ACI-35.030 anti-phospho Tau active immunotherapy produces antibodies that prevent pathological Tau seeding *in vitro*

Marija Vukicevic, PhD | ADPD, March 2024

Disclaimer

This presentation contains statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements are statements other than historical fact and may include statements that address future operating, financial or business performance or AC Immune's strategies or expectations. In some cases, you can identify these statements by forward-looking words such as "may," "might," "will," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "outlook" or "continue," and other comparable terminology. Forward-looking statements are based on management's current expectations and beliefs and involve significant risks and uncertainties that could cause actual results, developments and business decisions to differ materially from those contemplated by these statements. These risks and uncertainties include those described under the captions "Item 3. Key Information – Risk Factors" and "Item 5. Operating and Financial Review and Prospects" in AC Immune's Annual Report on Form 20-F and other filings with the Securities and Exchange Commission. These include: the impact of Covid-19 on our business, suppliers, patients and employees and any other impact of Covid-19. Forward-looking statements speak only as of the date they are made, and AC Immune does not undertake any obligation to update them in light of new information, future developments or otherwise, except as may be required under applicable law. All forward-looking statements are qualified in their entirety by this cautionary statement.

SupraAntigen® is a registered trademark of AC Immune SA in the following territories: AU, CH, EU, GB, JP, RU and SG. Morphomer® is a registered trademark of AC Immune SA in CH, CN, GB, JP, KR, NO and RU.

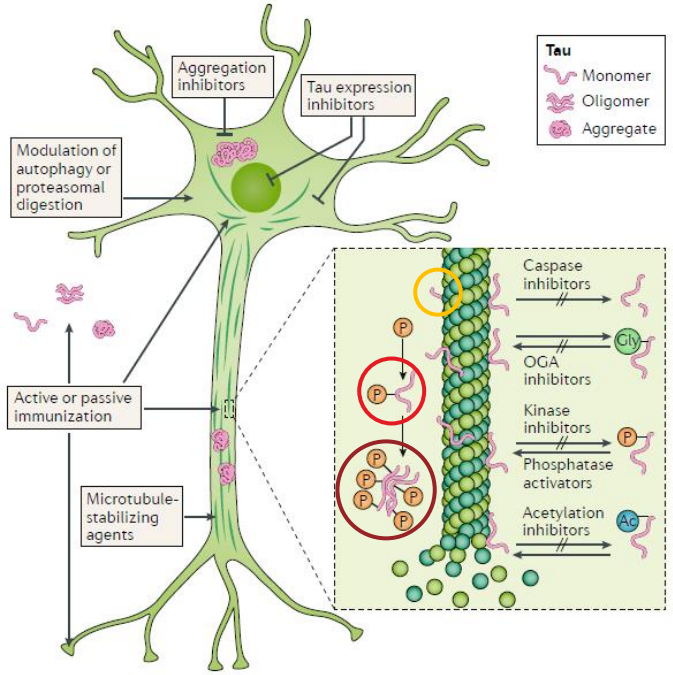
Conflict of interest disclosure

Marija Vukicevic is an employee of AC Immune entitled to stock options.

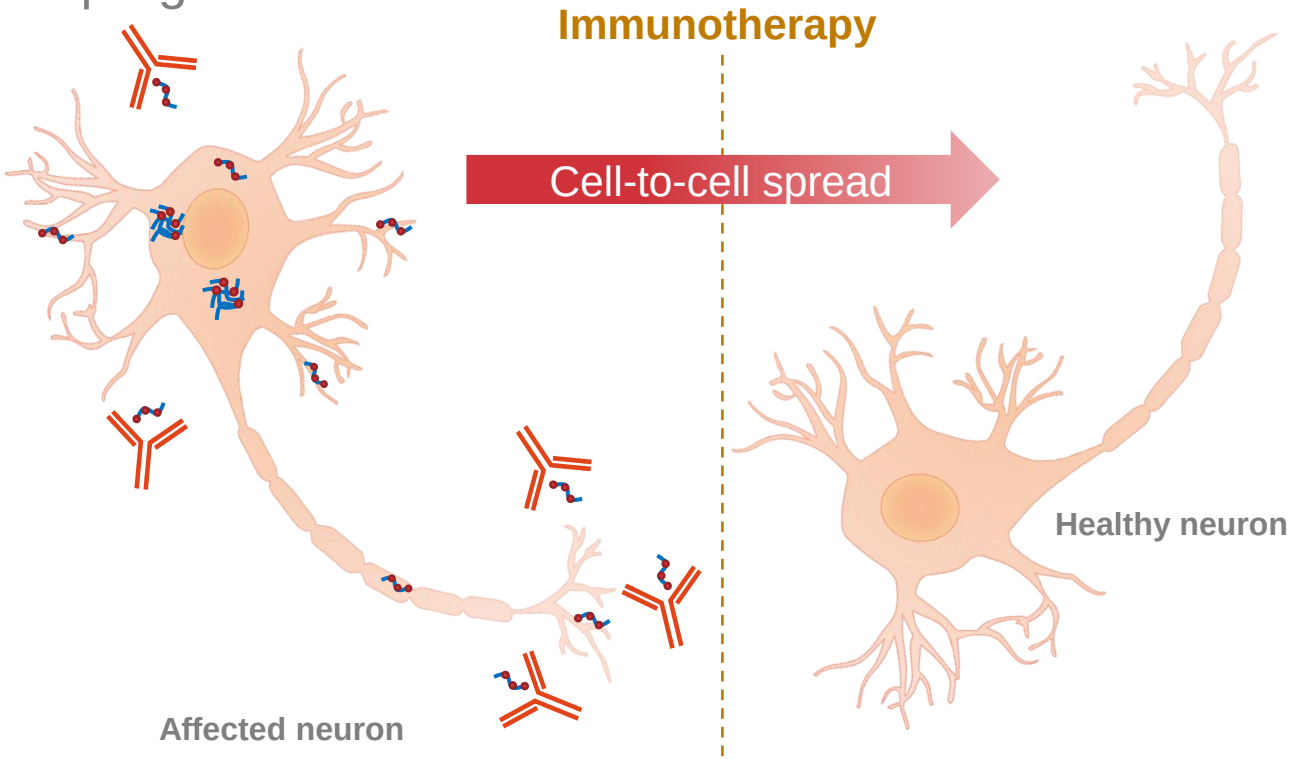
Active immunization for early intervention in Alzheimer's Disease

Preventing Tau spreading and disease progression

Hyperphosphorylated Tau aggregates in AD



Congdon et al., Nature Reviews Neurology, 2018



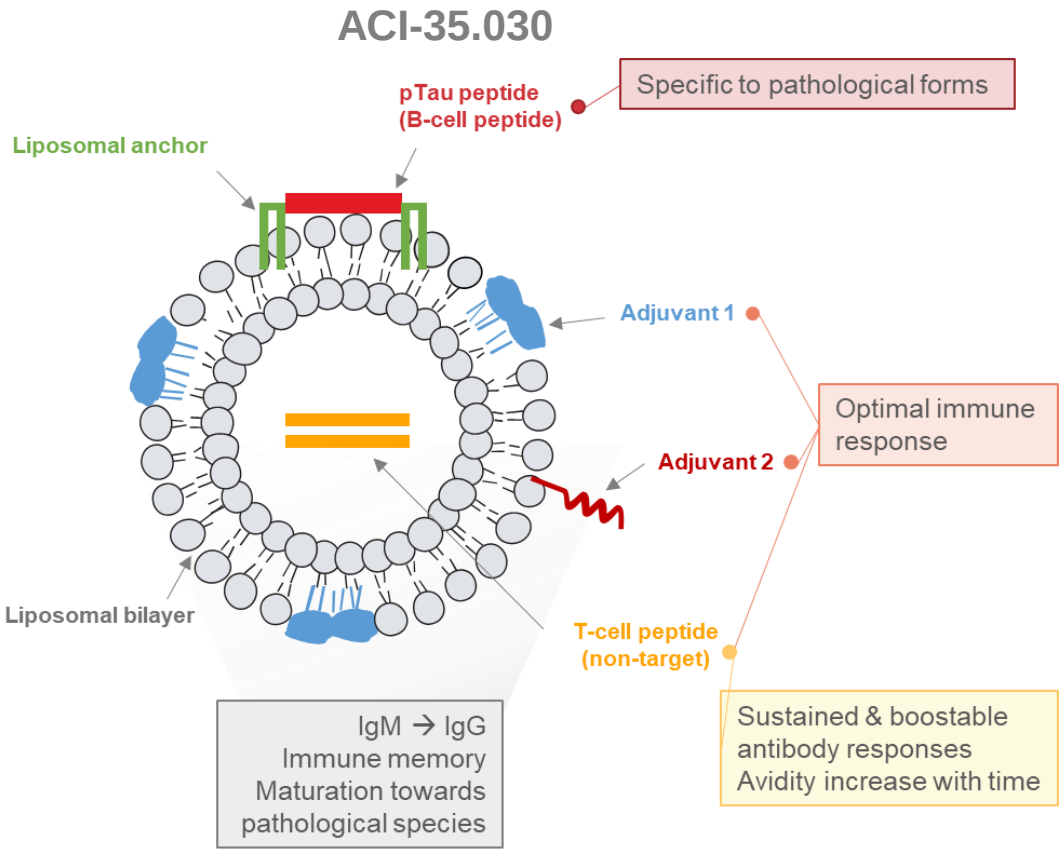
- Tau: a validated target through neuropathology and pre-clinical data
- Antibodies are suggested to selectively bind, trap and remove pathological Tau species to prevent cell-to-cell spread

- ACI-35.030 induces antibodies targeting the toxic forms of Tau (phosphorylated Tau) to prevent spreading of the pathology from cell-to-cell

AD, Alzheimer's Disease

ACI-35.030: anti-pTau active immunotherapy

Induces superior antibodies to fight Alzheimer's disease



Generates a target-specific antibody response

Safely engages Tau-unrelated T-cells to enhance & maintain immune responses

Preclinical and Clinical Performances

Immunogenicity against pTau species	++++
Specificity towards pathological Tau species	++++[1]
Sustainability of antibody response	++++
Boosting	+++
Class switching IgM to IgG	+++
Safety and tolerability	+++

(1) Increases over time

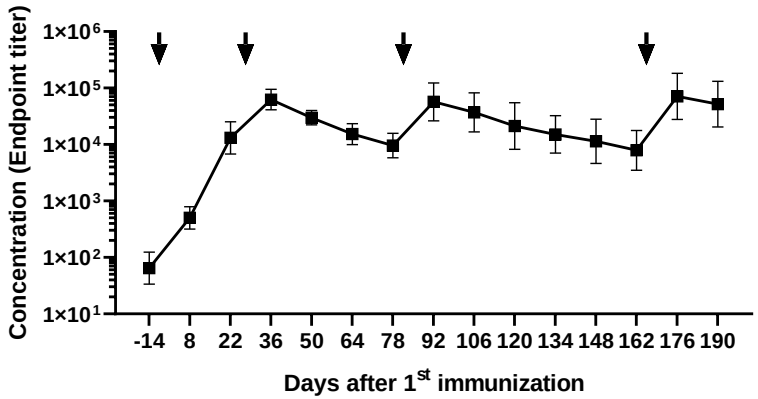
- ACI-35.030 Tau active immunotherapy shows excellent safety and tolerability, inducing IgG responses to the immunizing peptide as well as AD brain-derived pathological Tau

AD, Alzheimer's Disease; Ig, Immunoglobin; pTau, phosphorylated Tau

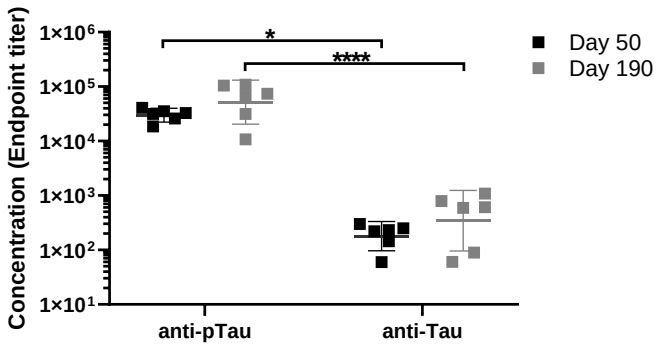
Immunogenicity of ACI-35.030 in non-human primates

Strong and sustained antibody response that matures towards the pathological target

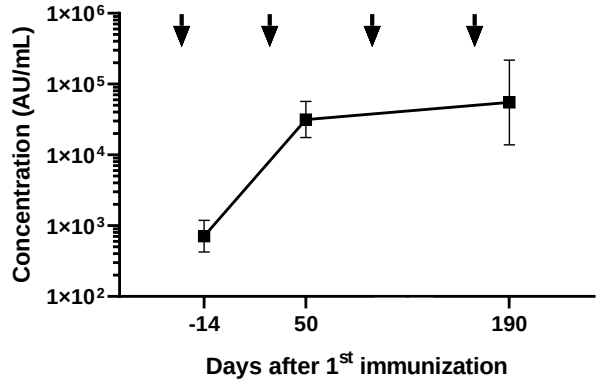
Anti-pTau peptide IgG titers



Anti-pTau & anti-Tau peptide IgG titers



Anti-ePHF IgG titers



Immunization schedule: Day 1, 29, 85 and 169 (arrows indicate injections)

Day 50: Three weeks after the 2nd injection
Day 190: Three weeks after the 4th injection
Two-Way ANOVA: *p < 0.05; ****p < 0.0001

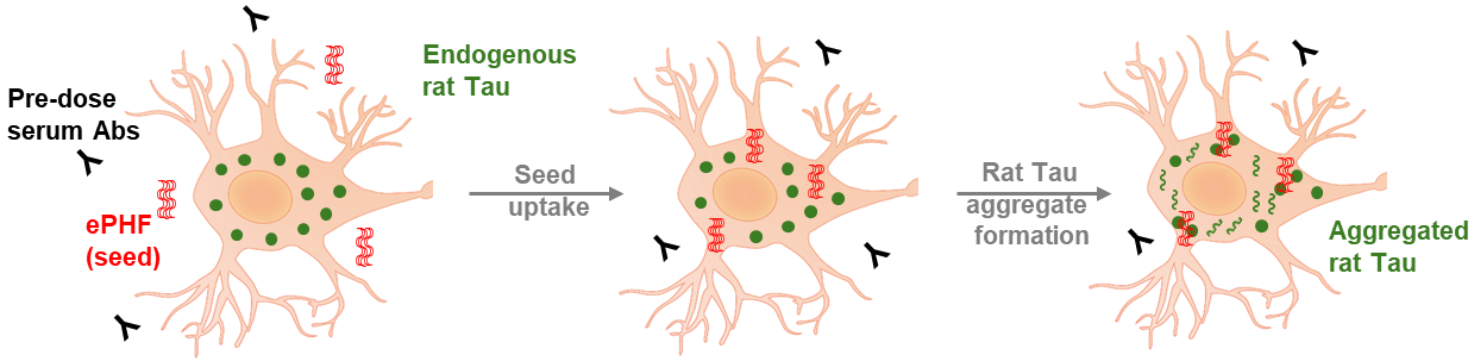
- Strong prime, boost and maintenance of antibody response in non-human primates
- Phospho-specific response, increasing in specificity for pathological species (ePHF) over time

ePHF, enriched paired helical filaments from human AD brain; Ig, Immunoglobin ; pTau, phosphorylated Tau

Functionality of ACI-35.030-induced antibodies

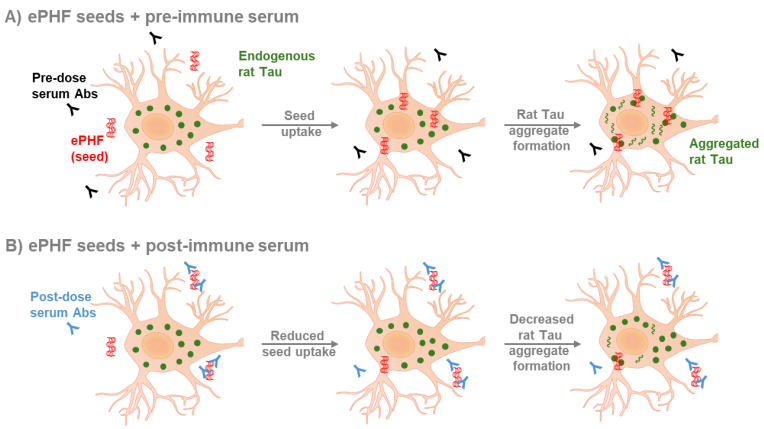
Can ACI-35.030-induced antibodies prevent seeding and intracellular Tau aggregation ?

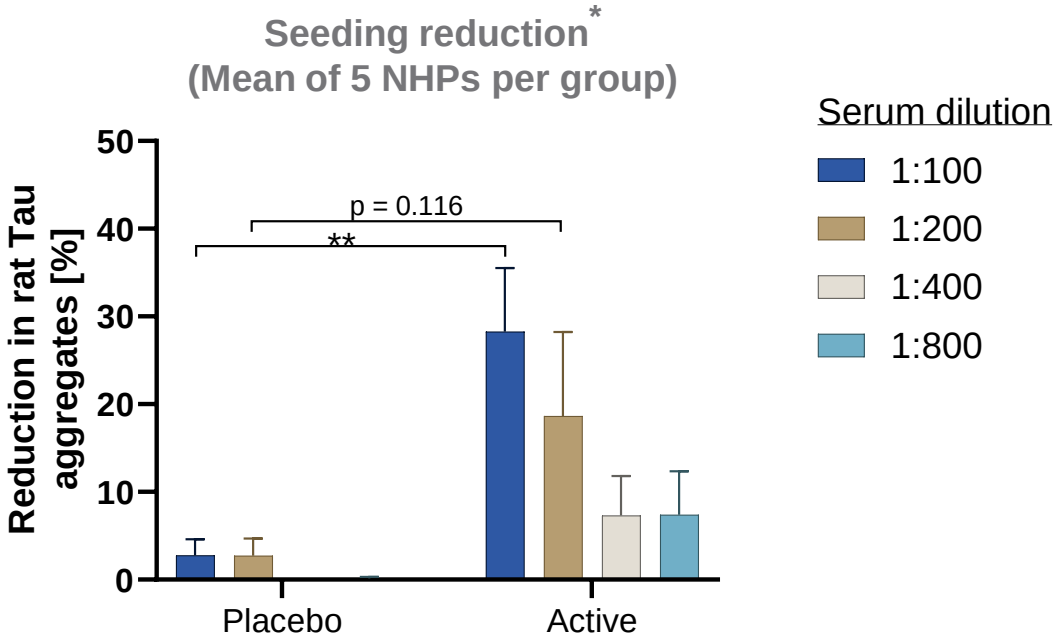
Assay principle: **A) ePHF seeds + pre-immune serum**



ACI-35.030 induces antibodies that prevent Tau seeding

Specific reduction of ePHF-seeded Tau aggregation using non-human primate immune sera





* Seeding reduction expressed as reduction in number of rat Tau aggregates between cells seeded in the presence of pre- and post-immunization serum samples

Immunization schedule: Day 1, 29 and 85
Analysis: Pre-dose and Day 99 (2 weeks after the 3rd immunization)
Seeding data is presented as mean ±standard error of mean in n=5/group
Statistical analysis: Two-Way ANOVA with Sidak's multiple comparison; **p < 0.01

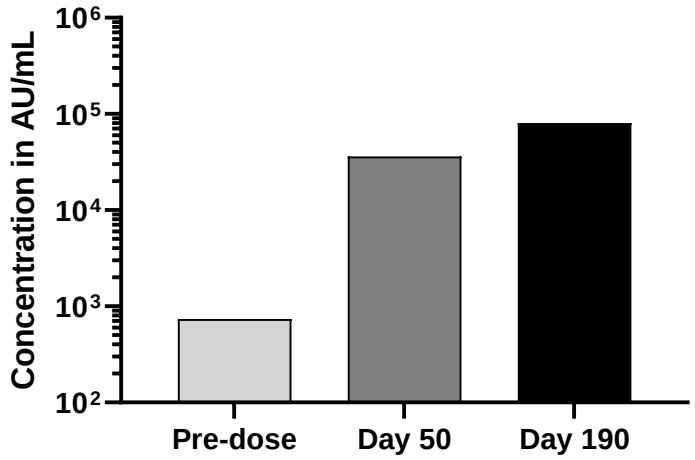
- ACI-35.030 immune sera decrease the seeding capacity of human ePHF as measured by a reduction in the number of induced Tau aggregates inside neurons
- No Tau aggregate reduction was observed with the placebo sera, confirming the specificity

ePHF, enriched paired helical filaments; NHPs, non-human primates

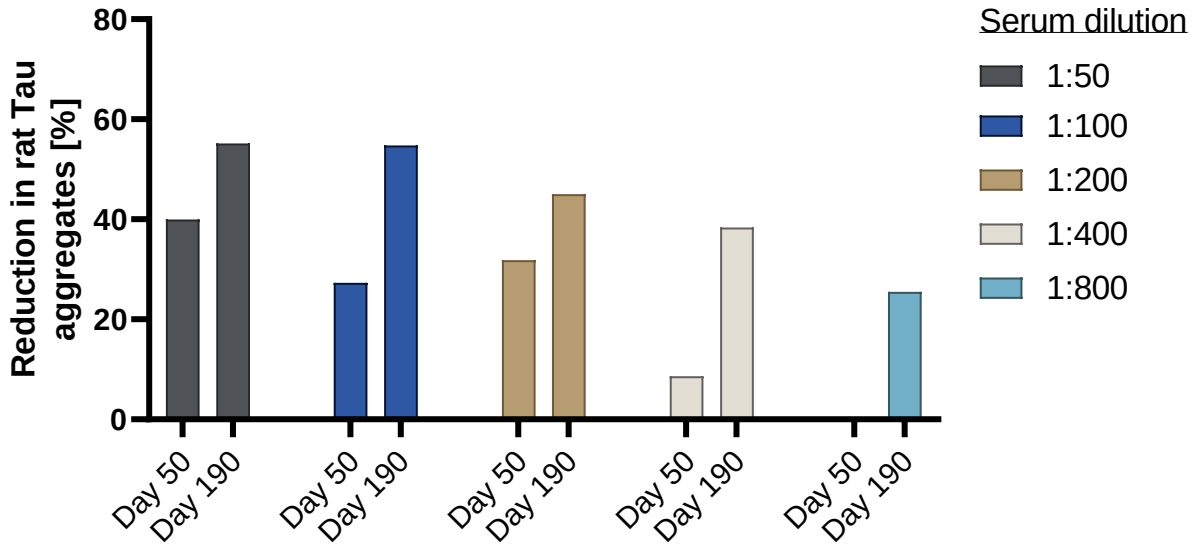
Over time increase in prevention of Tau seeding

Increasing seeding prevention with subsequent immunizations in non-human primates

Anti-ePHF IgG titers
(Serum pool from 6 immunized NHPs)



Seeding reduction*
(Serum pool from 6 immunized NHPs)



Immunization schedule: Day 1, 29, 85 and 169
Analysis: Pre-dose, Day 50 (3 weeks after the 2nd immunization) and Day 190 (3 weeks after the 4th immunization)
Antibody titers: Arithmetic mean titers from all monkeys included in the serum pool used for seeding analysis

* Seeding reduction expressed as the reduction in rat Tau aggregates between cells seeded in the presence of pre- and post-immunization serum samples

- ACI-35.030 immune sera decreased the seeding capacity of human ePHF
- Prevention of seeding was stronger using sera collected after the 4th (Day 190) as compared to 2nd (Day 50) immunization, suggesting maturation of the polyclonal immune response

ePHF, enriched paired helical filaments; Ig, Immunoglobulin; NHPs, non-human primates

ACI-35.030 anti-phospho Tau active immunotherapy

- ACI-35.030 induces:
  - ✓ strong and sustained antibody response
  - ✓ maturation of the antibody response over time towards the pathological target

- ACI-35.030 induces antibodies in non-human primates with:
  - ✓ capacity to specifically reduce ePHF-seeded de novo Tau aggregation
  - ✓ increased seeding prevention after subsequent immunizations

- In the next step, Tau seeding assay will be assessed and optimized for the testing of human sera from AD patients immunized with ACI-35.030

- ACI-35.030 is a safe and immunogenic Tau active immunotherapy that will be further clinically assessed in pre-clinical AD population in the upcoming Ph2b RETAIN study

AD, Alzheimer's Disease; ePHF, enriched paired helical filaments

Acknowledgements

AC Immune

Eva Gollwitzer
Emma Fiorini
Stefanie Siegert
Stefania Rigotti
Nathalie Chuard
Fabiana Tione
Laure Font

Marie Kosco-Vilbois
David Hickman
Madiha Derouazi
Andrea Pfeifer

J&J Innovative Medicine

Clara Theunis
Bruno Vasconcelos
Liesje Naessens

AC Immune

We continue to shape the future of neurodegeneration by discovering and developing breakthrough therapies through pioneering science and precision medicine

Web: https://www.acimmune.com/

Social media: www.linkedin.com/company/ac-immune

Business development: bd@acimmune.com

Investors and Media: communications@acimmune.com