**PRESS RELEASE**

# AC Immune Provides Update on Alzheimer's Prevention Initiative Study Evaluating Crenezumab in Autosomal Dominant Alzheimer's Disease

*Crenezumab did not statistically significantly slow or prevent cognitive decline in people with a specific genetic mutation which causes early-onset Alzheimer's disease*

*Numerical differences favouring crenezumab over placebo were observed across the co-primary, multiple secondary and exploratory endpoints*

*Initial data will be presented at the Alzheimer's Association International Conference (AAIC) on August 2, 2022*

**Lausanne, Switzerland, June 16, 2022** – AC Immune SA (NASDAQ: ACIU), a clinical-stage biopharmaceutical company pioneering precision medicine for neurodegenerative diseases, today announced results from the Alzheimer's Prevention Initiative (API) Autosomal Dominant Alzheimer's Disease (ADAD) Colombia Trial. The study evaluated the potential of crenezumab, an investigational medicine, to slow or prevent Alzheimer's disease in cognitively unimpaired people who carry a specific genetic mutation which causes early-onset Alzheimer's disease.

Numerical differences favouring crenezumab over placebo were observed across the co-primary, multiple secondary and exploratory endpoints, though none were statistically significant. The co-primary endpoints assessed the rate of change in cognitive abilities or episodic memory function, measured by the API ADAD composite cognitive total score and the Free and Cued Selective Reminding Test (FCSRT) Cueing Index, respectively. Crenezumab was generally well tolerated during the study and no new safety issues were identified. Further analyses of data are ongoing. Initial data will be presented at the Alzheimer's Association International Conference (AAIC) on August 2, 2022.

**Dr. Andrea Pfeifer, CEO of AC Immune commented**: "While we are disappointed that the primary endpoints were not met, crenezumab's safety profile and the favorable numerical differences observed across primary, secondary and exploratory endpoints, warrant further analyses of the data."

"We are grateful to all those involved in this landmark study, which will undoubtedly increase the scientific community's understanding of pre-symptomatic Alzheimer's disease and prevention studies conducted in this population. We would like to especially recognize the trial participants and their families, whose courage continues to inspire us. We also thank our colleagues and partners

at the Banner Alzheimer's Institute (BAI), Grupo de Neurociencias de Antioquia (GNA), at the University of Antioquia in Colombia, Genentech, a member of the Roche Group, and the National Institute on Aging for their faultless commitment to the diligent execution of this nine-year study."

The trial enrolled 252 people who are members of the world's largest extended family with ADAD in Colombia. Two-thirds of participants carried the Presenilin 1 E280A mutation which typically causes cognitive impairment due to Alzheimer's disease around age 44. Participants were randomised to receive crenezumab or placebo over five to eight years. During the trial, the dose of crenezumab was increased as knowledge about potential treatment approaches for Alzheimer's disease evolved.

The study, which was supported by National Institute on Aging, generous philanthropic contributions to Banner Alzheimer's Foundation, and Roche, has generated a wealth of data that will advance the early detection, tracking and study of Alzheimer's disease and inform the design of future Alzheimer's prevention trials.

Crenezumab is an investigational treatment discovered by AC Immune SA and designed to neutralise a pathological species of the beta-amyloid protein called oligomers. It is developed by Genentech, a member of the Roche Group, under a license and collaboration agreement established in 2006.

**About the Alzheimer's Prevention Initiative and the API ADAD (Colombia) Trial**

The Alzheimer's Prevention Initiative (API) is an international collaborative formed in 2009 to launch a new era of Alzheimer's prevention research. Led by the Banner Alzheimer's Institute, the API conducts prevention trials in cognitively healthy people at increased risk for Alzheimer's disease. API continues to establish brain imaging, fluid biomarker and cognitive endpoints needed to rapidly test promising prevention therapies. It also leads participant recruitment registries to accelerate enrollment into Alzheimer's-focused studies. API is intended to provide the scientific means, accelerated approval pathway and enrollment resources needed to evaluate the range of promising Alzheimer's prevention therapies and find ones that work without losing another generation.

First proposed by investigators from BAI, the API ADAD trial (NCT01998841) was a prospective, randomised, double-blind, placebo-controlled, parallel-group label enabling Phase II study of the efficacy of crenezumab versus placebo in cognitively unimpaired individuals who have no clinical symptoms of Alzheimer's disease and carry the PSEN1 E280A autosomal dominant mutation. Participants who are mutation carriers were randomised in a 1:1 ratio to receive either crenezumab or placebo for at least 260 weeks. Crenezumab was initially administered subcutaneously 300 mg every two weeks. Dosing was amended in 2015 to 720 mg subcutaneously every two weeks and in 2019 the option to increase the dose to 60 mg/kg, delivered intravenously every four weeks, was offered to participants. A cohort of participants (non-mutation carriers) were also enrolled and dosed solely on placebo.

The trial, which was supported by National Institute on Aging (NIA) generous philanthropic contributions to Banner Alzheimer's Foundation and Roche, was the first NIH-supported prevention trial of an experimental prevention therapy in cognitively unimpaired persons at known risk for the disease.

For more information, go to https://alzheimerspreventioninitiative.com/.

**About Autosomal Dominant Alzheimer's Disease**

Autosomal dominant Alzheimer's Disease (ADAD; also known as familial AD or dominantly-inherited AD [DIAD]) is a rare, inherited form of Alzheimer's disease caused by single gene mutations in the *APP*, *PSEN1* or *PSEN2* genes. Less than 1% of all Alzheimer's cases worldwide are thought to be caused by genetic mutations. It usually has a much earlier onset than the more common sporadic Alzheimer's disease, with symptoms developing in people in their 30s to 60s. If an individual has one of these mutations they are nearly certain to develop Alzheimer's and there is a 50% chance they will pass it on to each of their children.

**About the PSEN1 E280A mutation and the Antioquia kindreds**

The *PSEN1 E280A* or 'Paisa' mutation virtually guarantees that carriers will develop Alzheimer's at the average age of 44 and dementia at the average age of 49. The Colombian *PSEN1 E280A* kindred are the world's largest extended family with ADAD, with ~6,000 family members and ~1,200 with the mutation.

The API ADAD trial was conducted in collaboration with neurologist Francisco Lopera and his team, Grupo de Neurociencias de Antioquia (GNA), at the University of Antioquia in Medellín, Colombia. Dr Lopera followed the kindred for three decades prior to the start of the trial and has established a close relationship with many members.

**About crenezumab**

Crenezumab is a humanised monoclonal antibody, an investigational treatment designed to slow Alzheimer's disease progression by neutralising neurotoxic beta-amyloid oligomers. It was designed by AC Immune to be a conformation-specific monoclonal antibody targeting multiple forms of misfolded Abeta. Crenezumab has an antibody backbone (IgG4) designed to minimise the inflammatory response in the brain, which may result in a lower risk of certain MRI (magnetic resonance imaging) abnormalities known as ARIA (Amyloid-Related Imaging Abnormalities).

**About AC Immune SA**

AC Immune SA is a 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, RU and SG. Morphomer® is a registered trademark of AC Immune SA in CN, CH, GB, JP, NO and RU.

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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.