INTERVIEW

“We will find a cure for Alzheimer’s”

AC Immune could become the first biopharma company to see a treatment for Alzheimer’s disease entering the market. We meet CEO Andrea Pfeifer at the company’s headquarters in Lausanne.

BY BERTRAND BEAUTÉ / PHOTOS: NICOLAS RIGHETTI

Will a small Vaud-based company succeed where pharma giants have failed for years? In June 2018, following a series of inconclusive clinical trials, British laboratory AstraZeneca announced that it was abandoning its most advanced Alzheimer’s treatment. Prior to this, American giants Merck and Eli Lilly experienced similar disappointment. Since then, AC Immune has found itself in an excellent position to become the first biopharma company – together with its partner Roche/Genentech – to see a treatment for this disease, that diminishes cognitive function, entering the market. “I have every faith,” affirms Professor Andrea Pfeifer, founder and director of the company, which is based on the École Polytechnique Fédérale de Lausanne (EPFL) campus. Find out more in this interview. ▷

PORTRAIT

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Developed in AC Immune’s laboratory, the Crenezumab antibody seeks to cure patients with Alzheimer’s disease by activating their immune system.

AC IMMUNE IN NUMBERS

10
The number of molecules being developed in the AC Immune laboratory.

90
The number of employees working for the company.

148,000
The number of people with dementia in Switzerland, of whom a majority (70%) have Alzheimer’s.

7
In billion of Swiss francs, the social costs generated each year by dementia in Switzerland.

There is currently no cure for Alzheimer's disease. When will the first one appear?

The number of people affected by this terrible disease is colossal. According to the World Health Organization (WHO), 50 million people suffer from Alzheimer's around the world and this figure is set to rise to 152 million by 2050 due to ageing populations. It is therefore vital that a cure be found. Current treatments only lessen symptoms – they don't stop the disease progressing. But I'm convinced we'll get there soon.

For example, the American laboratory Biogen has developed a promising molecule called Aducanumab. Meanwhile, Roche is conducting two phase III clinical trials of our monoclonal antibody, Crenezumab. Results are expected in 2020. This is the final stage before applying for a marketing authorisation. If the trial results are positive, which I hope they will be, the product should be on the market soon thereafter. We could then become the first company with our partner Roche offering a cure for Alzheimer's disease.

Why would AC Immune succeed where pharmaceutical giants have failed?

We have made the right decisions, and probably had our fair share of luck too. For example, many years ago, some pharmaceutical companies placed a lot of hope in drug candidates called BACE, targeting the beta-amyloid protein found in Alzheimer's patients. We decided not to partake in these programmes as we weren't sure it was the right approach. It could have been a mistake, but we turned out to be right: these molecules cause too many undesirable side effects to be placed on the market, and so they were abandoned. This decision made by scientists a few years ago explains why we are still in the running today while other pharma companies had to give up on these programmes.

What approach have you decided to take?

We decided to go down the immunotherapy route with our most advanced product, Crenezumab. Alzheimer's disease is characterised by a build-up of amyloid plaques in the brain, and the so called oligomers or oligos, which are very toxic. They damage and kill brain cells, leading to well-known symptoms such as gradual memory loss. Crenezumab is a monoclonal antibody which binds specifically to these oligos, thus allowing the immune system to destroy them. A study conducted on 98 people with Alzheimer's disease, the results of which were revealed in July 2018, showed significant oligo reduction in the brains of patients treated with Crenezumab. This is a world first – no drug has ever had such a result. So, it's very promising. Especially given that our antibody causes very few side effects thanks to its highly specific nature. In particular, it doesn't trigger any inflammation, despite the immune response it generates.

Known for its drug candidates, AC Immune also works on developing diagnostic tools for Alzheimer's and Parkinson's diseases.

THE WOMAN WHO IS WAGING WAR ON CHRONIC DISEASES

Andrea Pfeifer has been fighting illness since a very young age. She was just 11 when she learned her mother had a chronic disease. Greatly affected by the news, this young girl, born in Munich in 1957, decided she would study medicine. She eventually decided on pharmacy. After obtaining a PhD in toxicology from Julius-Maximilians-Universität (JMU) in Germany, she worked at the National Cancer Institute in Bethesda, in the US. But disease caught up with her. "I came back to Europe to support my dying father," she says. Pfeifer then joined Nestlé, where she rose to the position of research director, with 600 people under her command. She left the Swiss giant in 2002 to found AC Immune. "I have always been driven by a desire to find solutions to chronic illnesses," she says. In fact, Pfeifer was already doing this in the US, where she worked on cancer treatments, and at Nestlé, where she helped develop health products, such as the LC1 yoghurt that enhances the immune system.

"A vaccine is the is the ultimate goal"

We are now hoping that the two clinical trials currently being conducted with 1,500 patients will demonstrate maximum clinical effectiveness – i.e. an improvement in patient condition.

But you are still exploring other ways to fight the disease. Why?

It's a matter of strategy: it's less risky and more beneficial for us to work on several projects at once. As such, we are developing small molecules, called Morphomer Tau, which enter neurons and act on diseased proteins. We are not as far along in this area compared to our immunotherapy treatment – the results of our phase II clinical trial should be revealed in 2019. However, should our leading treatment not succeed, we also have this project and a wealth of other clinical and pre-clinical programmes.

Investors should therefore realise that our value is not dependent on Crenezumab's phase III results alone.

We have many drug candidates in the pipeline whose value is substantial.

Currently, when patients are diagnosed, they already have some memory loss and the disease is at an advanced stage. Is this not a problem?

Indeed, it has now been established that the disease starts to silently attack the brain 10 or so years before the onset of symptoms. This means that by the time a patient is diagnosed, their brain has already suffered damage over a long period.

And that's the objective of the work you are conducting in Colombia...

Yes. As everyone knows, in our part of the world there is a link between Alzheimer's and ageing. At 60, people have a 10% chance of developing this neurological disease. At 80, this increases dramatically to 30%. However, in a region in north-west Colombia, people as young as 30–50 years old are developing the disease due to a certain genetic mutation. Members of this community have a 50% chance of developing the disease at birth.

"We have become a model of success for many Swiss start-ups"

Furthermore, once the disease reaches a certain stage of severity, when 70% of brain cells have been permanently destroyed for example, treatment becomes futile. It is therefore vital that an early diagnosis be made. Current cerebral imaging techniques make this possible, but they are expensive. Other techniques are therefore being developed. For example, Roche has been granted approval for an early testing technique based on assaying biomarkers in the cerebrospinal fluid (CSF). It's a tremendous breakthrough.
It's my belief that, one day, when you go to your doctor at age 50 or 60 to get your cholesterol or blood sugar levels tested, you'll also be able to screen for Alzheimer's disease and other dementia with a simple blood test. This would make it possible to begin treating patients right from the onset of symptoms, or even before that, as a preventative measure for people particularly at risk.

This very high probability therefore justifies developing a preventative treatment for Alzheimer's. Since 2015, we have been testing Crenezumab on 300 asymptomatic volunteers of which 200 are with the genetic mutation. We expect to have the first results in 2020. If they are positive, that is to say if fewer people develop the disease, it would be excellent news not just for this population but for others too. It would pave the way for a preventative treatment for all risk profiles.

You are also developing vaccines against Alzheimer's. How do these complement your treatments?

A vaccine is the ultimate goal. Alzheimer's is a chronic disease, meaning once a drug becomes available, patients have to take it for the rest of their lives. However, given the high number of sufferers around the world, this would be very costly for health systems. A vaccine would solve this problem by protecting people before the disease develops. So, we have begun phase II clinical trials for two vaccine candidates.

You are also developing treatments for Parkinson's disease, glaucoma and Down's syndrome. Is this not a bit too ambitious for a company with only ninety or so employees?

No. All the diseases we focus on are related to the same biological processes. We might seem to have a lot of projects in the pipeline, but they are based on the same principles, allowing us to use the same technological platforms, which are based on antigen detection.

ANALYST ADVICE

ALL OR NOTHING

If an effective treatment against Alzheimer's were to come on the market, it would be a sure-fire hit and generate more than a billion dollars per year. In other words, Lausanne company AC Immune is potentially sitting on a gold mine, provided the clinical trials it is currently conducting prove successful. Many analysts recommend buying AC Immune for its diverse pipeline of potential treatments against Alzheimer's, one of the most expensive diseases in the world, for which there is currently no cure. Nevertheless, it is still a risky investment. Should the phase III clinical trials of its most advanced molecule, Crenezumab, fail, the value of AC Immune could plummet. But for now, the interim results are positive.

The AC Immune laboratory, located at the Innovation Park on the École Polytechnique Fédérale de Lausanne campus.

In 2016, you listed AC Immune on the Nasdaq. Why did you not list the company in Switzerland?

Being a Swiss company, it was a difficult decision, but the number of investors, the volume of transactions and the capital available are all much greater in the US than in Europe. Being based in Switzerland puts us at a bit of a disadvantage in terms of capital. We have to do more to get the same recognition as an American company. With that said, we don't intend to move. People might not realise it, but we have an exceptional environment here in Switzerland. Research in the field of neuroscience is particularly good here and we have an excellent talent pool to choose from.

AC Immune issued new shares in July this year. What will the funds be used for?

We issued three new share subscription offerings, at the usual price of $11.75 per share, which has allowed us to raise a total of $117.5 million. These funds will allow us to continue our clinical trials. To be more specific, we have enough capital to continue until the third quarter of 2021. In other words, we are on a strong footing financially. Ultimately, our goal is to become a business that will live off the sale of its products. But for now, we are in the research stage. Our cash comes from investors and partnerships with pharmaceutical companies, such as Roche/Genentech and Biogen with whom we are developing Crenezumab and working on diagnostics for Parkinson's disease.

You founded AC Immune in 2003. What is your view of the journey so far?

I am very proud to have led our company to where it is today. AC Immune has become a model of success for many Swiss start-ups. The fact that my work helps a cause that is dear to me, and could be useful to society, makes me even happier. ◢