EDISON

OSE Immunotherapeutics

R&D update

Positive Tedopi step 1, rethinking its future

Pharma & biotech

On 1 April 2020, OSE announced that the primary endpoint was met in the predefined step 1 analysis of the Phase III Atalante 1 trial with OSE's cancer vaccine Tedopi in HLA-A2 positive, non-small cell lung cancer (NSCLC) patients after they failed checkpoint inhibitors (CPIs, anti-PD-1 or anti-PD-L1). The patients (n=99) were randomised and received treatment at least 12 months before step1 analysis. The 12-month survival rate in the Tedopi arm was 46% (29 out of 63; CI 33–59%), well above the predefined futility threshold of 25%, so a statistically strong result. In the chemotherapy control arm, the 12-month survival rate was 36% (13 out of 36). Due to the COVID-19 pandemic, OSE has decided to terminate enrolment into the step 2 part 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 virtually unchanged at €230m or €15.3/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/18	24.5	4.8	0.38	0.0	11.1	N/A
12/19	26.0	(1.2)	(0.30)	0.0	N/A	N/A
12/20e	0.0	(22.9)	(1.53)	0.0	N/A	N/A
12/21e	0.0	(23.1)	(1.55)	0.0	N/A	N/A

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

OSE-127 milestone payment brought forward

In March, OSE announced that it had renegotiated certain deal terms with Servier, which brought the €5m milestone payment forward (of €20m); this is now expected as soon as the first patient is recruited to the Phase II trial with OSE-127 (anti-IL-7R antibody). Notably, two Phase II trials with OSE-127 were planned to start in 2020, but the company indicated that the outbreak may affect these initiations. We note that given the circumstances trial initiation delays are preferable to trial interruptions.

Rethinking Tedopi's future

OSE had a clear plan for expansion of the Phase III trial and was ready to open more recruitment centres if step 1 analysis was positive. So, the announcement about the termination was unexpected and clearly a result of the COVID-19 pandemic. Because of underlying conditions and immunosuppression due to other treatments, NSCLC patients are vulnerable to coronavirus infections. The positive outcome of the futility analysis means the asset is not compromised and the newly obtained data will likely be used in regulatory and partnering discussions.

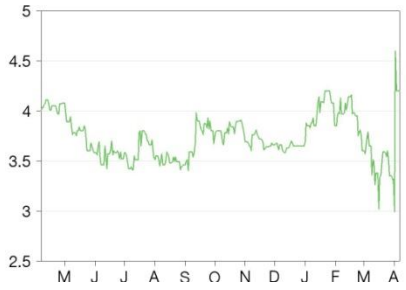
Valuation: €230m or €15.3/share

Our valuation of OSE is virtually unchanged at €230m or €15.3/share. We brought the expected €5m payment forward in our rNPV model (risk-adjusted; not yet included in our financial estimates as per our principles). 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. We reviewed recent R&D progress with other assets in our last report published in March.

7 April 2020

Price	**€4.2**
Market cap	**€63m**
Gross cash (€m) at end-FY19 (government debt not included)	25.8
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	15.1	9.7	5.0
Rel (local)	37.1	51.8	33.3
52-week high/low		€4.6	€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	2020
Initiation of Phase II trials with OSE-127	2020
Update on BiCKI platform	2020

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Edison profile page

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 vs 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, 99 patients were randomised and received treatment for at least 12 months. The results of the predefined step 1 assessment were:

- The 12-month survival rate in the Tedopi arm was 46% (29 out of 63). The predefined futility threshold was 25%, while the obtained confidence interval at 95% of significance level was 33–59%, so a statistically strong result.
- In the chemotherapy control arm, the 12-month survival rate was 36% (13 out 36).

Together with the Independent Data Monitoring Committee and the Steering Committee of the trial, OSE has reviewed the prospects for continuation of the trial in light of the COVID-19 pandemic. Since COVID-19 can cause serious complications to NSCLC patients, there is a risk that the trial data could be significantly affected by the outbreak. In addition, industry stakeholders (medical societies, some pharma companies) have recommended or have taken actions to introduce voluntary holds on the recruitment of new patients in oncology trials. OSE has therefore decided not to expand the trial into step 2.

OSE also announced 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.

Our view

Since step 1 was primarily a futility analysis, statistical significance between the active and control arms is not available at the moment. The absolute difference of 10% in 12-month survival between the arms seems encouraging. The fact that the lower boundary of the 95% confidence interval was well above the predefined futility threshold is a key finding, in our view.

OSE's intention to seek and establish a partnership is not surprising, as the company is mostly a translational and early- to mid-stage drug developer and never intended to develop its marketing capacity. We also include a licensing deal for Tedopi in our model. We did expect the trial to progress to step 2 of the Phase III Atalante 1 trial even with no partner on board, but the COVID-19 pandemic seems to be the deciding factor in terminating patient recruitment for now. Because of underlying conditions and immunosuppression due to other treatments, NSCLC patients are vulnerable to coronavirus infections. Recruitment and treatment in step 1 were completed in a very timely manner and OSE was able to present the results.

The positive outcome of the futility analysis means the asset is not compromised and the newly obtained data will likely be used in partnering discussions. 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.

Update on commercial partnerships

OSE has two commercial partnerships with a total remaining value of c €1.3bn in R&D and commercial milestones plus royalties.

- According to the terms of the licensing deal with Boehringer Ingelheim (BI), OSE is eligible to receive up to €1.1bn in milestones plus royalties if certain conditions are met. The €15m in milestones was paid on the initiation of the Phase I trial in 2019. BI will take over development after completion of the Phase I trial. The next milestone payment has not been guided by OSE, but we would expect it after initiation of the Phase II trial. The key message in the FY19 results release was that, unsurprisingly, the COVID-19 pandemic is affecting recruitment of new patients to the trial and 'further updates will be made when available'.
- Deal terms with Servier include total value of the deal, €272m, of which €22m has been received (upfront payment and step 1 milestone). In our last published note, we described the recently announced successful completion of the Phase I study. In March 2020, OSE reported that, together with Servier, it had signed an amendment to the two-step licensing option agreement for OSE-127, which relates to step 2 (for a summary of deal terms, see our initiation report). According to the new terms, €5m in milestones will be paid to OSE once the first patient is enrolled to the Phase IIa trial in Sjögren's syndrome, while the remaining €15m will be paid after completion of both trials (Sjögren's syndrome and ulcerative colitis). The previous version of the option agreement terms had the full €20m due after completion of the Phase II study in ulcerative colitis. Both trials were planned to start in 2020 but, as with the other trials, OSE indicated that the ongoing outbreak may have an effect on initiations. We note that given the circumstances, trial initiation delays are preferable to trial interruptions.

Financials

OSE reported a top line of €26.0m in FY19, which was mostly milestones from BI (€15m) and Servier (€10m), while the rest is R&D cost reimbursement to OSE.

Total FY19 operating expenses were €27.4m (81% related to R&D) vs €19.5m in FY18. Out-of-pocket R&D costs are mainly associated with the Tedopi Phase III NSCLC study, as other clinical studies are financed via partnerships. We therefore forecast lower R&D spending in 2020 and 2021 with total operating expenditure estimates of €22.9m and €23.1m respectively. We do not yet include the €5m milestone payment from Servier in our financial estimates (as per our principles), but the updated deal terms are reflected in our rNPV model.

As of end 2019, OSE had cash, cash equivalents and financial assets of €25.8m. The balance sheet also includes debt of €9.8m, which is mainly government loans. OSE guided that if the €5m payment from Servier and €3m in tax credits is received, funding is sufficient to Q121. This implies that OSE is well positioned to weather the COVID-19 pandemic. OSE also indicated that if the trials are significantly affected and delayed, the runway would also be longer as CRO costs would be delayed, which is a mitigating factor.

Valuation

Our valuation of OSE is virtually unchanged at €230m or €15.3/share compared to our note published in March. We have brought the €5m milestone payment from Servier forward in our rNPV model (risk-adjusted). We make no other changes to our assumptions, described in detail in our previous reports, primarily the initiation report. In the near term we will be focusing on:

- Any potential updates on further Tedopi programme, 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 2 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	291.9	19.5	25%	69.4	4.6
OSE-127 - ulcerative colitis	2027	843	184.0	12.3	15%	37.3	2.5
OSE-172 - multiple cancer indications (TNBC)	2027	1,801	273.1	18.2	10%	38.7	2.6
FR104 - rheumatoid arthritis	2026	1,056	242.9	16.2	15%	58.5	3.9
FY19e cash*			25.8	1.7	100%	25.8	1.7
Valuation			**1,017.7**	**67.8**		**229.7**	**15.3**

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	0	0
Cost of Sales	0	0	0	0
Gross Profit	24,456	25,952	0	0
Research and development	(15,057)	(21,655)	(17,000)	(17,000)
EBITDA	4,963	(897)	(22,838)	(23,026)
Operating Profit (before amort. and except.)	4,847	(1,220)	(22,939)	(23,117)
Intangible Amortisation	0	(251)	0	0
Exceptionals	0	0	0	0
Other	0	0	0	0
Operating Profit	4,847	(1,471)	(22,939)	(23,117)
Net Interest	0	8	(6)	(12)
Profit Before Tax (norm)	4,847	(1,212)	(22,945)	(23,129)
Profit Before Tax (reported)	4,847	(1,463)	(22,945)	(23,129)
Tax	783	(3,188)	0	0
Profit After Tax (norm)	5,630	(4,400)	(22,945)	(23,129)
Profit After Tax (reported)	5,630	(4,651)	(22,945)	(23,129)
Average Number of Shares Outstanding (m)	14.6	14.9	15.0	15.0
EPS - normalised (€)	0.38	(0.30)	(1.53)	(1.55)
EPS - normalised fully diluted (€)	0.36	(0.30)	(1.53)	(1.55)
EPS - reported (€)	0.38	(0.31)	(1.53)	(1.55)
Dividend per share (€)	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	N/A	N/A
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	5,256	2,747
Stocks	0	0	0	0
Debtors	2,253	747	747	747
Cash	9,573	25,842	4,509	2,000
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)	(16,067)	(35,085)
Long term borrowings	(3,832)	(9,211)	(9,211)	(28,229)
Other long term liabilities	(2,243)	(6,856)	(6,856)	(6,856)
Net Assets	53,416	52,063	30,629	9,011
CASH FLOW				
Operating Cash Flow	1,860	5,989	(21,327)	(21,515)
Net Interest	0	0	(6)	(12)
Tax	(783)	3,148	0	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	(21,333)	(21,527)
Opening net debt/(cash)	(4,761)	(5,113)	(16,083)	5,250
HP finance leases initiated	0	0	0	0
Other	(0)	0	0	0
Closing net debt/(cash)	(5,113)	(16,538)	5,250	26,777

Source: Company data, Edison Investment Research

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