OSE Immunotherapeutics Reports Full Phase 2 Induction Results for Anti-IL-7R mAb Lusvertikimab in Ulcerative Colitis at the 20th Congress of ECCO

- **Lusvertikimab achieved statistical significance on the primary and secondary endpoints** in moderate to severe active ulcerative colitis (UC) patients during the 10-week induction period of treatment in the randomized, double-blind CoTikiS Phase 2 study. These results were presented in the Top 10 congress highlights oral plenary session at ECCO 2025.
- **Lusvertikimab demonstrated high rates of clinical and endoscopic remission** after 10 weeks of treatment, along with clinically meaningful histological improvement and Histo-Endoscopic Mucosal Improvement (HEMI) rates.
- **Treatment with Lusvertikimab significantly reduced fecal calprotectin (FCP)** after 10 weeks of treatment, an objective biomarker of mucosal inflammation in UC patients and an early predictor of endoscopic and histological responses.
- **Statistically significant efficacy was demonstrated in clinical and endoscopic remission** in the UC patient subgroup with high baseline FCP (>250µg/g).
- **A good safety and tolerability profile was observed** with no clinically relevant safety signals.

NANTES, France – February 24, 2025, 7:30am CET - OSE Immunotherapeutics SA (ISIN: FR0012127173; Mnemo: OSE), presented full efficacy and safety data from the induction period of the randomized, double-blind, placebo-controlled, Phase 2 CoTikiS study of Lusvertikimab (OSE-127) in the Oral and Poster presentations at the 20th Congress of ECCO (European Crohn's and Colitis Organisation), demonstrating meaningful efficacy and a favorable safety profile in moderate to severe active UC patients.

Pr. Arnaud Bourreille, Associate Professor in Gastroenterology at the Institut des Maladies de l'Appareil Digestif, Nantes University Hospital, and Coordinating Investigator of the CoTikiS study, said: *"These full Phase 2 clinical induction results provide strong efficacy data for Lusvertikimab in UC, particularly highlighting the meaningful achievement in the key endpoints of endoscopic remission and histological improvement after only 10 weeks of treatment. The latest data showing high histo-endoscopic mucosal improvement (HEMI) and mucosal healing rates represent a strong signal of efficacy, as they are associated with the prediction of long-term prevention of future relapse and are important for UC patients in need of breakthrough therapeutic options and sustained healing."*

Pr. Walter Reinisch, Director of the IBD Study Group at the Medical University of Vienna, Department of Internal Medicine, Vienna, Austria, commented: *"Lusvertikimab has been shown to significantly decrease FCP, an objective inflammatory biomarker most commonly used in clinical practice to monitor treatment response in patients with ulcerative colitis. These data parallel and confirm the overall results of the primary and secondary endpoints from the CoTikiS study, highlighting the potential of Lusvertikimab as an efficacious therapy for all UC patients, also by normalising increased baseline FCP values."*

Week-10 Induction Period Results in the Global Population[1]

The randomized, double-blind Phase 2 clinical trial CoTikiS evaluated the efficacy and safety of Lusvertikimab versus placebo in 136 patients with moderate to severe active UC who failed or lost response to previous treatment(s)[2]. CoTikiS is a 50-week study, with a 10-week induction period evaluating two doses (450 mg or 850 mg) of Lusvertikimab against placebo, a 24-week open-label extension period (OLE) during which subjects received Lusvertikimab 850 mg infusions every four weeks and a 16-week safety follow-up period free of treatment. The induction data at week 10 in the full population and in the subgroup of severe UC patients with high baseline FCP were presented at ECCO 2025.

The overall induction results from the CoTikiS study show that the two doses evaluated, 450 mg and 850 mg, met the primary efficacy endpoint (Modified Mayo Score) at week 10 and demonstrated statistically significant and clinically meaningful results on secondary endpoints:

Primary End Point at Week 10[3]

Improvement of the Global Disease Activity Index of UC (Modified Mayo Score)

- Lusv 450mg group: difference of -1.16 point versus placebo (p= 0.019)
- Lusv 850mg group: difference of -0.9 point versus placebo (p=0.036)
- 450 + 850mg pooled group: difference of -1.00 point versus placebo (p= 0.010)

Secondary Endpoints at Week 10, included:

- **Clinical remission rate:** 16% for the pooled 450+850 mg group (n=85) versus 4% for placebo (n=49) (Odds ratio = 4.25; p=0.066)
- **Endoscopic improvement rate:** 32% for the pooled group versus 13% for placebo (Odds ratio = 3.29; p=0.027)
- **Endoscopic remission rate:** 25% for the pooled group versus 13% for placebo (Odds ratio = 2.33; p=0.120)
- **Ulcerative Colitis Endoscopic Index of Severity (UCEIS) mean score change:** -1.35 for the pooled group versus -0.32 for placebo (p=0.007)
- **Fecal Calprotectin (FCP):** +189 µg/g for the placebo group, -830 µg/g for the 450mg group (p = 0.009), -635 µg/g for the 850mg group (p=0.018), and -716 µg/g for the pooled group (p=0.004)

Exploratory objectives included histological score analysis (centralized and blinded), such as the number and proportion of patients with histological improvement at Week 10, defined by a Nancy Histological Index (NHI) score of 0 or 1, and the number and proportion of patients with histo-endoscopic mucosal

[1] *An interim futility analysis performed early (approx. 30% of patients) by the IDMC proposed stopping the 450 mg group due to the risk of futility. The 850 mg group was initially considered as the primary analysis; however, in the final analysis, the futility of the 450mg dose group was not confirmed. Statistical Analysis Plan (SAP) Addendum: results of 450mg group of patients were included in the analyses. In addition, the two groups were pooled for the active drug cohort to evaluate a global treatment effect.*

[2] *Previous corticosteroids, immunosuppressive agents or previous biological treatments.*

[3] *OSE Immunotherapeutics Press Release of November 4th 2024: EN_241104_Lusvertikimab-Phase-2.pdf*

improvement at week 10, defined by a NHI ≤ 1 with a Mayo Endoscopic score ≤ 1. Additional histological readouts included Robarts' histological index (RHI) and Geboes score (GS) changes from baseline.

- **Histological Improvement (NHI score ≤ 1) at W10:** Chi-square p < 0.01
  - 45.2% in the 450 mg group (n=31); difference versus placebo of 35.2% (p<0.01)
  - 31.0% in the 850 mg group (n=42); difference versus placebo of 21.0% (p=0.02)
  - 37.0% in the 450 + 850 mg pooled group (n=73); difference versus placebo of 27.0% (p<0.01)
  - 10.0% in the placebo group (n=40)
- **Histo-Endoscopic Mucosal Improvement (HEMI) (NHI score ≤ 1 + MES ≤ 1) at W10:** Chi-square p = 0.02
  - 32.3% in the 450 mg group; difference versus placebo of 24.8% (p<0.01)
  - 14.3% in the 850 mg group; difference versus placebo of 6.8% (p=0.33)
  - 21.9% in the 450+850 mg pooled group; difference versus placebo of 14.4% (p=0.05)
  - 7.5% in the placebo group
- **Histological Geboes score (GS) mean changes from baseline at W10:** Chi-square p = 0.05
  - 450 mg group: -2.9 (SD: 7.2)
  - 850 mg group: -4.2 (SD: 6.1; p<0.01 versus placebo)
  - 450+850 mg pooled group: -3.7 (SD: 6.6; p=0.02 versus placebo)
  - Placebo: -0.7 (SD: 5.1)
- **Histological Robarts Index (RHI) mean changes from baseline at W10:** Chi-square p < 0.01
  - 450 mg group: -3.5 (SD: 12.3)
  - 850 mg group: -8.5 (SD: 10.8; p<0.01 versus placebo)
  - 450+850 mg pooled group: -6.4 (SD: 11.7; p=0.01 versus placebo)
  - Placebo: -0.6 (SD: 9.2)

Week-10 Induction Results in Severe Active UC with High Baseline Fecal Calprotectin

Fecal calprotectin (FCP) is an objective marker of inflammation in UC patients and may predict sustained clinical and endoscopic response. The CoTikiS study included an exploratory endpoint assessing the efficacy of Lusvertikimab 850 mg and 450 mg compared to placebo in patients with FCP > 250 µg/g at baseline, considered the threshold for active and severe inflammatory UC disease.

High baseline FCP (> 250 µg/g) represented 69.5% (n=93) of the total Phase 2 population. Baseline FCP was not different between treatment groups. These additional analyses have shown that Lusvertikimab significantly decreased FCP after 10 weeks of treatment in both dose groups and achieved improvements in clinical and endoscopic outcomes in this UC patient population with active inflammation. These data strengthen the overall results of the primary and key secondary endpoints from the CoTikiS study.

- **Fecal Calprotectin (FCP) decreases at W10**
  - 450 mg group: difference of -1 169 µg/g versus placebo (p=0.025)
  - 850 mg group: difference of -966 µg/g versus placebo (p=0.034)
  - 450+850 mg pooled group: difference of -1 048 µg/g versus placebo (p=0.011)
- **Fecal Calprotectin (FCP) normalization to below 250 µg/g at W10**
  - 38% in the 450 mg group (n=22); difference versus placebo of 20% (p=0.1)
  - 45% in the 850 mg group (n=33); difference versus placebo of 27% (p=0.02)
  - 42% in the 450+850 mg pooled group (n=55); difference versus placebo of 24% (p=0.02)

- 18% in the placebo group (n=38)

- **Improvement of the Global Disease Activity Index of UC (MMS)**
  - 450 mg group; difference of -1.47 point versus placebo (p= 0.011)
  - 850 mg group; difference of -0.95 point versus placebo (p=0.055)
  - 450 + 850 mg pooled group; difference of -1.16 point versus placebo (p= 0.009)

- **Clinical Remission rate at W10:** Fisher-test p < 0.01
  - 28.3% in the 450 mg group; difference versus placebo of 28.3%
  - 9.4% in the 850 mg group; difference versus placebo of 9.4%
  - 16.9% in the 450+850 mg pooled group; difference versus placebo of 16.9%
  - 0% in the placebo group

- **Endoscopic Remission rate at W10**
  - 38% in the 450 mg group; difference versus placebo of 30.5% (p= 0.03)
  - 14% in the 850 mg group; difference versus placebo of 6.7% (p= 0.33)
  - 24% in the 450+850 mg pooled group; difference versus placebo of 16.3% (p= 0.11)
  - 7% in the Placebo group

- **Ulcerative Colitis Endoscopic Index of Severity (UCEIS) mean score change from baseline**
  - 450 mg group; difference of -1.69 point versus placebo (p= 0.003)
  - 850 mg group; difference of -0.74 point versus placebo (p=0.12)
  - 450+850 mg pooled group; difference of -1.12 point versus placebo (p= 0.01)

Safety Profile

Lusvertikimab displayed a good safety profile and was well tolerated, with no difference between both dose groups and placebo in the incidence of drug-related serious adverse events (SAEs), adverse events (AEs) leading to discontinuation, drug-related AE and severe drug-related AEs, opportunistic infections, or infusion reactions during the induction period.

ABOUT ULCERATIVE COLITIS (UC)

Ulcerative colitis is a chronic disease of the large intestine, or colon, and rectum, in which the lining of the gastrointestinal tract becomes inflamed and develops ulcers. This condition is the result of an overactive immune system. UC affects 3.3 million patients in the US, Europe and Japan (1). Despite broad therapeutic options, remission rates are only 25-30%, (2) leaving most patients without satisfactory treatments. 15% of patients (3) fail to respond to all therapies and undergo surgery as a last option.

(1) *EvaluatePharma*
(2) *Drugs Context. 2019; 8: 212572 –doi: 10.7573/dic.212572*
(3) *Scientific Reports volume 10, Article number: 12546 (2020)*

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

Contacts

Fiona Olivier
fiona.olivier@ose-immuno.com

Sylvie Détry
sylvie.detry@ose-immuno.com

France Media Contact
FP2COM
Florence Portejoie
fportejoie@fp2com.fr
+33 6 07 768 283

U.S. Media Contact
Rooney Partners LLC
Kate Barrette
kbarrette@rooneypartners.com
+1 212 223 0561

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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.