OSE Immunotherapeutics Announces Dosing of the First Participant in a Phase 1 Study of VEL-101/FR104, a Novel Investigational Drug for Kidney Transplant Immunosuppression

A Phase 1 Study Sponsored and Conducted by Veloxis Pharmaceuticals, Inc., the Company's Partner in Transplantation

Nantes, France – May 18, 2022, 6:00pm CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) today announced that the first participant has been dosed in a Phase 1 Study of VEL-101/FR104 [NCT05238493], a study sponsored and conducted by its partner in transplantation, Veloxis Pharmaceuticals, Inc., an Asahi Kasei company. VEL-101/FR104 is a novel investigational maintenance immunosuppressive agent being developed for prevention of acute rejection in kidney transplant recipients.

"Dosing our first participant in this study is a monumental step for Veloxis and our growth as a global pharmaceutical development company" said Mark Hensley, chief executive officer of Veloxis. *"This milestone demonstrates how our relationship with the Asahi Kasei Group is enabling us to deliver on our promise to improve the lives of transplant patients by developing innovative therapeutics."*

Dominique Costantini, chief executive officer of OSE Immunotherapeutics, comments: *"We thank Veloxis for this new step which marks a key advancement in the clinical development of CD28 antagonist VEL-101/FR104 and promising innovative immunosuppressive treatment addressing a key therapeutic challenge. To complement Veloxis' efforts, an investigator-initiated clinical trial* to evaluate VEL-101/FR104 in patients undergoing renal transplantation is being conducted at University Hospital of Nantes."*

The Veloxis study will assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of single ascending doses of VEL-101 or placebo when administered subcutaneously (SC) or intravenously (IV). Approximately 56 healthy participants will be enrolled and will undergo monitoring for 50 days.

VEL-101/FR104's prior Phase 1, randomized, double-blind, placebo-controlled study evaluated single and multiple ascending IV doses of VEL-101/FR104 in healthy participants. The current Phase 1 study will provide important data following SC administration before proceeding to studies in the kidney transplant population. A SC route of administration is being studied to potentially support self-administration at home.

"We are excited to initiate the development of VEL-101 with this study in healthy participants in the United States. The Phase 1 study will primarily provide data on the safety and tolerability of the investigational drug when administered using a subcutaneous route of administration and in a non-weight based fixed dose format", says Tunde Otulana MD, chief medical officer of Veloxis. *"The study will also generate data to support the selection of an appropriate dose-range to incorporate into the next study, which will be a Phase 2 proof of concept study in de novo kidney transplant patients."*

VEL-101 is a pegylated monoclonal antibody fragment that binds to and blocks CD28-mediated effector-T cell co-stimulation, without blocking CTLA-4, an important protein receptor found on T cells that acts as a natural brake on the body's immune responses. VEL-101 is, therefore, expected to have a dual-mechanism of action where in a direct manner, it blocks CD28-mediated T cell activation, and in an indirect way, it allows for CTLA-4 mediated immunosuppressive functions. VEL-101 will be developed for prevention of acute rejection in recipients of kidney transplants and potentially in recipients of other solid organs.

*NCT04837092

About the Study (NCT05238493)

VEL-101 is being studied in a Phase 1, randomized, double blind, placebo controlled, dose escalation study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of VEL-101 administered intravenously or subcutaneously in healthy participants. The primary objective is to assess the safety and tolerability of single ascending doses of VEL-101 when administered subcutaneously or intravenously. Approximately 56 participants will be enrolled in all the cohorts.

About the VEL-101 Clinical Program

VEL-101 has been evaluated in a first-in-human study to assess the safety, pharmacokinetics, pharmacodynamics, and potency of IV administrations in healthy subjects (read about the study here [1]). VEL-101, a pegylated monoclonal antibody fragment CD28 antagonist, selectively blunts CD28 co-stimulation while sparing the CTLA-4 co-inhibitory signal. The net effect of CD28 antagonism is downregulating effector T cells while potentially promoting regulatory T cell (Treg) activity.

VEL-101, also known as FR104, was licensed by Veloxis Pharmaceuticals, Inc. from OSE Immunotherapeutics in April 2021. As part of the license agreement, Veloxis Pharmaceuticals, Inc. obtained worldwide rights to develop, manufacture, and commercialize VEL-101 for all transplant indications.

About Veloxis Pharmaceuticals, Inc.

Veloxis Pharmaceuticals, Inc, an Asahi Kasei company, is a fully integrated specialty pharmaceutical company committed to improving the lives of transplant patients. Headquartered in Cary, North Carolina, USA, Veloxis is focused on the global development and commercialization of medications utilized by transplant patients and by patients with serious related diseases. For further information, please visit www.veloxis.com.

About Asahi Kasei

The Asahi Kasei Group contributes to life and living for people around the world. Since its foundation in 1922 with ammonia and cellulose fiber business, Asahi Kasei has consistently grown through the proactive transformation of its business portfolio to meet the evolving needs of every age. With more than 40,000 employees around the world, the company contributes to sustainable society by providing solutions to the world's challenges through its three business sectors of Material, Homes, and Healthcare. Its healthcare operations include devices and systems for acute critical care, dialysis, therapeutic apheresis, transfusion, and manufacture of biotherapeutics, as well as pharmaceuticals and diagnostic reagents. For further information, please visit www.asahi-kasei.com.

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 Immuno-Inflammation. Its balanced first-in-class clinical and preclinical portfolio has a diversified risk profile:

Immuno-Oncology first-in-class products

1 Poirier N et al. First-in-Human Study in Healthy Subjects with FR104, a Pegylated Monoclonal Antibody Fragment Antagonist of CD28. *J. Immunol*. 2016

- **Tedopi®** (innovative neoepitope combination): the Company's most advanced product; positive results for Phase 3 trial (Atalante 1) in Non-Small Cell Lung Cancer patients in secondary resistance after checkpoint inhibitor failure.
  Other ongoing combination trials sponsored by cooperative clinical research groups in oncology:
  Phase 2 in pancreatic cancer (TEDOPaM), sponsor GERCOR.
  Phase 2 in ovary cancer, in combination with pembrolizumab (TEDOVA), sponsor ARCAGY-GINECO.
  Phase 2 in non-small cell lung cancer in combination with nivolumab, sponsor Italian foundation FoRT.
- **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 and in combination with ezabenlimab (PD-1 antagonist); ongoing expansion Phase 1; BI sponsored international phase 1b clinical trial ongoing in combination with ezabenlimab alone or with other drugs in patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) or hepatocellular carcinoma (HCC).
- **OSE-279**, anti-PD1 – advanced preclinical stage.
- **BiCKI®**: bispecific fusion protein platform built on the key backbone component of anti-PD1 combined with a new immunotherapy target (for example: BiCKI®-IL7, preclinical stage) to increase anti-tumor efficacy.

Immuno-Inflammation first-in-class products

- **OSE-127/S95011** (humanized monoclonal antibody antagonist of IL-7 receptor): developed in partnership with Servier; positive Phase 1 results; ongoing Phase 2 in ulcerative colitis (sponsor OSE) and ongoing Phase 2a in Sjögren's syndrome (sponsor Servier).
- **FR104** (anti-CD28 monoclonal antibody): licensing partnership agreement with Veloxis Pharmaceuticals, Inc. in transplantation; ongoing Phase 1/2 in renal transplant (sponsored by the Nantes University Hospital); US IND obtained by Veloxis Pharmaceuticals, Inc. for a clinical trial; Phase 2 planned in an autoimmune disease indication.
- **OSE-230** (ChemR23 agonist mAb): preclinical stage therapeutic agent with the potential to resolve chronic inflammation by driving affected tissues to tissue integrity.

CoVepiT: a prophylactic second-generation vaccine activating cytotoxic T lymphocytes against COVID-19, developed using optimized epitopes from SARS-CoV2 viral proteins, epitopes non impacted by multi-variants. Shows good tolerance and very good level of T cell immune response. In clinical testing, a long-term memory response was confirmed at 6 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 2022, including the annual

financial report for the fiscal year 2021, 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.