Pioneering Precision Medicine for Neurodegeneration

NASDAQ: ACIU | Investor Presentation, March 2023

AC Immune

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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
Integrates therapeutics and diagnostics

Multiple global partnerships
>CHF 3 billion in potential milestones

Clinically validated technology platforms
Best-in-class small molecules and biologics

Strong Balance sheet
Funded into Q3 2024

- Based in Lausanne, Switzerland
- ~150 employees
- Listed September 2016 (NASDAQ: ACIU)
- 83.6 million shares outstanding[1]
- Cash of CHF 122.6 million[2] (~USD 132.5 million)

(1) As of December 31, 2022; excluding treasury shares; (2) As of December 31, 2022

Neurodegenerative diseases represent a large and growing market

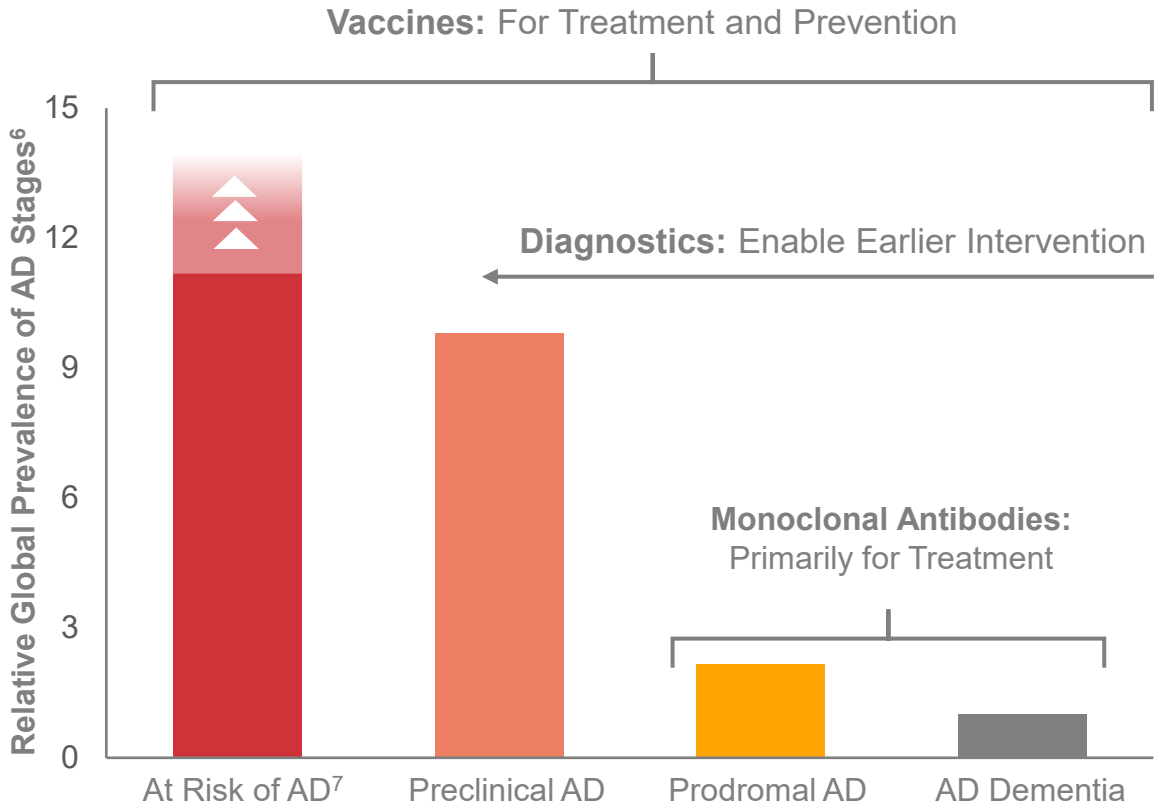
Prevalence of dementia expected to nearly double every 20 years[1]

>50 Million with dementia globally[1]

>1 Trillion global annual cost of dementia[1]

>6 Million with PD[2] globally[3]

20-50% of people over age 80 with LATE[4,5]



- Pairing earlier diagnosis with early vaccination can significantly expand NDD[8] market

(1) Alzheimer's Disease International; (2) Parkinson's disease; (3) Michael J Fox Foundation; (4) Limbic-predominant age-related TDP-43 encephalopathy; (5) Nelson et al. *Brain* 2019; (6) Gustavsson et al. Alzheimer's Dement. 2022; 1- 13. https://doi.org/10.1002/alz.12694; (7) Alzheimer's disease; (8) Neurodegenerative disease

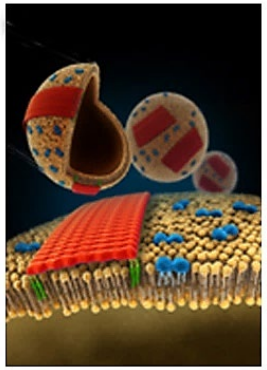
SupraAntigen® and Morphomer® platforms

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

CNS-optimized

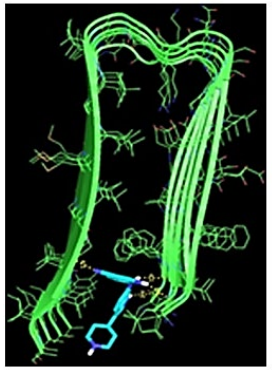
Clinically validated

SupraAntigen®



Vaccines & Antibodies

Morphomer®



Small Molecules

Conformation-specific

Precision medicine enabling

External validation and cash generated by 5 partnering[1] deals

Managing risk and retaining significant upside

	Product	Dev. phase	Total value[2]	Upfront[2]	Milestones received to date[2]	Royalties	Partners
Biologicals	Crenezumab (anti-Abeta antibody)	Phase 2	USD 340	USD 25	USD 40	Mid-single digits to mid-teens	Genentech, A Member of the Roche Group
Biologicals	Semorinemab (anti-Tau antibody)	Phase 2	CHF 430	CHF 17	CHF 42	Mid-single digits to low-double digits	Genentech, A Member of the Roche Group
Biologicals	ACI-35.030 (anti-pTau vaccine)	Phase 1b/2a	CHF 500	CHF 26	CHF 5	Low-double digits to mid-teens	Janssen
Small molecules	Tau PET[3] imaging agent	Phase 3[4]	EUR 160	EUR 0.5	EUR 7	Mid-single digits to low-teens	Life Molecular Imaging
Small molecules	Tau Morphomer® small molecules	Phase 1[5]	CHF 1,860	CHF 80 +USD 50[6]	CHF 40	Low-double digits to mid-teens	Lilly
	Total (millions)[7]		**CHF ~3,311**	**CHF 155.2[8]**	**CHF 132.4**		

- Outstanding potential milestone payments exceed CHF 3 billion

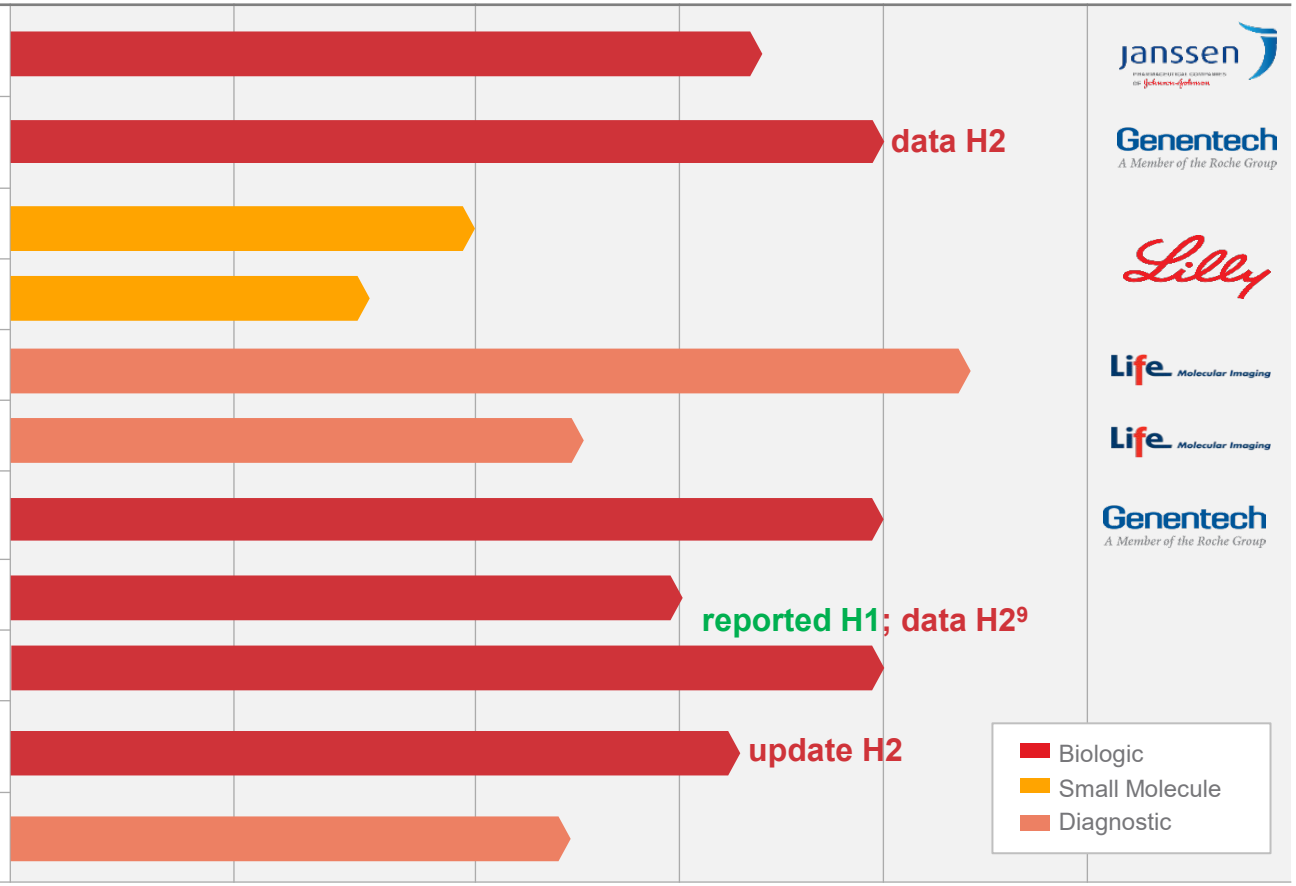
(1) Disclosure limited due to confidentiality agreements with collaboration partners; (2) In millions; (3) Positron emission tomography; (4) In Alzheimer's disease; (5) Phase 1 completed; (6) Equity investment; (7) Converted to CHF on date of receipt; (8) Excludes convertible note agreement of USD 50 million

Broad and robust pipeline in neurodegenerative diseases

Driven by validated proprietary technology platforms for sustained growth

Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	PARTNER
Tau	**ACI-35.030** *(anti-pTau vaccine)*	AD[1] treatment	Janssen
	Semorinemab *(anti-Tau antibody)*	AD treatment (*mild-to-moderate*)[2]	Genentech
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies	Lilly
		AD treatment	
	Tau-PET[3] tracer	AD diagnostic	Life Molecular Imaging
		PSP[4] diagnostic	Life Molecular Imaging
Abeta	**Crenezumab** *(anti-Abeta antibody)*	AD prevention[5]	Genentech
	ACI-24.060 *(anti-Abeta vaccine)*	AD treatment (*Down syndrome*[6])	
		AD treatment	
a-syn[7]	**ACI-7104.056** *(anti-a-syn vaccine)*	PD[8], a-synucleinopathies	
	a-syn-PET tracer	a-synucleinopathies (e.g. MSA[10])	



(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related Alzheimer's disease; (7) alpha-synuclein; (8) Parkinson's disease; (9) Refers to expected readouts from a Phase 1b/2 trial of an optimized formulation of ACI-24 (ACI-26.060) in patients with AD and patients with Down syndrome; (10) Multiple system atrophy

AC Immune 2022 highlights

Precision Medicine

- First ever live image of a-synuclein in a human brain

Pipeline deliverables

- Progressed towards 6 clinical milestones
- First AD[1] prevention study readout with anti-Abeta monoclonal antibody crenezumab

Pipeline maturation

- Initiated landmark Phase 1b/2 study of anti-Abeta vaccine in both sporadic AD and DS[2]
- Regulatory authorization to initiate first Phase 2 study of an anti-a-synuclein vaccine
- Partner (LMI[3]) initiated a Phase 3 study of Tau-PET[4] Tracer PI-2620

CMC process

- Established robust CMC process for anti-Abeta vaccine for pivotal and registrational supply
- Assured supply of anti-a-synuclein vaccine for Phase 2b/3

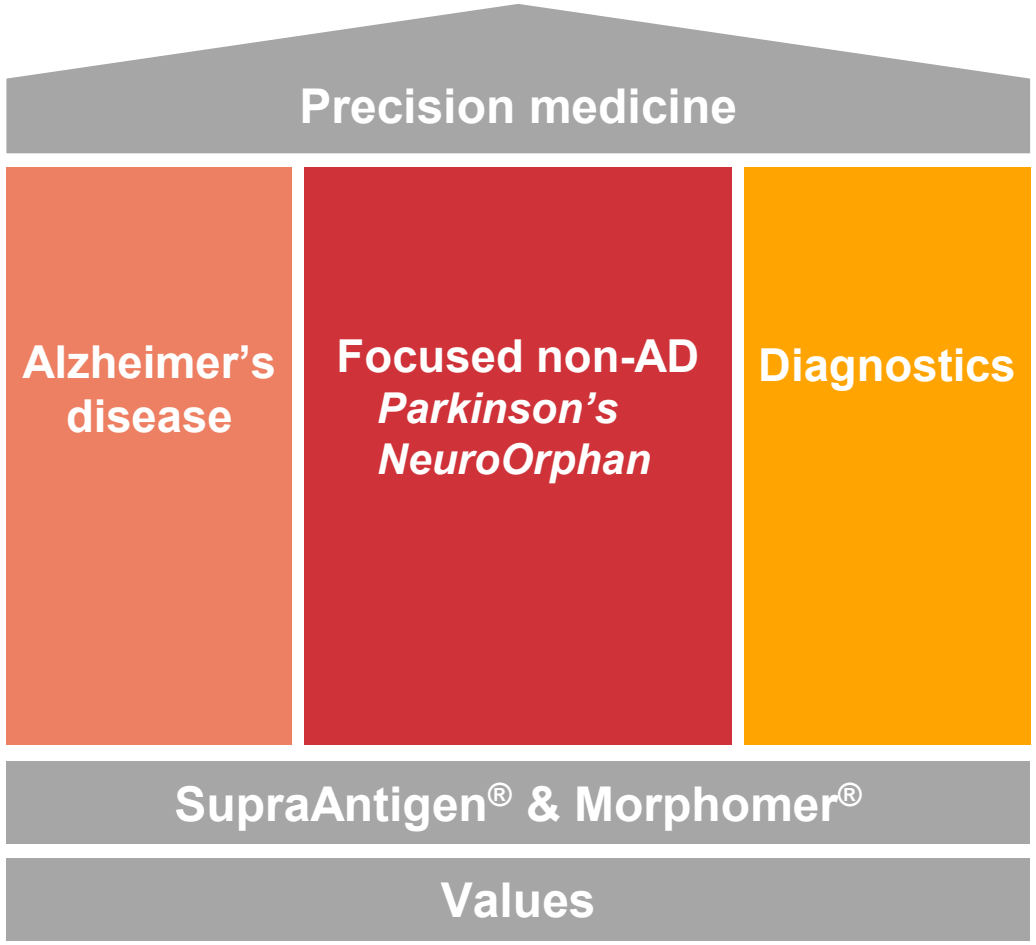
Maintained Financial Strength

- Cash runway into Q3 2024 without consideration of potential milestone payments

(1) Alzheimer's disease; (2) Down syndrome; (3) Life Molecular Imaging; (4) Positron emission tomography

Business Strategy 2023: advancing vaccine and non-AD portfolio

Focus on delivering Precision Medicine to enhance value creation



Alzheimer's disease

- Accelerate development of novel late-stage therapies with partners
- Accelerate wholly-owned optimized anti-Abeta vaccine (ACI-24.060) with parallel development in AD[1] and DS[2]

Non-AD and NeuroOrphans

- Increase strategic focus in non-AD to Parkinson's disease
- Advance anti-a-syn[3] vaccine into late-stage development

Diagnostics for precision medicine

- Advance our differentiated diagnostic pipeline for Parkinson's disease and TDP-43[4]-based pathologies

(1) Alzheimer's disease; (2) Down syndrome; (3) Alpha-synuclein; (4) TAR DNA-binding protein 43

Key milestones for value creation in 2023

Multiple clinical readouts for wholly-owned vaccines

✓ Achieved
● Clinical readouts
○ Other development events

Vaccines		H1	H2	
ACI-24.060	Abeta	○		Initiation of Down syndrome cohort of Phase 1b/2 ABATE study
		○		IND submission to enable expansion of ABATE study to U.S.
		✓	●	**Two interim analyses in AD[1] – safety, immunogenicity**
			●	**Interim analysis in Down syndrome – safety, immunogenicity**
ACI-35.030	Tau		○	Further development with initiation of next trial in AD followed by milestone payment
ACI-7104	a-syn[2]		●	**Phase 2 VACSYN study in PD update**
Monoclonal antibodies				
Semorinemab	Tau		●	**Phase 2 Lauriet Trial Open Label Extension results**
Monoclonal antibody	TDP-43[3]		○	Candidate into preclinical development (tox)
Diagnostics				
a-syn-PET[4] tracer	a-syn		○	Next clinical candidate declaration for PD[5]
TDP-43-PET tracer	TDP-43	○		Clinical candidate declaration

(1) Alzheimer's disease; (2) Alpha-synuclein; (3) TAR DNA-binding protein 43; (4) Positron emission tomography; (5) Parkinson's disease

Vaccine programs targeting neurodegenerative diseases

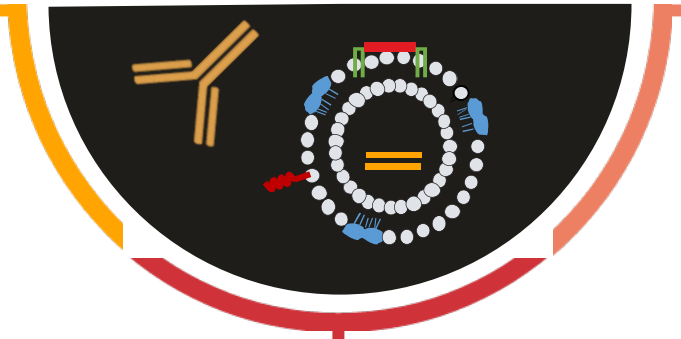
Vaccines as a new class of treatment for neurodegenerative disease

AC Immune vaccines: Potential for profound social and economic impact

Treatment

High efficacy with:

- Multiple epitope targeting
- Long-lasting immune response
- Steady titers
- Favorable safety and tolerability
- Convenient, annual dosing



Prevention

- Vaccination is the best strategy to preserve function and quality of life
- Cost-effective and global application

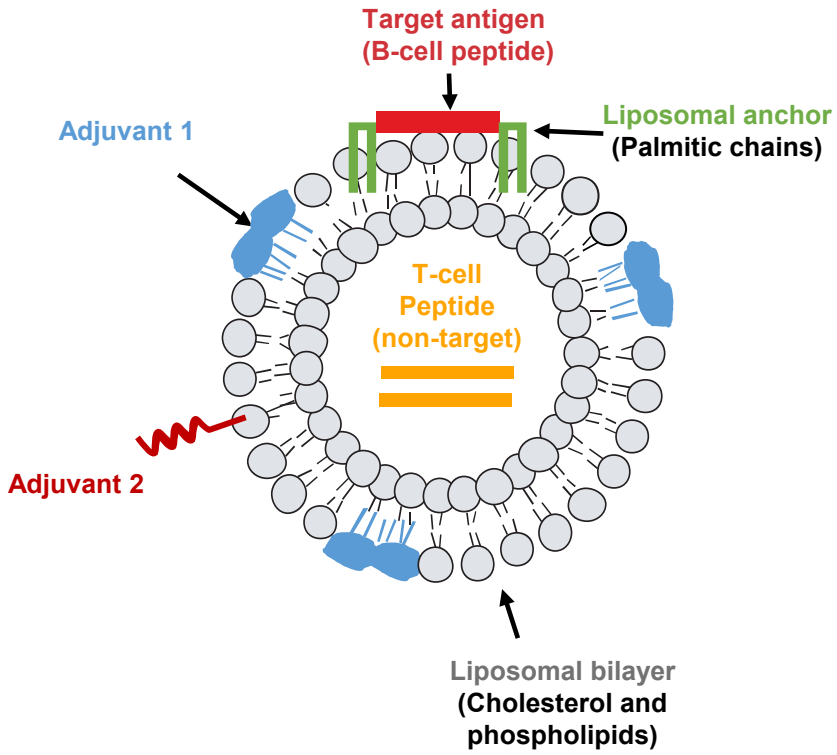
Maintenance

- Use as maintenance therapy after monoclonal anti-Abeta antibodies
- Convenient, annual dosing to maintain low plaque levels

- Goal: Global vaccines for neurodegenerative diseases

Disruptive potential of SupraAntigen®-V

Optimized vaccines delivering superior results in neurodegenerative diseases



Generates target-specific antibody response

Safely engages target-unrelated T-cells to enhance & maintain response

Unprecedented Clinical Performance

Immunogenicity	++++[1]
Target specificity	++++[2]
Conformation specificity	+++
Avidity increase over time	+++
Sustainability of response	+++
Boosting	+++
Class switching IgM to IgG	+++
Evidence of memory B cells	+++

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

(1) 100% response after 1st injection; (2) Increases over time

ACI-24.060: Vaccine targeting two pathological forms of Abeta

ACI-24.060 targets pyroGlu- and oligomeric Abeta, which are believed to drive AD progression

Clinical Stage Programs

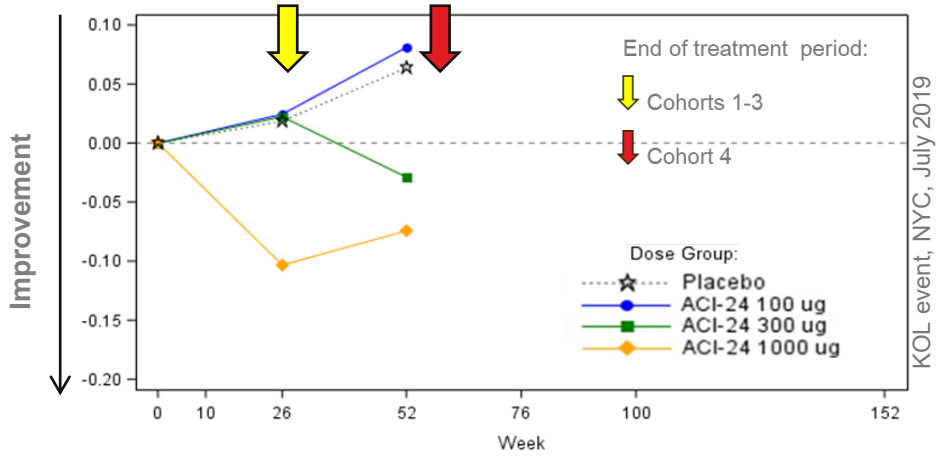
TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	ACI-35.030 *(anti-pTau vaccine)*	AD[1] treatment						janssen
	Semorinemab *(anti-Tau antibody)*	AD treatment *(mild-to-moderate)*[2]						Genentech
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies						Lilly
		AD treatment						
	Tau-PET[3] tracer	AD diagnostic						Life Molecular Imaging
		PSP[4] diagnostic						Life Molecular Imaging
Abeta	Crenezumab *(anti-Abeta antibody)*	AD prevention[5]						Genentech
	ACI-24 *(anti-Abeta vaccine)*	AD treatment (*Down syndrome*[6])				reported H1; data H2[9]		
		AD treatment						
a-syn[7]	ACI-7104 *(anti-a-syn vaccine)*	PD[8], a-synucleinopathies						
	a-syn-PET tracer	a-synucleinopathies (e.g. MSA[10])						

(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related AD; (7) alpha-synuclein; (8) Parkinson's disease; (9) Refers to expected readout from a Phase 1b/2 trial of an optimized formulation of ACI-24 in patients with AD and patients with Down syndrome; (10) Multiple system atrophy

ACI-24: Early clinical data support advancement of program

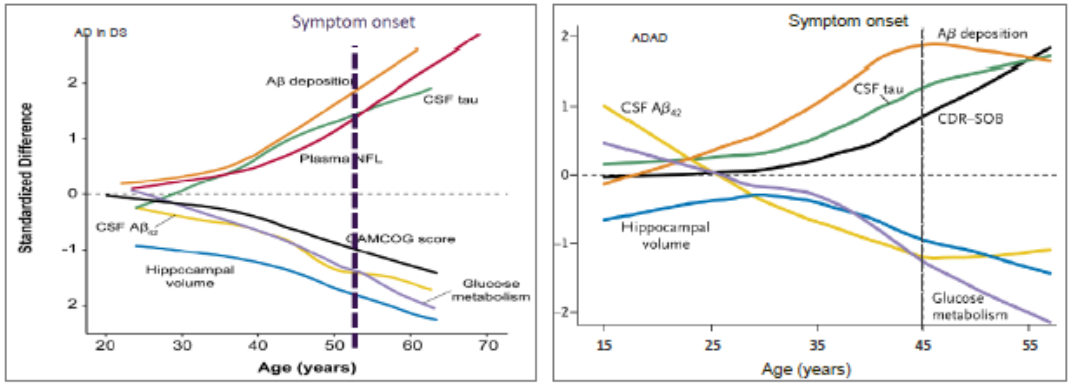
Optimized formulation (ACI-24.060) in next stage of clinical development in AD[2] and DS[3]-related AD

Abeta clearance measured by Abeta PET[4]
Change in composite summary SUVR-MCG[5]
Clinical evidence of target engagement



Alzheimer's disease in DS
Similar pathophysiology and biomarkers in DS and ADAD[6]
Virtually all individuals with DS go on to develop AD-like symptoms

DS, Fortea, AAIC 2019



ADAD, adapted from Bateman, NEJM 2012

1 Dose-dependent reduction of brain Abeta accumulation in a Phase 1b/2 trial in AD[7]

2 Encouraging immunogenicity: generated anti-Abeta antibodies in patients with AD & individuals with DS

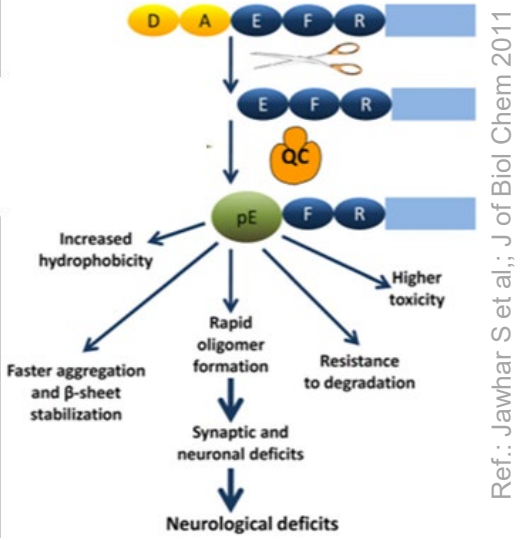
3 Positive pharmacodynamic response (increase in plasma Abeta) in a Phase 1b trial in DS

4 Safe and well tolerated with no treatment-related SAEs[8] in clinical trials in AD[9] and DS[10]

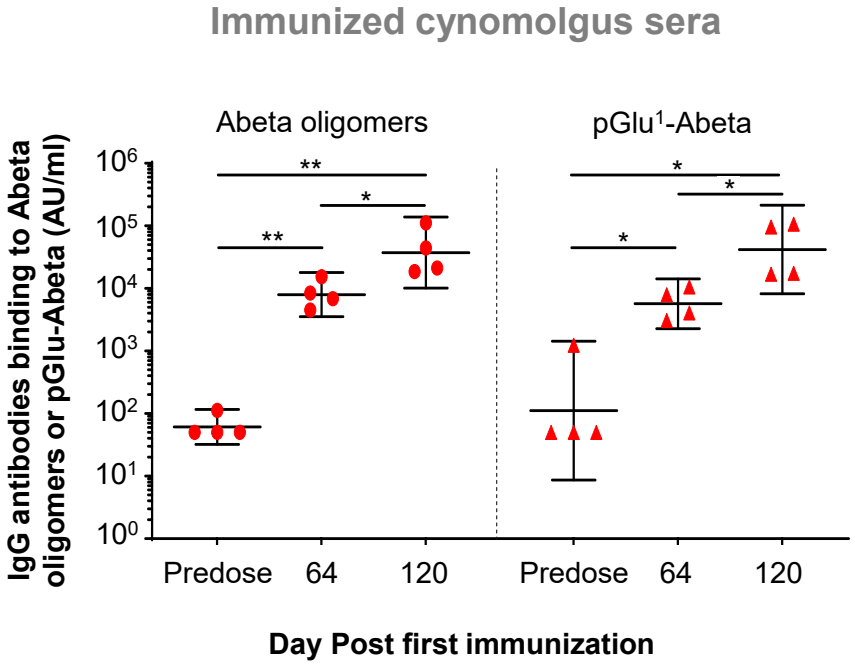
(1) Pyroglutamate Abeta; (2) Alzheimer disease; (3) Down syndrome; (4) Positron emission tomography; (5) Standardized Uptake Value Ratio-Mean Cerebellar Gray; (6) Autosomal dominant Alzheimer's disease; (7) Phase 1b/2 clinical trial in AD (trial ACI-0701); (8) Serious adverse events; (9) Phase 2 clinical trial in AD (trial ACI-1801); (10) Phase 1b clinical trial in DS (trial ACI-1301)

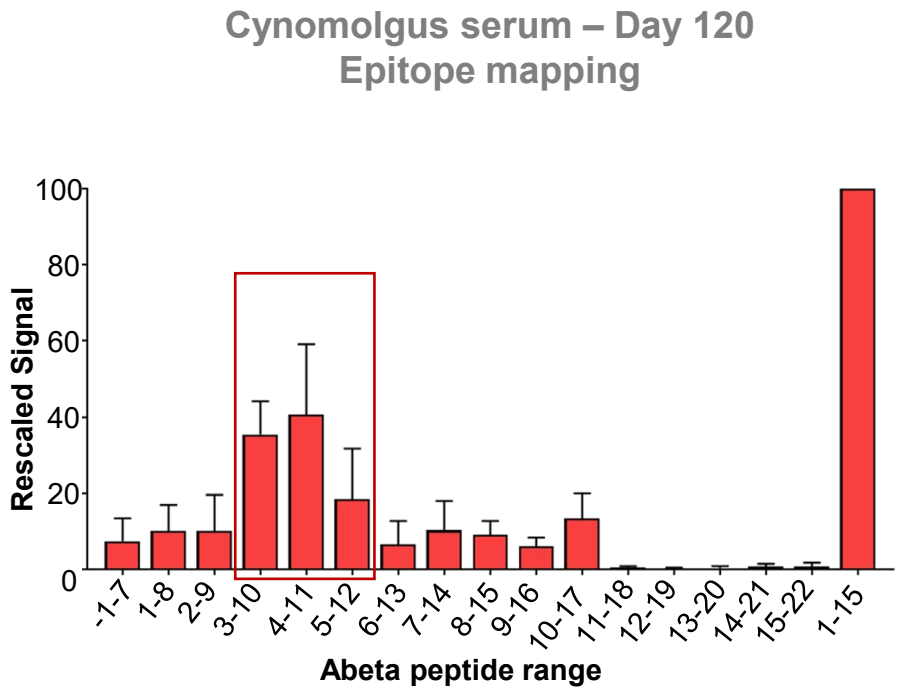
ACI-24.060: Strong immune response against toxic Abeta species

Targets oligomeric- and pyroGlu-Abeta (targets of lecanemab and donanemab, respectively)



Ref.: Jawhar S et al,; J of Biol Chem 2011





Ref.: Global Down Syndrome Forum 2021; M. Vukicevic, et al., Brain Comm, 2022

- Sustained and enhanced IgG response that binds Abeta(1-42) oligomers and pyroglutamate Abeta, the highly neurotoxic, truncated form of pathological Abeta
- The optimized vaccine represents a potential breakthrough compared to previous anti-Abeta vaccines

(1) Pyroglutamate * p<0.05, ** p<0.01

AβATE: Phase 1b/2 study of ACI-24.060 in AD[1] and AD in DS[2]

Innovative, translational, biomarker-based design offers key advantages

Precision Medicine

- **Defined populations** using clinical and biomarker measures to detect Abeta pathology and disease severity in **sporadic AD** and **individuals with DS**

Interim Analysis: Decision Points

- Abeta PET[3] lowering as key marker to benchmark against current monoclonal antibodies targeting oligomeric- and pyroGlu-Abeta (lecanemab & donanemab)
- Allows for early **interim analysis** for safety, immunogenicity and pharmacodynamics

Acceleration and De-Risking

- **Fast and informed transition** between cohorts and generation of meaningful readout on Abeta PET to allow **accelerated initiation of pivotal program**

Primary Prevention: Abeta PET

- DS is the largest **genetic AD population** with a strongly predictable initiation of Abeta pathology in the brain
- AβATE will inform use of Abeta PET as an outcome for primary prevention

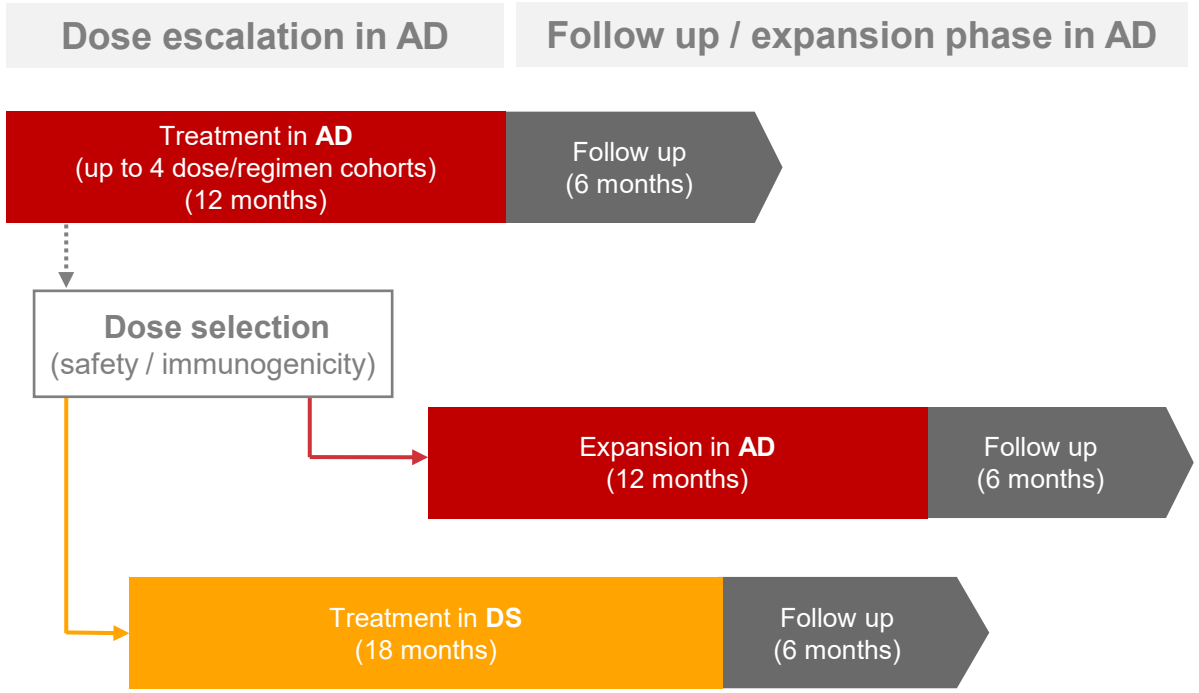
(1) Alzheimer's disease; (2) Down syndrome; (3) Positron Emission Tomography

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

Placebo-controlled Phase 1b/2 Study Overview

Inclusion criteria	Both	Multicenter, adaptive, placebo-controlled, dose-escalation, double-blind, randomized Phase 1b/2 study in people with: ▪ Abeta pathology confirmed by PET[3] scan
	AD	▪ Prodromal AD (CDR[4]-Global Score 0.5; age 50-75 years)
	DS	▪ Non-demented people living with DS (age 35–50 years)
Study design	Both	▪ IA[5] of safety/tolerability and immunogenicity ▪ Biomarker analyses including Abeta PET 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 ▪ Exploratory biomarkers and clinical endpoints

Trial Schematic



Interim analyses

- Safety/tolerability
- Immunogenicity – antibody titers
- Biomarkers – Abeta-PET, pharmacodynamics, target engagement

(1) Alzheimer's disease; (2) Down syndrome-related AD; (3) Positron emission tomography; (4) Clinical Dementia Rating; (5) Interim analyses

ACI-7104: Anti-a-syn[1] vaccine being developed for Parkinson's disease

Update on Phase 2 trial expected in H2

Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	ACI-35.030 *(anti-pTau vaccine)*	AD[2] treatment						janssen
	Semorinemab *(anti-Tau antibody)*	AD treatment *(mild-to-moderate)*[3]						Genentech
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies						Lilly
		AD treatment						
	Tau-PET[4] tracer	AD diagnostic						Life Molecular Imaging
		PSP[5] diagnostic						Life Molecular Imaging
Abeta	Crenezumab *(anti-Abeta antibody)*	AD prevention[6]						Genentech
	ACI-24 *(anti-Abeta vaccine)*	AD treatment (*Down syndrome*[7])						
		AD treatment						
a-syn	**ACI-7104** *(anti-a-syn vaccine)*	PD[8], a-synucleinopathies				update H2		
	a-syn-PET tracer	a-synucleinopathies (e.g. MSA[9])						

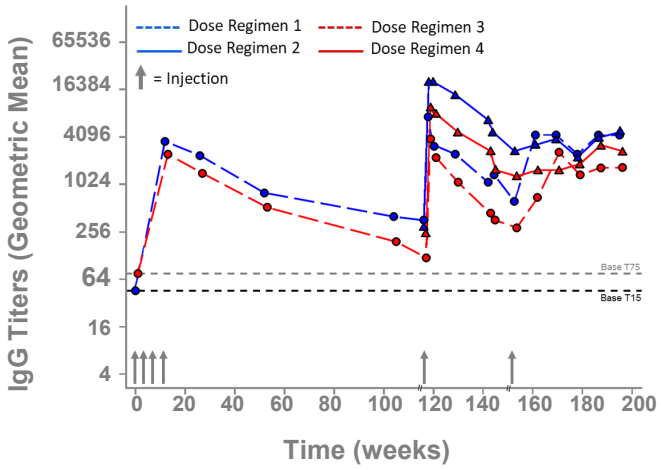
(1) Alpha-synuclein; (2) Alzheimer's disease; (3) Open label extension study is ongoing; (4) Positron emission tomography; (5) Progressive supranuclear palsy; (6) Prevention trial API-ADAD in Colombia; (7) Down syndrome-related Alzheimer's disease; (8) Parkinson's disease; (9) Multiple system atrophy

Anti-a-syn[1] vaccine is clinically validated[2] in Parkinson's disease

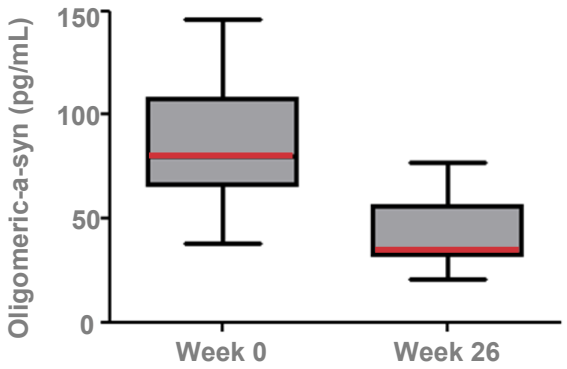
Phase 1 results in *The Lancet Neurology* support best-in-class profile

THE LANCET Neurology

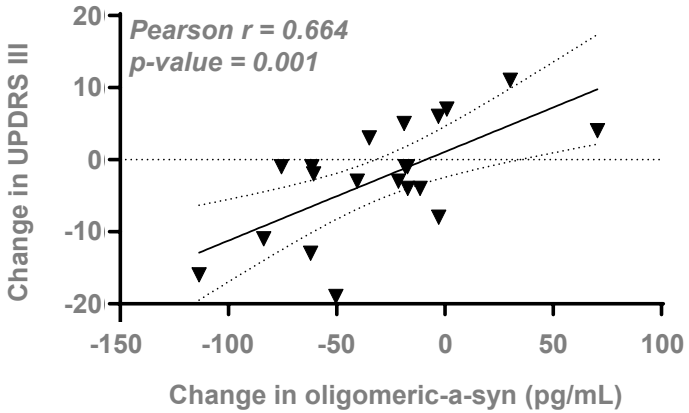
Strong and boostable antibody response



50% reduction[3] of pathological a-syn in CSF[4]



Changes[5] in oligo-a-syn and UPDRS III correlate



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

2 Strong and boostable antibody responses

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

4 Signal of clinical efficacy: stabilization of UPDRS[6] III scores correlated with reductions in oligomeric a-syn

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

AC Immune

VacSYn: an adaptive biomarker-based Phase 2 study in early PD[1]

Placebo-controlled Phase 2 Study Overview

Inclusion criteria

- Idiopathic PD; L-Dopa treatment (up to 300 mg per day, stable)
- A diagnosis of PD for 2 years or less at screening (not demented / no cognitive impairment)
- Dopaminergic deficit by DaT SPECT[2]

Study design

- 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
  - Understand biological signal for early transition to filing

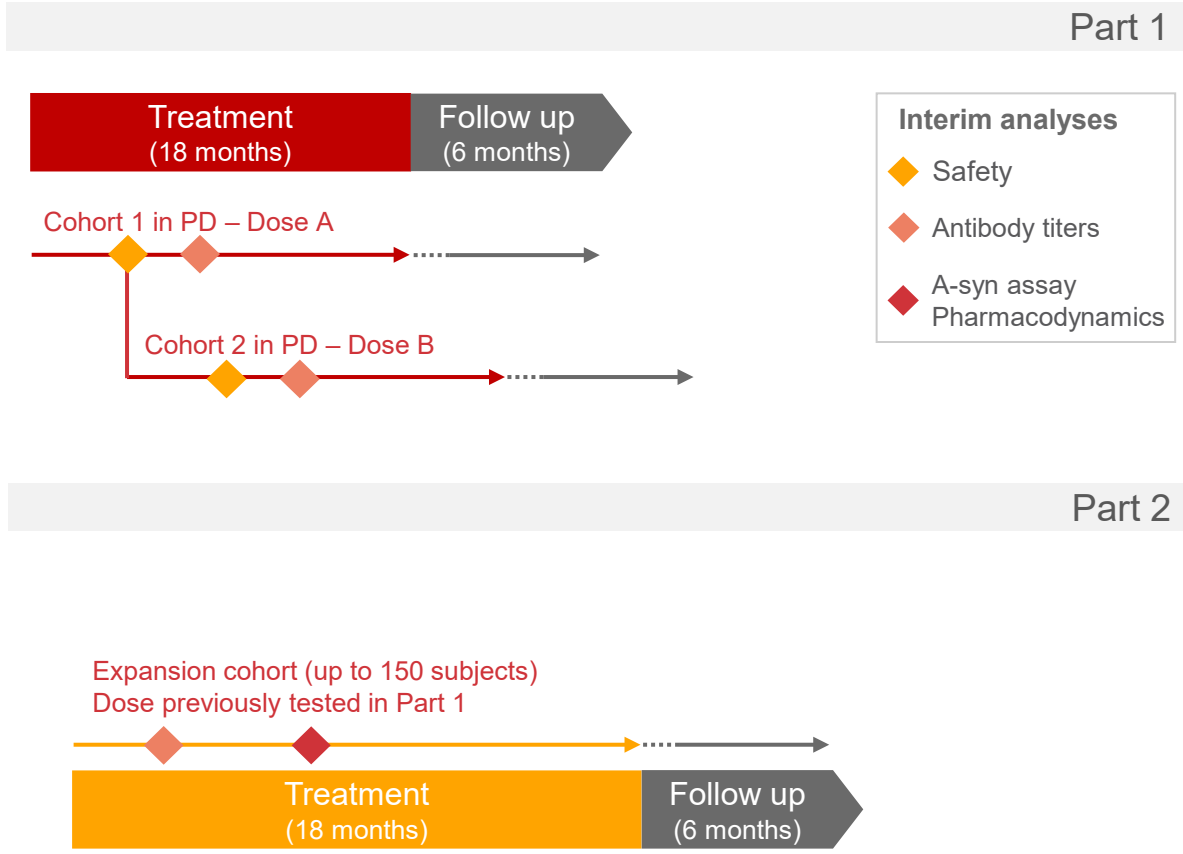
Part 1 Safety & PK/PD[3]

- Key immunogenicity measures
- Measures of pathological a-syn[4] and a-syn aggregation (phospho-a-syn and a-syn oligomers)

Part 2 PoC[5] in early PD

- Motor and Non-Motor Functioning (UPDRS[6] based)
- Neurodegeneration of dopaminergic terminals (DaT SPECT imaging)
- Digital biomarkers of motor and non-motor function
- Advanced MRI (including ASL[7] and DTI[8])
- Functional and patient reported outcomes

Study Dosing Schematic



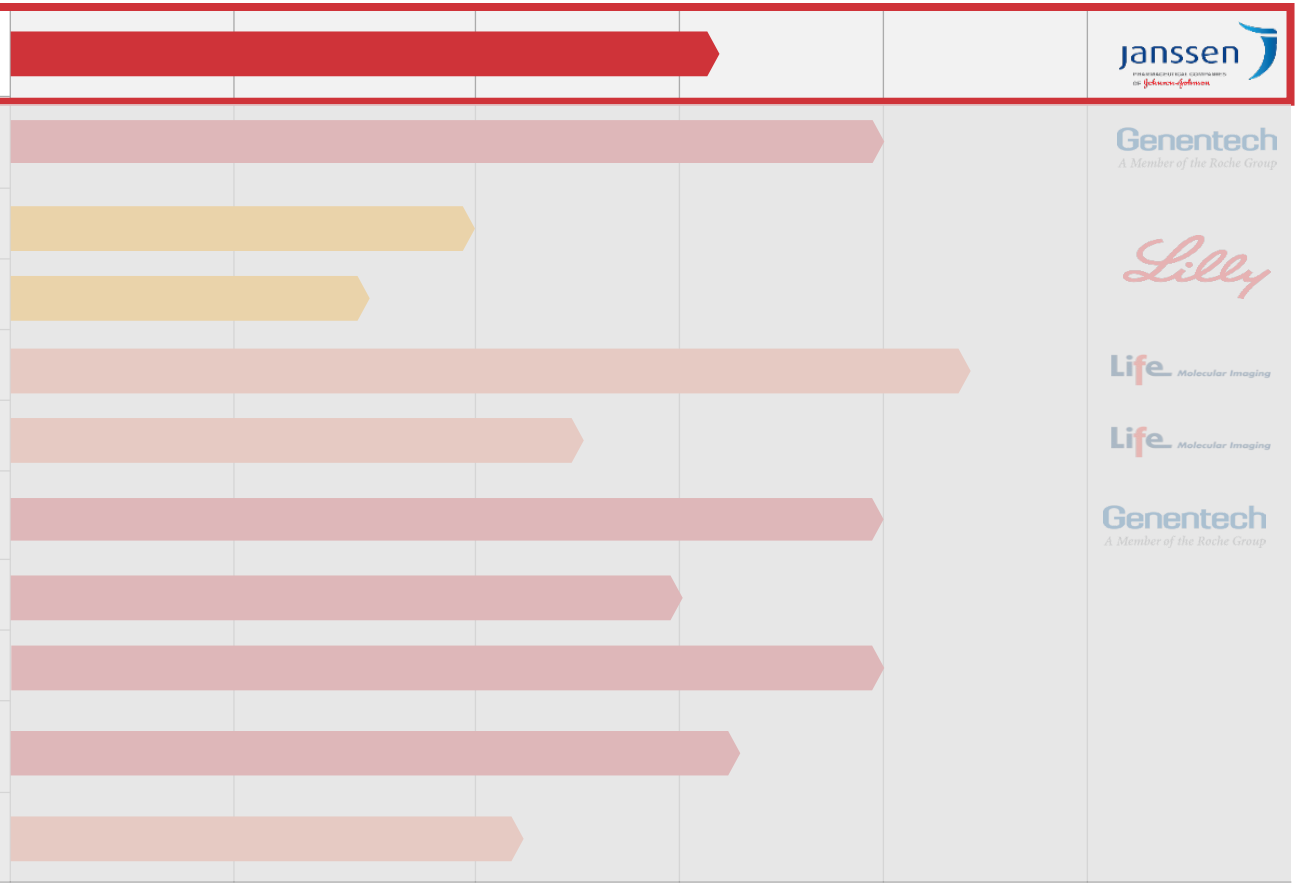
(1) Parkinson's disease; (2) Dopamine Transporter Single Photon Emission Computed Tomography; (3) Pharmacokinetics and Pharmacodynamics; (4) alpha-synuclein; (5) Proof-of-concept; (6) Unified Parkinson's disease rating scale; (7) Arterial spin labeling; (8) Diffusion tensor imaging

ACI-35.030: Anti-pTau vaccine being developed for AD[1]

Further clinical development in AD and milestone payment expected in H2

Clinical Stage Programs

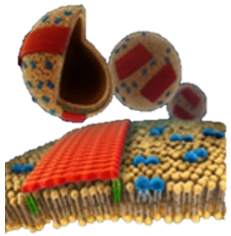
TARGET	PRODUCT CANDIDATE	INDICATION	PARTNER
Tau	**ACI-35.030** *(anti-pTau vaccine)*	AD treatment	Janssen
	Semorinemab *(anti-Tau antibody)*	AD treatment *(mild-to-moderate)*[2]	Genentech
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies	Lilly
		AD treatment	
	Tau-PET[3] tracer	AD diagnostic	Life Molecular Imaging
		PSP[4] diagnostic	Life Molecular Imaging
Abeta	**Crenezumab** *(anti-Abeta antibody)*	AD prevention[5]	Genentech
	ACI-24 *(anti-Abeta vaccine)*	AD treatment (*Down syndrome*[6])	
		AD treatment	
a-syn[7]	**ACI-7104** *(anti-a-syn vaccine)*	PD[8], a-synucleinopathies	
	a-syn-PET tracer	a-synucleinopathies (e.g. MSA[9])	



(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related Alzheimer's disease; (7) alpha-synuclein; (8) Parkinson's disease; (9) Multiple system atrophy

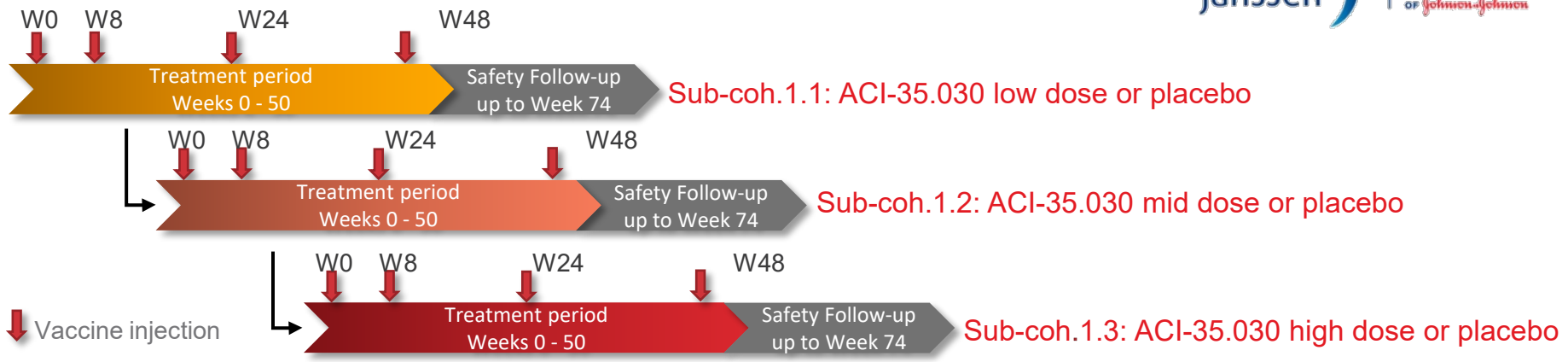
ACI-35.030: Very encouraging interim Phase 1b/2a results in AD[1]

SupraAntigen® platform



AC-35.030

- pTau selective
- T-cell independent (Tau)
- Optimized formulation



Interim results to date in all dose cohorts (safety/tolerability, immunogenicity):

- Anti-Tau IgG response preferentially targeting phosphorylated Tau in all participants
- 100% of participants demonstrated an anti-pTau IgG response[3] after the 1st injection
- Anti-pTau IgM response was also elicited in all participants
- Safe and well tolerated, no vaccine-related safety concerns observed to date

Expansion of the second dose cohort to generate additional patient data

1 Achieved high titers of anti-pTau antibodies in 100% of participants from week 2

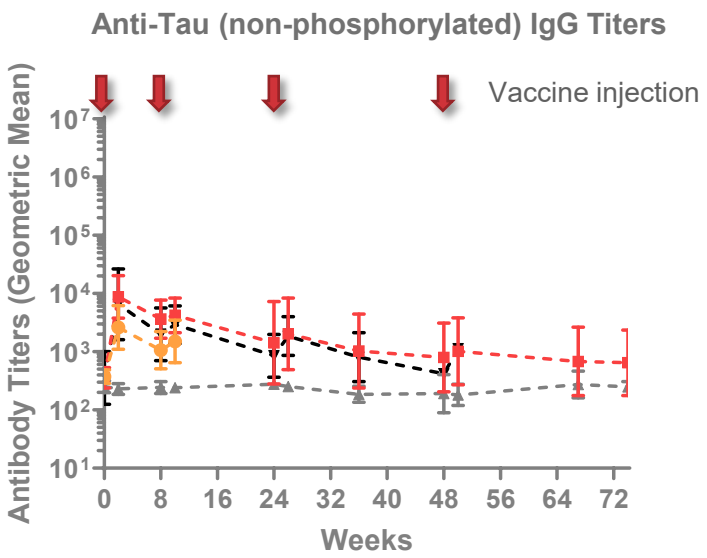
2 Strong safety and robust immunogenicity support advancing to late-stage development

(1) Alzheimer's disease; (2) Clinical Trials in Alzheimer's Disease Conference; (3) Responders were defined as higher than a pretreatment value multiplied by a threshold factor (>~2x)

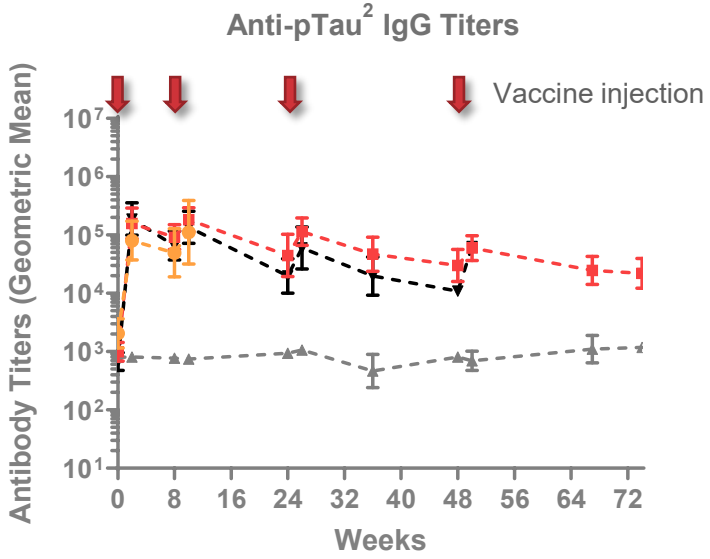
ACI-35.030 generates a potent Ab[1] response against pathological Tau

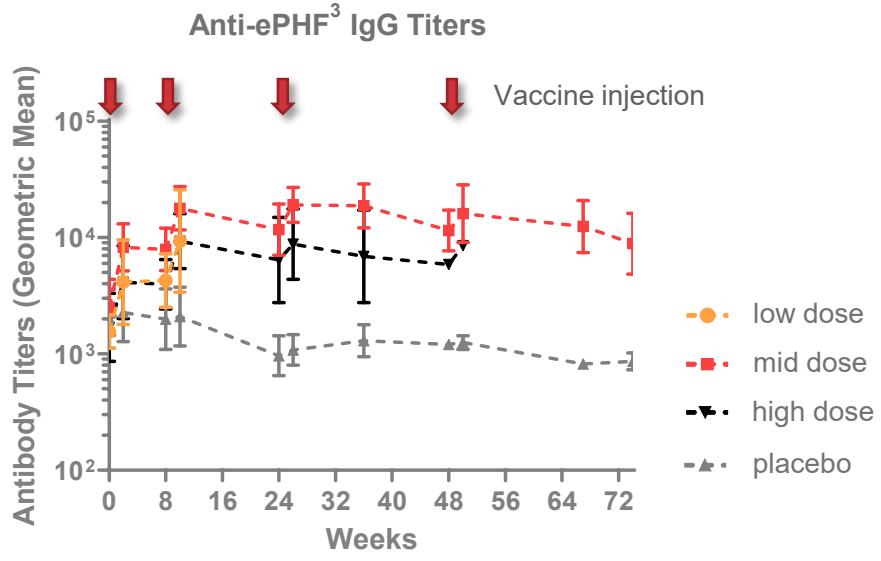
ACI-35.030 generates excellent Ab responses against pTau[2] in an older population

Non-Phosphorylated Tau



Phosphorylated & Pathological Tau species





1 Strong induction of Abs preferentially targeting pTau and its aggregated form (ePHF)

2 Anti-pTau titers increased by >100-fold[4] from baseline in the mid-dose cohort

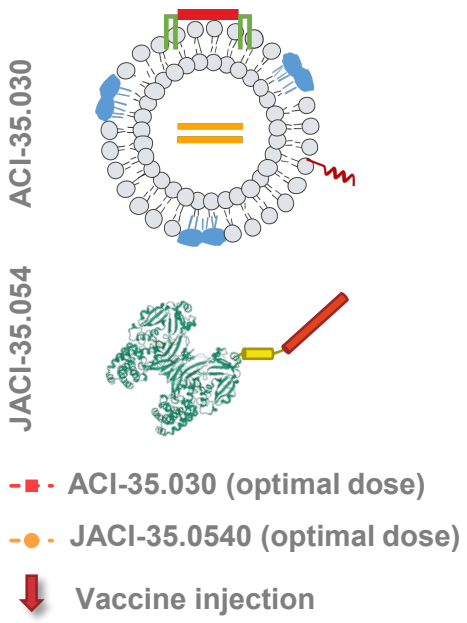
3 Anti-ePHF titers increased by approximately 10-fold[5] from baseline in the mid-dose cohort

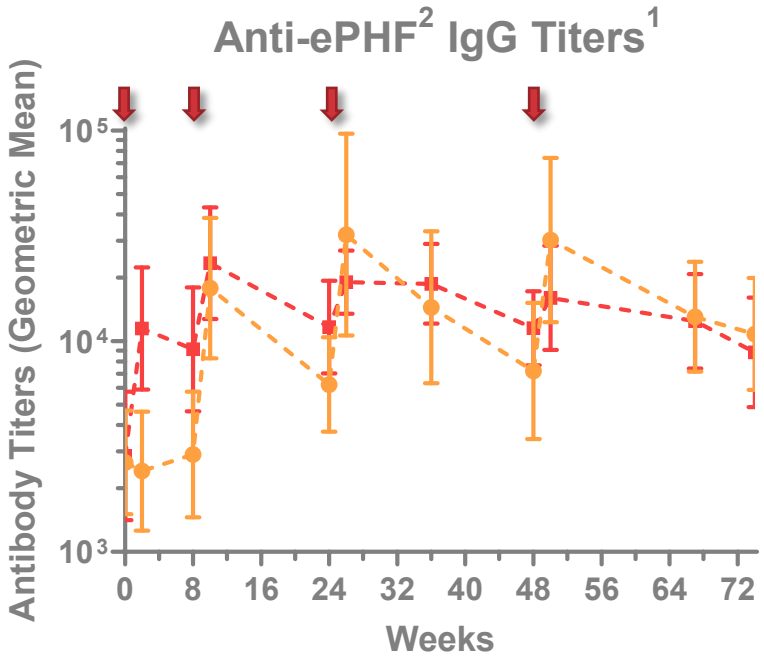
4 Antibody responses showed boostability following the second and third doses

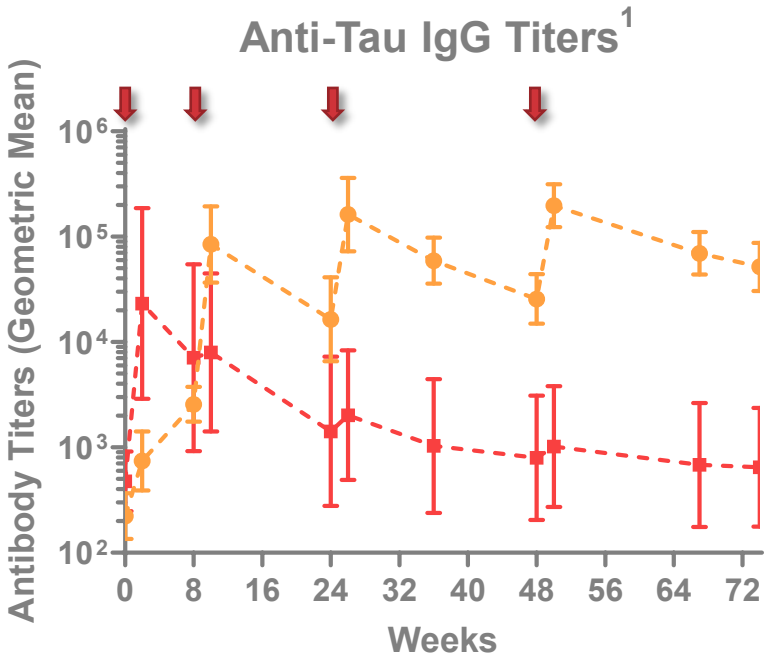
(1) Antibody; (2) phosphorylated Tau; (3) Enriched paired helical filaments; (4) at Weeks 2 and 10; (5) at Week 10

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







1 JACI-35.054 is a protein conjugate vaccine utilizing the same pTau[3] epitope as ACI-35.030

2 ACI-35.050 and JACI-35.054 were evaluated in parallel in the Phase 1b/2a trial in AD[4] patients

3 ACI-35.030 induced Ab[5] responses in 100% of patients after 1st injection compared to 50% with JACI-35.054

4 ACI-35.030-induced anti-ePHF Abs: longer apparent half-lives, less variability, lower peak-to-trough ratios

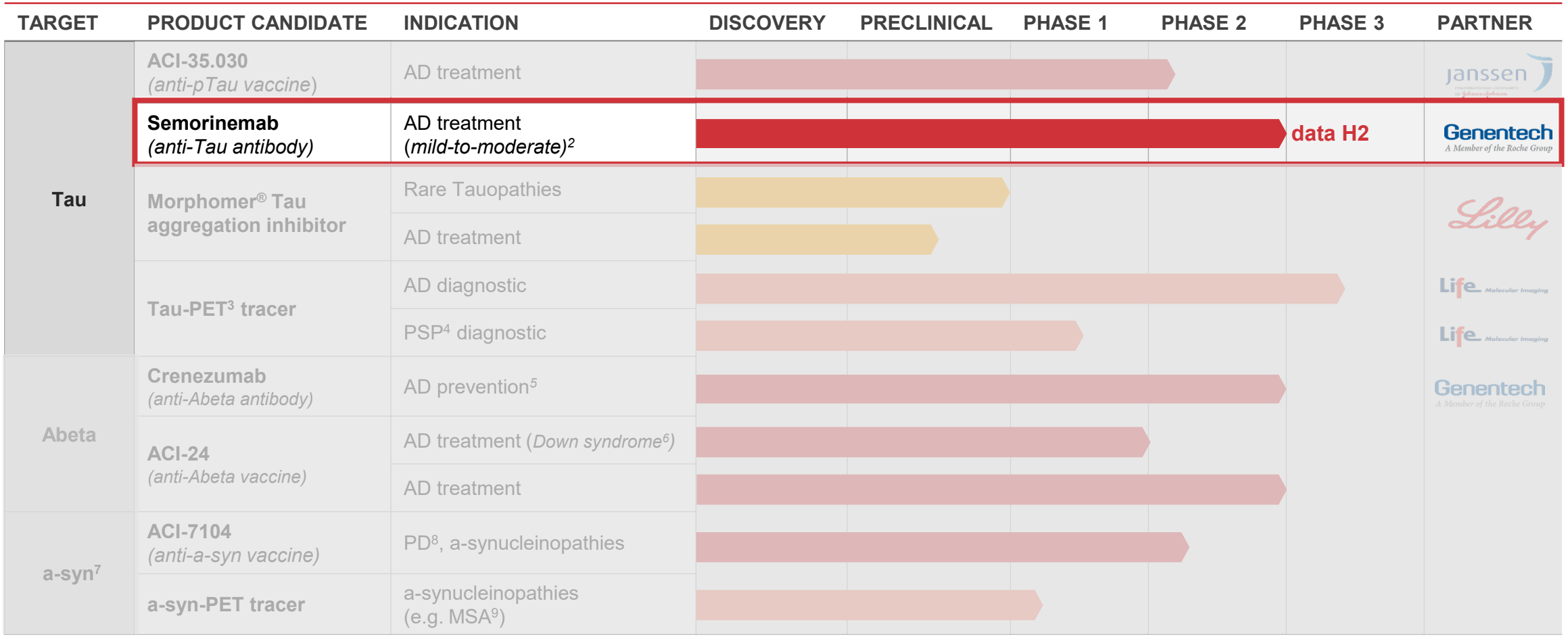
(1) ACI-35.030 original sub-cohort 1.2 data; (2) Enriched paired helical filaments; (3) phosphorylated Tau; (4) Alzheimer's disease; (5) Antibody

Clinical-stage monoclonal antibodies targeting neurodegenerative diseases

Semorinemab: Anti-Tau monoclonal antibody being developed for AD[1]

New Phase 2 open-label extension data expected in H2

Clinical Stage Programs



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Lauriet study evaluating the mAb[1] semorinemab in mild-to-moderate AD[2]

One co-primary endpoint met: first positive cognitive results for an anti-Tau mAb therapy in AD

1. Observed a statistically significant 2.89 point (42.2%) reduction in cognitive decline vs. placebo as measured by ADAS-Cog11[3] at week 49 (p=0.0008)
2. ADAS-Cog11 findings were consistent across prespecified subgroups and at week 61[4]
3. Results showing semorinemab's significant treatment effect on cognition achieved in a population where limited or no effect of anti-Abeta mAbs is observed
4. Semorinemab was well tolerated with an acceptable safety profile and no unanticipated safety signals
5. ADCS-ADL[5] co-primary endpoint and secondary efficacy endpoints (MMSE[6]; CDR-SB[7]) were not met

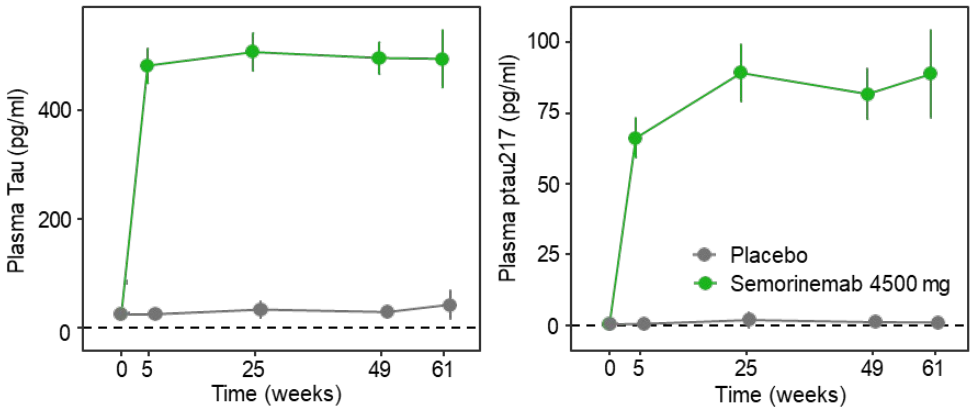
First evidence of therapeutic impact on cognition for a disease-modifying anti-Tau mAb in mild-to-moderate AD patients[8]

(1) Monoclonal antibody; (2) Alzheimer's disease; (3) Alzheimer's Disease Assessment Scale, Cognitive Subscale, 11-item Version; (4) In the subset of patients for whom the double-blind treatment period was extended to 60 weeks; (5) Alzheimer's Disease Cooperative Study - Activities of Daily Living; (6) Mini-mental state exam; (7) Clinical Dementia Rating-Sum of the Boxes; (8) MMSE of 16-21;

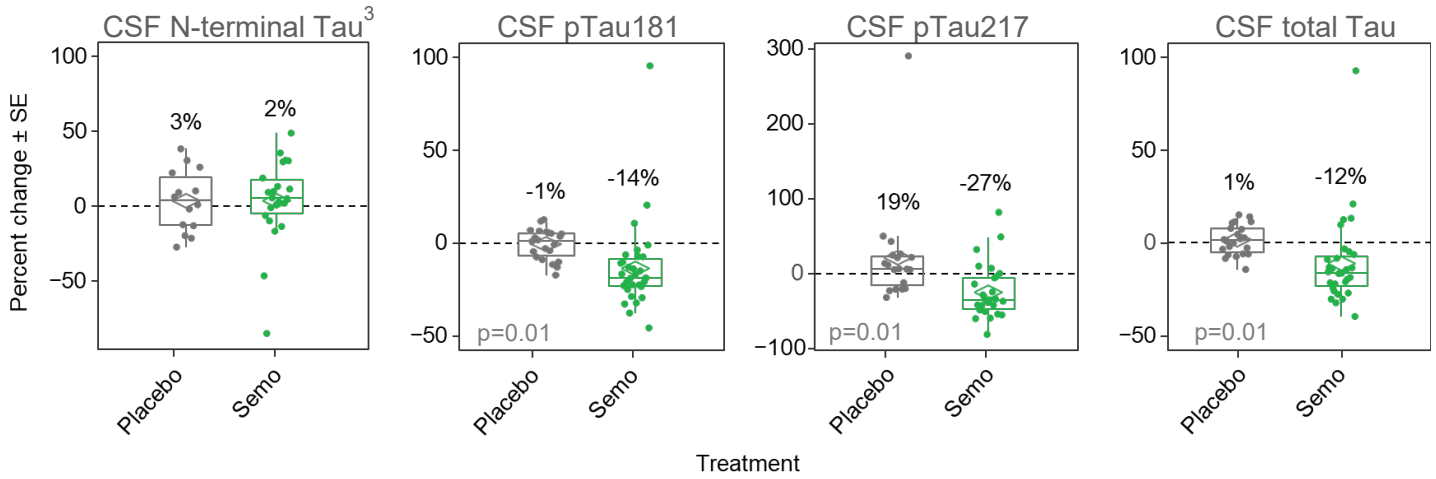
Key biomarker findings from Lauriet Phase 2 trial of semorinemab in AD[1]

Data provide further support for Tau as a target in AD

Plasma pharmacodynamics from Lauriet study[2]



Lauriet study (mild-to-moderate AD): CSF Tau pharmacodynamics



1 Observed rapid rise in plasma Tau levels following treatment with semorinemab, providing evidence of target engagement

2 CSF[4] biomarker analyses confirm target engagement and show significant reduction of pTau[5]

3 Treatment effect on Tau PET[6] signal was not observed

4 Data support the importance of soluble forms of pathological Tau in driving cognitive decline and warrant further analysis

(1) Alzheimer's disease; (2) Week 61 timepoint corresponds to a subset of Cohort 2 patient samples; (3) N-terminal Tau findings potentially linked to antibody-target binding; (4) Cerebrospinal fluid; (5) Phosphorylated Tau; (6) Positron emission tomography

Diagnostics to enable precision medicine

Successfully treating neurodegeneration requires precision medicine

From a mono- to a multi-target combination approach informed by cutting edge diagnostics

Imaging: AC Immune's Unique Capabilities

Positron Emission Tomography

- Tau
- a-syn[1]
- TDP-43[2]

Biofluids

- **Blood / Serum**
- **Cerebrospinal Fluid**

- a-syn
- TDP-43

Future Technologies

In collaboration:

- **Digital Health Technologies & Wearable Devices**

Treating the

right proteinopathies,

in the right patient,

at the right time

- Non-invasive diagnostics are critical for accurate patient selection and treatment to improve clinical outcomes
- Early and comprehensive diagnosis may eventually lead to disease prevention and combination therapy

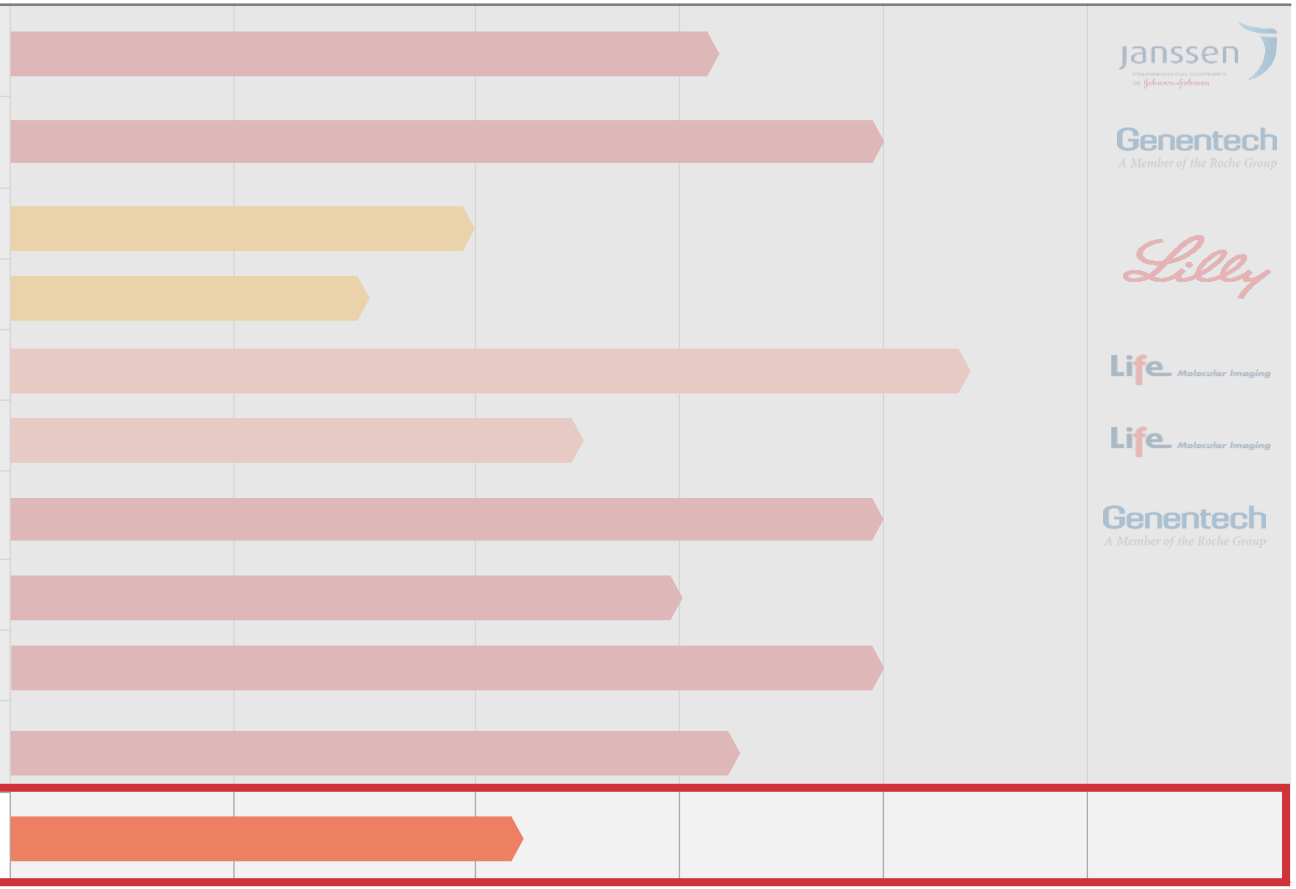
(1) alpha-synuclein; (2) TAR DNA-binding protein 43;

ACI-12589: a-syn PET tracer

Positive clinical proof-of-concept

Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	PARTNER
Tau	**ACI-35.030** *(anti-pTau vaccine)*	AD[1] treatment	janssen
	Semorinemab *(anti-Tau antibody)*	AD treatment *(mild-to-moderate)*[2]	Genentech
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies	Lilly
		AD treatment	
	Tau-PET[3] tracer	AD diagnostic	Life Molecular Imaging
		PSP[4] diagnostic	Life Molecular Imaging
Abeta	**Crenezumab** *(anti-Abeta antibody)*	AD prevention[5]	Genentech
	ACI-24 *(anti-Abeta vaccine)*	AD treatment (*Down syndrome*[6])	
		AD treatment	
a-syn[7]	**ACI-7104** *(anti-a-syn vaccine)*	PD[8], a-synucleinopathies	
	a-syn-PET tracer	a-synucleinopathies (e.g. MSA[9])	



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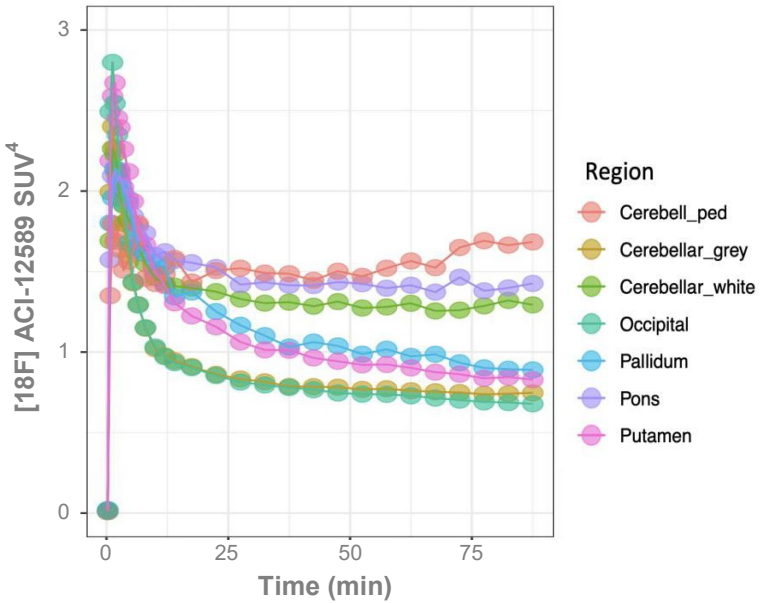
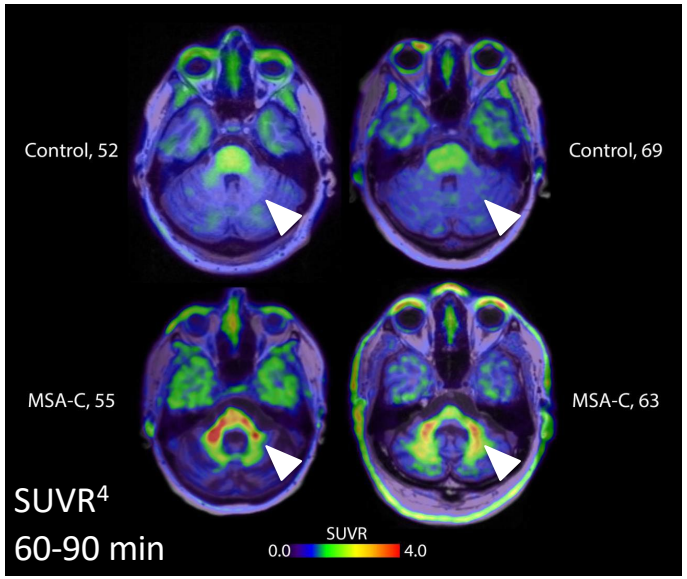
ACI-12589: Positive clinical proof-of-concept for an a-syn[1]-PET[2] tracer

First-in-class diagnostic for MSA[3] and monitoring a-syn drug target engagement

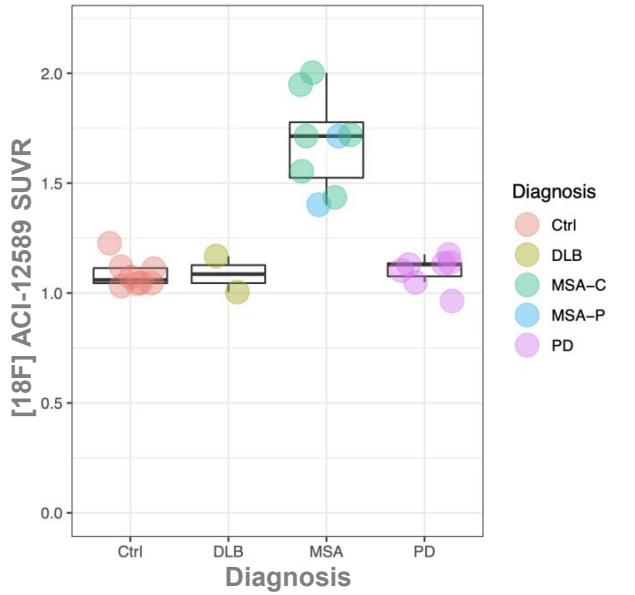
Rapid brain uptake and fast signal equilibrium



Strong signal in cerebellar white matter in MSA



Complete separation of MSA from other synucleinopathies and HC[5]



R. Smith *et al.*, AD/PD, 2022

1 ACI-12589 shows rapid brain uptake and fast signal equilibrium

2 Clearly separates MSA from other a-synucleinopathies with strong binding in expected regions (cerebellum)

3 ACI-12589 displays selectivity for a-syn over Abeta and Tau, and no relevant binding to MAO-B[6]

4 Ready for full development in MSA and enables future applications in PD[7] with ACI-12589 or next-gen tracers

(1) alpha-synuclein; (2) Positron emission tomography; (3) Multiple system atrophy; (4) Standardized uptake value; (5) Healthy controls; (6) Monoamine oxidase B; (7) Parkinson's disease

Key milestones for value creation in 2023

Multiple clinical readouts for wholly-owned vaccines

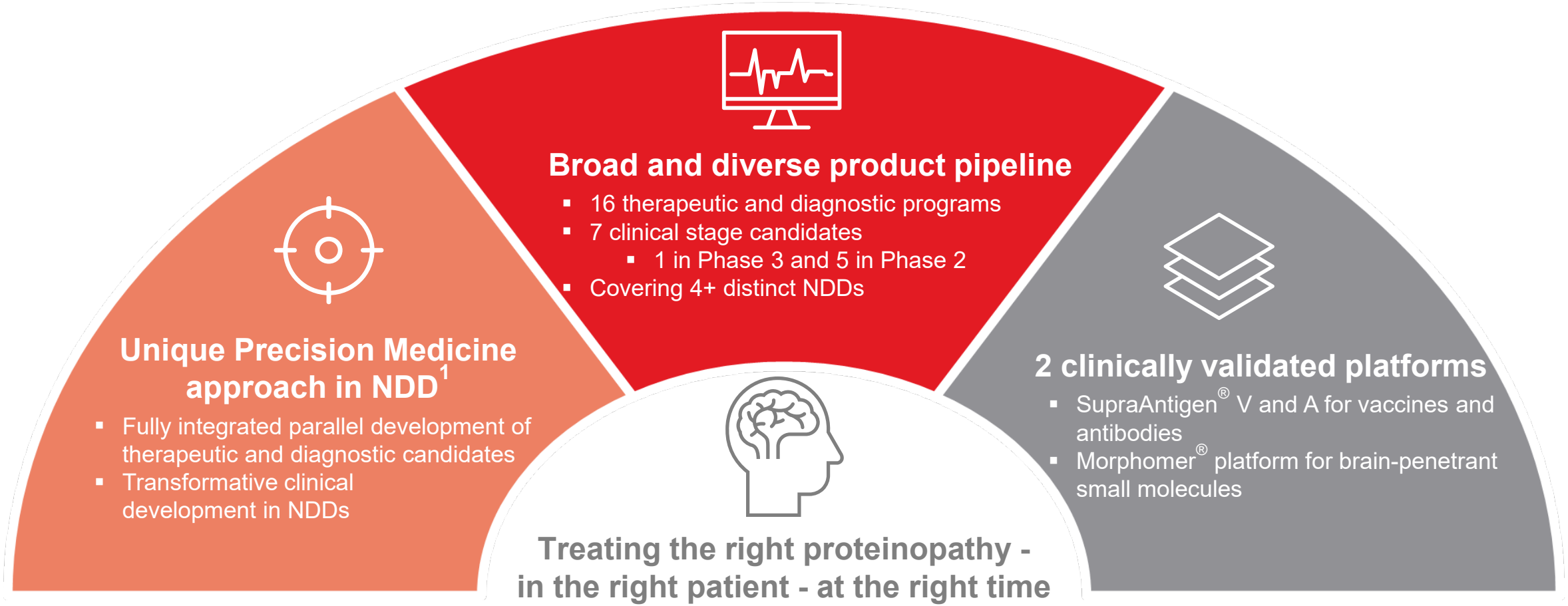
✓ Achieved
● Clinical readouts
○ Other development events

Vaccines		H1	H2	
ACI-24.060	Abeta	○		Initiation of Down syndrome cohort of Phase 1b/2 ABATE study
		○		IND submission to enable expansion of ABATE study to U.S.
		✓	●	**Two interim analyses in AD[1] – safety, immunogenicity**
			●	**Interim analysis in Down syndrome – safety, immunogenicity**
ACI-35.030	Tau		○	Further development with initiation of next trial in AD followed by milestone payment
ACI-7104	a-syn[2]		●	**Phase 2 VACSYN study in PD update**
Monoclonal antibodies				
Semorinemab	Tau		●	**Phase 2 Lauriet Trial Open Label Extension results**
Monoclonal antibody	TDP-43[3]		○	Candidate into preclinical development (tox)
Diagnostics				
a-syn-PET[4] tracer	a-syn		○	Next clinical candidate declaration for PD[5]
TDP-43-PET tracer	TDP-43	○		Clinical candidate declaration

(1) Alzheimer's disease; (2) Alpha-synuclein; (3) TAR DNA-binding protein 43; (4) Positron emission tomography; (5) Parkinson's disease

Summary: AC Immune Today

Differentiated leadership through Precision Medicine



(1) Neurodegenerative diseases

AC Immune: Pioneering science and precision medicine

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