EDISON

OSE Immunotherapeutics

R&D update

Solid new details from Step 1 of Tedopi Ph III trial

Pharma & biotech

On 21 September 2020, OSE presented additional data from step one of the Phase III Atalante 1 trial at the virtual ESMO conference. This followed the first announcement in April 2020. The totality of data now points to a favourable benefit/risk ratio of Tedopi treatment in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failed checkpoint inhibitor treatment. Due to the COVID-19 pandemic, OSE has decided to terminate enrolment into step two of the trial, as NSCLC patients are vulnerable to coronavirus infections and there was therefore a substantial risk of data loss. OSE will focus on regulatory interactions and partnering discussions, given the availability of new data. Our valuation is marginally higher at €240m or €16.0/share (from €15.3).

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/18	24.5	4.8	0.38	0.0	16.2	N/A
12/19	26.0	(1.2)	(0.30)	0.0	N/A	N/A
12/20e	9.0	(13.9)	(0.66)	0.0	N/A	N/A
12/21e	9.0	(14.1)	(0.94)	0.0	N/A	N/A

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

New details from step one of Tedopi Phase III trial

One the most interesting new details was the median over survival (mOS) reaching statistical significance in the Tedopi vs chemotherapy arm of the per-protocol (mPP) analysis. This is particularly encouraging as, due to the early end of the trial, the cross-arm comparison is limited. The time to ECOG deterioration (general health status of a patient) was also significantly longer in the Tedopi group, indicating better quality of life. Step one was primarily a futility analysis, with the primary endpoint of 12-month survival in the Tedopi arm reaching 46% in modified intention-to-treat analysis (mITT), significantly higher than the pre-specified boundary of 25%. The newly released mPP analysis confirmed this result.

Upcoming newsflow

Our most recent review of the developments with OSE's clinical-stage assets can be found in the report published in July 2020. A Phase I study with BI 765063, antagonist of SIRPα, in solid tumours is ongoing in partnership with BI and the first results are expected in H121. Two Phase II trials with OSE-127, an anti-IL-7Rα antibody, are planned to start in H220 in ulcerative colitis (sponsored by OSE) and Sjögren's syndrome (sponsored by Servier), although the pandemic may affect the start dates. The new project CoVepiT, a potentially prophylactic vaccine against the SARS-CoV-2 virus, is progressing as well, with the first preclinical data published in August 2020. The Phase I study is expected to start by end-2020 or early in 2021.

Valuation: €240m or €16.0/share

Our valuation of OSE is marginally higher at €240m or €16.0/share, as the lower cash position was offset by rolling our model forward. We make no changes to our rNPV model for Tedopi for the moment. However, some modifications to our model will be warranted once OSE releases more information.

28 September 2020

Price	**€6.14**
Market cap	**€92m**
Gross cash (€m) at end-H120 (government debt not included)	22.9
Shares in issue	15.0m
Free float	25%
Code	OSE
Primary exchange	Euronext Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(8.9)	3.4	60.7
Rel (local)	(3.6)	6.7	88.9
52-week high/low	€7.48		€3.0

Business description

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

Next events

Update on Tedopi development/ partnering	H220
Initiation of Phase II trials with OSE-127	H220
Update on BiCKI platform	H220

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Edison profile page

Second Phase III Atalante 1 trial update

As a reminder, this was a Phase III trial with Tedopi, an off-the-shelf cancer vaccine, as second- or third-line treatment versus standard of care (docetaxel or pemetrexed) in HLA-A2-positive patients (c 45% of the total population) with locally advanced (stage IIIB), or metastatic (stage IV) NSCLC. Patients who have failed post-checkpoint inhibitor treatment represent an area where no novel treatment has been approved yet. In total, 103 patients were randomised and received follow-up care for at least 12 months. The results of the predefined step one assessment were published for the first time in April 2020 and included:

- **mITT analysis**: the 12-month survival rate in the Tedopi arm was 46%. The predefined futility threshold was 25%, while the obtained confidence interval at 95% of the significance level was 33–59%, a statistically strong result.
- **mITT analysis**: the 12-month survival rate in the chemotherapy control arm was 36%.

On 21 September 2020, OSE released additional data at the virtual ESMO conference. These included:

- **mPP analysis**: 12-month survival rate in the Tedopi arm was 47.5% (95% CI: 34.3%, 60.9%), confirming the previous result in the mITT analysis.
- **mPP analysis**: 12-month survival rate in the chemotherapy arm was 34.4%.
- **ITT analysis**: mOS in the Tedopi arm was 9.8 months versus 8.7 months in the chemotherapy arm (HR: 0.71 [95% CI: 0.44, 1.16]; p = 0.17).
- **PP analysis**: mOS in the Tedopi arm was 11.1 months versus 8.7 months in the chemotherapy arm reaching statistical significance with p = 0.037 (HR: 0.57 [95% CI: 0.34, 0.97]).

Regarding the safety/tolerability profile, the new data showed that:

- time to ECOG deterioration was significantly longer in the Tedopi arm (8.4 versus 4.4 months; p = 0.002); and
- significantly fewer severe treatment emergent adverse effects were reported in the Tedopi arm, 14% versus SoC 43%, p < 0.001.

Our view

Step 1 was primarily a futility analysis, with the primary endpoint of 12-month survival in the Tedopi arm being better than the pre-specified boundary of 25%. In the mITT analysis (more conservative than mPP), the 12-month survival rate in the Tedopi arm was 46%, with the confidence interval of 33–59% at 95% of the significance level, a statistically strong result. The newly released mPP analysis confirmed this result.

The difference between ITT and PP methods is that in an ITT analysis all randomised patients are included in the final analysis. ITT is the gold-standard approach in large registrational trials, as it is a more conservative approach and potentially better reflects the real world. The drawback of this method is that it can overly punish the investigational drug (by underestimating the efficacy). For example, if an unusually high number of patients decided to stop the treatment early for various non-drug-related reasons, they would normally still be included in the ITT analysis, as long as they received at least one dose. In large trials, the rationale is that these deviations would not obscure the overall data; drop-outs can happen in the control arm, too. In smaller trials, however, it is enough for just a few patients to significantly deviate from the protocol and this can substantially skew the ITT analysis against the drug. For this reason, in smaller trials it is important to consider PP analysis, ie the effect of a drug in optimal conditions if all patients followed the protocol as designed. Both ITT and PP methods can be modified and adapted to the specific needs of a clinical trial, hence mITT and mPP.

Keeping all this in mind, one of the most interesting new details for us was the mOS reaching statistical significance in the Tedopi versus chemotherapy arm in the PP analysis. This is particularly encouraging as, due to the early end of the trial, the cross-arm comparison is limited. The time to ECOG deterioration was also significantly longer in the Tedopi group, indicating better quality of life.

Next steps

OSE planned to expand the Phase III trial and was ready to open more recruitment centres if the step-one analysis was positive. However, as reported in April 2020, the company, together with the Independent Data Monitoring Committee and the Steering Committee, reviewed the prospects for continuation of the trial, given the COVID-19 pandemic. Due to underlying conditions and immunosuppression from other treatments, NSCLC patients are vulnerable to coronavirus infections. Therefore, there was a substantial risk that the trial data could be significantly affected by the outbreak. OSE has, therefore, decided not to expand the trial into step two.

For the next steps, OSE indicated that it would like to discuss these results with the regulatory authorities and agree the best options for further development. In addition to regulatory interactions, OSE indicated that it will actively explore potential partnership opportunities for Tedopi. As is typical in these situations, the timelines for any partnership deals are uncertain. We do not expect any major announcements until the COVID-19 pandemic subsides. Once that happens, updates on partnering discussions and regulatory interactions will be of primary interest.

Financials and valuation

OSE reported a top line of €5.8m in H120, due to the reinvoicing of development costs of BI 765063 to the partner BI, the sales of OSE-127 vials to its partner Servier and the spreading of a milestone payment after the exercise of option one under the two-step option agreement with Servier. Total H120 operating expenses were €12.9m (77% related to R&D) versus €12.1m in H119 and largely in line with our expectations. Our updated top line forecasts for both FY20 and FY21 now stand at €9m to reflect the ongoing income from partners. This still does not include expected R&D related milestones payments if certain conditions are met (as per our principles), so the total income from OSE's partners could be higher in 2020/2021. Our higher revenue estimates have resulted in lower losses for FY20/21 (see Exhibit 2).

As of end-H120, OSE had cash, cash equivalents and financial assets of €22.9m, which is sufficient until Q321, according to the company. The balance sheet also includes debt of €16.2m, mainly government loans.

Our valuation of OSE is marginally higher at €240m or €16.0/share, compared to €230m or €15.3/share previously, due to a lower cash position, which was offset by rolling the model forward. We make no other changes to our assumptions, described in detail in our previous reports, in particular the initiation report. In the near term, we will be focusing on:

- Any potential updates on further Tedopi programmes, either partnering discussions or interactions with regulators. We make no changes to our rNPV model for Tedopi for the moment. However, we previously assumed that step two of the trial would start in 2020, so some modifications to our model will be warranted, once OSE releases more information.
- Updates on the COVID-19 effects on the ongoing clinical trial (Phase I with BI 765063 in multiple cancer indications) or those that were about to start (two Phase II trials with OSE-127 in Sjögren's syndrome and ulcerative colitis).
- Preclinical updates on the BiCKI platform.

Exhibit 1: Sum-of-the-parts OSE valuation

Product	Launch	Peak sales ($m)	Unrisked NPV (€m)	Unrisked NPV/share (€)	Probability (%)	rNPV (€m)	rNPV/share (€)
Tedopi – NSCLC	2023	657	311.1	20.7	25%	74.0	4.9
OSE-127 – ulcerative colitis	2027	843	196.1	13.1	15%	39.7	2.6
OSE-172 – multiple cancer indications (TNBC)	2027	1,801	291.1	19.4	10%	41.3	2.8
FR104 – rheumatoid arthritis	2026	1,056	258.9	17.3	15%	62.4	4.2
Cash, last reported*			22.9	1.5	100%	22.9	1.5
Valuation			**1,080.2**	**72.0**		**240.2**	**16.0**

Source: Edison Investment Research. Note: WACC = 12.5% for product valuations. Note: *OSE's debt, not shown above, consists of government loans, which are typically repayable on commercial success only.

Exhibit 2: Financial summary

€'000s	2018	2019	2020e	2021e
December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	24,456	25,952	9,000	9,000
Cost of Sales	0	0	0	0
Gross Profit	24,456	25,952	9,000	9,000
Research and development	(15,057)	(21,655)	(17,000)	(17,000)
EBITDA	4,963	(897)	(13,838)	(14,026)
Operating Profit (before amort. and except.)	4,847	(1,220)	(13,939)	(14,117)
Intangible Amortisation	0	(251)	0	0
Exceptionals	0	0	0	0
Other	0	0	0	0
Operating Profit	4,847	(1,471)	(13,939)	(14,117)
Net Interest	0	8	(6)	(12)
Profit Before Tax (norm)	4,847	(1,212)	(13,945)	(14,129)
Profit Before Tax (reported)	4,847	(1,463)	(13,945)	(14,129)
Tax	783	(3,188)	4,094	0
Profit After Tax (norm)	5,630	(4,400)	(9,851)	(14,129)
Profit After Tax (reported)	5,630	(4,651)	(9,851)	(14,129)
Average Number of Shares Outstanding (m)	14.6	14.9	15.0	15.0
EPS - normalised (€)	0.38	(0.30)	(0.66)	(0.94)
EPS - normalised fully diluted (€)	0.36	(0.30)	(0.66)	(0.94)
EPS - reported (€)	0.38	(0.31)	0.0	0.0
Dividend per share (€)	0.0	0.0		
Gross Margin (%)	100.0	100.0	100.0	100.0
EBITDA Margin (%)	20.3	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	19.8	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	53,879	55,871	55,770	55,679
Intangible Assets	52,600	52,600	52,600	52,600
Tangible Assets	904	1,009	908	817
Investments	375	2,262	2,262	2,262
Current Assets	14,687	26,589	25,350	12,823
Stocks	0	0	0	0
Debtors	2,253	747	747	747
Cash	9,573	25,842	24,603	12,076
Other	2,861	0	0	0
Current Liabilities	(9,075)	(14,330)	(14,330)	(14,330)
Creditors	(8,447)	(13,782)	(13,782)	(13,782)
Short term borrowings	(628)	(548)	(548)	(548)
Long Term Liabilities	(6,075)	(16,067)	(23,067)	(23,067)
Long term borrowings	(3,832)	(9,211)	(16,211)	(16,211)
Other long term liabilities	(2,243)	(6,856)	(6,856)	(6,856)
Net Assets	53,416	52,063	43,723	31,105
CASH FLOW				
Operating Cash Flow	1,860	5,989	(12,327)	(12,515)
Net Interest	0	0	(6)	(12)
Tax	(783)	3,148	4,094	0
Capex	(593)	0	0	0
Acquisitions/disposals	0	0	0	0
Financing	(37)	0	0	0
Other	(95)	2,288	0	0
Dividends	0	0	0	0
Net Cash Flow	352	11,425	(8,239)	(12,527)
Opening net debt/(cash)	(4,761)	(5,113)	(16,083)	(7,844)
HP finance leases initiated	0	0	0	0
Other	(0)	0	0	0
Closing net debt/(cash)	(5,113)	(16,538)	(7,844)	4,683

Source: OSE Immunotherapeutics, Edison Investment Research

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