10 September 2010

TopoTarget

Year End	Revenue (DKKm)	PBT* (DKKm)	EPS* (DKK)	DPS (DKK)	P/E (x)	Yield (%)
12/08	43.9	(306.1)	(4.68)	0.0	N/A	N/A
12/09	44.0	(142.7)	(1.41)	0.0	N/A	N/A
12/10e	128.8	(26.3)	(0.20)	0.0	N/A	N/A
12/11e	90.6	(50.2)	(0.36)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding goodwill amortisation and exceptional items, $0.170/DKK, €0.134/DKK.

Investment summary: Betting on belinostat

TopoTarget's prospects are closely tied to those of its lead drug, belinostat. It is in a pivotal Phase II trial for peripheral T-cell lymphoma (PTCL) and could gain approval in 2012. The drug is also being developed for cancer of unknown primary (CUP) and non-small cell lung cancer (NSCLC). The North American and India rights have been out-licensed to Spectrum Pharmaceuticals. We are forecasting that belinostat will generate peak revenues of $1.2bn.

Major catalyst in coming year

The pivotal clinical trial in PTCL is due to report in 2011 and Spectrum aims to file an NDA later that year. There is an SPA in place so if belinostat demonstrates 20% ORR (Phase II study: ORR=32% n=19) it should be approved in 2012 as it has been given fast-track status, assuming there are no additional safety signals.

Potential best in class drug

Belinostat belongs to the histone deacetylase inhibitor (HDACi) class of drugs, but appears to be differentiated from similar drugs by its safety profile. Limited haematological adverse events have been detected and the recommended dose is well tolerated in combination with standard chemotherapy treatments, including in solid tumours.

Main market opportunities beyond PTCL

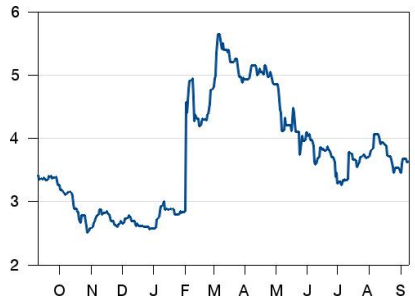
The niche indication of PTCL is being targeted to gain a rapid approval for belinostat, with larger markets being targeted subsequently. There are no approved therapies so far for CUP, despite c 2-6% of tumours falling into this class. NSCLC is the second most prevalent form of cancer.

Valuation: DKK990m based on DCF

TopoTarget was valued using a SOTP DCF at DKK994m. The current EV is c DKK250m, even though belinostat could be on the market in 2012 and generate revenues of over $1bn by 2020. The company is also well capitalised with DKK262m of cash at Q210.

Price	DKK3.66
Market Cap	DKK486m

Share price graph



Share details

Code	TOPO
Listing	OMX Copenhagen
Sector	Pharmaceuticals & biotech
Shares in issue	132.7m

Price

52 week	High	Low
	DKK5.85	DKK2.44

Balance Sheet as at 30 June 2010

Debt/Equity (%)	N/A
NAV per share (DKK)	3.17
Net cash (DKKm)	262

Business

TopoTarget is a Danish drug development and marketing company focused on the field of oncology. Its lead product is belinostat and it has out-licensed its North American and India rights to Spectrum.

Valuation

	2009	2010e	2011e
P/E relative	N/A	N/A	N/A
P/CF	N/A	N/A	N/A
EV/Sales	5.3	2.2	4.3
ROE	N/A	N/A	N/A

Revenues by geography

UK	Europe	US	Other
N/A	N/A	N/A	N/A

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Investment summary: Betting on belinostat

Company description: Danish oncology company

TopoTarget is a drug development and marketing company focused on oncology. It was founded in 2000 and listed on the Copenhagen Stock Exchange (now OMX) in 2005. Its headquarters are in Copenhagen and it also has operations in the UK and the US, with c 40 employees. To date it has raised a total of DKK1.06bn in equity. It has taken one drug to market, called Totect in the US and Savene in Europe, which prevents tissue damage caused by anthracycline extravasation (leakage of blood vessels) following chemotherapy. The product was approved in Europe in 2006 and in the US in 2007 and has been promoted by TopoTarget's own sales force, generating revenues of DKK39.7m in 2009. However, TopoTarget sold the rights for Savene (including its sales force) to SpePharm Holding for €5m and double-digit royalties up to €1m.

Its key product is belinostat, which is in a pivotal Phase II study. The North American and Indian rights to the drug were out-licensed to Spectrum Pharmaceuticals in a deal worth c $350m in February 2010. It is hoped that belinostat will initially be approved for PTCL in 2012, before having its label expanded to include cancer of unknown primary (CUP) and non-small cell lung cancer (NSCLC). We are forecasting potential peak sales of $1.2bn for belinostat.

Valuation

TopoTarget has been valued at DKK994m using a SOTP DCF valuation. The potential royalties from belinostat in PTCL are worth DKK564m, in CUP DKK604m and NSCLC DKK313m. The valuation of the different revenue lines is very sensitive to the eventual price of belinostat and whether belinostat is positioned for the mass oncology market or for niche indications.

Positive results of the pivotal trial in PTCL, which is due to be completed in 2011, should act as a major catalyst and enable belinostat to be approved in 2012.

Sensitivities

The prospects of the company are closely linked to that of its lead drug, belinostat. In the short term, the results of belinostat in its clinical trials and whether it is able to gain approval will be key. In the longer term, the ability of Spectrum to market belinostat successfully will be most important. Spectrum is a highly motivated and ambitious company, but it will be competing against much larger companies with better established oncology franchises, such as Merck & Co and Celgene.

Financials

TopoTarget is well capitalised following the rights issue in 2009 that raised DKK132.6m and the licensing deal with Spectrum (upfront payment of $30m); at Q210 it had a cash position of DKK262m. The company has sufficient cash to operate into H212 in the absence of any additional funding.

Its cash position could be enhanced further by the sale of assets and the achievement of milestones in its agreement with Spectrum (eg on submission of an NDA in PTCL, marketing approval). The company is currently undergoing a strategic review, the results of which will be announced at its Q310 results, which could lead to a change in spending assumptions.

Company description: Danish oncology company

The investment case in TopoTarget is linked to the prospects of belinostat, a histone deacetylase inhibitor (HDACi) that is being developed for a broad array of oncology indications. The drug is currently in a pivotal trial for PTCL as a monotherapy with a special protocol assessment (SPA) and the company is hoping to file its NDA during H211 under a fast track protocol. In parallel, belinostat is in 11 other clinical trials in various oncology indications (including CUP) and drug combinations, which are being funded by the firm, its partner Spectrum Pharmaceuticals and the National Cancer Institute in the US.

TopoTarget's most promising drug in development is belinostat, which belongs to a new class of oncology products called histone deacetylase inhibitors (HDACi). There are over 12 of them in development, with two on the market. They are primarily being developed for the oncology market, but also other indications including autoimmune disease. TopoTarget has out-licensed the rights to the drug for North America and India, with an option on China, to Spectrum Pharmaceuticals in a deal worth c $350m with double-digit royalties, including a $30m upfront payment.

There are three other products in clinical development. Exhibit 1 provides details of TopoTarget's products that are either on the market or in clinical development. François Martelet, who was appointed CEO in February 2010, is conducting a strategic review and will announce its results at TopoTarget's Q310 results. Consequently some of these assets might be divested or be placed on hold. An overview of belinostat's current clinical trial programme is shown in Exhibit 2.

Exhibit 1: R&D pipeline and marketed products

Product	Indication	Development stage	Notes
Totect/Savene dexrazoxane	Anthracycline extravasion	Marketed	Topoisomerase II catalytic inhibitor blocking the activity of anthracyclins. Generated sales in Europe of DKK26.8m (c €3.6m) and in the US of DKK17.1m (c €2.3m). European rights (Savene) sold to SpePharm Holding for €5m plus royalties up to €1m. Patents lapse in March 2020.
Belinostat	PTCL, CUP and other cancers	Pivotal study	HDAC inhibitor. Drug identified by TopoTarget; in 2004 entered into a licence and collaboration agreement with CuraGen to develop drug; in 2008 Topotarget bought back the product rights for $30m, 5m shares and up to $6m at the rate of 10% of the first $60m in belinostat sales (it received $3m following the licensing agreement with Spectrum, $3m is outstanding). In February 2010, it out-licensed the North American and Indian rights to Spectrum Pharmaceuticals in a deal worth c $350m. Composition of matter patent expires in September 2021; iv formulation patent until May 2026, if granted. Further details below.
APO866	Solid and haematological tumours	Phase II	A specific inhibitor of NMPRT, a key enzyme needed for the production of nicatinamide adenine dinucleotide (NAD+). It targets cells with a high turnover of NAD+ such as tumour cells. In open label Phase II study in 43 pts with melanoma, open label Phase II study in 23 pts with refractory or relapsed cutaneous T-cell lymphoma (CTCL) and PoC Phase I/II in 10 pts with refractory or relapsed B-chronic lymphocytic leukaemia (B-CLL). Company obtained an exclusive, worldwide licence for the product from Astellas by acquiring Apoxis for €14.5m in 2007. Astellas has the right to buy back the drug until the end of Phase II, and first right of negotiation at any time. Protected by four patent families until September 2026 if all patents granted.
Zemab	Breast, head and neck cancer	Phase I	An antibody/toxin recombinant protein that targets the ErbB2/HER2 receptor, similar to Herceptin but with a cytotoxin attached. In-licensed from Novartis in 2003, Topotarget will pay milestones and royalties to Novartis. The latter retains a buy-back option until the end of Phase II to the market. A patent has been filed which should give protection July 2028 after making improvements to recombinant protein technology.
APO010	Solid tumours	Phase I	A recombinant fusion protein derived from the human Fas ligand that promotes apoptosis. In dose escalation study with up to 35 pts with untreatable or refractory solid tumours. Obtained through acquisition of Apoxis.

Source: Edison Investment Research.

Exhibit 2: Belinostat development overview

Indication	Therapy	Funding	Comments
Relapsed or refractory PTCL	Monotherapy	100% Spectrum	Pivotal Phase II trial. Trial name: BELIEF: 1,000mg/m^2 by 30min iv infusion on days 1-5 of 21-day cycle, 120 pts. Primary endpoint is overall response rate of 20% in 100 evaluable pts. No active comparator. Started December 2008, estimated H111. NDA filing expected in 2011.
CUP	+ carboplatin + paclitaxel	100% TopoTarget	Phase II trial. Belinostat 1,000mg/m^2 iv over 30 min on days 1-3 with carboplatin (AUC 6) and paclitaxel (175mg/m^2) on day 3 and 2,000mg of oral belinostat on days 4 and 5 of 21-day cycle, 88pts. Open-label randomised trial, pts in active comparator do not receive belinostat (c 44 in each arm). Primary endpoint: PFS measured by RECIST criteria, started February 2009, estimated completion date is Q311.
NSCLC	+ carboplatin + paclitaxel	30% TopoTarget 70% Spectrum	Phase II trial to assess optimal dose and assess clinical activity, to be initiated possibly in H210.
Hepatocellular cancer	Monotherapy	Collaboration with NCI	Phase I/II trial. Phase I dose escalation study with iv belinostat and 24 pts given on days 1-5 of 21-day cycle until disease progression or unacceptable toxicity, followed by Phase II study with iv belinostat being given to 37 pts at MTD to assess tumour response. Started in May 2006.
Ovarian cancer	+ carboplatin + paclitaxel	Collaboration with NCI	Phase I/II trial. Phase I dose escalation study with iv belinostat up to 1,000mg/m^2 in combination with standard doses of carboplatin and/or paclitaxel and given on days 1-5 of 21-day cycle until disease progression or unacceptable toxicity, followed by Phase II study with iv belinostat being given to 18-32 pts with relapsed ovarian cancer and 15 pts with urothelial carcinoma of the bladder at MTD to assess tumour response, 80 pts in total. Started September 2005, completed April 2010.
Recurrent or metastatic Thymoma/ thymic carcinoma	Monotherapy	Collaboration with NCI	Phase II trial. Belinostat 1,000mg/m^2 iv delivered over 30 min on days 1-5 of 21-day cycle for 12 courses, 50 pts. No active comparator, all patients must have received platinum containing chemotherapy course previously. Primary outcome: ORR assessed by RECIST criteria. Started in December 2007, final data collection date for primary outcome is estimated to be in 2011.
Solid tumours/ STS	+ doxorubicin		Phase I/II trial. Phase I dose escalation study with iv belinostat in combination with doxorubicin, followed by Phase II study with iv belinostat being given to 20-40 pts at MTD to assess tumour response, 65 pts. Trial will be stopped if no more than two responses in first 20 pts in second part of trial. Started in May 2006, expected completion in 2011.
AML/MDS	+ azacitidine	Collaboration with NCI	Phase I dose escalation study with iv belinostat in combination with azacitidine. Primary endpoint to identify MTD with tumour response a secondary endpoint, 33 pts. Started June 2006.
SCLC, and other advanced cancers	+ cisplatin + etoposide	Collaboration with NCI	Phase I dose escalation study with iv belinostat in combination with cisplatin and etoposide, 44 pts. Primary endpoint to identify a safe and tolerable dose for Phase II study, with a secondary pharmacokinetic endpoint. Started June 2009, expected completion date is June 2012.
Advanced solid tumours and lymphomas	+bortezomib	Collaboration with NCI	Phase I dose escalation study with iv belinostat on days 1-5 in combination with bortezomib (Velcade) on days 1,4,8 and 11 (2,5,8,11 during course 1), 55 pts. Primary endpoint to identify MTD. Trial started March 2006.
Advanced Solid tumours and lymphomas	Monotherapy – Oral formulation	30% TopoTarget 70% Spectrum	Phase I dose escalation study with oral belinostat dosed once or twice daily, continuously or discontinuously, 100pts. Primary endpoint safety and to identify MTD. Trial started June 2006, estimated completion date December 2010.
1st line treatment of advanced or recurrent thymoma/ thymic carcinoma	+cisplatin +cyclo-phosphamide +doxorubicin	Collaboration with NCI	Phase I/II trial. Phase I dose escalation study with belinostat given civ infusion over 48hrs starting on day 1 of 21-day cycle, with doxorubicin on days 2 and 3, cisplatin on day 2 and cyclophosphamide on day 3, followed by Phase II study with iv belinostat being given to 37 pts at MTD; 58 pts. Phase II study to continue for 6 treatment cycles or until disease progression (belinostat monotherapy can be given after cycle 6). Primary endpoint of Phase I part to determine safe and tolerable Phase II dose; primary endpoint of Phase II part to determine clinical response. Trial began March 2010, estimated completion date February 2012.
Relapsed and refractory acute leukaemia and MDS	+bortezomib	Collaboration with Virginia Commonwealth University and MD Anderson	Phase I dose escalation study IV over 30 min on days 1-5 and 8-12 and bortezomib IV on days 1, 4, 8 and 11 on 21-day cycle for up to 12 cycles in the absence of disease progression or unacceptable toxicity. Primary objective to identify dose for Phase II together with safety and tolerance.

Source: Edison Investment Research

Belinostat

TopoTarget hopes to have belinostat approved for relapsed and refractory PTCL in 2012, before expanding the label to include CUP, NSCLC and other forms of cancer. Its partner, Spectrum, is aiming to file an NDA in 2011 to gain approval for the treatment of PTCL as a monotherapy. An SPA has been agreed with the FDA for the PTCL pivotal study and belinostat has also been granted fast-track approval and given orphan drug designation.

The results of some of the clinical trials to date are summarised in Exhibit 3. In total belinostat has been given to over 700 patients and has been shown to be well tolerated at the recommended dose of 1,000mg/m^2 with limited grade 3/4 adverse events (primarily nausea, vomiting and fatigue), limited haematological adverse events and no cardiac safety signal. Belinostat can be delivered at the recommended dose in combination with standard chemotherapy, and has tended to show a greater ORR in combination with other chemotherapy agents than as a monotherapy.

Exhibit 3: Completed studies with belinostat

Indication	Therapy	Notes
Advanced solid tumours	+5-fluorouracil	Phase I, 35pts, escalating doses of belinostat and 5-fluorouracil up to 1,000mg/m^2. Common AE were fatigue, nausea and vomiting, no clinically relevant effects on ECG parameters found. 9 SD observed.
Advanced solid tumours	+ carboplatin and/or paclitaxel	Phase I, 23pts. Primary endpoint was to identify MTD or DLT up to 1,000mg/m^2 in combination with standard doses of carboplatin and/or paclitaxel, no DLT observed, 5 grade 3 adverse events including thrombocytopenia in one case, no grade 4. 2 PR and 10 SD observed.
Relapsed ovarian cancer	+ carboplatin and paclitaxel	Phase II, 35pts, dose 1,000mg/m^2 iv over 30-60min. Generally well tolerated with most common adverse events, nausea, fatigue and vomiting, grade 3/4 neutropenia in 2 cases, although 5 discontinued study because of AEs and 1 withdrew consent. 3 CR and 16 PR observed (by RECIST and CA125 criteria).
Advanced solid tumours	Oral	Phase I, 60 pts, escalating doses with different dosing regimes. Most frequent AE were fatigue, nausea and anorexia, MTD for continuous (all of 28d cycle) QD dosing was 250mg/m^2, for continuous BID dosing was 250mg/m^2, and for discontinuous (days 1-14 of 28 day cycle) the MTD was not reached (max dose 750mg/m^2 QD and 500mg/m^2 in morning, 250mg/m^2 in evening).
Recurrent or refractory CTCL or PTCL	Monotherapy	Phase II, 20pts, 1,000mg/m^2 iv over 30min on days 1-5 of 21 day cycle. Nausea and fatigue most common AE, 1 Grade 3/4 AE of thrombocytopenia. CTCL efficacy: 1 CR; 2 PR; 8 SD (n=8). PTCL efficacy: 2 CR; 0 PR; 8 SD (n=12).
Haematological neoplasia	Monotherapy	Phase I, 16 pts, dosing of 600, 900 and 1,000mg/m^2 iv over 30 min on days 1-5 of 21 day cycle. Nausea, vomiting and fatigue were the most common AE, two Grade 4 AE of renal failure in two pts with MM, 1 haematological Grade 3 AE (lymphopenia), no cardiac AE. 0 CR; 0 PR; 5 SD and 2 achieved disease stabilisation during 2 of the 9 cycles.
Advanced solid tumours	Monotherapy iv	Phase I, 46 pts, dosing of 150-1200mg/m^2 iv over 30 min on days 1-5 of 21 day cycle. Three Grade 3 AE detected, all with 1200mg dose (lethargy, nausea and anorexia. 0 CR; 0 PR; 18 (39%) SD.
Relapsed/ refractory PTCL	Monotherapy	Ongoing Ph II study (recruitment ended) 1,000mg/m^2 iv over 30 min on days 1-5 of 21 day cycle. CR: 2 pts; PR: 4 pts; ORR: 32%; median durable response: +268 days.
MDS	Monotherapy	Phase II, 21 pts, dosing of 1,000mg/m^2 iv over 30 min on days 1-5 of 21-day cycle for 4 cycles. Grade 3/4 AE possibly related to belinostat: neutropenia (10 pts); thrombocytopenia (9 pts); anaemia (5 pts) and fatigue (2 pts). ORR 5% (1 pt). Trial not extended by 29 pts because of ORR <3 pts.

Source: Edison Investment Research

The current clinical development programme for belinostat as disclosed is detailed in Exhibit 2, including the eight studies that are being conducted in collaboration with the National Cancer Institute (NCI) in the US, for which TopoTarget supplies belinostat but has no additional financial commitment. The support of the NCI provides validation of the potential of belinostat, however it should be noted that it is also funding trials with other HDACi.

CEO François Martelet has a strong commercial background in the HDACi space. From 2005-07 he was vice president and worldwide franchise head, oncology at Merck & Co, during which time he was involved in the global launch of Zolinza (vorinostat), the first HDACi to be approved.

Licensing deal

In February 2010, TopoTarget out-licensed the North American and Indian rights to belinostat to Spectrum Pharmaceuticals (market cap: $201m, listed on NASDAQ, SPPI), which is a speciality pharmaceutical company that acquires and develops oncology products. It markets two products in North America (c 75 sales reps out of a total number of c 160 employees): ibritumomab tiuxetan (Zevalin) for non-Hodgkin's lymphoma (NHL); and levoleucovorin (Fusilev) for osteosarcoma.

The principal details of the licensing deal are:

- Spectrum has the exclusive right to commercialise belinostat in North America and India, and has an option on China.
- TopoTarget received $30m in an upfront payment, and could receive a further $313m and 1m shares of Spectrum (currently worth $3.8m) if certain development, regulatory and sales milestones are met.
- Spectrum will pay the entire costs of the PTCL clinical trial; TopoTarget will pay all the costs of the current Phase II CUP trial and the costs of the future clinical trials will be divided 70%:30% to Spectrum and TopoTarget respectively.
- There is a co-promote option for TopoTarget if Spectrum Pharmaceuticals does not maintain a minimum number of field reps over a certain period.

PTCL

Belinostat needs to have a 20% ORR from 100 evaluable patients to satisfy the requirements of the SPA in its pivotal trial (in a Phase II trial with 19 patients, an ORR of 32% was achieved). Should the pivotal clinical trial be a success, belinostat could be on the market in 2012. The trial is expected to be concluded in 2011, with the NDA Filing submitted by Spectrum by late H211, and the FDA has granted TopoTarget fast track designation for this orphan indication (belinostat has orphan status for PTCL and the associated seven years data exclusivity associated with it).

The number of new cases of PTCL per year in the US is estimated to be 8,200, c 12% of NHL cases. Chemotherapy regimens such as CHOP, EPOCH and hyperCVAD tend to be used in first-line treatment, however the five-year survival rate is only between 25-40% depending on the subtype of PTCL. The only treatment that is currently approved for this indication is pralatrexate (Folotyn) marketed by Allos Therapeutics. Pralatrexate appears to have a similar response rate to belinostat (ORR 27%, n=109), but a worse safety profile with 70% of patients experiencing mucositis and 41% with thrombocytopenia. We assume that Celgene is planning to submit an sNDA to get romidepsin's (Istodax) label expanded to include PTCL in the US later this year.

CUP

There is no drug therapy specific approved for treatment of CUP. It is a recognised diagnosis and the incidence rate is estimated to be between 2-6% of cancers in the US (30,000-90,000 new cases pa), although this will probably fall gradually as diagnostic techniques improve (including use of biomarkers). The prognosis for these patients is particularly poor; five-year survival rate is estimated to be c 11% compared to 68% for all forms of cancer, although this is partly because there are no targeted treatments for them.

Belinostat, in combination with carboplatin and paclitaxel, has the potential to become the first approved therapy for CUP, with approval for this indication possible in 2015 (cetuximab, everolimus and bevacizumab are also in Phase II trials for CUP). It could also become the first HDACi to be approved for the treatment of a solid tumour indication, as well as the first one approved in combination with an established standard of care. Both claims could enable belinostat to be differentiated from other HDACi, and enable belinostat to be positioned as a complementary treatment to the current established oncology treatments.

NSCLC

NSCLC is the second most common form of cancer (c 220,000 new cases in the US each year), but is also one of the most competitive oncology markets with 16 new treatments for NSCLC in Phase III trials. The partners believe that belinostat should demonstrate efficacy in a similar manner to Merck & Co's vorinostat (ORR of 34% compared to 12.5% with placebo in a Phase II study in combination with carboplatin and paclitaxel for first-line therapy; 62 patients in vorinostat arm and 32 in placebo arm), but without the haematological adverse events that the latter causes.

It is unlikely that it could be approved for this indication before 2015.

HDACi and competitive landscape

There are 11 HDACi that are in development or on the market for cancer indications, as shown in Exhibit 4, because of the promise that the class demonstrates (HDACi are also in development for other indications because they can have anti-inflammatory and immunosuppressive effects, eg Karus Therapeutics is developing an HDACi for the treatment of rheumatoid arthritis).

The precise mechanism by which the HDACi work is unclear. There are at least 11 HDACs that have an effect on a broad range of proteins. The HDACi have an epigenetic effect (non-specific effect on a cell's genes) through altering the level of acetylation of histones and causing the DNA to be in a more open form. But HDACi have other effects as they alter the activity proteins such as oestrogen receptors, hsp90 and p53, all known to be associated with oncology, and also tubulin which performs a key role during cell division. The range of effects explains the synergistic effects that occur with different chemotherapy agents.

The current clinical data suggests that the safety profiles of the products (primarily haematological and cardiac issues) will probably become a key differentiator, and importantly if they can be used in combination with other oncology products. Efficacy will also be important but there does not currently appear to be clear differences in clinical efficacy, despite *in vitro* data suggesting that some drugs are more potent than others (eg *in vitro* belinostat is 3-5x more potent than vorinostat). The delivery mechanism will influence the choice of some physicians, with oral products preferred. Finally the marketing power of the company promoting the product will determine its potential.

Belinostat's main strength appears to be its safety profile (885 patients have been treated to date with belinostat) compared to the other HDACi, with relatively limited haematological effects and a good cardiac safety profile, and the fact that it can be taken at the recommended dose of 1,000mg/m^2 in combination with all of the current oncology products with which it has been tested (these include doxorubucin, carboplatin, paclitaxel and bortezomib).

Exhibit 4: HDAC competitive summary

Note: Active trials refers to the clinical trials that are active according to clinicaltrials.gov.

Drug / Company	Development stage	Notes
Vorinostat/ SAHA/ Zolinza **Merck & Co**	Approved (CTCL)	**Main indications:** CTCL (approved) **Other indications:** NSCLC, breast, AML, MDS, NHL, MM, mesothelioma and others (106 active trials) **Efficacy:** CTCL: ORR 30% (n=74, mono), ORR 31% (n=33, mono); MM: ORR 0% SD 90% (n=10, mono), ORR 26% SD 53% (n=34, comb); Renal: ORR 18%, SD 67% (n=32, comb); CRC: ORR 5%, SD 52% (n=21, comb); NSCLC: ORR 47% SD 42% (n=19, comb); Breast: SD 29% (n=14, mono), ORR 17% (n=17, comb); Prostate: no efficacy shown because of toxicities. **Tolerability:** Nausea, fatigue, thrombocytopenia, anaemia, no QT prolongation **Approval date:** 2006 (CTCL)
Depsipeptide/ romidepsin/ Istodax **Celgene**	Approved (CTCL)	**Main indications:** CTCL, PTCL (pivotal Ph III expected to be completed in 2010), MM **Other indications:** melanoma, bladder, head & neck, GI, leukaemia (15 active trials) **Efficacy:** CTCL: ORR 35% (n=96+71, mono); PTCL ORR 34% (n=71, mono); solid tumours: ORR 3%, SD 36% (n=33, comb.); prostate: ORR 3% SD 6% (n=31, mono) **Tolerability:** Nausea, vomiting, fatigue and haematological AE (neutropenia, thrombocytopenia, anaemia), no QT prolongation observed **Approval date:** November 2009 (CTCL) **Other:** Obtained via acquisition of Gloucester Pharma. for $340m + $300m (milestones)
Panobinostat/ LBH589 **Novartis**	Phase III	**Main indications:** Hodgkin's lymphoma (filing expected in 2010), MM **Other indications:** Prostate, AML, thyroid, MDS, NHL, myelofibrosis (45 active trials) **Efficacy:** CTCL: ORR 16% (n=63, mono), Prostate ORR 19% (n=16, comb), breast: ORR 11% (n=18, comb), ORR 7%, SD 27% (n=15, comb); MM: ORR 57% SD 23% (n=30, comb); SCLC: ORR 11% (n=19, mono) **Tolerability:** dyspnea, thrombocytopenia, nausea, QT prolongation **Potential launch date:** 2011
Belinostat / PDX101 **TopoTarget (Spectrum)**	Pivotal Phase II	**Main indications:** PTCL (SPA, FTA, orphan status), CUP, NSCLC **Other indications:** thymic, HCC, ovarian, STS, MDS, AML, and others (17 active trials) **Efficacy:** PTCL: ORR 32% (n=19, mono); ovarian: ORR 30% (n=23, comb.); solid tumours: ORR 9%, SD 43% (n=23, comb.) and ORR 0%, SD 39% (n=46, mono); MDS: ORR 5% (n=21, mono) **Tolerability:** Nausea, vomiting and fatigue with limited haematological AE; can be taken at recommended dose in combination with chemotherapy **Potential launch date:** 2011 for PTCL **Other:** N. American and Indian rights acquired by Spectrum in $350m deal + royalties
Entinostat/ MS-245 **Syndax**	Phase II	**Main indications:** HL **Other indications:** NSCLC, breast, MDS, CML, AML (5 active trials) **Efficacy:** NSCLC: ORR 10% SD 20% (n=10, comb.); breast: ORR 4%, SD 4% (n=27, comb) **Tolerability:** Nausea, fatigue, diarrhoea, cytopenias **Potential launch date:** 2013 **Other:** Acquired from Bayer Schering Pharma AG in April 2007
Resminostat/ 4SC-201 **4SC**	Phase II	**Main indications:** HCC (with sorafinib), Hodgkin's lymphoma (monotherapy) **Other indications:** CRC (2 active trials) **Efficacy:** SD 61% (n=18, mono) **Tolerability:** Nausea, vomiting, fatigue, well tolerated (Phase I, n=19) **Potential launch date:** 2013
Givinostat/ ITF2357 **Italfarmaco**	Phase II	**Main indications:** HL, MM **Other indications:** 2 non-onc. indications: polycythemia vera, autoinflammatory disease (4 active trials) **Efficacy:** HL: SD 54% (n=15, mono) **Tolerability:** prolongation of QT, thrombocytopenia **Potential launch date:** 2014
Mocetinostat/ MGCD0103 **Methylgene (Taiho)**	Phase II	**Main indications:** lymphoma, AML, MDS **Other indications:** 1 active trial **Efficacy:** HL: ORR 38% (n=21, mono), AML: ORR 29% (n=24, comb) **Tolerability:** fatigue, diarrhoea, nausea, thrombocytopenia, neutropenia, anaemia, pericardial SAE **Potential launch date:** 2014
PCI-24781 **Pharmacyclics**	Phase I/II	**Main indications:** Follicular lymphoma **Other indications:** sarcoma, B-cell lymphoma (3 active trials) **Efficacy:** Lymphoma: ORR 31% SD 44% (n=16, mono) **Tolerability:** fatigue, nausea, few incidence of thrombocytopenia and anaemia **Potential launch date:** 2014 **Other:** Partnership with Servier for ex-US development worth $39m in payments
CHR-2845 **Chroma Therapeutics**	Phase I	**Main indications:** Haematological tumours (1 active trial) **Potential launch date:** 2015
CHR-3996 **Chroma Therapeutics**	Phase I	**Main indications:** Solid tumours (1 active trial) **Potential launch date:** 2015

Source: Edison Investment Research

Pricing

The future pricing of belinostat is difficult to predict because of the large price discrepancy between the two HDACi that have been approved; romidepsin costs a $22,800 per month and vorinostat $10,000 per month. The price of belinostat will depend on the results of the clinical trials and whether it is positioned as a drug for niche indications such as PTCL, in which case it will probably be priced at a similar level to romidepsin or pralatrexate ($30,000 per month) or as a mass market oncology product. In this situation its pricing will be anchored against drugs such as Avastin and be at c $30,000 per year. We believe it is more likely that belinostat will be priced for the wider oncology market at $30,000 per year.

Sensitivities

The performance of TopoTarget's shares is closely linked to the success of belinostat. The risk is concentrated in this product, although it is mitigated partially because of the range of tumours it is being developed to treat.

In the short term this depends on the results of the clinical trials, primarily the primary endpoints being met, and secondarily how its safety and efficacy compares to other HDACi. The safety profile of belinostat is as important as its efficacy (as a monotherapy and in combination with other oncology products), as this appears to be the key differentiator for belinostat.

In the longer term, the key uncertainty is Spectrum's ability to market successfully belinostat in the important US market. The company is very ambitious but it is competing against much larger companies with established oncology franchises. The future ownership of Spectrum is associated with this issue as a larger company might acquire it to gain control of belinostat, or Spectrum might sub-license the North American rights to belinostat.

Other issues that will affect the performance of TopoTarget's shares include:

- Marketing of belinostat outside North America and India: TopoTarget still retains the rights to belinostat in Europe. It is unclear at the moment if it will market belinostat itself, out-license it or enter a co-promote arrangement. If TopoTarget decides to market belinostat, there will be greater upside, but there will also be greater risk.
- Ability to expand belinostat's label: Belinostat is initially being targeted as a niche indication. If TopoTarget is able to gain approval in solid tumours, belinostat's market potential will increase significantly.
- Competitive products: The potential sales of belinostat are linked to the prospects of products in the same market, primarily of other HDACi. Thus the clinical results/ marketing of other HDACi or oncology drugs for the same indications as belinostat will affect its potential. TopoTarget hopes to limit the competitive pressures by becoming a complementary treatment to the established standards of care in solid tumours.
- The development/out-licensing of the other products in development: TopoTarget has three other products in clinical development, which could become significant value drivers if they demonstrate the potential to become successful oncology products or out-license them on good terms.

Valuation

TopoTarget has been valued using a sum-of-the-parts DCF valuation at DKK994m, suggesting that the fair price of the shares is DKK9.10. The main assumptions for the valuation are detailed in Exhibit 5. In addition, a discount rate of 12.5% has been used, belinostat has been priced at $30,000 per patient per year, in line with advanced general oncology products, and peak sales are achieved after five years. It is assumed that the company will not have to pay any taxes until 2016. No value has been assigned to the rest of TopoTarget's pipeline, or to the prospect of belinostat gaining approval for other indications beyond PTCL, CUP and NSCLC.

Exhibit 5: Main assumptions for valuation of TopoTarget

Note: We forecast that Totect will achieve sales of DKK20.9 in 2010, with an effective royalty rate of 10%.

Product	Launch date	Peak sales	Risk adjustment	Market penetration	Royalty
Totect*	On market	DKK20.9m	100%	N/A	10%
Belinostat - PTCL	2012	$72m	60%	15%	18%
Belinostat - CUP	2015	$540m	50%	15%	18%
Belinostat - NSCLC	2017	$560m	40%	5%	18%

Source: Edison Investment Research

The potential royalties from belinostat in PTCL are worth DKK564m, in CUP DKK604m and NSCLC DKK313m. The value of the different revenue streams is very sensitive to the eventual pricing of belinostat. We estimate that the value of the royalty stream for belinostat in PTCL could increase to DKK1,698m from DKK566m if belinostat is priced more in line with pralatrexate (cost per patient per year: $90,000, assuming its use for three months). However, such a price would exclude belinostat from the large oncology indications such as NSCLC, breast and colorectal cancer. The valuation highlights the pricing challenge for TopoTarget and Spectrum; before the launch of belinostat in PTCL, they will have to decide whether they can maximise the value of belinostat by positioning it as a broad or niche oncology product.

The royalty rate is also important; if the company only receives an effective royalty rate of 15% the valuation of the company decreases by 11% to DKK886m.

Financials

TopoTarget is in a strong financial position after completing the licensing deal with Spectrum (upfront fee of $30m) and raising DKK132.6m in a fully subscribed rights issue in July 2009. We forecast that it has sufficient cash to operate to the end of 2012 even if it does not receive any further milestones or out-licenses any of its products, including potentially belinostat in Europe. Its cash position at the end of Q210 was DKK262m. We are forecasting that it will be DKK202m at FY10 – net cash inflow of DKK74m – and DKK100m at FY11 – net cash outflow of DKK102m.

TopoTarget could receive milestone payments on approval of belinostat in various indications, probably be in the range of $20-30m according to the size of the indication. There could also be milestones payable on the filing of NDAs.

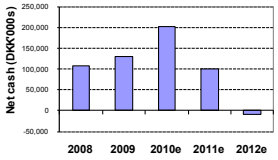
A summary of TopoTarget's financial statements is shown in Exhibit 6. The large increases in revenue in 2010 and 2011 are due to the upfront payment from Spectrum (recorded as other in the FY10e cashflow statement) being spread over 18 months.

Exhibit 6: Summary of financial statements

Note: The exceptional income in FY10 is from the divestiture of the European rights to Savene.

DKK'000s	2007	2008	2009	2010e	2011e	2012e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	**44,890**	**43,890**	**43,979**	**128,773**	**90,589**	**25,728**
Cost of Sales	(25,838)	(10,082)	(10,125)	(8,768)	(5,091)	(5,146)
Gross Profit	19,052	33,808	33,854	120,005	85,499	20,582
EBITDA	**(212,470)**	**(192,933)**	**(106,756)**	**(15,465)**	**(42,182)**	**(111,705)**
Operating Profit (before GW and except.)	**(219,801)**	**(294,371)**	**(132,491)**	**(24,197)**	**(45,203)**	**(114,840)**
Intangible Amortisation	0	0	0	0	0	0
Exceptionals	0	0	0	32,473	0	0
Other	0	0	0	0	0	0
Operating Profit	**(219,801)**	**(294,371)**	**(132,491)**	**8,276**	**(45,203)**	**(114,840)**
Net Interest	5,754	(11,737)	(10,250)	(2,118)	(4,986)	(6,589)
Profit Before Tax (norm)	**(214,047)**	**(306,108)**	**(142,741)**	**(26,315)**	**(50,189)**	**(121,429)**
Profit Before Tax (FRS 3)	**(214,047)**	**(306,108)**	**(142,741)**	**6,158**	**(50,189)**	**(121,429)**
Tax	2,447	4,899	2,277	0	2,011	2,176
Profit After Tax (norm)	**(211,600)**	**(301,209)**	**(140,464)**	**(26,315)**	**(48,178)**	**(119,253)**
Profit After Tax (FRS 3)	**(211,600)**	**(301,209)**	**(140,464)**	**6,158**	**(48,178)**	**(119,253)**
Average Number of Shares Outstanding (m)	54.0	64.3	99.5	132.6	132.6	132.6
EPS - normalised (DKK)	(3.92)	(4.68)	(1.41)	(0.20)	(0.36)	(0.90)
EPS - FRS 3 (DKK)	(3.92)	(4.68)	(1.41)	0.05	(0.36)	(0.90)
Dividend per share (DKK)	0.00	0.00	0.00	0.00	0.00	0.00
Gross Margin (%)	42.4	77.0	77.0	N/A	N/A	N/A
EBITDA Margin (%)	N/A	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	N/A
BALANCE SHEET						
Fixed Assets	**390,711**	**481,398**	**440,300**	**432,311**	**432,613**	**432,927**
Intangible Assets	370,639	467,381	431,885	426,448	426,448	426,448
Tangible Assets	18,415	12,094	7,044	4,923	5,225	5,539
Other	1,657	1,923	1,371	940	940	940
Current Assets	**443,464**	**137,634**	**145,113**	**226,966**	**121,571**	**11,662**
Stocks	3,310	2,566	1,944	841	488	493
Debtors	21,328	19,744	6,758	23,857	20,920	21,146
Cash	403,617	107,998	130,145	202,267	100,163	(9,977)
Other	15,209	7,326	6,266	0	0	0
Current Liabilities	**(120,452)**	**(83,781)**	**(58,920)**	**(108,019)**	**(41,674)**	**(41,692)**
Creditors	(113,868)	(42,811)	(37,299)	(42,883)	(41,674)	(41,692)
Short term borrowings	0	0	0	0	0	0
Other	(6,584)	(40,970)	(21,621)	(65,136)	0	0
Long Term Liabilities	**(48,655)**	**(105,875)**	**(114,695)**	**(130,510)**	**(137,141)**	**(143,980)**
Long term borrowings	0	0	0	0	0	0
Other long term liabilities	(48,655)	(105,875)	(114,695)	(130,510)	(137,141)	(143,980)
Net Assets	**665,068**	**429,376**	**411,798**	**420,748**	**375,370**	**258,918**
CASH FLOW						
Operating Cash Flow	**(218,407)**	**(175,563)**	**(104,807)**	**(84,456)**	**(102,437)**	**(109,117)**
Net Interest	9,474	4,097	1,231	10,576	1,645	250
Tax	0	1,922	4,377	0	2,011	2,176
Capex	(12,416)	(125,310)	2,016	(1,174)	(3,323)	(3,449)
Acquisitions/disposals	23,127	0	0	0	0	0
Financing	332,502	0	119,095	0	0	0
Dividends	0	0	0	0	0	0
Other	(510)	(266)	550	147,176	0	0
Net Cash Flow	133,770	(295,120)	22,462	72,122	(102,104)	(110,140)
Opening net debt/(cash)	**(269,847)**	**(403,617)**	**(107,998)**	**(130,145)**	**(202,267)**	**(100,163)**
HP finance leases initiated	0	0	0	0	0	0
Other	0	(499)	(315)	0	0	0
Closing net debt/(cash)	**(403,617)**	**(107,998)**	**(130,145)**	**(202,267)**	**(100,163)**	**9,977**

Source: Edison Investment Research

Growth	Profitability	Balance sheet strength	Sensitivities evaluation	
N/A	N/A		Litigation/regulatory	●
			Pensions	○
			Currency	◖
			Stock overhang	○
			Interest rates	○
			Oil/commodity prices	○

Growth metrics	%	Profitability metrics	%	Balance sheet metrics		Company details	
EPS CAGR 07-11e	N/A	ROCE 10e	N/A	Gearing 10e	N/A	Address:	
EPS CAGR 09-11e	N/A	Avg ROCE 07-11e	N/A	Interest cover 10e	N/A	Symbion Science Park Fruebjergvej 3 2100 Copenhagen 0	
EBITDA CAGR 07-11e	N/A	ROE 10e	N/A	CA/CL 10e	2.1		
EBITDA CAGR 09-11e	N/A	Gross margin 10e	93%	Stock turn 10e	2.4	Phone	+45 39 17 83 92
Sales CAGR 07-11e	19%	Operating margin 10e	N/A	Debtor days 10e	68	Fax	+45 39 17 94 92
Sales CAGR 09-11e	43%	Gr mgn / Op mgn 10e	N/A	Creditor days 10e	122	www.topotarget.com	

Principal shareholders	%
HealthCap AB	13
Avanza AB	5
Tredje AP-Fonden	3

Forthcoming announcements/catalysts	Date *
Q310 results	18 November 2010
PTCL interim clinical trial results	Q410*
CUP accrual data	Q410
Note: * = estimated	
Companies mentioned in this report:	
Spectrum Pharmaceuticals	

Management team

CEO: François Martelet

Joined in February 2010. Previously he worked at many of the major pharmaceutical companies, including Merck & Co as vice president and worldwide head of oncology (2005-2007), and was CEO and president of Avax Technologies (2007-09).

CFO: Anders Vadsholt

Joined in April 2010. He worked at BankInvest Biomedical Venture, a shareholder of TopoTarget (2005-10) and has been the CFO of many smaller companies as well as an investment banker.

Chairman: Bo Jesper Hansen

Joined the board in 2009. From 1998-2010, he was CEO and president of Swedish Orphan International (SOI). SOI was acquired by Biovitrum AB for SEK3.5bn in January 2010 and he is now the chairman for Swedish Orphan Biovitrum. He is also a medical doctor.