AC Immune Initiates Phase 1 Clinical Trial of NLRP3 Inhibitor

- ACI-19764 is an orally available highly brain-penetrant small molecule NLRP3 inhibitor
- NLRP3 inhibitors are a major new class of compounds linked to a broad spectrum of inflammatory conditions including both metabolic and neurological diseases
- ACI-19764 is an important addition to AC Immune's growing small molecule pipeline
- Phase 1 results in healthy volunteers are expected in H2 2026

Lausanne, Switzerland, February 24, 2026 -- AC Immune SA (NASDAQ: ACIU), a clinical-stage biopharmaceutical company pioneering precision therapeutics for neurodegenerative diseases, today announced that the first participant has been dosed in a Phase 1 clinical trial of ACI-19764, an orally administered small molecule inhibitor of the NLRP3 inflammasome.

Targeting the NLRP3 inflammasome provides an opportunity to reduce the chronic inflammation thought to be associated with disease progression in multiple inflammatory disorders, metabolic diseases, and neurological diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and frontotemporal dementia.

Dr. Andrea Pfeifer, CEO of AC Immune SA, commented: "We are delighted to announce the dosing of the first participant in the Phase 1 trial in healthy volunteers of our lead NLRP3 inhibitor. This is another important milestone in demonstrating the power of AC Immune's small molecule discovery capabilities for targeting key pathways that contribute to neurodegeneration and other diseases. Robust preclinical data have shown that ACI-19764 has best-in-class potential based on its potency and PK profile, as well as its ability to reduce neuroinflammation and limit neurodegeneration *in vivo*. This suggests ACI-19764 could have a disease-modifying effect relevant to neurodegenerative diseases, and we are looking forward to studying it further in the clinical setting."

The Phase 1 trial will investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ACI-19764 in healthy volunteers. The study is divided into two parts. Part A will evaluate single ascending doses while Part B will examine multiple ascending doses. The trial is being conducted in Europe. Primary outcome measures include the safety and tolerability of ACI-19764, as well as its pharmacokinetics in plasma and cerebrospinal fluid. A secondary outcome measure will assess target engagement (inhibition of IL-1β) and exploratory endpoints will include the influence of ACI-19764 on fluid biomarkers of the immune system, among others. Initial data from the Phase 1 trial are expected in the second half of 2026.

ACI-19674 has demonstrated a highly competitive profile in extensive preclinical studies, with optimal brain penetrance in animal models, high potency and selectivity in assays including whole human blood and in several *in vivo* models, and an excellent safety and tolerability profile. In a mouse model of diet-induced obesity (DIO), ACI-19764 showed excellent weight control both alone and in

combination with semaglutide, as well as reductions in activation of both microglia and astrocytes.

These preclinical data position ACI-19764 competitively among the best-in-class NLRP3 inhibitors for CNS indications.

About ACI-19764

ACI-19764 is an orally available, highly brain penetrant, small molecule drug candidate which specifically inhibits the NLRP3 inflammasome. In preclinical studies it has been shown to be safe and well tolerated and has shown high potency as demonstrated by the downstream inhibition of IL-1β production *in vitro* by human macrophages and human whole blood with an IC_{50} in the range of 2-20.5nM. It has shown an excellent level of brain penetration with Kp,uu values in rat brain and dog CSF of 0.71 and 1, respectively. ACI-19764 statistically significantly inhibited neuroinflammation *in vivo* through reduced activation of Iba1+ microglial cells and GFAP+ astrocytes in preclinical models (including mouse models of Diet-Induced Obesity and chronic LPS-mediated CNS inflammation), demonstrating its strongly competitive profile and high potential for broad application in both metabolic and neurologic therapeutic areas.

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 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 CA, 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.

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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. 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.