Novel Therapeutics and Diagnostics for Alzheimer’s and other Neurodegenerative Diseases presented by Prof. A. Pfeifer, CEO

Jefferies Healthcare Conference, November, 2018
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About AC Immune

- Pioneering new ways to treat neurodegenerative diseases associated with misfolded proteins
- Listed on Nasdaq since September 2016 (ticker: ACIU)
- 67.4 million shares outstanding
- Cash position of CHF 199.1 million following share capital increase in July 2018
- Based at the EPFL campus in Lausanne, Switzerland
- 90 full-time employees

(1) As of Q3, 2018, following completion of a common stock offering of 10 million shares totaling USD 117 million in gross proceeds which closed on July 31, 2018;
Key partners
External validation of technologies and platforms

Well-regarded foundations / institutions

Highly committed institutional investors

High-value partnerships

- Four out-licensing agreements over USD 1.4 billion in value and three research collaborations
- Five private financing rounds totalling ~USD 130 million
- IPO NASDAQ September 2016 raised USD 70.5 (CHF 69.4) million in net proceeds
- Share capital offering of 10 million common shares in July 2018 raising gross proceeds of USD 117.7 (CHF 116.4) million
- More than 300 pending patent applications
- More than 260 granted patents

(1) Exchange rate fixed as of closing date of last financing round

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To become a global leader in precision medicine\(^1\) of neurodegenerative diseases leveraging dual proprietary technology platforms to develop breakthrough therapies.

Dual Proprietary Technology Platforms

**SupraAntigen™**

Vaccines and antibodies specific to disease causing conformations

**Morphomer™**

Conformation-sensitive small molecules

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(1) The goal of precision medicine is to deliver optimally targeted and timed interventions tailored to the individual disease drivers.
Why do we need Precision Medicine in AD?

High level of other proteinopathies and co-pathologies in AD

- hAD (iAD) shows high levels of co-pathologies, i.e. 55% (41%) α-Synuclein; 40% (33%) TDP-43 with an overall pre-valence of 70% (65%)

The prevalence of co-pathologies in AD and other neurodegenerative diseases may indicate a need for different therapies at different stages
- Clinical trial participants may be better defined by their various proteinopathies
- Patient sub-classification may lead to improved clinical outcome
- Combination therapy may be the ultimate requirement

Adapted from Robinson et al., Brain, 2018
Business strategy: 3-pillar approach
Precision medicine creates ultimate differentiation

Vision

Alzheimer’s disease (AD)
Non-AD Neuro-orphans
Diagnostics

Alzheimer’s disease
- Develop best-in-class late stage assets in partnership
- Develop preventive/therapeutic vaccines as fully owned assets
- Establish a pipeline of disease modifying small molecules

Non-AD, neuro-orphans
- Discover therapeutics in Parkinson’s disease
- Leverage AD therapeutics in Down syndrome (DS), PSP\(^1\) and other neuro-orphan diseases

Diagnostics
- Accelerate diagnostic pipeline to late stage development
- Use diagnostics for improved clinical trials and external partnerships

(1) Progressive supranuclear palsy
# Broad and robust pipeline in neurodegenerative diseases

Driven by proprietary technology platforms for sustained growth

## Product candidate

<table>
<thead>
<tr>
<th>Target</th>
<th>Partner</th>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crenezumab (anti-Abeta antibody)</td>
<td>Abeta</td>
<td>AD treatment</td>
<td>AD prevention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevention trial (API-ADAD) Colombion population</td>
<td>Abeta</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ACI-24 (anti-Abeta vaccine)</td>
<td>Abeta</td>
<td>AD treatment</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>ACI-35 (anti-pTau vaccine)</td>
<td>Tau</td>
<td>AD treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-Tau antibody</td>
<td>Tau</td>
<td>AD treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphomer Tau (Tau inhibitor, small molecule)</td>
<td>Tau</td>
<td>AD treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACI-24 (anti-Abeta vaccine)</td>
<td>Abeta</td>
<td>Down syndrome (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphomer Abeta (Abeta inhibitor, small molecule)</td>
<td>Abeta</td>
<td>Glaucoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphomer a-syn (a-synuclein inhibitor, small molecule)</td>
<td>a-synuclein</td>
<td>Parkinson's</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-a-syn antibody</td>
<td>a-synuclein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-TDP-43 antibody</td>
<td>TDP-43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tau-PET(^2) tracer</td>
<td>Tau</td>
<td>AD and PSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVD(^3) (Tau, Abeta)</td>
<td>Abeta/Tau</td>
<td>AD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a-syn-PET(^2) tracer</td>
<td>a-synuclein</td>
<td>Parkinson's</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(1) AD and cognitive impairment associated with Down syndrome; (2) Positron emission tomography; (3) in-vitro diagnostics

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NASDAQ: ACIU | November 2018

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Successful delivery of strategy with multiple near-term catalysts

### Achievements 2017/18

<table>
<thead>
<tr>
<th>Data read-outs</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ ACI-24 in AD(^1): <strong>Phase 1/2</strong> reported in Q1 2018</td>
</tr>
<tr>
<td>✓ ACI-35: <strong>Phase 1b</strong> reported in Q1 2018</td>
</tr>
<tr>
<td>✓ Tau-PET(^2) imaging agent in AD(^1): <strong>Phase 1</strong> data with favorable kinetics and densitometry; specific binding to different Tauopathies</td>
</tr>
</tbody>
</table>

### Key milestones for 2018/19

- **Pivotal CREAD 1 Phase 3** read-out in 2020 with interim analysis in 2019
- **ACI-24 Phase 1b in DS\(^3\) interim data** in Q4 2018 (low dose cohort) and H1 2019 (high dose cohort); potential decision to start **Phase 2** early
- Morphomer Tau **IND\(^4\) enabling studies** in 2018
- First selective a-synuclein PET\(^2\) tracers **IND\(^4\) enabling studies** in H1 and H2 2018
- a-Synuclein antibodies **lead selection** in 2018
- TDP-43\(^5\) antibodies **lead selection** in 2019

### Clinical Trial Update

- Crenezumab: **Pivotal CREAD 1 and CREAD 2 trials** completed recruitment in Q4 2017 and Q3 2018 by Roche / Genentech, respectively
- Anti-Tau antibody: **Phase 2** recruitment on schedule
- **ACI-24 in AD\(^1\)**: Start of **Phase 2** and first patient enrolled in August 2018
- **ACI-24 in DS\(^3\)**: **Phase 1b high-dose cohort** fully recruited in Q2 2018

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(1) Alzheimer’s disease; (2) Positron emission tomography; (3) Down syndrome; (4) Investigational new drug; (5) TAR DNA-binding protein 43; (6) First-in-Human

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Highly productive and versatile dual technology platforms driving future growth

**SupraAntigen™**
Vaccines and antibodies specific to disease causing conformations

**Morphomer™**
Conformation sensitive small molecules

**Immunotherapy against conformation-specific targets**
- Highly selective conformation-specific immunotherapy
- Antibodies and vaccines
- Rapid antibody response
- Favorable safety (T-cell independent MoA\(^1\))

**Generation of conformation-specific small molecules**
- Conformation specific small molecules through rational design
- Robust library of small molecules
- Protein propagation inhibitors

- **Crenezumab** in AD\(^2\) (Ph 3)
- **ACI-24** in AD\(^2\) (Ph 2) and DS (Ph1b)
- **ACI-35** in AD\(^2\) (Ph 1b)
- **Anti-Tau antibody** in AD\(^2\) (Ph 2)
- **a-syn\(^3\)/TDP-43 antibodies** in PD\(^4\) and neuro-orphan indications (pre-clinical)

- **Tau-PET imaging agent** in AD\(^2\) and PSP\(^5\) (Ph 1)
- **Morphomers for different targets** in AD\(^2\) and PD\(^4\) (discovery / pre-clinical)
- **a-syn\(^3\)-PET\(^6\) imaging agent** in PD\(^4\) (pre-clinical)

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\(^1\) Mode of action; (2) Alzheimer’s disease; (3) a-synuclein; (4) Parkinson’s disease; (5) Progressive supranuclear palsy; (6) Positron emission tomography
AC Immune is focused on detecting and treating AD earlier

Early treatment translates into better outcomes for patients

- The future treatment paradigm for neurodegenerative diseases may involve **different disease-modifying treatments used at various points in the disease progression**

- Possible **combination** therapies:
  - Passive immunization targeting Abeta (e.g. crenezumab) together with anti-Tau antibodies
  - Immunotherapies and small molecules targeting Abeta or Tau

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Disease-modifying treatment</th>
<th>Symptomatic treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Abeta Tau?</td>
<td>Abeta Tau</td>
</tr>
<tr>
<td>Prevention</td>
<td>Presymptomatic 2ndry prevention</td>
<td>Abeta Tau</td>
</tr>
<tr>
<td>Prodromal MCI</td>
<td>Abeta Tau?</td>
<td>Abeta Tau, Tau?</td>
</tr>
<tr>
<td>Mild AD¹</td>
<td>Moderate – severe</td>
<td></td>
</tr>
</tbody>
</table>

(1) Alzheimer's disease; (2) Mild cognitive impairment
Clinical pipeline
Crenezumab – Phase 3 in AD

<table>
<thead>
<tr>
<th>Target</th>
<th>Misfolded Abeta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed to</td>
<td>Roche Genentech</td>
</tr>
</tbody>
</table>

**Key results in pre-clinical studies**
- Unique epitope, breaks up Abeta aggregation and prevents assembly
- Binds to monomers, oligomers (10x higher affinity to soluble oligomers) and fibrils of Abeta
- Crystal structure supports ability to block aggregation and promote disaggregation
- Reduced risk of ARIA-E\(^1\) and neuro-inflammation allows for higher dosing attributable to
  - Low effector function of IgG4 backbone limiting inflammatory cytokines
  - Lack of binding to vascular amyloid and dense core of Abeta plaques

**Development status**
- Phase 3 commenced in 2016 (CREAD 1) and 2017 (CREAD 2), fast-track designation
  - Recruitment completed: Q4 2017 (CREAD 1) and Q3 2018 (CREAD 2)
- Encouraging Phase 2 data in mild patients
- First-in-class drug in AD\(^2\) prevention trial (Phase 2)

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(1) Amyloid related imaging abnormality-edema; (2) Alzheimer’s disease
Crenezumab

Compelling binding characteristics with unique disaggregation and safety profile

Multiple neuroprotective mechanisms of action

Uniquely differentiated binding profile with favorable preliminary safety profile

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Binding profile</th>
<th>Stage</th>
<th>Phase 3 dosage Clinicaltrials.gov</th>
<th>Iso-type</th>
<th>ARIA-E (safety)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crenezumab (GNE/Roche/AC Immune)</td>
<td>Monomers + Oligomers +++ Fibrils ++</td>
<td>Ph 3</td>
<td>60mg/kg</td>
<td>IgG4</td>
<td>&lt; 0.2% in Ph2</td>
</tr>
<tr>
<td>Aducanumab (Biogen/Eisai)</td>
<td>Oligomers +++ Fibrils +++</td>
<td>Ph 3</td>
<td>ApoE4+: 3 or 10 mg/kg ApoE4-: 6 or 10mg/kg</td>
<td>IgG1</td>
<td>41%, 37% and 35% in Ph1b (DB)</td>
</tr>
<tr>
<td>Gantenerumab (Roche/Morphosys)</td>
<td>Oligomers ++ Fibrils +++</td>
<td>Ph 3</td>
<td>Double blind (DB): 1.5 or 3.2mg/kg Open Label (OLE): up to 17.1mg/kg</td>
<td>IgG1</td>
<td>10% in DB, 22.9% in OLE</td>
</tr>
<tr>
<td>Solanezumab (Eli Lilly)</td>
<td>Monomers +++</td>
<td>Ph 3</td>
<td>failed</td>
<td>IgG1</td>
<td>1% in Ph3</td>
</tr>
<tr>
<td>BAN2401 (Eisai/Biogen)</td>
<td>Soluble Protifibrils +++ Fibrils +</td>
<td>Ph 2</td>
<td>2.5mg/kg 5 mg/kg 10mg/kg</td>
<td>IgG1</td>
<td>9.9% in all subjects ≥ 14.6% (in ApoE4 carriers)</td>
</tr>
<tr>
<td>Bapineuzumab (Elan/Pfizer/J&amp;J)</td>
<td>Monomers ++ Oligomers +++ Fibrils ++</td>
<td>Ph 3</td>
<td>failed</td>
<td>IgG1</td>
<td>~10% in Ph3</td>
</tr>
</tbody>
</table>

Crenezumab’s multiple neuroprotective mechanisms of action, in particular direct binding and inhibition of toxic Abeta oligomers, may differentiate crenezumab’s clinical benefit

Crenezumab
Promotes Abeta oligomer engulfment by microglia without inflammatory activation

Abeta1-42 oligomers

Abeta1-42 oligomers + MABT

MABT is equivalent to crenezumab, MABT IgG1 is MABT on IgG1 backbone

Reduces Abeta 1-42 oligomer toxicity

Reduces microglia inflammatory activation

Modified from Adolfsson et al., 2012

Antibody-mediated increase in cell survival

Reduction in TNF-α production
Oligomeric ABeta in AD: ABBY / BLAZE Findings

- Significant 43% reduction of oligomeric CSF ABeta after 69 weeks in the high dose i.v. cohort
- Strong evidence for principle oligomeric ABeta engagement by Crenezumab

<table>
<thead>
<tr>
<th></th>
<th>Median Change</th>
<th>Oligo decrease</th>
<th>LLoQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-13%</td>
<td>54% (→)</td>
<td>0%</td>
</tr>
<tr>
<td>i.v.¹</td>
<td>-43%</td>
<td>86% (p = 0.01)</td>
<td>20%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Median Change</th>
<th>Monomer increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-9%</td>
<td>25% (→)</td>
</tr>
<tr>
<td>i.v.¹</td>
<td>10%</td>
<td>71% (p = 0.001)</td>
</tr>
</tbody>
</table>

(1) i. v. Intravenous; (2) Proportions of patients with negative change; (3) Proportions of patients below lowest level of quantification; (4) Proportions of patients with positive change
Crenezumab – Phase 3
Anti-Abeta antibody with potential to become best-in-class disease modifying treatment for Alzheimer’s disease (AD)

Dose-response simulation on cognitive endpoints in patients with mild AD (MMSE1 22-26)

- Choice of the dose for Phase 3 based on modelling of results from the Phase 2 in a drug-disease model
- Antibody exposure needed for maximal cognitive and clinical effect reached at 60/mg/kg
- Phase 1 safety results support use of 60mg/kg in Phase 3

Key ongoing clinical studies

Pivotal CREAD 1 and CREAD 2 trial design builds on ABBY/BLAZE findings and latest Abeta understanding

Study design
- 750 patients with prodromal to mild AD per study
- 60mg/kg every four weeks (4x higher than Phase 2 ABBY)

Key Eligibility
- MMSE1 22+ and CDR-GS4 0.5/1.0
- Brain amyloid positivity
- 50-80 years of age

Endpoints
- Primary endpoint: CDR-SB5 at 105 weeks
- Key secondary endpoint: ADAS-cog2 13 at 105 weeks
- Other endpoints: safety, biomarkers and economic

Study timelines
- CREAD 1 started in Q1 2016; fully recruited in Q4 2017
- CREAD 2 started in Q1 2017; fully recruited in Q3 2018

API-ADAD prevention trial in Colombian population
- 300 cognitively healthy individuals of whom 200 are genetically predisposed to develop early AD
- Study commenced in Q4 2013

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(1) Mini-mental state exam; (2) Alzheimer’s Disease Assessment Scale-cognitive subscale; (3) Subcutaneous; (4) Clinical Dementia Rating-Global Score; (5) Clinical Dementia Rating-Sum of the Boxes
# ACI-24 – Advancing to Phase 2 in AD and Phase 1b in DS

Anti-Abeta therapeutic vaccine

<table>
<thead>
<tr>
<th>Target</th>
<th>Misfolded Abeta</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>▪ Strong and robust antibody response(^1) specific for oligos and fibrils</td>
</tr>
<tr>
<td></td>
<td>▪ Favorable safety profile with lack of local inflammation and T-cell independent mode of action(^1)</td>
</tr>
<tr>
<td></td>
<td>▪ Significant reduction of Abeta levels in brain and compelling memory enhancement (AD and DS)</td>
</tr>
</tbody>
</table>

## Alzheimer’s Disease (AD) development status

- Clinical Phase 1/2a completed
  - Positive safety and tolerability across 4 cohorts confirmed
  - Cohort 3 and 4 showed a trend of reduction of accumulation of brain amyloid (PET\(^3\) imaging)
- **Start of Phase 2 trial and first patient enrolled in August 2018**

## Down Syndrome (DS) development status

- Clinical Phase 1b with interim data expected in 2018
- World first clinical trial for vaccine targeting Abeta in people with Down syndrome
- Dose escalation study in up to 24 adults with Down syndrome (25-45 years)
- Endpoints: safety and tolerability, anti-Abeta antibody titers and biomarkers
- Recruitment completed: low-dose cohort in Q3 2017 and high-dose cohort in Q2 2018

---

(1) Pihlgren et al., Blood 2013; (2) Object recognition test; (3) Positron emission tomography
# ACI-35 – Phase 1b in Alzheimer’s Disease

Anti-pTau therapeutic vaccine

## Target

| Aggregated pTau |

## Licensed to

| [Janssen Pharmaceutical Companies of Johnson & Johnson] |

## Key results in pre-clinical studies

- High specific antibody response to pathogenic Tau
- Improvement of cognition, physical performance, behavior and prolongation of survival
- Favorable safety profile with T-cell independent mode of action

### Immune response highly specific to phosphorylated Tau

ACI-35 vaccinated mice - pTau vs. Tau protein after 5 immunizations

<table>
<thead>
<tr>
<th>O.D. at 1/100 dilution</th>
<th>ACI-35 tg1 mice</th>
<th>ACI-35 wt2 mice</th>
<th>PBS tg1 mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
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</tbody>
</table>

- **pTau protein**
- **Tau protein**

### Highly significant improvement of behavior (P301S)

15 rpm ACI-R-40 Rotarod 5M vehicle vs. ACI-35

<table>
<thead>
<tr>
<th>Latency to fall (s)</th>
<th>vehicle</th>
<th>ACI-35</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td><strong>p=0.02</strong></td>
</tr>
</tbody>
</table>

## Development status

- Clinical Phase 1b treatment part finished and final data analysis ongoing
  - Acceptable safety and tolerability
  - Dose-dependent and target-specific antibody response to pTau
  - AC Immune and Janssen jointly decided to advance anti-Tau vaccine program, supported by regulatory authorities
  - Based on data available next stage of development in preparation

(1) Transgenic; (2) Wild type
**Anti-Tau antibody – Phase 2 in AD**

**Anti-Tau antibody (RO7105705)**

<table>
<thead>
<tr>
<th>Target</th>
<th>Designed to intercept the cell-to-cell spread of pathological tau in extracellular space of brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed to</td>
<td><a href="https://www.genentech.com/">Genentech</a></td>
</tr>
<tr>
<td>Key pre-clinical results</td>
<td></td>
</tr>
</tbody>
</table>
  - Tau pathological spread is dose dependently reduced independent of effector function  
  - Proven target engagement through dose-dependent rise of plasma Tau (mice, cynos) |

<table>
<thead>
<tr>
<th>Pre-clinical results</th>
<th>Clinical results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose dependent reduction of Tau pathology</strong></td>
<td><strong>Pharmacodynamic response: Plasma Tau concentration 2x higher in AD(^1) than in HV(^2)</strong></td>
</tr>
<tr>
<td><img src="image1" alt="Control" /> Anti-gp 20, 30mg/kg</td>
<td><img src="image2" alt="RO7105705" /> Anti-Tau DANG 30mg/kg</td>
</tr>
<tr>
<td>AD/PD conference, Vienna, April 2017</td>
<td>Compared to HV(^2), AD(^1) patients exhibited two-fold greater levels of plasma tau following RO7105705 administration…</td>
</tr>
<tr>
<td><img src="image3" alt="Control" /> Anti-gp 20, 30mg/kg</td>
<td>…despite identical RO7105705 exposures in the two populations</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Development status</th>
<th>Phase 1 data</th>
<th>Phase 2 design</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>
  - No dose-limiting toxicities up to high doses  
  - Dose-proportional Pharmacokinetics (PK) with median half-life of 32.3 days  
  - Detectable in CSF\(^3\), indicating CNS\(^4\) exposure  
  - Pharmacodynamic (PD) response: 2x higher plasma Tau concentrations observed in patients with AD\(^1\) than in HV\(^2\) |
|                   |  
  - 360 prodromal-to-mild AD\(^1\) patients (MMSE\(^5\) 20-30, CDR-GS\(^6\) 0.5 or 1)  
  - 3 active doses or placebo for 72 weeks, followed by 96 week open label study  
  - Primary endpoints: safety measures and CDR-SB\(^7\) |

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1. Alzheimer’s disease  
2. Healthy volunteers  
3. Cerebrospinal fluid  
4. Central nervous system  
5. Mini-mental state exam  
6. Clinical Dementia Rating-Global Score  
7. Clinical Dementia Rating-Sum of the Boxes

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Preclinical pipeline
# Tau Morphomer Therapeutics – Discovery in AD

<table>
<thead>
<tr>
<th>Target</th>
<th>Intracellular Tau seeds</th>
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<tbody>
<tr>
<td><strong>Target characteristics</strong></td>
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<tr>
<td>In AD(^1) Tau undergoes misfolding and aggregation and forms intra-cellular seeds</td>
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<td>Tau seeds are involved in spreading of Tau pathology in AD(^1) and other tauopathies</td>
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<tr>
<th>Preclinical results of leads</th>
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<td>In vitro</td>
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<td>Selective binding to pathological Tau</td>
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<td>Reduction of cellular misfolded Tau (MC1(^2))</td>
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<td>In vivo</td>
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<td>Target engagement demonstrated by reduction of misfolded Tau (MC1(^3))</td>
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<td>Reduction of Tau in CSF(^3) (biomarker)</td>
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<td>4-Week GLP toxicological studies successfully completed</td>
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<td>Significant reduction of activated microglia</td>
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<td>Promising safety profile with NOAEL(^4) at 300mg/Kg and 450mg/Kg in rodent and non-rodent</td>
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**Morphomer Platform**

- **Morphomer Technology**
  - Rational chemical design of CNS small molecules (sm) targeting proteinopathies
  - CNS\(^5\) library with more than 3500 sm

**Next steps**

- Initiate Phase\(^1\) clinical trial

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(1) Alzheimer’s Disease; (2) Conformational antibody; (3) Cerebrospinal fluid; (4) No adverse event levels; (5) Immunohistochemistry; (6) Transgenic mice tg4510; (7) Central nervous system; (8) Good laboratory practice
The significant inverse correlation between CSF Tau and ACI-3024 exposure in plasma might indicate an increase of Tau clearance from the brain.

CSF Tau concentrations will be explored as a biomarker for efficacy.
AC Immune’s targets pathological Tau at key points in the disease pathway

- Targeting both intracellular seeds and extracellular spreading by combination therapy of Morphomers and immunotherapy enables to fully control Tau pathology progression
- High selective Tau imaging diagnostic enables more precise patient characterization and potentially more precise prediction of AD progression
Diagnostics
Tau-PET imaging – Advancing to longitudinal study in AD and PSP

Morphomer Tau PI-2620

**Target**
- Misfolded Tau (4R and 3R)

**Licensed to**
- Life Molecular Imaging

**Key results**
- High specificity for pathological forms of human Tau in AD\(^1\) and other tauopathies
- Outstanding PET\(^2\) tracer-profile – excellent brain penetration and high selectivity even in early disease stage

**Development status**
- Clinical Phase with interim data
- Fast kinetics with robust brain uptake, fast wash-out in non-target regions and low off-target uptake
- Distinct and specific Tau distribution pattern in AD\(^1\) and PSP\(^3\) subjects
- Good reproducibility of PET\(^9\)-scans confirmed by test-retest study

**Pre-clinic:** High selectivity and absence of off-target binding

**Phase 1 clinical study:** distinct, specific Tau distribution pattern in AD\(^1\) and PSP\(^3\)

- NDC\(^4\): 53 y, MMSE\(^6\) 29, CDR\(^7\) 0, ADAS-cog\(^8\) 5
- Mild AD\(^1\): 70 y, MMSE\(^6\) 22, CDR\(^7\) 0.5, ADAS-cog\(^8\) 21
- Severe AD\(^1\): 63 y, MMSE\(^6\) 7, CDR\(^7\) 2, ADAS-cog\(^8\) 53
- PSP\(^3\) (SN\(^5\)): 75 y, MMSE\(^6\) 19, PSP\(^3\) scale 54

\(1\) Alzheimer’s disease; \(2\) Positron emission tomography; \(3\) Progressive supranuclear palsy; \(4\) Non-demented control; \(5\) Substantia nigra; \(6\) Mini-mental state exam; \(7\) Clinical Dementia Rating; \(8\) Alzheimer’s Disease Assessment Scale-cognitive subscale; \(9\) Positron emission tomography
Alpha-synuclein (a-syn) PET Tracer
Morphomer a-syn: ACI-3710

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<tr>
<th>Target</th>
<th>Misfolded, aggregated a-syn</th>
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<tr>
<td>Partner</td>
<td>Biogen (non-exclusive)</td>
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<td>Key results</td>
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<td>• Highly specific, low nanomolar binding to a-syn aggregates in human PD(^2); DLB(^3) and MSA(^4) brains</td>
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<td>• Between 500- to 1000-fold selectivity over potential amyloid-beta co-pathologies</td>
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<td>• Favorable pharmacokinetic (PK) profile in non-human primates (NHP) and mice</td>
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**Biochemical and histological radiography assays**

- **Binding to Lewy bodies in PD\(^2\) brains**
  - % competition vs. ACI-3710 concentration (nM)
  - \(K_i=0.6\) nM (\(R^2=0.97\))\(^6\)

- **Binding to PD\(^2\)-derived a-syn aggregates**
  - % competition vs. ACI-3710 concentration (nM)
  - \(K_i=1.7\) nM (\(R^2=0.88\))\(^6\)

**PK profile in NHP**

- **18F-PK profile in different brain regions**
  - SUV (g/ml) vs. Time (min)

- **Brain uptake**
  - Time to \(C_{\text{max}}\) 5min
  - ID/g\(^3\) brain (%) 4.0

- **Wash-out**
  - Peak/half Peak ~ 20min

**Development status**

- Potentially the first selective a-syn PET\(^1\) tracer
- IND\(^9\) enabling studies in H2 2018
- Start of Phase 1 in H2 2018

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(1) Positron emission tomography; (2) Parkinson’s disease; (3) Dementia with Lewy bodies; (4) Multiple system atrophy; (5) Inhibitory constant; (6) Square of the coefficient of multiple correlation; (7) Data shown for 18F-labeled ACI-3710 by PET\(^1\); (8) Injected dose per gram of brain; (9) Investigational new drug
Strategy for value creation

CONTINUE to leverage our dual platform technologies to efficiently advance commercially viable product candidates

INVEST to further build leadership in neurodegenerative diseases
- Accelerate diagnostic portfolio
- Pursue research in neuroinflammation
- Explore new targets

EVOLVE strategy and capture upside by developing late stage assets in-house

EXPAND into other neurodegenerative and neuro-orphan diseases
- Potential for streamlined regulatory pathway and favourable pricing / reimbursement