Inotrem Announces FDA Clearance of Investigational New Drug (IND) for the Phase IIB ASTONISH Trial in Septic Shock Patients to Demonstrate Nangibotide Efficacy

PARIS--(BUSINESS WIRE)--Inotrem S.A., a biotechnology company specialized in immunotherapy for acute inflammatory syndromes, announced today the U.S. Food and Drug Administration (FDA) has cleared the company's Investigational New Drug (IND) application for the ASTONISH trial (Phase IIb) where the safety, tolerance and efficacy of nangibotide (LR12), its lead compound for septic shock, will be studied. The IND is now effective allowing Inotrem to begin its planned Phase IIb study in septic shock patients in the US.

> Inotrem announces FDA clearance of IND for the ASTONISH trial (Phase IIb) in septic shock patients to demonstrate nangibotide efficacy
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The Phase IIb study will aim at demonstrating efficacy of nangibotide and bring a clinically relevant proof of clinical activity in septic shock patients. It will be a global multicentric study conducted in the United States and Europe. In addition, this study intends to validate a personalized medicine approach using soluble TREM-1 as potential companion diagnostic test to identify patients more likely to benefit from nangibotide treatment.

The FDA decision was based on the review of the information provided on the previous preclinical and clinical experience with nangibotide in particular the Phase IIa clinical study which demonstrated the safety and tolerability of nangibotide in patients suffering from septic shock. Preclinical models reviewed by the FDA showed that nangibotide was able to restore appropriate inflammatory response, vascular function, and improved survival in septic shock animal models. The design of the ASTONISH clinical trial has been previously discussed with the FDA during a preIND meeting. The regulatory process for clinical trial authorization in European countries is currently ongoing.

Septic shock is the ultimate complication of sepsis and currently constitutes a high unmet medical need. The incidence of septic shock continuously raises and mortality remains elevated (35%) in developed countries. There is currently no specific therapy approved for this indication besides antibiotics and symptomatic treatment. Inotrem's solution is based on a novel approach of immunomodulation which targets the TREM-1 pathway: a crucial mediator of the septic shock and has the potential to become the first mechanism-based treatment for septic shock.

Jean-Jacques Garaud, CEO of Inotrem, said: *"The FDA's clearance of IND for nangibotide is an important milestone for Inotrem. It confirms the strong potential of this novel therapeutic approach and gives us the opportunity to validate both the proof of clinical activity of nangibotide and our personalized medicine strategy in septic shock, a severe and often fatal condition for which there is currently no specific targeted therapies".*

Mitchell Levy, Division Chief of Pulmonary, Critical Care and Sleep Medicine at the Warren Alpert School of Medicine at Brown University and Medical Director, Medical Intensive Care Unit at Rhode Island Hospital and Inotrem's main investigator in the United States, added: "*We are thrilled by the FDA's decision which will allow to begin Inotrem's planned Phase IIb study in septic shock patients, and which as such recognizes the company's unique position around the TREM-1 pathway*".

About Inotrem
Inotrem S.A. is a biotechnology company specialized in immunotherapy for acute inflammatory syndromes, such as septic shock. 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 investors — Sofinnova Partners, Andera Partners, Biomed Invest and Inserm Transfert Initiative.
www.inotrem.com

About sTREM-1 and TREM-1 pathway.
TREM-1 pathway is an amplification loop of the immune response that triggers an exhuberant and hyperactivated immune state which is known to play a crucial role in the pathophysiology of septic shock and acute myocardial infarction. Today, there is an increasing number of publications indicating that the TREM-1 pathway is also implicated in chronic inflammatory diseases. Soluble TREM-1 (sTREM-1) is a plasma circulating protein which is released upon TREM-1 activation, and is thus a marker of TREM-1 pathway activation.

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 Effic**a**cy, **S**afety and **To**lerability of **n**angibotide **i**n Patients with Septic **Sh**ock (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.