

## **AC Immune to discontinue development of ACI-91 small molecule**

- **Phase II results do not demonstrate efficacy of ACI-91 in patients with advanced Alzheimer's disease**
- **ACI-91 drug in-licensed with different mode-of-action from in-house therapies under development**

**Lausanne, Switzerland, 31 January, 2013 – AC Immune SA today announced that it has stopped development of the small molecular entity ACI-91. This follows results of a Phase II trial in 63 patients with mild to moderate Alzheimer's disease.**

The Phase II clinical study was based on intriguing pre-clinical data which suggested that ACI-91 eliminates the Abeta peptide from the brain and improves cognition. Based on these results and the known peripheral effects outside the brain for short-term use of ACI-91, it was decided to conduct a limited Phase II study in Alzheimer's patients to evaluate the safety of long-term administration of the drug.

Although the overall tolerability of ACI-91 was rated as good in most patients, it was associated with a general, but statistically not significant, decrease of measures of cognitive performance and clinical function. There were also no consistent effects on biomarkers of the disease.

It is presumed that the negative effect on cognition is likely to be related to ACI-91's unexpected central anticholinergic properties, to which the study population may have been relatively susceptible. Consequently any potential positive peripheral effect of ACI-91, as shown in the pre-clinical studies, was not strong enough to outweigh these anticholinergic properties.

**Prof. Andrea Pfeifer, CEO of AC Immune** said: "We are disappointed at these Phase II clinical results, particularly in view of the convincing pre-clinical data and ACI-91's long-standing safety record in other indications. As a small biotechnology company we have to make judicious use of our scientific and financial resources, and so will now focus on our own home-grown molecules with different modes-of-action from ACI-91. We remain convinced that our strategy to target both the Abeta and Tau proteins will lead to a breakthrough therapy for Alzheimer's disease."

AC Immune has one of the industry's broadest pipelines focused on Alzheimer's disease, with two therapies in clinical trials and a rich portfolio of pre-clinical compounds. The anti-Abeta antibody (crenezumab) for passive immunization is partnered with Genentech and is in Phase II; it was selected in May 2012 by the Alzheimer's Prevention Initiative as the preferred therapy for the world's first preventative trial in patients. AC Immune's vaccine ACI-24 is being developed in-house and is in a Phase I/IIa trial.

### **About ACI-91**

ACI-91 (pirenzepine) was in-licensed. It is approved in a number of European countries for the treatment of stomach and intestinal ulcers.

ACI-91 is a muscarinic acetylcholine inhibitor which indirectly down-regulates the expression and activity of the beta-secretase BACE-1 in pre-clinical studies. BACE-1 is regarded as a key target for therapies treating Alzheimer's disease. Evidence suggests that inhibiting BACE-1 decreases the production of the Abeta peptide and therefore may reduce amyloid plaque formation which is associated with the disease.

### **About the Phase II trial**

The primary objective was to assess safety and tolerability including examination for potential negative effects on cognition during 12 months treatment with ACI-91 compared to placebo.

Secondary objectives included assessing the biochemical effects of ACI-91 on biomarkers of Alzheimer's disease such as BACE-1, Abeta and total Tau and to explore the effects of ACI-91 on cognition, global function, activities of daily living and neuropsychiatric symptoms.

The Phase II trial enrolled 63 patients with mild to moderate Alzheimer's disease in 16 centers across Germany and Austria. They were treated with oral doses of 75 mg of ACI-91 or placebo twice a day (total daily dose 150 mg) for 12 months, on top of standard therapy of an acetylcholinesterase inhibitor.

### **About Alzheimer's Disease**

Alzheimer's is the most common form of dementia. It is degenerative, irreversible and terminal. The memory and thinking of the patients is progressively destroyed. Besides the personal aspect there is a huge social and economic impact. Alzheimer's disease is recognized as a significant health crisis of the 21st century with currently more than 36 million patients worldwide. This number is expected to double in the next 20 years and to triple to more than 116 million by 2050. In 2010 global worldwide costs were estimated to be USD 604 billion and were exceeding 1% of the global domestic product (Reference: World Alzheimer Report 2011, Alzheimer's Disease International).

Scientists don't yet fully understand what causes Alzheimer's disease, but it has become increasingly clear that it develops because of a complex series of events that take place in the brain over a long period of time. Two proteins – Tau and Abeta - are perceived as the major causes of neurodegeneration: tangles and other abnormal forms of Tau protein accumulate inside the brain cells, while plaques and oligomers formed by Abeta occur outside the brain cells of people with Alzheimer's disease.

### **About AC Immune SA**

AC Immune SA is a Swiss-based biopharmaceutical company and a leader in Alzheimer's disease drug development. AC Immune develops innovative therapeutics with "best in class" potential against Alzheimer's disease and other conformational diseases along three axes: vaccines, antibodies and small molecules. The anti-Abeta antibody (crenezumab) for passive immunization is partnered with Genentech and is in

Phase II development; it has been selected for the first groundbreaking Alzheimer's prevention trial. The company pursues the Phase I/IIa in clinical development of the vaccine ACI-24. These two clinical programs are focused on Alzheimer's disease, and are backed by a rich portfolio of preclinical compounds. A preclinical stage anti-Tau antibody is also partnered with Genentech. The therapeutic molecules are leveraged for Alzheimer's disease diagnostic and other central nervous system and non-CNS diseases, such as Glaucoma. Since its foundation in 2003, AC Immune has raised CHF 64 million from private investors.

**For further information, please contact:**

Prof. Andrea Pfeifer  
Chief Executive Officer  
Phone: +41-21-693 91 21  
E-mail: [andrea.pfeifer@acimmune.com](mailto:andrea.pfeifer@acimmune.com)  
[www.acimmune.com](http://www.acimmune.com)

Eva Schier  
Corporate Communications Manager  
Phone: +41-21-693 91 34  
E-mail: [eva.schier@acimmune.com](mailto:eva.schier@acimmune.com)  
[www.acimmune.com](http://www.acimmune.com)

Nick Miles  
Senior Consultant  
Cabinet Privé de Conseils s.a.  
Phone : +41 22 321 45 40  
Mobile : +41 79 678 76 26  
E-mail : [miles@cpc-pr.com](mailto:miles@cpc-pr.com)

In the US  
Ted Agne  
The Communications Strategy Group Inc.  
Phone: +1 781 631 3117  
E-mail: [edagne@comstratgroup.com](mailto:edagne@comstratgroup.com)