OSE Immunotherapeutics Announces Latest Preclinical Efficacy Data on its Anti-IL-7 Receptor Antagonist OSE-127 in Acute Lymphoblastic Leukemia at the 2022 American Society of Hematology (ASH) Annual Meeting

Nantes, France – December 12, 2022, 7:30 a.m. CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) presented the latest preclinical data on the use of its anti-IL-7 receptor (IL-7R) antagonist OSE-127 for the treatment of B- and T-Cell Acute Lymphoblastic Leukemia (B- and T-ALL) at the American Society of Hematology (ASH) annual meeting [(1)] on December 11, 2022 (New Orleans, Louisiana). This oral presentation has received the merit-based "Abstract Achievement Award" from the peer-review committee.

The preclinical data on OSE-127 presented at ASH was generated from a collaborative research program between OSE Immunotherapeutics and the University Medical Center Schleswig-Holstein in Kiel (Germany). This collaboration is using patient-derived samples and in-vivo xenograft models to evaluate the therapeutic potential of anti-IL-7R antagonist OSE-127 in targeting and blocking the high and dysregulated IL-7R-expression observed in 84% of B- or T-Acute Lymphoblastic Leukemia (ALL) patients.

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, comments*: "We are very pleased to share our collaborative research on OSE-127 in B-ALL and T-ALL with the international scientific hematology research community. By targeting the oncogenic IL-7 pathway and simultaneously triggering leukemia clearance through macrophage-driven phagocytosis, OSE-127 demonstrated great therapeutic potential in both B-ALL and T-ALL patient-derived xenograft experiments to address a significant unmet need for a wide spectrum of leukemia subtypes".*

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), leading the research program in collaboration with OSE Immunotherapeutics, state: *"Treatment options for T-ALL remain very limited and there is an urgent need for novel immunotherapy approaches to reduce toxicity and to target relapsed or refractory disease in ALL patients. Due to its dual mode of action comprising both antibody-dependent cellular phagocytosis induction and IL-7R-pathway blockade, OSE-127 may represent a promising novel immunotherapy option for ALL patients, including cases with dysregulated IL-7R signaling, particularly in combination with standard of care polychemotherapy. When translated into the clinic, OSE-127 could significantly improve ALL-therapy and the outcome of relapsed/refractory disease."*

The 2022 ASH presentation, entitled "The IL7R-Antagonist OSE-127 Blocks Acute Lymphoblastic Leukemia Development Via a Dual Mode of Action" [(2)], reported on the preclinical efficacy of OSE-127 in ALL and on the mechanism of action underlying its anti-leukemic efficacy:

- In a large prospective ALL patient cohort, IL-7R positivity was detected in more than **84% of cases**.

- Mechanistically, OSE-127 efficiently targeted leukemic cells not only via its IL-7R antagonist activity but also through macrophage-mediated antibody dependent phagocytosis (ADCP).
- In vivo efficacy of OSE-127 treatment correlated with IL-7R expression levels on patient leukemic cells, independently of IL-7R pathway activity, highlighting IL-7R as a potential predictive biomarker for OSE-127 efficacy in ALL.
- High preclinical efficacy has been observed both in minimal residual disease (MRD) as well as in overt-leukemia patient derived xenograft (PDX) models.
- OSE-127 demonstrated preclinical in vivo efficacy as monotherapy in **96% of tested B- and T-ALL Patient Derived Xenografts** (PDXs), including samples from relapse and refractory patients.
- Standard of Care (SOC) poly-chemotherapy synergized with OSE-127 treatment, resulting in increased **survival** in overt-leukemia settings, with **clearance of the disease** in 56% of SOC + OSE-127 treated cases.

Additional patent applications were filed in 2021 and 2022 to strengthen the global intellectual property of OSE-127 by covering the use of anti-IL-7R antagonist antibodies with macrophage-redirected phagocytic activity for the targeted treatment of IL-7R-positive cancers.

About Acute Lymphoblastic Leukemia (ALL)

Acute lymphoblastic leukemia (ALL) is a heterogeneous group of lymphoid disorders resulting from clonal proliferation of immature lymphocytes of B-cell (85%) or T-cell (15%) lineages [(3)] in the blood, bone marrow, and other lymphoid organs.

Although it is one of the most common cancers in children, accounting for approximately 25% of all childhood cancer diagnoses among children under 15 years of age [(4)], adults can also develop ALL. About 40% cases of ALL diagnosed are in adults and among them about 50% present refractory disease or undergo relapse under current conventional therapies [(4)].

The American Cancer Society estimates that almost 6,660 new cases of ALL will be diagnosed in the United States in 2022[(5)]. In Europe, 7,000 cases of ALL are diagnosed each year [(6)]. The number of patients in Japan was reported to be about 5,000 in a survey by the Japanese MHLW in 2017. The number of diagnosed incident cases of acute lymphocytic leukemia (ALL) in Europe, US, Japan and China is estimated to achieve 26,482 cases in 2029[(7)].

(1) ASH Publication – Blood (2022) 140 (Supplement 1): 1045 - 1047
(2) Lennart Lenk, PhD, Irène Baccelli, PhD, Dorothee Winterberg, PhD, Anna Dietterle, Frédérique Corallo, MD, Julien Taurelle, Emma Narbeburu, Anna Laqua, PhD, Beat Bornhauser, PhD, Jean-Pierre Bourquin, MD, PhD, Fotini Vogiatzi, PhD, Martin Schrappe, MD, Gunnar Cario, Monika Brüggemann, MD, Nicolas Poirier, PhD and Denis Martin Schewe, MD*
(3) DeVita, Jr. VT, Hellman S, Rosenberg SA, eds.; Cancer: Principles and Practice of Oncology, 10th ed.; Lippincott-Raven, Philadelphia, PA; 2014.
(4) Childhood Acute Lymphoblastic Leukemia Treatment (PDQ®)–Health Professional Version, accessed October 2022
(5) American Cancer Society. Key 2022 Statistics for Acute Lymphocytic Leukemia (ALL). Available at: https://www.cancer.org/cancer/acute-lymphocytic-leukemia/about/key-statistics.html#references., accessed October 2022
(6) Gatta G, van der Zwan JM, Casali P, et al. Rare cancers are not so rare: The rare cancer burden in Europe. Eur. J. Cancer. 2011; 47: 2493-2511.
(7) Global Data

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, for which completion of patient enrollment has been announced in November 2022, and a Phase 2 study conducted in ulcerative colitis by OSE Immunotherapeutics.

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 primary 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.