OSE Immunotherapeutics Announces Publication Supporting Additional New Mechanism of Action for Selective Antibody Antagonist of SIRPα BI 765063 in the Journal of Clinical Investigation

The peer-reviewed publication identifies a new T-cell exclusion mechanism attributed to CD47-SIRPα signaling; selective SIRPα blockade overcomes this 'Don't Find Me' signal from tumors

Nantes, France, October 22, 2020, 6:00PM CET – OSE Immunotherapeutics (ISIN: FR0012127173; Mnemo: OSE) today announced a publication in the prestigious **Journal of Clinical Investigation** (JCI) of translational and preclinical study data in rodent *in vivo* and human *ex vivo* models characterizing the efficacy and mechanism of action of BI 765063, formerly OSE-172, the first selective antibody antagonist of SIRPα-mediated "Don't Eat Me" signals. Importantly, for the first time ever the OSE R&D team has identified a complimentary SIRPα-mediated "Don't Find Me" mechanism by which tumors evade immune detection by preventing T lymphocytes from entering the tumor core.

BI 765063 is currently being evaluated in a Phase 1 clinical trial conducted in patients with advanced solid tumors. The ongoing Phase 1 study is a dose finding study of the myeloid checkpoint inhibitor BI 765063 administered as a single agent and in combination with Boehringer Ingelheim's monoclonal antibody PD-1 antagonist BI 754091, a T lymphocyte checkpoint inhibitor. The study is conducted by OSE Immunotherapeutics as part of a collaboration and license agreement under which Boehringer Ingelheim obtained exclusive rights to BI 765063 and for which OSE has already received €30 million, in a deal worth up to €1.1 billion in milestones, plus royalties on sales.

Nicolas Poirier, Chief Scientific Officer of OSE Immunotherapeutics, commented: "O*ur studies show that macrophages are inhibited when in contact with tumors expressing CD47 via the SIRPα pathway and thus they no longer secrete chemokines - small protein mediators which attract immune cells. By overexpressing CD47, tumors not only induce a 'Don't Eat Me' signal to macrophages but, as we discovered, they also induce a 'Don't Find Me' signal and consequently T lymphocytes are no longer attracted to the tumor core by the secretion of chemokines from the macrophages. Our new anti-SIRPα strategy reverses this major mechanism of resistance named 'T-cell exclusion' by releasing the break on T lymphocyte chemotaxis and migration into the heart of the tumors."*

The article entitled: "*Selective SIRPα blockade reverses tumor T cell exclusion and overcomes cancer immunotherapy resistance*" (**https://www.jci.org/articles/view/135528/ga**) reports that the OSE's R&D team discovered that the anti-SIRPα strategy reverses a major mechanism of resistance and escape to immunotherapy called "T-cell exclusion," meaning that the activated T lymphocytes cannot penetrate the tumor core and remain blocked at its periphery. In *in vivo* models of resistance to anti-PD-1, PD-L1 or 4-1BB costimulation activators, studies demonstrated that T lymphocytes initially blocked at the tumor's margin could penetrate efficiently into the tumor when blocking SIRPα in parallel. Crossing this barrier is associated with positive modulation of macrophage expression and secretion of chemokines allowing the penetration of T lymphocytes into the heart of the tumor.

ABOUT BI 765063

BI 765063, a monoclonal antibody antagonist of the key myeloid cell checkpoint inhibitor SIRPα selectively blocks the SIRPα/CD47 interaction and thus increases the function of myeloid cells: phagocytosis of tumor cells by macrophages and presentation of tumor antigens by dendritic cells. BI 765063 is also a selective inhibitor of SIRPα that by virtue of this specificity and lack of binding and blocking of a very similar receptor called SIRPɣ, ensures that response of T lymphocytes is retained to enable T cell-mediated tumor killing.

ABOUT OSE Immunotherapeutics

OSE Immunotherapeutics is a clinical-stage biotechnology company focused on developing and partnering therapies to control the immune system for immuno-oncology and autoimmune diseases. The company has several scientific and technological platforms including neoepitopes and agonist or antagonist monoclonal antibodies, all ideally positioned to fight cancer and autoimmune diseases. Its first-in-class clinical and preclinical portfolio has a diversified risk profile:

- **Tedopi®** (innovative combination of neoepitopes): the company's most advanced product; **positive results for Step-1 of the Phase 3 trial** (Atalante 1) in **Non-Small Cell Lung Cancer** post checkpoint inhibitor failure.
  In **Phase 2 in pancreatic cancer** (TEDOPaM, sponsor GERCOR) in monotherapy and in combination with checkpoint inhibitor Opdivo®.
- **BI 765063** (OSE-172, anti-SIRPα monoclonal antibody): developed in **partnership with Boehringer Ingelheim**; myeloid checkpoint inhibitor in **Phase 1 in advanced solid tumors**.
- **FR104** (anti-CD28 monoclonal antibody): **positive Phase 1 results**; **Phase 2-ready asset in autoimmune diseases or in transplantation**.
- **OSE-127** (humanized monoclonal antibody targeting IL-7 receptor): developed in **partnership with Servier**; **positive Phase 1 results**; two independent **Phase 2** planned in **ulcerative colitis** (OSE sponsor) and in **Sjögren's syndrome** (Servier sponsor) to start in Q4 2020.
- **BiCKI®**: **bispecific fusion protein** platform built on the key backbone component anti-PD-1 (OSE-279) combined with new immunotherapy targets; 2nd generation of PD-(L)1 inhibitors to increase **antitumor efficacity**.
- **CoVepiT**: a **prophylactic vaccine** against **COVID-19**, developed using SARS-CoV-2 optimized neo-epitopes. **Positive preclinical and human ex vivo results in August 2020**, **clinical trial expected to start end of 2020/early 2021**.
  Due to the COVID-19 crisis, accrual of new patients in the clinical trial TEDOPaM is temporarily suspended and initiation timelines for both Phase 2 trials of OSE-127 could be impacted during the coming months.

For more information:
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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 2020, including the annual financial report for the fiscal year 2019, 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.