OSE Immunotherapeutics Presents Additional Preclinical Updates on CLEC-1, a Novel Myeloid Immune Checkpoint in Immuno-Oncology

At the 2023 American Association for Cancer Research (AACR) Annual Meeting

- **CLEC-1 inhibitory myeloid checkpoint blockade enhances antitumor responses and tumor phagocytosis by macrophages.**
- **TRIM21 has been identified by OSE Immunotherapeutics in collaboration with Dr Elise Chiffoleau's team [(1)] as a novel interaction partner for CLEC-1, and the CLEC-1/TRIM21 axis as a new target for cancer immunotherapy.**

Nantes, France – April 20, 2023, 7:30 a.m. CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) presented two additional posters reporting the latest research updates on CLEC-1 (new myeloid immune checkpoint), from its Myeloid platform, at the 2023 American Association for Cancer Research (AACR) Annual Meeting held in Orlando (Florida) on April 14-19.

CLEC-1, novel myeloid immune checkpoint target

The academic collaboration conducted with Dr Elise Chiffoleau's team at the Center for Translational Research in Transplantation and Immunology [(1)] has led to identify CLEC-1 as a checkpoint, a receptor expressed by myeloid cells inhibiting key pro-phagocytic and T-cell cross-priming functions and hence limiting anti-tumor immune responses.

Dr Aurore Morello, Head of Research of OSE Immunotherapeutics, comments: *"Altogether, the data presented at the AACR meeting demonstrate that CLEC-1 acts as a new immune checkpoint in myeloid cells and highlight the CLEC-1/new ligand TRIM21 axis as a new target for cancer immunotherapy. These latest data generated from our teams' collaboration provide evidence to further support the preclinical evaluation of monoclonal antagonist antibodies targeting CLEC-1. Importantly, this opens the way for further upcoming translational clinical studies aiming at developing a new myeloid immune checkpoint therapy releasing the breaks on macrophages and dendritic cells."*

"CLEC-1 inhibitory myeloid checkpoint blockade enhances antitumor responses and tumor phagocytosis by macrophages".

CLEC-1 blockade with proprietary monoclonal antibodies increases tumor rejection in monotherapy and synergizes with chemotherapy. Anti-CLEC-1 monoclonal antibodies profoundly impacted the tumor environment: frequencies of invigorated dendritic cells and macrophages, activated cells and memory T-cells were increased, while frequencies of immunosuppressive myeloid cells and PD1-expressing T-cells were largely decreased.

The findings presented also revealed a previously unrecognized function for CLEC-1 in myeloid cells as a specific sensor of non-homeostatic cell death. The data showed that the absence of CLEC-1 suppresses tumor growth and hinders immunosuppressive tumor microenvironment.

"TRIM21 is a novel endogenous partner of the inhibitory myeloid checkpoint CLEC-1 involved in tumor antigen cross-presentation".

TRIM21, an intra-cellular Fc receptor and E3 ubiquitin ligase, is identified as a novel interaction partner for CLEC-1 (a discovery published in *'Sciences Advances'* last November: Drouin et al., 2022). The research demonstrated the functional relevance of CLEC-1 interaction with its ligand. High TRIM21 expression is predictive of worse overall survival in patients with hepatocellular carcinoma, pancreatic cancer, or glioma. Mechanistically, CLEC-1 inhibition enhances the capacity of dendritic cells to cross-present tumor antigens to T lymphocytes, a process known to be regulated by TRIM21 through its E3 ubiquitin ligase activity. Antagonist anti-CLEC-1 or anti-TRIM21 antibodies are therefore being evaluated to further confirm the involvement of the newly identified CLEC-1 interaction with TRIM21 in the regulation of CLEC-1's function as an inhibitory myeloid checkpoint.

(1) *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).*

Poster presentation details:

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

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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Contacts

OSE Immunotherapeutics
Sylvie Détry
sylvie.detry@ose-immuno.com
+33 1 53 198 757

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

Investor Relations
Thomas Guillot
thomas.guillot@ose-immuno.com
+33 6 07 380 431

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.