OSE Immunotherapeutics Announces:

Positive Phase 3 Data from its Cancer Vaccine in Lung Cancer Patients with Resistance to Previous Immunotherapy Published in *Annals of Oncology*

Leading medical journal highlights peer-reviewed, randomized phase 3 clinical results with Tedopi® *off-the-shelf* T-cell epitope-based cancer vaccine monotherapy compared to chemotherapy in advanced non-small cell lung cancer (NSCLC) patients in secondary resistance to immune checkpoint inhibitors (ICI), with statistically significant and clinically meaningful data on:

- **Overall survival,**
- **Safety,**
- **and Quality of Life.**

Nantes, France – September 11, 2023, 6:00pm CET – OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE) today announced the peer-reviewed publication in *Annals of Oncology** of the randomized Phase 3 clinical trial (Atalante-1**) on T-cell epitope cancer vaccine Tedopi® in HLA-A2 positive patients with advanced or metastatic NSCLC in monotherapy in third line NSCLC with secondary resistance to immune checkpoint inhibitors (ICI).

Tedopi® is a novel T-cell epitope-based cancer vaccine targeting five tumor-associated antigens, an activating and differentiated *off-the-shelf* immunotherapy expanding tumor specific T-lymphocytes in HLA-A2 cancer patients. The article, titled *"Randomized Open-Label Controlled Study of Cancer Vaccine OSE2101 Versus Chemotherapy in HLA-A2-positive Patients with Advanced Non-Small Cell Lung Cancer with Resistance to Immunotherapy: ATALANTE-1"* features positive data from the randomized international Phase 3 study showing that novel cancer vaccine Tedopi® improves overall survival with a better safety and quality of life profile in monotherapy compared to chemotherapy in HLA-A2 positive patients with advanced or metastatic NSCLC who have progressed at least 12 weeks after sequential treatment with chemotherapy and immune checkpoint inhibitors (ICI).

Prof. Benjamin Besse, Director of Clinical Research at Gustave Roussy Institute (IGR, Villejuif, France), and Principal Investigator of the Atalante-1 clinical trial, commented: *"Tedopi® is the first cancer vaccine to demonstrate positive results on survival in a randomized Phase 3 trial in advanced and metastatic NSCLC cancer patients in 3rd line. A significant reduction of the risk of death by 41% was achieved with a better safety profile and a maintained quality of life. This study, conducted in patients*

* *Annals of Oncology*, Impact Factor 2023: 50.5, the journal of the European Society for Medical Oncology and the Japanese Society of Medical Oncology, provides rapid and efficient peer-review publications on innovative cancer treatments or translational work related to oncology and precision medicine.

** First results presented by Pr. Benjamin Besse at the 2021 ESMO congress (European Society for Medical Oncology), cf. press release of September 20, 2021.

with secondary resistance to immunotherapy, compared Tedopi® monotherapy with standard of care docetaxel or pemetrexed chemotherapies. Further evaluation is clearly warranted in a second line of treatment of advanced and metastatic NSCLC, to potentially make this cancer vaccine available to hard-to-treat patients in failure and with high medical needs."

Nicolas Poirier, Chief Executive Officer of OSE Immunotherapeutics, commented*: "Tedopi® is the most advanced therapeutic cancer vaccine in clinical development. These Phase 3 data, demonstrating the promising effects, have now been validated in the internationally recognized journal 'Annals of Oncology', a major achievement for all involved so, in particular, we'd like to thank warmly the investigators, the patients and their families for their commitment. This Phase 3 positive monotherapy data and moreover the recently announced positive Phase 1 and 2 results using other personalized cancer vaccines in combination to treat resected melanoma or pancreatic cancer patients, highlight the promise of this new therapeutic class of vaccines. The clinical value of our results, re-activating specifically the anti-tumor immune responses, is particularly interesting in patients showing immune escape from checkpoint inhibitors. The confirmatory pivotal Phase 3 trial in preparation (first patient expected early 2024) is planned to support the regulatory registration of Tedopi® in secondary resistance to immune checkpoint inhibitors, this time in second line NSCLC treatment."*

Main results of the first Phase 3 clinical trial of Tedopi® in HLA-A2+ patients with NSCLC

This Phase 3 clinical trial has demonstrated a significant therapeutic benefit in patients with secondary resistance [(1)] to immune checkpoint inhibitors (ICI) defined as patients with failure to platinum-based chemotherapy followed by a minimum of 12 weeks ICI treatment (main analysis of the trial). Tedopi® demonstrated a favorable benefit/risk ratio versus standard of care (SoC) docetaxel or pemetrexed in advanced HLA-A2+ NSCLC patients with secondary resistance to ICI.

The main results were:

Improved efficacy

1. Overall survival (primary endpoint) was statistically significantly improved for Tedopi®:
   HR=0.59 (95% CI: 0.38, 0.91) in favor of the Tedopi® arm, reduced risk of death by 41%.
   44.4% overall survival rate at 1 year with Tedopi® versus 27.5% with chemotherapy. A clinically meaningful gain in median overall survival of 3.6 months in favor of the Tedopi® arm with Tedopi® OS at 11.1 months versus 7.5 months for SoC (p=0.017).
2. Post progression survival was also significantly longer in the Tedopi® arm (7.7 months versus 4.6 months; p=0.004, HR=0.46).

Improved safety profile and Quality of Life

1. The ECOG performance status[(2)], of maintained general health condition with time to ECOG deterioration was significantly longer in the Tedopi® arm (9.0 months versus 3.3 months; p=0.006; HR=0.43).
2. A better quality of life was observed with Tedopi® (p= 0.04). (Global health status: p=0.045; Role Functioning: p=0.025).
3. A good tolerance profile of Tedopi® with fewer Severe Adverse Events grade 3-5 (Tedopi® 38% vs SoC 68%, p<0.001). No Treatment Emergent Adverse Effects of concern in the Tedopi® arm.

[(1)] *Secondary resistance is defined as failure after a minimum of 12 weeks of Immune checkpoint inhibitor given in sequential chemotherapy - checkpoint inhibitors treatment (Kluger HM et al; Journal for immunoTherapy of Cancer 2020 Defining tumor resistance to PD-1 pathway blockade: recommendations from the first meeting of the SITC Immunotherapy Resistance Taskforce)*

[(2)] *The ECOG score is a performance scale used to quantify the general health condition of a patient. It is subdivided into 5 grades from 0 to 5, ranging from fully active (0) to fully disabled, then to death (5).*

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** - *lusvertikimab* (humanized monoclonal antibody antagonist of IL-7 receptor); ongoing Phase 2 in Ulcerative Colitis (sponsor OSE Immunotherapeutics); ongoing preclinical 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 immunotherapies:

- **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 May 2, 2023, including the annual financial report for the fiscal year 2022, 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.