EDISON

Onxeo

Corporate outlook

LA VIE est BELle (LivAtag, ValidIvE, BELeodaq)

Pharma & biotech

The next major value inflection point for Onxeo will likely be availability of Phase III Livatag data for second-line liver cancer expected H117. This product could potentially be the first launched by Onxeo in Europe as part of the orphan oncology strategy. Prior to Livatag data, progression with Beleodaq and Validive is expected, with the start of further Phase III trials anticipated in H116. Our valuation, which is largely unchanged at €328m, suggests the current share price is ascribing limited value to these assets.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/13	1.5	(15.3)	(0.74)	0.0	N/A	N/A
12/14	22.1	0.2	(0.05)	0.0	N/A	N/A
12/15e	3.3	(21.8)	(0.61)	0.0	N/A	N/A
12/16e	7.0	(19.6)	(0.56)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation & exceptional items.

Moving forwards with three lead assets

Livatag Phase III liver cancer data are expected in H117; the 400-patient trial, which began in 2012, is now 50% enrolled and has been expanded during 2015 to accelerate recruitment; the next DSMB is anticipated in Q415. For Validive we expect Onxeo to begin a Phase III study in oral mucositis (in H&N cancer) in H116. The start of the Phase III Beleodaq trial in PTCL to satisfy regulatory requirements is expected in H116. We also expect Onxeo and partner Spectrum to provide an update on Beleodaq's future development strategy in 2016.

Orphan oncology strategy

Onxeo's three lead assets are focused on orphan oncology indications. Onxeo's strategy is to commercialise these alone in major European markets and seek partners in other regions, such as the US. Successful strategy execution could drive commercial operational synergies in the future if all three products are approved and in a timely manner. Livatag could be the first to market in 2018, with Beleodaq and Validive potentially in 2019.

Share price underpinned by approved products

Our valuation suggests that if the currently-approved products (Beleodaq in the US, and non-core assets Sitavig and Oravig) can achieve our peak sales forecasts, which could prove optimistic unless sales of the non-core products accelerate in the US, the current market capitalisation is more than justified by these assets alone together with net cash. Hence, there appears to be limited market value currently ascribed to Validive, Livatag or Beleodaq in Europe.

Valuation: rNPV of €328m or €8.1/share

Our updated Onxeo valuation is €328m (from €338m). We have made no major changes to our underlying assumptions for Validive, Livatag and Beleodaq, but have slightly lowered near-term sales of non-core products. Current cash should be sufficient to fund operations into 2017, including the start of Phase III trials in 2016.

8 September 2015

Price	**€3.65**
Market cap	**€148m**

Net cash (€m) at end June 2015	41.0
Shares in issue	40.6m
Free float	86%
Code	ONXEO
Primary exchange	Euronext Paris
Secondary exchange	OMX Copenhagen

Share price performance

%	1m	3m	12m
Abs	(21.2)	(31.5)	(41.4)
Rel (local)	(11.1)	(25.7)	(42.7)

52-week high/low	€7.3	€3.6

Business description

Onxeo is focused on orphan cancer and has three late-stage orphan oncology assets it could commercialise alone in Europe (Livatag, Beleodaq and Validive). Royalty-earning Beleodaq (belinostat) is launched in the US, along with two non-core, partnered, specialty products.

Next events

Livatag next DSMB	Q415
Phase I BelCHOP data	Q415
Start of Phase III Beleodaq trial	H116
Start of Validive Phase III oral mucositis study (in H&N cancer)	H116

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Edison profile page

Investment summary

Company description: Orphan oncology with three lead assets

Onxeo is a French orphan oncology company with three key products: (1) Beleodaq, which is approved and partnered with Spectrum in the US for rare blood cancer peripheral T-cell lymphoma (PTCL); (2) Livatag in Phase III development for second-line advanced liver cancer; and (3) Validive for oral mucositis arising from chemoradiotherapy, where a Phase III trial is planned. Onxeo plans to commercialise these assets in Europe, building out a salesforce and seeking operational efficiencies across this infrastructure. Onxeo also has two non-core specialty products (Sitavig and Oravig) that are out-licensed to multiple partners in exchange for royalties and milestone payments.

Exhibit 1: Onxeo's clinical stage and approved products pipeline

Product	Indication	Phase	Comments
Livatag	Liver cancer	Phase III	Next six-monthly DSMB in Q415 (October); Phase III preliminary data in H117
Validive	Oral mucositis	Phase III planned	Phase III expected to commence in H116 focused on H&N cancer patients
Beleodaq	Peripheral T-cell lymphoma	Phase I/II	US: approved & partnered with Spectrum (Onxeo receives royalties); EU: Phase III planned to start H116; An update on future development with partner Spectrum expected in 2016
Sitavig	Recurrent herpes labialis	Marketed	Partners include: Cipher/Innocutis (US); Daewoong Pharmaceutical (South Korea); Teva (Israel); Bruno Farmaceutici (Italy); EMS S/A (Brazil)
Oravig/Loramyc	Oropharyngeal candidiasis	Marketed	Partners include: Dara Biosciences/Midatech (US); Therabel (EU); Sosei (Japan); SciClone Pharmaceuticals (China)

Source: Edison Investment Research; Onxeo. Note: Non-core specialty products are shaded.

Valuation: Share price underpinned by approved products

Our updated Onxeo valuation is €328m or €8.1/share, which includes risk-adjusted contributions for Validive, Livatag and Beleodaq. This has been reduced slightly largely owing to a slowdown in near-term sales of non-core products, while maintaining our future peak sales forecasts (we forecast US Sitavig peak sales of €80m vs $0.5m reported in Q215, while Oravig sales are interrupted during transition to a new partner). Our valuation suggests that if approved products Beleodaq (US), Sitavig and Oravig can achieve our peak sales forecasts, which will require a pick-up in sales of the non-core products, the current market capitalisation is more than justified by these assets alone together with net cash. Hence, there appears to be limited market value currently ascribed to Validive, Livatag or Beleodaq in Europe.

Sensitivities: Progression with the orphan oncology pipeline

The main sensitivities in both the near and mid-term relate to the three orphan oncology assets, Livatag, Beleodaq and Validive, with the next main value inflection point likely to be the Phase III Livatag data expected in H117. Livatag is based on an approved anti-cancer agent and has already demonstrated survival benefits in a Phase II trial. However, the ongoing study is in harder to treat patients and uses an alternative administration method to overcome prior serious safety issues. Beleodaq US sales momentum and an update on the future development strategy in additional indications could drive the share price. For Validive, progression to Phase III development in oral mucositis will be the next event. Successful commercialisation of each of these assets and realising operational efficiencies will be key to Onxeo's longer-term investment case.

Financials: Sufficient cash to 2017

Onxeo reported cash and equivalents at end-June 2015 of €42.9m and has debt of €1.9m (including short-term debt of €1.8m and repayment of a conditional advance related to Livatag due by September). We believe this should be sufficient to fund operations into 2017, which includes ongoing Phase III costs of the Livatag ReLive trial, future costs of the planned Validive Phase III trial and Onxeo's 30% share of costs for the planned Beleodaq Phase III trial (to secure European approval in addition to post-approval US requirements). Development of Beleodaq in additional indications, which will need to be agreed with partner Spectrum, could affect the cash reach.

Livatag Phase III data in H117

The next key value inflection point for Onxeo will likely be the availability of Phase III Livatag data from the ongoing ReLive trial in liver cancer. During 2015 the trial has been expanded to additional countries and centres and is now c 50% recruited. Onxeo expects top-line data to become available during H117. We forecast peak Livatag sales of €250m (including the US, major European and Asian markets), assuming first launches from 2018. Our estimates suggest Livatag could potentially be Onxeo's most valuable asset, given the size of the liver cancer market, particularly in Asia.

A validated mechanism of action…

Livatag is based on the approved anti-cancer agent doxorubicin, which is currently used to treat a wide variety of solid tumours. Livatag is a nanoparticle formulation of doxorubicin developed with BioAlliance's Transdrug technology, facilitating diffusion of the drug into the tumour cell. In a previous Phase II trial in 28 liver cancer patients, Livatag demonstrated a 17-month overall survival improvement ($P<0.05$) compared to best supportive care (TACE, transarterial chemoembolization), with Livatag reporting median overall survival of 32 months compared to 15 months with TACE. Although this was a small trial in first-line liver cancer patients, ie less advanced than the ongoing ReLive trial, which is in second-line, with a different method of delivery (intra-arterial), these data do provide an indication of Livatag's potential efficacy in liver cancer.

…with prior safety concerns continuing to diminish

The trial was terminated early owing to three incidences of acute respiratory distress syndrome (ARDS) leading to two fatalities. It was thought that the rapid infusion rate via intra-arterial delivery was the key cause of this. In the Phase III ReLive trial, Livatag is now infused intravenously (IV) over a prolonged period (six hours) to ensure slower delivery. Given concerns over the potential lung toxicity, a data safety monitoring board (DSMB) reviews safety data every six months. To date, six DSMBs have concluded with the trial continuing as planned and around 450 IV infusions have occurred without pulmonary toxicity. The next DSMB is scheduled for October 2015.

Top-line Phase III ReLive data expected in H117

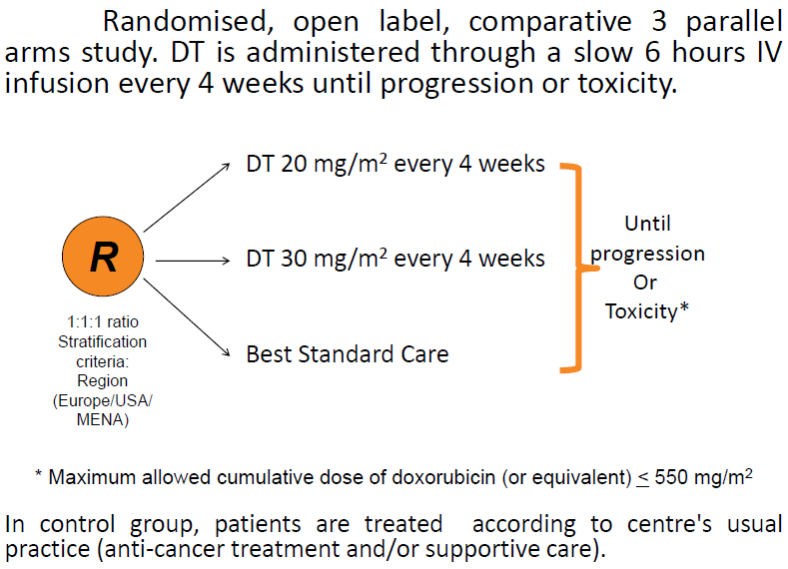
The Phase III ReLive trial in advanced hepatocellular carcinoma (HCC) patients who are refractory or intolerant to sorafenib (Nexavar) started in May 2012 and has now recruited around 50% of the targeted 400 patients. Earlier in 2015, the trial was expanded to include centres in the MENA region (Middle East and North Africa), in addition to existing centres in Europe and North America.

ReLive is an open-label trial investigating two doses of Livatag (20mg/m^2 and 30mg/m^2 every four weeks administered until progression or toxicity) compared to standard of care. The trial is investigating overall survival (OS) as the primary endpoint, in addition to RECIST[1] defined response and progression-free survival (PFS). An overview of the trial design is shown in Exhibit 2.

As ReLive is an event-driven trial (285 events or deaths are needed for analysis), timelines can be difficult to predict. Onxeo estimates that based on the current event rate and expected recruitment uptick, initial top-line data could become available during H117. If positive and approvals are granted within typical timelines, first launches could therefore be from 2018. Livatag has 'fast track' status with the FDA in addition to orphan drug status in the US and Europe.

[1] Response evaluation criteria in solid tumours.

Exhibit 2: ReLive Phase III trial design



Source: EASL 2015 e-poster, Merle P et al

Peak sales potential of €250m

We estimate that of the c 70k newly-diagnosed liver cancer patients in the US and major European markets per year, around 20k receive treatment for front-line advanced HCC. We assume the majority of these will require second-line therapy suggesting a potential eligible patient population of around 14-15k for Livatag in the US and Europe. Our peak sales forecast assumes that Livatag can attain 30% peak penetration in both markets, with pricing of €3,500 per month in the key five European markets (EU5) and $5,000 per month in the US (similar to sorafenib) and assuming an average six months of treatment. This suggests peak sales of €130m in the EU5 and the US by 2023. We assume a similar level of sales is possible in Asia, for combined global peak sales of €250m, with the higher patient numbers in Asia likely offset by lower overall pricing in this region.

Commercialise alone in EU but partner rest of world

We expect Onxeo to commercialise Livatag alone in Europe and to seek a partner in the US, in-line with its orphan oncology strategy. In the US we therefore include a partnership in our valuation, forecasting royalties of 20%, but excluding potential upfront or milestone payments. This is in addition to partnership deal(s) in Asia, including a royalty rate of 17.5%, which is below the US as this region will likely need bridging studies to secure regulatory approvals.

Treatment landscape and competition in liver cancer

Nexavar (sorafenib) is the only approved targeted agent to treat unresectable first-line HCC; sales were €771m (including €247m in the US) in 2014, which also includes sales in kidney cancer. However, treatment options for second-line therapy are limited, with current US treatment guidelines recommending liver transplantation, surgical resection, ablation or palliative therapy.

There have been a number of high-profile failures in recent years in second-line advanced HCC, highlighting the difficulty in treating these patients; these include Novartis' Afinitor in addition to Eli Lilly's ramucirumab. However, only recently, Eli Lilly announced plans to initiate a further Phase III trial of ramucirumab as second-line treatment in a subgroup of advanced liver cancer patients, highlighting the unmet need in this indication. Phase III data from potential Livatag competitors tivantinib (METIV-HCC trial, ArQule) and regorafenib (RESORCE trial, Bayer) are expected in 2016.

Beleodaq future development strategy in 2016

With Onxeo now receiving royalty income from US partner Spectrum on Beleodaq US PTCL sales, the next key event will be initiation of a further Phase III trial, expected in H116, both to secure European approval and to satisfy post-approval US commitments. Onxeo and Spectrum are also discussing future development plans in further indications and we expect an update during 2016.

Current status in PTCL

Beleodaq was approved in the US for relapsed or refractory peripheral T-cell lymphoma (r/r PTCL) in July 2014, leading to a $25m milestone payment to Onxeo (fully recognised in the P&L). Onxeo is now receiving royalty payments (mid-teens) from Spectrum. Sales in Q215 were $1.7m and $4.5m in H115. We continue to forecast peak US sales of €80m.

A confirmatory Phase III trial comparing Beleodaq in combination with CHOP (Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone) therapy vs CHOP alone is required as a condition of the FDA approval. In Europe a controlled Phase III trial (the US-based Phase II BELIEF study in PTCL was an open-label, single-arm study in 120 patients) will be required for approval.

Onxeo and Spectrum plan to address both the US and European regulatory requirements with a further Phase III controlled trial in first-line PTCL combining Beleodaq with CHOP (BelCHOP) compared to CHOP alone. Initiation of a further Phase III trial will be subject to data anticipated in Q415 from an ongoing Phase I safety study, which is assessing the BelCHOP combination. Hence, further development could begin in H116. Assuming the trial takes around two to three years, this could allow for European filing in 2018 and launches from in 2019. As per the co-development terms of the deal with Spectrum, costs will be shared, with Onxeo contributing 30%, which we include in our financial forecasts and valuation.

Beleodaq could have potential beyond PTCL

Beleodaq is a histone deacetylase inhibitor (HDACi), similar to Celgene's romidepsin (Istodax) and Merck & Co's vorinostat (Zolinza), both of which are approved in CTCL. Beleodaq is a pan HDACi, therefore inhibiting the activity of several HDAC enzymes. Beleodaq Phase I/II clinical trials have already been completed in a number of oncology indications, including blood cancers and solid tumours, both as monotherapy and in combination therapy, providing Onxeo and Spectrum with a wealth of data to help shape the future development strategy.

Most recently, data were presented at ASCO including Beleodaq with doxorubicin in soft tissue sarcoma, confirming the combination was well-tolerated with progression-free survival data suggesting preliminary efficacy. With Onxeo focused on orphan oncology, a selection of previous Beleodaq data in such indications are shown in Exhibit 3.

Exhibit 3: Beleodaq development in other orphan oncology indications

Indication	Activity of belinostat
Thymic malignancies	In Phase II monotherapy trial (n=41) 2 PR and 25 SD, median PFS was 5.8 months and median OS was 19.1 months. In Phase I/II trial (n=13) in combination with cisplatin, doxorubicin and cyclophosphamide (PAC) one CR, six PR and six SD. In preclinical studies synergistic effects detected between belinostat and PAC.
MDS	In Phase II monotherapy trial (n=21) one haematological improvement. In Phase II trial (n=32) in combination with azacitidine eight CR, one PR and eight haematological improvements. In Phase I/II trial with idarubicin, the two patients with MDS responded to therapy.
HCC	In Phase I/II study (n=42) one PR and 19 SD; median PFS was 2.6 and median OS was 6.6. In preclinical studies synergistic effects detected between belinostat and sorafenib.
STS	In Phase I/II study (n=41) in combination with doxorubicin; Phase II MTD portion of the study one CR, one PR and nine SD, with median duration of response of 7.9 months. Median time to progression of six months.

Source: Edison Investment Research, Onxeo (Topotarget)

Joint future development of Beleodaq outside PTCL will depend on Onxeo and Spectrum agreeing future development plans, and we expect an update in 2016 (Spectrum has publicly made very few comments on the future development strategy for Beleodaq). Until these are disclosed our valuation only focuses on Beleodaq in PTCL. The agreement with Spectrum includes co-development, with Onxeo contributing only 30% of future development costs. According to Spectrum's most recent SEC filing, Spectrum has "final decision-making authority for all developmental activities in North America and India (and China upon exercise of its option). Topotarget [Onxeo] has final decision-making authority for all developmental activities in all other jurisdictions." Hence, should Spectrum and Onxeo choose to focus on slightly different indications for Beleodaq, there is scope that Onxeo could conduct future development alone, or perhaps as part of academic collaborations in Europe.

A potential area of interest beyond already completed trials of Beleodaq could include in combination with cancer immunotherapy (which aims to stimulate the immune system against tumour cells). Immunotherapy is set to potentially revolutionise cancer treatment; hence, synergistic products that could enhance immunotherapy effects could become much sought after assets. Although HDACs have largely been thought to be immunosuppressive, which would preclude combination with cancer immunotherapies, more recent studies[2] [3] have suggested that there could be potential synergies with immunotherapy.

However, it is very early days and any such strategy would require careful consideration, given the agreement already in place with Spectrum and the likely costs of running development in the absence of an immunotherapy partner. Nevertheless, if Spectrum and Onxeo decide to pursue an immunotherapy strategy, and can secure funds or a partner, this could significantly expand Beleodaq's potential.

Validive progression to Phase III in H116

Towards the end of 2014, Onxeo reported top-line data from the Phase II trial examining Validive as a preventative treatment for oral mucositis in patients with head and neck (H&N) cancer. Detailed data have since been presented at a number of conferences during 2015, including at ASCO, helping to raise awareness of the product. A Phase III study in a similar patient population is planned to start during H116. We estimate Validive could have peak sales potential in H&N cancer of €200m, which is at the bottom-end of Onxeo's estimate of €200-400m.

Detailed Phase II data presented at ASCO

Validive is based around the widely-used antihypertensive, anti-inflammatory agent clonidine delivered via BioAlliance's Lauriad technology as a mucoadhesive buccal tablet (MBT), which adheres to the gums, gradually releasing clonidine. The Phase II Validive trial included 183 patients with H&N cancer (in the oral cavity, oropharynx, hypopharynx or larynx) undergoing postoperative chemoradiotherapy. The trial assessed two doses of Validive (50µg and 100µg) compared to placebo with treatment initiated one to three days before radiotherapy. The primary endpoint of the trial was based on incidence of severe oral mucositis (defined as WHO grade 3 or 4).

Data from the two Validive doses were pooled and demonstrated a numerically lower overall incidence of severe oral mucositis (45%) compared to the placebo group (60%), although this was not statistically significant (Exhibit 4). The median time to onset of severe oral mucositis was 45 days with Validive (pooled doses) compared to 36 days with placebo (p=0.235). Validive-treated patients were also able to tolerate a higher cumulative dose of radiotherapy (60Gy) before onset of severe oral mucositis, compared to placebo (48Gy) (p=0.211). Validive was generally well tolerated

[2] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4196144/

[3] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3672064/

(Exhibit 5) with statistically lower incidences of nausea, dysphagia (swallowing difficulties) and abnormal weight loss, all of which are typically associated with severe oral mucositis resulting from radiotherapy.

Exhibit 4: Phase II incidence of severe oral mucositis

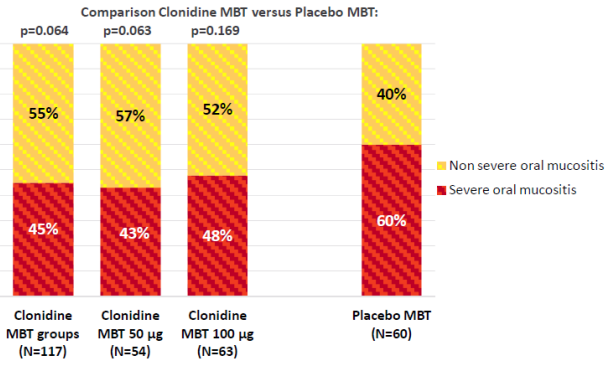


Fig 6: Overall incidence of severe oral mucositis during radiotherapy in ITT population
(6 patients without OM assessment during radiotherapy)

Source: ASCO 2015 poster #6058, Giralt J et al

Exhibit 5: Phase II summary of adverse events

	Clonidine MBT groups (N=119)		Placebo MBT (N=62)	
	No	%	No	%
Patients with at least one AE	108	91	61	98
Patients with at least one AE related to study treatment	32	27	18	29
Patients with at least one severe AE	59	50	29	47
Patients with at least one severe AE related to study treatment	12	10	4	6
Patients with at least one SAE	37	31	14	23
Patients with at least one SAE related to study treatment	2(1)	2	2(2)	3
Patients permanently removed from the study due to AE	6	5	1	2
No of death	1(3)	1	-	-

- (1) Two cases of hypotension were reported as SAE in Clonidine MBT group; (2) One case of dysphagia and one case of dehydration were reported as SAE in placebo MBT group
- (3) Death due to tumor progression not related to study treatment

Source: ASCO 2015 poster #6058, Giralt J et al

Phase III trial planned to start in H116

Following the positive trends observed in the Phase II trial, Onxeo plans to begin a Phase III study in H116 in a similar patient population (H&N cancer). We expect a trial of similar scope to the Phase II. Allowing two years to complete the trial and around one year for regulatory review, first Validive launches could potentially occur from 2019.

In-line with its orphan oncology strategy, we continue to expect Onxeo to commercialise Validive alone in the major European markets, while seeking a partner in other regions, including the US. We believe the priority is initiating the Phase III trial, supported by current resources, prior to any formal partnering initiatives. However, the availability of Phase II data, in addition to presentations at a recent scientific conference, particularly high-profile events such as ASCO, may have already prompted interest in Validive, which could facilitate the partnering process. Although we have limited visibility on the timing and terms of any partnerships, our valuation assumes Onxeo is able to secure a deal in exchange for a 17.5% royalty stream; we do not include any upfront or milestone payments.

Peak oral mucositis sales of €200m in H&N cancer alone

We have maintained our combined peak US/Europe Validive sales forecast of €200m, which only includes Validive for oral mucositis in H&N cancer. This indication is where the incidence of severe oral mucositis is highest, affecting oral function and leading to difficulty in eating; in the most severe cases it can lead to hospitalisation and cancer treatment interruption. This will also be the patient setting for the planned Phase III study. However, oral mucositis, which is a painful consequence of chemotherapy and radiotherapy, does occur in other cancers, to which we currently ascribe no value.

Onxeo estimates that around 65% of radiotherapy-treated H&N cancer patients experience severe oral mucositis (in the Phase II study 60% of placebo-treated patients developed severe oral mucositis, in-line with this estimate). We estimate around 75% of the c 63k newly-diagnosed H&N cancer patients per year in major European markets receive radiotherapy, ie. 47k, suggesting an eligible severe oral mucositis patient market of c 34k in Europe, with a likely similar number in the US. With limited current treatment options (mouthwashes and rinses focused on pain control), and Validive potentially set to be the first preventative treatment for oral mucositis, we estimate 50%

penetration of this market is possible. Assuming treatment costs of €5,000 per patient per course in Europe and a 20% premium to this in the US suggests combined Europe/US peak sales of €200m in 2025, six years post launch. If Validive can be more broadly approved in other cancer indications, given there were around 14 million cancer cases and 8.2 million deaths in 2012, there could be significant upside potential to our forecasts.

Validive has 'fast track' designation from the US FDA and has been awarded orphan drug status in Europe for the prevention of radiotherapy-induced oral mucositis in H&N cancer patients.

Sensitivities

Onxeo is subject to the usual drug development risks, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, financing and commercial risks. The main sensitivities in both the near and mid-term relate to the three orphan oncology assets: (1) Phase III Livatag data expected in H117; (2) Beleodaq US sales progression in PTCL in addition to an outline of the future development strategy; and (3) progression into Phase III with Validive in oral mucositis.

Initial Phase III Livatag data are expected in H117. Timing of event-driven trials such as ReLive is difficult to predict as it depends on the efficacy and hence survival length of both the study drug Livatag and the control arm (best supportive care). We believe an uptick in recruitment will likely be needed to achieve this timeline, which should be facilitated by the recent expansion to additional countries and centres. If the data are positive and regulatory approvals are obtained, this could be the first orphan oncology product that Onxeo commercialises alone in Europe.

Beleodaq is approved in the US for PTCL with partner Spectrum responsible for commercialisation. Sales momentum in the US could be a driver for the share price. A further study will be needed in Europe to secure approval, which is expected to start in H116. Beleodaq could have potential in a range of other cancers, although clinical studies will need to be conducted to gain regulatory approvals. Onxeo and Spectrum share Beleodaq development costs (with 30% funded by Onxeo), assuming the future development strategy is agreed by both. If Onxeo elects to conduct development outside of any agreed indications, costs will likely need to be borne entirely by Onxeo.

With Phase II data now reported for Validive in oral mucositis, progressing to Phase III development will be the next key event. There could be considerable upside to our forecasts if Validive can be successfully developed in indications outside of head and neck cancer.

In the longer term, securing approval for these assets will be key to Onxeo's orphan oncology strategy, where Onxeo plans to commercialise alone in Europe, leveraging the commercial base and generating operational efficiencies. There is execution risk around commercialisation, especially in a fragmented market like Europe. Furthermore, these synergies could be compromised if any of the products fail to reach the market. To crystallise value from each asset, Onxeo will also need to seek a partner in other regions, including the US. Although Onxeo does have considerable experience in executing out-licensing deal, we have limited visibility on the timelines and terms of any such deal(s).

Valuation

Our Onxeo valuation is reduced slightly to €328m (from €338m) or €8.1/share, with the main changes owing to a slowing of the near-term sales ramp while maintaining our peak forecasts for the time being for non-core products Oravig and Sitavig (outlined in more detail in the Financials section). There are no major changes to our underlying assumptions for Validive, Livatag and

Beleodaq (maintaining our peak sales, launch year and probability of success for each), although slightly higher near-term US Beleodaq sales forecasts have led to a corresponding small increase in valuation. Our valuation has also been rolled forwards in time and has been updated to include last reported net cash. Our valuation, which is based on a risk-adjusted NPV analysis using a 12.5% discount rate is shown in Exhibit 6.

Exhibit 6: Onxeo rNPV valuation

Product	Indication	Launch	Peak sales (€m)	NPV (€m)	Probability (%)	rNPV (€m)	NPV/share (€/share)
Validive	Oral mucositis (H&N cancer)	2019	200	113.4	60	65.0	1.6
Livatag	Liver cancer	2018	250	149.6	40	55.0	1.4
Beleodaq US	PTCL	2014	80	42.8	100	42.8	1.1
Beleodaq EU	PTCL	2019	60	53.8	70	35.9	0.9
Loramyc/Oravig	Oropharyngeal candidiasis	2007	50	23.7	100	23.7	0.6
Sitavig	Recurrent herpes labialis	2014	110	64.9	100	64.9	1.6
Net cash				41.0	100	41.0	1.0
Valuation				**489.2**		**328.4**	**8.1**

Source: Edison Investment Research. Note: Specialty products shaded. PTCL: peripheral T-cell lymphoma.

For each of the three orphan oncology products we assume that Onxeo will commercialise alone in Europe, factoring in costs for the build-out of a commercial infrastructure, with partnerships in other key regions, such as the US, in exchange for a royalty on sales. Where deals are already in place and if milestone payments are known or expected, we include these within our NPV assessments. Elsewhere, owing to the limited visibility on out-licensing deals, we generally model a simple royalty on sales and do not include upfront or milestone payments. We assume the non-core specialty products will be fully partnered, with Onxeo receiving a royalty on sales.

For both Validive and Beleodaq, we only include a contribution in indications that are currently being pursued (oral mucositis in H&N cancer for Validive, and PTCL for Beleodaq). Development in additional indications would therefore provide upside to our current forecasts. We expect an update on future Beleodaq development plans in 2016.

For Validive we assign a fairly typical 60% probability of success, commensurate with a Phase III asset. Although Livatag is in Phase III development, we assign a lower 40% probability of success despite the validated mechanism of action and prior positive Phase II efficacy data; this reflects both the harder to treat second-line liver cancer indication (the Phase II trial was in front-line) in addition to a more cautious stance owing to the severe safety issues observed in the Phase II trial. For Beleodaq in Europe where a Phase III controlled trial will need to be conducted prior to approval, we assign a 70% probability of success given the US approval.

If peak sales of Validive and Livatag approach the top end of Onxeo's current estimates (€400m for Validive and €800m for Livatag, in contrast to our current €200m for Validive and €250m for Livatag), and if Beleodaq is developed in regions beyond the core European markets (Onxeo has worldwide rights outside of the territories where Beleodaq is partnered with Spectrum and could therefore seek additional partners) and/or in indications outside of PTCL, effectively doubling our current €140m peak sales forecast, our rNPV would be around €650m, all else being equal. Maintaining these more optimistic projections and unwinding the current assumed risk-adjustments (ie increasing the probability to 100% for each product) suggests an NPV of around €1.1bn.

Financials

Onxeo's H115 revenues were €1.5m, with €1.2m generated by royalty income from partner marketed products (Beleodaq, Sitavig and Oravig); we believe the bulk of this originated from Beleodaq US sales, which were $4.5m in H115 on which Onxeo earns a mid-teens royalty. We

have increased our FY15 US Beleodaq sales to $14m (from $7.5m) given the H115 trends, driving higher Beleodaq-related royalty income. However, with decreases in our royalty forecasts for both Sitavig and Oravig (described below), overall we have reduced our FY15 revenue forecast to €3.3m (from €4.9m).

This reduction includes a lowering of Sitavig sales (Sitavig's US partner Innocutis was acquired by Cipher Pharmaceuticals in April 2015; Cipher reported Q215 US Sitavig sales of $0.5m vs our expectation for FY15 US-based royalties of €1.8m on $15m of revenues; we also now only include a minor contribution for Sitavig in Europe from new Italian partner Bruno Farmaceutici, whereas we had assumed more extensive sales across Europe). We have also reduced our Oravig royalty income forecast owing to interrupted sales following termination of the agreement with Vestiq in 2014; Oravig was partnered with Dara BioSciences (under proposal to be acquired by Midatech) in March 2015, with relaunch planned for Q415. We have maintained our peak sales forecasts for each for the time being pending further sales updates. Both Sitavig and Oravig are non-core products.

H115 operating expenses were €13.5m, including €3.7m personnel costs and €8.4m of external expenses; operating expenses included €7.8m of R&D costs. Our last published FY15 forecasts are broadly in-line with the H115 trend, and hence we make no major changes to our cost forecasts; our future cost forecasts include an uptick in R&D spend to include initiation of a Phase III trial with Validive, in addition to Onxeo's share of Beleodaq development costs (30%) on the start of the CHOP combination Phase III PTCL trial.

Our lowered FY15 revenue forecast has led to a corresponding decrease in operating and net loss. A summary of the main changes to our financial forecasts is shown in Exhibit 7.

Exhibit 7: Summary of the main changes to our Onxeo financial forecasts

€m	2015e Old	2015e New	% change	2016e Old	2016e New	% change
Revenue	4.909	3.328	-32	8.743	7.049	-19
Personnel costs	(8.616)	(8.624)	+0	(9.026)	(9.056)	+0
External expenses	(16.422)	(16.437)	+0	(17.204)	(17.260)	+0
Operating profit	(20.791)	(24.380)	+17	(18.183)	(21.576)	+19
Profit before tax (reported)	(20.169)	(23.371)	+16	(17.762)	(21.195)	+19
Profit after tax (reported)	(23.135)	(26.337)	+14	(20.728)	(24.161)	+17

Source: Edison Investment Research

Onxeo reported cash and equivalents at end-June 2015 of €42.9m and has debt of €1.9m (including short term-debt of €1.8m and repayment of a conditional advance related to Livatag due by September). We believe this should be sufficient to fund operations into 2017. Development of Beleodaq in additional indications, which is under discussion with partner Spectrum, could affect the cash reach.

Following the merger with Topotarget, effective from 1 July 2014, Topotarget financials are now fully consolidated within the financial accounts in 2015. Our financial summary in Exhibit 9 displays the historic BioAlliance standalone data only (which only include a contribution from Topotarget from H214). For comparison purposes, Onxeo has provided both standalone financial data and pro forma financial statements, which we have summarised in Exhibit 8, in addition to our financial forecasts. Note that 2014 revenues included non-recurring milestone income from Spectrum related to Beleodaq NDA filing in H114 ($10m, only included in the pro forma numbers) and US approval in H214 ($25m, which is included in the standalone financials).

Exhibit 8: Select Onxeo standalone and pro forma financials

€m	2013		2014		2015e	2016e
	Standalone	Pro forma	Standalone	Pro forma	Forecast	Forecast
Net sales	1.467	2.585	22.081	35.300	3.328	7.049
Personnel costs	(5.347)	(7.684)	(7.116)	(8.266)	(8.624)	(9.056)
External expenses	(10.687)	(13.653)	(13.563)	(14.646)	(16.437)	(17.260)
Merger costs	0.000	0.000	(4.861)	(9.734)	0.000	0.000
Net Income (reported)	(15.325)	(20.009)	(7.699)	(2.406)	(26.337)	(24.161)

Source: Edison Investment Research, Onxeo accounts

Exhibit 9: Financial summary

€000s	2009	2010	2011	2012	2013	2014	2015e	2016e
Year-end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS								
Revenue	7,536	22,532	3,231	4,028	1,467	22,081	3,328	7,049
Cost of Sales	(399)	(859)	(750)	(375)	(264)	(249)	(324)	(324)
Gross Profit	7,138	21,673	2,481	3,653	1,202	21,832	3,004	6,725
EBITDA	(15,024)	3,065	(14,429)	(11,300)	(15,189)	(4,505)	(22,399)	(19,591)
Operating Profit (before amort. and except.)	(15,362)	2,698	(14,841)	(11,506)	(15,412)	184	(22,784)	(19,990)
Intangible Amortisation	(117)	(105)	(97)	(9)	(10)	(800)	(1,586)	(1,586)
Exceptionals	0	0	0	0	0	(4,861)	0	0
Other	0	0	0	0	(29)	(77)	(10)	0
Operating Profit	(15,478)	2,593	(14,938)	(11,515)	(15,450)	(5,554)	(24,380)	(21,576)
Net Interest	95	217	316	(33)	126	5	1,009	381
Profit Before Tax (norm)	(15,266)	2,914	(14,525)	(11,539)	(15,286)	189	(21,776)	(19,609)
Profit Before Tax (reported)	(15,383)	2,809	(14,622)	(11,548)	(15,325)	(5,549)	(23,371)	(21,195)
Tax	0	(0)	0	0	0	(2,150)	(2,966)	(2,966)
Profit After Tax (norm)	(15,266)	2,914	(14,525)	(11,539)	(15,315)	(2,038)	(24,752)	(22,575)
Profit After Tax (reported)	(15,383)	2,809	(14,622)	(11,548)	(15,325)	(7,699)	(26,337)	(24,161)
Average Number of Shares Outstanding (m)	12.9	13.6	17.7	17.7	20.7	40.5	40.5	40.6
EPS - normalised (€)	(1.18)	0.21	(0.82)	(0.65)	(0.74)	(0.05)	(0.61)	(0.56)
EPS - normalised and fully diluted (€)	(1.18)	0.21	(0.82)	(0.65)	(0.74)	(0.05)	(0.61)	(0.56)
EPS - (reported) (€)	(1.19)	0.21	(0.83)	(0.65)	(0.74)	(0.19)	(0.65)	(0.60)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	94.7	96.2	76.8	90.7	82.0	98.9	90.3	95.4
EBITDA Margin (%)	N/A	13.6	N/A	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	12.0	N/A	N/A	N/A	0.8	N/A	N/A
BALANCE SHEET								
Fixed Assets	2,319	2,083	1,793	1,540	1,300	89,052	87,238	85,605
Intangible Assets	130	117	27	33	23	87,932	86,346	84,760
Tangible Assets	1,919	1,632	1,401	1,086	908	711	492	446
Investments	270	334	366	422	369	409	399	399
Current Assets	19,017	24,251	32,288	20,581	16,432	62,946	38,903	17,402
Stocks	21	38	1	3	3	65	85	85
Debtors	957	243	456	2,089	338	582	365	772
Cash	14,710	20,947	28,666	14,503	11,329	57,227	33,381	11,472
Other	3,328	3,023	3,164	3,986	4,762	5,073	5,073	5,073
Current Liabilities	(6,794)	(5,737)	(7,051)	(6,147)	(6,357)	(12,919)	(12,792)	(13,053)
Creditors	(6,719)	(5,680)	(6,881)	(6,090)	(6,266)	(11,290)	(11,162)	(11,423)
Short term borrowings	(75)	(57)	(170)	(57)	(91)	(1,630)	(1,630)	(1,630)
Long Term Liabilities	(1,780)	(1,745)	(4,128)	(4,231)	(3,487)	(17,108)	(16,950)	(16,950)
Long term borrowings	(1,067)	(1,131)	(2,237)	(511)	(303)	(138)	0	0
Other long term liabilities	(714)	(614)	(1,891)	(3,720)	(3,185)	(16,970)	(16,950)	(16,950)
Net Assets	12,761	18,852	22,902	11,742	7,888	121,971	96,399	73,004
CASH FLOW								
Operating Cash Flow	(17,426)	3,492	(11,614)	(14,076)	(14,020)	(7,733)	(21,788)	(18,971)
Net Interest	(359)	3	(0)	1,788	345	821	1,009	381
Tax	0	0	0	0	0	0	(2,762)	(2,966)
Capex	(230)	(108)	(148)	(39)	(119)	(2)	(166)	(352)
Acquisitions/disposals	0	0	0	0	0	14,208	0	0
Financing	(107)	2,803	18,261	3	10,795	37,229	0	0
Dividends	0	0	0	0	0	0	0	0
Net Cash Flow	(18,122)	6,191	6,499	(12,324)	(3,000)	44,524	(23,708)	(21,909)
Opening net debt/(cash)	(31,691)	(13,569)	(19,760)	(26,259)	(13,935)	(10,935)	(55,459)	(31,751)
HP finance leases initiated	0	0	0	0	0	0	0	0
Other	0	(0)	(0)	0	0	0	0	0
Closing net debt/(cash)	(13,569)	(19,760)	(26,259)	(13,935)	(10,935)	(55,459)	(31,751)	(9,842)

Source: Edison Investment Research, Onxeo accounts. Note: Historic financials display standalone data only, with Topotarget consolidated from H214.

Contact details	Revenue by geography
49, boulevard du Général Martial Valin 75015 Paris France +33 (0)1 45 58 761 00 www.onxeo.com	N/A

Management team

CEO: Judith Greciet	CFO: Nicolas Fellmann
Judith Greciet became CEO in 2011. From 2007 to 2010, she was president of Eisai France, focusing on Alzheimer's disease. She has held former operational and strategic managerial positions at Wyeth, LFB Group, Zeneca and Pharmacia. She is a pharmacist and has headed up oncology and hospital departments.	Nicolas Fellmann became CFO in November 2006. From 1996 to 2006, he held various finance positions at Pfizer France and was notably director of treasury tax and audit from 1999. From 1992 to 1995, he was a financial auditor at Ernst & Young. He has a MBA from EM Lyon Business School.
CSO: Graham Dixon	
Graham Dixon joined Onxeo in February 2015 with 20 years' experience in research and development in the pharmaceutical industry, particularly oncology, having held senior management positions in big pharma and biotech. Prior to Onxeo Dr Dixon was Director of R&D at Galapagos for 10 years. He has a PhD in biochemistry from the University of Swansea, Wales.	

Principal shareholders	(%)
Financière de la Montagne	14.00
Healthcap funds	2.30

Companies named in this report

Spectrum Pharmaceuticals (SPPI.US); Cipher Pharmaceuticals (CPHR.US); Dara BioSciences (DARA.US); Midatech (MTPH.LN)