OSE Immunotherapeutics Announces Publication of Peer-Reviewed Data on CLEC-1, its Novel Myeloid Immune Checkpoint in '*Science Advances*'

Nantes, France – November 21, 2022, 6:00 p.m. CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) today announced the publication of data in the peer-reviewed journal *Science Advances* on a first-in-class preclinical program with CLEC-1, its novel myeloid immune checkpoint target for cancer immunotherapy.

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.

The article, entitled ***"CLEC-1 is a death sensor that limits antigen cross-presentation by dendritic cells and represents a target for cancer immunotherapy"*** [(2)], reports on fundamental discoveries and preclinical results showing that CLEC-1 is a novel myeloid checkpoint interacting with a new ligand TRIM-21 and highlighting the therapeutic potential of CLEC-1 antagonist antibodies (Abs) as innovative cancer immunotherapy.

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, commented: "*We are very pleased to have this data on CLEC-1 published in the journal 'Science Advances'. It recognizes both the significant therapeutic potential of the research program from our cutting-edge myeloid platform in immuno-oncology and the quality of our strategic academic collaboration with Dr Elise Chiffoleau' team on CLEC-1. These findings on the first CLEC-1-ligand over-expressed in several human tumor types, such as pancreatic, liver or colon cancers with high unmet needs, alongside novel preclinical efficacy data generated with our proprietary antagonist antibodies, open the pathway for future clinical development beyond the myeloid SIRPα/CD47 axis, with anti-SIRPa antibody already in clinical development at OSE.*"

Elise Chiffoleau, INSERM scientist, said: "*We are honored by the publication of our collaborative research with OSE Immunotherapeutics in this journal with the highest scientific standards. Our teams worked closely on CLEC-1 target and identified for the first time TRIM-21 as an endogenous ligand induced during cell stress and/or death. CLEC-1 is a death receptor and binds to dead cells induced by secondary necrosis. We have discovered that CLEC-1 represents a novel type of myeloid checkpoint within the C-Type Lectin family controlling the ability of type-1 dendritic cells to activate T-cell responses against tumor antigens. Furthermore, we have selected anti-human CLEC-1 monoclonal antibodies able to prolong survival in colon carcinoma and hepatocarcinoma preclinical models and recapitulating the tumor-microenvironment modifications observed in these same models by genetic ablation of CLEC-1A with more CD8+ T cells, and a shift in myeloid cell composition towards fewer immunosuppressive myeloid cells (MDSCs - Myeloid Derived Suppressor Cells - and macrophages) and more mature dendritic cells.*"

The results described in the research article highlight that:

- Overall, CLEC-1 genetic deletion leads to a profound reinvigoration of the tumor immune microenvironment by enhancing infiltrates of dendritic cell (antigen presenting cells), increasing memory and activated T lymphocyte infiltrates, decreasing infiltrates of exhaustion marker PD1-expressing T lymphocytes and limiting the recruitment of immunosuppressive cells such as myeloid derived suppressor cells (MDSCs).
- Importantly, CLEC-1 blockade using monoclonal antibody treatment demonstrates robust anti-tumor activity, also by reinvigorating the tumor immune microenvironment in several preclinical oncology models, thereby faithfully recapitulating the effect of CLEC-1 genetic deletion in the context of human CLEC-1-expressing mice. 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.

(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).*

(2) ***"****CLEC-1 is a death sensor that limits antigen cross-presentation by dendritic cells and represents a target for cancer immunotherapy."*
Marion Drouin, Javier Saenz, Vanessa Gauttier, Bérangère Evrard, Géraldine Teppaz, Sabrina Pengam, Caroline Mary, Ariane Desselle, Virginie Thepenier, Emmanuelle Wilhelm, Emmanuel Merieau, Camille Ligeron, Isabelle Girault, Maria-Dolores Lopez, Cynthia Fourgeux, Debajyoti Sinha, Irène Baccelli, Aurélie Moreau, Cedric Louvet, Régis Josien, Jérémie Poschmann, Nicolas Poirier, Elise Chiffoleau.

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** *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

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.