

## **AC Immune ACI-24 Data in *Brain Communications* Show Abeta Vaccine-Candidate Induces Immunity Against pyroGlu-Abeta, Key Driver of Alzheimer's Disease**

*Results differentiate ACI-24 as potential best-in-class Abeta vaccine in development*

*Strong response against neurotoxic pyroGlu-Abeta variants observed in non-human primates*

*Data further support advancing optimized ACI-24 into the next stage of clinical development for Alzheimer's disease and Down syndrome-related AD in 2022*

**Lausanne, Switzerland, February 04, 2022** – AC Immune SA (NASDAQ: ACIU), a Swiss-based, clinical-stage biopharmaceutical company with a broad pipeline focused on neurodegenerative diseases, today announced that preclinical data on the optimized formulation of its wholly-owned amyloid-beta (Abeta) vaccine program, ACI-24, were published in the peer reviewed journal [Brain Communications](#). Based on these and other preclinical data, as well as the results of three clinical trials with ACI-24, AC Immune plans to advance clinical development of the optimized formulation to the next stage for both Alzheimer's disease (AD) and Down syndrome (DS) related AD in 2022.

Pyroglutamate Abeta (pyroGlu-Abeta) peptides, truncated forms of the Abeta protein, are highly neurotoxic Abeta species, which are observed only in brain amyloid plaques and believed to be key drivers of AD<sup>1</sup>. PyroGlu-Abeta peptides' altered biochemical properties make them more prone to aggregation compared to full-length Abeta and they are a major component of neurotoxic amyloid plaques. A recently [published](#) Phase 2 clinical trial showed that a monoclonal antibody targeting pyroGlu-Abeta epitope demonstrated slowing of cognitive and functional decline in early Alzheimer disease patients<sup>2</sup>.

Data published today in the [Brain Communications](#) paper show the optimized ACI-24 formulation induced a broad polyclonal anti-Abeta response, including high titers of antibodies targeting pyroGlu-Abeta variants, and was well tolerated in non-human primates and mice. Specifically, in the study, conducted in mice and non-human primates, optimized ACI-24 generated a strong immune response against both the full length Abeta (Abeta1-42) and pyroGlu-Abeta. Importantly, the anti-pyroGlu-Abeta immune response observed in this newly published study was substantially stronger in animals vaccinated with the optimized ACI-24 vaccine formulation compared to those vaccinated with earlier Abeta vaccines from other companies that have been clinically tested (AN1792 and ACC-001) in this study.

**Dr. Michael Rafii, Medical Director of the Alzheimer's Therapeutic Research Institute and Professor of Neurology at the Keck School of Medicine, commented:** "Thanks to its strong immunogenicity against pyroGlu-Abeta, the optimized ACI-24 formulation represents a potential breakthrough in Abeta vaccination that warrants further study in the clinic. The inability of currently

available therapies to reverse neuronal damage highlights the promise and need for active vaccination approaches that can delay or prevent AD.”

**Prof. Andrea Pfeifer, CEO of AC Immune SA, commented:** “These data suggest that ACI-24 likely is the best-in-class Abeta vaccine in development because of the robust polyclonal immune response, including high concentrations of antibodies against highly neurotoxic pyroGlu-Abeta variants, which are thought to be key drivers of early AD. These neurotoxic pyroGlu-Abeta species are not strongly targeted by competing anti-Abeta vaccines. We are honored that the data are published in this prestigious peer-reviewed publication.”

“This new year, we are proudly emerging as the leader in developing active vaccines to prevent neurodegenerative diseases, with three vaccine candidates advancing in mid-stage clinical development: ACI-24 to treat AD and DS-related AD; ACI-35 anti-pTau vaccine to treat AD, in partnership with Janssen; and ACI-7104, our wholly-owned anti-alpha synuclein vaccine to treat Parkinson’s disease and other synucleinopathies,” Prof. Pfeifer said.

ACI-24 is wholly-owned by AC Immune and derived from the Company’s SupraAntigen® platform. It is designed to prevent Abeta plaque accumulation and enhance plaque clearance by generating antibodies against pathological Abeta, including oligomeric Abeta and pyroGlu-Abeta. An earlier formulation of ACI-24 has been evaluated in a Phase 1b/2 and a Phase 2 trial in AD patients, and a Phase 1b trial in individuals with DS. AC Immune will be initiating clinical testing of the optimized ACI-24 formulation in H1 2022.

Further data will be presented at the AD/PD™ 2022 hybrid congress, held on March 15-20.

## References

1. Schlenzig D, Röncke R, Cynis H, Ludwig H, Scheel E, Reymann K, et al. N-Terminal pyroglutamate formation of Aβ38 and Aβ40 enforces oligomer formation and potency to disrupt hippocampal long-term potentiation. *J Neurochem.* 2012;121:774–84.
2. Mintun MA, Lo AC, Duggan Evans C, et al. Donanemab in Early Alzheimer’s Disease. *N Engl J Med.* 2021;384(18):1691-1704.

## About AC Immune SA

AC Immune SA is clinical-stage biopharmaceutical company that aims to become a global leader in precision medicine for neurodegenerative diseases, including Alzheimer’s disease, Parkinson’s disease, and NeuroOrphan indications driven by misfolded proteins. The Company’s two clinically validated technology platforms, SupraAntigen® and Morphomer®, fuel its broad and diversified pipeline of first- and best-in-class assets, which currently features ten therapeutic and three diagnostic candidates, six of which are currently in clinical trials. AC Immune has a strong track record of securing strategic partnerships with leading global pharmaceutical companies

including Genentech, a member of the Roche Group, Eli Lilly and Company, and Janssen Pharmaceuticals, Inc., resulting in substantial non-dilutive funding to advance its proprietary programs and >\$3 billion in potential milestone payments.

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

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