OSE Immunotherapeutics and Nantes University Hospital Present Positive Phase 1/2 Study Evaluating FR104/VEL-101 Immunotherapy in Renal Transplant

At the American Transplant Congress 2024 (June 1-5 Philadelphia)

Nantes, France – June 5, 2024, 7:30am CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) and Nantes University Hospital present positive Phase 1/2 analysis from first use of anti-CD28 FR104/VEL-101 in kidney transplantation in oral presentation at the Annual American Transplant Congress (ATC) held in Philadelphia (June 1-5, 2024). A total of three oral presentations on FR104/VEL-101 were presented at this congress.

A first oral communication, entitled *"First use of FR104, an anti-CD28 molecule in human kidney transplantation"*, presented by Pr. Gilles Blancho, Head of the ITUN* at the University Hospital in Nantes / Nantes University and Principal Investigator of the study, reported on the positive data from the completed Phase 1/2 clinical trial FIRsT evaluating FR104/VEL-101 in patients undergoing renal allotransplant. This study is sponsored and conducted by the University Hospital of Nantes as part of a collaboration agreement with OSE Immunotherapeutics.

A second oral communication, entitled "*Safety, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Fixed-Dose, Subcutaneous (SQ) Administration of VEL-101, an Anti-CD28 Pegylated Monoclonal Antibody Fragment, in Healthy Participants*", presented by OSE Immunotherapeutics partner Veloxis Pharmaceuticals, featured the results from the Company's Phase 1 dose escalation clinical trial evaluating the safety, tolerability, pharmacodynamics and pharmacokinetics of single ascending doses of subcutaneous administration of FR104/VEL-101 in healthy participants.

A third oral communication, entitled "*Combined blockade of the CD154 and CD28 co-stimulation pathways attenuates pathogenic alloimmunity and prolongs survival in cynomolgus cardiac allografts*", presented by the group of Pr. Richard Pierson (Massachusetts General Hospital, Harvard university, Boston, USA), reported on the positive preclinical efficacy data of FR104/VEL-101 injection in monotherapy or in combination with anti-CD40L antibody to protect from acute and chronic heart allograft rejection.

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, said: *"We thank the University Hospital of Nantes for this important step with the first clinical study evaluating FR104/VEL-101 in transplanted patients. Our partner Veloxis presented its positive subcutaneous Phase 1 clinical trial results in oral session, which will facilitate dose selection in preparation for a Phase 2 study in kidney transplant recipients. At last, we are excited about the promising preclinical results of our academic collaborator in the field of cardiac transplantation, further enhancing the future market potential."*

Pr. Gilles Blancho commented: *« We are very pleased to share the positive results of the FIRsT study at international congress on post-transplant immune response and one-year safety in patients treated with FR104/VEL-101, developed for years in our own research laboratory, CR2TI**/UMR Inserm 1064. The data presented show the safety of the product used in combination and the first signs of efficacy in kidney transplant recipients with no episodes of acute rejection after one year follow-up in all patients of the study. The exploration of FR104/VEL-101's safety profile seems promising and encourages moving to a Phase 2 trial for patients undergoing renal transplant who require innovative solution."*

The purpose of the FIRsT Phase 1/2 clinical trial is to investigate the safety, tolerability, and pharmacokinetics of FR104/VEL-101, a novel antagonist pegylated anti-CD28 Fab' antibody fragment, as well as its potential clinical efficacy on acute rejection prophylaxis and renal function in a *de novo* renal transplant population receiving an allograft from standard criteria donors (NCT number: NCT04837092). A one-year safety and efficacy of FR-104/VEL-101 treatment assessment was performed after transplantation, including renal function, incidence of rejection and suspected reported adverse events.

Ten patient candidates eligible to a first kidney transplant at low risk of rejection, as planned in the protocol, have been included in the FIRsT study for eight analyzable patients (two patients were screened and enrolled but not transplanted for technical reasons). Tacrolimus (a calcineurin inhibitor) was withdrawn after 6 months post-transplantation. The eight patients completed 1-year treatment with FR104/VEL-101.

No safety alert was detected for FR104/VEL-101. Adverse events were those conventionally observed in kidney transplantation. Pharmacological monitoring made it possible to optimize exposure to FR104/VEL-101 and to maintain high receptor occupancy during the one-year follow-up. With a follow-up of 1 year in all patients, not only no acute rejection under FR104/VEL-101 was observed, and notably no acute rejection episodes occurred after discontinuation of tacrolimus, but also no immunization against the donor occurred. One of the key challenges in organ transplantation remains calcineurin inhibitors alternatives with effective immunosuppressive treatments and minimal side effects, particularly on renal function in order to preserve patients' quality of life, and long-term control of post-transplant immune reaction.

* *Urology and Nephrology* Transplant Institute *(ITUN)*

*** Center for Research in Transplantation and Translational Immunology (CR2TI)*

DETAILS OF THE PRESENTATIONS
OSE IMMUNOTHERAPEUTICS ***"First Use of FR104, an Anti-CD28 Molecule in Human Kidney Transplantation, Interim Analysis"*** - Rapid Fire Oral Abstract Session - Abstract 1050 - Tuesday, June 04 - 3:50PM – 4 :00PM G. J. Blancho, *Institute of Transplantation - Urologie - Nephrologie (ITUN), Centre Hospitalier Universitaire, Nantes, France*
VELOXIS PHARMACEUTICALS ***"Safety, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Fixed-Dose, Subcutaneous (SQ) Administration of VEL-101, an Anti-CD28 Pegylated Monoclonal Antibody Fragment, in Healthy Participants"*** - Rapid Fire Oral Abstract Session - Abstract 1049 - Tuesday, June 04 - 3:40PM 3:50PM S. Tremblay [{1}], A. Abaigar[{2}], P. Allton[{1}], D. Sardinha[{1}], S. Patel[{1}], U. Meier-Kriesche[{1}], K. Shah[{1}], J. Maynard[{3}], B. Otulana[{1}], *[{1}]Veloxis Pharmaceuticals, Cary, NC, [{2}]CTI Clinical Trial & Consulting Services, Bilbao, Spain, [{3}]CTI Clinical Trial & Consulting Services, Cincinnati, OH*
CENTER FOR TRANSPLANTATION SCIENCES, MASSACHUSETTS GENERAL HOSPITAL, HARVARD UNIVERSITY, BOSTON ***"Combined blockade of the CD154 and CD28 co-stimulation pathways attenuates pathogenic alloimmunity and prolongs survival in cynomolgus cardiac allografts"*** - Rapid Fire Oral Abstract Session - Abstract 860 - Tuesday, June 04 - 9:45AM 9:55PM Kohei Kinoshita[1], A Maenaka[1], Z Habibabady[1], I Ileka1, M Ma[1], V Diaz[1], T Zhang[3], N O'Neill[3], I Rosales[2], S Fogarty[4], P Maguire[4], B Daugherty[4], S Lederman[4], U Meier-Kriesche[5], N Poirier[6], A Azimzadeh[1,3], R Pierson III[1], [1]*Center for Transplantation Sciences, Massachusetts General Hospital, Boston,* [2] *Department of Pathology, Massachusetts General Hospital, Boston, ,* [3] *University of Maryland School of Medicine, Baltimore,* [4] *Tonix Pharmaceuticals,* [5] *Veloxis Pharmaceuticals,* [6] *OSE Immunotherapeutics*

ABOUT FR104/VEL-101

FR104/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. FR104/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.

ABOUT VELOXIS PHARMACEUTICALS

Veloxis Pharmaceuticals, an Asahi Kasei company, is a fully integrated specialty pharmaceutical company committed to improving the lives of transplant patients. Headquartered in Cary, N.C., 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 OSE IMMUNOTHERAPEUTICS

OSE Immunotherapeutics is a biotech company dedicated to developing first-in-class assets in immuno-oncology (IO) and immuno-inflammation (I&I).
The Company's current well-balanced first-in-class clinical pipeline includes:

- **Tedopi®** (immunotherapy activating tumor specific T-cells, off-the-shelf, neoepitope-based): this cancer vaccine is the Company's most advanced product; positive results from the Phase 3 trial (Atalante 1) in Non-Small Cell Lung Cancer patients in secondary resistance after checkpoint inhibitor failure. Other Phase 2 trials, sponsored by clinical oncology groups, of Tedopi® in combination are ongoing in solid tumors.
- **OSE-279** (anti-PD1): first positive results in the ongoing Phase 1/2 in solid tumors.
- **OSE-127** - *lusvertikimab* (humanized monoclonal antibody antagonist of IL-7 receptor); ongoing Phase 2 in Ulcerative Colitis (sponsor OSE Immunotherapeutics); ongoing preclinical research in leukemia (OSE Immunotherapeutics).
- **FR-104/VEL-101** (anti-CD28 monoclonal antibody): developed in partnership with Veloxis Pharmaceuticals, Inc. in transplantation; ongoing Phase 1/2 in renal transplant (sponsor Nantes University Hospital); successful Phase 1 in the US (sponsor Veloxis Pharmaceuticals, Inc.).
- **Anti-SIRPα monoclonal antibody** developed in partnership with Boehringer Ingelheim in advanced solid tumors and cardiovascular-renal-metabolic diseases (CRM); positive Phase 1 dose escalation results in monotherapy and in combination; Phase 2 in CRM diseases planned to be initiated end of 2024.
- **OSE-230** (ChemR23 agonist mAb) developed in partnership with AbbVie in chronic inflammation.

OSE Immunotherapeutics expects to generate further significant value from its three proprietary drug discovery platforms, which are central to its ambitious goal to deliver next-generation first-in-class immunotherapies:

- **Pro-resolutive mAb platform** focused on targeting and advancing inflammation resolution and optimizing the therapeutic potential of targeting Neutrophils and Macrophages in I&I. **OSE-230** (licensed to AbbVie) is the first candidate generated by the platform, additional discovery programs ongoing on new pro-resolutive GPCRs.

- **Myeloid Checkpoint platform** focused on optimizing the therapeutic potential of myeloid cells in IO by targeting immune regulatory receptors expressed by Macrophages and Dendritic cells. **BI 765063** and **BI 770371** (licensed to Boehringer Ingelheim) are the most advanced candidates generated by the platform. Ongoing additional discovery programs, in particular with positive preclinical results obtained in monotherapy with new anti-**CLEC-1** mAbs.

- **BiCKI® Platform** is a bifunctional fusion protein platform built on the key backbone component of anti-PD1 combined with a new immunotherapy target to increase anti-tumor efficacy.

Additional information about OSE Immunotherapeutics assets is available on the Company's website: www.ose-immuno.com. Click and follow us on X and LinkedIn.

Contacts

Sylvie Détry
sylvie.detry@ose-immuno.com

Nicolas Poirier
Chief Executive Officer
nicolas.poirier@ose-immuno.com

French Media: FP2COM
Florence Portejoie
fportejoie@fp2com.fr
+33 6 07 768 283

U.S. Media Contact
RooneyPartners LLC
Kate Barrette
kbarrette@rooneypartners.com
+1 212 223 0561

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 April 30, 2024, including the annual financial report for the fiscal year 2023, 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.