Inotrem's COVID-19 Phase IIa Clinical Trial declared "National Priority Research" by the French government's Clinical Trial Council

Paris, December 24. 2020. Inotrem S.A., a biotechnology company specialized in the development of immunotherapies targeting the TREM-1 pathway, announces today that its Phase IIa study of nangibotide, the company's lead product, for the treatment of severe forms of COVID-19 has been declared "National Priority Research" by the French government' steering committee for therapeutic clinical trials and other research (CAPNET).

In the context of a substantial amount of COVID-19-related research and the launch of numerous clinical trials, the French government created this steering committee to prioritize and accelerate high potential clinical trials. The "National Priority Research" designation, granted by CAPNET on the basis of assessment conducted by the REACTing Scientific Council, facilitates accelerated enrollment of patients in clinical trials, the activation of fast-track reviews and approval processes conducted by the French regulatory authorities (ANSM) and the French Ethics Committee (CPP), and for better valuing research centers' active contribution.

Inotrem's Phase IIa clinical trial which takes place in France, Belgium and the United States will determine the safety, tolerability and potential signals of efficacy of nangibotide, the company's lead product, in critically ill COVID-19 patients. This Phase IIa trial follows a preliminary study conducted by Prof. Sébastien Gibot at the CHU of Nancy, which showed that the TREM-1 pathway was activated in critically ill COVID-19 patients and associated with outcome. TREM-1 is an immunomodulatory receptor expressed on innate immune and endothelial cells which amplifies and maintains inflammation. Based upon an interim analysis, an independent DMC recommended on December 21. 2020 the continuation of Inotrem's Phase IIa clinical trial which results are expected early Q2 2021.

Jean-Jacques Garaud, CEO of Inotrem, indicates: *"This Research National Priority designation is an endorsement of both the work we have accomplished so far in fighting the COVID-19 pandemic and of the high potential of our lead product, nangibotide, for treating patients in ICU suffering from severe forms of COVID-19. Thanks to the strong commitment of regulatory bodies and the funding provided by Bpifrance, France's public investment bank, we were able with our partners, CHRU of Nancy and CHU of Limoges, to launch this study in timely manner. This governmental designation will allow us to accelearate this study and more rapidly assess the therapeutic potential for patients suffering from severe forms of COVID-19".*

Prof. Sebastien Gibot, lead study investigator, adds: *« We are very pleased with this decision which will allow us to accelerate patients' enrollment in France; we plan on enrolling a total of 60 patients. Results of the study are expected early Q2 2021 and will determine the safety, tolerability and potential signals of efficacy of nangibotide in COVID-19 patients. Previous clinical studies have demonstrated nangibotide's safety and tolerability in patients suffering from septic shock, which is also characterized by acute inflammatory syndromes".*

In parallel, Inotrem is currently conducting a Phase IIb trial (ASTONISH) to treat septic shock patients with nangibotide in six European countries and in the United States. Previous clinical studies with nangibotide in septic shock demonstrated that it was safe, well tolerated and showed signals towards clinically relevant efficacy. Pre-clinical models have shown that nangibotide modulates the amplification of the immune response caused by the activation of TREM-1 and is able to restore

appropriate inflammatory response and vascular function, resulting in improved survival in septic shock models.

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.

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