OSE Immunotherapeutics Updates on Anti-IL-7 Receptor Antagonist OSE-127/S95011, a Breakthrough Approach in Chronic Inflammatory Autoimmune Diseases and Hematology

- **Positive Phase 1 clinical results published in *'The Journal of Immunology'* (online)**
- **Two ongoing Phase 2 clinical trials in Ulcerative Colitis and primary Sjögren's Syndrome**
- **Positive preclinical efficacy data in Acute Lymphoblastic Leukemia**

Nantes, France – February 22, 2023, 6:00 p.m. CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) today announced the online publication in the peer-reviewed 'The Journal of Immunology' of positive Phase 1 clinical results with OSE-127/S95011, an anti-IL-7 receptor (IL-7R) antagonist, and provides an overall update on the product, which is being developed in immuno-inflammation through two ongoing Phase 2 clinical trials in Ulcerative Colitis (sponsor OSE) and in primary Sjögren's Syndrome (sponsor Servier), and in hematology where promising preclinical data in Acute Lymphoblastic Leukemia (ALL) has already been reported.

OSE-127/S95011 is being developed in partnership with Servier* via a collaboration agreement. Two clinical studies evaluating OSE-127/S95011 are ongoing: a Phase 2a study conducted by Servier in primary Sjögren's syndrome and a Phase 2 study conducted by OSE Immunotherapeutics in ulcerative colitis (UC).

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, comments: *"We are very pleased to have this peer-reviewed data on OSE-127 published in 'The Journal of Immunology'. It recognizes the value of our Phase 1 data which marked an important step towards understanding the safety and efficacy of OSE-127. It confirms the interest in the novel and differentiated mechanism of action of the only full-antagonist of IL-7R for the treatment of chronic autoimmune diseases. OSE-127 is the only compound targeting IL-7R under clinical development in the primary Sjögren's syndrome and ulcerative colitis.*

Based on this strong scientific rationale, we are confident that the ongoing Phase 2 trials conducted by OSE in ulcerative colitis and Servier in primary Sjögren's syndrome will start to establish OSE-127 as a potential new best-in-class treatment for these disabling chronic inflammatory diseases.

Patient enrolment is completed in the Phase 2a trial in primary Sjögren's syndrome, and we are looking forward to the results that are expected in H1 2023.

Besides autoimmune diseases, OSE-127 has also demonstrated great therapeutic potential in Acute Lymphoblastic Leukemia (ALL), a very aggressive tumor arising from B or T cell precursors. Our collaboration with the University of Kiel aims at evaluating the therapeutic potential of OSE-127 in targeting and blocking the high and dysregulated IL-7 receptor-expression observed in more than 80%

Servier is a global pharmaceutical group

of B- or T-ALL patients. Relapse remains a clinical challenge in B-ALL in high-risk patients and treatment options for T-ALL remain very limited. Novel targeted immunotherapy approaches are urgently needed to meet these patients' high medical need."

Peer-reviewed data in 'The Journal of Immunology' with strong rationale for a potential new breakthrough therapeutic approach

An article, selected as 'Top Read' for the March 15th issue, was published online in 'The Journal of Immunology' (online). The publication, entitled "*First-in-Human Study in Healthy Subjects with the Non-Cytotoxic 1 Monoclonal Antibody OSE-127, a Strict Antagonist of the IL-7Rα*" reports on the Phase 1 positive results. These showed a good safety and tolerability profile for OSE-127/S95011, with no signs of significant lymphopenia, cytokine release syndrome or T-cell compartment alterations. All pharmacokinetic and pharmacodynamic parameters were consistent and demonstrated a dose-proportionality across the several dose-levels up to 10 mg/kg. A decreased IL-7 pathway gene signature in human peripheral blood cells has been demonstrated confirming the efficient blockade of the target.

Enrollment completed in Phase 2a clinical trial in primary Sjögren's syndrome (Servier)

- Patient enrollment in the Phase 2a clinical trial of OSE-127/S95011 in primary Sjögren's syndrome conducted by Servier was completed in October 2022.
- This international, randomized, double-blind, placebo-controlled, Phase 2a study is designed to evaluate the efficacy and tolerance of the monoclonal antibody OSE-127/S95011 in primary Sjögren's syndrome. The multicenter study in the United States, Australia and Europe includes 48 patients. Results are expected in H1 2023.
- The estimated prevalence of Sjögren's varies from 2.5 million to 4 million patients (Sjögren's Syndrome Foundation) in the US alone, with a worldwide estimate of up to 7.7 million in the key markets (US, France, Germany, Italy, Spain, UK and Japan) by the year 2024 (Global Data Research).
- To date there is no treatment approved in altering the course of the disease for primary Sjögren's syndrome, a disease with significant unmet medical need, and only a few molecules are being evaluated in Phase 2/3 clinical development.

Phase 2 clinical trial in ulcerative colitis (UC) with interim analysis (OSE Immunotherapeutics)

- The randomized, double-blind Phase 2 clinical trial aims to assess the efficacy and safety of OSE-127/S95011 versus placebo in patients with moderate to severe active UC who have previously failed or lost response or are intolerant to previous treatment(s).
- An interim futility analysis was conducted on the prespecified first 50 patients (i.e., 33% of the total patient enrollment in the study) having completed the Induction Phase. After completion of the planned safety and efficacy assessment for futility, the trial's Independent Data Monitoring Committee (IDMC) recommended the continuation of the study.

- UC is a debilitating and chronic inflammatory bowel disease which affects 3.3 million patients in US, Europe and Japan [(1)] representing 12.2 per 100,000 people by year [(2)]. Despite broad options, remission rates are only 25-30% [(3)] leaving most patients without satisfactory treatments.

- UC is characterized by a heavy burden on patients' lives with a strong medical need for new therapeutic options.

Positive preclinical efficacy data in B- and T-Cell Acute Lymphoblastic Leukemia (B- and T-ALL)

- The research program of IL-7R antagonist OSE-127 in Acute Lymphoblastic Leukemia (ALL) is being conducted through 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 OSE-127 in targeting and blocking the high and dysregulated IL-7R-expression observed in 84% of B- or T-ALL patients.

- The latest preclinical data on the use of OSE-127 for the treatment of B- and T-Cell ALL (B- and T-ALL) were presented at the American Society of Hematology (ASH) annual meeting in December 11, 2022. This oral presentation has received the merit-based "Abstract Achievement Award" from the peer-review committee. The presentation, entitled "*The IL7R-Antagonist OSE-127 Blocks Acute Lymphoblastic Leukemia Development Via a Dual Mode of Action*", 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 cell positivity was detected in more than 84% of cases.
  . 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.

- The American Cancer Society estimated that almost 6,660 new cases of ALL will have been diagnosed in the United States in 2022[(4)]. In Europe, 7,000 cases of ALL are diagnosed each year[(5)]. The number of patients in Japan was reported to be about 5,000 in a survey by the Japanese MHLW (Ministry of Health, Labour and Welfare) in 2017. The number of diagnosed incident cases of ALL in Europe, US, Japan and China is estimated to achieve 26,482 cases in 2029[(6)].

A global patent protection

Given the potential of OSE-127, OSE Immunotherapeutics has strengthened its global intellectual property until 2037. This has been achieved through the grant of a large number of patents worldwide, notably in major territories including Europe, the US, China and Japan.

These patents protect anti-IL-7R antagonist OSE-127 and its therapeutic applications, in particular in autoimmune and inflammatory diseases.

(1) EvaluatePharma
(2) Updated Incidence and Prevalence of Crohn's Disease and Ulcerative Colitis in Olmsted County, Minnesota (1970-2011). Loftus EV et al. October 2014.
(3) Drugs Context. 2019; 8: 212572 –doi: 10.7573/dic.212572

(4) 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 Oct. 2022
(5) 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.
(6) Global Data

ABOUT OSE-127/S95011

OSE-127/S95011 is a monoclonal immunomodulatory antibody targeting the CD127 receptor, the alpha chain of the interleukin-7 receptor (IL-7R) that induces a powerful antagonist effect on effector T lymphocytes. Interleukin-7 is a cytokine which specifically regulates the tissue migration of human effector T lymphocytes. The blockage of IL-7R prevents the migration of pathogenic T lymphocytes while preserving regulator T lymphocytes which have a positive impact in autoimmune diseases.

ABOUT ULCERATIVE COLITIS (UC)

Ulcerative colitis is a chronic disease of the large intestine, in which the lining of the colon becomes inflamed and develops tiny open sores, or ulcers. This condition is the result of the immune system's overactive response. UC affects 3.3 million patients in US, Europe and Japan [(1)]. Despite broad options, remission rates are only 25-30% [(2)] leaving most patients without satisfactory treatments. 15% of patients [(3)] fail to respond to all therapies and get surgery as last option.

(1) *EvaluatePharma*
(2) *Drugs Context. 2019; 8: 212572 –doi: 10.7573/dic.212572*
(3) *Scientific Reports volume 10, Article number: 12546 (2020)*

ABOUT SJÖGREN'S SYNDROME

Primary Sjögren's syndrome is an autoimmune disease characterized by lymphocytic infiltration of salivary and lacrimal glands, causing dryness of mouth and eyes and negatively impacting quality of life. Other organs can be affected. Primary Sjögren's syndrome is one of the most common chronic systemic autoimmune diseases, with a prevalence of 60.82 per 100,000 population according to an epidemiological meta-analysis of primary Sjögren's syndrome.
https://ard.bmj.com/content/74/11/1983#

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 [(1)] 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 [(2)], 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 [(2)].

(1) DeVita, Jr. VT, Hellman S, Rosenberg SA, eds.; Cancer: Principles and Practice of Oncology, 10th ed.; Lippincott-Raven, Philadelphia, PA; 2014.
(2) Childhood Acute Lymphoblastic Leukemia Treatment (PDQ®)–Health Professional Version, accessed October 2022

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

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.