OSE Immunotherapeutics Presents Positive Preclinical Results and Human Ex Vivo Data for OSE-127 (Effi-7) to Support Next Clinical Applications in Inflammatory Bowel Diseases

at the « Federation of Clinical Immunology Societies » (FOCIS) Conference

- **OSE-127 Blocks Pathological Homing of Human T Lymphocytes to Inflamed Colon**
- **Ex vivo, OSE-127 Reduces Production of Gamma Interferon by Human Proinflammatory Bowel T lymphocytes in Patients' Biopsies**

NANTES, France, June 15, 2017, 6 p.m. CET. - OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnémo: OSE) today presented new data for OSE-127 (Effi-7), an antagonist of the interleukin-7 receptor (IL-7R), at the 2017 Federation of Clinical Immunology Societies held in Chicago from June 14 to 17.

The communication entitled "*IL-7 pathway controls human T cell homing to the gut and culminates in inflammatory bowel disease mucosa*" [(1)] shows efficacy results for OSE-127 in various preclinical acute or chronic colitis models and ex vivo human biopsies.

In preclinical humanized models reconstituted with human T lymphocytes, OSE-127 significantly blocked pathological homing of human T lymphocytes to the inflamed colon thereby preventing destruction of gut mucosa by the T lymphocytes.

In a separate translational study conducted in human in collaboration with Professor Thomas McDonald (Blizard Institute, Barts and the London School of Medicine), OSE-127 significantly reduced production of gamma interferon expressed by proinflammatory mucosal T lymphocytes ex vivo in colon biopsies from patients with inflammatory bowel disease.

Increased expression of IL-7R, IL-7 and genes involved in the IL-7R signalling pathway was observed in the patients' inflammatory colon biopsies and correlates with a lack of response to current immunosuppressive treatments. The expression of the product's target (IL-7R) in human tissues in case of therapeutic escape represents a major clinical interest for OSE-127, with potential identification of responder patients.

Nicolas Poirier, Chief Scientific Officer of OSE Immunotherapeutics, said: *"Strengthened by first-class academic collaborations, our studies demonstrate a differentiated mechanism of action for OSE-127 able to fight pathologic local homing of inflammatory T lymphocytes, key players in the inflammatory bowel disease's chronicity. The strong presence of the product's target in situations of therapeutic escape implies an important medical need as more than 40% of these patients are in therapeutic failure [(2)]. These findings provide additional evidence of OSE-127 therapeutic potential in these patients."*

ABOUT OSE-127

OSE-127 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, especially in the gut. The blockage of IL-7R prevents the migration of pathogenic T lymphocytes while preserving regulator T lymphocytes [3, 4] which have a positive impact in autoimmune diseases.

OSE Immunotherapeutics has signed a license option agreement with Servier in December 2016 for the development and commercialization of OSE-127. Under this agreement, OSE Immunotherapeutics is eligible to receive up to €272 M including a €10.25 M upfront payment and additional payments of €30 M upon the exercise of a two-steps option license until Phase 2 completion in ulcerative colitis. Further payments will be linked to the achievement of clinical development and registration in multiple indications, as well as sales milestones with double-digit royalties on sales.

(1) *"IL-7 pathway controls human T cell homing to the gut and culminates in inflammatory bowel disease mucosa"*
L. Belarif[1,2,3], L. Kermarec[4], V. Daguin[1,2], C. Mary[1,2,3], R. Danger[1,2], A. Kucik[5], T. MacDonald[5], G. Blancho[2,3], P. Naveilhan[4], B. Vanhove[1,2,3], N. Poirier[1,2,3]
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(2) *Sandborn WJ et al; The present and future of inflammatory bowel disease treatments; Gastroenter. Hepatol 12, 438-441 (2016)*

(3) *Powell, N. et al. The transcription factor T-bet regulates intestinal inflammation mediated by interleukin-7 receptor+ innate lymphoid cells. Immunity 37, 674–684 (2012)*

(4) *Yamazaki, M. et al. Mucosal T cells expressing high levels of IL-7 receptor are potential targets for treatment of chronic colitis. J. Immunol. 171, 1556–1563 (2003)*

ABOUT THE « Federation Of Clinical Immunology Societies » (FOCIS)

The annual FOCIS meeting highlights the best science in the field of clinical immunology. In addition, the FOCIS meeting is an incubator for developing scientists and practitioners alike to meet with one another and representatives of the relevant biotech and pharmaceutical industry whose combined support is invaluable to the success of the field of clinical immunology.

ABOUT OSE IMMUNOTHERAPEUTICS

Our ambition is to become a world leader in activation and regulation immunotherapies

OSE Immunotherapeutics is a biotechnology company focused on the development of innovative immunotherapies for immune activation and regulation in the fields of immuno-oncology, auto-immune diseases and transplantation. The company has a balanced portfolio of first-in-class products with a diversified risk profile ranging from clinical phase 3 registration trials to R&D:

In immuno-oncology:

- **Tedopi®, a combination of 10 optimized neo-epitopes** to induce specific T activation in immuno-oncology - **Currently in registration Phase 3 trial advanced NSCLC HLA A2+ patients EU /US -** Orphan Status in the US **- Registration expected in 2019 - A Phase 2 with Tedopi® in combination with a checkpoint inhibitor** in NSCLC is considered in 2017**.**
- **OSE-172 (Effi-DEM), new generation checkpoint inhibitor** targeting the **SIRP-α receptor - In preclinical development** for several cancer models.

In auto-immune diseases and transplantation:

- **FR104,** CD28-antagonist in immunotherapy - **Phase 1 trial completed** – For the treatment of autoimmune diseases and for use with transplantation - **Licensed to Janssen Biotech Inc.** to pursue clinical development.
- **OSE-127 (Effi-7),** interleukin receptor-7 antagonist - **In preclinical development** for inflammatory bowel diseases and other autoimmune diseases. **License option agreement with Servier** for the development and commercialization.

The portfolio's blockbuster potential gives OSE Immunotherapeutics the ability to enter global agreements at different stages of development with major pharmaceutical players.

Immunotherapy is a highly promising and growing market. By 2023 Immunotherapy of cancer could represent nearly 60% of treatments against less than 3% at present * and the projected market is estimated at $67 billion in 2018 **.

There are more than 80 autoimmune diseases that represent a significant market including major players in the pharmaceutical industry with sales towards $10 billion for the main products. The medical need is largely unmet and requires the provision of new innovative products involved in the regulation of the immune system.

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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 Reference Document filed with the AMF on 28 April 2017 under the number R.17-038, including the annual financial report for the fiscal year 2016, 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.