EDISON

Onxeo

Company update

Phase I with AsiDNA iv starts; first data in H218

Pharma & biotech

On 24 April, Onxeo announced that the first patient had been treated with AsiDNA, a first-in-class DNA break repair inhibitor, via systemic administration in the Phase I trial. AsiDNA has already generated supportive data from a Phase I trial in melanoma using intratumoural injection. Alongside the Phase I trial Onxeo is conducting a broad preclinical programme that explores AsiDNA in various settings and combinations with other drugs. Two abstracts with preclinical data were presented at the American Association for Cancer Research conference in April potentially demonstrating unique characteristics of its mechanism of action. Our valuation is marginally higher at €221m or €4.4/sh.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/16	4.4	(20.4)	(0.45)	0.0	N/A	N/A
12/17	9.5	(19.7)	(0.24)	0.0	N/A	N/A
12/18e	2.6	(12.2)	(0.24)	0.0	N/A	N/A
12/19e	3.9	(11.2)	(0.22)	0.0	N/A	N/A

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

First patient recruited to Phase I with AsiDNA

The new Phase I study is exploring AsiDNA via intravenous administration for the first time. The study, now introduced as DNA Repair Inhibitor administered IntraVenously (DRIIV), will enrol patients with various advanced solid cancers with the goal of evaluating the safety profile, establishing the clinical dose and determining the active dose at the tumour level. Onxeo is also exploring various biomarkers that might help to stratify patients in later trials. AsiDNA is part of the proprietary, novel platON platform, a major R&D expansion announced in October 2017, and is based on decoy oligonucleotides. The platON platform belongs to the so-called DNA damage response (DDR) technology, a domain to which recently marketed PARP inhibitors also belong (for detailed analysis, see our outlook report, published in November 2017). Interim results from the DRIIV trial are expected in H218. The final results and the findings from Onxeo's broad preclinical programme will help to inform further R&D strategy.

Fresh preclinical data at AACR

Onxeo presented two abstracts in a poster session at the AACR's annual meeting on 14-18 April 2018 in Chicago, Illinois. The new data added to the growing body of evidence backing AsiDNA's potential and, surprisingly, revealed a potentially new mechanism of action. According to this evidence, unlike the majority of drugs in oncology that develop resistance, the tumour cell's sensitivity to AsiDNA could actually increase as the treatment progresses. If confirmed in future studies, it could be the first known drug with such an effect.

Valuation: Marginally up to €221m or €4.4/share

Our valuation is €221m or €4.4/share, marginally higher than our previous value of €218m, or €4.3/share, mainly due to rolling our model forward, which was partly offset by lower cash. Interim data from the DRIIV trial and the potential start of other clinical trials with AsiDNA are catalysts for the share price in the near term.

27 April 2018

Price	**€1.33**
Market cap	**€67m**
Net cash (€m) at end Q417	14.1
Shares in issue	50.7m
Free float	80%
Code	ONXEO
Primary exchange	Euronext Paris
Secondary exchange	OMX Copenhagen

Share price performance

%	1m	3m	12m
Abs	(6.3)	(27.0)	(48.6)
Rel (local)	(12.3)	(25.9)	(50.5)
52-week high/low	€5.4		€1.0

Business description

Onxeo is focused on orphan cancer indications, specialising in epigenetics and DNA break repair inhibition. Beleodaq, an HDAC inhibitor, is approved for PTCL in the US and partnered with Spectrum Pharmaceuticals. AsiDNA, a novel DNA break repair inhibitor from Onxeo's platON platform, is in a Phase I trial with interim data expected in 2018.

Next events

Interim data from the DRIIV trial	H218
AsiDNA + HDACi Phase I start	2018
AsiDNA + PARPi Phase I start	2018

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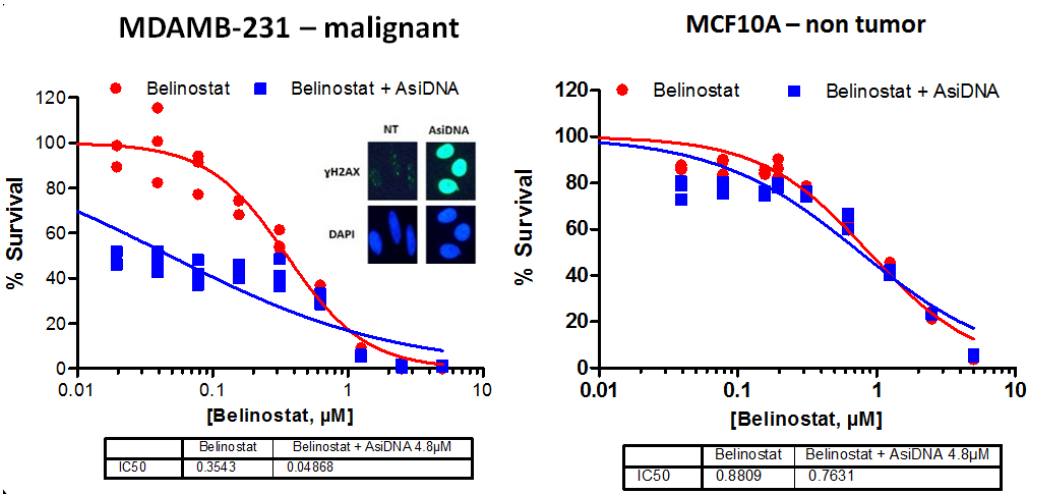
Cross-potentiation between AsiDNA and belinostat

One of the abstracts summarised the data of AsiDNA administered in combination with belinostat (Beleodaq), Onxeo's HDAC inhibitor, in several tumour cell lines. The results showed:

- Belinostat treatment caused DNA break accumulation and genetic instability in tumour cells.
- Importantly, AsiDNA increased belinostat's activity on its targets. AsiDNA increased histone acetylation by belinostat, and prevented DNA repair mechanisms in the tumour cells that would otherwise be activated on DNA damage by belinostat. This cross-potentiation between the two drugs resulted in high synergistic anti-tumour efficacy (Exhibit 1).
- While repeated treatments with belinostat alone caused drug resistance, this was not seen in the combination treatment with AsiDNA, indicating the combination's potential to prevent the tumour from developing resistance to treatment.

Exhibit 1: Efficacy of AsiDNA + belinostat combination indicated by survival of tumour cell line MDAMB-231 compared with MCF10A, a non-tumour cell line

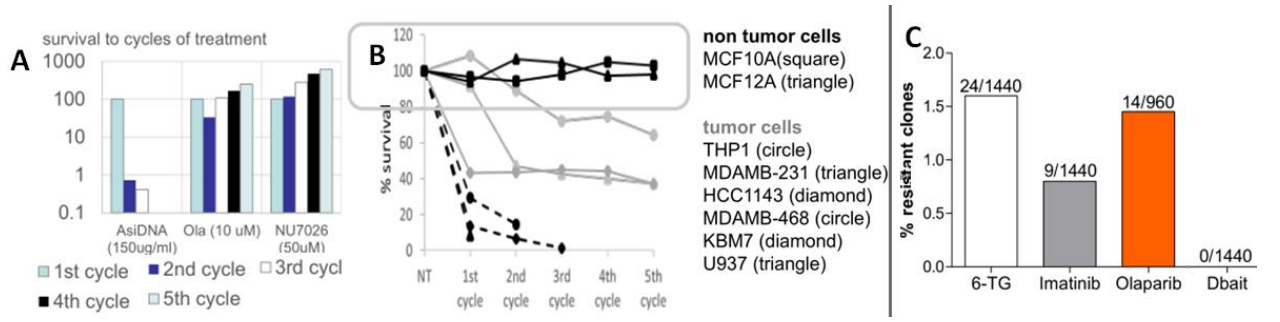


Source: Jdey et al. AsiDNATM and HDAC inhibitors: a cross-potentiation team working to kill tumor cells. Poster presentation at AACR, 14-18 April 2018.

AsiDNA causes tumour cell "autosensitization"

The second abstract described the *in vitro* data for a study that explored AsiDNA's effects in six different tumour cell lines. Cells were treated with AsiDNA and various targeted therapy agents, namely imatinib (original brand Glivec, Novartis), olaparib (Lynparza, AstraZeneca) and 6-thioguanine. The results showed for the first time that long-term treatment with AsiDNA increases the sensitivity of tumour cells to AsiDNA itself. All six cell lines tested became more sensitive to AsiDNA and did not develop resistance. This is a unique feature in oncology, as tumours developing resistance to drugs is an almost universal problem. All tumour cell lines developed some resistance to other targeted therapy agents. In addition, normal cells were not affected by the standalone treatment with AsiDNA.

Exhibit 2: AsiDNA causes "autosensitization" (A and B), but no drug resistance (C)



Source: Kozlack et al. Evolution of tumor cells under Dbait (AsiDNA) treatment results in "autosensitization". Poster presentation at AACR, 14-18 April 2018. Dbait – AsiDNA technology

Next steps

While the new publications describe early *in vitro* data, in our view, the unique value lies in the identification of a potentially new mechanism of action of AsiDNA, which Onxeo has termed autosensitization. If the findings are replicated in further trials, AsiDNA could potentially be the first known drug with this effect.

Onxeo believes that the synergistic potential of AsiDNA with belinostat is sufficient to investigate the combination treatment further. However, this is only one of the potential R&D directions. The company's ongoing broad preclinical programme explores AsiDNA's potential in various combinations including with PARP inhibitors and conventional established chemotherapy drugs, or even standalone. The final results from the DRIIV study and the findings from Onxeo's preclinical programme will help inform further R&D strategy. Onxeo also believes the broad data package will be a key component in future discussions with potential partners.

Financials

Onxeo recently reported its FY17 results. The top line figure of €9.5m was close to our estimate of €10.2m and consisted of €3.0m in recurring revenues. This came from royalties on Beleodaq (belinostat) sales and sales of now-divested Loramyc/Sitavig. The remaining €6.5m was one-off income, mainly comprising of €4m after the divestment of the aforementioned products to Vectans Pharma in July 2017 and €0.8m in upfront fees after out-licensing the non-core product, Validive, to Monopar Therapeutics.

Operating costs were €28.7m, up 4% y-o-y, largely in line with our expectations. Onxeo also reported €47.2m in non-recurring costs. Of that amount, €38.1m was an impairment of R&D assets related to belinostat, which led to a reduction in deferred tax liability and a tax income of €7.8m in the P&L. R&D assets were acquired through the merger with Topotarget in 2014. According to Onxeo, the impairment was required after a routine test to reflect a change in market dynamics for Beleodaq, namely increased competition in the peripheral T-cell lymphoma market. We revised our projections for royalty income from Beleodaq previously and for the time being make no changes to our top-line estimates. Another non-recurring expense was €9.2m put in an escrow account after the Commercial Court of Paris ordered the company to pay following its dispute with SpeBio/SpePharm. Onxeo appealed the decision and the outcome is uncertain, partly due to the fact that Onxeo owns 50% of SpeBio.

We have already reflected the divestment in our top-line projections and have revised our operating cost projections downwards as Onxeo indicated that it will aim to implement cost reduction

measures. Overall, opex will be substantially lower in 2018 after completion of the Phase III trial with Livatag. The company expects cash reach to mid-2019, largely in line with our expectations.

Exhibit 3: Key changes to our financial forecasts

€m	2017			2018e			2019e
	Est.	Act.	Change	Old	New	Change	New
Revenue	10.248	9.505	-7%	2.623	2.623	+0%	3.898
Operating profit (normalised))	(17.160)	(19.189)	+12%	(15.672)	(12.209)	-22%	(11.230)
Profit before tax (normalised)	(15.692)	(19.680)	+25%	(14.020)	(12.212)	-13%	(11.232)
Profit after tax (normalised)	(11.692)	(11.883)	+2%	(14.020)	(12.212)	-13%	(11.232)
EPS (norm, €)	(0.24)	(0.24)	-2%	(0.28)	(0.24)	-13%	(0.22)

Source: Onxeo accounts, Edison Investment Research

Valuation

We substantially revised our model in our last outlook report and, following the FY17 results we make no changes to our R&D assumptions. Our valuation is €221m or €4.4/share, which is marginally higher compared to our previous valuation of €218m or €4.3/share. This is mainly due to rolling our model forward, which was offset by lower net cash.

Exhibit 4: Onxeo rNPV valuation

Product	Indication	Launch	Peak sales (€m)	NPV (€m)	Probability (%)	rNPV (€m)	NPV/share (€/share)
Core assets							
AsiDNA	TNBC	2024	2,170	378.1	15%	78.0	1.5
Beleodaq (US)	PTCL	2014	80	34.6	100%	34.6	0.7
Beleodaq (EU + US)	PTCL	2022	60	59.6	70%	41.7	0.8
Other assets							
Livatag			250	226.3	5%	11.3	0.2
Validive			70	55.2	50%	27.6	0.5
Est. earn-outs associated with Loramyc/Sitavig				45.8	30%	13.7	0.3
Net cash at end FY17				14.1	100%	14.1	0.3
Valuation				813.7		221.1	4.4

Source: Edison Investment Research. Note: PTCL = peripheral T-cell lymphoma, TNBC = triple negative breast cancer.

Exhibit 5: Financial summary

€000s	2015	2016	2017	2018e	2019e
Year-end December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	3,482	4,423	9,505	2,623	3,898
Cost of Sales	(337)	(655)	(634)	(530)	(530)
Gross Profit	3,145	3,768	8,871	2,093	3,368
EBITDA	(20,355)	(21,304)	(17,393)	(12,109)	(11,130)
Operating Profit (before amort. and except.)	(20,574)	(21,542)	(19,189)	(12,209)	(11,230)
Intangible Amortisation	(1,600)	(1,626)	0	(1,000)	(1,000)
Exceptionals	(160)	(43)	(47,188)	0	0
Operating Profit	(22,334)	(23,211)	(66,377)	(13,209)	(12,230)
Other	(29)	0	0	0	0
Net Interest	602	1,107	(491)	(3)	(3)
Profit Before Tax (norm)	(19,972)	(20,435)	(19,680)	(12,212)	(11,232)
Profit Before Tax (reported)	(21,761)	(22,104)	(66,868)	(13,212)	(12,232)
Tax	2,353	(566)	7,797	0	0
Profit After Tax (norm)	(17,648)	(21,001)	(11,883)	(12,212)	(11,232)
Profit After Tax (reported)	(19,408)	(22,670)	(59,071)	(13,212)	(12,232)
Average Number of Shares Outstanding (m)	40.5	47.0	50.4	50.5	50.5
EPS - normalised (€)	(0.44)	(0.45)	(0.24)	(0.24)	(0.22)
EPS - normalised fully diluted (€)	(0.44)	(0.45)	(0.24)	(0.24)	(0.22)
EPS - (reported) (€)	(0.48)	(0.48)	(1.17)	(0.26)	(0.24)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	90.3	85.2	93.3	79.8	86.4
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	87,539	88,232	48,111	47,011	45,911
Intangible Assets	86,367	87,213	47,535	46,535	45,535
Tangible Assets	841	713	344	244	144
Investments	331	306	232	232	232
Current Assets	41,697	36,868	30,857	19,604	16,139
Stocks	106	184	30	25	25
Debtors	1,036	1,548	740	204	303
Cash	33,793	29,243	14,277	3,564	0
Other	6,762	5,893	15,810	15,810	15,810
Current Liabilities	(10,606)	(12,417)	(18,841)	(18,841)	(18,841)
Creditors	(10,537)	(12,311)	(18,711)	(18,711)	(18,711)
Short term borrowings	(69)	(106)	(130)	(130)	(130)
Long Term Liabilities	(15,831)	(18,594)	(9,358)	(8,918)	(15,670)
Long term borrowings	0	0	0	0	(6,753)
Other long term liabilities	(15,831)	(18,594)	(9,358)	(8,918)	(8,918)
Net Assets	102,799	94,089	50,769	38,856	27,538
CASH FLOW					
Operating Cash Flow	(20,067)	(16,838)	(20,974)	(11,029)	(10,249)
Net Interest	579	(1,560)	317	382	(3)
Tax	(2,448)	538	(7,801)	0	0
Capex	(410)	(316)	(65)	(66)	(66)
Acquisitions/disposals	0	0	0	0	0
Financing	611	13,589	13,533	0	0
Dividends	0	0	0	0	0
Net Cash Flow	(21,735)	(4,587)	(14,990)	(10,713)	(10,317)
Opening net debt/(cash)	(55,459)	(33,724)	(29,137)	(14,147)	(3,434)
HP finance leases initiated	0	0	0	0	0
Other	0	0	0	0	0
Closing net debt/(cash)	(33,724)	(29,137)	(14,147)	(3,434)	6,883

Source: Company accounts, Edison Investment Research

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