



Effimune

Effimune and In Cell Art collaborate to develop a novel therapeutic approach in immunology

The two biotechnology companies in Nantes develop a novel approach aiming at the production of therapeutic antibodies directly by the patient

Nantes, 11th February 2016 ó Effimune and In Cell Art announce today their collaboration to launch the öEfficaceö project. This project aims to develop an innovative cancer immunotherapy strategy combining a novel therapeutic target and a transfer approach based on the synthetic intracellular delivery of mRNA (messenger Ribonucleic Acid) encoding validated monoclonal antibodies. This new approach consists of producing therapeutic antibodies from the patient's body rather than those produced in bioreactors (classical approach).

This 12-month project will allow to demonstrate preclinical concept and to initiate future clinical studies. The efficacy of this antibody production approach using Nanotaxi® will be compared to the classical approach in relevant models of cancer.

Each startup receives grant coming from the funds öPays de la Loire Territoires d'Innovationö - Future Investment Program (FTI-PIA), financed equally by the Government and by the Region öPays de la Loireö and implemented by Bpifrance. The Region öPays de la Loireö is one of the four regions in France to experiment this partnership strongly supporting investment in SMEs' R&D.

öThis ambitious project was labelled by the cluster Atlanpole Biotherapiesö, explains its General delegate, Jean-François Balducchi, who points out that öit is perfectly in line with two thematic priorities of the cluster : "Immunobiothérapies" and "innovative technologies for biologics" and with the Pays de la Loire regional pattern of research and innovation. We are delighted to get two innovative companies from Nantes and members of Atlanpole Biotherapy cluster collaborating together. Both companies have a recognized and complementary expertise, Effimune in the field of immune regulation for cancer and In-Cell-Art in the expertise of new generations of vaccines and biotherapeutics using its technology Nanotaxi ®.ö

The objective is to produce antibodies directly by the body using the technology of öNanotaxi®ö developed by In Cell Art. This technology is an effective and credible alternative to bioreactors for

the production of therapeutic antibodies. Once the therapeutic antibodies are selected, the RNA sequences of these antibodies are formulated with Nanotaxi® and used to produce them directly by the patient in order to obtain the desired pharmacological activities.

Enabling the body to produce their own therapeutic antibodies in the body has a double advantage:

- To improve the potential efficacy of the treatments in oncology reducing significantly the risk of intolerance since the body will produce the antibodies/medicines in the same way as their own antibodies.
- To achieve substantial economy of scale in terms of processes, number of injections and costs of production with a positive impact on the expenses of public health.

Bernard Vanhove, Effimune CEO is pleased to say *“The interest for Effimune is to diversify our products and to have eventually new antibodies products to inject”* and specifies *“This novel therapeutic antibodies approach marks a turning point. The mRNA will be the product to inject into the patient, which will reduce the costs of production and could be more efficient.*

“InCellArt unlocks the promise of nucleic acids using Nanotaxi® for the development of vaccines and biotherapeutics to treat acquired or inherited diseases” says Bruno Pitard CEO and CSO of In Cell Art who explains *“We are delighted to use in this project our Nanotaxi®/mRNA technology to produce antibodies involved in the control of immune reaction against tumor cells and also to evaluate its synergistic effects with In-Cell-Art's Nanotaxi® formulated DNA vaccine (HepaVacö) to treat hepatocellular carcinoma which is currently under regulatory preclinical and clinical development”*.

About Effimune

Located in Nantes, France, Effimune is a Biotech company specialized in Immune Regulation for applications in transplantation, autoimmunity and cancer immunotherapy. The originality of Effimune's therapeutic strategy, compared to conventional immunosuppression, is the modification in the balance between effector and regulatory immune cells. The biological drugs Effimune develops, such as monoclonal antibodies, are aimed at restoring the natural balance of these cells by targeting the molecular checkpoint.

The expertise of the company lies in its ability to identify new therapeutic targets and to develop effective biomolecules for the pharmaceutical industry by guaranteeing the manufacture of pilot and clinical batches and by validating preclinical and clinical proofs of concept.

Effimune is a spin-off of the Nantes Institute of Transplantation Urology Nephrology-(ITUN), created in December 2007. Since then, Effimune is an active member of the cluster, Atlanpole Biotherapy. After chairing the board of the pole, Maryvonne Hiance, Effimune Chairman, became vice president of the "Immunobiothérapies" research focus.

About In Cell Art

In Cell Art (ICA), based in Nantes (France) is a biopharmaceutical company specializing in the preclinical and pharmaceutical development of nanocarriers named Nanotaxi® for macromolecular drugs. Its founder and research team, which includes a Nobel Laureate, have designed new classes of vectors that are organized on a nanometric scale, which enables them to cross the cell barrier efficiently and safely. In-Cell-Art offers a range of reagents and biotechnology development services:

1. ICANTibodies

In the absence of recombinant antigen, ICANTibodies allows, from an in silico DNA antigenic sequence, the production of the most ambitious functional antibodies against any natively expressed nuclear, cytoplasmic, secreted or membrane proteins. ICANTibodies has allowed, in less than 3 years, the production of more than 300 different functional antibodies. In-Cell-Art has worked with a number of pharmaceutical firms (Sanofi, GlaxoSmithKline, Geneuro etc.) and public research institutions and universities (Institut Cochin, Cancer Research UK, Institute of Neurology UK etc).

2. ICA Nanotaxi®

- DNA Vaccine

ICA614 Nanotaxi®, an innovative DNA synthetic formulation, offers unique efficient and industrial features such as the dramatic enhancement of the immunogenicity of plasmid DNA-encoding tumours or pathogen-derived antigens, a reduction in the dose of plasmid DNA, as well as an excellent safety profile. ICA614 Nanotaxi® represents a crucial step in DNA vaccine development, and is currently being tested by major vaccine companies (Sanofi-Pasteur, Merial etc.).

- mRNA Vaccine

Some other ICA Nanotaxi® are also being assessed in \$33.1 million RN-ARMORVAX consortium, co-funded by US Defense Advanced Research Projects Agency (DARPA). The consortium would validate the new application of ICA Nanotaxi® for mRNA-based vaccines for infectious diseases in collaboration with CureVac and Sanofi-Pasteur.

- mRNA Replacement Therapy

Some other ICA Nanotaxi® are also developed to improve the limited efficacy and stability of mRNA therapeutics, leading to the dramatic increase in therapeutic protein expression without DNA-encoded gene.

3. ICAfectin® transfection reagents

ICAfectin® transfection reagents are innovative breakthrough synthetic vectors for in vitro nucleic acid delivery. They are becoming the reagents of choice for efficient DNA and siRNA transfections as demonstrated by their increasing use in numerous studies published in high impact factor

journals including Journal of Biological Chemistry, Nucleic Acids Research, PLOS ONE, PLOS Pathogen, Human Gene Therapy and more.

In-Cell-Art is a privately held company, which was founded in 2005. It is a member of the Atlanpole Biotherapies high-tech cluster of biotechnology companies in western France.

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