OSE Immunotherapeutics and Nantes University Hospital Announce Initiation of a Phase 1/2 Clinical Trial to Evaluate CD28 Antagonist FR104 in Patients Undergoing Renal Transplantation

- ***University Hospital of Nantes will sponsor and conduct the clinical trial***
- ***OSE Immunotherapeutics will provide its FR104 product***
- ***Post-transplant immune response is a key therapeutic issue for patients and a new development indication for FR104***

Nantes, France, December 3, 2020, 7:30AM CET – OSE Immunotherapeutics (ISIN: FR0012127173; Mnémo: OSE), and **Nantes University Hospital (CHU de Nantes)** today announced that the French National Agency for Medicines and Health Products Safety (ANSM) and the French Central Ethics Committee (CPP) approved the initiation of a Phase 1/2 trial evaluating first administration of FR104, a monoclonal antibody CD28 antagonist, in patients undergoing renal transplant. This study will be conducted as part of a collaboration agreement between OSE Immunotherapeutics and the University Hospital of Nantes.

Alexis Peyroles, Chief Executive Officer of OSE Immunotherapeutics, comments: *"We are very pleased to be collaborating with the University Hospital of Nantes and the ITUN, a very high-level clinical investigation center, with a team of excellence in renal graft at European level. The initiation of a first clinical trial of FR104 in renal transplantation is a key step in the product's development. Since graft rejection is a major issue for patients that results in need for lifelong immunosuppressive treatment, the evaluation of FR104 immunotherapy in the long-term control of post-transplant immune reaction addresses a key therapeutic challenge that requires innovative solutions. OSE Immunotherapeutics is also working on a new Phase 2 clinical trial with FR104 in a niche indication in autoimmune diseases as the product has showcased a strong development potential in a number of indications."*

The purpose of this Phase 1/2 clinical trial is to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of FR104 in renal transplant patients.

A long-term follow up assessment will be performed one year after the end of the study. Long term safety and efficacy will be evaluated in terms of renal function, incidence of rejection and all suspected FR104 related adverse events.

The study will be conducted under the sponsorship of Nantes University Hospital. Pr. Gilles Blancho, Head of the ITUN (Institute of Urology and Nephrology Transplantation) within the University Hospital, will serve as the coordinating investigator. OSE Immunotherapeutics will provide its product FR104 and a financial support.

Pr. Gilles Blancho, Head of the ITUN, added: *"Despite continuous progress in immunosuppressive treatments, the need for medical advances for renal transplant recipients remains very strong. Through FR104, we are hoping to develop an innovative and promising immunotherapy. The key issue in organ transplant is having available efficient immunosuppressive treatments with minimal side effects, thus preserving patients' quality of life. Moreover, the clinical collaboration between ITUN and OSE fits into Nantes hospital's commitment to foster partnerships with the pharmaceutical industry in order to help our clinicians participate in clinical trials while simultaneously enabling our patients to benefit from the latest therapeutic advancements."*

FR104 is a monoclonal antibody and an antagonist of CD28. This pegylated monovalent antibody selectively inhibits the CD28 receptor and has potential clinical applications in autoimmune diseases and transplantation.

Due to its selective immunosuppressive activity directed at effector T cells, OSE plans to investigate FR104 for use in kidney transplantation. Selective CD28 blockage by FR104 might represent an effective immunomodulation strategy by reducing the activation of T lymphocytes, while sparing the activity of regulatory T lymphocytes.

Several studies conducted with FR104 in preclinical models of transplant and other immune-mediated diseases have generated significant immune data demonstrating its ability to promote immunological modulation[(1)] and ability to reinforce immunosuppression[(2)]. In particular, when used as a monotherapy or in combination according to the models, FR104 has shown to efficiently control graft-versus-host disease (GVHD) or renal graft rejection and this control was superior to the one observed with non-selective CD28-antagonist CTLA4-Ig[(3, 4)]. Additionally, the results from the Phase 1 clinical [(5)] study of FR104 have shown a good clinical and biological safety with an immunosuppressive activity potentially applicable to transplantation and immune-mediated diseases.

(1) Selective blockade of CD28 on human T cells facilitates regulation of alloimmune responses
Masaaki Zaitsu, Fadi Issa, Joanna Hester et al.; JCI Insight. 2017

(2) FR104, an antagonist anti-CD28 monovalent fab' antibody, prevents alloimmunization and allows calcineurin inhibitor minimization in nonhuman primate renal allograft
Poirier N, Dilek N, Mary C et al.; Am J Transplant. 2015 Jan.

(3) CD28 blockade controls T cell activation to prevent graft-versus-host disease in primates
Benjamin K. Watkins, Victor Tkachev, Scott N. Furlan et al.; J Clin Invest. 2018 Aug 13

(4) Anti-CD28 Antibody and Belatacept Exert Differential Effects on Mechanisms of Renal Allograft Rejection
Ville S, Poirier N et al., J Am Soc Nephrol. 2016

(5) First-in-Human Study in Healthy Subjects with FR104, a Pegylated Monoclonal Antibody Fragment Antagonist of CD28
Nicolas Poirier, Gilles Blancho, Maryvonne Hiance et al.; The Journal of Immunology, Nov. 2016

ABOUT CHU DE NANTES

Nantes University Hospital (CHU Nantes), the 6th largest French university hospital, provides high-quality comprehensive health services. Among the top research institutions in France, CHU de Nantes focuses on excellence and innovation. Nantes University Hospital participates each year in about 1,300 clinical trials, involving approximately 6,500 patients, leading to over 1,200 publications in peer-reviewed journals. Over the years, CHU de Nantes has developed numerous research partnerships with SMEs and major actors of the biotech and medtech industry. We believe opening up to our ecosystem is a real game-changer for the development of innovations for the benefit of patients and health professionals.

ABOUT OSE Immunotherapeutics

OSE Immunotherapeutics is an integrated biotechnology company focused on developing and partnering therapies to control the immune system for immuno-oncology and autoimmune diseases. The company's

immunology research and development platform is focused on three areas: T-cell-based vaccination, Immuno-Oncology (focus on myeloid targets), Auto-immunity & Inflammation. Its balanced first-in-class clinical and preclinical portfolio has a diversified risk profile:

Vaccine platform

- **Tedopi®** (innovative combination of neoepitopes): the company's most advanced product; positive results for Step-1 of the Phase 3 trial (Atalante 1) in Non-Small Cell Lung Cancer post checkpoint inhibitor failure.
  In Phase 2 in pancreatic cancer (TEDOPaM, sponsor GERCOR) in monotherapy and in combination with checkpoint inhibitor Opdivo®.
- **CoVepiT**: a prophylactic vaccine against COVID-19, developed using SARS-CoV-2 optimized neo-epitopes. Positive preclinical and human ex vivo results in August 2020, clinical trial expected to start Q1 2021.

Immuno-oncology platform

- **BI 765063** (OSE-172, anti-SIRPα mAb on the SIRPα/CD47 pathway): developed in partnership with Boehringer Ingelheim; myeloid checkpoint inhibitor in Phase 1 in advanced solid tumors.
- **CLEC-1** (novel myeloid checkpoint target): identification of mAb antagonists of CLEC-1 blocking the "Don't Eat Me" signal that increase both tumor cell phagocytosis by macrophages and antigen capture by dendritic cells.
- **BiCKI®**: bispecific fusion protein platform built on the key backbone component anti-PD-1 (OSE-279) combined with new immunotherapy targets; 2nd generation of PD-(L)1 inhibitors to increase antitumor efficacity.

Auto-immunity and inflammation platform

- **FR104** (anti-CD28 monoclonal antibody): positive Phase 1 results; Phase 2-ready asset in autoimmune diseases or in transplantation.
- **OSE-127** (humanized monoclonal antibody targeting IL-7 receptor): developed in partnership with Servier; positive Phase 1 results; two independent Phase 2 planned in ulcerative colitis (OSE sponsor) and in Sjögren's syndrome (Servier sponsor) to start in Q4 2020.
- **OSE-230** (ChemR23 agonist mAb): first-in-class therapeutic agent with the potential to resolve chronic inflammation by driving affected tissues to tissue integrity.
  Due to the COVID-19 crisis, accrual of new patients in the clinical trial TEDOPaM is temporarily suspended and initiation timelines for both Phase 2 trials of OSE-127 could be impacted during the coming months.

For more information: **https://ose-immuno.com/en/**
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Forward-looking statements

This press release contains express or implied information and statements that might be deemed forward-looking information and statements in respect of OSE Immunotherapeutics. They do not constitute historical facts. These information and statements include financial projections that are based upon certain assumptions and assessments made by OSE Immunotherapeutics' management in light of its experience and its perception of historical trends, current economic and industry conditions, expected future developments and other factors they believe to be appropriate.

These forward-looking statements include statements typically using conditional and containing verbs such as "expect", "anticipate", "believe", "target", "plan", or "estimate", their declensions and conjugations and words of similar import. Although the OSE Immunotherapeutics management believes that the forward-looking statements and information are reasonable, the OSE Immunotherapeutics' shareholders and other investors are cautioned that the completion of such expectations is by nature subject to various risks, known or not, and uncertainties which are difficult to predict and generally beyond the control of OSE Immunotherapeutics. These risks could cause actual results and developments to differ materially from those expressed in or implied or projected by the forward-looking statements. These risks include those discussed or identified in the public filings made by OSE Immunotherapeutics with the AMF. Such forward-looking statements are not guarantees of future performance. This press release includes only summary information and should be read with the OSE Immunotherapeutics' Universal Registration Document filed with the AMF on 15 April 2020, including the annual financial report for the fiscal year 2019, available on the OSE Immunotherapeutics' website. Other than as required by applicable law, OSE Immunotherapeutics issues this press release at the date hereof and does not undertake any obligation to update or revise the forward-looking information or statements.