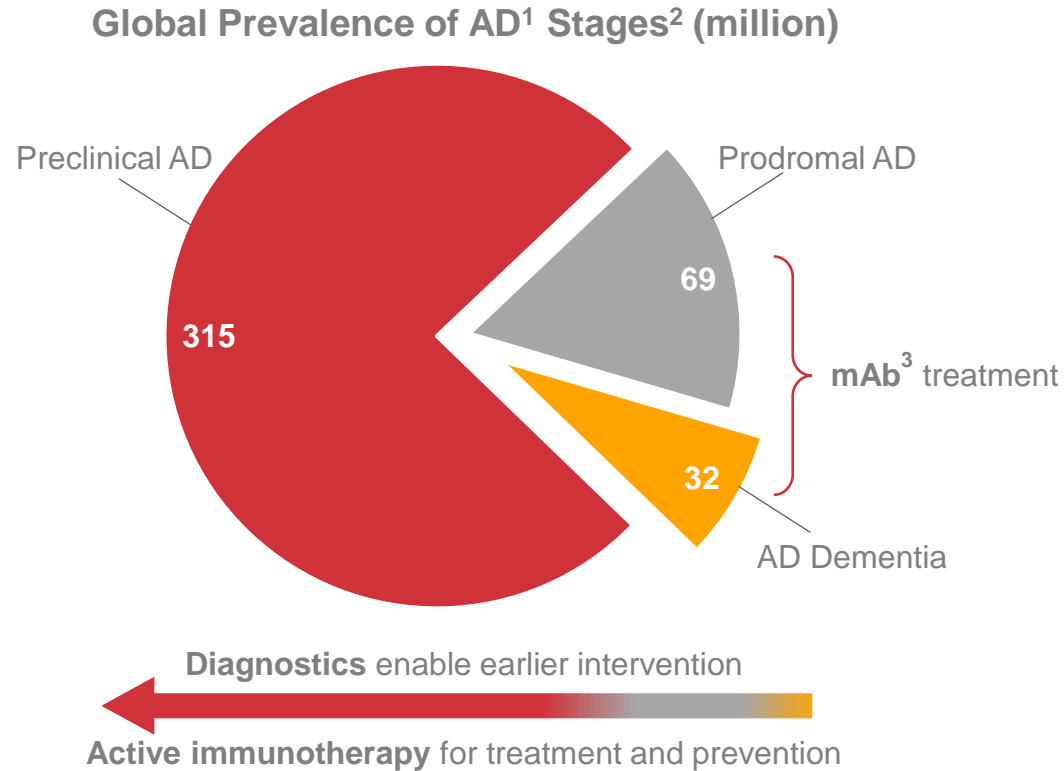
- Based in Lausanne, Switzerland
- ~150 employees
- Listed September 2016 (NASDAQ: ACIU)
- 99.7 million shares outstanding¹
- Cash of CHF 175.2 million²



(1) As of June 30, 2024; excluding treasury shares; (2) as of June 30, 2024; (3) assumes second ACI-35-related milestone payment of CHF25 million received in 2025 and no other milestones

Neurodegenerative diseases

Prevention as the only approach to long-term preservation of neurological health







- AD prevention through combination of earlier diagnosis with early active immunotherapy
- Global disease prevention market potentially over 300 million people

(1) Alzheimer's disease; (2) Gustavsson et al. Alzheimer's and Dement. 2023 19:658-670. <https://doi.org/10.1002/alz.12694>; (3) Monoclonal antibody; (4) Neurodegenerative disease; (5) alpha-synuclein; (6) TAR DNA-binding protein 43; (7) Amyotrophic lateral sclerosis; (8) Limbic-predominant age-related TDP-43 encephalopathy

Broad and robust pipeline in neurodegenerative diseases

Driven by validated proprietary technology platforms for sustained growth

Clinical Stage Programs





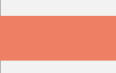
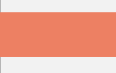
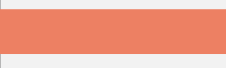
CLASS	PRODUCT CANDIDATE	INDICATION	Lead Discovery	Preclinical	PHASE 1	PHASE 2	PHASE 3	News	Partner	
Active Immunotherapy	ACI-24.060 (<i>anti-Abeta</i>)	AD ¹ treatment	[Red bar]						Program on track	
		AD treatment (<i>Down syndrome</i> ²)	[Red bar]							
	ACI-7104.056 (<i>anti-a-syn</i> ³)	PD ⁴ , a-synucleinopathies	[Red bar]						data H2 '24	
	ACI-35.030 (<i>anti-pTau</i>)	AD treatment	[Red bar]							
Small Molecule Morphomer®	Tau-PET ⁵ tracer	AD diagnostic	[Orange bar]							
		PSP ⁶ diagnostic	[Orange bar]							
	a-syn-PET tracer ⁷	MSA ⁸ , a-synucleinopathies	[Orange bar]							
	a-syn-PET tracer ⁹	PD, a-synucleinopathies	[Orange bar]							
	Tau aggregation inhibitor	Rare Tauopathies treatment	[Orange bar]							
		AD treatment	[Orange bar]							

(1) Alzheimer's disease; (2) Down syndrome-related Alzheimer's disease; (3) alpha-synuclein; (4) Parkinson's disease; (5) Positron emission tomography; (6) Progressive supranuclear palsy; (7) ACI-12589, a-syn PET tracer for MSA; (8) Multiple system atrophy; (9) ACI-15916, a-syn PET tracer for PD

Broad and robust pipeline in neurodegenerative diseases

Diversification into non-AD¹ and non-CNS² diseases

Novel Targets Pipeline

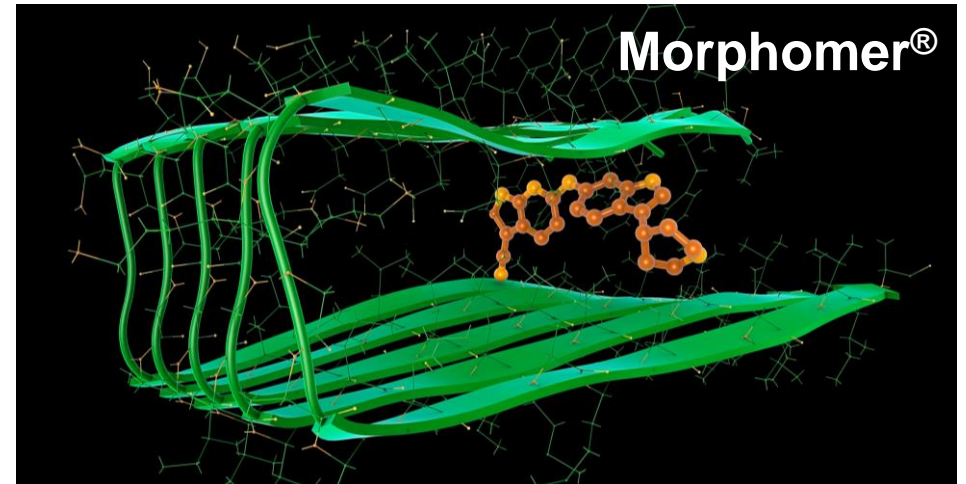
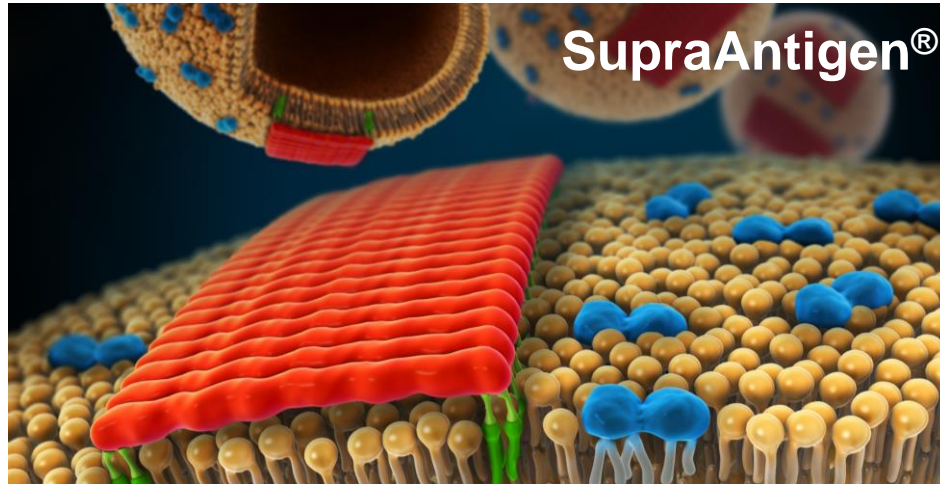
CLASS	PRODUCT CANDIDATE	INDICATION	Lead Discovery	Preclinical	PHASE 1	PHASE 2	News	Partner
Monoclonal antibody	Anti-TDP-43 ³	LATE ⁴ , NeuroOrphan						
	Anti-a-syn ⁵	PD ⁶ , NeuroOrphan						
	Anti-NLRP3 ⁷ -ASC ⁸	CNS, NeuroOrphan						
Small Molecule Morphomer [®]	TDP-43-PET ⁹ tracer	TDP-43-opathies						
	Morphomer [®] a-syn (a-syn inhibitor)	PD, a-synucleinopathies						
	Morphomer [®] NLRP3-ASC	Non-CNS						
	Morphomer [®] NLRP3-ASC	CNS, NeuroOrphan						

(1) Alzheimer's disease; (2) Central nervous system; (3) TAR DNA-binding protein 43; (4) Limbic-predominant age-related TDP-43 encephalopathy; (5) alpha-synuclein; (6) Parkinson's disease; (7) (NOD)-like receptor protein 3; (8) Apoptosis-associated speck-like protein containing a CARD, also PYCARD; (9) Positron emission tomography (TDP-43 PET tracer, ACI-19626)

AC Immune technology platforms driving validating pharma deals

Strategy: optimize value to risk ratio and retain significant upside

Platform



Unpartnered Programs

- a-syn active immunotherapy
- Anti-TDP-43 mAb¹
- Anti-NLRP3-ASC mAb

- Mor-a-syn
- Mor-TDP-43 PET
- Mor-NLRP3-ASC

- Considerable additional potential value in our unpartnered clinical and preclinical programs

(1) Monoclonal antibody

AC Immune financial position

Value-driven cash management



Cash of CHF 175.2 million¹



2024 annual cash burn guidance
CHF 65m – 75m





Strong Balance Sheet²
3-year cash runway










Prudent
investment
strategy focused
on major value
drivers and near-
term catalysts

(1) As of June 30, 2024; (2) Assumes second ACI-35.030 milestone payment of CHF 25m received in 2025, no other milestones or deals included.

Key milestones in 2024

Multiple catalysts across pipeline

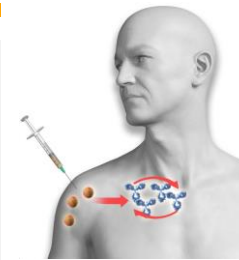
-  Clinical readouts
-  Other development events

Active immunotherapies		H1	H2	
ACI-24.060 (Takeda)	Abeta			ABATE Phase 2 trial in AD ¹ on track ²
				ABATE: First DS ³ data on safety and immunogenicity
ACI-35.030 (Janssen)	pTau			First Patient In Phase 2b clinical trial (ReTain)
ACI-7104.056	a-syn ⁴			Interim safety and immunogenicity Phase 2 VacSYn clinical trial in PD ⁵
Monoclonal antibodies and small molecule drugs				
Monoclonal antibody	TDP-43 ⁶			Completion of regulatory tox studies
Morphomer-NLRP3	NLRP3 ⁷			Clinical candidate declaration
Morphomer-a-syn	a-syn			Lead candidate declaration
Diagnostics				
TDP-43-PET ⁸ tracer	TDP-43			Phase 1 initiation
a-syn-PET tracer (ACI-15916)	a-syn			PD candidate, IND ⁹ -enabling studies completed

(1) Alzheimer's disease; (2) see Q2 2024 earnings release; (3) Down syndrome; (4) alpha-synuclein; (5) Parkinson's disease; (6) TAR DNA-binding protein 43; (7) (NOD)-like receptor protein; (8) Positron emission tomography; (9) Investigational new drug

Major advantages

- ✓ Long-lasting specific immunity for pathological target, consistent, boostable, durable
- ✓ Limited annual dosing (once or twice) after priming year
- ✓ No observed ARIA-E¹ to date (safety profile well suited to long-term use)
- ✓ Cost-effective (attractive healthcare economics across global populations)
- ✓ Improved access (ease of administration, simple logistics)

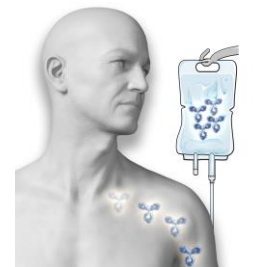


Active immunotherapy

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

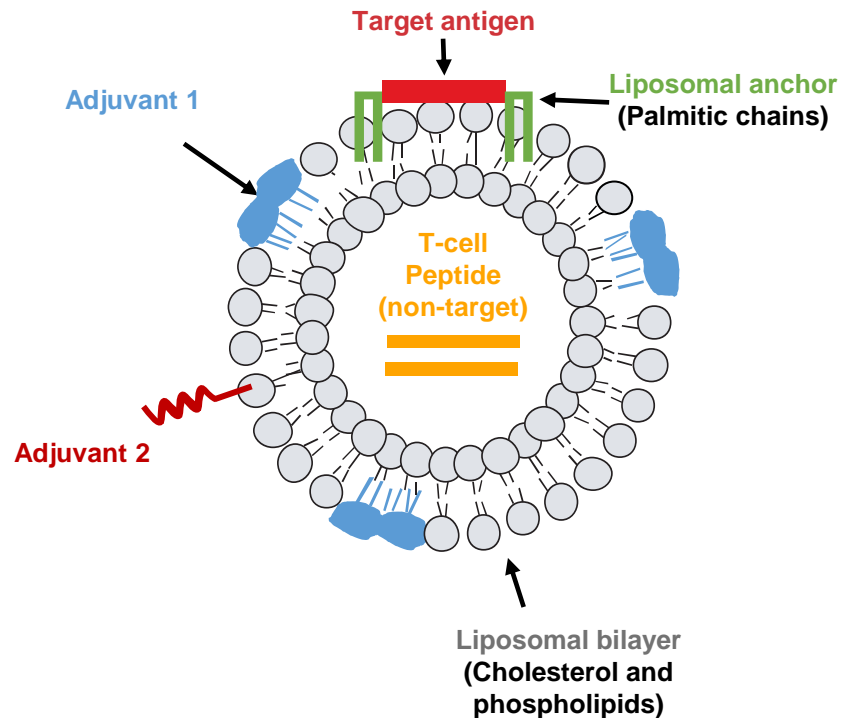
Passive immunotherapy

Externally generated mAb requires administration every two to four weeks



Disruptive potential of SupraAntigen®

Active immunotherapies delivering superior results in neurodegenerative diseases



Target-specific antibody response

Helper T-cells safely engaged **(target-unrelated)**

Unprecedented Clinical Performance

Immunogenicity	✓
Target & conformation specificity	✓
Avidity increase over time	✓
Sustainable response	✓
Boostable response	✓

- Robust immunogenicity and strong safety demonstrated in humans
- Evidence for lasting immune response supporting a disease prevention approach

For ACI-35.030: (1) 100% response after 1st injection; (2) Increases over time

A microscopic view of a neuron, showing a central cell body (soma) with a prominent nucleus, surrounded by numerous branching processes (dendrites and axons) extending outwards. The image is rendered in a blue and white color scheme, giving it a scientific and clinical appearance.

ACTIVE 
Immune Therapy

ACI-24.060: Anti-Abeta for Alzheimer's disease

Landmark deal for ACI-24.060 in Alzheimer's disease

Supports promise of active immunization for neurodegenerative diseases



- The deal with Takeda covers AC Immune's unique, class-leading Abeta targeted active immunotherapy ACI-24.060



- Deal terms:
 - \$100 million upfront payment received for exclusive option to license global rights
 - Option exercise fee in the low-to-mid nine-figure range linked to ABATE clinical data
 - Up to approximately \$2.1 billion in potential payments including option exercise fee and development, commercial and sales-based milestones
 - Royalties in the mid-to-high teens on global sales



- Combines AC Immune's leadership in developing products for NDDs¹ with Takeda's clinical development expertise and history of driving neuroscience innovation

(1) Neurodegenerative diseases

ABATE: Biomarker-based Phase 1b/2 study of ACI-24.060 in AD¹ and DS²

Placebo-controlled Phase 1b/2 Study Overview

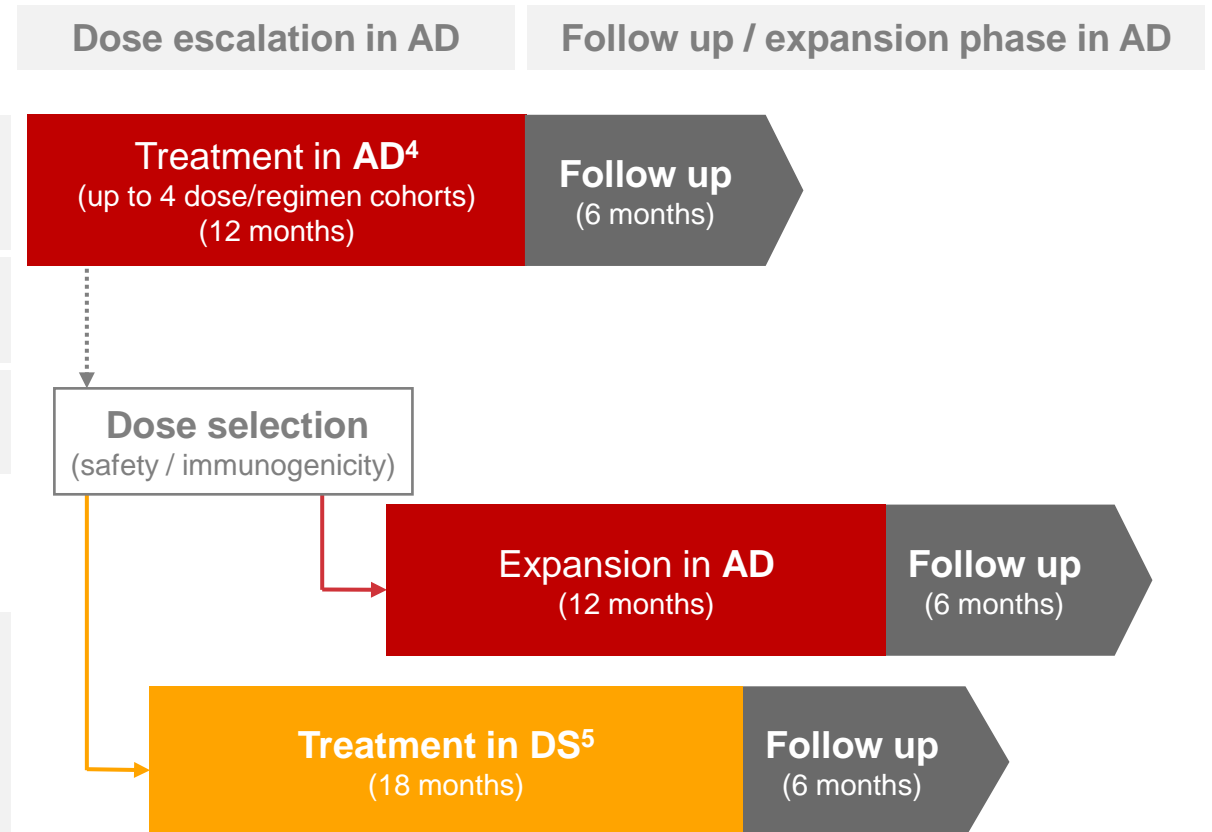
Adaptive Study Design

Both	<ul style="list-style-type: none"> Interim analyses of safety/tolerability & immunogenicity Biomarker analyses including Abeta PET³ and others
AD	<ul style="list-style-type: none"> Up to 4 different doses and/or dose regimens Expansion of one cohort to assess effect on Abeta PET
DS	<ul style="list-style-type: none"> Initiation using selected dose identified in AD (based on safety/tolerability and immunogenicity)

Outcome measures

Both	<ul style="list-style-type: none"> Safety/tolerability Pharmacodynamics: Serum anti-Abeta antibody titers Abeta-PET imaging Exploratory biomarkers and clinical endpoints
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Trial Schematic

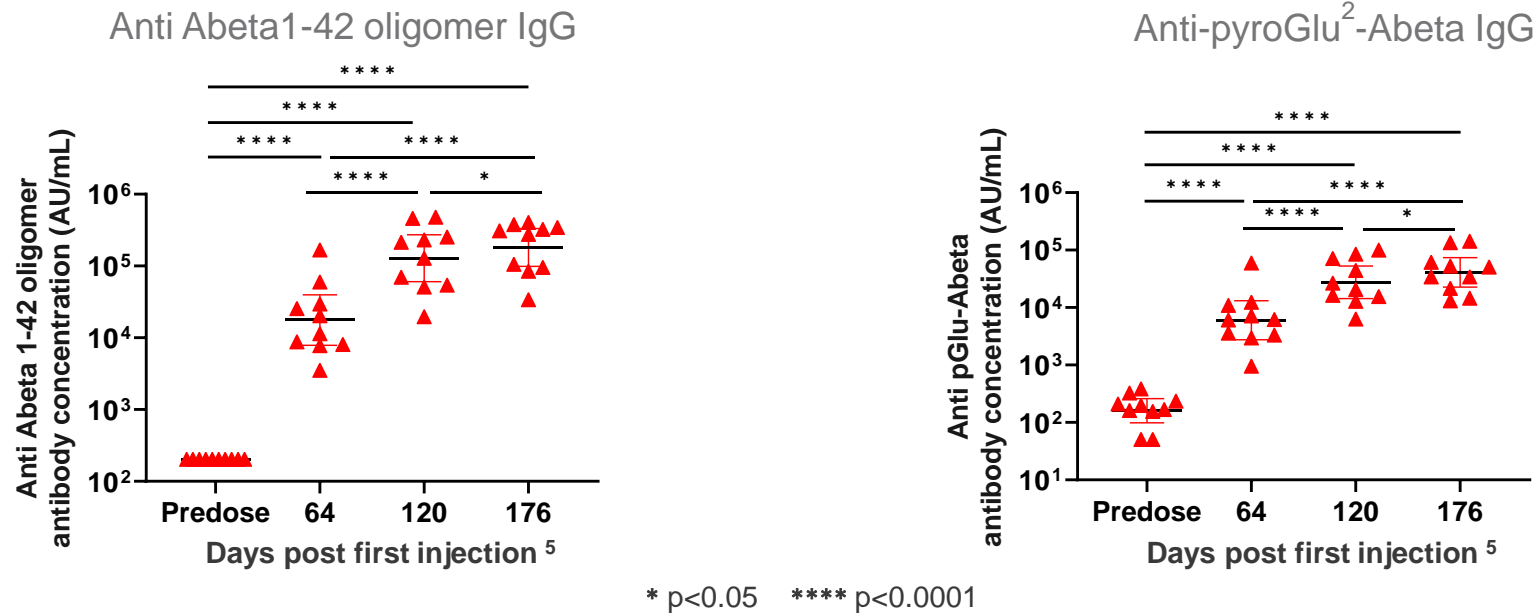


(1) Alzheimer's disease; (2) Down syndrome-related AD; (3) Positron emission tomography; (4) AD participants must be between 50 – 85 years of age and have prodromal AD with Clinical Dementia Rating Global Score of 0.5 and Abeta pathology confirmed by PET scan; (5) Cohort comprised of non-demented people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

ACI-24.060: Potent immune response against toxic Abeta species

Strong antibody response against targets of lecanemab and donanemab (NHP¹)

ACI-24.060 in NHPs

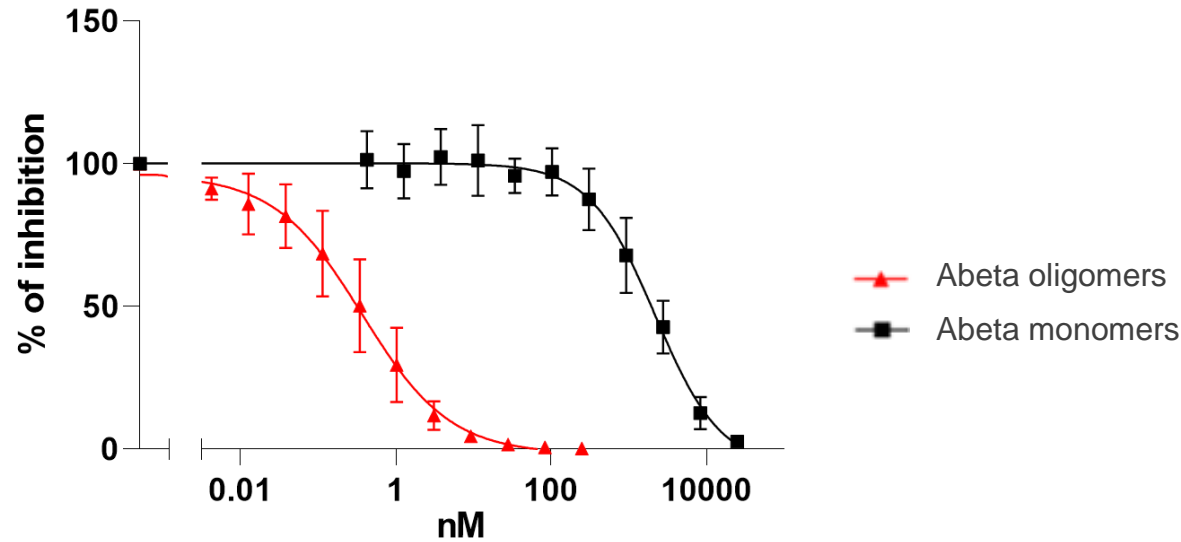


- Sustained, boostable IgG response against Abeta oligomers³ and pyroglutamate⁴ Abeta
- ACI-24.060 represents a potential breakthrough compared to previous anti-Abeta therapeutics

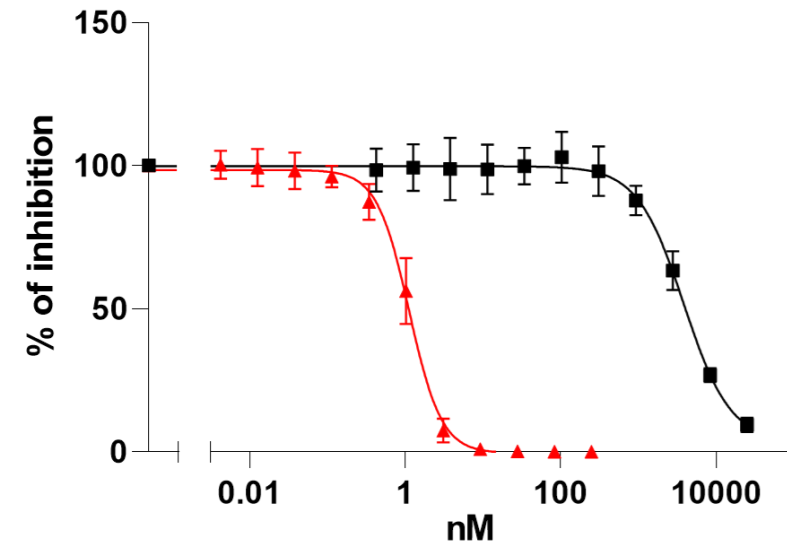
(1) Non-human primates; (2) Pyroglutamate; (3) Target of lecanemab; (4) Target of donanemab (5) Injections on days 0, 29, 57, 85, 113, 141, 169

ACI-24.060: antibodies highly specific for pathologic oligomeric Abeta

Antibodies in NHP¹ immune sera have >1000-fold preference for oligomers over monomers



NHP immunized with ACI-24.060



Lecanemab

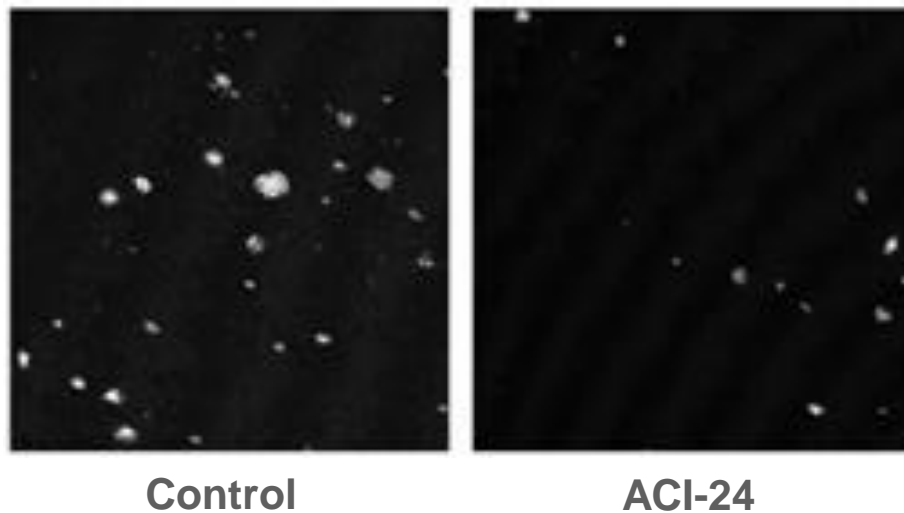
- ACI-24.060 induced antibodies in NHPs: >1000-fold stronger recognition of Abeta oligomers than monomers, similar to lecanemab

(1) Non-human primates

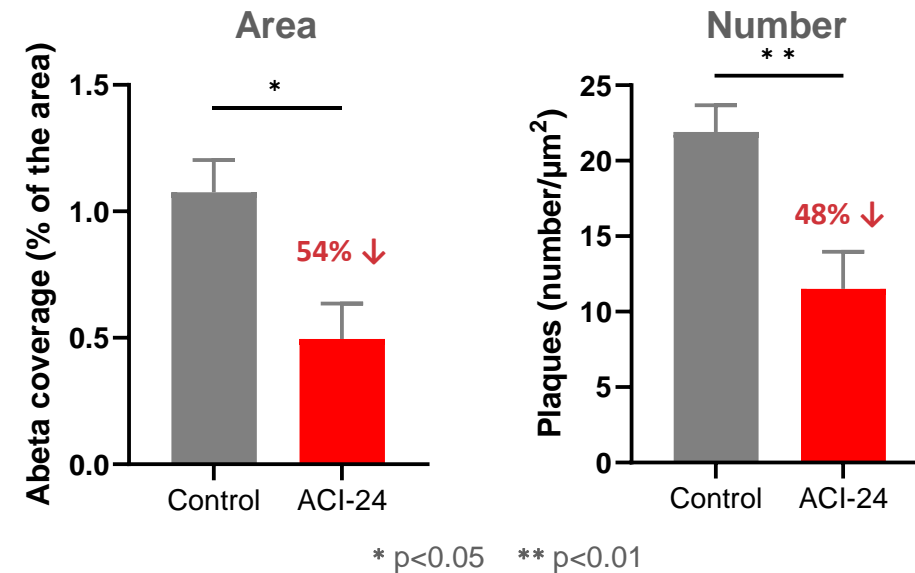
ACI-24 active immunotherapy reduces Abeta plaque burden

Significant Abeta plaque reduction *in vivo* in preclinical APPxPS1 model¹

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



Quantification of Abeta Plaques



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; (2) Alzheimer's disease; (3) Antibodies



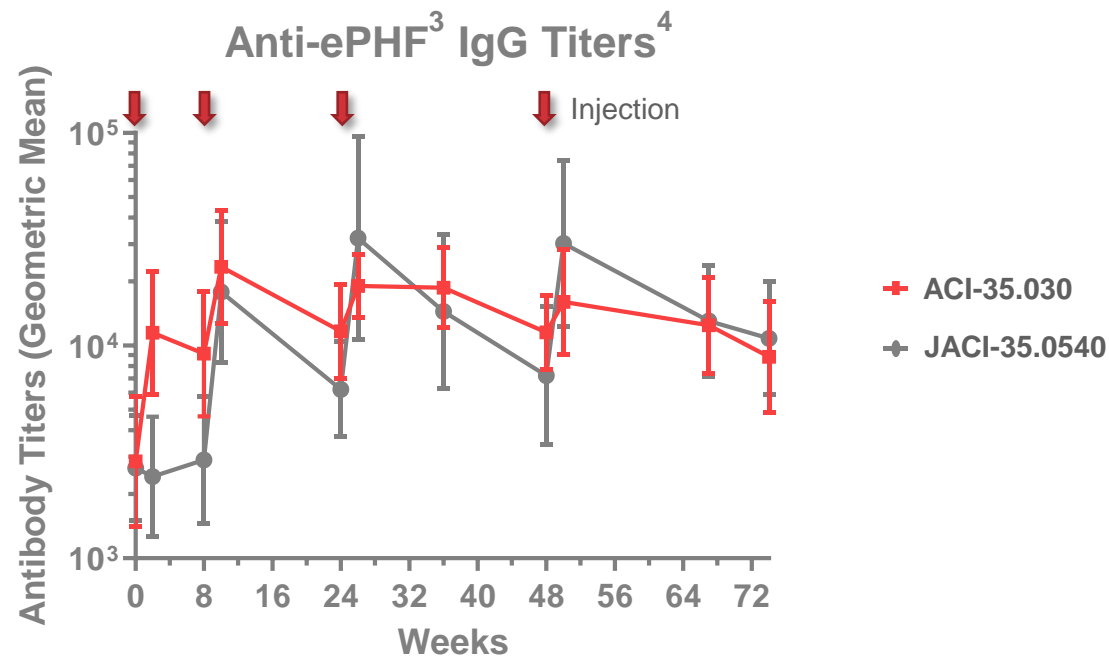
ACTIVE 
Immune Therapy

ACI-35.030: Anti-pTau for Alzheimer's disease

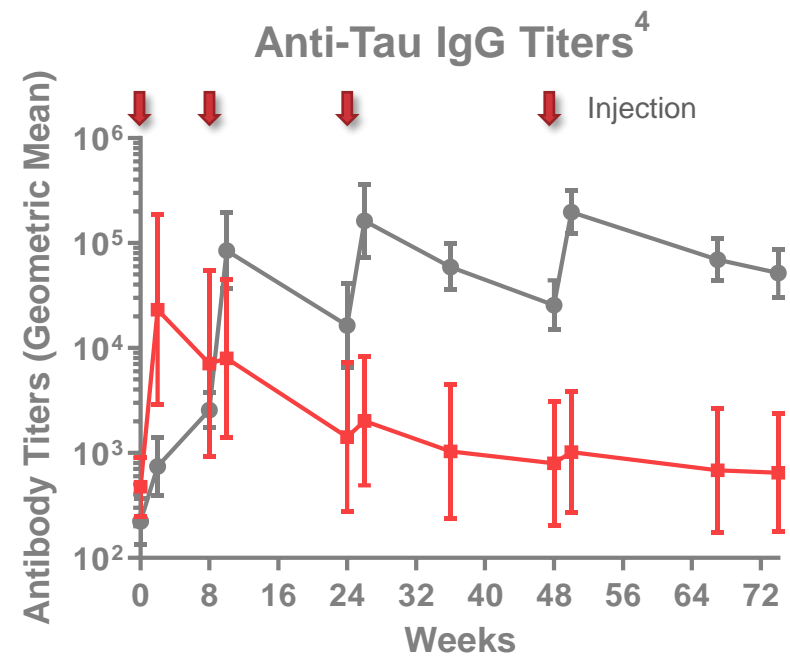
ACI-35.030 selected for further development by partner Janssen

Follows data showing ACI-35.030's superior specificity for pathological Tau vs. JACI-35.054

ACI-35.030 and JACI-35.054 utilized the same pTau¹ epitope – compared head-to-head in Phase 1b/2a trial in AD² patients



ACI-35.030 induced anti-ePHF Ab⁵ responses in 100% of patients after 1st injection



ACI-35.030-induced Abs against normal Tau returned to baseline levels as Ab response matured

(1) Phosphorylated Tau; (2) Alzheimer's disease; (3) Enriched paired helical filaments; (4) ACI-35.030 original sub-cohort 1.2 data; (5) Antibody

ReTain: a Phase 2b study of ACI-35.030 in preclinical AD¹

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

Study population

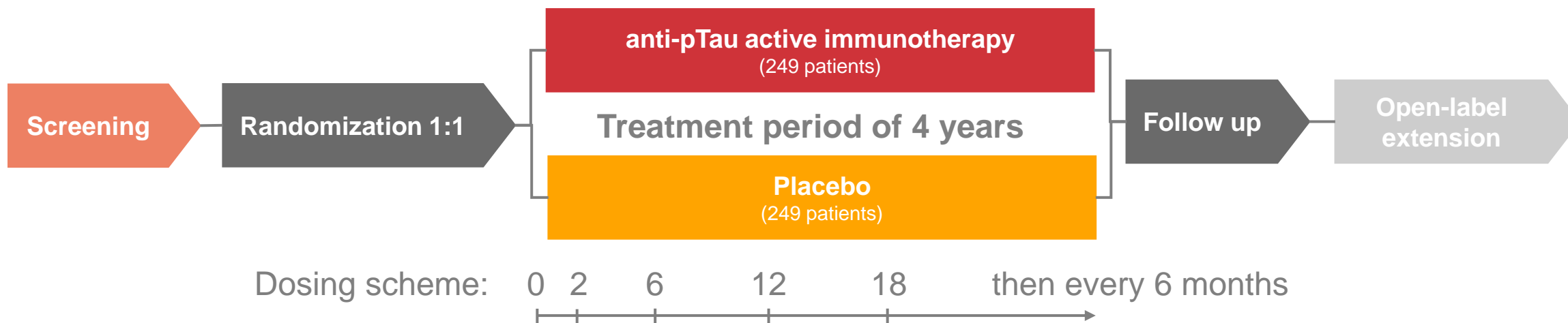
- ~500 participants with **preclinical AD**:
 - Cognitively normal
 - Tau PET positive
 - Amyloid positive²
- Prior to appearance of clinical symptoms

Biomarker readouts

- Tau pathology compared with placebo:
 - Tau-PET imaging³
 - Baseline and annually for 4 years
- Potential **BLA filing** and **accelerated approval**

Primary cognitive endpoint

- Preclinical AD Cognitive Composite 5⁴:
 - Episodic memory
 - Timed executive function
 - Global cognition
- Potential **traditional approval**



(1) Alzheimer's disease; (2) Implied Abeta positivity (A+) because of Tau positivity (T+), but not part of the inclusion criteria; (3) Tau-PET measured in the Tau-naïve composite region; (4) PACC-5



ACI-7104.056: Anti-a-syn for Parkinson's disease



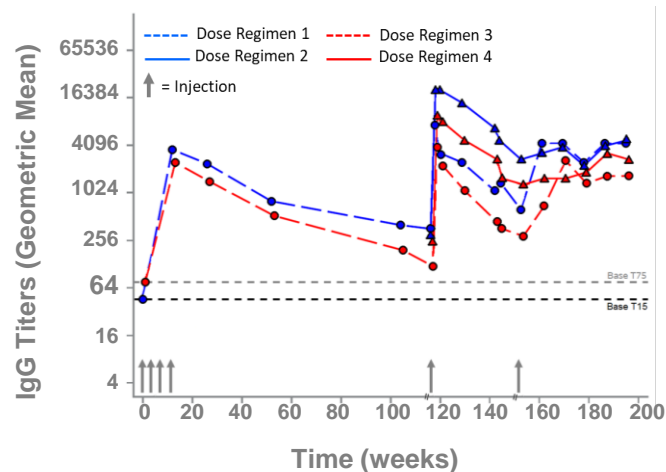
Clinically validated¹ anti-a-syn² active immunotherapy in PD³

Phase 1 results in *The Lancet Neurology* support best-in-class profile

THE LANCET
Neurology

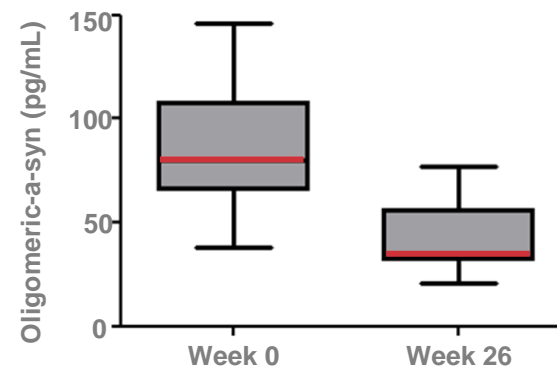
Safe and well tolerated with no safety concerns noted in patients followed for more than 3.5 years

Strong and boostable antibody response



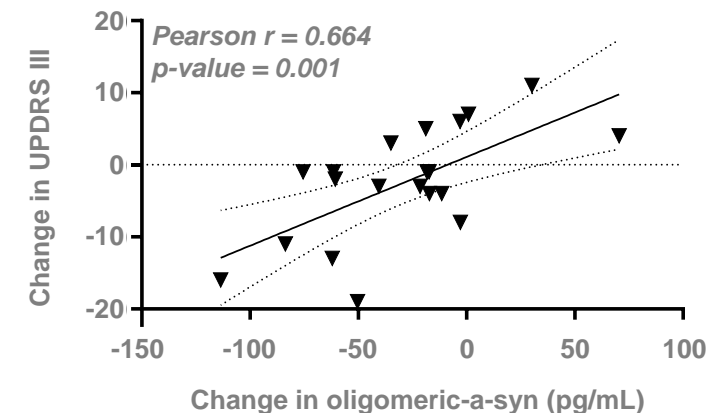
Strong and boostable antibody responses

50% reduction⁴ of pathological a-syn in CSF⁵



Target engagement evidence: 50% reduction in pathological (oligomeric) a-syn in the CSF

Changes⁶ in oligo-a-syn and UPDRS III correlate



Signal of clinical efficacy: stabilization of UPDRS⁷ III scores correlated with reductions in oligomeric a-syn

(1) Volc *et al.*, *Lancet Neurol.* 2020; (2) alpha-synuclein; (3) Parkinson's disease; (4) Data from 75 µg dose group; (5) Cerebrospinal fluid; (6) Change in oligomeric a-syn calculated at week 26, change in UPDRS III calculated at week 100; (7) Unified Parkinson's Disease Rating Scale

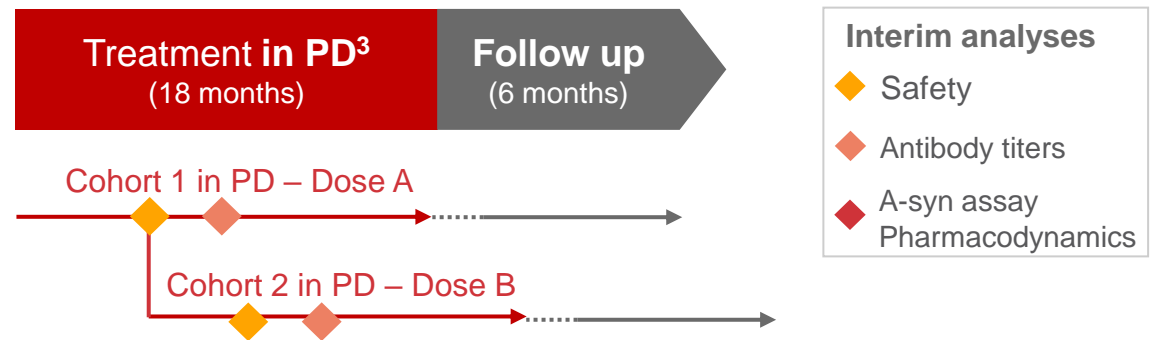
VacSYn: an adaptive biomarker-based Phase 2 study of ACI-7104 in early PD¹

Placebo-controlled Phase 2 Study Overview

- Seamless transition
 - 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

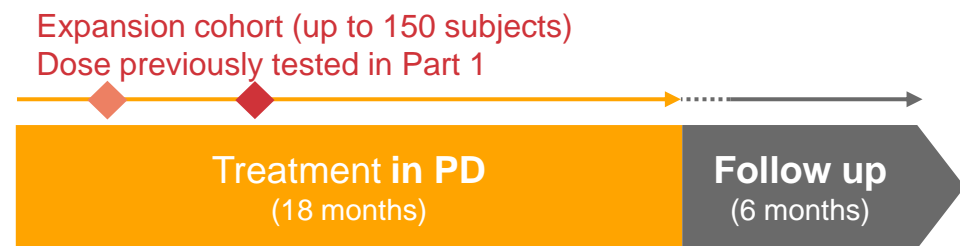
Part 1: Safety & PK/PD²

- Key immunogenicity measures
- Measures of pathological a-syn⁴ (a-syn oligomers and aggregates)



Part 2: PoC⁵ in early PD

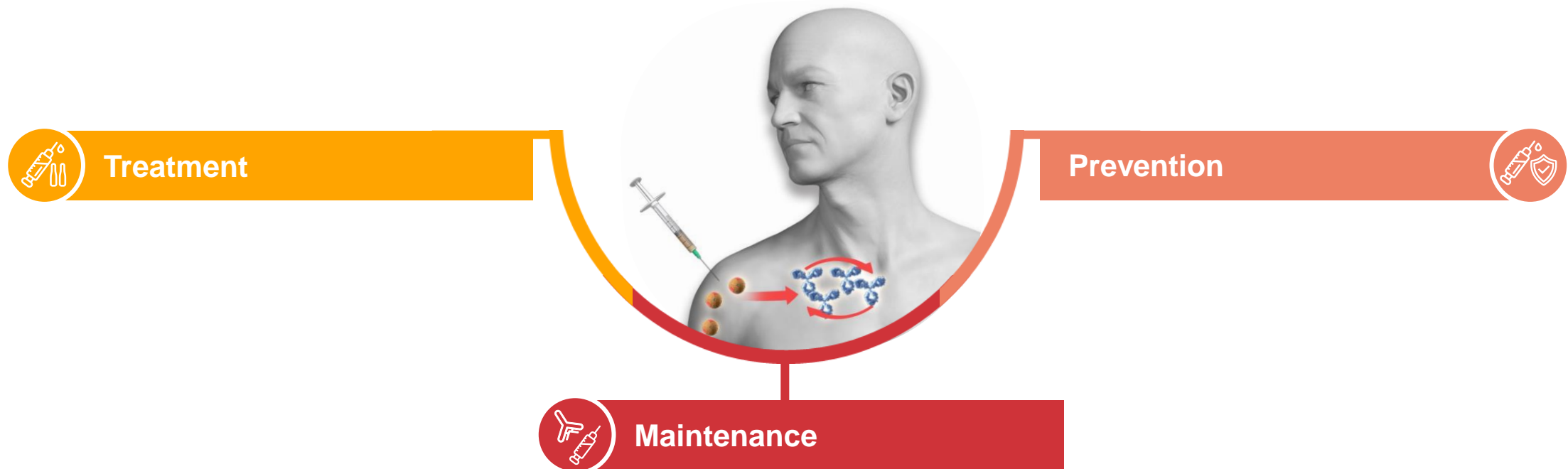
- Motor and Non-Motor Functioning (UPDRS⁶ based)
- Degeneration of dopaminergic terminals (DaT SPECT⁷ imaging)
- Advanced MRI (including ASL⁸ and DTI⁹)
- Digital biomarkers of motor and non-motor function
- Functional and patient reported outcomes



(1) Parkinson's disease; (2) Pharmacokinetics and Pharmacodynamics; (3) 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; (4) alpha-synuclein; (5) Proof-of-concept; (6) Unified Parkinson's disease rating scale; (7) Dopamine Transporter Single Photon Emission Computed Tomography; (8) Arterial spin labeling; (9) Diffusion tensor imaging

Active immunotherapy: a new class of treatment for neurodegenerative diseases

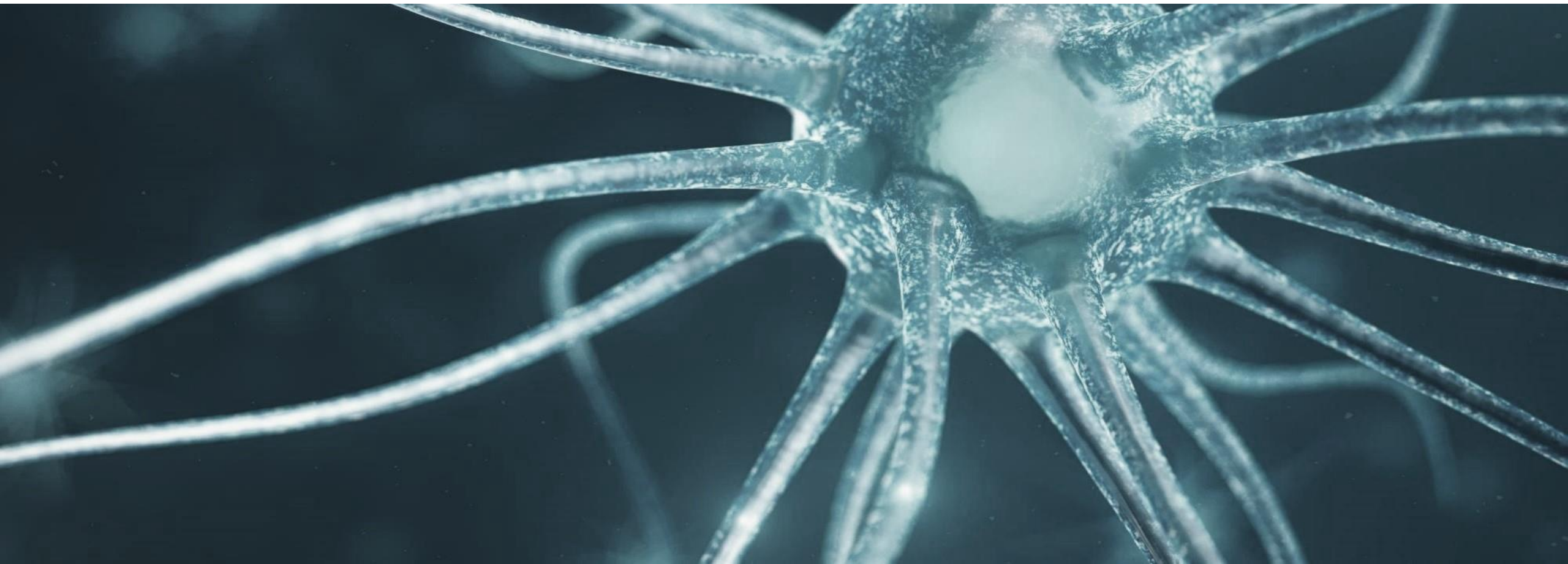
Potential for profound social and economic impact



ACTIVE 
Immune **Therapy**

for global treatment and prevention of neurodegenerative diseases

Future perspective



Creating the future of Precision Medicine in neurodegeneration

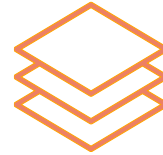
The foundation for early detection and treatment



Advance clinical-stage active immunotherapies

Targeted active immunotherapies:

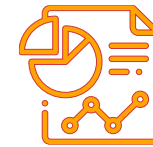
- **ACI-24.060** (Takeda)¹
- **ACI-35.030** (Janssen J&J)²
- **ACI-7105.056** (wholly-owned)³



Valorize pioneering technology platforms

SupraAntigen[®] & Morphomer[®]

- Clinical entry of a-syn⁴ and TDP-43⁵ PET⁶ tracers
- Clinical candidates for NLRP3⁷ inhibitors for CNS⁸ and non-CNS indications



Strong financial position

Operating capital foundation:

- Equity markets:
 - follow-on financing Dec 2023
- Partner payments:
 - Janssen ACI-35.030 milestones
 - Takeda ACI-24.060 upfront

3-year cash runway permits achievement of key milestones & execution of value-generating innovation

(1) Phase 1b/2; (2) Phase 2b; (3) Phase 2; (4) Alpha-synuclein; (5) TAR DNA-binding protein 43; (6) Positron emission tomography; (7) (NOD)-like receptor protein 3; (8) Central nervous system

AC Immune's leadership in Precision Medicine

Scientific excellence drives landmark **partnering deals** and shareholder value

Confirmed leadership in **active immunotherapies** in NDD¹

Multiple **unpartnered high-value assets**

Strong Balance Sheet with 3-year cash runway²

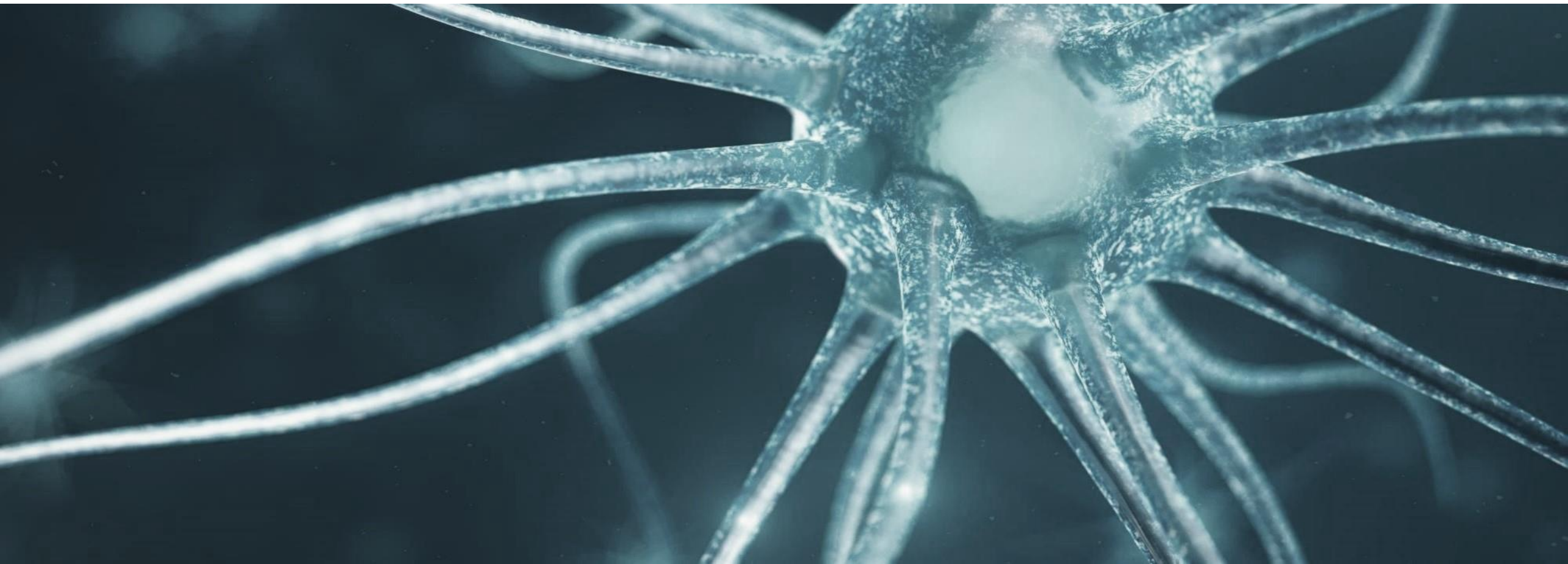


(1) Neurodegenerative disease; (2) assumes second ACI-35-related milestone payment of CHF25 million received in 2025 and no other milestones

AC Immune: Pioneering science and precision medicine

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

Supplementary information



Enable preventative therapies for rapid global application

Active immunotherapy is the most realistic approach

Science-driven innovation for optimal outcomes for patients

Advanced biomarker-based prevention trials for efficient market entry

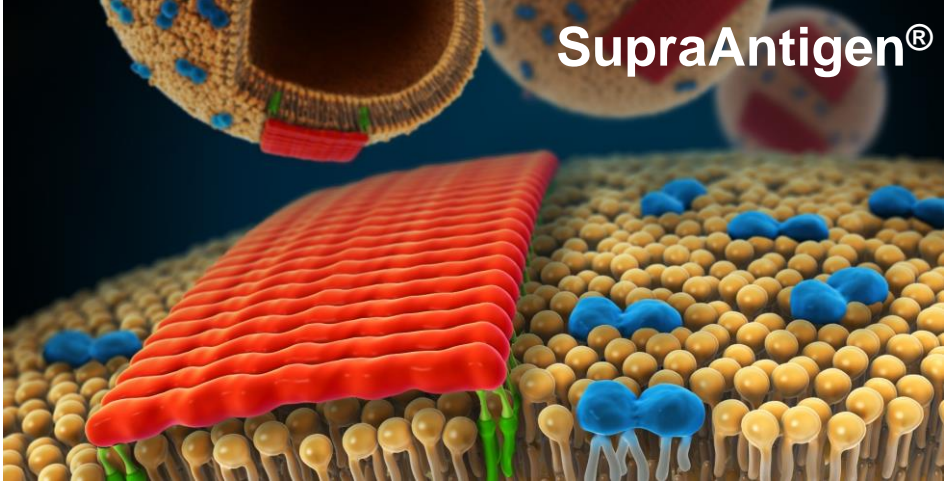
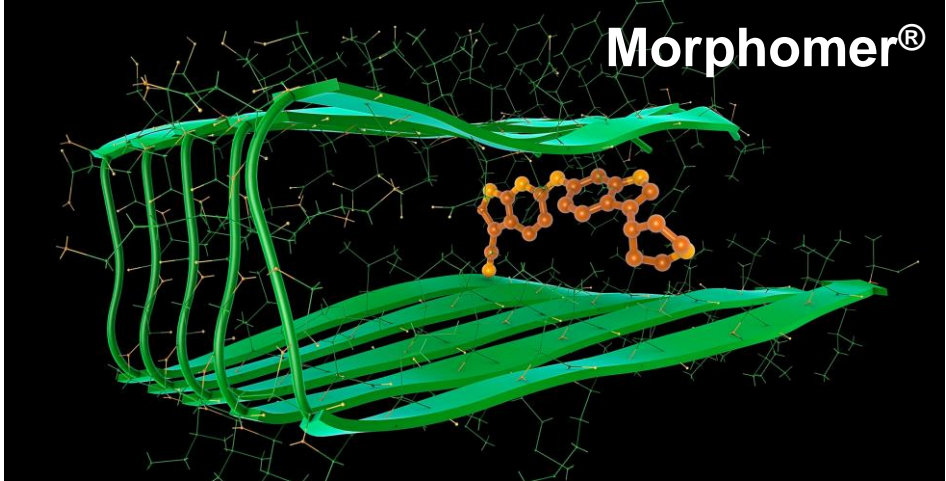




AD therapeutics with best-in-class features to ease use

Global partnerships to accelerate clinical development and worldwide distribution



AC Immune technology platforms driving validating pharma deals




Strategy: optimize value to risk ratio and retain significant upside

Platform	 SupraAntigen®		 Morphomer®	
Program	ACI-24.060	ACI-35.030	Mor Tau	Tau PET
Partner				

- An integrated approach to Central Nervous System (CNS)-specific therapies

AC Immune strong track record in deals¹ 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-24.060 (anti-Abeta active immunotherapy)	Phase 1b/2	>USD 2,100	USD 100		Mid-to-high teens	
ACI-35.030 (anti-pTau active immunotherapy)	Phase 2b	CHF 500	CHF 26	CHF 20	Low-double digits to mid-teens	
Tau Morphomer[®] drugs	Phase 1 ⁶	CHF 1,860	CHF 80 +USD 50 ⁷	CHF 40	Low-double digits to mid-teens	
PI-2620 (Tau PET ⁴ tracer)	Phase 3 ⁵	EUR 160	EUR 0.5	EUR 7	Mid-single digits to low-teens	
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 147.4		

■ 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)