Peer-reviewed results from Phase 1b/2a Trial of Anti-pTau Active Immunotherapy from AC Immune Published in eBioMedicine

September 25, 2025

Peer-reviewed results from Phase 1b/2a Trial of Anti-pTau Active Immunotherapy from AC Immune Published in eBioMedicine

- Detailed results from completed Phase 1b/2a trial of ACI-35.030 and JACI-35.054 demonstrated that two different active immunotherapy formulations against the same target can induce a differential antibody response in individuals with early Alzheimer's disease
- ACI-35.030, developed using AC Immune's SupraAntigen® technology, generated rapid, potent polyclonal response against pathological forms of Tau after first dose
- No clinically relevant safety and tolerability observations were reported
- ACI-35.030 (JNJ-64042056) selected to advance and now in ongoing potentially registration-enabling Phase 2b ReTain clinical trial in preclinical Alzheimer's disease

Lausanne, Switzerland, 25, 2025 -- AC Immune SA (NASDAQ: ACIU), a clinical-stage biopharmaceutical company pioneering precision therapeutics for neurodegenerative diseases, today announced the peer-reviewed publication in eBioMedicine of results from the completed Phase 1b/2a trial of active immunotherapy ACI-35.030's (JNJ-2056) partnered with Janssen Pharmaceuticals, Inc., a Johnson & Johnson company. ACI-35.030 generated a rapid, robust and durable polyclonal response against pathological forms of Tau including phosphorylated Tau (pTau) and brain-derived Tau (enriched paired helical filament, ePHF). There were no clinically relevant safety or tolerability observations for either ACI-35.030 or JACI-35.054.

Dr. Andrea Pfeifer, CEO of AC Immune SA, commented: "These data show that ACI-35.030 (JNJ-2056) was well tolerated at all tested doses and induced a rapid and sustained response against pathological Tau, while requiring less frequent dosing to maintain titers as compared to monoclonal antibodies. Safety and rapid, durable responses are key advantages of active immunotherapies, which make them particularly well suited to the long-term treatment needed to achieve precision prevention. ACI-35.030 is continuing to progress according to plan in the Phase 2b ReTain trial, being conducted by our development partner Johnson & Johnson."

Dr. Pfeifer added: "This study also demonstrated the ability of AC Immune's SupraAntigen® platform to generate active immunotherapies that are highly differentiated from other approaches even when the immunogen is identical. We are encouraged by the excellent performance of the SupraAntigen® technology as this also powers our ACI-24.060 anti-Abeta active immunotherapy program in Phase 2 development where further results are expected in H1 next year."

The publication is entitled "Safety and immunogenicity of two Tau-targeting active immunotherapies, ACI-35.030 and JACI-35.054, in participants with early Alzheimer's disease: a Phase 1b/2a, multicentre, double-blind, randomised, placebo-controlled study" and reports the following key findings from the completed trial (NCT04445831):

- ACI-35.030 is based on AC Immune's proprietary SupraAntigen® technology which anchors the pTau peptide in a liposome and also incorporates non-Tau T-cell epitopes and adjuvants. JACI-35.054 covalently linked the immunogen to the carrier protein CRM197 and was mixed with adjuvants. Both active immunotherapies used the same target pTau peptide sequence.
- ACI-35.030 required only one injection to induce anti-pTau Immunoglobulin G (IgG) antibody titers in all participants and consistently boosted levels with subsequent immunizations. JACI-35.054 raised a more heterogenous anti-pTau IgG antibody response and required multiple administrations to reach consistent titers.
- All participants across all dose-levels were considered anti-pTau IgG responders at 2 weeks post treatment with ACI-35.030. In the two high-dose cohorts, response rates remained between 94% and 100% until week 74. Most participants generated an anti-ePHF antibody response after the first administration and antibody levels further increased with additional immunizations.
- Antibody titers against unphosphorylated (normal) Tau declined and were not boosted with subsequent administrations of ACI-35.030, demonstrating specific targeting of the pathological Tau species. In contrast, JACI-35.054 induced antibody titers against normal Tau after the second treatment and these increased with subsequent administrations.
- An exploratory post-hoc analysis showed that at multiple time points for the two highest doses ACI-35.030, treatment resulted in a significant ($p<0.05$) change from baseline of plasma pTau and brain-derived Tau plasma levels compared to the pooled placebo group.

Based on the results from this trial, ACI-35.030 was selected for further clinical testing and is now being investigated in the ongoing Phase 2b ReTain trial (NCT06544616). It is the first active immunotherapy targeting Tau to be investigated in approximately 500 participants with preclinical AD.

Reference

Sol O. et al, Safety and immunogenicity of two Tau-targeting active immunotherapies, ACI-35.030 and JACI-35.054, in participants with early Alzheimer's disease: a Phase 1b/2a, multicentre, double-blind, randomised, placebo-controlled study, eBioMedicine, 2025; 120: 105940.

About ACI-35.030 (JNJ-64042056)

ACI-35.030 (JNJ-64042056) is an investigational active immunotherapy designed using AC Immune's SupraAntigen® platform. Its liposomal formulation incorporates a conformationally-constrained, membrane bound target peptide antigen, phosphorylated Tau (pTau), in addition to adjuvants and non-Tau T-helper peptides. Immunization with ACI-35.030 has been shown in a recent Phase 1b/2a clinical trial to rapidly elicit antibodies after the first injection against extracellular pathological pTau in 100% of patients with early Alzheimer's disease. Importantly, the antibody response was sustained, boostable, and focused on pathological Tau aggregates, including neurotoxic enriched paired helical filaments (ePHF). Antibodies against non-phosphorylated Tau diminished over time. To date, no safety or tolerability issues have been observed following ACI-35.030 immunization.

About the Phase 2b ReTain Study (ClinicalTrials.gov Identifier: NCT06544616)

The Phase 2b ReTain trial is a potentially registration-enabling randomized, multicenter, double-blind, placebo-controlled clinical study in participants with preclinical AD to assess the clinical effect of active immunization with JNJ-64042056 (JNJ-2056). It is designed to test the hypothesis that JNJ-2056 has a disease-modifying effect that can delay or prevent the onset of cognitive impairment or other clinical symptoms in individuals with preclinical AD through inhibition of seeding and spreading of pathological Tau.

The study will include approximately 500 participants with preclinical AD (cognitively normal, Tau positive), who will be randomized in a 1:1 ratio to a single dose level of JNJ-2056 or placebo and administered as intramuscular injections for a maximum of 4 years. It is currently being conducted at more than 40 clinical trial sites in the U.S., Japan, UK and Australia, and more are expected to open shortly.

The primary endpoint will measure cognitive decline as assessed by the Preclinical AD Cognitive Composite 5 (PACC-5) score. The key secondary efficacy endpoint will assess the effect of JNJ-2056 on the propagation and/or accumulation of Tau pathology compared with placebo, as measured by Tau PET imaging.

The ReTain trial is fully funded and conducted by Janssen Pharmaceuticals, Inc., a Johnson & Johnson company, pursuant to a global license, development and commercialization agreement with AC Immune.

About AC Immune SA

AC Immune SA is a clinical-stage biopharmaceutical company and a global leader in precision prevention 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 a range of therapeutic and diagnostic programs, including candidates in Phase 2 and Phase 3 development. AC Immune has a strong track record of securing strategic partnerships with leading global pharmaceutical companies, resulting in substantial non-dilutive funding to advance its proprietary programs and >$4.5 billion in potential milestone payments plus royalties.

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

The information on our website and any other websites referenced herein is expressly not incorporated by reference into, and does not constitute a part of, this press release.

For further information, please contact:

SVP, Investor Relations & Corporate Communications

Gary Waanders, Ph.D., MBA
AC Immune
Phone: +41 21 345 91 91
Email: gary.waanders@acimmune.com

International Media

Chris Maggos
Cohesion Bureau
Phone: +41 79 367 6254
Email: chris.maggos@cohesionbureau.com

Forward looking statements

This press release 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. 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.

Attachment

- 20250924__ACIU ACI-35.030 eBioMedicine_FINAL

Source: AC Immune SA