

AC Immune Provides Update on Alzheimer's Disease Vaccine Candidates Targeting Pathological Amyloid-Beta

Optimized vaccine candidate generates enhanced polyclonal antibody response against pyroglutamate Abeta in non-human primates

Phase 2 interim analysis of ACI-24 confirms good safety and tolerability profile in people with mild Alzheimer's disease

Lausanne, Switzerland, June 2, 2021 – AC Immune SA (NASDAQ: ACIU), a clinical-stage biopharmaceutical company pioneering precision medicine for neurodegenerative diseases, today provided key clinical and preclinical updates for its SupraAntigen®-derived liposomal vaccine candidates, which are designed to convey active, long-lasting immunization against pathological forms of amyloid-beta (Abeta). AC Immune is completing a Phase 2 study of its first clinical candidate, ACI-24, in people with mild Alzheimer's disease (AD), and is also advancing an optimized ACI-24 formulation, which demonstrates enhanced and sustained immunogenicity in non-human primate studies, particularly against key pathological forms of Abeta such as oligomeric and pyroglutamate Abeta.

Pyroglutamate Abeta (pyroGlu-Abeta) is a highly neurotoxic form of Abeta that is N-terminally truncated and post-translationally modified to form pyroglutamate. Extracellular pyroGlu-Abeta is an important target for immunotherapy, as the peptide's altered biochemical properties make it more prone to aggregate compared to full-length Abeta, and it is a major component of Abeta plaques. Passive immunization with a monoclonal antibody specific for pyroglutamate Abeta demonstrated encouraging clinical results in a [recently published Phase 2 clinical study](#).

In non-human primates, vaccination with the optimized ACI-24 vaccine generated a [strong, conformation-specific antibody response against oligomeric and pyroGlu-Abeta](#). A robust boosting effect was also observed, the magnitude of which was substantially greater against pyroGlu-Abeta compared to full-length Abeta (approx. 8-fold vs 4-fold increase, respectively, between the 3rd and 5th injections). Epitope mapping studies using sera from immunized cynomolgus monkeys showed the strongest signals for sites binding to peptides covering N-terminal regions of Abeta located just beyond where cleavage occurs to form pyroGlu-Abeta (amino acids 3-10, 4-11, 5-12). This further supports the strong response observed against this key pathological variant.

Prof. Andrea Pfeifer, CEO of AC Immune SA, commented: “We believe the optimized ACI-24 formulation represents a potential breakthrough in Abeta vaccination, as it elicits a strong immune response against oligomeric and truncated Abeta, the suggested key culprits in the Abeta pathway driving early Alzheimer's disease. These exciting preclinical results, combined with the encouraging clinical safety and efficacy we have demonstrated to date for our optimized pTau vaccine ACI-35.030 as well as our first anti-Abeta vaccine candidate ACI-24, highlight the strength and versatility of our SupraAntigen®-V platform for delivering safe and long-lasting active immunization against key proteinopathies in neurodegenerative diseases. We are planning to file an Investigational New Drug (IND) application for the optimized ACI-24 formulation by year-end, followed by an

accelerated clinical development in Down syndrome-related AD, with start of Phase 2 as early as 2022/23.”

In addition, AC Immune completed an 18-month interim assessment of safety and tolerability in the Phase 2 study evaluating ACI-24 in patients with mild AD. Confirming earlier interim results, there have been no safety concerns nor evidence for CNS inflammation or ARIA (amyloid-related imaging abnormalities) related to ACI-24 in any subject. AC Immune will complete the Phase 2 study with the 24-month analysis on the basis of currently enrolled patients.

About the SupraAntigen® platform

AC Immune’s clinically validated SupraAntigen® platform uses proprietary liposomes to rapidly generate novel vaccines (SupraAntigen®-V) for active immunization as well as best-in-class monoclonal antibodies (SupraAntigen®-A) for passive immunization against key neurodegenerative disease targets. Antibodies generated by the platform are highly specific for the pathological conformations of misfolded proteins and show good safety in AD patients and animals. The SupraAntigen® platform has successfully generated two vaccines and two monoclonal antibody candidates that have been validated in clinical studies and has led to multiple global partnerships with world-leading pharmaceutical companies. In addition to targeting Abeta and Tau, AC Immune has generated conformation-specific antibodies against emerging targets in neurodegenerative diseases including alpha-synuclein, TDP-43 and the NLRP3 inflammasome pathway.

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

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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. 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.