



aptaTargets starts Phase Ib / IIa clinical trial with ApTOLL in stroke patients

October 2020. The Spanish Agency for Medicines and Health Products, AEMPS, has authorized the biotechnology company aptaTargets to start the APRIL study, a Phase Ib / IIa clinical trial with ApTOLL, a new and powerful immunomodulator and anti-inflammatory, capable of reducing brain damage in stroke patients. This is the first study in acute stroke patients after the results observed in animal models of cerebral ischemia confirmed a protective effect, which translated into smaller infarcts and less disability.

In the first phase of the trial (Ib), 32 patients will be recruited in five hospitals in Spain: Vall d'Hebron and Bellvitge (Barcelona), Can Ruti / Germans Trias i Pujol (Badalona), La Princesa (Madrid) and Virgen del Rocío (Seville). This part is expected to be completed in the first quarter of 2021, followed by Phase IIa, which will extend the study to a greater number of patients (up to 150), expanding up to 20 more centres, in Spain, France, Portugal and Germany.

In March 2020, Phase Ia was completed at La Princesa hospital. In this study, increasing doses of the drug were administered to 46 healthy volunteers and no relevant adverse effects were detected, confirming the excellent safety profile observed in preclinical studies.

ApTOLL is the only drug in development for the treatment of stroke that blocks the activation of TLR4, a receptor on the membrane of immune system cells, such as microglia, neutrophils, macrophages, and lymphocytes. Activation of TLR4 initiates the inflammatory cascade that leads to the death of neurons and the consequent worsening of brain injuries. Therefore, by acting as a TLR4 antagonist, ApTOLL regulates the unwanted immune response, preventing the inflammatory cascade that occurs in the first hours after the onset of stroke.

To date, no neuroprotectant has shown any efficacy in clinical trials in ischemic stroke patients. Current treatments focus on the recanalization of occluded arteries, via the administration of thrombolytic drugs (which dissolve the thrombus) or, more recently, by catheter removal of the thrombus (endovascular therapy or mechanical thrombectomy).

Administered after stroke and combined with endovascular treatment, ApTOLL may provide important benefits for patients by slowing the growth of the brain lesion even before recanalization of the affected artery achieved. In this way, the chances of neurological recovery increase, which will directly affect the patient's quality of life. "Our treatment is a neuroprotective molecule that reduces inflammation in the acute phase of stroke. We intend to combine this neuroprotective effect with mechanical thrombectomy, a combination that is expected to generate synergistic and positive effects in patients", explains Dr. Marc Ribó, Medical Director of aptaTargets and coordinator of the APRIL study. "In this first study, we target patients with severe strokes in whom a greater benefit is expected, but we are already planning

new trials to assess the effect of Aptoll in patients with lower stroke severity or even with cerebral haemorrhage, where inflammation also causes significant damage"

About stroke

Stroke is more a disabling than a fatal disease , being considered the leading cause of disability in adults, the second cause of death and the second cause of dementia after Alzheimer's disease, as well as the most frequent cause of Admission to neurology services and extension of hospital stay, according to *The Burden of Stroke in Europe*. The social and health consequences that it entails make it essential to rapidly develop new therapeutic strategies to slow down the evolution of the disease and to improve long-term functionality of patients.

Stroke has a high incidence, estimating an average of 200-250 cases per 100,000 inhabitants per year. In Europe, 650,000 people die every year from this disease, 40,000 in Spain where 120,000 new cases are detected annually, according to the Iberictus study and the Spanish Ictus Atlas. In Europe, it is the second leading cause of mortality after ischemic heart disease and, according to data from the Stroke Observatory and the World Health Organization, it entails annual costs of 27,000 million euros.

Ischemic-type stroke is the most common in approximately 86% of cases (vs.haemorrhagic stroke, which amounts to 14% of cases).

Other indications

In addition to neuroprotection in stroke patients, ApTOLL has also shown a significant protective effect in preclinical models of other therapeutic indications, including haemorrhagic stroke, myocardial infarction and multiple sclerosis. "Recently, a study has been published in which the inhibition of the TLR4 receptor with ApTOLL, in a model of myocardial infarction in pigs, a significant functional improvement is observed", comments Dr. Macarena Hernández, Scientific Director of aptaTargets.

About aptaTargets

Founded in 2014 by David Segarra and Maria Eugenia Zarabozo, aptaTargets span-out from Aptus Biotech, an aptamer technology platform. AptaTargets started a drug development program, in collaboration with the Complutense University and the Ramón y Cajal University Hospital. In 2017, Caixa Capital Risc and Inveready Asset Management, venture capital funds specialized in biotechnology, completed the first financing round for the company (2.7 million euros).

In June 2019, aptaTargets started clinical trials, a First-in-Human study in healthy volunteers. that was successfully completed in March 2020. ApTOLL is the first aptamer (single-stranded DNA molecule) targeting TLR4, a receptor that triggers the immune response in human subjects in the first steps of the inflammatory pathway after stroke, and in other pathologies.

The company has just closed the second round of financing, with the participation of Inveready and the CDTI, through its INNVIERTE program, which will allow it to mobilise up to 5 million

euros between 2020 and 2022. With these funds, aptaTargets aims to complete a clinical proof-of-concept in acute ischemic stroke patients and close a licensing agreement.

For more information:

AptaTargets Communications Department

comunicacion@aptatargets.com

Phone: +34 670419322

<https://aptatargets.com/>

<https://www.linkedin.com/company/aptatargets/>