OSE Immunotherapeutics Provides an Update on the First Positive Results and Clinical Development of CoVepiT, its Multi-Target T-cell Anti-COVID Vaccine

- **New clinical data confirm the good tolerance of CoVepiT and a very good level of T cell response in healthy volunteers vaccinated.**
- **Promising preclinical efficacy signals guide development in immunocompromised patients with poor antibody response to present registered anti-COVID vaccines.**
- **Results on the 6-month long-term memory T response, expected in the first quarter of 2022, will be a key element in further clinical development.**
- **CoVepiT epitopes* remain independent of mutations identified in current and emerging variants.**

Nantes, France – November 30, 7:30am CET - OSE Immunotherapeutics (ISIN: FR0012127173; Mnemo: OSE) today announces the positive analysis of the first data of CoVepiT, its prophylactic vaccine candidate against COVID-19, in particular positive interim immunological results on T cell response obtained in 100% of the treated population, with in parallel a resolution of local indurations observed during vaccination.

Last July, the company voluntarily suspended the recruitment and administration of CoVepiT in the Phase 1 clinical trial as a precaution due to a limited number of adverse reactions (nodule-like indurations at the injection site) grade 1 and a grade 2 adverse reaction in one participant. Since then, the data have been analyzed regularly with the Independent Safety Monitoring Committee in charge of evaluating the safety of the trial and the Ghent (Belgium) investigation center. The indurations were resolved within a few weeks for most of the participants (without systemic reaction, without fever, nor inflammation, without local ulceration) and the follow-up continues to show a good safety profile. This profile, with frequent indurations, is close to that of vaccines inducing T cell responses [1;2;3] and is regularly linked to this T cell mechanism of action.

The immunological response was measured on the eight healthy volunteers who received CoVepiT, showing the expected efficacy at six weeks after the injection, the primary endpoint of the phase 1 trial, with good immunogenicity of the T cells against the viral epitopes. Interferon-gamma responses measured by Elispot was observed in 100% of participants, from the 22nd day to the 6th week. These immunological results are significantly better than those obtained in convalescent patients and confirm the interest and the mechanism of action of the vaccine on the T cell response.

In addition, new preclinical studies have shown that the intensity and the quality of the immunogenicity of the T cells induced by the CoVepiT vaccine were not altered by concomitant immunosuppressive treatments such as antimetabolites (mycophenolate mofetil, MMF, inhibiting immunosuppressant proliferation of B and T cells) or by a strong depletion of B cells producing antibodies (observed with rituximab, used in autoimmune diseases and certain cancers). The interest in generating T cells is

enhanced especially for immunocompromised patients with weak antibody responses despite repeated administration of current registered vaccines.

Alexis Peyroles, CEO of OSE Immunotherapeutics, comments: *"All of the first results generated, on tolerance and immunological results, confirm that the modified epitope platform acts by amplifying the response of T cells and makes it possible to consider longer term protection. For immunocompromised populations, current recommendations relate to the administration of additional doses of vaccines already registered, in an attempt to strengthen the antibody response which currently makes access to these patients and the clinical development of CoVepiT difficult. During the first quarter of 2022, we are awaiting additional 6-month immunogenicity results on the long-term memory T response, and if positive, we will prepare a meeting with the health Agencies to prioritize development in immunocompromised patients.*

This therapeutic approach of modified epitopes has already enabled us to obtain a T response against tumor antigens in oncology, resulting in a significant benefit in terms of survival for our Tedopi® product in advanced non -small cell lung cancer patients (NSCLC) with secondary resistance to immunotherapy (Atalante-1 ESMO phase 3 results 2021). These new CoVepiT results confirm the value of our epitope platform, in particular for the most fragile populations."

**These epitopes, fragments of viral proteins, are antigenic determinants recognized by T cell receptors during an adaptive T immune response. They are not currently impacted by the mutations described for the existing variants (Delta) and emergent variants (Omicron).*

(1) Pleguezuelos et al. 2020
(2) Rodo et al. PLoS Pathog 2019
(3) Heitmann, J. S. et al. Nature 2021

ABOUT CoVepiT

CoVepiT is a next-generation multi-target, multi-variant vaccine against SARS-CoV-2 in clinical Phase 1. The vaccine candidate was designed using optimized epitopes selected after screening more than 67,000 global SARS-CoV-2 genomes, as well as those of previous human-infective CoVs, SARS and MERS, to identify vaccine targets with the lowest chance of natural mutation. Targeting 11 virus proteins including Spike, M, N and several non-structural proteins, this second-generation vaccine covers all initial and novel SARS-CoV-2 variants identified globally to date. In preclinical testing, CoVepiT demonstrated the ability to activate T cell defenses through CD8 T-cell multi-epitope responses for long-term T memory cell immunity.

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 Phase 3 trial (Atalante 1) in Non-Small Cell Lung Cancer patients after secondary resistance to checkpoint inhibitors.
  In Phase 2 in pancreatic cancer (TEDOPaM), sponsor GERCOR.
  In Phase 2 in ovary cancer, in combination with pembrolizumab (TEDOVA), sponsor ARCAGY-GINECO.
  In Phase 2 in non-small cell lung cancer in combination with nivolumab, sponsor Italian foundation FoRT.

- **CoVepiT**: a prophylactic second-generation vaccine against COVID-19, developed using SARS-CoV-2 optimized epitopes against multi variants. Positive preclinical and human ex vivo results. Voluntary and temporary Phase 1 enrollment suspension on-going (July 2021).

Immuno-oncology platform

- **BI 765063** (OSE-172, anti-SIRPα mAb on CD47/SIRPα pathway): developed in partnership with Boehringer Ingelheim in advanced solid tumors; positive Phase 1 dose escalation results of BI 765063 in monotherapy or in combination with ezabenlimab (PD-1 antagonist); Expansion Phase 1 open for screening.
- **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): Licensing partnership agreement with Veloxis in the organ transplant market; ongoing Phase 1/2 in renal transplant (sponsored by the Nantes University Hospital); Phase 2-ready asset in an autoimmune disease indication.
- **OSE-127/S95011** (humanized monoclonal antibody targeting IL-7 receptor): developed in partnership with Servier; positive Phase 1 results; in Phase 2 in ulcerative colitis (OSE sponsor) and an independent Phase 2a ongoing in Sjögren's syndrome (Servier sponsor).
- **OSE-230** (ChemR23 agonist mAb): first-in-class therapeutic agent with the potential to resolve chronic inflammation by driving affected tissues to tissue integrity.

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

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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 2021, including the annual financial report for the fiscal year 2020,

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.