# Inotrem announces publication of two key articles on nangibotide Phase II programs in peer-reviewed medical journals

- Data of ASTONISH Phase 2 trial in septic shock patients is published in *The Lancet Respiratory Medicine* and data of ESSENTIAL Phase 2 study in critically ill COVID-19 patients is published in *eClinicalMedicine*.

- Both studies show that a therapeutic intervention with nangibotide can control the TREM-1 pathway in major life-threatening immune dysregulations caused by severe infections, whether it is septic shock or severe forms of COVID-19, leading to improved patient outcome.

**Paris (France). June 1st. 2023.** Inotrem, an advanced clinical stage biotech company specializing in immunotherapies for acute and chronic inflammatory conditions, announced today the publication of the results of two phase 2 clinical studies in the *The Lancet Respiratory Medicine* and in *eClinicalMedicine*. The first article presents the ASTONISH Phase 2b trial in septic shock patients and the second one the ESSENTIAL Phase 2 trial for the treatment of critically ill COVID-19 patients. Both studies reveal that the TREM-1 pathway plays a central role in major life-threatening immune dysregulations caused by severe infections, whether it is septic shock or severe forms of COVID-19. The findings presented further validate Inotrem's innovative approach to treat inflammatory diseases by targeting TREM-1.

The two studies suggest that nangibotide, which targets TREM-1, is pathogen agnostic and has the potential to treat those very severe inflammatory conditions caused by both viral and bacterial infections. Both studies highlight the potential of nangibotide in the treatment of septic shock patients and of patients with severe forms of COVID-19 with a biomarker guided approach using soluble TREM-1 as predictive marker of response to targeted therapy.

The first manuscript in *The Lancet Respiratory Medicine* is entitled "Prospective evaluation of the efficacy, safety, and the optimal biomarker enrichment strategy for nangibotide, a TREM-1 inhibitor, in patients with septic shock: a double-blind, randomized, controlled, phase 2b trial" and presents results from 355 septic shock patients. The primary outcome was the change in SOFA at day 5 compared to placebo in the pre-defined high soluble TREM-1 (≥ 400 pg/ml) group and in the overall population. Planned evaluation of the optimal sTREM-1 cut-off revealed increased clinically relevant benefits of high dose nangibotide at higher cutoffs (sTREM-1 ≥ 532 pg/ml). The manuscript can be accessed via the following link: The Lancet Respiratory Medicine.

The second manuscript in *eClinicalMedicine,* entitled "Evaluation of the efficacy and safety of TREM-1 inhibition with nangibotide in patients with COVID19 receiving respiratory support: results of the ESSENTIAL randomized, double-blind trial" presents the Phase 2 results obtained in 220 COVID-19 patients receiving ventilatory support. In this study, nangibotide has a significant and positive impact on the clinical progression of the disease, as well as on the severity of the respiratory failure, secondary infection rates and notably mortality. The trial showed that sTREM-1 is an effective prognostic marker of outcome in severe COVID-19. The manuscript can be accessed via the following link: eClinicalMedicine.

"Nangibotide is the first TREM-1 inhibitor and has the potential to become the first causal treatment of life-threatening immune dysregulations. This is an area with a major unmet medical need" said Professor Bruno François, Limoges University Hospital, and lead author on the two manuscripts.

"We are excited to see this data published in *The Lancet Respiratory Medicine* and in *eClinicalMedicine,* two of the most established peer-reviewed medical journals in our field. These two publications come as a strong recognition of Inotrem's innovative scientific leadership regarding the role of the TREM-1 pathway and of our solid therapeutic approaches" said Sven Zimmermann, CEO of Inotrem. "We look forward to bringing this potential new treatment option to patients suffering from severe and often fatal inflammatory conditions."

**About nangibotide**

Nangibotide is a TREM-1 inhibitor peptide with the potential to restore appropriate inflammatory response, vascular function, and improve post septic shock survival. 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. Nangibotide in septic shock has been granted the fast-track status in September 2019 by the FDA and the PRIME status in 2017 by the EMA.

**About ASTONISH Study**

The Efficacy, Safety and Tolerability of nangibotide in Patients with Septic Shock (ASTONISH) phase 2b trial is a Randomized, Double-blind, Placebo Controlled Dose Selection Study that was performed in Europe and in the US. The study compared the effect of nangibotide at two different doses (0.3 and 1mg/kg/h continuous i.v. infusion for 3 to 5 days) versus standard of care. Results for Phase IIb ASTONISH clinical trial in septic shock patients were disclosed for the first time at the International Sepsis Forum held in Barcelona on October 13. 2022.

**About ESSENTIAL Study**

The ESSENTIAL phase 2 trial is a double-blind randomized controlled trial assessing efficacy, safety, and optimum treatment population of nangibotide (1·0 mg/kg/h) compared to placebo. The study was stopped after 220 patients had been recruited; of them, 219 were included in the mITT analysis. Patients aged 18-75 years were eligible within 7 days of SARS-CoV-2 documentation and within 48 hours of onset invasive or non-invasive respiratory support because of COVID-19-related ARDS. ESSENTIAL data were disclosed for the first time at the ESICM meeting held in Paris in October 25. 2022.

**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, nangibotide, with potential applications in a number of therapeutic indications such as septic shock, severe forms of COVID-19 and myocardial infarction. In parallel, Inotrem has also launched an antibody-based 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 Inotrem is part of the French Tech 120, a government program dedicated to support the development of fast-growing startups. www.inotrem.com

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