



# Pioneering Precision Medicine for Neurodegeneration

NASDAQ: ACIU | Annual General Meeting, June 24, 2022



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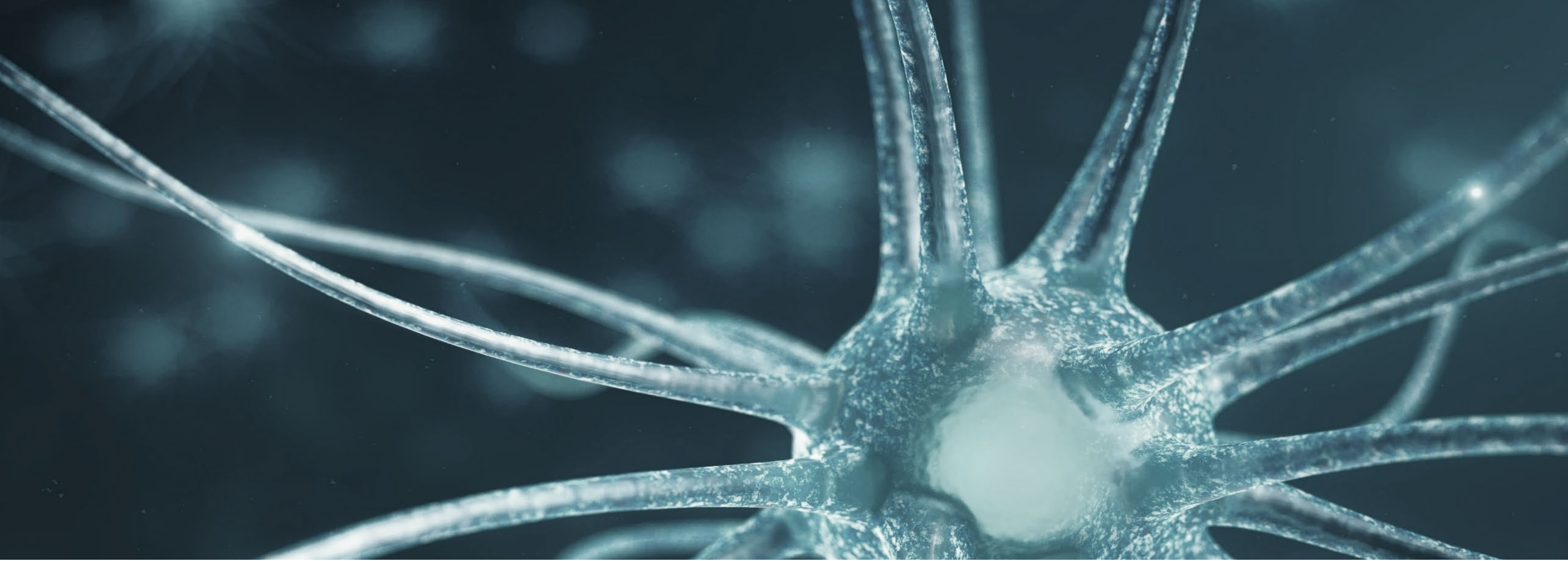
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# Agenda

1. AC Immune's leadership in neurodegenerative diseases
2. Achievements 2021/22
3. AC Immune's business strategy
4. Pipeline update
5. Clinical-stage vaccine programs
6. Clinical-stage monoclonal antibodies
7. First-in-class diagnostic for precision medicine
8. Near-term inflection points
9. Financial figures
10. Strategic outlook

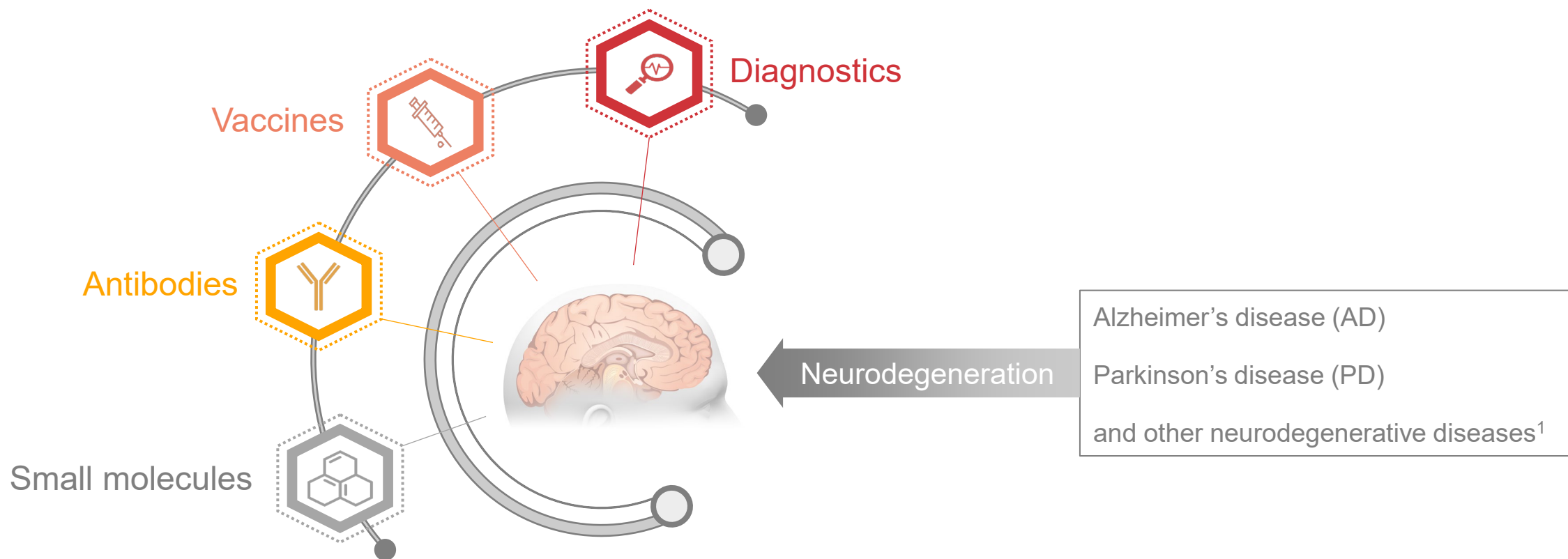




## 1. AC Immune's leadership in neurodegenerative diseases

# What are we doing?

Developing novel treatments and diagnostics for neurodegenerative diseases



- **First-in-class precision diagnostics** to identify and analyze neurodegenerative diseases
- **Breakthrough therapeutic modalities** to support treatment and prevention of neurodegeneration

(1) Dementia with Lewy bodies (DLB), Limbic-predominant Age-related TDP-43 Encephalopathy (LATE), Multiple systems atrophy (MSA), Progressive Supranuclear Palsy (PSP)

# Investment highlights



## **Broad, diversified pipeline in neurodegeneration**

Six Phase 2 programs; seven clinical readouts in 2022



## **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 through Q1 2024

Pioneering  
precision medicine  
for neurodegenerative  
diseases

# Neurodegenerative diseases represent a large and growing market

Prevalence expected to increase drastically as the population ages

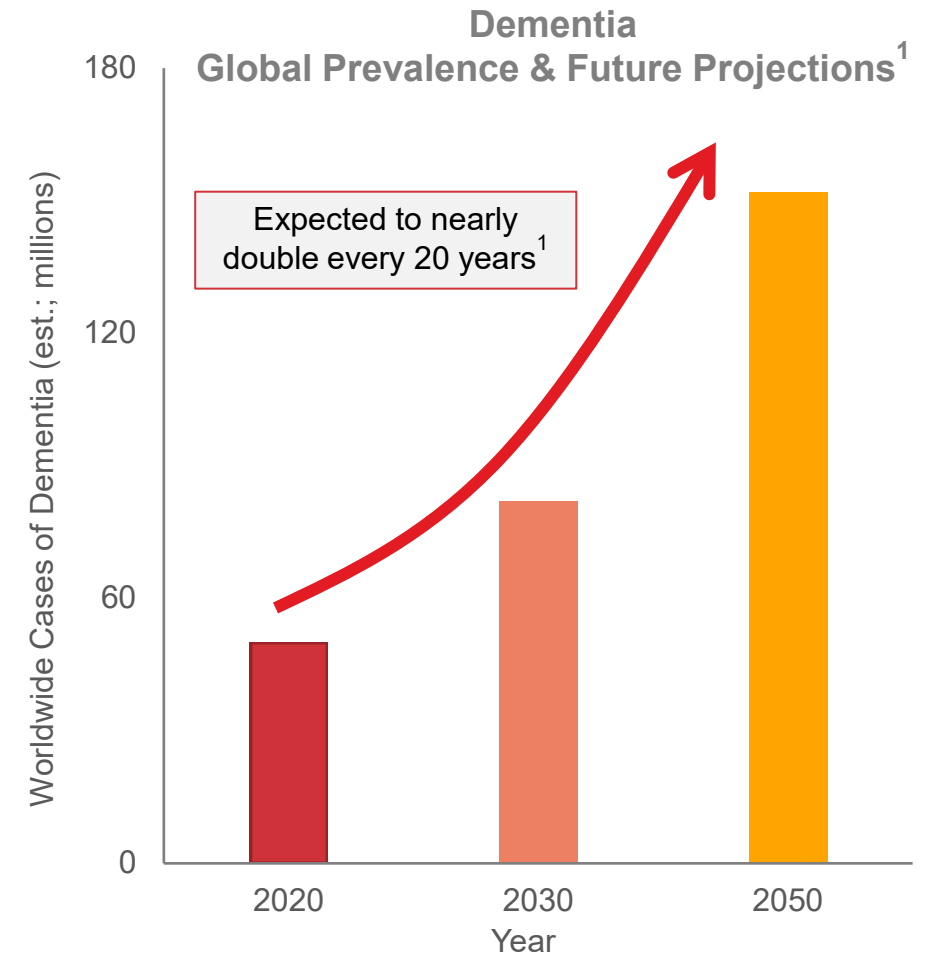
**>50 Million** people worldwide living with dementia<sup>1</sup>

**>\$1 Trillion** global annual cost of dementia<sup>1</sup>

**>6 Million** people worldwide living with PD<sup>2,3</sup>

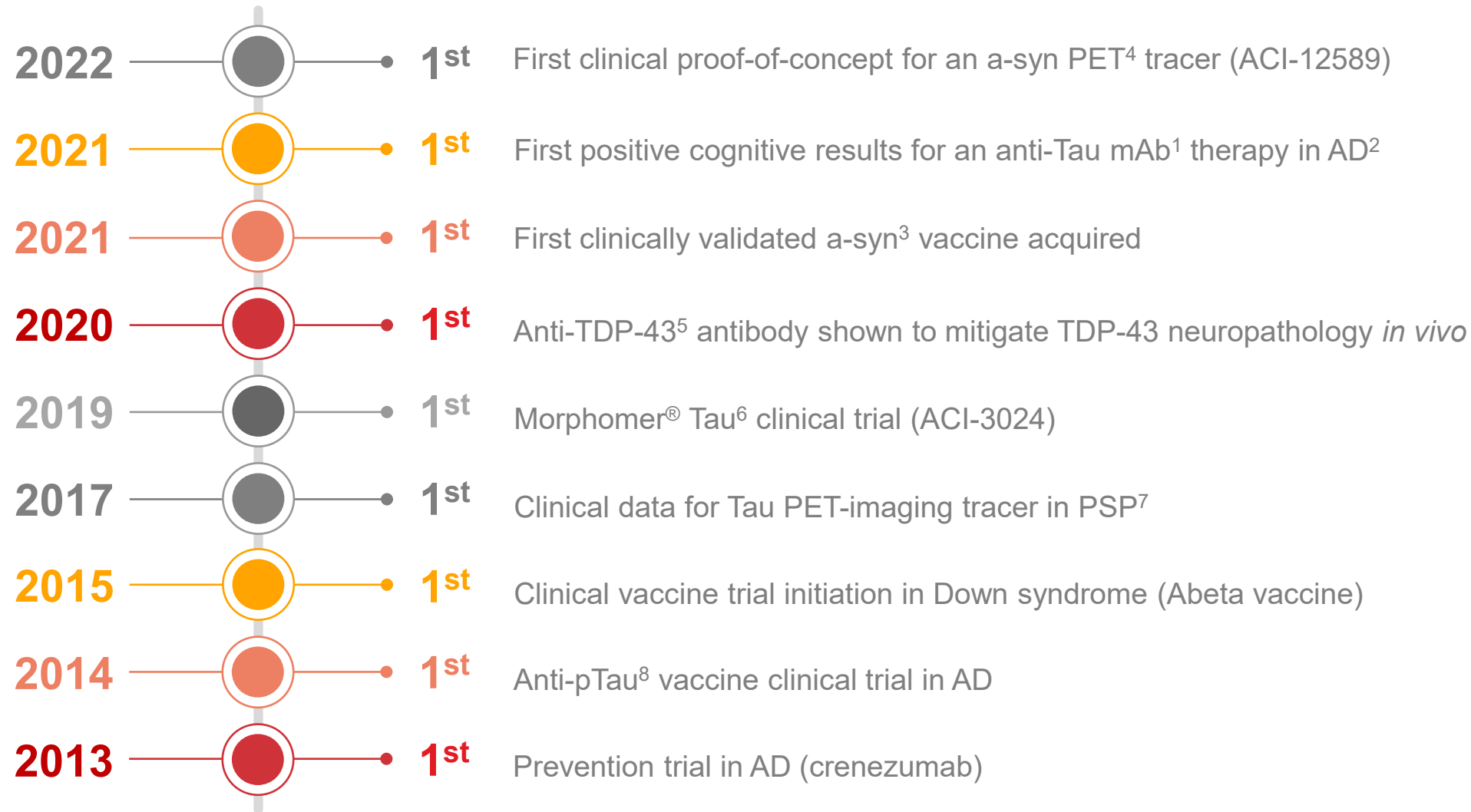
**20-50%** of people over age 80 with LATE<sup>4,5</sup>

**>8 Million** in USA<sup>6</sup> with different NeuroOrphan diseases



(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) [National Institute of Neurological Disorders and Stroke](#)

# “Firsts” reflect ACIU’s leadership in neurodegenerative disease



**Genentech**  
A Member of the Roche Group

*Lilly*

**Life** Molecular Imaging

**janssen**  
PHARMACEUTICAL COMPANY  
OF Janssen-Cilag

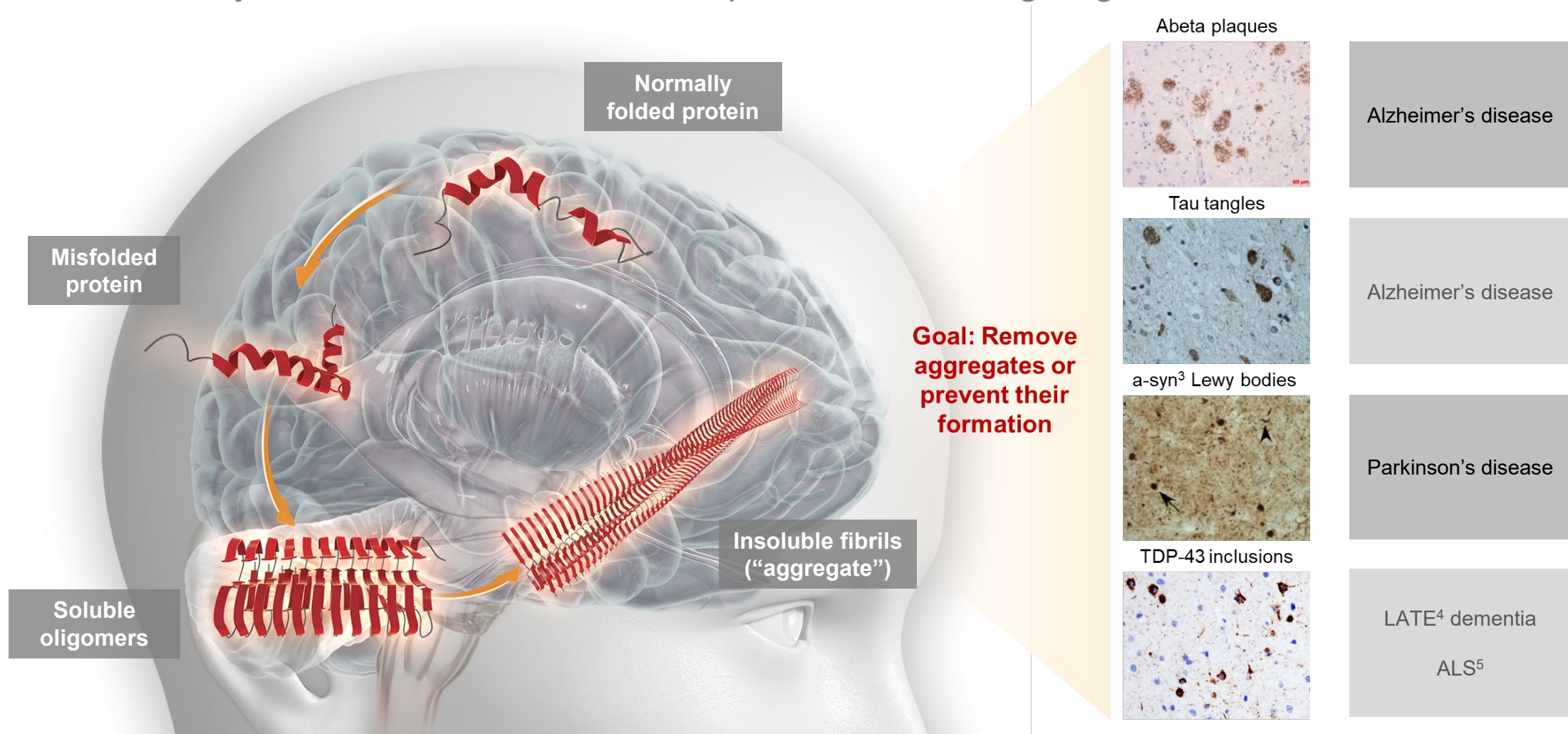
**Genentech**  
A Member of the Roche Group

(1) Monoclonal antibody; (2) Alzheimer's disease; (3) alpha-synuclein; (4) Positron emission tomography; (5) TAR DNA binding protein-43; (6) Small molecule Tau-specific aggregation inhibitor; (7) Progressive supranuclear palsy; (8) Phosphorylated Tau



# Misfolded proteins: Leading targets in neurodegenerative diseases

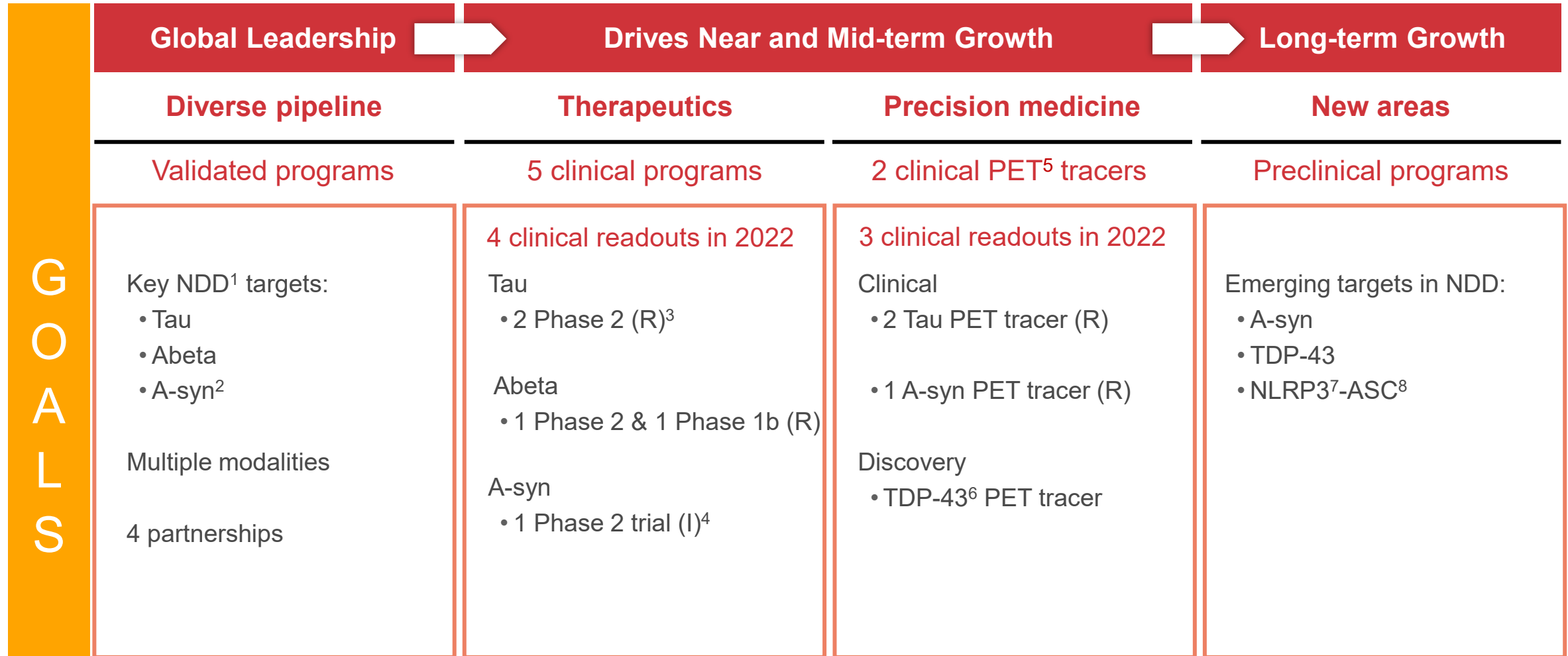
Abeta, Tau, a-synuclein, and TDP-43<sup>1</sup> are important NDD<sup>2</sup> drug targets



Refs: Soto 2003, <http://www.alz.org/brain>; Nag *et al.* Acta Neuropathologica Communications (2018) 6:33;

(1) TAR DNA-binding protein 43; (2) Neurodegenerative disease; (3) a-synuclein; (4) Limbic-predominant age-related TDP-43 encephalopathy; (5) Amyotrophic lateral sclerosis

# Growth initiatives for 2022 and beyond



(1) Neurodegenerative disease; (2) alpha-synuclein; (3) (R) – readout; (4) (I) – initiation; (5) Positron emission tomography; (6) TAR DNA-binding protein 43; (7) (NOD)-like receptor protein 3; (8) Apoptosis-associated speck-like protein containing a CARD, also PYCARD

# Successfully treating neurodegeneration requires precision medicine

From a mono- to a multi-target combination approach

**1** **Non-invasive diagnostics** are critical for identifying and monitoring disease

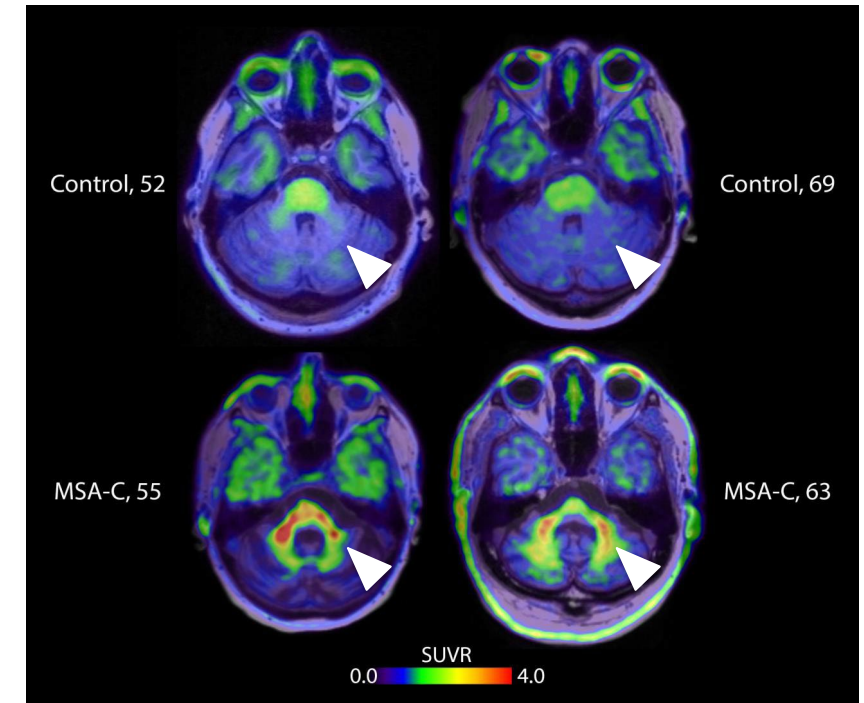
**2** **Earlier, more reliable diagnosis** may eventually lead to disease **prevention**

**3** Different therapies at different stages

**4** Patients selected and treated according to their underlying pathologies

**5** **Combination therapy** may be required

First a-syn<sup>1</sup>-PET<sup>2</sup> tracer to effectively detect a-syn in human brains and distinguish MSA<sup>3</sup> from HC<sup>4</sup>



Courtesy of Dr Ruben Smith, Skåne University Hospital

■ Treating the right proteinopathies, in the right patient, at the right time

(1) Alpha-synuclein; (2) Positron emission tomography; (3) Multiple system atrophy; (4) Healthy controls





## 2. Achievements 2021/22

# AC Immune 2021 Highlights



**Expanded Phase 1b/2a ACI-35.030 trial to support advancement to late-stage development**



**Promising data readouts from Phase 1b (DS<sup>1</sup>) and Phase 2 (AD<sup>2</sup>) trials of ACI-24**



**Phase 2 Lauriet trial in mild-to-moderate AD met 1 of 2 co-primary endpoints**



**Moved to the forefront of PD<sup>3</sup> drug development with alpha-synuclein vaccine acquisition**

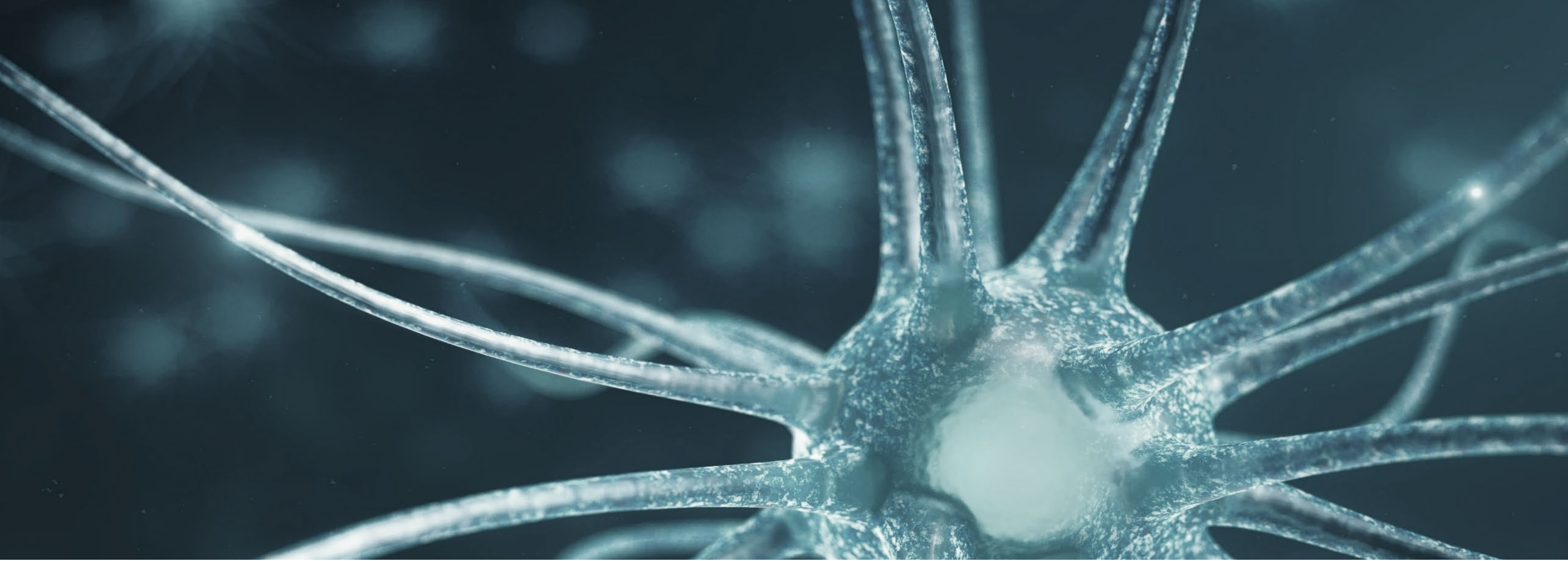


**External validation and global recognition from MJFF<sup>4</sup> and Swiss Economic Forum**

Our accomplishments  
in 2021 have us on  
track to achieve  
seven clinical data  
readouts in 2022

(1) Down syndrome; (2) Alzheimer's disease; (3) Parkinson's disease; (4) Michael J. Fox Foundation

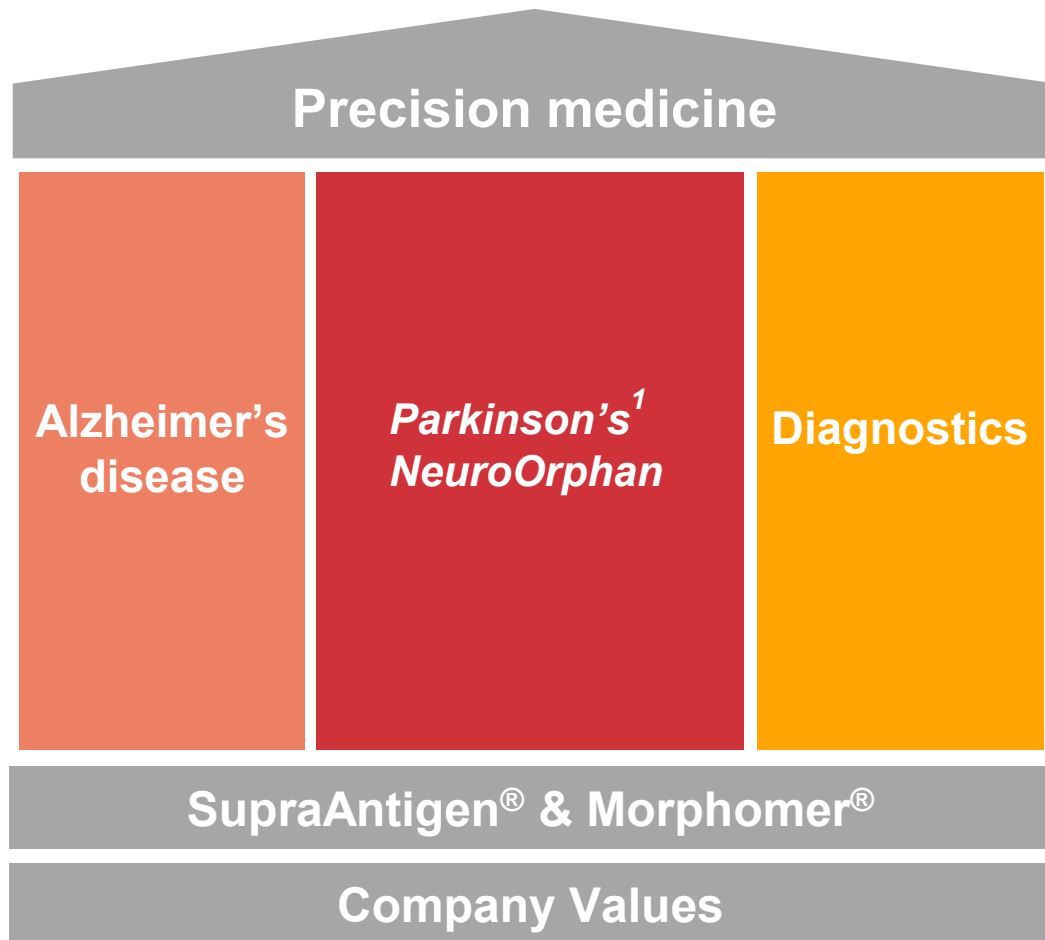




### 3. AC Immune's business strategy

# Business strategy 2022: further focus the execution strategy of 2021

Enhance value creation through acceleration of vaccine and PD<sup>1</sup> portfolio



## Alzheimer's disease

- Accelerate development of novel late-stage therapies with partners
- Accelerate optimized anti-Abeta vaccine development in DS<sup>2</sup>

## Parkinson's and NeuroOrphans

- Broaden strategic activity in other NDD<sup>3</sup>, e.g. Parkinson's disease
- Genetic FTD/MAPT population for Morphomer® Tau

## Diagnostics for precision medicine

- Advance our differentiated diagnostic pipeline for a-synucleinopathies (e.g. MSA<sup>4</sup>) and TDP-43<sup>5</sup>-based pathologies

(1) Parkinson's disease; (2) Down syndrome; (3) Neurodegenerative diseases; (4) Multiple system atrophy; (5) TAR DNA-binding protein 43

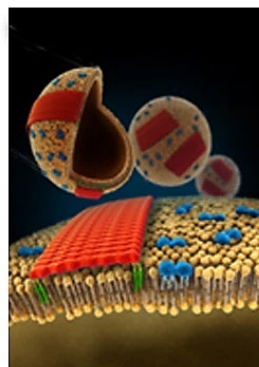
# SupraAntigen® and Morphomer® platforms

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**



## 4. Pipeline update



# Broad and robust pipeline in neurodegenerative diseases

Driven by validated proprietary technology platforms for sustained growth

## Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	<b>ACI-35.030</b> (anti-pTau vaccine)	AD <sup>1</sup> treatment					reported H1	Janssen <small>Pharmaceutical Companies of Johnson &amp; Johnson</small>
	<b>Semorinemab</b> (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>					data H2	
	<b>Morphomer® Tau</b> aggregation inhibitor	Rare Tauopathies (ACI-3024)						Lilly
		AD treatment						
	<b>Tau-PET<sup>3</sup> tracer</b>	AD diagnostic					data H2	Life Molecular Imaging
		PSP <sup>4</sup> diagnostic					data H2	
Abeta	<b>Crenezumab</b> (anti-Abeta antibody)	AD prevention <sup>5</sup>					data H1	Genentech <small>A Member of the Roche Group</small>
	<b>ACI-24</b> (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )					data H2 <sup>9</sup>	
		AD treatment						
a-syn <sup>7</sup>	<b>ACI-7104</b> (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies						
	<b>a-syn-PET tracer</b>	a-synucleinopathies (e.g. MSA <sup>10</sup> )					reported H1	

■ Biologic  
■ Small Molecule  
■ Diagnostic








(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 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

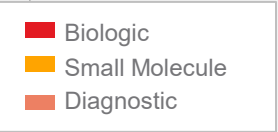


# Broad and robust pipeline in neurodegenerative diseases

Diversification into non-AD<sup>1</sup> and non-CNS<sup>2</sup> diseases

## Novel Targets Pipeline

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2
a-synuclein (a-syn)	Anti-a-syn antibody	PD, NeuroOrphan				
	Morphomer® a-syn (a-syn inhibitor)	PD, a-synucleinopathies				
TDP-43	Anti-TDP-43 <sup>5</sup> antibody	LATE <sup>6</sup> , NeuroOrphan				
	TDP-43-PET tracer	TDP-43-opathies				
Inflammasome	Anti-NLRP3 <sup>7</sup> -ASC <sup>8</sup> antibody	NeuroOrphan				
	Morphomer® NLRP3-ASC	Non-CNS				
	Morphomer® NLRP3-ASC	NeuroOrphan; non-CNS				



■ Biologic  
■ Small Molecule  
■ Diagnostic

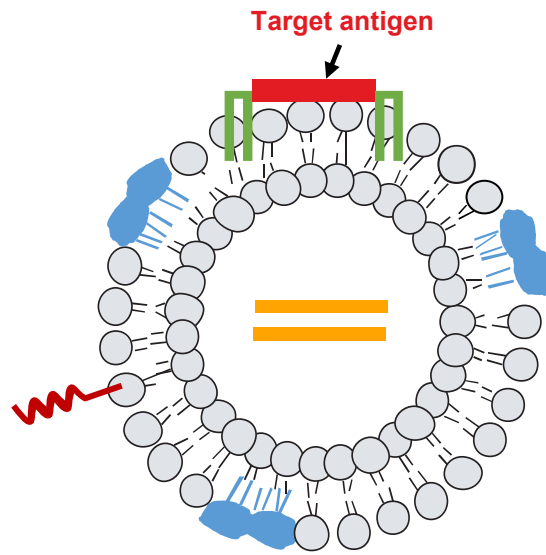
(1) Alzheimer's disease; (2) Central nervous system; (3) Parkinson's disease; (4) Positron emission tomography; (5) TAR DNA-binding protein 43; (6) Limbic-predominant age-related TDP-43 encephalopathy; (7) (NOD)-like receptor protein 3; (8) Apoptosis-associated speck-like protein containing a CARD, also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



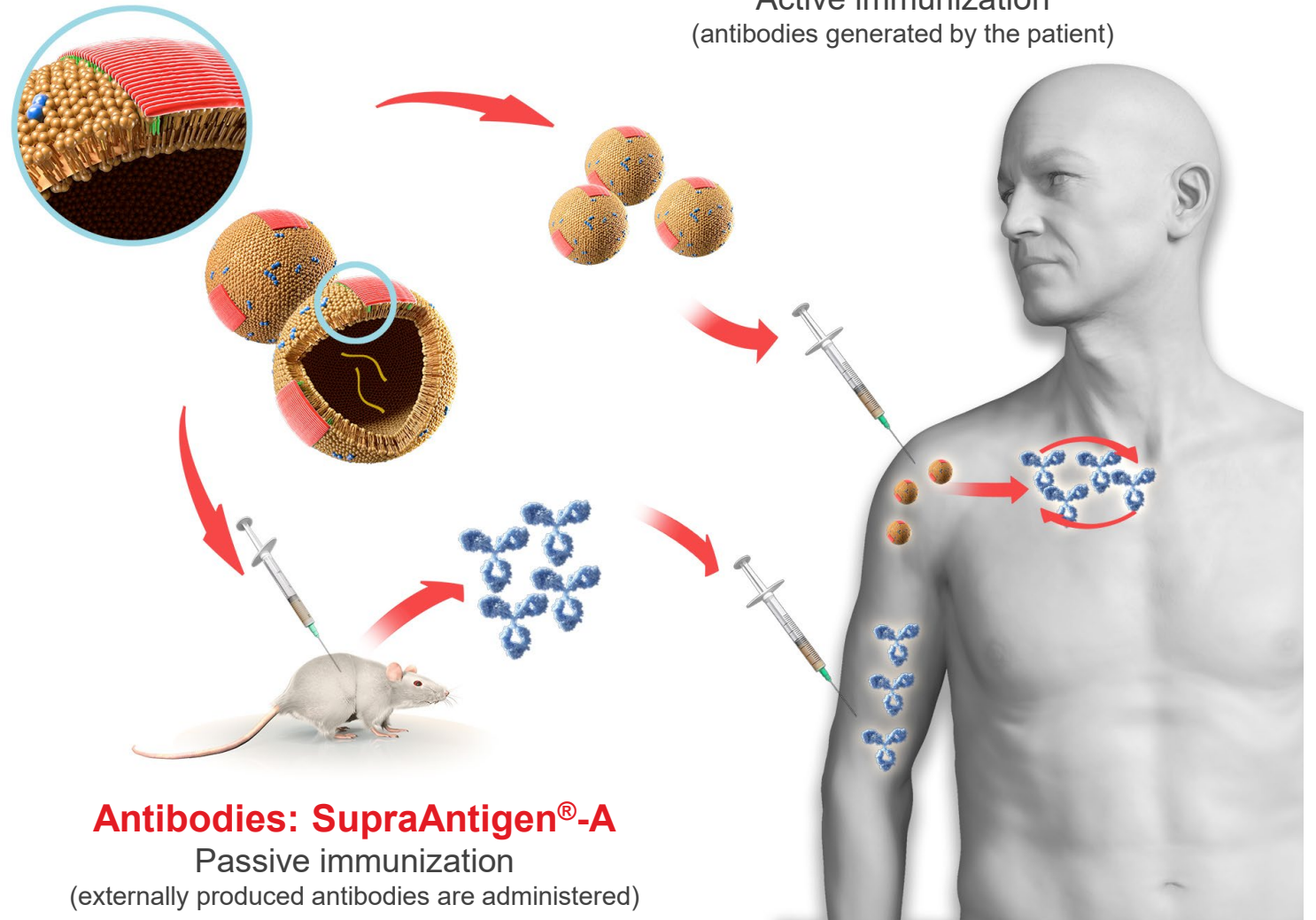
## 5. Clinical-stage vaccine programs

# Proprietary SupraAntigen® discovery platform

Generation of vaccines and monoclonal antibodies



SupraAntigen® allows optimal configuration of liposomes for each application



## Vaccines: SupraAntigen®-V

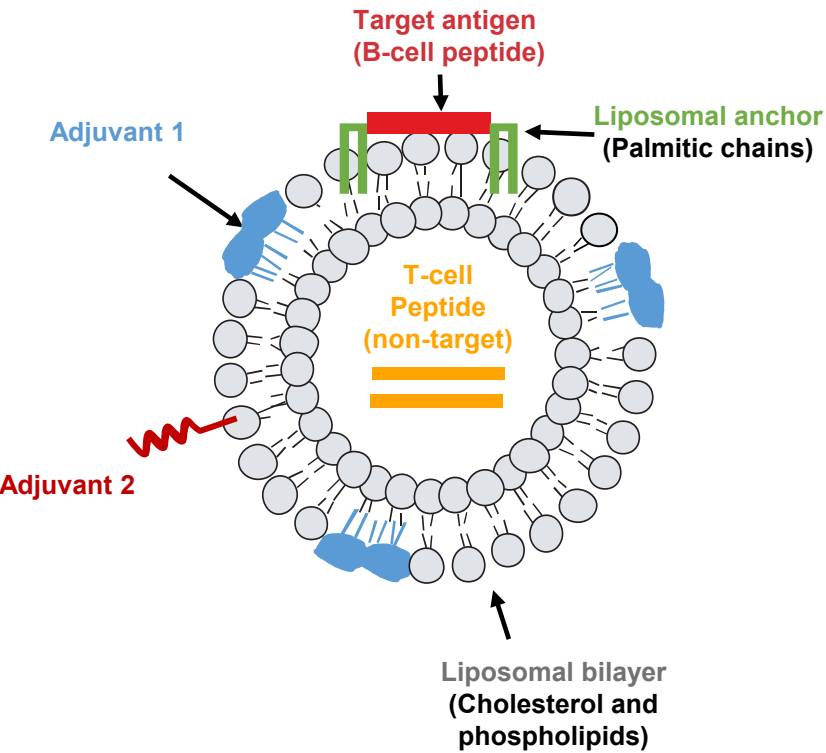
Active immunization  
(antibodies generated by the patient)

## Antibodies: SupraAntigen®-A

Passive immunization  
(externally produced antibodies are administered)

# 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	++++ <sup>1</sup>
Target specificity	++++ <sup>2</sup>
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 1<sup>st</sup> injection; (2) Increases over time

# ACI-35.030: Anti-pTau vaccine being developed for AD<sup>1</sup>

## Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	<b>ACI-35.030</b> (anti-pTau vaccine)	AD treatment	<div></div>					
	<b>Semorinemab</b> (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>	<div></div>					 <small>A Member of the Roche Group</small>
	<b>Morphomer® Tau aggregation inhibitor</b>	Rare Tauopathies (ACI-3024)	<div></div>					
		AD treatment	<div></div>					
	<b>Tau-PET<sup>3</sup> tracer</b>	AD diagnostic	<div></div>					
		PSP <sup>4</sup> diagnostic	<div></div>					
Abeta	<b>Crenezumab</b> (anti-Abeta antibody)	AD prevention <sup>5</sup>	<div></div>					 <small>A Member of the Roche Group</small>
	<b>ACI-24</b> (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )	<div></div>					
		AD treatment	<div></div>					
a-syn <sup>7</sup>	<b>ACI-7104</b> (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies	<div></div>					<div><div></div> Biologic</div> <div><div></div> Small Molecule</div> <div><div></div> Diagnostic</div>
	<b>A-syn-PET tracer</b>	a-synucleinopathies (e.g. MSA <sup>9</sup> )	<div></div>					

■ Biologic  
■ Small Molecule  
■ Diagnostic

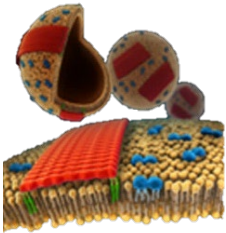
(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related Alzheimer's disease; (7) alpha-synuclein; (8) Parkinson's disease; (9) Multiple system atrophy



# ACI-35.030 – very encouraging interim Phase 1b/2a results in AD<sup>1</sup>

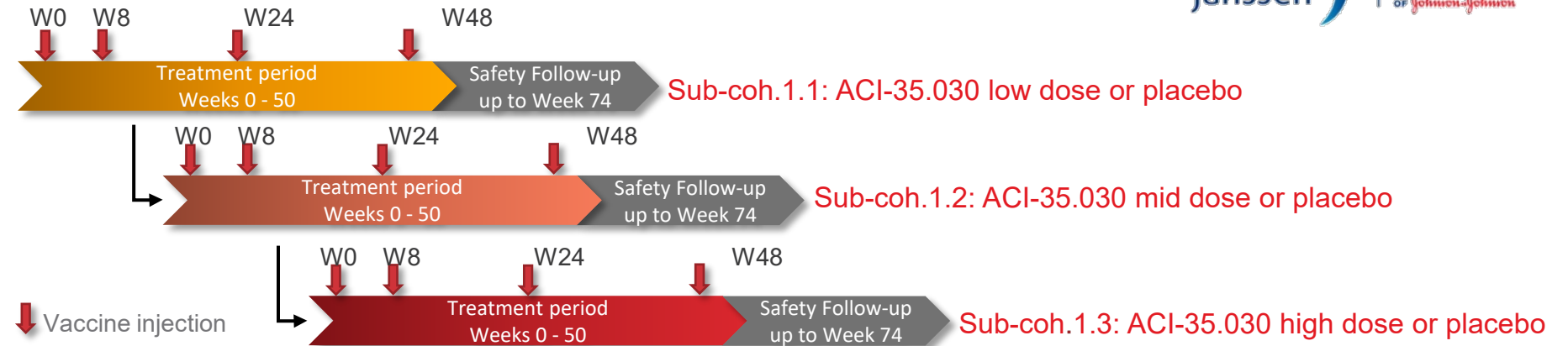


SupraAntigen<sup>®</sup>  
platform



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<sup>3</sup> after the 1<sup>st</sup> 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

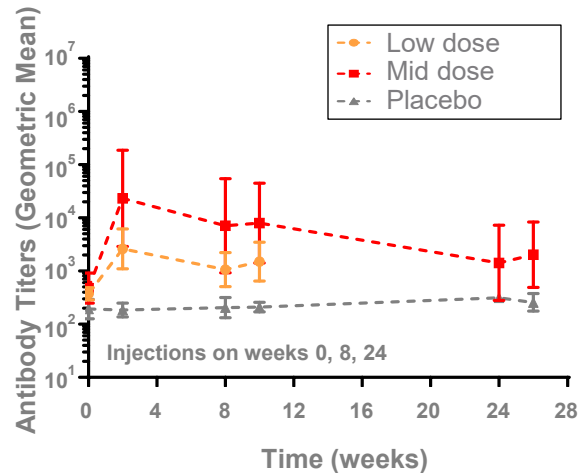
Strong safety and robust immunogenicity support advancing to late-stage development

(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)

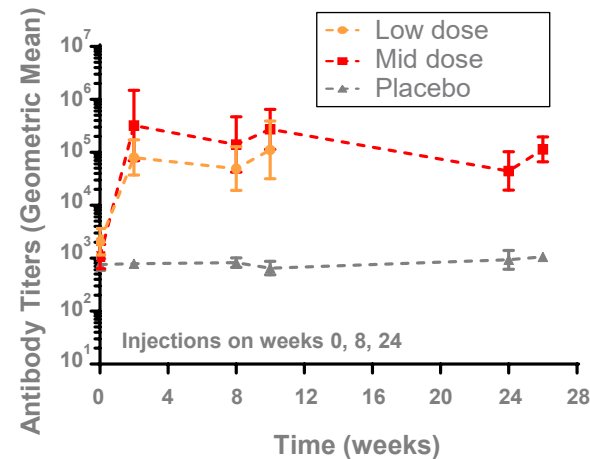
# ACI-35.030 generates a potent Ab<sup>1</sup> response against pathological Tau

ACI-35.030 generates excellent Ab responses against pTau<sup>2</sup> in an older population

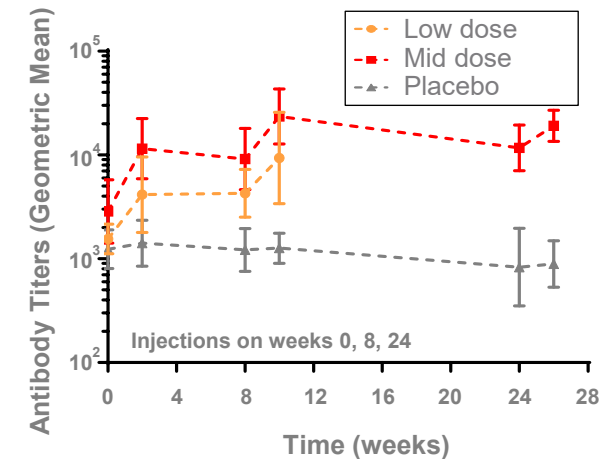
Anti-Tau (non-phosphorylated) IgG Titers



Anti-pTau IgG Titers



Anti-ePHF<sup>3</sup> IgG Titers



1

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

3

Anti-ePHF titers increased by approximately 10-fold<sup>5</sup> from baseline in the mid-dose cohort

2

Anti-pTau titers increased by >100-fold<sup>4</sup> from baseline in the mid-dose cohort

4





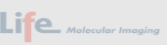

Antibody responses showed boostability following the second and third doses

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

# ACI-7104: Anti-a-syn vaccine being developed for Parkinson's disease

Phase 2 trial initiation 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 treatment						 
	Semorinemab (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>						
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies (ACI-3024)						
		AD treatment						
	Tau-PET <sup>3</sup> tracer	AD diagnostic						 
		PSP <sup>4</sup> diagnostic						
Abeta	Crenezumab (anti-Abeta antibody)	AD prevention <sup>5</sup>						
	ACI-24 (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )						
		AD treatment						
a-syn <sup>7</sup>	<b>ACI-7104</b> (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies						
	A-syn-PET tracer	a-synucleinopathies (e.g. MSA <sup>9</sup> )						

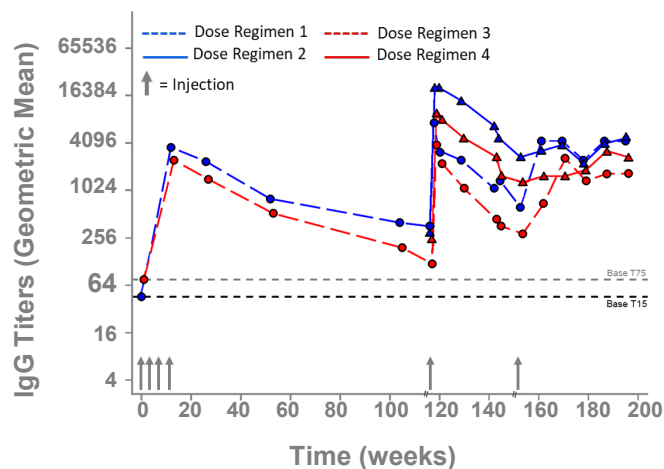
(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related Alzheimer's disease; (7) alpha-synuclein; (8) Parkinson's disease; (9) Multiple system atrophy

# Anti-a-syn<sup>1</sup> vaccine is clinically validated<sup>2</sup> in Parkinson's disease

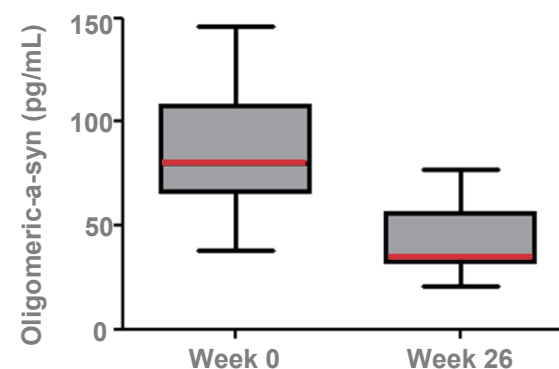
Phase 1 results in *The Lancet Neurology* support best-in-class profile

THE LANCET  
Neurology

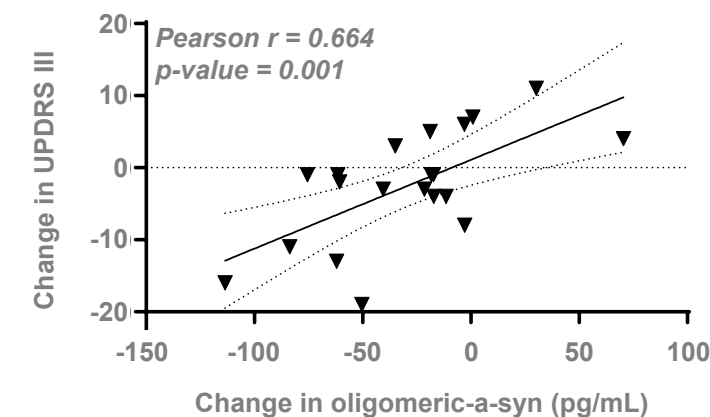
Strong and boostable antibody response



50% reduction<sup>3</sup> of pathological a-syn in CSF<sup>4</sup>



Changes<sup>5</sup> 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

3

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

2

Strong and boostable antibody responses

4

Signal of clinical efficacy: stabilization of UPDRS<sup>6</sup> III scores correlated with reductions in oligomeric a-syn

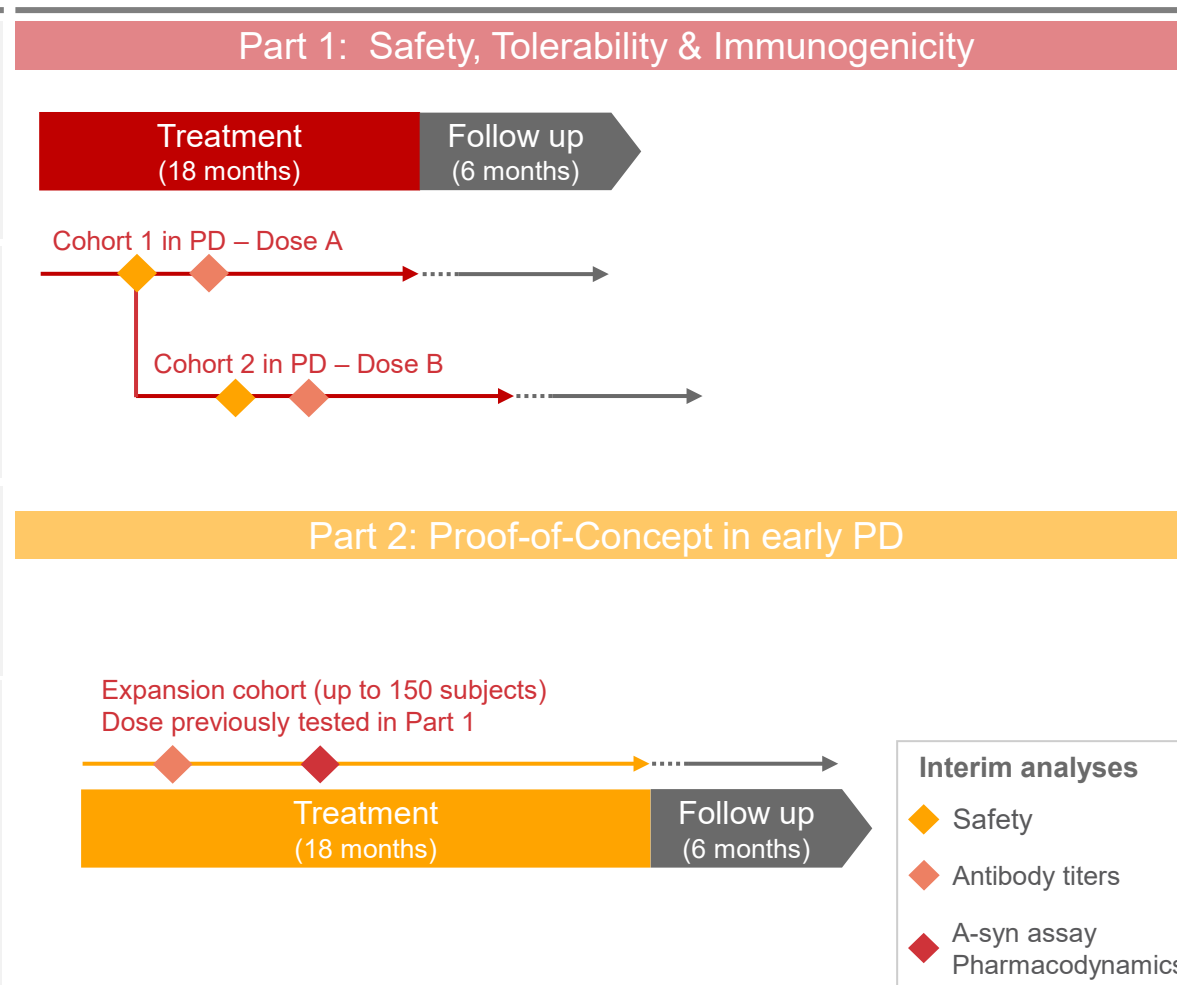
(1) alpha-synuclein; (2) Volc *et al.*, Lancet Neurol. 2020; (3) Data from 75 µg dose group; (4) Cerebrospinal fluid; (5) Change in oligomeric a-syn calculated at week 26, change in UPDRS III calculated at week 100; (6) Unified Parkinson's Disease Rating Scale

# ACI-7104: an adaptive biomarker-based Phase 2 study in early PD<sup>1</sup>

## Placebo-controlled Phase 2 Study Overview

Inclusion criteria	<ul style="list-style-type: none"> <li>Idiopathic PD untreated or treated with MAO-B<sup>2</sup> inhibitor</li> <li>A diagnosis of PD for 2 years or less at screening (not demented / no cognitive impairment)</li> <li>Dopaminergic deficit by DaT SPECT<sup>3</sup></li> </ul>
Study design	<ul style="list-style-type: none"> <li>Seamless transition                             <ul style="list-style-type: none"> <li>All participants from Part 1 will contribute to final analysis</li> </ul> </li> <li>Biomarker based interim analyses                             <ul style="list-style-type: none"> <li>Early immunogenicity to tailor dose and/or dose regimen</li> <li>Understand biological signal for early transition to filing</li> </ul> </li> </ul>
Part 1: Safety & PK/PD <sup>4</sup>	<ul style="list-style-type: none"> <li>Key immunogenicity measures</li> <li>Measures of pathological a-syn<sup>5</sup> and a-syn aggregation (phospho-a-syn and a-syn oligomers)</li> </ul>
Part 2: PoC <sup>6</sup> in early PD	<ul style="list-style-type: none"> <li>Motor and Non-Motor Functioning (UPDRS<sup>7</sup> based)</li> <li>Neurodegeneration of dopaminergic terminals (DaT SPECT or VMAT2<sup>8</sup> imaging)</li> <li>Digital biomarkers of motor and non-motor function</li> <li>Advanced MRI (including ASL<sup>9</sup> and DTI<sup>10</sup>)</li> <li>Functional and patient reported outcomes</li> </ul>

## Dosing Schematic



(1) Parkinson's disease; (2) Monoamine Oxidase Type B; (3) Dopamine Transporter Single Photon Emission Computed Tomography; (4) Pharmacokinetics and Pharmacodynamics; (5) alpha-synuclein; (6) Proof-of-concept; (7) Unified Parkinson's disease rating scale; (8) Vesicular monoamine transporter 2; (9) Arterial spin labeling; (10) Diffusion tensor imaging



# ACI-24: Vaccine targeting two pathological forms of Abeta for AD<sup>1</sup>

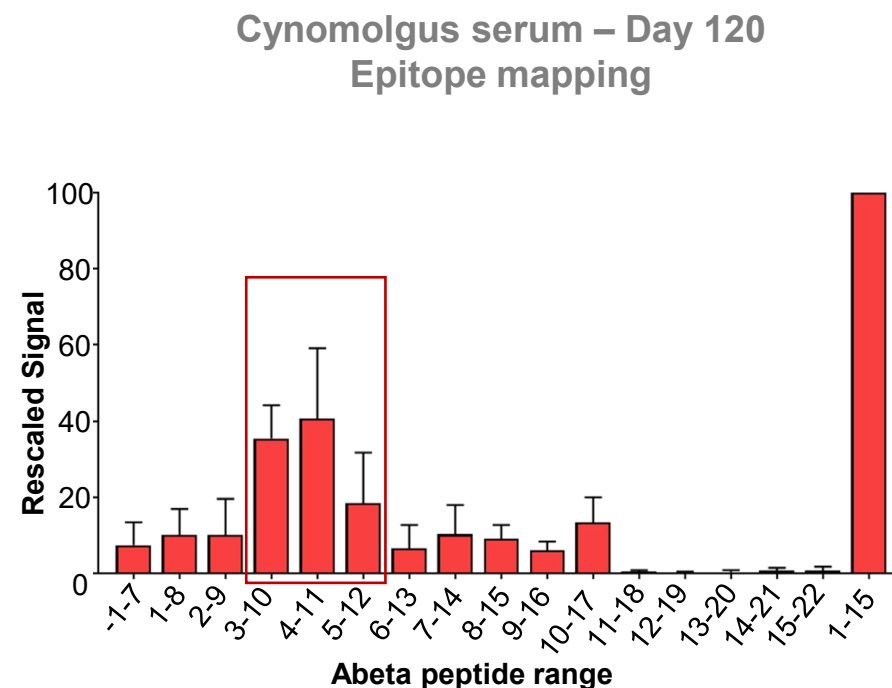
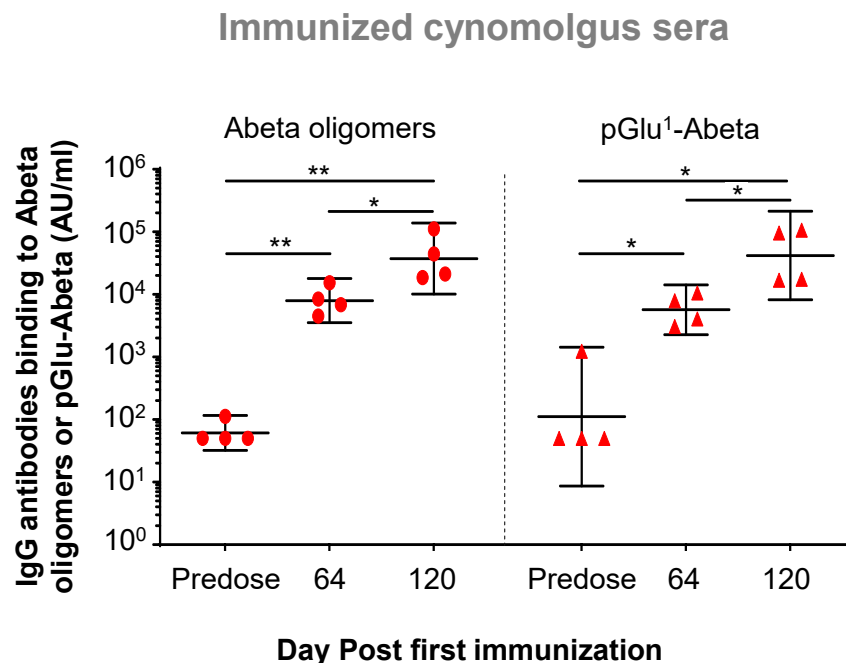
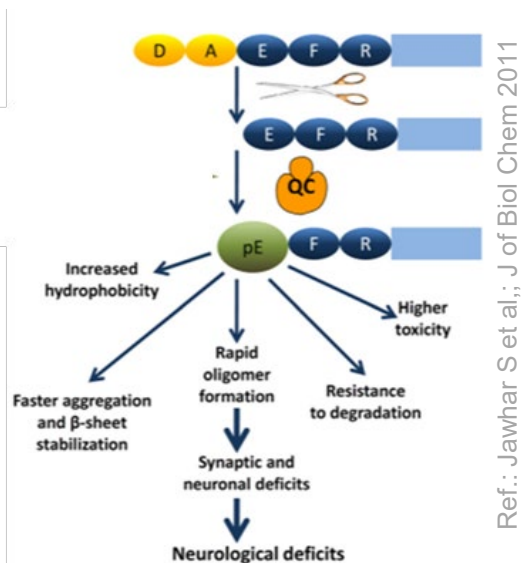
ACI-24 targets pyroGlu- and oligomeric Abeta, which are believed to drive the progression of AD

## Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	ACI-35.030 (anti-pTau vaccine)	AD <sup>1</sup> treatment						Janssen <small>Research Triangle Institute in Johnson &amp; Johnson</small>
	Semorinemab (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>						
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies (ACI-3024)						Lilly
		AD treatment						
	Tau-PET <sup>3</sup> tracer	AD diagnostic						Life Molecular Imaging
		PSP <sup>4</sup> diagnostic						
Abeta	Crenezumab (anti-Abeta antibody)	AD prevention <sup>5</sup>						Genentech <small>A Member of the Roche Group</small>
	ACI-24 (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )					data H2 <sup>9</sup>	
		AD treatment						
a-syn <sup>7</sup>	ACI-7104 (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies						
	A-syn-PET tracer	a-synucleinopathies (e.g. MSA <sup>10</sup> )						

(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 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

# Optimized anti-Abeta ACI-24: Strong immune response against pyroglutamate Abeta



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

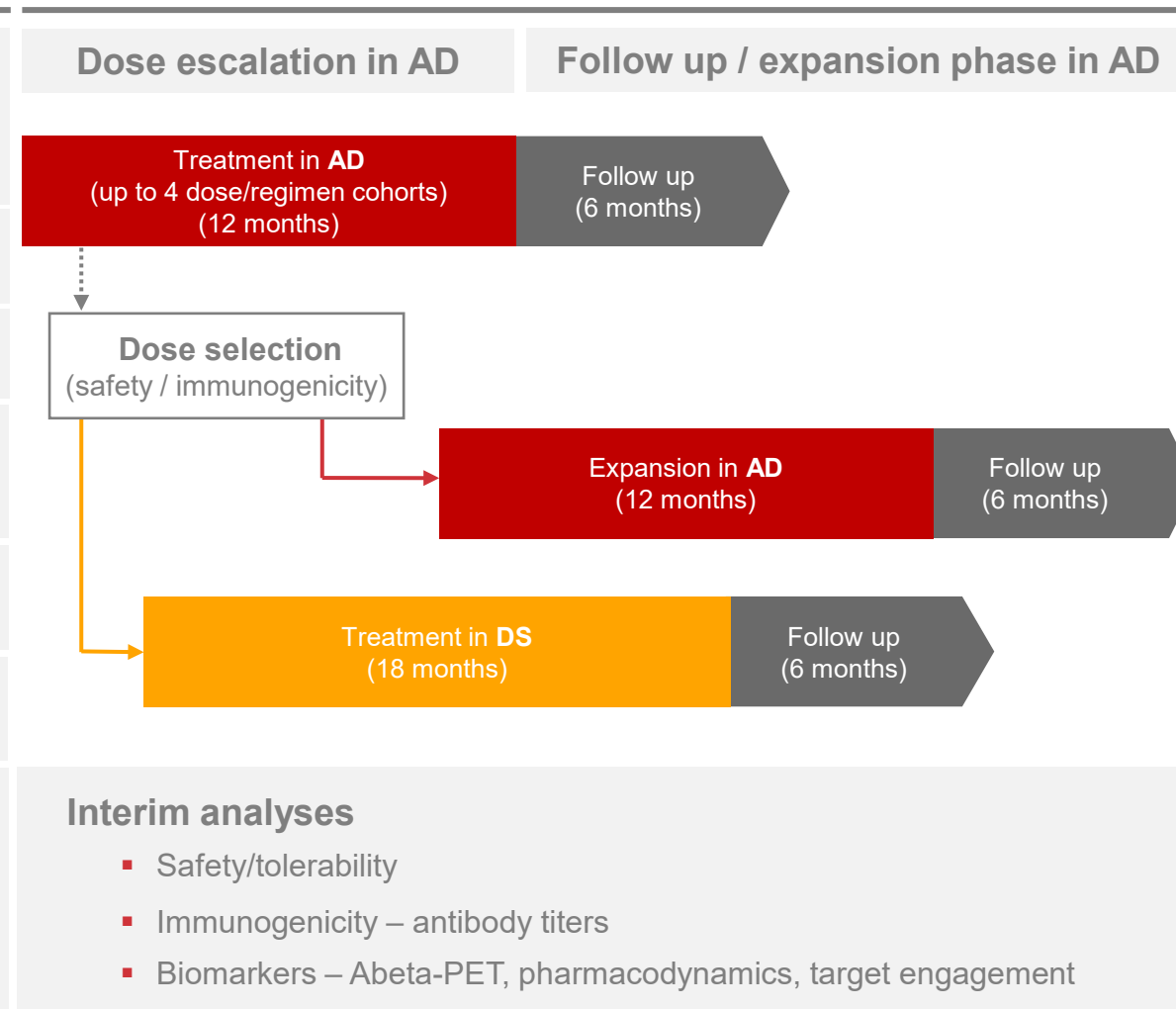
(1) Pyroglutamate \* p<0.05, \*\* p<0.01

# ACI-24: Biomarker-based development in AD<sup>1</sup> and AD in DS<sup>2</sup>

## 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: <ul style="list-style-type: none"> <li>Abeta pathology confirmed by PET<sup>3</sup> scan</li> </ul>
	AD	<ul style="list-style-type: none"> <li>Prodromal AD (CDR<sup>4</sup>-Global Score 0.5; age 50-75 years)</li> </ul>
	DS	<ul style="list-style-type: none"> <li>Non-demented people living with DS (age 35–50 years)</li> </ul>
Study design	Both	<ul style="list-style-type: none"> <li>IA<sup>5</sup> of safety/tolerability and immunogenicity</li> <li>Biomarker analyses including Abeta PET and others</li> </ul>
	AD	<ul style="list-style-type: none"> <li>Up to 4 different doses and/or dose regimens</li> <li>Expansion of one cohort to assess effect on Abeta PET</li> </ul>
	DS	<ul style="list-style-type: none"> <li>Initiation using selected dose identified in AD (based on safety/tolerability and immunogenicity)</li> </ul>
Outcome measures	Both	<ul style="list-style-type: none"> <li>Safety/tolerability</li> <li>Pharmacodynamics: Serum anti-Abeta antibody titers</li> <li>Exploratory biomarkers and clinical endpoints</li> </ul>

## Trial Schematic



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



## 6. Clinical-stage monoclonal antibodies



# Semorinemab: Anti-Tau monoclonal antibody being developed for AD<sup>1</sup>

New Phase 2 biomarker and open-label extension data expected in H2 2022

## Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	ACI-35.030 (anti-pTau vaccine)	AD treatment						Janssen
	<b>Semorinemab</b> (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>					data H2	Genentech A Member of the Roche Group
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies (ACI-3024)						Lilly
		AD treatment						
	Tau-PET <sup>3</sup> tracer	AD diagnostic						Life Molecular Imaging
		PSP <sup>4</sup> diagnostic						Life Molecular Imaging
Abeta	Crenezumab (anti-Abeta antibody)	AD prevention <sup>5</sup>						Genentech A Member of the Roche Group
	ACI-24 (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )						
		AD treatment						
a-syn <sup>7</sup>	ACI-7104 (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies						
	A-syn-PET tracer	a-synucleinopathies (e.g. MSA <sup>9</sup> )						

(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



# Lauriet study evaluating the mAb<sup>1</sup> semorinemab in mild-to-moderate AD<sup>2</sup>

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<sup>3</sup> at week 49 (p=0.0008)

2

ADCS-ADL<sup>4</sup> co-primary endpoint and secondary efficacy endpoints (MMSE<sup>5</sup>; CDR-SB<sup>6</sup>) were not met; treatment effect on Tau PET<sup>7</sup> signal was not observed

3

Semorinemab was well tolerated with an acceptable safety profile and no unanticipated safety signals

4

ADAS-Cog11 findings were consistent at week 61<sup>9</sup>

5

Lauriet open label extension continues and biomarker analyses of semorinemab's effect on soluble forms of pathological Tau are ongoing

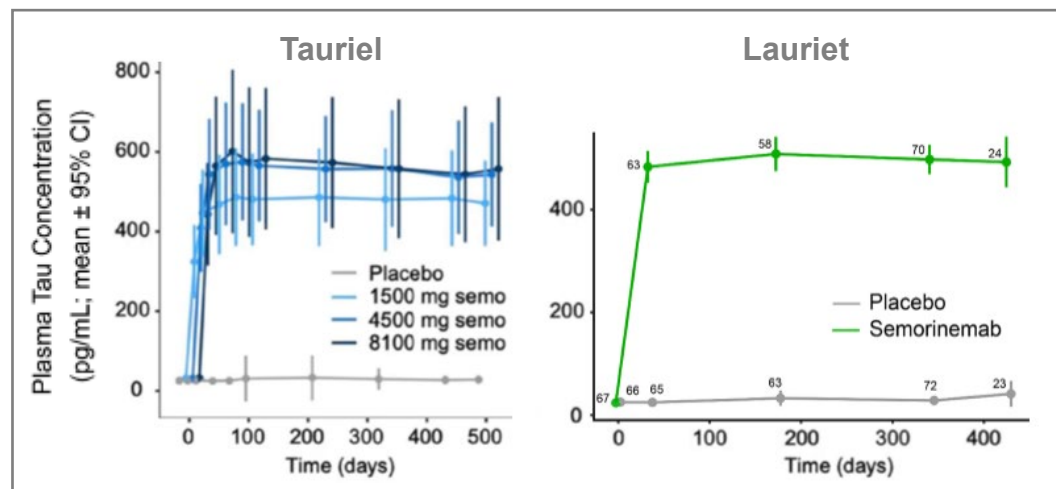
First evidence of therapeutic impact on cognition for a disease-modifying anti-Tau mAb in mild-to-moderate AD patients<sup>8</sup>

(1) Monoclonal antibody; (2) Alzheimer's disease; (3) Alzheimer's Disease Assessment Scale, Cognitive Subscale, 11-item Version; (4) Alzheimer's Disease Cooperative Study - Activities of Daily Living; (5) Mini-mental state exam; (6) Clinical Dementia Rating-Sum of the Boxes; (7) Positron emission tomography; (8) MMSE of 16-21; (9) In the subset of patients for whom the double-blind treatment period was extended to 60 weeks.

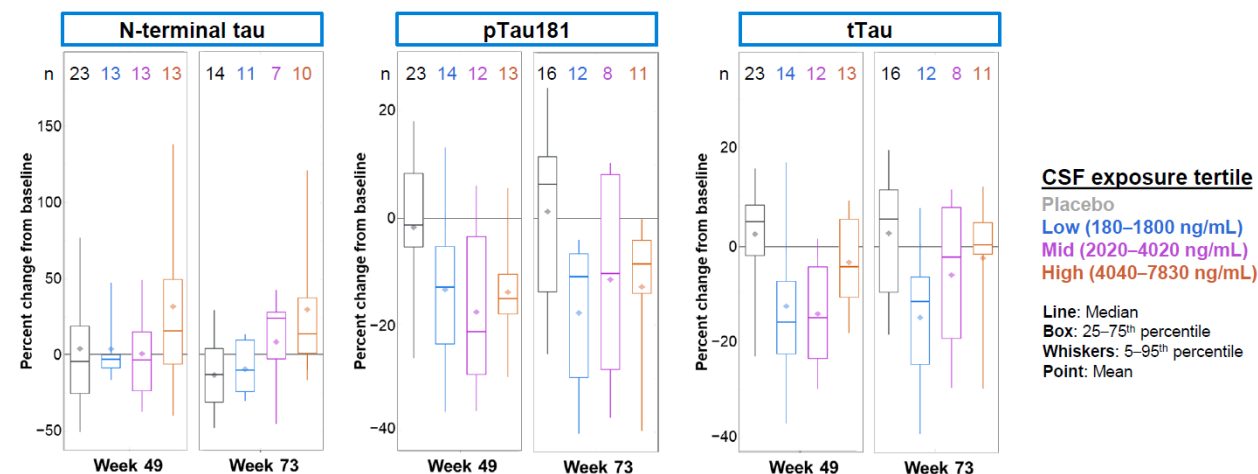
# Key findings from Phase 2 trials of semorinemab in AD<sup>1</sup>

Data provide further support for Tau as a target in AD

Plasma Tau Pharmacodynamic Data<sup>2</sup>



Tauriel Trial (prodromal-to-mild AD): Target Engagement Data



1

Significant semorinemab treatment effect on cognition in a patient population where limited or no effect of anti-Abeta mAbs is observed

2

Semorinemab treatment effect observed in Lauriet was consistent across prespecified subgroups

3

Tauriel's CSF<sup>3</sup> biomarker analyses confirm target engagement despite lack of clinical effect in prodromal to mild AD. Lauriet's CSF analyses are ongoing

4

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

(1) Alzheimer's disease; (2) Plasma pharmacodynamics are similar between studies; (3) Cerebrospinal fluid

# Crenezumab: Monoclonal anti-Abeta antibody being developed for AD<sup>1</sup>

Top line results from foremost Alzheimer prevention trial expected in H1 2022

## Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Tau	ACI-35.030 (anti-pTau vaccine)	AD <sup>1</sup> treatment						Janssen <small>Pharmaceutical Companies a Johnson &amp; Johnson</small>
	Semorinemab (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>						
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies (ACI-3024)						Lilly
		AD treatment						
	Tau-PET <sup>3</sup> tracer	AD diagnostic						Life Molecular Imaging
		PSP <sup>4</sup> diagnostic						
Abeta	<b>Crenezumab</b> (anti-Abeta antibody)	AD prevention <sup>5</sup>					data H1	Genentech <small>A Member of the Roche Group</small>
	ACI-24 (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )						
		AD treatment						
a-syn <sup>7</sup>	ACI-7104 (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies						
	A-syn-PET tracer	a-synucleinopathies (e.g. MSA <sup>9</sup> )						

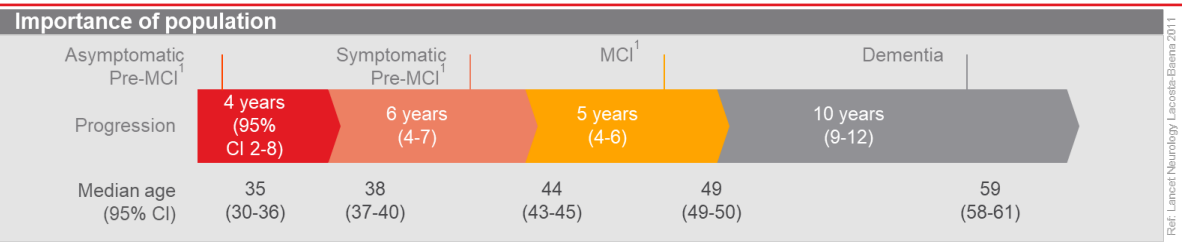
(1) Alzheimer's disease; (2) Open label extension study is ongoing; (3) Positron emission tomography; (4) Progressive supranuclear palsy; (5) Prevention trial API-ADAD in Colombia; (6) Down syndrome-related Alzheimer's disease; (7) alpha-synuclein; (8) Parkinson's disease; (9) Multiple system atrophy

# Crenezumab: Alzheimer Prevention Initiative (API-ADAD<sup>1</sup>) trial

Top line results from foremost Alzheimer prevention trial expected in H1 2022

## Patient population

- Colombian family clan with Paisa mutation leading to Abeta accumulation and early onset AD<sup>2</sup>
- Largest autosomal-dominant AD cohort
- Nearly 100% certainty of disease development due to a PSEN-1<sup>3</sup> gene mutation
- Unique opportunity to study prevention and treatment in defined population



**nature**  
International journal of science  
NEWS • 27 MARCH 2018

### Pioneering Alzheimer's study in Colombia zeroes in on enigmatic protein

Researchers tracking a genetic mutation that causes an early-onset form of the disease hope to uncover new drug targets.

## Study design

- Phase 2 double-blind, placebo-controlled study
- 252 subjects were enrolled with MMSE  $\geq 24^x$  or  $>26^y$
  - 169 mutation carriers randomized equally (1:1) to crenezumab or placebo
  - 83 non-carriers received a placebo as an additional control
  - Two primary cognitive endpoints measuring rate of change over at least 260 weeks (and up to approximately 416 weeks);
    - API-ADAD Composite Cognitive Test Total Score
    - Free and Cued Selective Reminding Test (FCSRT)
  - Secondary endpoints: Safety, time to MCI<sup>4</sup>; biomarkers (Abeta PET<sup>5</sup>, FDG<sup>6</sup> PET, Tau PET, CSF<sup>7</sup>, and blood-based biomarkers)
  - Study started December 2013

## Upcoming milestones

H1 2022



H2 2022

Milestone

Report top line results

Note: X: less than 9 years of education; Y: more than 9 years of education; (1) Alzheimer's Prevention Initiative – Autosomal-Dominant Alzheimer's disease; (2) Alzheimer's disease; (3) Presenilin-1; (4) Mild cognitive impairment; (5) Positron emission tomography; (6) Fluorodeoxyglucose; (7) Cerebrospinal fluid

# API<sup>1</sup> study evaluating crenezumab in familial AD<sup>2</sup>: Primary Endpoints

Numerical differences favoring crenezumab versus placebo were observed, but were not statistically significant

1

Crenezumab **did not statistically significantly slow or prevent cognitive decline** in people with a specific genetic mutation which causes early-onset Alzheimer's disease

2

Numerical differences favoring crenezumab were observed across the co-primary, multiple secondary and exploratory endpoints

3

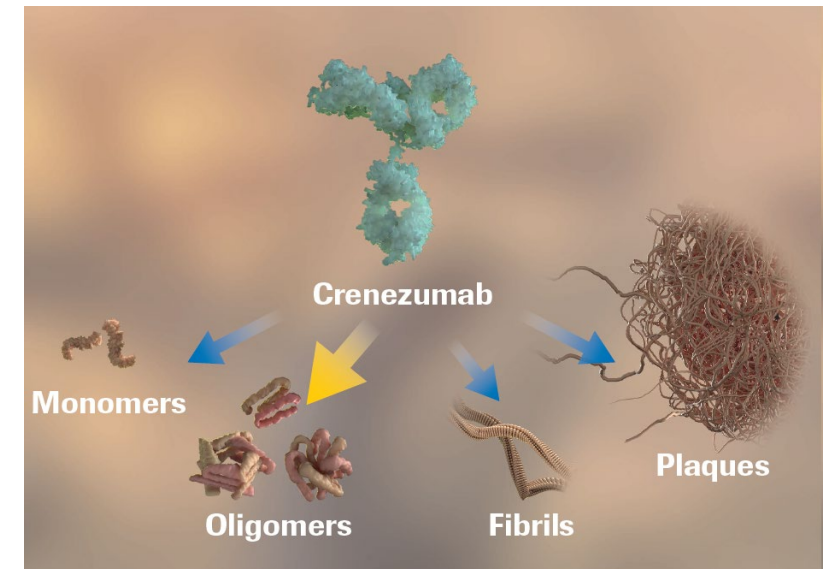
Crenezumab was **generally well tolerated**, and no new safety issues were identified. There was no case of ARIA-E<sup>3</sup>.

4

Patients from the trial can **continue receiving crenezumab** in a blinded extension of the study while Roche further analyzes the **data**.

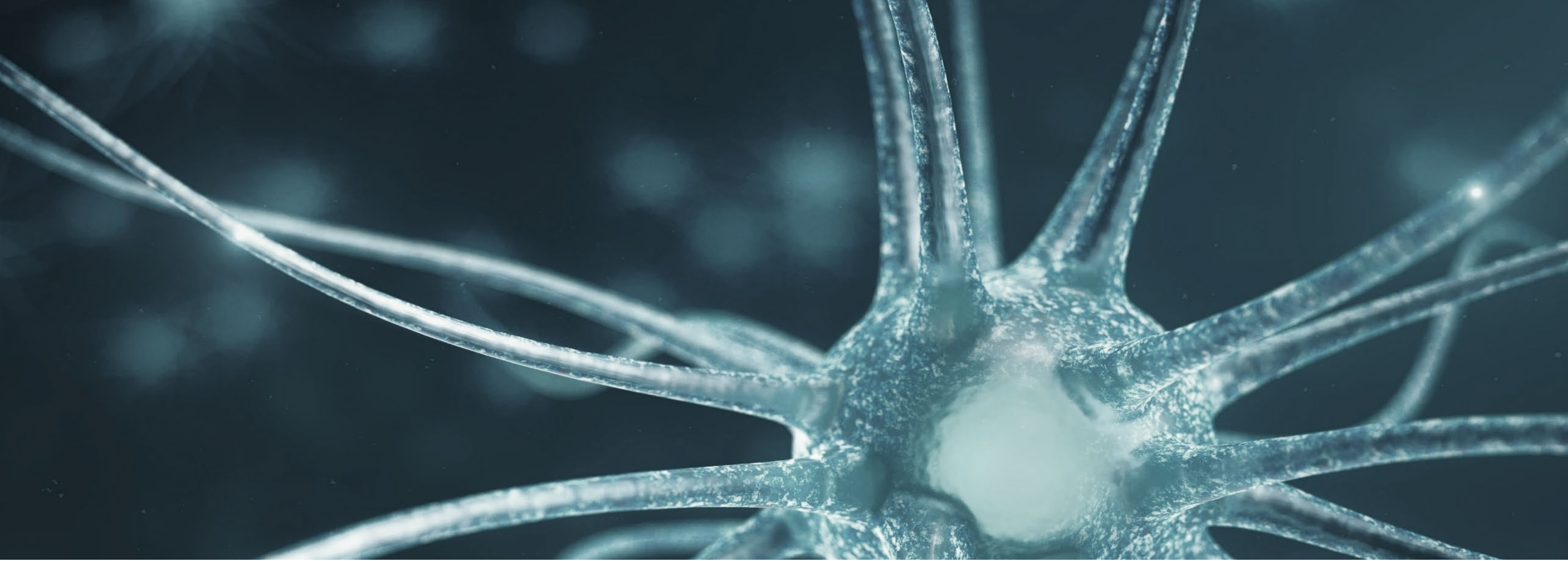
5

Further analyses are ongoing, and Partner Genentech and Roche will present initial data at **AAIC<sup>4</sup> on August 2, 2022**



(1) Alzheimer's Prevention Initiative; (2) Alzheimer's disease; (3) Amyloid-related imaging abnormalities refers to cerebral edema; (4) Alzheimer's Association International Conference





## 7. First-in-class diagnostic for precision medicine

# ACI-12589: a-syn PET tracer

Positive clinical proof-of-concept

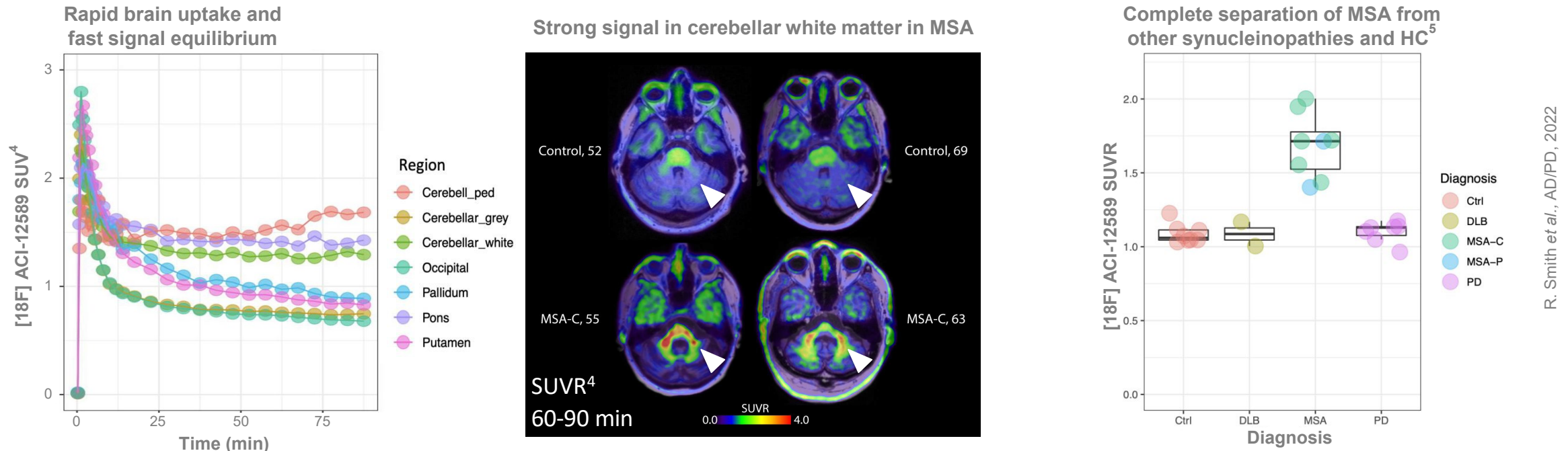
## Clinical Stage Programs

TARGET	PRODUCT CANDIDATE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
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	Semorinemab (anti-Tau antibody)	AD treatment (mild-to-moderate) <sup>2</sup>						
	Morphomer® Tau aggregation inhibitor	Rare Tauopathies (ACI-3024)						Lilly
		AD treatment						
	Tau-PET <sup>3</sup> tracer	AD diagnostic						Life Molecular Imaging
		PSP <sup>4</sup> diagnostic						
Abeta	Crenezumab (anti-Abeta antibody)	AD prevention <sup>5</sup>						Genentech <small>A Member of the Roche Group</small>
	ACI-24 (anti-Abeta vaccine)	AD treatment (Down syndrome <sup>6</sup> )						
		AD treatment						
a-syn <sup>7</sup>	ACI-7104 (anti-a-syn vaccine)	PD <sup>8</sup> , a-synucleinopathies						
	<b>A-syn-PET tracer</b>	a-synucleinopathies (e.g. MSA <sup>9</sup> )						

(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-12589 - positive clinical proof-of-concept for an a-syn<sup>1</sup>-PET<sup>2</sup> tracer

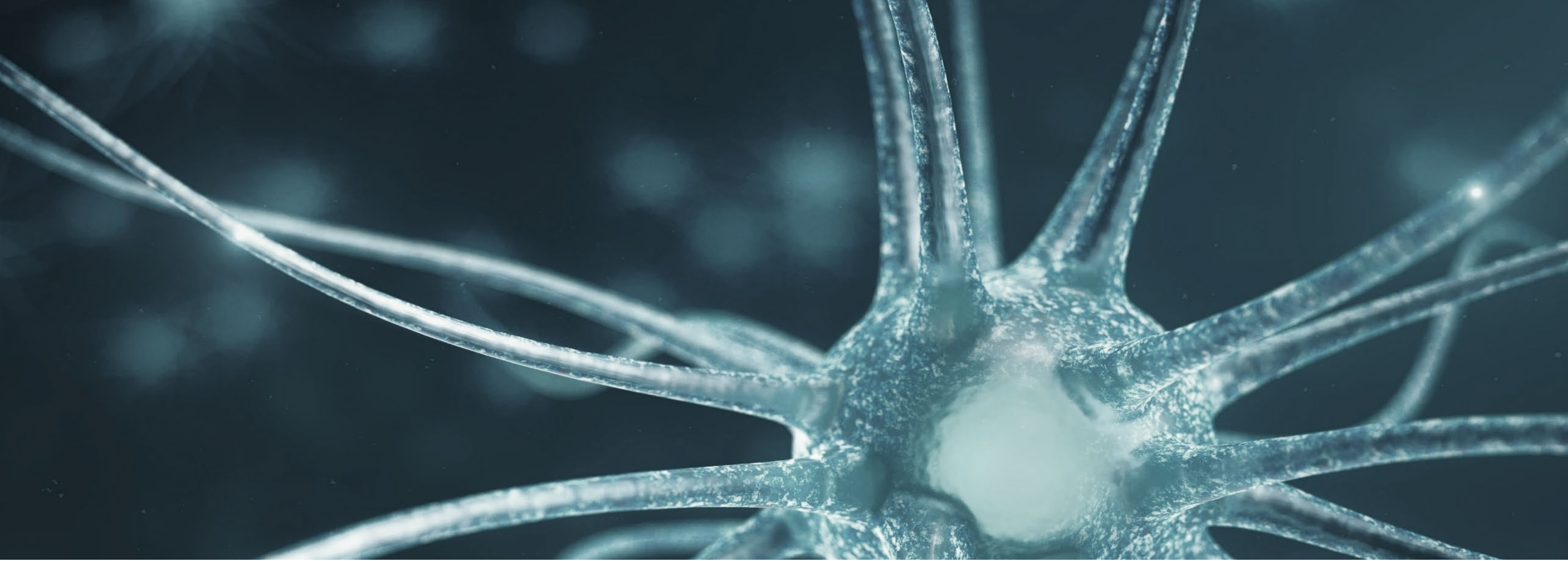
First-in-class diagnostic for MSA<sup>3</sup> and monitoring a-syn drug target engagement



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

(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





## 6. Near-term inflection points

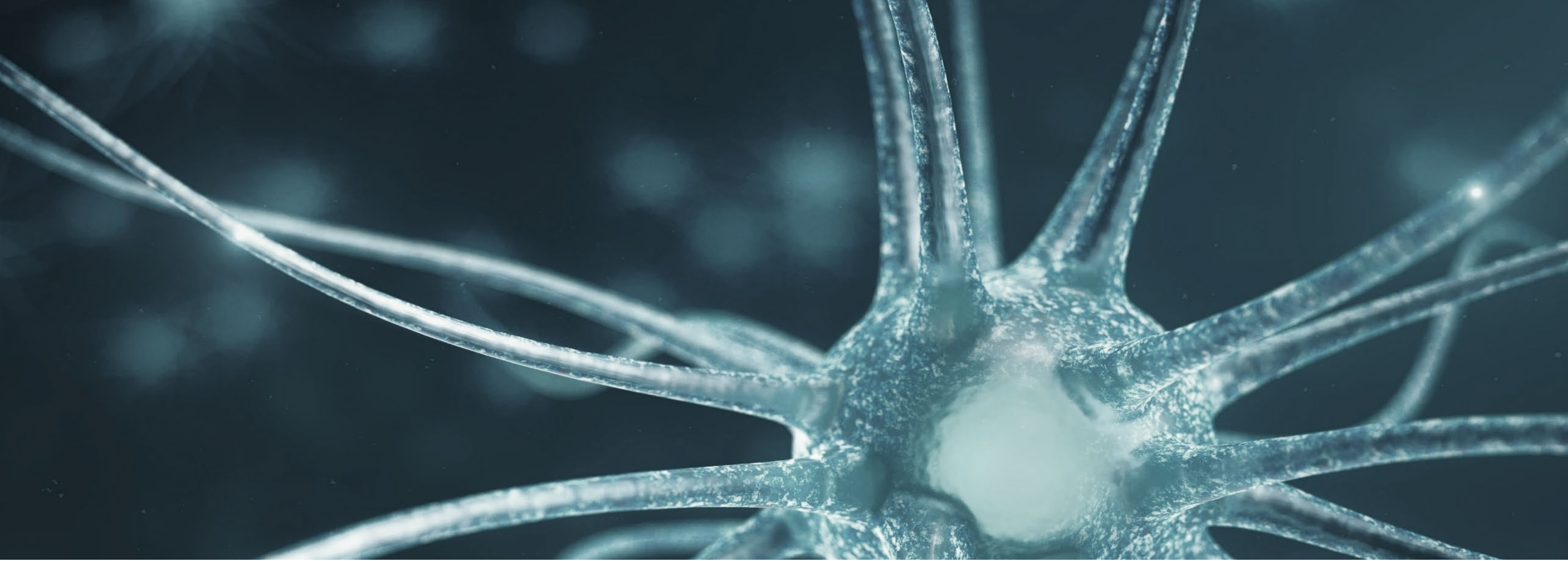
# Clinical catalysts to drive further value creation

Seven clinical data readouts expected in 2022

2022				
		H1	H2	
Tau	ACI-35.030 (anti-pTau vaccine)	✓		Phase 1b/2a interim analysis (highest dose) of ACI-35.030
			●	Decision to enter into late-stage development
	Semorinemab (anti-Tau antibody)		●	Report new Phase 2 Lauriet data (biomarkers)
	Tau-PET <sup>1</sup> Tracer (PI-2620)		●	Clinical PET study readout in orphan indication
			●	Phase 2 results in AD <sup>2</sup>
Abeta	ACI-24 (anti-Abeta vaccine)	✓		ACI-24 (optimized vaccine formulation) Phase 1b/2a First-Patient-In (AD)
			●	Phase 1b in AD readout and decision to move into DS <sup>3</sup>
	Crenezumab (anti-Abeta antibody)	✓		Top line results of Phase 2 Alzheimer's prevention trial
a-syn <sup>4</sup>	ACI-7104 (anti-a-syn vaccine)		●	Phase 2 First-Patient-In
	a-syn-PET tracer	✓		First clinical proof of concept in alpha-synucleinopathies ( e.g. MSA <sup>5</sup> )

(1) Positron emission tomography; (2) Alzheimer's disease; (3) Down syndrome-related AD; (4) alpha-synuclein; (5) Multiple system atrophy





## 7. Financial figures

- Pioneering new ways to **treat neurodegenerative diseases** such as Alzheimer's and Parkinson's
- **Listed on Nasdaq** since September 2016 (ticker: ACIU)
- **83.5 million shares** outstanding<sup>1</sup> (free float approximately 39%<sup>2</sup>)
- Cash position of **CHF 173.8 million (USD ~188 million)**<sup>3</sup>
- Based at the **EPFL**<sup>4</sup> campus in Lausanne, Switzerland
- **~145 employees**



(1) As of March 31, 2022 – excluding treasury shares; (2) Source: Refinitiv;  
(3) As of March 31, 2022; (4) École Polytechnique Fédérale de Lausanne

# External validation and cash generated by 5 partnering<sup>1</sup> deals

Managing risk and retaining significant upside

Biologicals

Small molecules

Product	Dev. phase	Total value <sup>2</sup>	Upfront <sup>2</sup>	Milestones received to date <sup>2</sup>	Royalties	Partners
<b>Crenezumab</b> (anti-Abeta antibody)	Phase 2	USD 340	USD 25	USD 40	Mid-single digits to mid-teens	<b>Genentech</b> <i>A Member of the Roche Group</i>
<b>Semorinemab</b> (anti-Tau antibody)	Phase 2	CHF 430	CHF 17	CHF 42	Mid-single digits to low-double digits	<b>Genentech</b> <i>A Member of the Roche Group</i>
<b>ACI-35</b> (pTau Vaccine)	Phase 1b/2a	CHF 500	CHF 26	CHF 5	Low-double digits to mid-teens	<b>janssen</b> <small>PHARMACEUTICAL COMPANY OF Janssen-Cilag</small>
<b>Tau PET<sup>3</sup> imaging agent</b>	Phase 2	EUR 160	EUR 0.5	EUR 3	Mid-single digits to low-teens	<b>Life</b> Molecular Imaging
<b>Tau Morphomer<sup>®</sup> small molecules</b>	Phase 1 <sup>4</sup>	CHF 1,860	CHF 80 + USD 50 <sup>5</sup>	CHF 40	Low-double digits to mid-teens	<b>Lilly</b>
<b>Total (millions)<sup>6</sup></b>		<b>CHF ~3,311</b>	<b>CHF 155.2<sup>7</sup></b>	<b>CHF 128.5</b>		

■ 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) Phase 1 completed; (5) Equity investment; (6) Converted to CHF on date of receipt; (7) Excludes convertible note agreement of USD 50 million

# First Quarter 2022 financial update

## Strong cash position

- CHF 173.8 million on March 31, 2022, compared to CHF 198.2 million on December 31, 2021

## R&D expenses

- Increased by CHF 1.8 million to CHF 15.1 million for the three months ended March 31, 2022, compared to the prior comparable quarter

## G&A expenses

- Decreased by CHF 0.2 million to CHF 4.2 million for the quarter ended March 31, 2022, for the comparable period in 2021

## Other operating income

- Recognized CHF 0.5 million in grant income, an increase of less than CHF 0.1 million compared to the prior period

## IFRS income/(loss)

- Net loss after taxes of CHF 18.8 million for the quarter ended March 31, 2022, compared with net loss of CHF 16.7 million for the comparable period in 2021

**Sufficiently funded to reach multiple value inflection points through at least Q1 2024<sup>1</sup>**

(1) Excluding potential future milestone payments

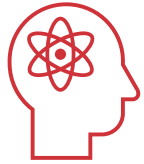




## 8. Strategic Outlook



# Acceleration of value creation in 2022 and beyond



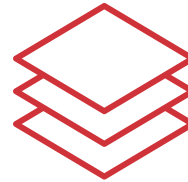
## Leading with Science

First- or best-in-class candidates



## Precision Medicine

Developing integrated diagnostics and therapeutics for single or combination therapies



## Enabling Platforms

Fuel development pipeline & create growth opportunities



## Execution Strategy

Partnerships for late-stage AD<sup>1</sup> assets; retain program lead until Ph 3 or further in other programs




## Financial Strength

Substantial partnership revenues & vision to become a fully integrated commercial company

Advancing world-class science to develop breakthrough therapies for neurodegenerative diseases

(1) Alzheimer's disease

# AC Immune: pioneering science and precision medicine



By pairing cutting-edge diagnostics with highly selective therapeutic agents, we aim to shift the treatment paradigm of neurodegenerative disease towards earlier diagnosis and disease prevention