Inotrem announces that its ESSENTIAL Phase II study for the treatment of critically ill COVID-19 patients meets its primary and key secondary endpoints

- **Results demonstrate statistically significant efficacy of drug candidate nangibotide in the treatment of patients with severe forms of COVID-19**
- **Nangibotide treatment improves patients' clinical status and shows a relative 43% reduction in mortality**
- **The company will consult with regulatory authorities to advance a new treatment option to severe COVID-19 patients**
- **ESSENTIAL was made possible thanks to the strong support from French public authorities and their commitment to fight COVID-19**

Paris (France), October 25. 2022. Inotrem, an advanced clinical stage biotech company specializing in immunotherapies for acute and chronic inflammatory syndromes, announced today at the European Society of Intensive Care Medicine's Annual Congress, held in Paris, positive results for ESSENTIAL, its Phase II clinical trial in COVID-19 patients hospitalized in critical care units and experiencing acute respiratory distress. The study was funded as part of the Capacity Building call for proposals, financed by the Programme d'Investments d'Avenir (PIA), operated on behalf of the French government by Bpifrance, the French national investment bank.

The ESSENTIAL study was terminated at 220 randomized ICU patients requiring ventilatory support (stage 5 or 6 on a 7-point clinical status ordinal scale) and compared infusion of nangibotide at 1mg/kg/hr for up to 5 days of treatment with standard of care. Despite a lower than anticipated sample size, the study met its primary endpoint of an improvement in clinical status according to 7-point clinical status ordinal scale from baseline to Day 28 (p value = 0.040).

Nangibotide treatment also showed a statistically and clinically meaningful 12% absolute and 43% relative reduction in Day 28 mortality (key secondary endpoint) in the overall trial population (p value = 0.030). Among the subpopulation of patients with levels of the TREM-1 pathway activation marker, soluble TREM-1 (sTREM-1) above the median, the absolute and relative reduction in mortality was even more pronounced, amounting to 20% and 47%, respectively (p value = 0.023).

The study showed that nangibotide has a significant and positive impact on the progression of the disease in patients receiving ventilatory support due to COVID-19, as well as on the severity of the respiratory failure, and length of stay in ICU. The trial showed that sTREM-1 is an effective prognostic marker of outcome in severe COVID-19 and, consistent with the results from the company's prior ASTONISH study, confirmed that sTREM-1 is a predictive marker of a positive response to the treatment by nangibotide.

Jean-Jacques Garaud, Senior VP Head of scientific and medical affairs at Inotrem said: "This new trial brings compelling evidence that the TREM-1 pathway plays a central role in major life-threatening immune dysregulations caused by severe infections, whether it is severe forms of COVID-19 or septic shock. This study strongly suggests 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."

Sven Zimmermann, CEO of Inotrem, added: “We are grateful for the continued financial support and confidence awarded to us by the French public authorities to fight COVID-19. This attests of the relevance of our innovative approach to treat inflammatory diseases. The data we obtained is extremely encouraging, and we plan on quickly consulting regulatory authorities in the US and EU.”

Thierry Hercend, Independent Board member at Inotrem, said: “The effect of nangibotide on severe forms of COVID 19 added to the recent announcement of the ASTONISH Phase II data in septic shock confirms that targeting the TREM-1 pathway is beneficial in other conditions, infectious or not, leading to severe immune dysregulation in the critical care setting.”

Substantial support from public funding to fight COVID-19

At the start of the pandemic in 2020, Inotrem team set out to build on the similarities between the immune dysregulation in severe forms of COVID-19 with those observed in septic shock patients. Building on its deep scientific and medical understanding of the TREM-1 pathway, and with the strong support of the French government, Inotrem launched ESSENTIAL, its clinical trial to assess the efficacy of its drug lead candidate, nangibotide, for COVID-19 patients in the ICU.

In July 2020, the CoviTREM-1 consortium which includes the Nancy and Limoges university hospitals and Inotrem, obtained a first public funding of 7.5 million euros under a call for projects operated by the Secretary General for Investment and Bpifrance. In December 2020, the trial was declared a “Research National Priority” by the French government. In July 2021, Inotrem was authorized to pursue the clinical development of nangibotide up to registration for COVID-19 patients and can draw on additional public funding of up to 45 million euros from Bpifrance, as part of the Programme d’Investments d’Avenir (“PIA”).

About the drug candidate 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 and has recently reported positive results from a Phase IIb trial (ASTONISH) in septic shock patients.

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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