EDISON

OSE Immunotherapeutics

Clinical update

Full Lusvertikimab results reflect potential in UC

Pharma and biotech

OSE Immunotherapeutics' final analysis of the CoTikiS trial in ulcerative colitis (UC) confirmed that Lusvertikimab met the primary endpoint with statistical significance, highlighting its potential to offer a clinically meaningful solution for the condition. In our view, this marks a positive step forward for the candidate, which, to our knowledge, has a unique mechanism of action to address chronic inflammatory and autoimmune diseases. We believe that OSE plans to advance this programme to the next stages of development (Phase IIb or Phase III) once a partner is onboard. Based on the encouraging full results, we have increased our probability of success for Lusvertikimab in UC to 35% (from 17%), resulting in a valuation upgrade for OSE to €541.2m or €24.8/share (from €465.7m or €21.3/share previously).

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/22	18.3	(18.0)	(0.96)	0.0	N/A	N/A
12/23	2.2	(23.2)	(1.18)	0.0	N/A	N/A
12/24e	98.5	64.5	2.80	0.0	3.1	N/A
12/25e	86.3	50.9	2.33	0.0	3.7	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Statistically significant & clinically meaningful results

The full CoTikiS results confirmed the potential efficacy and safety of Lusvertikimab in UC. The primary endpoint (improvement of the Modified Mayo Score (MMS) at Week 10) was met with statistical significance at the two tested doses, with the pooled group showing a -1.00 point difference compared to placebo (p=0.01). Key secondary endpoints showed high rates of clinical and endoscopic remission, and in addition, the candidate was found to be comparable to placebo in terms of safety and tolerability, demonstrating its potential as a first-in-class interleukin-7 (IL-7) antagonist. In our view, the decision to advance the programme in partnership represents a sensible strategy, and we highlight that big pharma has shown interest in the disease area, exemplified by Eli Lilly's $3.2bn acquisition of Morphic.

Registrational Tedopi trial remains the top priority

OSE's strategic priority remains the registrational ARTEMIA trial, which commenced in September 2024, assessing Tedopi as a monotherapy in the second-line non-small cell lung cancer setting. We expect interim updates in 2026, top-line results in 2027, and provided the data are positive, a commercial launch from 2028. For a more detailed discussion, we direct readers to our prior note.

Valuation: Upgrades to €541.2m or €24.8 per share

We expect the release of the full data for the Phase II CoTikiS trial to support OSE's discussions with potential partners for Lusvertikimab's next phase of development in UC. We therefore increase our probability of success for the programme to 35%, from 17% previously. This results in our overall valuation for OSE rising to €541.2m or €24.8/share, from €465.7m or €21.3/share previously.

21 November 2024

Price	**€8.65**
Market cap	**€189m**
	€0.89/US$
Gross cash and cash equivalents at 30 June 2024	€80.8m
Shares in issue	21.8m
Free float	65%
Code	OSE
Primary exchange	Euronext Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(12.0)	18.5	86.8
Rel (local)	(7.0)	23.0	88.2
52-week high/low	€10.74		€3.20

Business description

OSE Immunotherapeutics is based in Nantes and Paris in France and is listed on the Euronext Paris exchange. It is developing immunotherapies for the treatment of solid tumours and autoimmune diseases and has established several partnerships with large pharma companies.

Next events

OSE-279: Phase I/II trial update	Q424
Tedopi: ARTEMIA interim updates	2026

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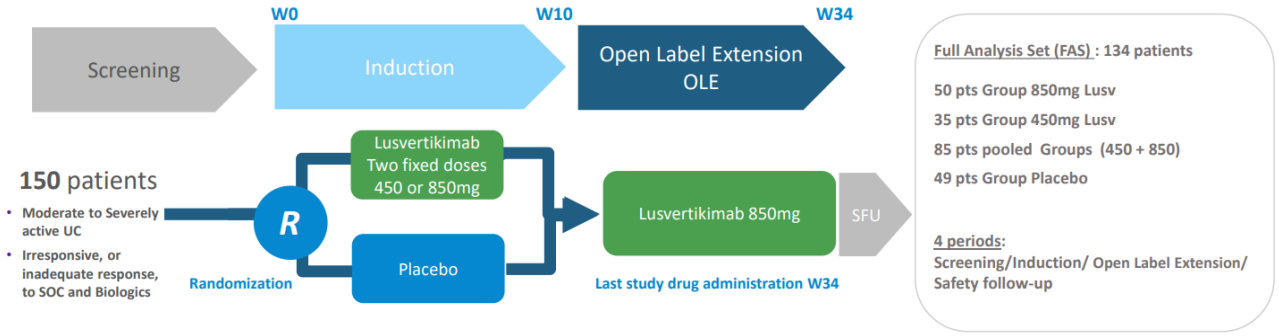
Edison profile page

CoTikiS: A Phase II trial of Lusvertikimab in UC

The CoTikiS trial was a multicentre, randomised, double-blind, placebo-controlled, parallel-group study designed to assess Lusvertikimab in UC patients. The study included participants with moderate to severe UC, who were either unresponsive or had inadequate response to the standard of care and other biologics. Participants were randomised to receive a dose of either 850mg or 450mg, or placebo, and the primary endpoint was based on MMS improvements, a FDA-recognised outcome measure (Exhibit 1). The MMS is a nine-point scale measuring disease activity in patients with UC, based on three parameters – stool frequency, rectal bleeding and endoscopic sub-scores – with each component assigned a score between zero and three, where higher scores correspond to greater disease severity.

134 patients were analysed in the Phase II study in the period up to week 10 (850mg group: n=50; 450mg group: n=35; placebo group: n=49). 120 patients treated with Lusvertikimab participated in the 24-week open-label extension.

Exhibit 1: CoTikiS trial design

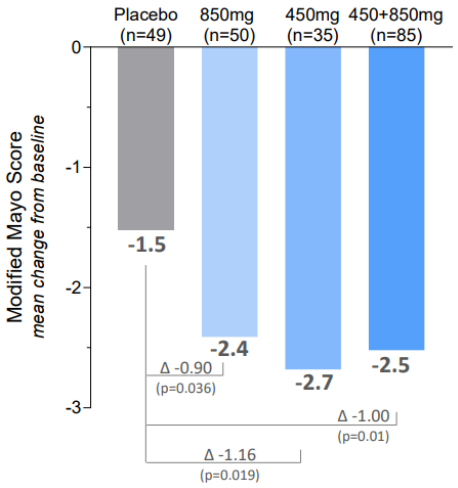


Source: OSE corporate presentation (November 2024). Note: Induction: Lusvertikimab at 450mg/850mg or placebo: IV infusions at Week 0; 2; 6. Analysis at Week 10; Open-label extension at week 10: additional infusions at 850mg every 4 weeks for 6 months.

While the topline results were first published in July 2024, OSE shared the full results in November 2024, including the final analysis of the primary endpoint at week 10. The primary endpoint was met with statistical significance at both tested doses. While the placebo group reported a 1.5-point improvement on the MMS from baseline, the higher dose group of 850mg recorded a 2.4-point improvement, while the 450mg dose cohort saw a 2.7-point improvement. The pooled cohort recorded a 2.5-point improvement from baseline. On a placebo-adjusted basis, these results translated to a 0.9-point difference versus placebo (p=0.036) in the 850mg group, and notably, a higher 1.16-point difference versus placebo (p=0.019) in the 450mg cohort. For the pooled cohort (n=85), a 1.00-point difference versus placebo (p=0.01) was recorded at week 10 (Exhibit 2).

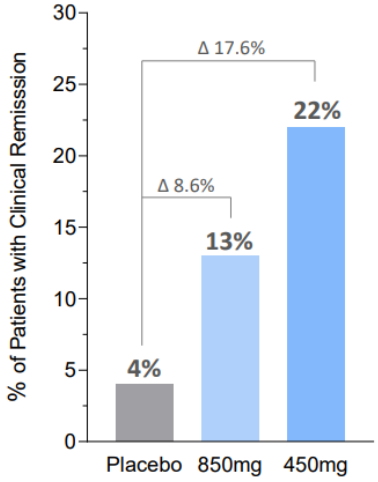
Importantly, the trial also reported encouraging results on key secondary endpoints. One of the key secondary endpoint measures was clinical remission, defined by an MMS of ≤2 points, including a rectal bleeding score of zero. The results showed that, compared to 4% for the placebo group, 13% of patients in the 850mg group (odds ratio, OR, 3.26), and 22% of patients in the 450mg group (OR 6.19), achieved clinical remission, again showing superior result at the lower of the two tested doses (Exhibit 3). Data from the lower dose cohort compares favourably to results from the Phase III induction trial data for AbbVie's second-generation biologic Skyrizi, which received FDA approval in June 2024 for moderate to severe UC. This study evaluated 975 patients (2:1 active arm to placebo) and reported a clinical remission rate of 20.3% for the candidate versus 6.2% for placebo following a 12-week treatment period. However, we caution that while this data provides directional guidance, one cannot draw firm conclusions given the possible differences in patient populations, trial design, treatment dosage and duration.

Exhibit 2: CoTikiS primary endpoint data – MMS improvement



Source: OSE corporate presentation. Note: MMS improvement defined on mean change at week 10 from baseline on the three sub-scores: rectal bleeding, stool frequency, endoscopic.

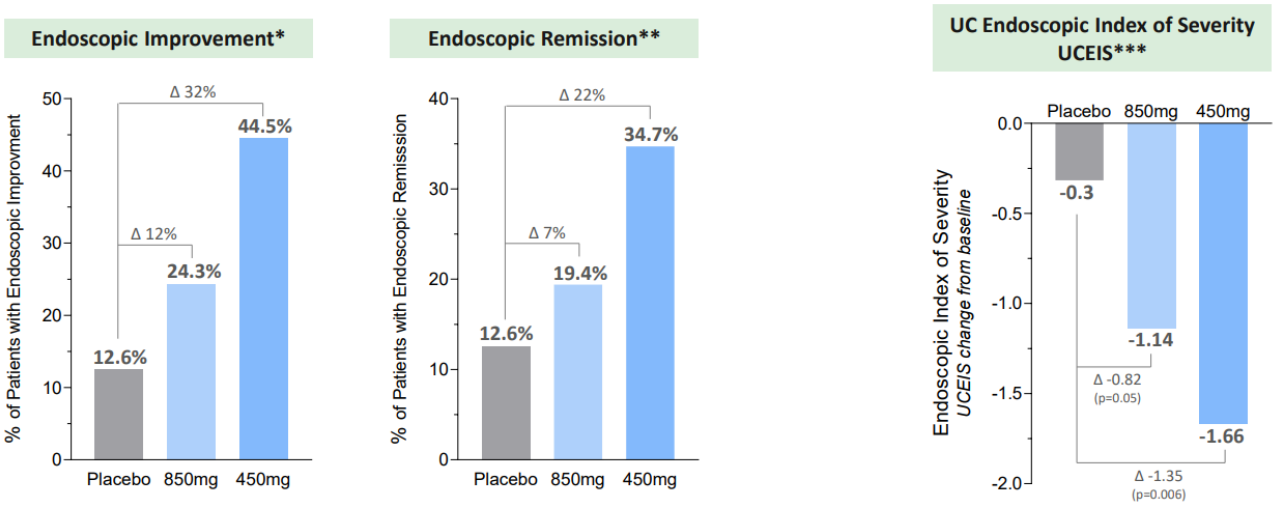
Exhibit 3: CoTikiS clinical remission data



Source: OSE corporate presentation. Note: Clinical remission defined by a modified Mayo score of ≤2 points with no individual sub-score of >1 point and a rectal bleeding sub-score at 0.

For CoTikiS, clinically meaningful benefits were also observed across measures of endoscopic improvement and endoscopic remission, as well as in measures on the UC endoscopic index of severity (UCEIS) (Exhibit 4). As with the primary endpoint measure and the clinical remission data, the 450mg group appeared to outperform the 850mg group. We note that an early interim futility analysis (including c 30% of patients) had proposed an interruption of the 450mg group, and as such, the 850mg group was initially considered for the primary analysis. However, in the final analysis the futility of the 450mg group was not confirmed, and the Statistical Analysis Plan (SAP) Addendum confirmed the inclusion of 450mg group. The two groups were pooled to assess the global treatment effect on the primary efficacy measure.

Exhibit 4: CoTikiS endoscopic improvement, remission and index of severity data



Source: Source: OSE corporate presentation. Notes: *Endoscopic remission defined by endoscopic MMS sub-score =0. **Endoscopic improvement defined by endoscopic Mayo sub-score ≤1 point. ***Defined by three sub-scores: vascular pattern: 0 to 2, bleeding: 0–3, erosions-ulcerations: 0–3.

In terms of safety, Lusvertikimab exhibited a desirable safety and tolerability profile throughout the 24-week label extension period (up to week 34), bolstering its data package. Importantly, there were no differences observed between the two tested doses and placebo in terms of serious

adverse events, adverse events leading to discontinuation, severe drug-related adverse events, opportunistic infections or infusion reactions during the induction period.

Collectively, we view these full results as favourable for the potential of Lusvertikimab to address moderate to severe UC. This latest update indicated that OSE will look to advance the programme with a development partner, which we anticipate could materialise in 2025.

Ulcerative colitis: Seeking novel treatments

UC is a form of inflammatory bowel disease, associated with inflammation around the lining of the large intestines (colon) and rectum. Symptoms include abdominal pain, cramping, bloating, blood in the stool and diarrhoea. The condition most commonly affects people between 15–30 years of age and can range from mild to severe. The prevalence of UC was estimated to be five million cases globally (as of 2023). The US prevalence is estimated to be between 600–990k. According to a report by Market Research Future, the global UC treatment market was valued at US$7.2bn in 2022, and projected to reach US$10.8bn by 2032, at a CAGR of 5.1%.

Standard UC treatment regimens include aminosalicylates (5-ASA drugs) in the first-line setting, which work more effectively where cases are mild to moderate. For patients not benefiting from 5-ASA drugs, other treatment options include corticosteroids (such as prednisone), immunomodulators (such as methotrexate and azathioprine), biologics and JAK inhibitors. Biologics typically work by inhibiting or blocking proteins/cytokines that cause inflammation, and since the first biologics approval in the indication in the late-1990s (Remicade, approved in 1998), they have become the standard of care in moderate to severe UC. Three separate categories of biologics are currently approved for the condition:

- Anti-tumour necrosis factor (anti-TNF) inhibitors: Humira (adalimumab), Remicade (infliximab) and Simponi (golimumab),
- Integrin receptor antagonists: Entyvio (vedolizumab), and
- Interleukin-12 and interleukin-23 antagonists: Stelara (Ustekinumab) and Skyrizi (risankizumab).

While anti-TNFs were the first biologics to receive the regulatory green light in UC, recent years have seen second-generation biologics, such as interleukin (IL) antagonists, gain prominence. As noted previously, the most recently approved biologic for UC is Skyrizi (an IL-23 antagonist), which received FDA approval in June 2024 in moderate to severe UC.

While available biologics continue to be an effective treatment option for UC, a portion of patients remain either unresponsive or eventually develop resistance to the treatments. Reports note that treatment efficacy tends to plateau over time, with less than 50% of patients achieving remission over one year. In our view, this highlights the need for alternative treatments with novel mechanisms of action.

OSE's Lusvertikimab targets IL-7 and its receptor IL-7R, a cytokine implicated in UC and other inflammatory bowel diseases, and, to our knowledge, is the most clinically advanced IL-7R antagonist in clinical development, targeting CD127 (a cytokine that modulates the proliferation, apoptosis and activation of CD4 and CD8 T-cells). Reported scientific data suggests that high expression of IL-7R is associated with poor responses to other biological treatments, such as anti-TNF therapies and could, therefore, offer a solution as a potentially more effective treatment compared to other biologics.

Valuation

We expect the release of the additional positive data on the primary and secondary endpoints of the Phase II CoTikiS trial to support OSE's discussions with potential partners for Lusvertikimab's next phase of development in UC. We therefore increase our probability of success for the programme to 35%, from 17% previously. This results in our overall valuation of OSE rising to €541.2m or €24.8/share, from €465.7m or €21.3/share previously.

Exhibit 5: OSE rNPV valuation

Product	Launch	Peak sales (€m)	NPV (€m)	NPV/share (€)	Probability	rNPV (€m)	rNPV/share (€)
Tedopi – NSCLC	2028	541	421.1	19.3	67%	274.3	12.6
OSE-127 – ulcerative colitis	2028	819	318.4	14.6	35%	125.9	5.8
BI 765063 – multiple cancer indications (MSS CRC)	2029	513	202.2	9.3	14%	40.5	1.9
FR-104 – Veloxis deal milestones (kidney transplantation)	2029	92	149.7	6.9	17%	27.7	1.3
OSE-279 solid tumours (SCLC)	2029	416	206.0	9.4	14%	35.9	1.6
Net cash at 30 June 2024 (including lease liabilities)			36.9	1.7	100%	36.9	1.7
Valuation			**1,334.2**	**61.1**		**541.2**	**24.8**

Source: Edison Investment Research

Based on our cash burn projection, we estimate the current cash reserves to be sufficient for the company to fund operations into 2027, in line with management guidance. We note that this does not consider further licensing or milestone-related inflows from partners, which should widen the runway further.

Exhibit 6: Financial summary

€000s	2022	2023	2024e	2025e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	18,302	2,227	98,480	86,271
Cost of Sales	0	0	0	0
Gross Profit	18,302	2,227	98,480	86,271
Research and development	(26,893)	(17,158)	(23,575)	(26,696)
Overhead expenses	(6,673)	(6,015)	(7,218)	(7,435)
EBITDA	(14,992)	(19,566)	66,673	53,348
Operating Profit (before amort. and excepts.)	(18,478)	(22,986)	65,523	52,140
Intangible Amortisation	0	0	0	0
Exceptionals	0	0	0	0
Other	0	0	0	0
Operating Profit	(18,478)	(22,986)	65,523	52,140
Net Interest	455	(235)	(1,070)	(1,231)
Profit Before Tax (norm)	(18,023)	(23,221)	64,453	50,910
Profit Before Tax (reported)	(18,023)	(23,221)	64,453	50,910
Tax	263	219	(3,540)	0
Profit After Tax (norm)	(17,760)	(23,002)	60,913	50,910
Profit After Tax (reported)	(17,760)	(23,002)	60,913	50,910
Average Number of Shares Outstanding (m)	18.5	19.6	21.7	21.8
EPS - normalised (c)	(95.86)	(117.58)	280.20	233.23
EPS - reported (€)	(0.96)	(1.18)	2.80	2.33
Dividend per share (€)	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	N/A	67.7	61.8
Operating Margin (before GW and except.) (%)	N/A	N/A	66.5	60.4
BALANCE SHEET				
Fixed Assets	54,580	51,576	55,950	49,108
Intangible Assets	48,784	46,401	45,594	44,787
Tangible Assets	743	464	471	520
Investments	5,053	4,711	9,885	3,801
Current Assets	37,200	30,478	85,599	139,027
Stocks	0	0	0	0
Debtors	403	982	1,031	1,083
Cash and cash equivalents	25,620	18,672	73,744	127,121
Other	11,177	10,824	10,824	10,824
Current Liabilities	16,268	18,799	17,108	24,520
Creditors	8,539	9,299	9,764	10,252
Short term borrowings	3,093	6,403	4,247	11,171
Other	4,636	3,097	3,097	3,097
Long Term Liabilities	42,855	40,280	38,175	26,439
Long term borrowings	37,231	35,508	34,261	23,090
Deferred tax liabilities	1,514	1,311	1,311	1,311
Other long term liabilities	4,110	3,461	2,603	2,038
Net Assets	32,657	22,975	86,267	137,177
CASH FLOW				
Operating Cash Flow	(17,760)	(23,002)	60,913	50,910
Movements in working capital	(3,142)	(835)	416	437
Depreciation and other	3,486	3,420	1,150	1,208
Net Interest	(3,066)	(657)	0	0
Tax	(499)	(435)	0	0
Others	2,728	1,746	2,164	0
Net Cash Flows from Operations	(18,253)	(19,763)	64,642	52,554
Capex	(274)	(232)	(350)	(450)
Acquisitions/disposals	0	0	0	0
Others	300	(275)	0	0
Net Cash Flow from Investing Activities	26	(507)	(54,330)	54,440
Equity Financing	6	11,357	215	0
Debt financing	11,046	2,304	(3,403)	(4,247)
Other	(785)	(337)	(858)	(565)
Dividends	0	0	0	0
Net Cash Flow from Financing Activities	10,267	13,324	(4,046)	(4,812)
Effect of FX	0	0	0	0
Net Cash Flow	(7,960)	(6,946)	6,266	102,182
Opening net debt/(cash)	(1,167)	14,704	23,239	(35,236)
Change in debt	7,912	1,587	(3,403)	(4,247)
Change in cash	7,960	6,946	(6,266)	(102,182)
Closing net debt/(cash)	14,704	23,239	(35,236)	(92,860)

Source: Company reports, Edison Investment Research

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