

Inotrem receives clearance from French, Belgian and US authorities to launch a Phase II clinical trial aimed at assessing nangibotide in mechanically ventilated patients with COVID-19

- **Inotrem's clinical study on Covid-19 was selected by the French government to be part of its €78 M action plan aimed at reinforcing the countries' research capabilities for therapeutic solutions.**
- **Pre-clinical studies have demonstrated nangibotide's capacity to restore an appropriate immune response by targeting the TREM-1 pathway which is activated in patients suffering from COVID-19.**



Paris, July 23rd. 2020. Inotrem S.A., a biotechnology company specialized in the development of immunotherapies targeting the TREM-1 pathway, announced today that it has obtained authorization to launch its phase IIa clinical trial in COVID-19 patients in France, Belgium and the USA.

For this study, Inotrem received a non-dilutive funding as part of the call for proposals PSPC Covid, financed by the Investments d'Avenir Program which managed on behalf of the French government by Bpifrance, France's public investment bank. Inotrem with its partners the CHRU of Nancy and the CHU of Limoges, was one of the 6 French biotech companies who benefited from this programme to support the research and development of therapeutic solutions targeting COVID-19.

The goal of this first exploratory study is to determine the safety and tolerability and potential signals of efficacy of nangibotide in critically ill patients with COVID-19 with features of systemic inflammation. The objective of this project is to have a positive impact on the severity of the respiratory failure, reduce duration of mechanical ventilation, length of stay in ICU and reduce mortality. Sixty patients will be enrolled in Europe and in the United States. This study follows an observational study in 27 patients, conducted by Prof. Sébastien Gibot at the CHRU of Nancy, which showed an increased expression of the TREM-1 pathway in severe COVID-19 patients. TREM-1 is an immunomodulatory receptor expressed on innate immune cells which amplifies and maintains inflammation.

Previous clinical studies with nangibotide demonstrated its safety and tolerability in patients suffering from septic shock, which is also characterized by a systemic inflammatory reaction. Pre-clinical models have shown that nangibotide inhibits the amplification of the immune response caused by the activation of TREM-1 and was able to restore appropriate inflammatory response, vascular function, and improved survival in septic shock models. Inotrem is currently conducting a Phase IIb trial (ASTONISH) to treat septic shock patients with nangibotide in 6 European countries and in the United States. It is also developing, with Roche Diagnostics, a companion diagnostic test to identify septic shock patients more likely to benefit from its nangibotide treatment.

Coronavirus disease 2019 is a new pandemic disease that arises as a consequence of infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The optimum treatment strategy in the management of critically ill patients with COVID-19 continues to evolve and, in addition to



supportive therapies such as mechanical ventilation, vasopressors and renal replacement therapy, may include immunomodulatory approaches, such as nangibotide, in patients with severe disease.

Professor Sébastien Gibot, Nancy University Hospital and coordinating investigator said *“We observed that the TREM-1 pathway was activated in severe forms of COVID-19. Nangibotide is a TREM-1 inhibitor and has the potential to restore an appropriate immune response. We are hoping to demonstrate that nangibotide will reduce the duration of hospitalization and mortality of critically ill patients suffering from COVID-19”*.

Jean-Jacques Garaud, CEO of Inotrem, declared: *“We are very pleased with both the granting of this financial support and the clearance to start our clinical trial. The French administration has been very effective in working in a coordinated and rapid fashion.”*

About Inotrem

Inotrem S.A. is a biotechnology company specialized in immunotherapy for acute and chronic inflammatory syndromes. The company has developed a new concept of immunomodulation that targets the TREM-1 pathway to control unbalanced inflammatory responses. Through its proprietary technology platform, Inotrem has developed the first-in-class TREM-1 inhibitor, LR12 (nangibotide), with potential applications in a number of therapeutic indications such as septic shock and myocardial infarction. In parallel, Inotrem has also launched another program to develop a new therapeutic modality targeting chronic inflammatory diseases. The company was founded in 2013 by Dr. Jean-Jacques Garaud, a former head of research and early development at the Roche Group, Prof. Sébastien Gibot and Dr. Marc Derive. Inotrem is supported by leading European and North American investors.

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About TREM-1 pathway

TREM-1 pathway is an amplification loop of the immune response that triggers an exuberant and hyperactivated immune state which is known to play a crucial role in the pathophysiology of septic shock and acute myocardial infarction.

About Nangibotide

Nangibotide is the formulation of the active ingredient LR12, which is a 12 amino-acid peptide prepared by chemical synthesis. LR12 is a specific TREM-1 inhibitor, acting as a decoy receptor and interfering in the binding of TREM-1 and its ligand. In preclinical septic shock models, nangibotide was able to restore appropriate inflammatory response, vascular function, and improved animals' survival post septic shock.

About ASTONISH Study

The Efficacy, Safety and Tolerability of nangibotide in Patients with Septic Shock (ASTONISH) phase IIb trial is a Randomized, Double-blind, Placebo Controlled Dose Selection Study that will be performed Europe and the US. Four hundred and fifty patients are planned to be included in this study in 48 clinical sites. The study will compare the effect of nangibotide at two different doses versus standard of care.

About Bpifrance

Bpifrance is the French national investment bank: it finances businesses – at every stage of their development – through loans, guarantees, equity investments and export insurances. Bpifrance also provides extrafinancial services (training, consultancy...) to help entrepreneurs meet their challenges (innovation, export...).

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About French Strategic Investment Program

Endowed with 57 billion euros, the “French Strategic Investment Program” (PIA), lead by the General Secretary for Investment under the authority of the Prime minister, has been implemented to finance innovative and promising investments all over the territory, in order to allow France to increase its potential for long-term growth and jobs creation. The third component of the PIA, endowed with 10 billion euros, is part of the 57 billion euros Grand Plan d'Investissement (GPI) committed by the Government in 2017 and for a five years period in order to support structural reforms and respond to four major challenges in France : carbon neutrality, better access to employment, competitiveness through innovation and building the digital state.



Media contact for Inotrem

Anne REIN

Strategies & Image (S&I)

anne.rein@strategiesimage.com

+33 6 03 35 92 05