OSE Immunotherapeutics Presents New "Cis-Demasking" Bispecific Technology for the Design of Cytokine Drugs with Improved Therapeutic Index

NANTES, France, October 17, 6:00pm CET - OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE), today announced it will be presenting its novel OSE-CYTOMASK Cis-Demasking[1] cytokine technology in oral presentations selected for international conferences:

- The Festival of Biologics in Basel, Switzerland (October 17, 2024)
- The 16th Annual Protein & Antibody Engineering Summit (PEGS) Europe Summit in Barcelona, Spain (November 7, 2024)
- The Antibody Therapeutics Xchange in Brussels (November 18, 2024)

OSE-CYTOMASK is an innovative proprietary non-cleavable linker technology to create a new class of regulated and targeted cytokine therapeutics that deliver highly active medicines with improved therapeutic index. The presentations highlight the rational design of the technology through two first preclinical programs based on anti-PD1 masked cytokine (IL-2, IL-15) in oncology with conditional Cis-Demasking and Cis-Potentiation of tumor-specific T cells expressing PD1 or other immune targets.

Aurore Morello, Head of Research, OSE Immunotherapeutics, said: *"We are very happy to present our novel OSE-CYTOMASK technology at upcoming leading scientific conferences. Our novel linker technology allows conditional Cis-Demasking of cytokine, through PD1-targeting on tumor-specific T cells, without relying on protease-cleavable technology or mutagenesis of cytokine to abrogate off-tumor activity associated with significant toxicity of the majority of cytokines from this class of drugs. The high preclinical efficacy observed in monotherapy and good tolerance profile of the first two drug candidates selected open the way to a potential novel first-in-class treatment for patients in high need of new therapeutic options in oncology."*

Nicolas Poirier, Chief Executive Officer, OSE Immunotherapeutics, adds: *"We are proud of the achievements from our research team on the advancement of these programs. This highly innovative technology promises to unleash the full potential of cytokines in oncology by dramatically increasing the therapeutic index of this class of drugs. We are also interested in potential applications of this innovative technology in autoimmune and inflammatory diseases."*

Immunostimulatory cytokines are a highly potent class of drug to reactivate the immune system against tumors. Their narrow therapeutic index is associated with significant peripheral toxicity and limited drug exposure in the tumor microenvironment (TME), limiting their clinical development.

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[1] *Cis-Demasking: Bispecific antibodies (*) have the capability to target cells either in a Cis- targeting (on the same cell) or in a Trans-binding orientation (between two different cells). Cis-Demasking bispecific technology targets two antigens expressed on the same cell, with one masked modality (eg. Cytokine) and enabling conditional activity of the cytokine on the desired immune cell types upon antibody binding.*

(*) Segués A. et al. International Review of Cell and Molecular Biology 2022.

Current conditional cytokine masking approaches relying on theoretical demasking activity in the TME with cleavable linker technologies by enzymes produce more selectively by the tumors have already demonstrated their limitation due to the heterogenous protease expression in tumors (variable on-tumor activation across patients) and non-specific protease expression in non-tumor sites (off-tumor cytokine activity). We have engineered an innovative non-cleavable recombinant linker technology allowing specific conditional delivery of cytokine activity only where needed based on an original targeted Cis-Demasking mechanism independent of proteases expression.

OSE-CYTOMASK technology has been used first to implement our proprietary anti-PD1 BiCKI® platform in order to improve the therapeutic index of highly active cytokines (eg., IL-2, IL-15…). The Company presented two first preclinical programs with anti-PD1/masked IL-2 and anti PD1/masked IL-15 with robust preclinical efficacy demonstrated in monotherapy leading to a high rate of anti-tumor response and eradication in different models (eg. orthotopic pancreatic tumor, melanoma or colon cancer) in the absence of peripheral toxicity in dose-response illustrating significantly improved therapeutic index of both IL-2 or IL-15 using the OSE-CYTOMASK technology.

Presentations: details

Festival of Biologics (October 17), Basel
Presenter: Aurore Morello, PhD., Head of Research, OSE Immunotherapeutics
"OSE- Cytomask Technology: Cis-Demasking Cytokine Technology for targeted Delivery"
October 17, 11:30

Protein & Antibody Engineering Summit (PEGS) Europe Summit (November 7), Barcelona
Presenter: Nicolas Poirier, PhD, Chief Executive Officer, OSE Immunotherapeutics
"OSE-CYTOMASK: Cis-Demasking Cytokine Technology with Non-Cleavable Linker"
November 7, 16:40

Antibody Therapeutics Xchange (November 18), Brussels
Presenter: Aurore Morello, PhD., Head of Research, OSE Immunotherapeutics
"Addressing challenges faced for optimal bi-specific and Immunocytokines engineering"
November 18, 09:05 - 10:05

About OSE Immunotherapeutics

OSE Immunotherapeutics is a biotech company dedicated to developing first-in-class assets in immuno-oncology (IO) and immuno-inflammation (I&I).
The Company's current well-balanced first-in-class clinical pipeline includes:

- **Tedopi®** (immunotherapy activating tumor specific T-cells, off-the-shelf, neoepitope-based): most advanced therapeutic cancer vaccine in development; positive results from a randomized Phase 3 trial (Atalante 1) in Non-Small Cell Lung Cancer patients in third-line secondary resistance after checkpoint inhibitor failure. Ongoing randomized registration Phase 3 study (Artemia) in second-line NSCLC in HLA-A2+ patients with secondary resistance. Other Phase 2 trials, sponsored by clinical oncology groups, of Tedopi® in combination are ongoing in solid tumors.

- **OSE-127** - *Lusvertikimab* (humanized monoclonal antibody antagonist of IL-7 receptor); Positive Phase 2 (CoTikiS) study in Ulcerative Colitis; ongoing preclinical research in leukemia.
- **OSE-279** (anti-PD1): first positive results in the ongoing Phase 1/2 in solid tumors.
- **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); successful Phase 1 in the US (sponsor Veloxis Pharmaceuticals, Inc.).
- **Anti-SIRPα monoclonal antibody** developed in partnership with Boehringer Ingelheim in advanced solid tumors and cardiovascular-renal-metabolic diseases (CRM); positive Phase 1 dose escalation results in monotherapy and in combination; Phase 2 in CRM diseases planned to be initiated end of 2024.
- **ABBV-230** (ChemR23 agonist mAb) developed in partnership with AbbVie in chronic inflammation.

OSE Immunotherapeutics expects to generate further significant value from its three proprietary drug discovery platforms, which are central to its ambitious goal to deliver next-generation first-in-class immunotherapies:

- **Pro-resolutive mAb platform** focused on targeting and advancing inflammation resolution and optimizing the therapeutic potential of targeting Neutrophils and Macrophages in I&I. **ABBV-230** (licensed to AbbVie) is the first candidate generated by the platform, additional discovery programs ongoing on new pro-resolutive GPCRs.
- **Myeloid Checkpoint platform** focused on optimizing the therapeutic potential of myeloid cells in IO by targeting immune regulatory receptors expressed by Macrophages and Dendritic cells. **BI 765063** and **BI 770371** (licensed to Boehringer Ingelheim) are the most advanced candidates generated by the platform. Ongoing additional discovery programs, in particular with positive preclinical results obtained in monotherapy with new anti-**CLEC-1** mAbs.
- **BiCKI® Platform** is a bifunctional fusion protein platform built on the key backbone component of anti-PD1 combined with a new immunotherapy target to increase anti-tumor efficacy by "cis-potentiating" tumor-specific T cells. A first program has been acquired by Boehringer Ingelheim. **OSE-CYTOMASK** is an innovative technology to create cytokine therapeutics with improved therapeutic index.
- **mRNA Therapeutic platform** allows local delivery into the inflammatory site of innovative immunotherapies encoded by RNA to locally controls and/or suppress immune responses and inflammation.

Additional information about OSE Immunotherapeutics assets is available on the Company's website: www.ose-immuno.com. Click and follow us on X and LinkedIn

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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 April 30, 2024, including the annual financial report for the fiscal year 2023, 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.