PRESS RELEASE

First Characterization of a TDP-43 PET Tracer Published in *Nature Communications* Showing Potential of AC Immune's ACI-19626 in Precision Medicine

- Aggregated TDP-43 is a pathological hallmark of neurodegenerative diseases including ALS, FTD and LATE, and a co-pathology in Alzheimer's and Parkinson's diseases
- PET imaging of aggregated TDP-43 could facilitate precision medicine in these diseases, whose shared clinical features complicate differential diagnosis, potentially delaying therapy
- Based on specificity, sensitivity, and pharmacokinetic properties, ACI-19626 was advanced into a Phase 1 clinical study with initial readout expected in Q4 2025

Lausanne, Switzerland, October 24, 2025 -- AC Immune SA (NASDAQ: ACIU), a clinical-stage biopharmaceutical company pioneering precision therapeutics for neurodegenerative diseases, today announced the publication in Nature Communications of preclinical data on its first-in-class brain positron emission tomography (PET) tracers for imaging TDP-43 pathology. The selected candidate, ACI-19626, potentially enables a precision medicine approach to multiple neurodegenerative diseases that are currently difficult to diagnose and differentiate from each other.

TDP-43 is the main component in inclusions found in the brains of people with amyotrophic lateral sclerosis (ALS), frontotemporal degeneration (FTD) and limbic-predominant age-related TDP-43 encephalopathy (LATE), as well as a co-pathology in Alzheimer's disease (AD) and Parkinson's disease (PD). These conditions share many of the same clinical signs and symptoms, making differential diagnosis a difficult and lengthy process in the absence of reliable biomarkers. PET imaging of aggregated TDP-43 offers a new era for the development of disease-modifying therapies for TDP-43 proteinopathies, potentially revolutionizing both diagnosis and treatment.

The data showed that ACI-19626, a Morphomer®-based TDP-43 PET tracer, demonstrates high specificity and selectivity for the target, with rapid brain uptake and fast and complete washout, supporting the potential to detect TDP-43 pathology by PET in the brains of living patients.

Dr. Andrea Pfeifer, CEO of AC Immune SA, commented: "Accurate PET imaging of TDP-43 pathology could significantly improve the diagnosis of multiple neurodegenerative diseases, paving the way to precision prevention with the possibility of intervening before damage occurs. This important diagnostic tool also has tremendous potential to improve the design and interpretation of clinical trials by enabling patient stratification, optimizing the timing of therapeutic intervention, and facilitating evaluation of target engagement and pharmacodynamic effects. Based on its advantageous profile, we took ACI-19626 forward into Phase 1 development and are looking forward to initial readout from that trial in Q4 2025, as we continue to pioneer the precision prevention of neurodegenerative diseases."

Dr. Francesca Capotosti, VP Research of AC Immune added: "PET imaging biomarkers have been proven to be potential game changers in the field of neurodegenerative diseases, as seen with

amyloid PET in Alzheimer's disease. We strongly believe that the detection of TDP-43 pathology by PET could not only support earlier and more definitive diagnosis but also accelerate drug development and open new avenues for combination therapies." The paper in Nature Communications, entitled "Development of [18F]ACI-19626 as a first-in-class brain PET tracer for imaging TDP-43 pathology", reports the characterization of ACI-19626 with the preferred profile for the successful visualization of TDP-43 pathology in human brain by PET.

Nature Communications also published an accompanying commentary on the potential of TDP-43 PET ligands for biological diagnosis of TDP-43 proteinopathies.

Specifically, data on ACI-19626 in the paper showed:

- High affinity for pathological TDP-43 aggregates, but not physiological TDP-43
- Excellent selectivity for TDP-43 over common co-pathologies including Abeta, Tau and alpha-synuclein
- No off-target binding against a panel of more than 100 receptors, enzymes, ion channels and transporters
- A pharmacokinetic profile in non-human primates suitable for human brain PET imaging, with rapid brain uptake, homogenous distribution across different brain regions. and fast and complete washout in absence of the target, suggesting minimal background in healthy controls

Based on these data, ACI-19626 was selected for further evaluation and is now in an ongoing Phase 1 clinical trial for its promising potential to detect pathological TDP-43 in the brains of patients with TDP-43 proteinopathies compared to healthy volunteers.

Reference

Efthymia Vokali *et al*., Development of [18F]ACI-19626 as a first-in-class brain PET tracer for imaging TDP-43 pathology, Nature Communications, 2025 16:9358.

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.

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