OSE Immunotherapeutics Presents Clinical and Preclinical Data from its Immuno-Oncology Portfolio

At the 2023 American Association for Cancer Research Annual Meeting

- **BI 765063, first-in-class SIRPα inhibitor on the SIRPα/CD47 myeloid pathway in advanced solid tumors.**
- **OSE-127, monoclonal immunomodulatory antibody targeting the CD127 receptor, the alpha chain of the interleukin-7 receptor (IL-7R) in Acute Lymphoblastic Leukemia.**
- **BiCKI®-IL-7, bifunctional therapy targeting PD1 and IL-7 to sustain exhausted T cell function and to disarm Treg suppressive activity.**

Nantes, France – April 18, 2023, 7:30 a.m. CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) announces three presentations at the American Association for Cancer Research (AACR) Annual Meeting in Orlando (Florida), April 14-19, 2023. The presentations include the first data on biomarker analyses from the Phase 1 study of BI 765063 (anti-SIRPα monoclonal antibody on the CD47/SIRPα pathway) in advanced solid tumors. Two other presentations report the latest preclinical updates on OSE-127 (anti-IL-7 receptor antagonist) in hematology and on BiCKI®-IL-7 (new bifunctional therapy targeting PD1 and IL-7).

In addition, preclinical characterization data on CLEC-1 (new myeloid immune checkpoint) binding mechanism will also be presented on April 19.

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, comments: *"We are very pleased to share our latest scientific advances with the leading international cancer scientific community. The solid clinical and preclinical data derived from our innovative research programs in immuno-oncology demonstrate our continued commitment and progress to delivering first-in-class immunotherapies for cancer patients in high need for new therapeutic options."*

BI 765063, a first-in-class selective SIRPα inhibitor on the SIRPα/CD47 myeloid pathway targeting myeloid cells in immuno-oncology, with a strong biological rationale for clinical response.

The escalation Phase 1 clinical trial data on selective SIRPα antagonist BI 765063 showed preliminary clinical efficacy results in monotherapy and in combination with PD1 inhibitor ezabenlimab in patients with advanced solid tumors. A biomarker analysis from this escalation Phase 1 study was performed to characterize the impact of BI 765063 on the tumor environment.

The AACR presentation featured analysis results showing a predictive response of identified biomarkers:

High levels of myeloid cells expressing SIRPα (CD11b+, SIRPα+ myeloid cells) in tumor microenvironment at baseline (but not CD47 tumor cell expression) correlate with longer survival. MDSC (Myeloid-Derived Suppressor Cells) signature in tumor microenvironment at baseline correlates also with clinical response.

Three clinical studies of BI 765063 in combination are currently being conducted:

- NCT05249426: in patients with 1st or 2nd line hepatocellular carcinoma in combination with anti-PD1 ezabenlimab +/- VEGF/Ang2 inhibitor and 2nd line head and neck squamous cell carcinoma in combination with cetuximab or chemotherapy and who received no prior anti-PD-L1 inhibitors (in the United States, Europe and Japan).
- NCT03990233: in patients with microsatellite stable (MSS) advanced colorectal cancer and MSS advanced endometrium cancer whose disease relapsed after standard of care and who received no prior anti-PD-L1 inhibitors (in Europe) (1).
- NCT04653142: in patients with solid tumors (in Japan).

OSE-127, a monoclonal immunomodulatory antibody antagonist of IL-7 receptor, represents a novel promising immunotherapy option in Acute Lymphoblastic Leukemia. (2)

The CD127 receptor is over-expressed by acute lymphoblastic leukemia and is efficiently targeted by the IL-7R-antagonist OSE-127 through macrophage-mediated antibody dependent phagocytosis. Targeting IL-7R CD127 is a promising novel strategy in B-Cell Precursor ALL (BCP-ALL) and T-ALL (T-Cell ALL) since CD127 signalling is important for B- and T-cell development, survival and proliferation. Despite the favourable prognosis of BCP-ALL, relapse remains a clinical challenge and novel targeted immunotherapy options are urgently needed. T-ALL is an aggressive haematological cancer for which treatment options are limited at relapse.

The poster presentation concluded on the strong rationale that OSE-127 may represent a powerful novel immunotherapy option for ALL patients based on a unique dual mechanism of action. This antibody both blocks oncogenic interleukin-7 fuel pathway and simultaneously triggers macrophage-driven phagocytosis of leukemic cells.

This research program, conducted on patient-derived xenograft experiments, is led by OSE Immunotherapeutics in collaboration with Pr. Denis Schewe (Head of the Pediatrics Department, Otto-von-Guericke-University, Magdeburg and formerly from the University Medical Center Schleswig-Holstein of Kiel) and Dr. Lennart Lenk (Department of Pediatrics I, Christian-Albrechts University Kiel and University Medical Center Schleswig-Holstein, Kiel).

BiCKI®IL-7, a bifunctional immunotherapy targeting PD1 and IL-7, represents a high potential asset for cancer patients suffering from immune escape following checkpoint inhibitor treatments.

BiCKI®IL-7, the most advanced candidate from OSE Immunotherapeutics' BiCKI® platform, is a novel bifunctional therapy which targets PD1 and at the same time selectively deliver IL-7 pro-survival cytokine to tumor-specific T-cells expressing PD1. 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.

The presentation reports that anti-PD1/IL-7v BiCKI®-IL-7 showed significant monotherapy anti-tumor efficacy in different *in vivo* models. In addition, BiCKI®-IL-7 showed significant anti-tumor efficacy post-anti-PD-(L)1 failure in a preclinical model, highlighting the clinical potential of BiCKI®-IL-7v in immune checkpoint inhibitor resistant patients.

These results validate the rationale of selective delivery of IL-7 to PD1 tumor-specific T-cells to limit risk of I-O/I-O immunotoxicity and sustain long-lasting proliferation and survival of stem-like CD8 T-cells to strengthen anti-PD-(L)1 therapy.

(1) This Phase 1 clinical trial with BI 765063 is being conducted by OSE Immunotherapeutics as part of a collaboration and license agreement under which Boehringer Ingelheim obtained exclusive rights to BI 765063.

(2) In parallel, OSE-127 is currently being developed in clinical stage in partnership with Servier. Two clinical studies are ongoing in inflammatory diseases: a phase 2a study conducted in primary Sjögren's syndrome by Servier and a Phase 2 study conducted in ulcerative colitis by OSE Immunotherapeutics.

Poster presentation details:

Poster BI 765063

Title: "Predictive response biomarkers from Phase I clinical trial of a SIRPalpha inhibitor BI765063, stand-alone and in combination with ezabenlimab, a PD1 inhibitor, in patients with advanced solid tumors"
Session Category: Clinical Research Excluding Trials
Session Title: Biomarkers of Therapeutic Benefit 2
Date & Time: April 17, 2023 - 9:00 AM - 12:30 PM
Location: Poster Section 39, Poster Board 3
Poster Number: 2129

Poster OSE-127

Title: "CD127 is expressed by acute lymphoblastic leukemias and is efficiently targeted by the IL7R-antagonist OSE-127 through macrophage-mediated antibody dependent phagocytosis"
Session Category: Immunology
Session Title: Therapeutic Antibodies 3
Session Date and Time: April 17, 2023 - 1:30 PM - 5:00 PM
Location: Poster Section 24
Poster Board Number: 4

Poster BiCKI®-IL-7

Title: "Anti-PD-1/IL-7v bispecific antibody promotes TCF1+ stem like CD8 T cells expansion and long-lasting in vivo efficacy"
Session Category: Immunology
Session Title: Therapeutic Antibodies 3
Session Date and Time: April 17, 2023 - 1:30 PM - 5:00 PM
Location: Poster Section 24
Poster Board Number: 2

Poster CLEC#1*

Title: **"**CLEC-1 inhibitory myeloid checkpoint blockade enhances antitumor responses and tumor phagocytosis by macrophages""
Session Category: Immunology
Session Title: Immune Checkpoints
Session Date and Time: April 19, 2023 - 9:00 AM – 12:30 PM
Location: Section 23
Poster Board Number: 2

Poster CLEC#2*

Title: "TRIM21 is a novel endogenous partner of the inhibitory myeloid checkpoint CLEC-1 involved in tumor antigen cross-presentation"
Session Category: Immunology
Session Title: Immune Checkpoints
Session Date and Time: April 19, 2023 - 9:00 AM - 12:30 PM
Location: Poster Section 23
Poster Board Number: 9

** 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): ongoing Phase 1/2 in solid tumors or lymphomas (first patient included). OSE-279 is the backbone therapy of the BiCKI® platform.
- **OSE-127/S95011** - *lusvertikimab* (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).
- **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); Phase 1 ongoing in the US (sponsor Veloxis Pharmaceuticals, Inc.).
- **OSE-172/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 in monotherapy and in combination, in particular with anti-PD-1 antibody ezabenlimab; 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.