OSE Immunotherapeutics Presents Positive Preclinical Data on Combination of Anti-IL-7 Receptor Lusvertikimab in Chronic Colitis In Oral Presentation at 20th Congress of ECCO

NANTES, France – February 20, 2025, 6:00pm CET - OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE), today presented positive preclinical data on the combination of anti-IL-7 receptor (IL-7R) with anti-IL-12/23 monoclonal antibody (mAb) in chronic colitis at the 20th Congress of ECCO (European Crohn's and Colitis Organization), held from February 19-22, 2025, in Berlin (Germany).

The oral communication, entitled *"Anti-IL-7 Receptor Plus Anti-IL12/23 Combination Induces Complete Histological Normalization in Chronic Colitis"*, presented by Nicolas Poirier, reported that IL-7 drives resistance to anti-IL-23 inhibition. The administration of anti-IL-7R in combination with an anti-IL-12/23 acts synergistically to achieve profound preclinical control of chronic colitis, characterized by complete histological healing.

Nicolas Poirier, CEO of OSE Immunotherapeutics, comments: "*Our latest research shows that IL-7 prevents the inhibitory effect of IL-23 antagonists on the control of human Th17 T lymphocytes. Additionally, IL-7R overexpression in the colon of ulcerative colitis or Crohn's disease patients correlates with high IL-23 expression. We demonstrated that combining anti-IL-7R with anti-IL-12/23 mAb is well tolerated and synergizes to control chronic colitis symptoms in a validated preclinical model. It also demonstrates complete histological normalization compared to monotherapies.*

"Together with the positive efficacy seen in the Phase 2 Lusvertikimab monotherapy clinical results on endoscopic and histological remission in ulcerative colitis, to be presented in the Top-10 highlighted plenary session at ECCO, these latest preclinical data for the combination of the inhibition of upstream (IL-7) and downstream (IL-23) inflammatory mechanisms expand and strengthen the potential positioning of our first-in-class drug candidate in the Immuno-Inflammation (I&I) therapeutic landscape. I would like to warmly thank the OSE research, translational, computational biology and clinical teams for their coordinated efforts in achieving these significant milestones."

More details on the presentation:

- Interleukin-7 (IL-7) drives not only the survival but also the differentiation of human T lymphocytes subsets, such as Th17 (IL-17-secreting pathogenic T lymphocytes). IL-23 is the primary driver of Th17 differentiation, and IL-23 antagonists (currently one of the standards of care in Inflammatory Bowel Diseases [IBD]) inhibit the generation of Th17 cells. However, in the presence of IL-7, IL-23 antagonists lose their inhibitory activity *in vitro*. Combining Lusvertikimab with an anti-IL-23 monoclonal antibody (eg. Guselkumab) restores the inhibition of human Th17 cells in the presence of both IL-7 and IL-23.
- High IL-7R tissue expression has previously been observed in the colon of IBD patients with resistance to anti-TNF or anti-integrin therapies[1]. OSE Immunotherapeutics' R&D team has shown

[1] *Belarif L et al.IL-7 receptor influences anti-TNF responsiveness and T cell gut homing in inflammatory bowel disease. Journal of Clinical Investigation 2019*

that IL-7R is also overexpressed in the mucosa of patients with resistance to anti-IL-12/23 antagonist therapy, and that IL-7R expression correlates with high mucosal IL-23 expression.

- Using a well-validated preclinical chronic colitis model, OSE Immunotherapeutics' R&D team reported that while the IL-12/23 antagonist mAb is efficient, it is not sufficient in monotherapy to achieve complete remission at both macroscopic and histological levels. In contrast, the combination of anti-IL-7R mAb and anti-IL-12/23 mAb has been shown to induce significant reduction of all colitis symptoms (e.g. macroscopic colon weight and length ratio) as well as complete microscopic histological remission and normalization, with no histological lesions, immune cell infiltrates, or epithelial cell hyperplasia. Additionally, a significant decrease in T-lymphocyte immuno-staining was observed in the colon, along with a significant increase in the Foxp3+ to Treg ratio, confirming the original mechanism of action of the IL-7R antagonist.

***Upcoming oral and poster presentations at ECCO'25 congress**:*

Oral Presentation			
Title	Presenter	Session	Date and time
OP36 - "LUSVERTIKIMAB, A FIRST-IN-CLASS IL7 RECEPTOR ANTAGONIST, IN MODERATE TO SEVERE ULCERATIVE COLITIS: RESULTS OF A MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED PHASE II STUDY "	Arnaud Bourreille	Session name: Sustainability in IBD and beyond Session 10: Hot topics in IBD Session hall: Plenary Hall / Hall B	Session date: February 22, 2025 Session time: 08:30 -10:50 Presentation time: 10:10 - 10:20
Selected amongst the Top 10 oral abstracts for 20th Congress of European Crohn's and Colitis Organization (ECCO) Highlights.			
Poster Presentation			
Title	Presenter	Session	
PO916 – "LUSVERTIKIMAB IS EFFICACIOUS IN SEVERE ULCERATIVE COLITIS (UC) PATIENTS WITH HIGH FECAL CALPROTECTIN (FCP): RESULTS FROM THE COTIKIS STUDY"	Walter Reinisch	Poster sessions: February 20, 2025, 10:30 to 18:00 February 21, 2025, 08:00 to 18:00 February 22, 2025, 09:00 to 13:00 Guided poster session: February 21, 2025, 12:40-13:40	

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) that address the unmet patient needs of today and tomorrow. We partner with leading academic institutions and biopharmaceutical companies in our efforts to develop and bring to the market transformative medicines for people with serious diseases. OSE Immunotherapeutics is based between Nantes and Paris and is quoted on Euronext.

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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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.