OSE Immunotherapeutics Builds a Strong R&D Strategy Through Innovative First-in-Class Multi-Platform Programs

Nantes, France – November 8, 2022, 6:00 p.m. CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) presents scientific updates in oral and poster presentations selected for international conferences: the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting in Boston, MA, November 8 – 12 and the Protein & Antibody Engineering Summit (PEGS) Europe 14th Annual Meeting in Barcelona, Spain, November 14 – 16. The communications feature the latest research on pre-IND programs from the pioneering Myeloid and BiCKI® platforms, namely presentations on OSE-230 (first pro-resolutive monoclonal antibody) in chronic inflammation, CLEC-1 (new myeloid immune checkpoint) and BiCKI®-IL-7 (new bifunctional therapy targeting PD-1 and IL-7) in immuno-oncology.

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, comments*: "We are very proud to share our latest scientific advances with the international scientific community on our innovative research platforms delivering next-generation first-in-class immunotherapies".*

Dr Aurore Morello, Head of Research of OSE Immunotherapeutics, explains: *"The communications highlight the potential therapeutic value of our 3 pre-IND assets. BiCKI®-IL-7, our bispecific anti-PD1/IL-7 program, presents an innovative cytokine approach, selectively targeting tumor-specific T-cells to improve the quality and durability of memory T-lymphocyte responses. CLEC-1 is our novel myeloid checkpoint beyond the SIRPα/CD47 axis. OSE-230 stands as the first pro-resolutive agonist monoclonal antibody, capable to clear chronic neutrophil infiltrates and to inhibit the pathogenic NETosis* process and fibrosis".*

Myeloid Platform

OSE-230 program in the Resolution of Inflammation (PEGS Europe 2022)

Resolution of inflammation is triggered by pro-resolving lipids activating GPCRs (G-Protein Coupled Receptor) targets. The ChemR23 GPCR is expressed on inflammatory myeloid immune cells, such as macrophages and neutrophils, and is over-expressed in tissues affected by chronic inflammatory diseases, such as lung inflammatory diseases or severe IBD (Inflammatory Bowel Disease) unresponsive to anti-TNF or anti-integrin therapies. ChemR23's over-expression is associated with chronic neutrophil accumulation in damaged tissues. OSE-230 is the first monoclonal antibody (mAb) to activate a pro-resolutive GPCR target (ChemR23). Its innovative mechanism of action drives inflammatory neutrophil tissue clearance through apoptosis and inhibition of the pathogenic NETosis* process. This mAb triggered resolution demonstrated positive preclinical efficacy in chronic colitis or chronic arthritis models with significant decrease in tissue fibrosis and restoration of tissue healing.

CLEC-1 program in Immuno-Oncology (SITC 2022)

CLEC-1 is a novel myeloid immune checkpoint beyond the SIRPα/CD47 axis inhibiting key functions of myeloid cells and hence limiting anti-tumor responsiveness of T-lymphocytes. Myeloid cells can accumulate in the tumor microenvironment and deregulate the immune activation of T-lymphocytes. The academic collaboration with Dr Elise Chiffoleau's team** highlights that CLEC-1 inhibition represents a novel target for cancer immunotherapy. The latest data presented at the SITC 2022 show the ability of CLEC-1 to sense dead or stress tumor cells through the identification of a CLEC-1 protein ligand (CLEC-1 ligand) over-expressed in cancer cells. Mechanistically, CLEC-1's expression by dendritic cells controls the cross-presentation of dead-cell tumor associated antigens and hence CD8+ T-cell cross-priming. Reversely, the absence of CLEC-1 increases the phagocytosis of tumor cells by macrophages *in vivo*. Proprietary anti-CLEC-1 mAbs increase survival in monotherapy in orthotopic model of hepatocellular carcinoma while combination with chemotherapy increases preclinical tumor eradication in colon carcinoma model.

<u>BiCKI® Platform</u>

BiCKI®-IL-7 program in Immuno-Oncology (SITC 2022)

BiCKI®-IL-7, the most advanced candidate from the BiCKI® platform, is a bifunctional therapy which targets PD-1 and at the same time provides selectively the IL-7 pro-survival cytokine to PD1-expressing T-cells. BiCKI®-IL-7 restores exhausted T-cell function, disarms Treg suppressive activity and extends stem-like memory T-cells, the key T-cell subpopulation associated with anti-PD(L)1 clinical responses. This bifunctional immunotherapy preferentially delivers the IL-7 pro-survival cytokine to the right T-cells (tumor-specific T-cells expressing high level of PD1) and at the right place (PD1-expressing T-cells located in the tumor microenvironment and in the draining lymph nodes where the anti-tumor response is initiated and amplified). The latest data presented at the SITC 2022 show high IL-7 receptor (IL-7R) pathway expression in TILs (Tumor-Infiltrating Lymphocytes) and tumor-specific T-cell clonotypes, predictive of long-term ICI (Immune Checkpoint Inhibitor) clinical responses. Reversely, decreased IL-7R pathway expression is associated with metabolic stress and apoptosis of tumor-specific T-cells. Redirecting IL-7 selectively on PD1 + T-cells provides stemness, proliferative and survival signals to tumor-specific T-cells inducing durable responses. Additional data presented provides a strong rationale for selective delivery of IL-7 to tumor-specific T-cells to sustain long-lasting preclinical response, as well as selective proliferation and survival of stem-like memory T-cells *in vivo*.

SITC 2022 communications

- **Title: *"IL7R TME expression correlates with immunotherapy response and is associated with T-cell stemness with decreased apoptosis"*** (abstract #826), poster presentation by I. Girault et al.
- **Title: *"Anti-PD-1/IL-7v bispecific antibody promotes TCF1+ stem like T-cells expansion and long-lasting in-vivo efficacy"*** (abstract #1366), poster presentation by A. Morello et al.
- **Title: *"Blockade of the myeloid CLEC-1 checkpoint enhances antitumor responses and tumor antigen cross-presentation"*** (abstract #484), poster presentation by V. Gauttier, I. Baccelli et al.

PEGS 2022 communication

- **Title: "*Agonist Anti-ChemR23 Antibody for Inflammatory Diseases*"**, oral presentation in the session "Biotherapeutics for GPCR Targets" on November 16th at 5:30pm by N. Poirier.

** NETosis is a program for formation of neutrophil extracellular traps (NETs), which consists of modified chromatin decorated with bactericidal proteins from granules and cytoplasm. Recent research has highlighted that neutrophils, and in particular NETs that can be released upon activation, have central roles in the initiation and perpetuation of systemic autoimmune disorders and trigger complex and chronic inflammatory responses that lead to organ damage and fibrosis.*

*** Collaborative academic program between OSE Immunotherapeutics and Dr Elise Chiffoleau's research teams (Center for Research in Transplantation and Translational Immunology (CR2TI), UMR1064, INSERM, Nantes University at Nantes University Hospital, https://cr2ti.univ-nantes.fr/research/team-1).*

ABOUT OSE Immunotherapeutics

OSE Immunotherapeutics is a biotech company dedicated to developing first-in-class assets in immuno-oncology and immuno-inflammation. 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): advanced preclinical stage.
- **OSE-127/S95011** (humanized monoclonal antibody antagonist of IL-7 receptor) developed in partnership with Servier; ongoing Phase 2 in ulcerative colitis (sponsor OSE Immunotherapeutics) and ongoing Phase 2a in Sjögren's syndrome (sponsor Servier); ongoing pre-clinical research in leukemia (OSE Immunotherapeutics).
- **VEL-101/FR104** (anti-CD28 monoclonal antibody): developed in partnership with Veloxis Pharmaceuticals, Inc. in transplantation; ongoing Phase 1/2 in renal transplant (sponsor Nantes University Hospital); Phase 1 ongoing in the US (sponsor Veloxis Pharmaceuticals, Inc.).
- **BI 765063** (anti-SIRPα monoclonal antibody 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, in particular with anti-PD-1 antibody ezabenlimab; BI sponsored international Phase 1b ongoing clinical trial in combination with ezabenlimab alone or with other drugs in patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) and hepatocellular carcinoma (HCC).

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

- **BiCKI® platform** focused on immuno-oncology (IO) is a bispecific fusion protein platform built on the key backbone component of anti-PD1 combined with a new immunotherapy target to increase anti-tumor efficacy. BiCKI-IL-7 is the most advanced BiCKI® candidate targeting anti-PD1xIL-7.
- **Myeloid platform** focused on optimizing the therapeutic potential of myeloid cells in IO and immuno-inflammation (I&I). **OSE-230** (ChemR23 agonist mAb) is the most advanced candidate generated by the platform, with the potential to resolve chronic inflammation by driving affected tissues to tissue integrity.

Additional information about OSE Immunotherapeutics assets is available on the Company's website: www.ose-immuno.com

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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 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.