Annual report **2011**

topotarget

Strategy for 2012 and beyond

Topotarget strives towards establishing belinostat as one of the most successful HDAC inhibitors in selected indications. In particular, we aim to:

- Finalize the late-stage PTCL and CUP studies
- Submit an NDA to the FDA for belinostat in PTCL together with our partner Spectrum Pharmaceuticals
- Explore commercial opportunities outside the US, including Europe, Asia/Pacific, Latin America, and the rest of the world, in order to maximize the value of belinostat
- Unlock the full potential for belinostat by initiating further clinical studies in the most advantageous indications within hematology and solid tumor oncology, based on the data from the PTCL and CUP studies

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VP BD&L /
Strategic Planning

FRANCOIS MARTELET
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CFO

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Director of Pharmaceutical Operations

AXEL MESCHEDER
CMDO

Financial highlights and ratios

DKK ' 000	2011	2010	2009	2008	2007
Financial highlights and ratios*)					
Consolidated financial highlights and ratios					
Revenue	65,598	107,826	43,979	43,890	44,890
Research and development costs	(54,345)	(71,608)	(89,884)	(146,906)	(129,111)
Write-down of research and development projects	-	(189,541)	(21,200)	(93,500)	-
Sales and distribution costs	-	-	(29,136)	(44,796)	(57,722)
Operating loss	(31,352)	(197,543)	(132,492)	(294,371)	(219,801)
Net financials	1,087	68,773	(10,250)	(11,737)	5,754
Net loss from continued operations	(29,012)	(84,785)	-	-	-
Net loss discontinued operations	(3,999)	29,096	-	-	-
Total comprehensive income for the year	(33,011)	(55,689)	(140,464)	(301,209)	(211,600)
Basic and diluted EPS continued operations	(0.22)	(0.64)			
Basic and diluted EPS continued and discontinued operations	(0.25)	(0.42)	(1.41)	(4.68)	(3.92)
Consolidated balance sheets					
Cash and cash equivalents	114,302	205,068	130,145	107,998	403,617
Equity	330,729	360,219	411,798	429,376	665,068
Total assets	370,476	465,824	585,413	619,032	834,175
Investment in tangible assets (net)	(1,844)	(1,633)	2,016	(164)	(7,965)
Consolidated cash flow statement					
Cash flows from operating activities	(88,847)	40,101	(99,197)	(169,545)	(208,933)
Cash flows from investing activities	(1,919)	34,686	37,861	(44,366)	25,666
Cash flows from financing activities	-	138	118,780	(499)	332,026
Consolidated ratios					
Number of fully paid shares, year-end	132,652,050	132,652,050	132,609,020	66,304,510	61,304,510
Average number of shares for the period	132,652,050	132,640,379	99,456,765	64,323,636	53,955,186
Assets/equity	1.1	1.3	1.4	1.4	1.2
Market price, year-end (DKK)	2.51	3.57	2.59	3.62	16.76
Net asset value per share (DKK)	2.49	2.73	3.11	6.48	10.85
Average number of full-time employees	42	50	58	109	141

*) The figures for 2007 also include Topotarget Switzerland S.A. from June 27, 2007
Finally the figures for 2008 also include Topotarget Netherlands B.V. from January 1, 2008

Figures for 2010 has been changed as Savene® and Totect® activities now are presented as discontinued operations. Other years are presented as continued operations.

Management letter to shareholders

Francois Martelet
Chief Executive Officer

During 2011, Topotarget A/S took further transformative steps towards ensuring a cost-effective organization fully focused on belinostat and the future. Two vital events included the reorganization plan for Topotarget followed by the divestiture of all remaining Savene®/Totect® activities in North and South America including the US subsidiary. Both initiatives represent significant steps that will allow us to devote our focus on the late-stage clinical development and commercialization of belinostat, in line with our core strategy and commitment to our shareholders, and ensure a cost-effective operational structure for this purpose.

2011 was also the year when we established a Global Oncology Advisory Board (GOAB) intended to improve the understanding of the pre-clinical and clinical work of belinostat, to assist in creating effective development strategies for belinostat, and to provide advice on the best possible design regarding potential new clinical studies to be initiated. Hence, we will make utmost use of our GOAB to discuss and identify the most advantageous indications and optimal development strategies for belinostat. The GOAB is led by Professor Jean-Louis Misset.

Throughout 2011, Topotarget presented 15 abstracts, including presentations held at the ASCO (annual meeting of the American Society of Clinical Oncology), ESMO (European Multidisciplinary Cancer Congress), and ASH (American Society of Hematology) conferences. Further, we made important progress in our clinical development studies, and we remain on track with the clinical development of belinostat within both hematological cancer indications and solid tumors.

Our overarching strategy is to develop belinostat in indications in which we have strong reasons to believe potential clinical efficacy exists, and to establish belinostat as one of the most successful HDAC inhibitors within these indications. Further, we remain focused on maintaining a cost-effective operational structure.

Clinical progress in PTCL
– BELIEF study
Belinostat is currently in a registrational, pivotal trial for the treatment of relapsed or refractory PTCL (peripheral T-cell lymphoma), which is sponsored, conducted, and finalized by our partner, Spectrum Pharmaceuticals, Inc. This study in a hematological cancer indication is considered the main value driver of Topotarget.

A key milestone was reached in September 2011, when Topotarget and Spectrum Pharmaceuticals achieved the target enrollment of 129 patients for the pivotal BELIEF trial. Topotarget is expecting top-line phase IIb data to be announced by Spectrum Pharmaceuticals in the second half of 2012. A subsequent New Drug Application (NDA) submission to the FDA is expected by the end of 2012, with an estimated approval from the FDA during 2013.

In addition to PTCL, we believe that belinostat may hold potential for other oncology indications (e.g. for MDS (myelodysplastic syndromes)) and support our commitment to developing novel treatments for lymphoma. Further, it is also Topotarget's strategy to seek to maximize the commercial potential of belinostat through exploration of the best strategic opportunities outside the US.

Clinical progress in CUP
– CLN-17 study
The CLN-17 study in CUP (cancer of unknown primary) within solid tumors is currently in a randomized phase II clinical study. The CUP study is fully sponsored by Topotarget.

Topotarget is currently awaiting the study's progression-free survival (PFS) results to be available. These results will provide important evidence of belinostat's potential and may guide us in regard to which benefits the HDAC inhibitor may add in terms of efficacy in an established chemotherapy regimen (BelCaP). The obtained results will therefore be used to evaluate and potentially support further clinical studies in other solid tumor indications, including cancers related to bladder, ovarian, colorectal, and NSCLC (non-small cell lung cancer).

Top-line data from the CUP study is expected to be reported during the first half of 2012.

Other clinical studies
Topotarget's other clinical studies include seven on-going clinical studies with belinostat, conducted by both Topotarget alone, in collaboration with Spectrum Pharmaceuticals, and several studies in collaboration with other partners, including the NCI (National Cancer Institute, USA).

Reorganization
A reorganization plan was initiated during December 2011 as a proactive and necessary step to secure financing capabilities of our main activities until expected significant milestone payments related to the belinostat development in PTCL.

The main elements in the initiated reorganization included:

- Directing relevant development efforts and investments into the

finalization of the PTCL pivotal study for belinostat and the subsequent NDA filing together with Topotarget's partner, Spectrum Pharmaceuticals

- Finalizing the randomized phase II CUP study for belinostat

- Continuing the clinical development of belinostat in solid tumor diseases, e.g. NSCLC and hematological cancer indications. These studies are run by Topotarget in collaboration with the NCI and other entities

- Divestiture of the Totect®-related operations in the US

- Reducing the number of employees in Denmark by approximately 40%

Divestiture of Totect®
In late December 2011, Topotarget announced the completion of the divestiture of Totect® to Apricus Biosciences, Inc.

The divestiture was made in line with our core strategy to focus on the late-stage clinical development and commercialization of belinostat, as well as maintaining a cost-effective operational structure.

Looking forward
2012 will be another exciting year for Topotarget, where our dedicated clinical focus will be concentrated on Topotarget's two late-stage clinical belinostat studies within PTCL and CUP, which remain our two most important value drivers, where the main objective is to complete a timely submission of an NDA to the FDA for PTCL.

We are dedicated to the clinical development of innovative treatment concepts for malignant diseases. Cancer remains one of the most relevant challenges in medicine with many patients suffering from the progression of the disease, aggressive treatment regimens, and resulting sequelae. Belinostat is aiming to improve patients' outcome combined with a favorable safety and tolerability profile. We focus our clinical development on the treatment of malignancies with a, still, highly unmet medical need. It is our aim to provide a meaningful contribution for the benefit of the patients.

Finally, I wish to thank our employees for their hard and dedicated work during 2011 and to express my gratitude to our shareholders for their continued support.

Value drivers

PTCL – BELIEF study

- Phase IIb
- Registrational and pivotal study with 129 patients enrolled (complete)
- Study sponsored, conducted, and finalized by partner, Spectrum Pharmaceuticals
- Topotarget is expecting top-line phase IIb data to be announced by Spectrum Pharmaceuticals in H2 2012
- NDA submission to the FDA expected by end 2012, with estimated approval in 2013
- Expected milestone payments from Spectrum Pharmaceuticals:

1. Following FDA acceptance of NDA (one million shares of common stock in Spectrum Pharmaceuticals, and a double-digit million USD cash payment)
2. Upon FDA approval (double-digit million USD cash payment)

- Following market launch, Topotarget will receive double-digit royalty payments from Spectrum Pharmaceuticals
- Possibility of subsequent drug approval in emerging markets for PTCL indication (provided FDA approval)
- Topotarget pursues partnerships regarding Europe, Asia/Pacific, Latin America, and in the rest of the world (ROW)
- Potential value of belinostat may exist in other liquid tumor indications, e.g. MDS

CUP clinical study (CLN-17)

- Phase II
- Randomized, controlled study with 89 patients enrolled (complete)
- Fully sponsored by Topotarget
- Announcement of top-line phase II data expected in H1 2012
- Based on the design and modest powering of the CUP study, the study does not serve as a registration study
- However, an obtained PFS improvement rate of 20-40% will be viewed as a positive trend warranting further studies in this indication

Other clinical studies

- Seven clinical studies with belinostat on-going, conducted by both Topotarget alone, in collaboration with Spectrum Pharmaceuticals, and several in collaboration with other partners, including the NCI
- Phase II clinical studies expected to be initiated in bladder and MDS, respectively, during 2013

Global Oncology Advisory Board

JEAN-LOUIS MISSET
Chairman

Jean-Louis Misset is Professor of Oncology at the University and at the St. Louis Hospital Oncology Division in Paris, France. Professor Misset has a strong oncology background as an advisor in the field of drug development.

As a member of many scientific boards and as an advisor, Professor Misset has extended experience with the clinical development of drugs, including Eloxatin® (Sanofi), Topotecan® (SmithKlineBeecham), Taxotere® (Aventis), Alimta® (Eli Lilly), and Herceptin® (Roche).

Jean-Louis Misset has published more than 200 publications in internationally well-known referenced journals.

ALAIN CATALIN MITA
GOAB member

MD, Co-Director of the Experimental Therapeutics Program at the Samuel Oschin Comprehensive Cancer Center, Cedars-Sinai Medical Center, Los Angeles, California, USA.

HANS-JOACHIM SCHMOLL
GOAB member

MD, Professor of Internal Medicine and Director of the Department of Hematology and Oncology at the Martin Luther University, Halle-Wittenberg, Germany.

DANIEL D. VON HOFF
GOAB member

MD, F.A.C.P., Physician in Chief, Senior Investigator and Director of Clinical Translational Research Division at TGen (Translational Genomics Research Institute), USA.

MATTI AAPRO
GOAB member

MD, Director of the Multidisciplinary Oncology Institute at the Clinique de Genolier in Genolier, Switzerland.

Belinostat – put into perspective

By Professor Jean-Louis Misset*)

Cancer cells are characterized by dysfunction of regulatory proteins driving the cellular processes of proliferation, differentiation, and cell death. Dysfunction may be consecutive to various abnormalities. The gene coding for the protein may be mutated giving rise to proteins that can be either non- or over-functional. Gene rearrangements can give rise to fusion proteins, also non- or over-functional. The gene may be partially deleted resulting in a truncated, either non-functional protein or even missing. Finally, the gene may be amplified and/or overexpressed resulting in an excess of functional protein as observed in Her2 positive breast cancer.

Mechanisms contributing to oncogenesis

Modification of the activation of certain genes, but not the basic structure of the DNA, can also be modified in cancer cells. In addition, even if the protein of interest is qualitatively and quantitatively normal, it remains subject to physiologic regulation processes through allosteric mechanisms affecting protein function through modification of its quaternary structure. These mechanisms such as phoshorylation-dephosphorylation and acetylation-deacetylation are also referred to as epigenetics. They can also be modified in cancer cells and contribute to the oncogenesis.

Histones in general as anti-tumor agents

Histones belong to a family of nuclear proteins which regulates protein translation and expression. When histones are acetylated, they are "open" for the access to the DNA for the enzymatic machinery for translation which allows protein synthesis. When deacetylated, histones wind up around DNA precluding access for the translation enzymatic machinery thus inhibiting protein expression. Histone deacetylases have consistently been shown to be overexpressed in a large variety of cancer cells, making their inhibition a potential epigenetic therapeutic target. The universal implication of histone deacetylase (HDAC) in oncogenesis suggests that targeting HDAC may have wide applications, both in the field of hematological malignancies as well as in solid tumors. Indeed, HDAC inhibitors (HDACi) have proven to be active anti-tumor agents in a large variety of pre-clinical models, in vitro and in vivo.

– and belinostat in particular

Belinostat is an HDACi belonging to the family of hydroxamic acid and is the lead product of Topotarget. As compared to other HDACi undergoing pre-clinical or clinical development, it has several advantages. First, on a molecular basis, belinostat is much more potent than many other HDACis, including several belonging to the same chemical family. Second, it has a much wider spectrum of anti-tumor activity: Not a single cancer cell line has been resistant to belinostat. Third, the safety profile has proven to be highly favorable, both in pre-clinical animal models and in the frame of already acquired clinical experience. For example, full doses of belinostat (1000mg/m^2/day) could be combined with full doses of the widely used combination of carboplatin+paclitaxel without additional toxicity. This observation has been confirmed with many other chemotherapy drugs or combinations.

Clinical experience with belinostat

Clinical experience of belinostat includes several large clinical studies paving the way to registration, and a large array of supporting evidence in many hematological malignancies and solid tumors on smaller numbers of patients. A large phase II study (129 patients enrolled) on peripheral T-cell lymphoma (PTCL) has completed accrual. The results are presently being analyzed and will be submitted to regulatory agencies. A randomized, controlled phase II study on cancer of unknown primary (CUP) comparing carboplatin and paclitaxel with or without belinostat has also completed accrual. Results will be available within a few months and may guide the further development of combination therapy in solid malignancies.

Additional supporting evidence includes encouraging early data on hematological malignancies such as cutaneous T-cell lymphoma (CTCL), relapsed acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), and multiple myeloma (MM). Signals of clinical activity and a favorable safety profile have been observed in a number of solid tumors, such as ovarian cancer, including tumors resistant to platinum, bladder cancer, lung cancer, thymoma, hepatocellular cancer, and colorectal cancer.

Global Oncology Advisory Board

Topotarget's management has sought scientific advice from a wide range of internationally acknowledged clinical experts within the field of new drug development or various malignancies targeted in the development of belinostat. In 2011, several meetings involving high-caliber, international experts were performed.

Future prospects

Future prospects for belinostat may include further investigation of the administration and dosing seeking to alleviate the inconveniency of a five-day infusion schedule. Above all, the development of belinostat may provide patients and physicians with a new therapeutic opportunity based on an innovative mechanism of action and well-tolerated treatment in malignancies facing unmet needs in hematology and solid tumors. Belinostat has the potential to increase survival and improve the outcome for cancer patients in many cases. This will require completion of pivotal registration studies, which are presently in consideration in the above-mentioned clinical situations. Conclusively, belinostat appears to be one of the promising new drugs in the field of oncology and targeted therapies.

*) Chairman of Topotarget's Global Oncology Advisory Board
Professor of Oncology at the St. Louis Hospital Oncology Division in Paris, France


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FOR CLINICAL TRIAL

Belinostat

Mode of action
Belinostat belongs to a class of anti-cancer agents, HDACi, which by enzymatic process (acetylation) works to normalize the abnormal gene function pattern characteristic of cancer cells.

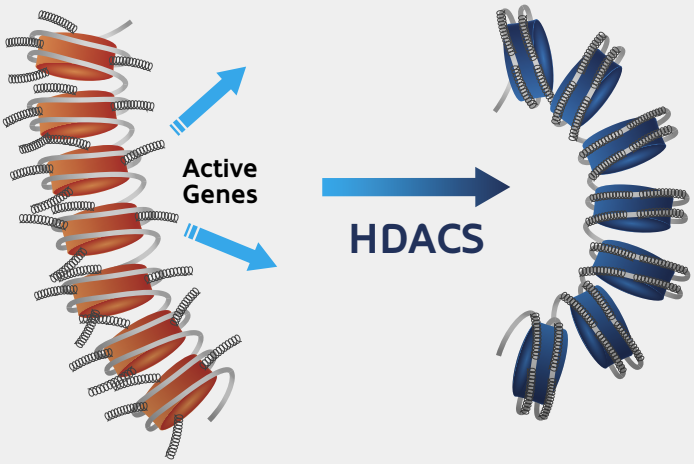
Belinostat is a strong member of the HDACi group as it:

- Has demonstrated anti-cancer activity against a variety of human tumors
- Is well-tolerated with minimal or no impact on bone marrow function
- Can be administered both by infusion and orally

Clinical use
Following extensive testing in the laboratory and in animal models with human tumors, the first-in-man clinical study was successfully completed in 2006. Belinostat has since been investigated in 30 clinical studies as monotherapy and in combination chemotherapy and more than 1050 patients have been exposed to the drug.

Overall, patients have experienced clinical benefit from both belinostat monotherapy and in combination with other anti-cancer agents, as defined by objective responses or prolonged stabilization of disease. Clinical benefit has been observed in patients with solid tumors and hematological malignancies. The favorable safety profile for both intravenously and orally administered belinostat and the encouraging anti-tumor activity indicates a favorable risk/benefit ratio and justifies the continued development of belinostat in multiple solid tumor and hematological malignancy indications.

The clinical study program of on-going or recently completed studies includes:



Histone DeACetylase inhibitors (HDACi)

Bypassing natural apoptosis is a hallmark of the cancer disease

Main characteristics of belinostat
- "Turns on" suppressor genes
  - Inhibiting HDACs activate silenced genes
  - Some of these are apoptotic (cell death) genes
  - Activation causes selective cancer cell death
- "Turns off" oncogenes
  - Results in inhibitions of cancer cell growth

Other mechanisms of action
- Inhibition of the growth and development of new blood vessels, in effect starving cancer cells
- Induction of immune system to target cancer cells
- Interacts with for example tubulin, thus synergizing with various chemotherapies and potentially overcoming drug resistance, which is the main reason for failure of cancer treatment

Hematological diseases
- Peripheral T-cell lymphoma (PTCL)
- Myelodysplastic syndrome (MDS)
- Acute myeloid leukemia (AML)

Solid tumor indications
- Cancer of unknown primary (CUP)
- Bladder cancer
- Ovarian cancer
- Liver cancer (HCC)
- Soft tissue sarcoma (STS)
- Thymoma
- Non-small cell lung cancer (NSCLC)
- Colorectal cancer (CRC)

Safety profile
Belinostat has an excellent safety profile as one of the drug's key characteristics. In clinical trials, comprising more than 1050 patients, belinostat is well-tolerated. The most frequently reported adverse events are mild and manageable.

Belinostat has been administered as monotherapy and combination therapy for the treatment of the cancers. The combination therapies include idarubicin, doxorubicin, 5-fluorouracil, carboplatin/paclitaxel, and bortezomib. Considering the cancers treated and the chemotherapies used in combination therapy studies, the adverse events observed are acceptable.

> Compared to other HDACis, belinostat's preliminary safety data show lower incidences of grade 3-4 adverse events*)

Compared to other HDACis, belinostat's preliminary safety data show lower incidences of the grade 3-4 adverse events (AE) within the most commonly reported AEs (nausea, fatigue, diarrhea, vomiting). In addition, other HDACis have significant side effects with hematological toxicity in drug combinations while belinostat seemingly does not.

Serious AEs related to belinostat have been relatively infrequent and no clusters that suggest a significant risk for the patients can be identified.

In a safety analysis in patients treated with belinostat as either mono- and/or combination therapy, the potential benefit of belinostat treatment outweighs the risks for the patients. Considering the cancers treated, the benefit-risk ratio for belinostat mono- and combination therapy appears favorable.

Trial definition

Phase I is the initial introduction of the drug candidate into healthy human volunteer subjects or patients with the disease. These studies are designed to determine the safety and side effects associated with increasing dosages, absorption, metabolism, distribution and excretion, pharmacologic and mechanism of action of the drug candidate in humans, and, if possible, to gain early evidence of effectiveness. Sufficient information about a drug candidate's pharmacokinetics and pharmacological effects should be obtained in order to design well-controlled, scientifically valid phase II studies.

Phase II involves clinical studies conducted to evaluate the effectiveness of the drug candidate for a particular indication in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug candidate. These studies are typically closely monitored and conducted in a relatively small number of patients, usually involving a couple of hundred patients.

Phase III studies are performed after preliminary evidence suggesting that effectiveness of the drug candidate has been obtained. Phase III studies are intended to generate additional information about the drug candidate's effectiveness and safety that is required to evaluate the overall benefit-risk relationship of the drug candidate and to provide an adequate basis for labeling. The studies may include anything from several hundred to several thousand subjects.

Phase IV studies are undertaken after a drug has been granted a marketing authorization. The main reasons for running phase IV studies are to find out more about the side effects and safety of the drug, to conduct risk-benefit assessments in a larger and more heterogeneous population than what is seen during clinical development.

Cancer at a glance

Commercial perspectives
Cancer represents a significant unmet medical need. Each year, more than 11 million people around the world are diagnosed with cancer. The World Health Organization (WHO) projects an increase to 16 million people a year over the next 15 years.

The majority of cancer patients die within a short time span of diagnosis. Seven million people die from cancer every year, corresponding to 13% of all deaths. The WHO projects an increase to 10 million by 2020.

Cancer is close to overtaking the position of cardiovascular diseases as the disease with the highest mortality rate in the western world, where the most common forms of lethal cancer are prostate cancer, breast cancer, lung cancer, and colorectal cancer.

*) Although no direct comparisson has been made

BELINOSTAT KEY CLINICAL STUDIES (TOPOTARGET OR SPECTRUM PHARMACEUTICALS)

Indication	Study	Sponsor	Phase I	Phase II	Randomized phase II or pivotal	Target #	Enrollment status	Milestone	Time frame
PTCL	BELIEF (CLN-19)	SPPI*)	→	→	→	100-120	Completed	Top-line results NDA filing	2012
CUP	CLN-17	TT**)	→	→	→	88	Completed	Top-line results	H1 2012
NSCLC	SPI-1014-Bel	SPPI/TT	→			35	Recruiting	Recruitment completed	-
Solid + STS	CLN-14	TT	→	→		55	Phase I completed Phase II recruiting	Results stage I LPFV stage I in phase II	H1 2012
Drug-Drug interaction	CLN-20	SPPI/TT	→			39	Recruiting	Top-line results	2012
Solid tumors	CLN-9	TT	→			92	Completed	Scientific publication	2012
Lymphoma	CLN-9	TT	→			30	Completed	Top-line results	2012

*) Spectrum Pharmaceuticals
**) Topotarget

The strong growth in global sales of cancer therapeutics witnessed within the past few years is primarily due to the launch of a number of new and highly specific targeted anti-cancer drugs. In 2006, the global expenditure for oncology drugs was USD 44 billion, up from USD 12 billion in 2000 and the expenditure increased to USD 65 billion in 2010 and is expected to increase by USD 72 billion in 2012.

In the years ahead, a continuing trend towards more targeted cancer therapies is expected. Additionally, a large number of more biologically specific cancer drugs will reach the market, further expanding the market for cancer therapeutics. Topotarget considers itself an important player in the targeted cancer therapeutics market and is committed to making a substantial contribution to the development of more effective anti-cancer drugs.

Indications and clinical program

The final spectrum of indications to be pursued in the future development program is subject to the ultimate evaluation of the results from the many on-going studies. So far, 20 phase II studies have been initiated by Topotarget and its partner, Spectrum Pharmaceuticals, the NCI in addition to some investigator-initiated studies in PTCL, MDS, CUP, ovarian cancer, HCC, STS, thymoma, and NSCLC.

The clinical trial process

Topotarget has allocated most of its resources in the clinical study process. All clinical studies must be conducted by qualified investigators in accordance with Good Clinical Practice's (GCP) regulations. Clinical studies are typically conducted in three and sometimes four sequential phases that, however, often overlap or are combined.

BELINOSTAT CLINICAL STUDY OVERVIEW

Belinostat clinical studies in malignant diseases

Peripheral T-cell lymphoma (PTCL)
CLN-6
CLN-19 (BELIEF study)
Studies initiated in preparation for NDA filing
CLN-20
NCI8846
Belinostat in treatment of advanced solid and hematological tumors
CLN-9

1. Belinostat in combination with carboplatin and paclitaxel (BelCaP) **p. 12**
Safety profile of BelCaP
a) BelCaP in CUP
CLN-17
b) BelCap in ovarian cancer
CLN-8
GOG-0126T
c) BelCap in bladder cancer
CLN-8
d) BelCaP in NSCLC
SPI-1014-Bel

2. Belinostat in combination with anthracyclines **p. 14**
Safety profile of belinostat in combination with anthracyclines
a) Belinostat + doxorubicin in STS
CLN-14
b) Belinostat + idarubicin in AML or MDS
CLN-15

3. Belinostat in combination with 5-fluorouracil **p. 14**
Safety profile of belinostat in combination with 5-fluorouracil
CLN-4

4. Belinostat in combination with azacitidine (Vidaza®) **p. 15**
Safety profile of belinostat in combination with azacitidine
a) NCI7258
b) NCI 7265
c) CLN-15
d) NCI7285

5. Belinostat in combination with bortezomib (Velcade®) **p. 15**
Safety profile of belinostat in combination with bortezomib
a) CLN-5
b) NCI7281
c) CLN-16
d) MCC-12517

Belinostat clinical studies in malignant diseases

Since 2006, the clinical development program of belinostat*) comprises more than 30 studies sponsored by Topotarget and Spectrum Pharmaceuticals, the NCI in addition to some investigator-initiated studies. These studies are a mix of monotherapy studies in hematological malignancies and in solid tumors. The early studies were designed to obtain information on how well belinostat was tolerated by patients with cancer as a single agent.

Single agent belinostat has been studied for both intravenous (i.v.) and oral administration. Later studies have utilized a combination strategy where i.v. administration of belinostat has been combined with carboplatin+paclitaxel, anthracyclines such as idarubicin or doxorubicin, 5-fluorouracil, azacytidine, or bortezomib.

Peripheral T-cell lymphoma (PTCL)
PTCL is a hematological disease including a heterogeneous group of malignancies of T-cell origin that represents about 10-15% of all cases of non-Hodgkin's lymphoma. It is an aggressive, high-grade type of cancer with a poor prognosis of expected survival of approximately two years from diagnosis. The projections from annual cancer incidences point to 15,500 new cases of PTCL in the US, Japan, and in top-5 EU countries.

CLN-6, a phase II clinical study of belinostat in patients with recurrent or refractory CTCL and PTCL. In this early clinical study, patients with either CTCL or PTCL were treated with i.v. belinostat monotherapy. A total of 25 patients with PTCL were enrolled and of 19 evaluable patients, six patients had a response (31.6%), two had complete remission, while four had par-

*) PXD101 (belinostat) is the prefix of all clinical study names investigating belinostat, but will not be explicitly used in this annual report.

tial remission. The results were presented by the investigators during the American Society of Hematology's (ASH) annual conference in 2009[1]. The results from this trial lead to initiation of our pivotal study CLN-19.

CLN-19 (BELIEF study), a multi-center, open-label study of i.v. belinostat in patients with relapsed or refractory PTCL. The BELIEF study is a pivotal, open-label, multi-center, single-arm efficacy and safety study. In total, the study included approximately 100 clinical centers globally. The primary endpoint is the objective response rate (ORR). As communicated during 2011, Topotarget obtained a positive recommendation following the futility analysis by the Independent Data Monitoring Committee in March 2011[2] and a follow-up safety update meeting in November 2011. The BELIEF study is fully sponsored by our US partner Spectrum Pharmaceuticals and the expectation is to file an NDA to the FDA in the second half of 2012. The trial was initiated in December 2008[3]. Enrollment of 129 patients into this trial was completed in September 2011[4].

Studies initiated in preparation for NDA filing

Spectrum Pharmaceuticals and Topotarget are committed to the NDA filing based on positive outcome of the BELIEF study. In preparation, a study, which looks at a possible drug-drug interaction (CLN-20) in addition to an NCI-sponsored (NCI8846) study in patients with impaired hepatic function, has been initiated. Both studies are on-going and use i.v. belinostat given as monotherapy. Available data will be part of the safety package for the NDA filing.

CLN-20, a phase I study of belinostat in combination with warfarin in patients with solid tumors or hematological malignancies. This drug-drug interaction study is conducted in the Topotarget/Spectrum Pharmaceuticals collaboration. Approximately 39 patients are expected to be included and the primary endpoint is safety.

NCI8846, a phase I pharmacokinetic study of belinostat for solid tumors and lymphomas in patients with varying degrees of hepatic dysfunction. Up to 80 patients are expected to be included and the primary endpoint is safety.

Belinostat in treatment of advanced solid and hematological tumors

CLN-9, an open-label, dose-escalation study of oral belinostat in patients with advanced solid tumors. Later the protocol was amended to also include patients with hematological diseases.

Patient recruitment for the CLN-9 study was concluded in April 2011. The study is an open-label, non-randomized, multi-center, dose-escalation phase I trial examining dose and schedule of the oral administration of belinostat. In total, 92 patients with refractory solid tumors and 28 patients with lymphoma have been included in the study. The recommended dose levels are being evaluated through dose escalation of belinostat from 250 to 2000 mg/day and testing different dosing schedules such as daily for 28 days, daily for two weeks in a three-week cycle, and daily for five days in a three-week cycle. Initial results from the solid tumor part of the study was presented by the authors during ASCO in 2009[5] with the final results estimated to be submitted for publication in H1 2012 and safety data from the hematological part of the study was presented by the investigators during the ASH annual meeting in December 2011.

The favorable tolerability of oral belinostat led to the inclusion of oral belinostat as maintenance in the randomized phase II study in patients with CUP. This study will be described later.

Belinostat in combination with ...

1) Carboplatin and paclitaxel (BelCaP)
2) Antracyclines
3) 5-fluorouracil
4) Azacitidine (Vidaza®)
5) Bortezomib (Velcade®)

1. Belinostat in combination with carboplatin and paclitaxel (BelCaP)

Topotarget has performed pre-clinical experiments and demonstrated encouraging synergies between belinostat in combination with carboplatin or paclitaxel. The synergistic effect seems further enhanced using the triple combination of belinostat, carboplatin, and paclitaxel (BelCaP). Carboplatin and paclitaxel are the backbone of anti-cancer treatment in many malignancies i.e. CUP (1st-line treatment), NSCLC (1st-line treatment), ovarian cancer (2nd-line treatment), and bladder cancer (2nd-line treatment).

The demonstrated pre-clinical synergy between these drugs and belinostat has led to several studies where this combination has been included:

a) CLN-17 in CUP
b) CLN-8 and GOG-0126T in ovarian cancer
c) CLN-8 in bladder cancer
d) SPI-1014-Bel in NSCLC

Safety profile of BelCaP

In total, more than 150 patients have been treated with BelCaP without unexpected toxicity. Furthermore, it has been shown that belinostat can be combined with full doses of the two anti-neoplastic drugs: Carboplatin and paclitaxel. Finally, in the on-going phase I/II study where BelCaP is given to previously untreated patients with NSCLC, the issue of potentially increasing the dose of belinostat is addressed.

a) BelCaP in CUP

CUP is by definition a cancer where the origin of the primary tumor remains unknown despite the use of intensive diagnostic tools. The histological characteristics detected in the biopsy yield some information of the origin, i.e. the tumor is either an adenocarcinoma, a squamous cell carcinoma, or an undifferentiated or poorly differentiated carcinoma/adenocarcinoma. Approximately 2-5% of all solid tumors are CUP and despite treatment with chemotherapy most patients die within one year.

CLN-17, an open-label randomized phase II study of belinostat in combination with carboplatin and paclitaxel (BelCaP) compared to carboplatin and paclitaxel in patients with previously untreated cancer of unknown primary. The study is a multinational, multi-center, randomized, comparative efficacy and safety study. Patients have been randomized to either BelCaP or CaP administered every 3rd week. In total, 89 patients have been randomized and the study has been closed for recruitment as communicated in December 2010. The primary study endpoint is progression-free survival (PFS), hence providing an estimate of the hazard ratio of treatment effect. Initial safety data were presented during ASCO 2010 and top-line results are expected in H1 2012.

b) BelCaP in ovarian cancer

Ovarian cancer is a growth of malignant cells that begins in the ovaries (women's reproductive glands). Ovarian cancer is the fifth-leading cause of cancer-related deaths among women. In 2010, approximately 60,000 women in the US, Japan, and five major EU markets were diagnosed with ovarian cancer and about 40,000 women die of the disease every year.

CLN-8, a phase I safety, pharmacodynamic, and pharmacokinetic study of intravenously administered belinostat plus carboplatin or paclitaxel or both in patients with advanced solid tumors. After the maximal tolerated dose was found in the phase I part of the protocol, a cohort expansion was approved which included 35 women with ovarian cancer. The results have been presented at several major scientific meetings, last time during ASCO 2008[8]. The main results demonstrated that 15 patients (43%) responded to the combination treatment.

> Topotarget has demonstrated encouraging synergies between belinostat in combination with carboplatin and paclitaxel in preclinical studies

GOG-0126T, a phase II evaluation of belinostat and carboplatin (not the BelCap combination) in the treatment of recurrent or persistent platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer. This study, initiated by the Gynecologic Oncology Group (GOG) in the US, included patients that were resistant to both paclitaxel and platinum, therefore these patients were more refractory than patients in the CLN-8 study. The primary endpoint in the study was response rate and called for at least three responses. The study was evaluated after 27 evaluable patients had been included and two responses were seen. As the primary endpoint of three responses was not met, the study was terminated as communicated in March 2011[9].

Collectively, the experience with belinostat in the treatment of ovarian cancer is based on these two studies. The GOG terminated the phase II study of belinostat and carboplatin in women with platinum-resistant ovarian cancer after the first stage due to a lack of responses. While disappointing, the result does not negate the activity of the triple drug combination of BelCaP explored in the CLN-8 study, but suggests that belinostat may require the combination of both carboplatin and paclitaxel for maximal activity. The synergy between carboplatin, paclitaxel, and belinostat has been demonstrated previously in an in vitro model system. The pre-clinical data coupled with the clinical data from the BelCaP study provides sufficient interest to carry forward further studies in ovarian cancer. Further investigation of the BelCaP combination may be conducted in very well-defined populations of women with ovarian cancer, stratified by platinum sensitivity.

c) BelCaP in bladder cancer

Bladder cancer originates from the bladder and the urinary tract affecting more than one million people worldwide. It is the fourth most common malignancy in men and the 10th in women. The vast majority of the tumors are low-grade and 90% of patients will survive more than 10 years.

CLN-8, a phase I safety, pharmacodynamic, and pharmacokinetic study of intravenously administered belinostat plus carboplatin or paclitaxel or both in patients with advanced solid tumors. After the maximum tolerated dose was reached in the phase I part of the protocol, a cohort expansion was approved which included 15 patients with heavily pretreated bladder cancer. The results have been presented at several major scientific meetings, last time during ESMO 2011[10]. The main efficacy results were presented in 2008 and demonstrated that of 14 evaluable patients, four (29%) responded to the treatment[11].

d) BelCaP in NSCLC

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer accounting for more than 75% of all lung cancers. It is estimated that ap-

proximately 350,000 patients per year will be diagnosed with lung cancer in the US, Japan, and five major EU markets. Of these approximately 250,000 patients will die from NSCLC.

SPI-1014-Bel, a phase I/II maximum tolerated dose study of belinostat in combination with carboplatin plus paclitaxel in chemotherapy-naive patients with stage IV non-small cell lung cancer. This is a multicenter, open-label, single-arm study.

Patients will receive up to six cycles of combination therapy of belinostat plus carboplatin (AUC 6) and paclitaxel 200 mg/m^2. A dose escalation study will be conducted, using traditional escalation rule of 3+3 design, during the first cycle of therapy to determine the maximum tolerated dose (MTD). The trial was initiated in March 2011[12] and it is expected that up to 35 patients will be enrolled.

2) Belinostat in combination with anthracyclines

a) CLN-14 with doxorubicin in patients with solid tumors and soft tissue sarcoma (STS) in the expansion cohort
b) CLN-15 with idarubicin in patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS)

Safety profile of belinostat in combination with anthracyclines
Collectively, the results demonstrate that the combination of belinostat and anthracyclines is safe and full doses of anthracyclines can be given in combination with full doses of belinostat.

a) Belinostat + doxorubicin in STS
Soft tissue sarcomas (STS) are defined by cancer in the soft tissues arising from mesenchymal cells such as muscles, tendons, and blood vessels. It excludes sarcomas arising from bone. STS is a rare disease and less than 1% of all cancers are STS.

CLN-14, a phase I/II clinical study of belinostat in combination with doxorubicin in patients with STS. This open-label, multi-center, dose-escalation study was initiated to evaluate safety, efficacy, pharmacodynamics, and pharmacokinetics of the combination of belinostat with doxorubicin administered every third week. After the maximum tolerated dose of belinostat in combination with doxorubicin was established in patients with solid tumors, a cohort expansion was initiated in patients with STS. The cohort expansion was planned in two stages, with 20 patients to be included at the first stage, and since less than three patients showed response, no additional 20 patients were enrolled. The initial results from the phase I part of the study have been presented at AACR-NCI-EORTC 2008[13]. The enrollment into the first part of the phase II has been completed and results are expected in H1 2012.

b) Belinostat + idarubicin in AML or MDS
Myelodysplastic syndrome (MDS) constitutes a heterogeneous group of bone marrow diseases characterized by inefficient hematopoiesis affecting one or more cell lines of the bone marrow. Most patients have anemia at diagnosis but a considerable number of patients have neutropenia and thrombocytopenia as well. Approximately 50% of patients have cytogenetic abnormalities, which are of prime prognostic importance. In some instances, MDS is caused by previous chemotherapy or radiation, so-called therapy-related MDS. These tend to have complex cytogenetics and a dismal prognosis. MDS is a rare disease accounting for slightly less than 1% of all malignancies. MDS may progress into acute myeloid leukemia (AML). AML is characterized by deregulated proliferation of myeloid blasts with limited differentiation. AML affects both younger and elderly patients with a higher incidence of elderly patients (13-15/100,000). It is a highly heterogeneous disease in terms of morphology, cytochemistry, immunophenotype, cytogenetics, and molecular abnormalities.

Treatment outcomes for both MDS and AML still remain suboptimal. Most patients receiving chemotherapeutic regimen relapse and die due to the disease or associated complications.

CLN-15, a phase I/II clinical study of belinostat in combination with idarubicin in patients with AML not suitable for standard intensive therapy. This open-label, non-randomized, multi-center, phase I/II study was initiated to assess the efficacy and safety of two schedules of belinostat in combination with idarubicin therapy in patients with AML (patients with MDS also included) not suitable for standard intensive therapy. The initial results from the phase I part of the study were presented during ASH 2008[14]. Analysis of trial outcome showed higher response rates (partial and complete, 5/16 patients) for the group of patients receiving constant infusion therapy with belinostat. Belinostat was given as a 48-hour infusion.

3) Belinostat in combination with 5-fluorouracil

The effect of belinostat in combination with 5-fluorouracil (5-FU) has been investigated in CLN-4 in patients with solid tumors and colorectal cancer in the expansion cohort.

Colorectal cancer (CRC) belongs to one of the most frequent malignancies, accounting for approximately 10% of all malignancies. CRC originates from either the colon or the rectum and the vast majority is adenocarcinomas. Approximately a quarter of the patients have disseminated disease at the time of diagnosis, i.e. metastatic disease (mCRC). Over the last couple of years, CRC has been divided into two nearly equal sized populations based on

whether the tumor cell expresses normal K-Ras or has the mutated form. Despite the use of targeted agents such as monoclonal antibodies, the overall survival in patients with mCRC remains poor at around two years.

Safety profile of belinostat in combination with 5-fluorouracil

Belinostat in combination with 5-FU has been generally well-tolerated up to 1000 mg/m²/day belinostat plus 250 mg/m²/day 5-FU. Toxicities were generally ≤ grade 2.

CLN-4, a phase I safety, pharmacodynamic, anti-tumor activity, and pharmacokinetic study of belinostat alone and in combination with 5-FU in patients with advanced solid tumors. This study was an open-label, multi-center, dose-escalation, safety, and pharmacodynamic study in patients with advanced solid tumors, with an expansion arm at the maximum tolerated dose (MTD) to confirm safety and assess pharmacodynamics, anti-tumor activity, and pharmacokinetics in patients with advanced colorectal cancer. The phase I part of the study enrolled various solid tumors to establish the safety profile of the combination of belinostat and 5-FU. Once this had been established, a cohort of patients with CRC was included. The main results relating to safety and pharmacodynamics and efficacy have been presented during the AACR-NCI-EORTC meeting in 2006, during ASCO in 2007, and ASCO GI 2009[15]. In a considerable number of patients, disease stabilization was observed as best clinical outcome.

4) Belinostat in combination with azacitidine (Vidaza®)

The effect of belinostat in combination with azacitidine has been investigated in NCI7285 in patients with AML or MDS.

Safety profile of belinostat in combination with azacitidine

Collectively, the data suggests that belinostat in combination with azacitidine has clinical activity. Furthermore, the combination of belinostat and azacitidine is well tolerated.

MDS is described above. In total, four studies have been performed in patients with acute myeloid leukemia (AML) and/or MDS.

a) **NCI7258,** a phase II study of belinostat, for the treatment of myelodysplastic syndrome. In this study, belinostat was used as a single agent. Amongst the 21 patients included, 17 were evaluable and a stable disease was seen in 15 of these patients.

b) **NCI7265,** a phase II study of belinostat in patients with relapsed or refractory AML or patients over 60 with newly diagnosed AML. In this study belinostat was used as a single agent but no responses were seen.

c) **CLN-15** has been described above.

These three studies (NCI7258, NCI7265, and CLN-15) paved the way for investigating belinostat in combination with azacitidine in AML/MDS patients (NCI7285).

d) **NCI7285,** a phase I pharmacodynamic study of belinostat plus azacitidine (5-AZA) in advanced myeloid neoplasms. In this study, 56 patients were included of which 24 were included to establish the maximum tolerated dose and an additional 32 patients were included at the maximum dose. Combining the two study sections, 39 patients were treated at the maximum dose and amongst these 13 patients responded (33%). These data were presented during ASCO 2011[16].

5) Belinostat in combination with bortezomib (Velcade®)

Bortezomib is a proteasome inhibitor, which in pre-clinical studies has been implied a synergistic neoplastic effect in combination with belinostat, possibly through a concerted action on proteasomal pathways or targeting of independent protein disposal mechanisms. After running pre-clinical studies testing this hypothesis, several studies have been initiated at Topotarget, at the NCI as well as investigator-driven studies.

Safety profile of belinostat in combination with bortezomib

Collectively, the data demonstrate that the combination of belinostat and bortezomib is well-tolerated. Caution should be taken when targeting tumors with a tendency to give rise to tumor lysis syndrome. Signs of clinical activity of the combination have been demonstrated in a few patients.

a) **CLN-5,** a phase Ib/II safety, pharmacokinetic, pharmacodynamic, and anti-tumor activity study of belinostat in combination with bortezomib in patients with relapsed refractory multiple myeloma. The study was closed while a new phase II trial with the same patient population was initiated[17].

b) **NCI7281,** a phase I study of belinostat in combination with bortezomib (PS-341) in patients with advanced solid tumors and lymphoma. Only patients with solid tumors were enrolled and no unexpected toxicity was seen at full doses. These results were presented at the AACR-NCI-EORTC scientific conference in 2009[18]. The study was performed in parallel with CLN-5 and demonstrated good tolerability of higher dose levels, leading to the initiation of CLN-16. At the same time the CLN-5 study was closed.

c) **CLN-16,** a phase II study of belinostat in combination with bortezomib in patients with relapsed refractory multiple myeloma. The initial dose level was 600 mg/m² and 1.0 mg/m², respectively. Among the first four patients, two had renal insufficiency, which in one patient was pre-existing. In the


belinostat
topotarget

other, creatinine levels were elevated but within normal limits at baseline. The sudden load of Bence-Jones proteins to the kidneys due to increased lysis of tumor celles, makes tumor lysis a complication well-known in myeloma. No nephrotoxicity was seen in the larger NCI7281 study where even higher doses of belinostat and bortezomib were used. Additionally, tumor lysis syndrome is rarely seen in patients with solid tumors. Tumor lysis may be a signal of efficacy, however other causes for the SAEs could not be ruled out and by protocol the study was terminated[19].

d) MCC-12517, a phase I study of belinostat and bortezomib in patients with relapsed or refractory acute leukemia and myelodysplastic syndrome. This study is run by a group of investigators at the University of Virginia, where the dose of belinostat and bortezomib is increased. No unexpected toxicities had been reported at the time of the American Association of Hematology´s (ASH) annual conference in December 2011[20].

Other clinical studies in malignant diseases

Human FAS ligand in solid tumors
APO010 is a recombinant form of the human FAS ligand. The FAS receptor is often over expressed cancer and after binding, APO010 induces apoptosis and cell death. In pre-clinical experiments, APO010 has demonstrated pronounced anti-tumor activity against a wide range of experimental and human tumors. One clinical study has been conducted so far:

SO65APOX01, a phase I dose finding and pharmacokinetic study of intravenous APO010 in patients with solid tumors, was initiated in 2007 by Apoxis and continued by Topotarget. After a cautious dose-escalation program, 25 patients were treated with i.v. bolus every other week at dose levels from 2.5 to 60 µg/m^2. The treatment was well tolerated up to 45 µg/m^2. At 60 µg/m^2 further dose escalation was stopped due to two episodes of transient cerebral ischemia. Relationship to the study medication could not be ruled out. Pharmacokinetic results limited by few patients at the higher doses suggested a dose-concentration relationship and a very short half-life of five minutes. The study showed that APO010 is well-tolerated at doses below 60 µg/m^2. Further studies are required to define the optimal FAS positive tumor targets and clinical schedules.

NMPRT in hematological and solid tumors
APO866, a first-in-class anti-cancer drug, is a potent and specific inhibitor of nicotinamide phosphoribosyl transferase (NMPRT), a key enzyme involved in the synthesis of nicotinamide adenine dinucleotide (NAD). APO866 exhibits broad anti-neoplastic activity in pre-clinical cancer models. A phase I study using APO866 administered as a 96-hour continuous intravenous infusion (CIV) was completed by Astellas in the US in January 2004 satisfactory and APO866 0.126 mg/m^2/hr for 96 hours in a 28-day schedule was recommended for phase II. On a license from Astellas, three phase II clinical studies were initiated by Apoxis and continued by Topotarget.

a) APO866-3001, a multi-center, open-label phase II study to assess the efficacy and safety of APO866 in patients with refractory or relapsed CTCL. The study was carried out in six centers in Europe from 2007 to 2011. A futility analysis was planned after the first eleven eligible patients had completed therapy. By December 2010, 13 patients had entered the study and received at least one cycle of therapy. Eleven patients had at least one repeated tumor assessment and were evaluable for efficacy. One of 11 patients had partial remission (PR), five had stable disease (SD), and five had progressive disease. Thus APO866 as CIV demonstrated clinical anti-neoplastic activity in CTCL, but the requirements for continuation of the study, three responders among the first 11 evaluable patients, were not met. Conclusively, the activity of the schedule and investigated dose were regarded as insufficient and the study was terminated. No major safety issues were reported during the study.

b) APO866-3003, a multi-center, two-stage, open label phase II study to assess the efficacy and safety of APO866 in the treatment of patients with advanced melanoma. The study was carried out in six centers in Switzerland, Germany, Austria, and France from 2006 to 2008. It was planned to enroll 20 evaluable patients in the first stage of the study. 25 patients were recruited in the first stage, resulting in 23 evaluable patients. The futility analysis failed to demonstrate responders and the study was therefore stopped due to lack of efficacy of APO366 administered as 96-hour CIV. Safety signals included a transient bilateral macular edema in one patient and were otherwise mild and reversible.

c) APO866-3005, an open phase I/II clinical study assessing the safety and tolerability of APO866 in patients with refractory B-cell lymphocytic leukemia not amenable to allogenic hematopoietic stem cell transplantation. The study was carried out in four centers in the UK (2007-2009) and accrued the planned 10 patients who all received a 96-hour CIV cycle of APO866. Four patients received 2-3 cycles. The treatment had a clear anti-neoplastic effect where five of eight patients with elevated peripheral CLL cells had a 30-40% reduction in their peripheral counts. But none of the patients

reached the 50% level defining partial remission and, conclusively, APO866 had insufficient anti-leukemic effect in the present dose and schedule. No major safety aspects were reported during the study.

2-PPA in treatment of familial adenomatous polyposis

The anti-epileptic drug valproic acid (VPA) became of oncologic interest when it was shown to be an HDACi known as PEAC, 2-propyl pentanoic acid (2-PPA). Several investigator-driven phase II studies in patients with leukemia and solid tumors have demonstrated a moderate anti-neoplastic effect.

Based on pre-clinical findings of reduced adenoma formation in a murine model of familial adenomatous polyposis (FAP), a clinical phase II study was initiated in January 2006 by the German company G2M and was, after the merging of the companies, continued by Topotarget.

Study G2M-777 SYSO1/2004 was a randomized, double-blind, placebo-controlled parallel group study to assess the safety and efficacy of an oral formulation of 2-propyl pentanoic acid (2-PPA, PEAC® minitablets) in the treatment of colorectal adenomas in patients with FAP.

The study was carried out in six centers in Germany, Russia, and Denmark. FAP patients were randomized to receive 2-PPA (in a new oral formulation, PEAC®) or placebo for a six-month period. The response was to be evaluated by videotaped colonoscopies before and after treatment. The study was planned to include 66 patients, but was stopped for further accrual in January 2009 at 49 patients included as it was clear that patient enrollment was extremely slow, and additionally, of 49 patients included, 13 patients could not be evaluated. This combined with major difficulties in interpretation of the colonoscopies from several patients made it unlikely that the study could be completed within a reasonable time frame.

As for the efficacy endpoints, the study was inconclusive. The safety pattern demonstrated AEs comparable to that of VPA used as an anti-epileptic drug, and they were mild to moderate in severity. Three SAEs were unrelated to study treatment.

Belinostat publications in 2011

Please visit www.topotarget.com for an overview of belinostat publications in 2011. The overview consists of review papers, clinical research, and pre-clinical research, including abstracts.

[1] Announcement December 8, 2009
[2] Announcement March 28, 2011
[3] Announcement December 17, 2008
[4] Announcement September 26, 2011
[5] Announcement May 29, 2009
[6] Announcement December 23, 2010
[7] Announcement May 21, 2010
[8] Announcement June 2, 2008
[9] Announcement March 14, 2011
[10] Announcement September 13, 2011
[11] Announcement October 22, 2008
[12] Announcement March 14, 2011
[13] Announcement October 23, 2008
[14] Announcement December 8, 2008
[15] Announcement November 10, 2006, April 19, 2007, and January 19, 2009
[16] Announcement May 19, 2011
[17] Announcement March 26, 2007
[18] Announcement November 17, 2009
[19] Announcement August 7, 2007
[20] Announcement November 9, 2011

Partnerships

Partner status

Spectrum Pharmaceuticals, Inc. (2010) – belinostat

- In February 2010, Topotarget out-licensed North American and Indian rights on belinostat to Spectrum Pharmaceuticals
- Under the terms of the agreement, Spectrum Pharmaceuticals made an upfront payment of USD 30 million and took over 100% funding of the PTCL BELIEF trial
- In September 2011, Spectrum Pharmaceuticals completed recruitment i.e. Last Patient First Visit of the PTCL BELIEF trial and is targeting submission of an NDA on belinostat for the orphan drug indication PTCL in end 2012
- Resources for co-development in additional indications will have cost sharing, with Spectrum Pharmaceuticals contributing 70% and Topotarget contributing 30%
- Further indications such as cancer of unknown primary (CUP), ovarian cancer, and non-small cell lung cancer (NSCLC) are being considered
- Topotarget is eligible to receive milestone payments upon successful achievement of certain development and commercial milestones of up to USD 320 million as well as double-digit royalties on sales in addition to the upfront payment
- The first expected milestone will be upon acceptance to file by the FDA, which can happen approximately 60 days after the submission of the NDA to the FDA

Multimeric Biotherapeutics, Inc. (2011) – license of IP rights to proteins containing TNF superfamily ligands (non-core asset)

- In October 2011, Topotarget out-licensed the exclusive rights to the further development of the multimeric TNF superfamily ligands (TNFSFs) for all therapeutics used to Multimeric Biotherapeutics, Inc.
- Under the agreement, Multimeric Biotherapeutics will license the rights to all multimeric fusion proteins containing TNFSFs which are covered by Topotarget's issued and pending patents in Europe, the US, Canada, Japan, Australia, South Korea, and other territories. The agreement also grants Multimeric Biotherapeutics the rights to sub-license. TNFSFs are not a core activity of Topotarget IP assets

National Cancer Institute (NCI), USA – academic collaboration

Topotarget is party to a Clinical Trial Agreement (CTA) with the NCI under which the NCI sponsors a number of clinical trials evaluating the activity of belinostat, either alone or in combination with other anti-cancer therapies, for the treatment of hematological cancers and solid tumors, e.g. ovarian cancer and thyroid cancer.

Termination of license agreements related to non-core pipeline activities

As a follow-up to the financial write-down of pipeline activities by the end of 2010, Topotarget has terminated the following license agreements and handed back the rights:

Astellas DE regarding APO866, Novartis regarding Zemab, and Mochida regarding patents relating to Fas/FasL.

Commercial opportunities for belinostat

Topotarget is actively exploring the commercial opportunities in Europe, Asia/Pacific and ROW and thereby continues to evaluate how we can commercialize belinostat most optimally outside Spectrum Pharmaceuticals' territory in order to maximize the shareholder value.

Corporate Governance

The Board of Directors defines the objectives, goals, and strategies of the company and makes decisions on matters of major significance and unusual nature. On behalf of the shareholders, the Board of Directors furthermore supervises the organization and ensures that the company is managed appropriately and in accordance with legislation and the company's Articles of Association. The Board of Directors does not participate in the day-to-day management of the company.

In addition to undertaking the overall controlling of Topotarget, it is the primary responsibility of the Board of Directors to define the strategic framework for the activities and action plans of the company and to maintain a constructive dialogue with the Management Board regarding the implementation of the strategies. In addition, the Board of Directors appoints the Management Board, sets out its terms and tasks, and supervises its work and the company's procedures and responsibilities.

Openness and transparency
Topotarget's current and future shareholders as well as other stakeholders have different requirements in terms of corporate information. However, all rely on the quality of the information available. Openness and transparency are therefore pivotal for evaluating Topotarget and its prospects and Topotarget seeks to maintain open communication through company announcements, investor meetings, and company presentations. As a result, Topotarget's annual report, interim reports, and other company announcements are available in both Danish and English. Topotarget seeks to ensure a timely convening of the company's annual general meetings, allowing its shareholders and others to consider the issues on the agenda for the general meeting.

Diversity
Topotarget fully understands and supports the importance of diversity in the organization. We believe that a diverse work force and work place results in greater quality of work as well as a broader understanding of various organizational tasks. This mindset is thus also clearly supported in Topotarget when looking at the composition of both our Board of Directors, our management team, and in the company in general.

Composition of the Board of Directors
Pursuant to Article 14 of Topotarget's Articles of Association, a maximum of seven members can serve on the Topotarget Board of Directors. The article further stipulates that board members must retire when they reach the age of 70. Topotarget seeks to ensure that at least a majority of the board members are independent of special interests. As such, six of Topotarget's seven board members are independent. All board members are evaluated by the entire Board of Directors on a yearly basis.

The key considerations made in relation to the appointment of the Board of Directors were the professional background and industry experience of each candidate. The activities of the Board of Directors are governed by an internal set of procedural rules. For relevant background information on the individual board members, please go to page 26 or visit
http://www.topotarget.com/about-us/board-of-directors.aspx

The Board of Directors has established a formal process for evaluating management, and objectives are agreed upon in connection with the budgeting procedure and evaluated finally at year-end. The Board of Directors continuously discusses the goals and strategies and Topotarget's ability to implement the strategies and live up to expectations. The Chairman of the Board has well-defined tasks, duties, and responsibilities. Among these to make sure that the board members have the competencies that are required for a governing board. The entire Board of Directors evaluates the board's composition to ensure that the needed competencies are at hand and also to ensure a transparent process on election of board members at the annual general meeting.

In 2011, the Board of Directors held 14 meetings (either in person, via telephone, or by way of written resolutions).

Audit Committee
Topotarget has established an Audit Committee and thus complies with the recommendations stipulated by the Danish Committee on Corporate Governance. The committee's main purpose is to review the financial controls and to work with the independent auditors in connection with their audit of the company's financial statements and to make reports and recommendations to the Board of Directors on these matters. The members of the Audit Committee are Bo Jesper Hansen (Chairman) and Per Samuelsson.

Internal rules in the form of a Management Instruction governing the allocation of powers between the company's Board of Directors and the senior management have been established, and the company intends to have an on-going policy of actively pursuing a strategy of good corporate governance.

Remuneration and Nomination Committee
The Board of Directors has moreover established a Remuneration and Nomination Committee. In regard to nomination, the committee's tasks are to describe and evaluate the required qualifications of the two governing bodies as well as making recommendations on changes. Furthermore, the committee considers and recommends proposals for candidates for executive positions in the company. With regard to remuneration, the sole purpose of the committee is to evaluate and make recommendations to the Board of Direc-

tors on the remuneration paid to board members and the senior management as well as recommendations concerning employee incentive programs. The committee consists of the following members: Bo Jesper Hansen (Chairman), Per Samuelsson, Ingelise Saunders, and Anker Lundemose.

Exceptions

It is the view of the Board of Directors that Topotarget complies with the Recommendations on Corporate Governance from August 2011, however, with the following exceptions:

Topotarget has, due to its size, not formally elected a Deputy Chairman.

The Chairman of the Board of Directors and the Chairman of the Audit Committee and the Remuneration and Nomination Committee are identical reasoned by the qualifications of the Chairman.

Topotarget offers share-based remuneration programs to board members, the reason being that the company considers share-based remuneration programs essential and necessary tools to attract and retain board members with international experience and profiles and to secure alignment with the company strategy.

Topotarget does not disclose remuneration of board members or managers at an individual level. Topotarget considers this information to be private and believes that information at an individual level is of limited value to shareholders.

A full description on Topotarget's approach to Corporate Governance can be found on our homepage
http://investor.topotarget.com/governance.cfm

Corporate Social Responsibility

Topotarget does not have a formal policy on Corporate Social Responsibility (CSR).

Despite not having a formal policy on the area, we recognize the significance of CSR. We therefore continue to develop and implement new operating standards and procedures to support and fulfill our obligations to both our internal and external stakeholders.

Risk profile and risk management

Risk profile
With the divestment of Topotarget's American subsidiary, Topotarget USA, Inc., and with the planned closures of our dorment Dutch, German, and Swiss subsidiaries, we are currently reducing our facilities outside Denmark – a reduction that is based on our undivided focus on our lead development compound, belinostat.

Topotarget performs development activities with global clinical studies for belinostat and are therefore, through these activities, exposed to a variety of risks – some of which are beyond our control. Risks that, if not properly assessed and controlled, may have significant impact on our business.

Risk management approach
Active management of operational, financial, and compliance risks is a prerequisite for Topotarget. Risks are identified and reported through a systematic process. Consolidation, analysis, and evaluation take place with stakeholders within Topotarget. Management is responsible for the final calibration of risks and review of mitigating actions. Management and the Board of Directors discuss and decide on the risk tolerance for the most significant risks.

Risk management initiatives in 2011
In 2011, Topotarget launched an initiative to enhance its risk management capabilities. The company completed the rollout of a risk management business process with semi-annual reporting to the Board of Directors as well as ad hoc reporting to relevant stakeholders.

The risk management business process defines clear responsibilities for the Board of Directors as well as the management. The Board of Directors is responsible for:

- Approval of the Risk Policy, including risk tolerance levels
- Review and approval of top risk scenarios
- Review of the current level of mitigation of top risks
- Proposals for additional mitigation, if required
- Verification of the adequacy of the risk management infrastructure

Management is directly responsible for management and mitigation of key risks as well as for the maintenance of a robust risk management business process, including the reporting cycle.

Below you will find a summary of the company's main risk areas and a summary of how the company seeks to address these risks.

Development and scientific risks
With the establishment of a Global Oncology Advisory Board, Topotarget seeks to ensure the optimal selection of future disease targets. Also, we have formed a Scientific Committee consisting of board members and key Topotarget employees, who are closely monitoring and assessing data and other information from our clinical trials. Both will help us in complying with the extensive governmental regulations that we are subject to up until our product candidate receives regulatory approval.

In general, there is a risk that the inclusion of patients in clinical studies is insufficient and that lack of efficacy and unexpected, SAEs are registered on a drug. Moreover, unforeseen safety issues or changes of regulatory requirements can influence the timing and nature of our clinical development activities, costs, and related revenues such as milestone payments and cost reimbursement.

Risks related to the market and partners
Our reliance on the collaboration with Spectrum Pharmaceuticals is very important for our business as our future growth and a significant part of our future revenues, in particular milestones and royalties, may depend on the continued collaboration. Our business might be negatively affected if Spectrum Pharmaceuticals does not devote sufficient resources to the belinostat development programs, if they become unable to meet their obligations, or if we are not able to establish additional partnerships for Asia and Europe.

Topotarget is furthermore subject to a range of normal biopharmaceutical commercial risks, including:

- Competition from existing treatment and/or new drugs
- Market size of lead indications
- Product pricing and reimbursement policies
- Interest from potential partners and investors
- Development time of new clinical trials
- Patent protection and ability to prevent infringements

Risks related to legal requirements
Topotarget's activities are also affected by legal requirements and changes from health authorities in several countries. Modified legislation and reinterpretation of legislation in Topotarget-relevant countries may result in unintended or unexpected issues.

Another risk scenario is that Topotarget's ability to protect itself in potential patent lawsuits is insufficient; for instance if our

intellectual property is not protected or our products infringe on a competitor's intellectual property. We therefore continue to file necessary patent applications in an effort to protect our product and technologies. We maintain strict confidentiality standards and agreements for internal employees and any collaborating parties in order to protect business secrets.

Financial risks
We are reducing our exposure to fluctuations in exchange rates by mainly concentrating our facilities in Denmark. However, as we are conducting global studies and have shared clinical costs with Spectrum Pharmaceuticals, we are exposed to exchange rate fluctuations.

The company's cash holdings consist of deposits held in money market funds and in cash. The interest rate risk is insignificant relative to Topotarget's combined operations.

Capital resources
With the divestment of Totect® Topotarget has become a drug development company without commercial revenue. We will, excluding revenue from collaboration partners, be cash consuming until belinostat becomes commercially available. It is therefore crucial that the company at all times ensures sufficient financial resources.

Risk management
A number of factors concerning Topotarget and our strategies contribute to a reduction of the overall risks:

- We are pursuing a partnering strategy which reduces a large part of the financial risks; we have a strong development agreement for belinostat with Spectrum Pharmaceuticals for North America and India, who will handle the commercialization of belinostat in its geographical regions; we are exploring commercial opportunities for belinostat in Asia and Europe

- We have developed an effective technology with validated tumor models to evaluate the effect of its therapeutics on cancer diseases; we have cross-disciplinary and complementary expert teams that continuously evaluate the results of studies with drug candidates and optimize the development process

- Topotarget collaborates with several scientific organizations and has a large representation of medical expertise within the company, ensuring bridge-building between science and the treatment of patients

- Topotarget is a professional organization which strives to be updated on and complying with laws affecting the company's activities

- We are dependent on contract manufacturers for the manufactory of belinostat, and therefore we are continually exploring our options to alleviate the risk of supply issues

- Our Board of Directors continuously evaluates the need to increase the company's financial resources based on financial reporting prior to board meetings

The process of accounts preparations

The overall responsibility for the company's control and risk management in relation to the financial reporting process, including compliance with applicable legislation and other financial reporting regulations, rests with Topotarget's Board of Directors and Management Board.

Financial report process
The company has an Audit Committee consisting of members of the company's Board of Directors. The Audit Committee reviews and discusses auditing and accounting matters with the company's auditors elected by the shareholders and the Management Board in accordance with the Audit Committee's terms of reference.

Topotarget's primary focus is to ensure that the financial statements are in accordance with relevant accounting legislation and other provisions and regulations and give a true and reliable view of the company's activities and financial position.

The preparation of the company's financial reporting follows a planned structure involving segregation of duties.

Topotarget has established internal monthly reporting with a view to effectively managing its financial status. The reporting process involves analyses of deviations between actual results, business plans, and budgets and the most recently updated estimate for the financial year. The monthly report, including explanation of deviations for the principal business areas, is reviewed by the Management Board before it is distributed to the Board of Directors.

The company's statutory reports are prepared according to the same structure as the monthly reports.

The quarterly reports are reviewed at an Audit Committee meeting before they are approved at a board meeting and subsequently released for publication.

The annual audit and reporting process comprise detailed planning of individual assignments, planning meetings between Investor Relations, the Finance Department and the external auditors. The audit and planning process is based on an approved audit strategy.

The annual report is prepared in close collaboration with key management personnel and individuals from each business unit. In addition, the auditors ensure that the financial statements provide a reliable and true view of the company's assets, liabilities and financial position, ensuring that the annual report is presented in accordance with the accounting policies adopted.

Control environment
The Audit Committee and subsequently the Board of Directors assess, at least once a year, the Group's organizational structure, its risk of fraud as well as the existence of in-house rules and guidelines.

The Group's control and risk management systems may provide reasonable, but not absolute, assurance that misappropriation of assets, losses and/or significant errors and omissions in the financial reporting are avoided.

The Board of Directors and the Management Board are responsible for establishing and approving general policies, procedures and controls in key areas in relation to the financial reporting process. The Board of Directors approves the overall policies, procedures, and controls, which are maintained and monitored by the Management Board and key employees representing each business area.

Topotarget has established policies and procedures for the key areas in relation to the financial reporting process, including business procedures for financial reporting and planning, business procedures for the finance function and other key business units and for IT security.

Risk assessment
At least annually, the Board of Directors makes a general assessment of risks in relation to the financial reporting process. The objective of Topotarget's internal risk management system is to maintain effective procedures for identification, monitoring, and reporting of such risks. This includes an assessment of IT security.

As part of the risk assessment, the Board of Directors considers the risk of fraud and the measures to be taken to reduce and/or eliminate such risk.

Board of Directors and Management

Board of Directors

BO JESPER HANSEN, MD, PhD
Danish, 53
Chairman since 2010
Independent board member since 2009

Special competences
Experience in the field of international contract negotiations and deal-making, including execution of high-impact license agreements and significant M&A transactions; international marketing, extensive knowledge of legislative conditions, pharmaco surveillance, medical marketing, business development, and many connections within the medical industry and especially within the orphan drug market.

Board positions
Chairman: Swedish Orphan Biovitrum AB (publ)
Member: MipSalus ApS, Zymenex A/S, Gambro AB, Orphazyme ApS, Novagali Pharma S.A., CMC Kontrast AB, Hyperion Therapeutics Inc., and Genspera Inc.

Stocks: 300,000
Warrants: 100,000

INGELISE SAUNDERS, MPh, BSc
Danish, 62
Independent board member since 2004

Special competences
Extensive executive management experience, experience in international operations, in sales, marketing, and global commercial operations, M&A transactions and business development, healthcare strategy, and life science investments.

Board positions
Member: AdvanDx A/S

Stocks: 25,000
Warrants: 133,278

JEFFREY H. BUCHALTER, BS, MBA
American, 54
Independent board member since 2006

Special competences
Experience in executive management, industry, development, manufacturing, and commercialization of pharmaceutical products as well as therapies for cancer patients.

Board positions
Chairman: The National Childhood Cancer Foundation
Member: Archimedes Pharma Limited

Warrants: 154,097

PER SAMUELSSON, MSc
Swedish, 51
Board member since 2009

Special competences
Experience in biotech, venture capital, investment banking, merger transactions, initial public offerings, and equity incentive programs.

Board positions
Member: Algeta ASA, BioStratum Inc., Cardoz AB, Nordic Vision Clinics AS, Oncos Therapeutics Oy, Optivy AB, and Sweden BIO

ANKER LUNDEMOSE, MD, PhD, Doctor of Medical Science
Danish, 50
Independent board member since 2010

Special competences
Experience within academia, executive management, large pharma, biotech, and business and corporate development. Has an international track record in R&D productivity, deal making, including execution of high-impact license agreements, and significant M&A transactions. Currently Managing Partner at BioTesch.

Board positions
Chairman: InteRNA Technologies BV
Member: Adenium Biotech AS

Stocks: 25,000
Warrants: 50,000

GISELA SCHWAB, MD
German, 55
Independent board member since 2011

Special competences
Experience within the pharmaceutical industry in managing early and late-stage development activities (target selection, pre-clinical, pharmacokinetic, clinical, and regulatory development) of biotechnological compounds and small molecules, filing of INDs and BLAs/MAAs, and in building and managing development teams.

Warrants: 25,000

KARSTEN WITT, MD
Danish, 55
Independent board member since 2011

Special competences
Experience in clinical strategy and execution of development programs as well as drug safety/pharmacovigilance, development of small-molecule targeted oncology therapies, filing of INDs, BLA/sBLA, and NDA/sNDA.

Warrants: 25,000

Management team

FRANCOIS MARTELET, MD
Company officer
French, 52
Chief Executive Officer

Special competences
Seasoned senior executive in general management with a track record of shaping business units and associates of pharma and biotech companies towards goals that deliver tangible, sustainable returns. Strong general P&L management and late-stage clinical development oncology experience.

Has a proven track record of launching successful multiple oncology drugs and specialty medicine products globally. In-depth knowledge of HDACi drug class and cancer vaccines therapy. Master's Degree in Business and a Medical Degree.

Warrants: 1,600,000

AXEL MESCHEDER, MD
Company officer
German, 53
Chief Medical & Development Officer

Special competences
Sound medical experience, clinical judgment, scientific and development skills. Experience in drug development, medical marketing, product development with focus on oncology. Experienced in building and managing international development teams.

Has a proven track record of developing and registering drugs internationally both with the FDA and EMA.

Experience in evaluating individual compounds as well as portfolios in order to make strategic decisions regarding business development and partnering.

Warrants: 270,000

ANDERS FINK VADSHOLT, MSc, MBA
Company officer
Danish, 42
Chief Financial Officer

Special competences
Operational experience from biotech companies within legal, finance, and investor relations. Experience from venture capital and corporate finance in raising private and public capital, mergers and acquisitions, restructuring and divestments of companies as well as communication with investors and stakeholders.

Has a proven track record in managing the available financial resources in a strategic and cost-efficient manner.

Stocks: 25,000
Warrants: 400,000

INGE HOLM LAURITZEN, BSc
Danish, 45
VP Business Development & Licensing/Strategic Planning

Special competences
Senior biotech and pharma executive with more than 15 years of contract negotiation and alliance management experience in the pharmaceutical and biopharmaceutical industry.

ELISABETH V. CARSTENSEN, PhD
Danish, 42
Director of Pharmaceutical Operations

Special competences
Extended experience within the area of pharmaceutical operations and more than 10 years' experience with Topotarget, including work with manufacturing operations, supply chain management, and registration processes. Manages CMC (chemistry, manufacturing, and controls) for clinical and commercial products in Topotarget's pipeline.

Shareholder information

Topotarget A/S' shares were listed on the Copenhagen Stock Exchange (now NASDAQ OMX Copenhagen A/S) in June 2005 under the securities/ISIN code DK0060003556 and the trading symbol TOPO. The company's Reuters symbol is TOPO.CO and its Bloomberg symbol is TOPO:DC. Trading of the company's shares commenced on June 10, 2005.

The closing price for our shares on December 31, 2011 was DKK 2.51 which was a decrease of 30% compared to the company's share price of DKK 3.57 at year-end 2010.

The average daily trading volume for the company's shares in 2011 was DKK 0.3 million.

At December 31, 2011, Topotarget's share capital was DKK 132,652,050 corresponding to 132,652,050 shares of DKK 1 nominal value. The company only has one class of shares and all shares have equal rights. Topotarget's Articles of Association do not contain provisions on limitations of ownership or voting rights for each individual shareholder.

Ownership structure

As of December 31, 2011, Topotarget had 8734 registered shareholders, who held 59% of the share capital compared to 9136 registered shareholders at the end of 2010.

At December 31, 2011, the company's 10 largest shareholders held 30% of the total share capital, and the following investors have informed Topotarget that they hold more than 5% of the shares:

- HealthCap funds
- Avanza Bank

IR policy, goals, and activities

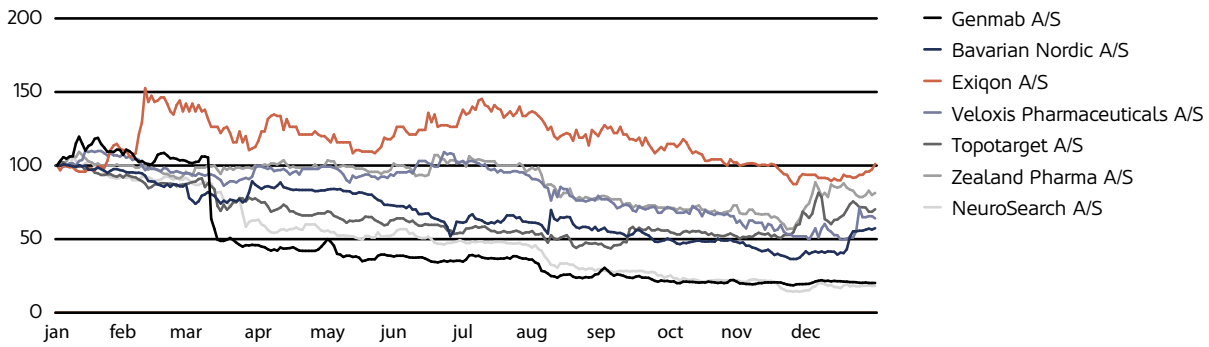
Topotarget aims to maintain an open and continuous dialogue with existing and potential shareholders, other stakeholders, and the general public. The company thus strives to provide transparent communication with equal access for all stakeholders. With open communication, the company aims to ensure fair pricing of the company's shares in order to reflect the company's willingness to generate higher earnings to its shareholders.

In compliance with the disclosure requirements of NASDAQ OMX Copenhagen, Topotarget will publish information on the company that is deemed important to the pricing of its shares. The company will also publish quarterly reports on the company's development, including relevant financial information. Topotarget also observes so-called 'quiet periods' (two weeks) before the publication of each company financial report. During these periods, the company will refrain from holding investor and analyst meetings or meetings with the media. The company maintains an insider register and will publish any changes to certain insiders' shareholdings in accordance with the rules that apply for NASDAQ OMX Copenhagen. Such publication will be made immediately after the transaction.

Topotarget has also adopted in-house rules, which stipulate that insiders may only purchase and sell shares in the company during a period of six weeks after the company's publication of interim financial statements.

Any information published by the company will be published in full accordance with disclosure requirements under Danish law and all announcements are posted on the company's website www.topotarget.com.

TOPOTARGET AND OTHER SHARE DEVELOPMENT 2011



Announcements and investor news 2011

Announcements	
Jan 3	Topotarget issues warrants to Management
Mar 4	Articles of Association of Topotarget A/S
Mar 8	Topotarget announces financial results for the year ended December 31, 2010
Mar 11	Notice to Convene Annual General Meeting
Mar 14	Topotarget announces updates on belinostat in two clinical trials - NSCLC and ovarian cancer
Mar 28	Independent Data Monitoring Committee recommends continuation of the belinostat pivotal BELIEF study in Peripheral T-Cell Lymphoma (PTCL)
Apr 5	Topotarget expects a pre-tax loss of DKK 20-40m for 2011
Apr 5	Passing on Topotarget A/S annual general meeting
Apr 6	Articles of Association of Topotarget A/S
Apr 8	Establishment of Global Oncology Advisory Board
Apr 26	Recruitment into the Phase I trial of oral belinostat has been completed
May 10	Topotarget announces the interim report for Q1 2011
May 19	Belinostat abstracts at ASCO 2011
Jul 1	Topotarget issues warrants to Employees, Management and the Board of Directors
Aug 3	Notice to Convene Extraordinary General Meeting
Aug 17	Topotarget announces the interim report for Q2 2011
Aug 25	Articles of Association of Topotarget A/S
Aug 29	Passing of extraordinary general meeting
Sep 13	Belinostat abstracts at the European Multidisciplinary Cancer Congress 2011
Sep 26	Belinostat PTCL trial fully enrolled
Oct 6	Topotarget publishes financial calendar for Q3 2011 and 2012
Oct 28	Topotarget issues warrants to board members
Nov 9	Belinostat abstracts at The American Society of Hematology 53rd annual 2011 meeting
Nov 9	Articles of Association of Topotarget A/S
Nov 18	Interim report for Q3 2011
Dec 7	Topotarget announces reorganization plans
Dec 16	Topotarget A/S announces the divestiture of Totect® to Apricus Biosciences, Inc., and improved financial expectations for 2011
Dec 30	Topotarget A/S announces the successful completion of the divestiture of Totect® and Topotarget USA, Inc. to Apricus Biosciences, Inc.

Investor news	
Mar 4	Topotarget announces time and date for telephone conference related to the publishing of the Annual Report 2010
May 4	Time and date for telephone conference related to the publishing of the Q1 2011 interim report
Aug 12	Time and date for telephone conference related to the publishing of the Q2 2011 interim report
Oct 28	Topotarget A/S grants Multimeric Biotherapeutics, Inc. an exclusive license to the MegaLigand Platform of TNF Superfamily ligands
Nov 14	Time and date for telephone conference related to the publishing of the Q3 2011 interim report

Financial review

The annual report comprises the Parent Company Topotarget A/S and the five wholly owned subsidiaries.

Unless otherwise stated, the financial review is based on the Group's consolidated financial information for the year ended December 31, 2011 as included in this annual report with comparative figures for the Group in 2010 in brackets.

A loss on continued operations before write-down activities of DKK 29.0 million (2010: loss of DKK 84.8 million) was recorded for the year.

The Group's net cash and cash equivalents as of December 31, 2011 totaled DKK 114.3 million (2010: DKK 205.0 million.) and equity stood at DKK 330.7 million (2010: DKK 360.2 million).

Consolidated income statement
Topotarget recognized revenues of DKK 65.6 million in 2011 (2010: DKK 107.8 million). Revenues are primarily composed of income of DKK 62.8 million from the Spectrum Pharmaceuticals upfront payment of USD 30 million as well as income from partnership.

Production costs, which amounted to DKK 1.8 million (2010: DKK 5.4 million), include Topotarget personnel costs related to the Spectrum Pharmaceuticals collaboration agreement.

Research and development costs were DKK 54.3 million (2010: DKK 71.6 million). The reduction is primarily due to the near completion of most studies. The finalization of data and study reports are ongoing.

Write-down of research and development projects acquired from third parties amounted to DKK 0 million (2010 DKK 189.5 million). For a more detailed description on the individual projects please see Note 12.

Sales and distribution costs for the Group have been reclassified to discontinued operations due to the divestiture of the US subsidiary including the IP for Totect®.

Administrative expenses were DKK 40.8 million (2010: DKK 38.8 million). The small increase is mainly due to increased support for partnering activities.

Net financial income was DKK 1.1 million (2010: Net income of DKK 68.8 million), primarily consisting of exchange rate adjustments in subsidiaries. (2010: Primarily consisting of the reversal of the APO provision for debt with the amount of DKK 66.5 million).

The tax income was DKK 1.2 million (2010: 44.0 million) and relates solely to Topotarget Switzerland S.A.

Net loss from discontinued operations DKK 4.0 million (2010: Profit 29.1 million). The loss from discontinued operations consists of all costs relating to the sales activities of Totect® for the year as well as the sale transaction of the IP and subsidiary in the amount of DKK 9.1 million. The comparative 2010 number also includes all elements of the year's activities as well as the sale proceeds of Savene®.

Topotarget recorded a net loss of DKK 33.0 million (2010: DKK 55.7 million).

Consolidated balance sheet
Total assets amounted to DKK 370.5 million (2010: DKK 465.8 million.), which primarily consist of acquired research and development projects, cash and cash equivalents, while the Group's liabilities mainly comprise equity and trade payables.

Cash and cash equivalents were DKK 114.3 million (2010: DKK 205.0 million).

Current liabilities have reduced from DKK 91.5 million to DKK 26.2 million due to the finalization of the deferred income release in the year.

Consolidated equity
Equity amounted to DKK 330.7 million (2010: DKK 360.2 million). The change in equity consists of the loss for the year of DKK 33.0 million and share-based payment of DKK 3.5 million.

Consolidated cash flow
Topotarget's cash flow from operating activities for 2011 was an outflow of DKK 88.4 million (2010: In-flow DKK 40.1 million). The Group's 2011 cash flow from investing activities excluding the buying and selling of securities was an outflow of DKK 1.9 million (2010: Inflow DKK 34.7 million). The Group's cash flow from financing activities was DKK 0.0 million (2010: Inflow of DKK 0.1 million).

Comparing the actual financial performance with financial guidance
The Group recorded a loss on continued operations before write-down activities of DKK 29.0 million. The financial performance is in line with our guidance announced at the annual general meeting on April 5, 2011.

Outlook
Topotarget expects an estimated pre-tax loss in the range of DKK 75–95 million for the full year financial result of 2012. The expected net cash and cash equivalents will be around DKK 35–55 million at year-end 2012.

Parent Company financial statements
The Parent Company recorded a loss of DKK 33.0 million (2010: DKK 55.7 million). The Parent Company's equity amounted to DKK 330.7 million (2010: DKK 360.2 million). The change in equity consists of the loss for the year of DKK 33.0 million and share-based payment of DKK 3.5 million.

Treatment of loss
The Board of Directors proposes that the loss for the year be carried forward to next year.

Statement by the Board of Directors and executive management

The Board of Directors and executive management today discussed and adopted the annual report for 2011 of Topotarget A/S.

The consolidated financial statements are presented in accordance with International Financial Reporting Standards as adopted by the EU, and the Parent financial statements are presented in accordance with the Danish Financial Statements Act. Further, the annual report is prepared in accordance with additional Danish disclosure requirements for listed companies.

In our opinion the consolidated financial statements and the Parent financial statements give a true and fair view of the Group's and the Parent Company's assets, liabilities, and financial position at December 31, 2011 and of the results of the Group's and the Parent Company's operations and cash flows for the year 2011.

We also believe that the management commentary contains a fair review of the development in the Group's and the Parent's business and of their financial position as a whole together with a description of the principal risks and uncertainties that they face.

The annual report will be submitted to the general meeting for approval.

Copenhagen, March 14, 2012

Executive management

Francois R. Martelet
CEO

Anders F. Vadsholt
CFO

Axel Mescheder
CMDO

Board of Directors

Bo Jesper Hansen
Chairman

Per Samuelsson

Jeffrey H. Buchalter

Ingelise Saunders

Anker Lundemose

Gisela Schwab

Karsten Witt

Independent auditors' report

To the shareholders of Topotarget A/S

Report on the consolidated financial statements and the Parent financial statements

We have audited the consolidated financial statements and the Parent financial statements of Topotarget A/S for the financial year January 1, 2011 to December 31, 2011, which comprise the statement of comprehensive income, balance sheet, statement of changes in equity, cash flow statement and notes, including accounting policies, for the Group as well as the Parent. The consolidated financial statements have been prepared in accordance with the International Financial Reporting Standards as adopted by the EU and Danish disclosure requirements for listed financial enterprises, and the Parent financial statements have been prepared in accordance with the Danish Financial Statements Act.

Management's responsibility for the consolidated and Parent financial statements

Management is responsible for the preparation of consolidated financial statements that give a true and fair view in accordance with International Financial Reporting Standards as adopted by the EU and Danish disclosure requirements for listed companies as well as the preparation of Parent financial statements that give a true and fair view in accordance with the Danish Financial Statements Act. Management is also responsible for the internal control that it considers necessary for preparing consolidated financial statements and Parent financial statements that are free from material misstatement, whether due to fraud or error.

Auditor's responsibility

Our responsibility is to express an opinion on the consolidated financial statements and Parent financial statements based on our audit. We conducted our audit in accordance with International Standards on Auditing and additional requirements under Danish audit regulation. This requires that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements and Parent financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the consolidated financial statements and the Parent financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the consolidated financial statements and the Parent financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the preparation of consolidated financial statements and Parent financial statements that give a true and fair view. The purpose of this is to design procedures that are appropriate in the circumstances but not to express an opinion on the effectiveness of the company's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements and the Parent financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Our audit has not resulted in any qualification.

Opinion

In our opinion, the consolidated financial statements give a true and fair view of the Group's financial position at December 31, 2011 and of the results of its operations and cash flows for the financial year January 1 to December 31, 2011 in accordance with the International Financial Reporting Standards as adopted by the EU and Danish disclosure requirements for listed companies.

Further, in our opinion, the Parent financial statements give a true and fair view of the Parent's financial position at December 31, 2011, and of the results of its operations and cash flows for the financial year January 1 to December 31, 2011 in accordance with the Danish Financial Statements Act.

Statement on the management's commentary

Pursuant to the Danish Financial Statements Act, we have read the management's commentary. We have not performed any further procedures in addition to the audit of the consolidated financial statements and Parent financial statements.

On this basis, it is our opinion that the information provided in the management's review is consistent with the consolidated financial statements and Parent financial statements.

Copenhagen, March 14, 2012

Deloitte
Statsautoriseret Revisionspartnerselskab

Jens Rudkjær
State-authorized public accountant

Carsten Vaarby
State-authorized public accountant

Consolidated statement of comprehensive income for the year

		Group		Parent	
DKK '000	Note	2011	2010	2011	2010
Revenues	3,4	65,598	107,826	68,015	111,620
Production costs	5,6	(1,840)	(5,442)	(4,351)	(10,319)
Research and development costs	5,6	(54,345)	(71,608)	(47,878)	(62,546)
Write-down of research and development projects	5	-	(189,541)	-	(11,275)
Divestiture of rights in Europe to Savene®		-	-	-	32,473
Sales and distribution costs	5,6	-	-	-	(1,788)
Administrative expenses	5,6	(40,765)	(38,778)	(40,065)	(37,181)
Operating loss		**(31,352)**	**(197,543)**	**(24,279)**	**20,984**
Income after tax from investments in subsidiaries	14		-	(19,946)	(180,780)
Financial income	7	11,729	80,863	20,183	116,056
Financial expenses	8	(10,642)	(12,090)	(8,969)	(11,950)
Loss from continued operations before tax		**(30,265)**	**(128,770)**	**(33,011)**	**(55,689)**
Tax on profit/(loss) for the year	9	1,253	43,985	-	-
Net loss from continued operations		**(29,012)**	**(84,785)**	**(33,011)**	**(55,689)**
Net loss from discontinued operations	10	(3,999)	29,096	-	-
Total comprehensive income for the year		**(33,011)**	**(55,689)**	**(33,011)**	**(55,689)**
Total comprehensive income attribuable to:					
Owners of the company		(33,011)	(55,689)	(33,011)	(55,689)
Non-controlling interests		-	-	-	
Total comprehensive income for the year		**(33,011)**	**(55,689)**	**(33,011)**	**(55,689)**
Basic and diluted EPS continued operations	11	(0.22)	(0.64)		
Basic and diluted EPS continued and discontinued operations	11	(0.25)	(0.42)	(0.25)	(0.42)

Balance sheet – assets

		Group		Parent	
DKK '000	Note	2011	2010	2011	2010
Acquired research and development projects		229,626	235,717	202,828	208,919
Intangible assets	5,12	**229,626**	**235,717**	**202,828**	**208,919**
Other fixtures and fittings, tools and equipment		4,963	5,991	4,961	5,973
Tangible assets	5,13	**4,963**	**5,991**	**4,961**	**5,973**
Investment in subsidiaries	14	-	-	31,134	27,941
Receivables from subsidiaries	14	-	-	20	26,625
Other receivables	14	608	972	608	787
Non-current investments	14	**608**	**972**	**31,762**	**55,353**
Non-current assets		**235,197**	**242,680**	**239,552**	**270,245**
Inventories – raw materials		-	766	-	766
Inventories – saleable goods		-	859	-	859
Inventories		**-**	**1,625**	**-**	**1,625**
Trade receivables	15	1,643	3,721	1,643	2,543
Other receivables		8,775	11,816	8,664	11,618
Prepayments		792	913	824	746
Receivables		**11,210**	**16,450**	**11,131**	**14,907**
Short-term securities	16	**9,768**	**-**	**9,768**	**-**
Cash and cash equivalents	19	**114,302**	**205,068**	**106,881**	**165,013**
Current assets		**135,279**	**223,143**	**127,780**	**181,545**
Assets		**370,476**	**465,824**	**367,331**	**451,789**

Balance sheet – equity and liabilities

		Group		Parent	
DKK '000	Note	2011	2010	2011	2010
Share capital	17	132,652	132,652	132,652	132,652
Share-based payments	18	34,743	31,222	34,743	31,222
Retained earnings		163,333	196,345	163,333	196,345
Equity		**330,729**	**360,219**	**330,729**	**360,219**
Deferred tax	9	-	-	-	-
Pension liabilities		-	-	-	-
Other payables	20	13,585	14,116	13,585	14,116
Non-current liabilities		**13,585**	**14,116**	**13,585**	**14,116**
Trade payables		16,274	16,868	13,673	17,091
Deferred income	22	-	63,455	-	56,804
Debt to subsidiaries		-	-	-	82
Other payables	19	9,889	11,163	9,345	3,478
Current liabilities		**26,163**	**91,486**	**23,018**	**77,454**
Liabilities		**39,748**	**105,602**	**36,603**	**91,570**
Equity and liabilities		**370,476**	**465,824**	**367,331**	**451,789**

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Cash flow statements

		Group		Parent	
DKK '000	Note	2011	2010	2011	2010
Operating loss		(31,352)	(197,543)	(24,279)	20,982
Operations loss from discontinued operations		(6,560)	(3,376)	-	-
Reversal of share-based payments		3,521	3,969	3,143	3,056
Reversal of pension commitments		-	(315)	-	-
Reversal of divestment of Savene®		-	-	-	(32,473)
Depreciation, amortization, and impairment losses	5	414	193,101	264	14,996
Working capital changes	25	(58,458)	31,742	(49,035)	32,981
Cash flows from operating activities before interest		**(92,435)**	**27,577**	**(69,907)**	**39,542**
Interest income etc. received		11,729	14,327	9,240	20,830
Interest expenses etc. paid		(9,394)	(1,827)	(5,161)	(1,901)
Refunded income taxes		1,253	24	-	-
Cash flows from operating activities		**(88,847)**	**40,101**	**(65,828)**	**58,471**
Purchase of tangible assets		(2,283)	(3,746)	(2,299)	(3,747)
Sale of tangible assets		-	2,113	56	475
Capital increase in subsidiary		-	-	3,147	(2,050)
Change of loan to subsidiary		-	-	6,613	(45,537)
Purchase of investments		364	399	179	400
Divesture of Savene®		-	-	-	35,920
Discontinued operations			35,920		-
Cash flow from investing activities		**(1,919)**	**34,686**	**7,696**	**(14,539)**
Installment on lease commitments			-		-
Proceeds from the issuance of shares	27		138		138
Cash flows from financing activities		**-**	**138**	**-**	**138**
Increase/decrease in cash and cash equivalents		(90,766)	74,923	(58,132)	44,068
Cash and cash equivalents at January 1		205,068	130,145	165,013	120,945
Cash and cash equivalents at December 31		**114,302**	**205,068**	**106,881**	**165,013**
Total cash and cash equivalents at December 31		**114,302**	**205,068**	**106,881**	**165,013**

Equity – Group

Consolidated statement of changes in equity for the period January 1 to December 31, 2011

DKK '000	Number of shares	Share capital	Share preminum account	Retained earnings	Total
Equity at January 1, 2011	132,652,050	132,652	31,222	196,345	360,219
Net loss for the year	-	-	-	(33,011)	(33,011)
Other comprehensive income for the year	-	-	-	-	-
Total comprehensive income for the year	-	-	-	(33,011)	(33,011)
Recognition of share-based payment	-	-	3,521	-	3,521
Equity at December 31, 2011	132,652,050	132,652	34,743	163,334	330,729

The share capital is an undistribuable reserve, while the other reserves are distributable for dividend purposes subject to the provisions of the Danish Public Companies Act.

Consolidated statement of changes in equity for the period January 1 to December 31, 2010

Equity at January 1, 2010	132,609,020	132,609	31,140	248,049	411,798
Net loss for the year	-	-	-	(55,689)	(55,689)
Other comprehensive income for the year	-	-	-	-	-
Total comprehensive income for the year	-	-	-	(55,689)	(55,689)
Recognition of share-based payment	-	-	3,940	31	3,971
Reversal of expired warrants			(3,858)	3,858	-
Share capital increase through warrant exercise	43,030	43	-	95	138
Equity at December 31, 2010	132,652,050	132,652	31,222	196,345	360,219

The share capital is an undistributable reserve, while the other reserves are distributable for dividend purporses subject to the provisions of the Danish Public Companies Act.

Equity – Parent

Parent Company statement of changes in equity for the period January 1 to December 31, 2011

DKK '000	Number of shares	Share capital	Share preminum account	Retained earnings	Total
Equity at January 1, 2011	132,652,050	132,652	31,222	196,345	360,219
Net loss for the year	-	-	-	(33,011)	(33,011)
Other comprehensive income for the year	-	-	-	-	-
Total comprehensive income for the year	-	-	-	(33,011)	(33,011)
Recognition of share-based payment	-	-	3,521	-	3,521
Equity at December 31, 2011	132,652,050	132,652	34,743	163,334	330,729

The share capital is an undistributable reserve, while the other reserves are distributable for dividend purposes subject to the provisions of the Danish Public Companies Act.

Parent Company statement of changes in equity for the period January 1 to December 31, 2010

Equity at January 1, 2010	132,609,020	132,609	31,140	248,049	411,798
Net loss for the year	-	-	-	(55,689)	(55,689)
Other comprehensive income for the year	-	-	-	-	-
Total comprehensive income for the year	-	-	-	(55,689)	(55,689)
Recognition of share-based payment	-	-	3,940	31	3,971
Reversal of expired warrants			(3,858)	3,858	-
Share capital increase through warrant exercise	43,030	43	-	95	138
Equity at December 31, 2010	132,652,050	132,652	31,222	196,345	360,219

The share capital is an undistributable reserve, while the other reserves are distributable for dividend purposes subject to the provisions of the Danish Public Companies Act.

Notes

1. Changes in accounting policies

Basis of preparation
The annual report for Topotarget, including consolidated financial statements, is prepared in accordance with the International Financial Reporting Standards (IFRS) as adopted by the EU, as well as additional Danish disclosure requirements for annual reports of listed companies. Topotarget presents its financial statements in accordance with all applicable IFRS standards. The accounting policies for the Group are unchanged from 2010. The financial statements for the Parent Company is prepared in accordance with the Danish Financial Statements Act (reporting class D) and is unchanged from 2010.

Standards and interpretations which have come into force and affect recognition and measurement
The annual report for 2011 is presented in accordance with the new and revised standards (IFRS/IAS) and interpretations (IFRIC) which apply for financial years starting on or after January 1, 2011. New standards and interpretations have not affected recognition and measurement.

Standards and interpretations which have come into force and affect disclosures
The annual report for 2011 is presented in accordance with the new and revised standards (IFRS/IAS) and interpretations (IFRIC) which apply for financial years starting on or after January 1, 2011. New standards and interpretations have not affected disclosures.

Standards and interpretations not yet in force
Standards and interpretations not yet in force at the time of publishing the present annual report have not yet taken effect and therefore have not been incorporated into the present annual report. Management believes that implementation of new and amended standards and interpretations will not affect the financial statements for 2012.

2. Significant accounting assumptions and estimates

In using the Group's accounting policies, the management is required to use judgments, estimates, and assumptions concerning the carrying amount of assets and liabilities which cannot be immediately inferred from other sources. Management's estimates are based on historical experience and other factors, including expectations of future events based on existing events. The actual outcome may differ from these estimates.

Estimates and assumptions are re-assessed in an on-going process. Changes to accounting estimates are recognised in the reference period in which the change occurs and in future reference periods if the change affects the period in which it is made as well as subsequent reference periods.

Areas in which the Group makes significant assumptions and estimates are described below. The Group's accounting policies are described in Note 29 to the financial statements.

Revenue recognition
Revenue is recognised when it is probable that future economic benefits will flow to the company and such economic benefits can be measured reliably. In addition, recognition requires that all significant risks and rewards of ownership of the rights or services included in the transaction have been transferred to the buyer. Income from agreements with multiple components and where the individual components cannot be separated is recognised over the period of the agreement. In addition, recognition requires that all significant risks and rewards of ownership of the goods or services included in the transaction have been transferred to the buyer. If all risks and returns have not been transferred, revenue is recognised as deferred income until all components of the transaction have been completed.

On February 2, 2010, Topotarget entered into a license and cooperation agreement with Spectrum Pharmaceuticals, Inc. covering the development and commercialization of belinostat. Topotarget has received an upfront payment of USD 30.0 million. According to the agreement, the initial upfront payment concerns several components which cannot be separated. The amount was recognised over a period of 18 months which commenced February 2, 2010.

Capitalization of development costs
Capitalization of development costs requires that the development of the technology or the product in the company's opinion has been completed, that all necessary public registration approvals and marketing approvals have been obtained, that costs can be reliably measured and that the technology or the product can be commercialized and that the future income from the product can cover, not only production, sales and distribution costs and administrative expenses, but also development costs. As none of the company's products have obtained the status required for capitalization, no development costs had been capitalised at December 31, 2011.

Notes

2. Significant accounting assumptions and estimates – continued

Impairment test of acquired research and development projects
The value of acquired research and development projects recognised in the balance sheet as at December 31, 2011 consist of the belinostat program acquired in conjunction with the acquisition of Topotarget UK in 2002 and the buy back of full control of belinostat from the company´s former partner CuraGen in April 2008.

In the period, until a marketing approval has been obtained, the acquired research and development project is tested for impairment annually. After marketing approval has been obtained, an impairment test is performed only where events or other circumstances indicate that the carrying amount may not be recoverable.

Included in the factors taken into account when testing for impairment are, among other things, expected market size and penetration thereof, the costs of development, manufacture and sales and marketing, and the risk that development will not prove successful, all of which have an effect on the value of the amount recognized. Especially for projects in early phases such assumptions include high uncertainty.

Based on the impairment test performed no write-down was made in 2011 (2010: DKK 189.5 million).

3. Revenue

	Group		Parent	
DKK '000	2011	2010	2011	2010
Sale of goods	-	-	9,319	16,237
Sale of services	2,436	8,119	2,436	6,291
Milestone payments	63,162	99,707	56,260	89,092
Total	**65,598**	**107,826**	**68,015**	**111,620**

Notes

4. Segment information

The Group's revenue is divided geographically as follows:

	Revenue	
DKK '000	2011	2010
Denmark	-	218
Europe	375	7,676
US	65,223	99,932
Total	**65,598**	**107,826**

Upfront payment from Spectrum Pharmaceuticals exeeds 10% of total revenue, 2011 82% (2010: 77%).

The Group's assets and additions to acquired research and development projects plus other fixtures and fittings, tools and equipment are divided geographically as follows:

	Assets		Additions to acquired research and development projects plus other fixtures and fittings, tools and equipment	
DKK '000	2011	2010	2011	2010
Denmark	337,157	397,225	2,299	3,747
Europe	35,388	65,986	-	-
US	-	2,613	-	-
Total	**372,545**	**465,824**	**2,299**	**3,747**

Due to the divestiture of Totect® and Topotarget USA, Inc., the company no longer has segmented information as the only operation on-going in 2011 is development activities.

The comparative figures for 2010 have been reclassified accordingly.

Notes

5. Depreciation, amortization, and impairment

		Group		Parent	
DKK '000	Note	2011	2010	2011	2010
Acquired research and development projects		750	190,416	750	12,150
Other fixtures and fittings, tools and equipment		3,311	4,192	3,294	3,058
Gain/loss from sale of equipment		-	(1,507)	-	(212)
Total		**4,061**	**193,101**	**4,044**	**14,996**
Allocated by function:					
Research and development costs		1,128	1,652	1,112	2,030
Write-down of research and development projects	12	-	189,541	-	11,275
Administrative expenses		2,183	768	2,182	768
Discontinued operations		750	1,140	750	923
Total		**4,061**	**193,101**	**4,044**	**14,996**

6. Staff costs

Wages and salaries		42,244	48,239	36,144	37,562
Share-based payments		3,505	3,969	3,144	3,056
Pension contributions, defined contribution plans		2,322	4,787	1,993	3,678
Other social security costs		661	1,718	261	314
Total		**48,732**	**58,712**	**41,542**	**44,609**
Allocated by function:					
Production cost		1,786	5,443	1,786	5,443
Research and development costs		23,386	22,151	23,257	19,490
Administrative expenses		16,514	19,715	16,499	19,676
Discontinued operations		7,046	11,403	-	-
Total		**48,732**	**58,712**	**41,542**	**44,609**
Remuneration to the Board of Directors*)		2,324	2,067	1,798	1,918
Remuneration to the Management*),**)		9,248	12,194	9,248	12,194
Average number of employees		**42**	**50**	**34**	**40**

*) Of this, share-based payments to the Board of Directors in 2011 equalled DKK 186,000 and DKK 278,000 in 2010.

**) Of this, share-based payments to the Management equalled DKK 1,715,000 in 2011 and DKK 879,0000 in 2010.

For share-based payments please see Note 18

Notes

7. Financial income

	Group		Parent	
DKK '000	2011	2010	2011	2010
Financial income from subsidiaries	-	-	9,130	7,161
Exchange rate adjustment of payables and receivables in foreign currencies	11,593	11,678	10,943	40,987
Financial income from securities and bank deposits	136	1,392	110	1,366
Write-down net of potential debt	-	67,793	-	66,542
Total financial income	**11,729**	**80,863**	**20,183**	**116,056**

During 2010 a write-down of APO projects and Zemap project in Topotarget Switzerland S.A. and Topotarget Germany A.G. have been made. As a consequence of the write-down of the APO and Zemap projects the capitalized potential debt and milestone payments previously recognized as a liability are reversed as financial income.

8. Financial expenses

Exchange rate adjustment of payables and receivables in foreign currencies	(8,829)	(1,836)	(7,293)	(1,900)
Amortization of debt concerning milestone payment	(1,664)	(10,150)	(1,664)	(10,050)
Other financial expenses	(149)	(104)	(12)	-
Total financial expenses	**(10,642)**	**(12,090)**	**(8,969)**	**(11,950)**

Notes

9. Tax on loss for the year

	Group		Parent	
DKK '000	2011	2010	2011	2010
Current tax	(1,253)	-	-	-
Adjustment of deferred tax	-	(43,985)	-	-
Tax on loss for the year	**(1,253)**	**(43,985)**	**-**	**-**
Deferred tax asset, net	**238,041**	**265,435**	**113,989**	**111,627**
Deductible temporary differences are attributable to the following terms:				
Intangible assets	(137,454)	(111,807)	(116,164)	(91,550)
Property, plant, and equipment	29,514	25,966	19,902	16,607
Other temporary differences	(4,258)	52,546	(4,258)	52,546
Tax losses carried forward	1,004,350	992,561	556,475	468,905
Total	**892,152**	**959,266**	**455,955**	**446,508**
Tax asset, not recognised	**238,041**	**265,435**	**113,989**	**111,627**

It is believed that at the present time there is not sufficient evidence that or when the tax asset can be utilized. It is therefore believed that capitalization does not meet the requirement for recognition of assets in accordance with the accounting policies applied.

Of the consolidated loss to be carried forward, DKK 1,004 million, (2010: DKK 993 million), DKK 197 million (2010: DKK 202 million) is subject to foreign local restrictions with respect to application (source-of-loss restriction)

Due to the divestment of Topotarget USA, Inc., the unrecognized tax asset has been reduced with DKK 31 million.

Reconciliation of the changes for the year:

Loss for the period before tax	**(34,264)**	**(99,674)**	**(33,011)**	**(55,689)**
Calculated tax	**(8,483)**	**(22,003)**	**(8,253)**	**(13,922)**
Changes in tax losses carried forward, not recognized	10,598	(8,185)	21,893	(26,765)
Changes in tax assets, not recognized	(6,754)	(32,754)	(19,531)	11,288
Other adjustments, not recognized	5,891	18,957	5,891	29,399
Total	**1,252**	**(43,985)**	**-**	**-**
Tax rate	(3.7%)	44.1%	-	-

Notes

10. Discontinued operations

On December 29, 2011, Topotarget concluded the agreement to divest the subsidiary Topotarget USA, Inc, which was responsible for the sale of Totect® in the US. The decision to divest the US activity was taken in 2011 so that the main focus of the Parent Company could be continued, that of belinostat and bringing this product to market.

The divestment was complete with effect from December 29, 2011 after which control of the activity was passed to the buyer Apricus Biosciences, Inc.

The sales price was agreed to USD 2.0 million of which Topotarget received common stock in Apricus Biosciences, Inc. equal to one million seven hundred thousand dollars on December 29, 2011, and on December 29, 2012 (the one-year anniversary of the Closing Date), Topotarget will receive common stock in Apricus Biosciences, Inc. equal to three hundred thousand dollars.

An potential payment of up to USD 2.0 million in shares in Apricus Biosciences, Inc based on achievement of certain milestones has been agreed upon.

	Group	
DKK '000	2011	2010
Operating income for the period until transfer of control	(6,560)	(3,376)
Profit on sale of net asset	2,561	32,473
Result from discontinued operations	**(3,999)**	**29,097**
Operating income for the period until the transfer of control can be specified as		
Revenue	12,536	21,212
Production cost	(5,579)	(5,490)
Gross profit	**6,957**	**15,722**
Sales and distribution costs	(13,056)	(19,098)
Administration costs	-	-
Profit from operations	**(6,099)**	**(3,376)**
Financial expenses/financial income	(461)	-
Loss/profit before tax	**(6,560)**	**(3,376)**
Tax for the period	-	-
Result	**(6,560)**	**(3,376)**

Notes

10. Discontinued operations – continued

	Group	
DKK '000	2011	2010
The discontinued operations in the financial year impacted cash flow statement as		
Cash flow from operating activities	(6,866)	24,991
Cash flow from investing activities	178	(175)
Cash flow from financing activities	-	
Sales of the discontinued operations are as follows		
Book value of net assets	**(6,559)**	**(2,822)**
	(6,559)	**(2,822)**
Net proceeds on sale less sales costs	9,120	35,295
Profit on sale	**2,561**	**32,473**

11. Basic and diluted EPS in DKK

Basic EPS
Basic EPS is calculated as the net result of the period's continuing activities, attributed to the ordinary shares of the company divided by the weighted average number of ordinary shares.

Diluted EPS
Diluted EPS is calculated as the net result of the period's continuing activities, attributed to the ordinary shares of the company divided by the weighted average number of ordinary shares adjusted for assumed dilution effect of issued equity instruments like convertible debts and issued outstanding warrants which can be converted to ordinary shares.

As the result is a net loss, no adjustment for dilution effects has been made since these are anti-diluting.

Basic and diluted EPS are as follow:

	Group		Parent	
DKK '000	2011	2010	2011	2010
Loss for the year attributable to equity holder of the Parent	(29,012)	(84,785)		
Weighted average number of ordinary outstanding shares	132,652,050	132,640,379		
Basic and diluted EPS from continued operations	**(0.22)**	**(0.64)**		
Loss for the year attributable to equity holder of the Parent	(33,011)	(55,689)	(33,011)	(55,689)
Weighted average number of ordinary outstanding shares	132,652,050	132,640,379	132,652,050	132,640,379
Basic and diluted EPS from continued and discontinued operations	**(0.25)**	**(0.42)**	**(0.25)**	**(0.42)**

Notes

12. Intangible assets

	Group		Parent	
DKK '000	2011	2010	2011	2010
Acquired research and development projects still in progress				
Cost at January 1	535,570	536,384	215,806	216,620
Adjustment of acquisition value	(1,779)	(814)	(1,779)	(814)
Cost at December 31	**533,791**	**535,570**	**214,027**	**215,806**
Amortization at January 1	(304,241)	(114,700)	(11,275)	-
Write-down of research and development projects	-	(189,541)	-	(11,275)
Amortization at December 31	**(304,241)**	**(304,241)**	**(11,275)**	**(11,275)**
Carrying amount at December 31	**229,550**	**231,329**	**202,752**	**204,531**
Acquired research and development projects available for use				
Cost at January 1	7,576	15,076	7,576	15,076
Disposals	(7,500)	(7,500)	(7,500)	(7,500)
Cost at December 31	**76**	**7,576**	**76**	**7,576**
Amortization at January 1	(3,188)	(4,875)	(3,188)	(4,875)
Amortization	(750)	(875)	(750)	(875)
Amortization regarding disposals for the year	3,938	2,562	3,938	2,562
Amortization at December 31	**-**	**(3,188)**	**-**	**(3,188)**
Carrying amount at December 31	**76**	**4,388**	**76**	**4,388**
Total acquired research and development projects	**229,626**	**235,717**	**202,828**	**208,919**
The weighted average residual term of licenses and rights is approximately (number of years)	0.50	5.75	0.50	5.75

Impairment test of acquired research and development projects

The value of acquired research and development projects recognized in the balance sheet as at December 31, 2011 consists of the belinostat program acquired in conjunction with the acquisition of Topotarget UK in 2002 and in April 2008 in conjunction with the purchase from the former American partner to obtain the full control of this program.

In the period until a marketing approval has been obtained, the acquired research and development project is tested for impairment annually. After marketing approval has been obtained, an impairment test is performed only where events or other circumstances indicate that the carrying amount may not be recoverable.

Included in the factors taken into account when testing for impairment are, among other things, expected market size and penetration thereof, the costs of development, manufacture and sales and marketing, and the risk that development will not prove successful, all of which have an effect on the value of the amount recognized.

Write-down in 2010 DKK 189.5 million relates to write-down of non-belinostat projects as a result of belinostat being the primary focus of the Group.

There was no down-writing in 2011.

Notes

13. Property plant, and equipment

	Group		Parent	
DKK '000	2011	2010	2011	2010
Other fixtures and fittings, tools, and equipment				
Cost at January 1	16,286	15,192	24,505	22,148
Additions	2,299	3,747	2,299	3,747
Disposals	(655)	(2,653)	(655)	(1,390)
Cost at December 31	**17,931**	**16,286**	**26,150**	**24,506**
Depreciation at January 1	(10,295)	(8,149)	(18,533)	(16,601)
Depreciation	(3,311)	(4,193)	(3,294)	(3,058)
Depreciation regarding disposals for the year	638	2,047	638	1,126
Depreciation at December 31	**(12,968)**	**(10,295)**	**(21,189)**	**(18,533)**
Carrying amount at December 31	**4,963**	**5,991**	**4,961**	**5,973**

14. Non-current investments

Investments in subsidiary				
Cost at January 1			468,973	466,923
Adjustment of acquisition value			-	-
Addition through capital increase in subsidiary			3,147	2,050
Cost at December 31			**472,120**	**468,973**
Net impairment at January 1			(441,032)	(430,110)
Income after tax from investments in subsidiaries			(19,946)	(180,780)
Negative equity transferred to set off against receivables from subsidiaries			19,992	169,776
Negative equity transferred to debt to subsidiaries			-	82
Net impairment at December 31			**(440,986)**	**(441,032)**
Value at December 31			**31,134**	**27,941**

Notes

14. Non-current investments – continued

	Ownership interest	Parent	
DKK '000		2011	2010
Investments in subsidiaries comprise:			
Name			
Topotarget UK Limited, England	100%	30,690	27,682
Topotarget Germany AG, Germany	100%	360	265
Topotarget USA, Inc., USA	100%	-	(85,060)
Topotarget Switzerland S.A., Switzerland	100%	(154,975)	(147,637)
Topotarget Netherlands B.V., The Netherlands	100%	84	84
Total equity		**(123,841)**	**(204,666)**
Negative equity transferred to set off against receivables from subsidiaries/debt to subsidiaries		154,975	232,607
Value at December 31		**31,134**	**27,941**
Receivables from subsidiaries			
Cost at January 1		229,062	183,525
Additions		20,176	45,537
Disposals		(26,789)	-
Cost at December 31		**222,449**	**229,062**
Net impairment at January 1		(202,437)	(62,398)
Negative equity transferred to set off against receivables from subsidiaries		(19,992)	(169,776)
Exchange adjustments etc.		-	29,737
Net impairment at December 31		**(222,429)**	**(202,437)**
Value at December 31		**20**	**26,625**

Notes

14. Non-current investments – continued

	Group		Parent	
DKK '000	2011	2010	2011	2010
Other receivable				
Cost at January 1	972	1,371	787	1,187
Disposals	(364)	(399)	(179)	(400)
Cost at December 31	**608**	**972**	**608**	**787**
Net impairment at January 1	–	–	–	–
Exchange adjustments etc.	–	–	–	–
Net impairment at December 31	–	–	–	–
Value at December 31	**608**	**972**	**608**	**787**

15. Trade receivables

Trade receivables	1,643	3,721	1,643	2,543
Total	**1,643**	**3,721**	**1.643**	**2,543**
The table below shows the due dates of trade receivables:				
Undue	268	2,934	268	1,756
Falling due within 90 days	1,375	528	1,375	528
Falling due after more than 90 days	–	259	–	259
Total	**1,643**	**3,721**	**1,643**	**2,543**

The average credit period for trade receivables is 73 days (2010: 56 days). The company is entitled to charge interest of 5% per annum after the due date, which is 30 days from the invoice date. Provisions are made for losses based on any uncertainties at any given time. Management performs analyses on the basis of customer´s expected ability to pay, historical information about payment patterns, and doubtful debtors and customer concentrations, customer credit worthiness and economic conditions in the company´s sales channels.

Notes

16. Short-term sercurites

	Group		Parent	
DKK '000	2011	2010	2011	2010
Listed shares	9.768	-	9.768	-
Total	**9.768**	**-**	**9.768**	**-**
Current assets	9.768	-	9.768	-
Non current assets	-	-	-	-
Total	**9.768**	**-**	**9.768**	**-**

17. Share capital

The share capital consists of 132,652,050 ordinary shares of 1 DKK each.
Each share carries one vote. The shares are fully paid.
Changes in share capital from 2007 to 2011:

	Date	Total DKK
Share capital January 1, 2007		45,684,880
Share issue through warrant exercise	30.03.2007	21,600
Share issue through warrant private placement	21.06.2007	12,000,000
Share issue through non-cash payment	27.06.2007	3,598,030
Share issue through non-cash payment	07.05.2008	5,000,000
Share issue through rights issue	02.07.2009	66,304,510
Share issue through warrant exercise	12.04.2010	43,030
Share capital December 31, 2011		132,652,050

Notes

18. Warrants

For the purpose of motivating and retaining employees and other associated persons, the company has established stock option schemes in the form of warrants for members of the Board of Directors and employees/consultants as well as the company's advisors.

The table below shows the extent of the individual programs that are active in the financial year or the comparative year.

	Time of issue	Number warrants***	Time of grant	Subscription period – two weeks after the release of interim and annual reports	Estimated fair value	Number exercised or expired	Outstanding warrants	Exercise price
DKK '000								
Program 1*	2001	1,652,320	26 March 2003 or later	March and August 2006-2012 and March 2013	N/A	970,798	681,523	6.1
Program 2*	2003	1,226,976	26 March 2003 or later	March and August 2006-2012 and March 2013	N/A	577,424	649,552	12.2
Program 3**	2005, March	622,501	11/mar/05	August and November 2006, March, May, August and November 2007-2012 and March 2013	5,879	622,501	–	N/A
Program 4*	2005, September	793,364	16/sep	August 2006 and March, and August 2007-2012	7,281	150,087	643,277	17.5
Program 4*	2005, September	688,474	16/sep/05	March and August 2007-2012 and March 2013	6,318	95,836	592,638	17.5
Program 5*	2006, October	299,486	04/okt/06	March and August 2008-2013 and March 2014	3,707	47,793	269,193	23.8
Program 5*	2006, October	299,486	04/okt/06	March and August 2009-2013 and March 2014	3,707	47,793	269,193	23.8
Program 5*	2006, October	598,972	04/okt/06	March and August 2010-2013 and March 2014	7,414	95,586	538,386	23.8
Program 5*	2007, September	388,988	27/sep/07	March and August 2009-2014 and March 2015	4,098	89.355	315	17.4
Program 5*	2007, September	389	27/sep/07	March and August 2010-2014 and March 2015	4,098	89,355	315	17.4
Program 5*	2007, September	777,975	27/sep/07	March and August 2011-2014 and March 2015	8,196	178,710	629,265	17.4
Program 5*	2009, January	438,041	30/jan/09	August 2010-2016 and March 2017	1,028	88,006	375,036	3.2
Program 5*	2009, January	438,041	30/jan/09	August 2010-2016 and March 2017	1,028	88,006	375,036	3.2
Program 5	2009, January	876,083	30/jan/09	August 2010-2016 and March 2017	2,056	176,011	750,071	3.2
Program 5	2010, March	35,687	26/mar/10	March 2012-2017 and March 2018	148	-	35,687	5.3
Program 5	2010, March	35,688	26/mar/10	March 2012-2017 and March 2018	148	-	35,688	5.3
Program 5	2010, March	71,375	26/mar/10	March 2012-2017 and March 2018	295	-	71,375	5.3
Program 5	2010, July	398,062	09/jul/10	March 2012-2017 and March 2018	1,063	-	398,062	3.4
Program 5	2010, July	398,062	09/jul/10	March 2012-2017 and March 2018	1,063	-	398,062	3.4
Program 5	2010, July	796,126	09/jul/10	March 2012-2017 and March 2018	2,126	-	796,126	3.4
Program 5	2010, December	63,750	30/dec/10	March 2012-2017 and March 2018	154	-	63,750	3.2
Program 5	2010, December	63,750	30/dec/10	March 2012-2017 and March 2018	154	-	63,750	3.2
Program 5	2010, December	127,500	30/dec/10	March 2012-2017 and March 2018	307	-	127,500	3.2
Program 5	2011, February	22,500	07/feb/11	March 2012-2017 and March 2018	55	-	22,500	3.3
Program 5	2011, February	22,500	07/feb/11	March 2012-2017 and March 2018	55	-	22,500	3.3
Program 5	2011, February	45,000	07/feb/11	March 2012-2017 and March 2018	110	-	45,000	3.3
Program 5	2011, July	398,063	30/jun/11	March 2013-2017 and March 2018	609	-	398,063	2.0
Program 5	2011, July	398,063	30/jun/11	March 2013-2017 and March 2018	609	-	398,063	2.0
Program 5	2011, July	796,125	30/jun/11	March 2013-2017 and March 2018	1,218	-	796,125	2.0
Program 5	2011, October	12,500	27/okt/11	March 2013-2017 and March 2018	16	-	12,500	1.9
Program 5	2011, October	12,500	27/okt/11	March 2013-2017 and March 2018	16	-	12,500	1.9
Program 5	2011, October	25,000	27/okt/11	March 2013-2017 and March 2018	33	-	25,000	1.9
Total programs					62,989	3,317,261	9,496,050	

*) The holders have earned complete and final rights.
**) Issued in connection with company acquisitions. The holders have earned complete and final rights.
***) After conversion in connection with rights issue July 2, 2009.

Notes

18. Warrants – continued

Under the programs, each warrant entitles the holder to subscribe for one share against cash payment of the exercise price, as illustrated in the table. The warrant program is conditional upon the warrant holder being employed with or acting as a consultant to the company or being a member of the company's Board of Directors. Warrants subsequently vest after 12 months for 25% of the allocated warrants, after 24 months for another 25% of the allocated warrants, and the remaining 50% of the allocated warrants vest after 36 months. If an employee/consultant/board member resigns, the person in question is obliged to exercise the vested warrants in the first coming exercise period after the date of resignation.

If issuing bonus shares, the number of shares which can be subscribed in accordance with the warrants is increased proportionally and the subscription price of the shares must be reduced proportionally so that the profit potential is retained. This is also the case, if shares are issued at a price beneath the market price. The number of shares which can be subscribed must be reduced proportionally and the subscription price has to be increased proportionally if the company reduces the capital by reserves to a special fund, cf. the Danish Public Companies Act, or in cover of loss, cf. section 44 of the Act. Last time bonus shares were issued was in Spring 2004.

In the event that a decision is made to liquidate the company, to merge or demerge the company, or to reduce the share capital through a subsequent disbursement, the warrant owners are entitled to exercise their warrants within 14 days.

The estimated values of warrants issued in 2011, 2010, 2009, 2007, 2006, and 2005 are calculated using the Black & Scholes model. The value is expensed on the income statement during the period in which the warrants vest.

The following assumptions provide the basis for the estimated fair values:

DKK '000	2011	2010
Weighted average share price (DKK per share)	2.4	4.3
Weighted average exercise price (DKK per share)	1.7	3.5
Weighted average expected volatility (%)	76.0	83.0
Weighted average risk-free interest rate (%)	2.5	2.6
Expected dividend payout ratio (%)	-	-
Period until expiry (number of years)	7	7

The expected volatility was calculated based on historic volatility of the share price of the Parent Company's shares during the period from the IPO in June 2005.

Period until expiry is calculated on the basis of the most recent potential exercise of the warrant adjusted for expected termination of employment and other causes of non-exercise of the warrants.

Notes

18. Warrants – continued

	Number of warrants	Weighted average exercise prices	Number of warrants	Weighted average exercise prices
DKK '000	2011	2011	2010	2010
Outstanding warrants January 1	8,392,435	7.6	6,461,685	11.5
Granted in the financial year	1,732,250	2.0	1,990,000	3.5
Exercised in the financial year	–	–	(59,250)	3.2
Expired in the financial year (resignation)	(230,000)	–	–	–
Outstanding warrants, December 31	**9,894,685**	**9.7**	**8,392,435**	**18.2**
Hereof outstanding vested warrants, December 31	**5,919,864**		**5,652,364**	

The weighted average remaining contractual maturity was three years at December 31, 2011 and three years at December 31, 2010.

There was no warrants exercised in 2011 (2010: 59,250).

The above assumptions were applied in connection with the calculation of the fair value of the warrants being vested.

The following values were recognised for the programs:

	Group		Parent	
DKK '000	2011	2010	2011	2010
Recognized share-based payment, equity schemes	3,521	3,971	3,521	3,971
	3,521	**3,971**	**3,521**	**3,971**

As a part of their contract the CEO, CFO, and CMDO (executive management) are eligible to receive up to a total of 3,060,000 warrants over a period of three years, each conferring a right to subscribe nominal DKK 1 share in the company. Any grant of warrants is subject to the shareholders of the company granting the Board of Directors authority to issue the warrants.

Notes

19. Financial instruments

Capital risk management

It is Group policy to minimize financial risks. The company does not use hedging transactions. Management carefully assesses and monitors the company's currency and interest rate exposure.

The Group manages its capital with a view to ensuring at all times that all Group entities can meet their payment obligations and give investors the best possible return on their investment through the best possible ratio of debt to equity. The Group's overall strategy is primarily focused on belinostat.

The Group's capital structure is composed of debt, as appears from the liabilities stated in the balance sheet with the exception of deferred tax, cash and cash equivalents and securities and equity, comprising both share capital, reserves, and retained losses.

The carrying amount of financial assets and financial liabilities equals the fair value of such assets and liabilities.

Cash and cash equivalents

The company is a development-stage company generating income in 2011 from the sale of Totect® and from the sale of services. The company has a net cash outflow.

Group management regularly reviews the company's capital structure and, in this respect, takes into account both the price of capital and the risk related to the capital.

The company has cash and cash equivalents to fund the day-to-day cash requirements of the business. Cash and cash equivalents amounted to DKK 114 million at December 31, 2011 (2010: DKK 205 million).

Significant accounting policies

Note 1 to the financial statements sets out the significant accounting policies and the methods applied, including policies on recognition and measurement.

Financial instrument categories

The carrying amount of each financial asset and liability is recognized in the balance sheet. The company's financial assets include receivables, while its financial liabilities include current and non-current liabilities exclusive of deferred tax.

Financial risk management areas

The company monitors and reports on financial risk areas, including movements in exchange rates, interest rates, and liquidity. The company does not use financial hedging instruments.

No changes were made to the Group's risk exposure or to the way in which risks are monitored compared with 2010.

Risk management – interest rates

The company is exposed to interest rate risk on marketable securities and cash on the asset side and to lease obligations and short-term loans on the liabilities side.

Notes

19. Financial instruments – continued

In its management reporting, the company quantifies the interest rate risk by calculating a change in financial results and equity in case of a 50 basis point change in interest rates. Such a change is considered to be within a likely range.

The company's interest rate exposure at December 31 is stated below:

	Group		Parent	
DKK '000	2011	2010	2011	2010
Cash - demand deposit	114,302	205,068	106,881	165,013
Average interest	0.30%	0.50%	0.30%	0.67%
Total cash	**114,302**	**205,068**	**106,881**	**165,013**
Inter-company balances			155,165	148,159
Average interest			6.00%	6.00%
In case of a 50 basis point change in nominal interest rates, results and equity would be impacted by	150	1,025	150	825

Intercompany balances are written down to nil.

The interest exposure is believed to be insignificant compared to the Group´s overall operations.

Risk management – exchange rates
It is company policy to monitor exchange rate developments and, to the extent possible, to even out income and expenses in the same currency in order to reduce the overall exposure.

The company is primarily exposed to exchange rate fluctuations with respect to two areas. One of these areas represents the strategic investment in subsidiaries, while the other area relates to the company's on-going short-term activities.

Notes

19. Financial instruments – continued

		Group		Parent	
DKK '000		2011	2010	2011	2010
The company's exposure in foreign currencies at December 31 are stated below:					
Currency	**Payment/expiry**				
Receivables:					
GBP	0-12 months	-	-	4	7
USD	0-12 months	9,196	9,016	9,196	32,045
EUR	0-12 months	778	802	798	805
SEK	0-12 months	-	250	-	250
CHF	0-12 months	-	-	155,150	147,656
Total receivables		**9,974**	**10,068**	**165,148**	**180,763**
Payables:					
GBP	0-12 months	1,952	3,140	87	55
USD	0-12 months	5,938	55,163	5,938	54,215
USD	More than 12 months	13,585	14,111	13,585	14,111
EUR	0-12 months	3,198	728	2,841	520
CHF	0-12 months	1,312	2,325	361	-
Total payables		**25,985**	**75,467**	**22,812**	**68,901**

Notes

19. Financial instruments – continued

GBP, USD, EUR, and CHF are the currencies that have the greatest impact on results and equity and, accordingly, these are the currencies reported on in-house reports to the management. Management believes that the most likely fluctuations in these currencies are restricted to a 10% range. A 10% change upwards or downwards in the exchange rate at December 31 will have the following numerical impact on results and equity figures:

	Group		Parent	
DKK '000	2011	2010	2011	2010
GBP	195	314	8	5
USD	1,033	6,026	1,033	3,636
EUR	242	7	204	29
CHF	131	232	15,479	14,766

The exchange rate exposure is believed to be insignificant compared to the Group's overall operations.

Credit risk management
The company's credit risk relates primarily to trade receivables from the sale of Savene®/Totect®.

Customer payment compliance is carefully monitored, and any late payments are followed up immediately.

Due to the divestiture of Topotarget USA, Inc. on December 29, 2011 the company no longer has sales activities, and therefore finds that there are no material credit risk.

Liquidity risk management
The Board of Directors is ultimately responsible for the company's risk management. The Board of Directors has defined appropriate limits for how the company may procure adequate liquidity in the long term and in the short term to cover its on-going activities.

The company regularly monitors the liquidity requirements through renewed calculation of expected cash flows based on the cash flows realized.

All receivables and payables recognized in the balance sheet fall due within 12 months except the conditioned liabilities in relation to belinostat.

Other obligations falling due after 12 months are listed in Note 21. Other commitments.

Notes

20. Fair value of financial assets and financial liabilities

Included in the non-current liabilities is the potential payment of USD 3.0 million to CuraGen (2010 USD 3.0 million) in relation to the purchase of the full belinostat rights in April 2008.

The carrying value of other financial assets and financial liabilities is equivalent to the same assets´and liabilities´ fair value.

21. Other commitments

	Group		Parent	
DKK '000	2011	2010	2011	2010
A rent agreement has been concluded with notice of termination of six months equivalent to	2,596	2,935	1,528	2,935
Other lease contracts	-	873	-	-
Lease commitment, operational lease	131	223	131	223
Total	**2,727**	**4,031**	**1,659**	**3,158**
Other obligations are due as follows:				
Up to one year	2,667	3,903	1,599	3,030
One to five years	60	128	60	128
Total	**2,727**	**4,031**	**1,659**	**3,158**

The Parent has an obligation to finance Topotarget Switzerland S.A. activities for a period of 12 months after the balance sheet date.

22. Deferred income

The company signed a license and collaboration agreement concerning research and development of the belinostat project. The agreement is a contract comprising of multiple componets and the amount received of DKK 162.9 million (USD 30 million) is recognized over a period of 18 months from February 2, 2010. Please see Note 2.

As at December 31, 2011 all deferred income from the Spectrum Pharmaceuticals agreement has been recognized.

Notes

23. Related parties

Related parties include the following:

Group and Parent:

Shareholders
HealthCap funds, Stockholm, cf. Note 24
Avanza Bank, Stockholm, cf. Note 24
2011 No transactions
2010 No transactions

The company's Board of Directors and senior management
2011 Renumeration and salaries, cf. Note 6
2011 Shares and warrants, see section on Board of Directors and Note 18
2010 Renumeration and salaries, cf. Note 6
2010 Shares and warrants, see the table in "Corporate Governance" and Note 18

Other related paties
2011 Related parties to the Board of Directors and the executive management have received remuneration of TDKK 715 and warrants of TDKK 0.

2010 Related parties to the Board of Directors and the executive management have received remuneration of TDKK 761 and warrants of TDKK 75.

For the Parent Company:

The subsidiary Topotarget UK Limited
2011 Intra-Group balance of TDKK 4 and interest on the intra-Group balance of TDKK 78
2010 Intra-Group balance of TDKK 25 and interest on the intra-Group balance of TDKK 35

The subsidiary Topotarget Germany AG
2011 Intra-Group balance of TDKK 20 and interest on the intra-Group balance of TDKK 1
2010 Intra-Group balance of TDKK 19 and interest on the intra-Group balance of TDKK 0

The subsidiary Topotarget USA, Inc.
2011 Intra-Group balance of TDKK 0 and interest on the intra-Group balance of TDKK 5,763
2010 Intra-Group balance of TDKK 86,806 and interest on the intra-Group balance of TDKK 4,170

The subsidiary Topotarget Schwitzerland S.A.
2011 Intra-Group balance of TDKK 155,150 and interest on the intra-Group balance of TDKK 2,826
2010 Intra-Group balance of TDKK 147,656 and interest on the intra-Group balance of TDKK 2,955

The subsidiary Topotarget Netherlands B.V.
2011 Intra-Group balance of TDKK (18) and interest on the intra-Group balance of TDKK 1
2010 Intra-Group balance of TDKK (18) and interest on the intra-Group balance of TDKK 1

Movements in intercompany balances all consists of transfer of cash to finance activities in subsidiaries.

Notes

24. Ownership

	Ownership
As per December 31, 2011 the following shareholders hold more than 5% of the company's share capital:	
- HealthCap funds	13.01%
The HealthCap funds, that hold stocks in the Company are, HealthCap 1999 KB, HealthCapKB, HealthCap 1999 GbR, HealthCap III Sidefund KB, OFCO Club III Sidefund, HealthCap IV LP, HealthCap IV BisLP, HealthCap IV KB, OFCO Club 1999 and OFCO Club IV	
- Avanza Bank, Stockholm	6.35%
Insurance company Avanza Pension.	

25. Working capital changes

	Group		Parent	
DKK '000	2011	2010	2011	2010
Changes in current assets	6,865	2,621	5,401	1,782
Changes in current liabilities	(65,323)	29,120	(54,436)	31,199
Total	**(58,458)**	**31,742**	**(49,035)**	**32,981**

26. Non-cash transactions

The company has had no non-cash transactions during 2010 and 2011.

27. Proceeds from capital increases

There has been no transactions in 2011.
DKK 138 warrants were exercised in 2010.

Notes

28. Fees to auditors appointed at the annual general meeting

	Group		Parent	
DKK '000	2011	2010	2011	2010
Statutory audit services	415	455	340	375
Other assurence engagements	20	20	20	20
Tax services	-	-	-	-
Other services	1,017	593	974	480
Total	1,452	1,068	1,334	875

Separate audit of Topotarget Germany AG, Topotarget S.A., Topotarget Netherland B.V., Topotarget USA, Inc. has not been carried out as the companies are not deemed material to the consolidated financial statements for 2011.

29. Accounting policies

In addition to the description in Notes 1 and 2, the accounting policies are as described in the following.

Consolidated financial statements
The consolidated financial statements comprise the Parent Company and Group enterprises in which the Parent Company is entitled to determine finance and operating policies, which normally applies for ownership interests of more than half of the voting rights.

Basis of consolidation
The consolidated financial statements are prepared on the basis of the financial statements of the Parent Company and its subsidiaries. The consolidated financial statements are prepared by adding items of a uniform nature. On consolidation intra-Group income and expenses, intra-Group accounts, dividends as well as gains and losses on transactions between the consolidated enterprises are eliminated.

The financial statements used for consolidation are prepared in accordance with the Group's accounting policies.

Acquisitions of subsidiaries are accounted for using the purchase method. Costs related to an acquisition are measured at the fair value of remuneration in the form of assets, the equity instruments granted and the liability incurred at the date of acquisition with the addition of costs directly connected to the takeover. From January 1, 2010 costs are recognized in the income statement.

Acquired identifiable assets, liabilities, and contingent liabilities in a business combination are measured on initial recognition at fair value at the acquisition date. Identifiable intangible assets are recognized if they can be separated or arise from a contractual right and the fair value can be reliably measured. Positive differences between cost and fair value of the Group's share of the identifiable net assets are recognized as goodwill.

Newly acquired subsidiaries are consolidated at the time when the controlling influence is established in the Group.

Recognition and measurement
The items included in the financial statements of each entity of the Group are measured by using the currency that best reflects the economic substance of the underlying events and conditions applicable for the entity in question. The financial statements are presented in Danish Kroner (DKK), the Parent Company's and the subsidiaries' functional currency.

On initial recognition, assets and liabilities are measured at cost. Revenue and costs, assets and liabilities are subsequently measured as described below.

The preparation of financial statements assumes the use of certain critical accounting estimates. It also requires management to exercise its judgment in the process of applying the Group's accounting policies.

Assets are recognized in the balance sheet when it is probable that future economic benefits will flow to the Group and the value of the asset can be measured reliably.

Notes

Liabilities are recognized in the balance sheet when the Group has a legal or constructive obligation as a result of a prior event, and it is probable that future economic benefits will flow out of the Group, and the value of the liabilities can be measured reliably.

Recognition and measurement take into consideration anticipated gains, losses, and risks that arise before the time of adoption of the annual report and that confirm or invalidate matters and conditions existing at the balance sheet date.

Income is recognized in the income statement as and when earned, whereas expenses are recognized as incurred. Value adjustments of financial assets and liabilities are recognized in the income statement as financial income or financial expenses.

Foreign currency translation
On initial recognition, transactions denominated in foreign currency are translated at the exchange rate ruling on the transaction date. Receivables, payables, and other monetary items denominated in foreign currencies that have not been settled on the balance sheet date are translated at the exchange rates ruling at the balance sheet date. Exchange differences between the exchange rate at the date of the transaction and the exchange rate at the date of payment or the balance sheet date, respectively, are recognized in the income statement as financial income or financial expenses.

On recognition in the consolidated financial statements of foreign subsidiaries in which Danish kroner (DKK) is the functional currency but which present their financial statements in another currency, monetary assets, and monetary liabilities are translated at the exchange rate at the balance sheet date. Non-monetary assets and liabilities measured based on historical cost are translated at the exchange rate at the transaction date. Non-monetary assets and liabilities measured at fair value are translated at the exchange rates at the most recent date of fair value adjustment.

Income statement items are translated at average monthly exchange rates, except for items derived from non-monetary assets and liabilities, which are translated at historical rates for the non-monetary assets and liabilities.

Income statement

Revenue
Revenue comprises of milestone payments and other income from research and development agreements. Revenue is recognized when it is probable that future economic benefits will flow to the company and such economic benefits can be measured reliably. Income from agreements with multiple components and where the individual components cannot be separated is recognized over the period of the agreement. In addition, recognition requires that all significant risks and rewards of ownership of the goods and services included in the transaction have been transferred to the buyer. If all risks and benefits have not been transferred, the revenue is recognized as deferred income until all components in the transaction have been completed.

Production costs
Production costs comprise costs incurred to generate the revenue. Production costs are comprised of salaries, contributions to pension schemes, costs of share-based payments, and other costs including depreciation, impairment write-down and amortization attributable to the Group's production activities.

Research and development costs
Research costs comprise salaries, contributions to pension schemes, costs of share-based payments and other costs, including patent costs, as well as depreciation and amortization attributable to the Group's research activities. Research costs are recognised in the income statement as incurred.

Development costs comprise salaries, contributions to pension schemes, costs of share-based payments and other costs, including depreciation and amortization attributable to the Group's development activities. Capitalization assumes that the development of the technology or the product in the Group's opinion has been completed, that all necessary public registration and marketing approvals have been obtained, and that costs can be reliably measured. Furthermore, it has to be established that the technology or the product can be commercialized and that the future income from the product can cover, not only production costs, sales, and distribution costs and administrative expenses, but also development costs.

Development costs are recognized in the income statement as incurred if the conditions for capitalization of the development costs are deemed not to be met.

Research and development costs also comprise any impairment write-down on acquired research and development projects made before the time when the project is available for use.

Notes

Sales and distribution costs
Sales and distribution costs comprise costs incurred for the distribution of goods sold and for sales campaigns, including salaries, contributions to pension schemes for sales and distribution staff, office expenses and depreciation and other indirect costs.

Administrative expenses
Administrative expenses comprise salaries, contributions to pension schemes to the management and administrative functions, office supplies as well as depreciation and amortization and other indirect costs.

Financial income and expenses
These items comprise interest income and expenses, interest on capitalized milestone payments, the interest element of finance lease payments, realised gains and losses on marketable securities and realised and unrealised gains and losses on payables and transactions in foreign currencies.

Income taxes
Tax for the year, consisting of the year's current tax and movements in deferred tax, is recognized in the income statement as regards the amount that can be attributed to the profit/loss for the year and posted directly in equity as regards the amount that can be attributed to movements taken directly to equity. Current tax payable or receivable is recognized in the balance sheet as calculated tax on the taxable income for the year adjusted for prepaid tax.

The deferred tax charge is recognized and measured using the balance sheet liability method on all temporary differences between the carrying amount and the tax values of assets and liabilities. The tax value of the assets is calculated based on the planned use of each asset.

Deferred tax is measured based on the tax rules and rates in the respective countries that will apply under the legislation in force on the balance sheet date when the deferred tax asset is expected to crystallise as current tax. Changes in deferred tax resulting from changes in tax rates are recognized in the income statement.

Deferred tax assets, including the tax value of tax loss carry-forwards, are recognized at the value at which they are expected to be realized, either through a set-off against deferred tax liabilities or as net assets.

Deferred tax assets and liabilities are not recognised if the temporary difference arises on initial recognition (in cases other than in connection with a business combination) of other assets and liabilities in a transaction not affecting the results for tax or accounting purposes.

Provision is made for tax on temporary differences arising on investments in subsidiaries, unless the Group can control the timing of the reversal of the temporary difference and it is probable that the temporary difference will not be reversed in the foreseeable future.

Discontinued operation
Discontinued operations are business areas or that has been sold or is intended for sale. Subsidiaries, which alone are for resale, are considered to be a discontinued operation.

The results of discontinued operations are presented in the income statement as a separate note (Note 10), which consists of operating profit after tax with respect to that activity and any gains or losses from fair value adjustment or sale of assets and liabilities associated with the activity.

Non-current assets and groups of assets held for sale are presented separately in the balance sheet as current assets. Liabilities directly associated with those assets are presented as current liabilities in the balance.

Non-current assets held for sale are not amortized, but are written down to fair value less costs to sell if this value is lower than the carrying value.

Segment reporting
The company in 2011 has only one segment of activity that of research and development. As only one segment is operated there is no need for a separate note on segment reporting.

The reason for the company only having one segment of activity in 2011 is due to the discontinued operations that of Totect®/ Savene®.

The Group does not allocate assets and liabilities to the segments.

Notes

Share-based payment

All warrants granted after January 1, 2005 are equity instruments that are measured at fair value at the date of grant. Where warrants are included as part of an acquisition price of a subsidiary, the value of the equity instrument is recognized together with the remaining cost, and the balancing item is taken directly to equity to the reserve for share-based payment. Where warrants are issued as incentive programs, the compensation cost is charged to the income statement of the over the period when the warrants vest. The expense is allocated to production costs, research and development costs, sales, and distribution costs and administrative expenses, and the balancing item is taken directly to equity to the reserve for share-based payment.

The fair value is calculated using the Black&Scholes model, taking into consideration the anticipated exercise of the warrants granted. On each balance sheet date, Topotarget estimates the anticipated number of warrants that will vest. Any change to the original estimates of number of warrants will result in a change of the expensed cost over the remaining vesting period. Prior year changes are recognized in the income statement in the year in which the change is identified.

Balance sheet

Goodwill

Goodwill is the amount at which the cost of an enterprise taken over exceeds the fair value of the Group's share of the net assets acquired at the time of the takeover.

Goodwill is tested for impairment at every balance sheet date. In the event of an impairment loss, the carrying amount of the goodwill is written down to the recoverable amount. Write-downs are recognized in the income statement.

Acquired research and development projects

Costs of acquiring research and development projects are measured at cost price and recognized as intangible assets. The assets are amortized over their expected economic lives from the time when the project is ready for use (marketing approvals have been obtained). In the period until a marketing approval has been obtained, the acquired research and development project is tested for impairment annually. After marketing approval has been obtained, an impairment test is performed when events or other circumstances indicate that the carrying amount may not be recoverable.

Property, plant, and equipment

Other fixtures and fittings, tools and equipment as well as assets held under finance leases are measured at cost less accumulated depreciation and impairment losses.

Cost comprises the acquisition price, costs directly attributable to the acquisition, and preparation costs of the asset until the time it is ready to be put into operation. In the case of assets produced in-house, cost comprises direct and indirect costs for materials, components, third-party suppliers and labor. The cost price of assets held under finance leases is determined as the lower of the present value of future lease payments and the fair value.

The basis for depreciation is cost less estimated residual value after the end of useful life. The expected residual value is re-assessed every year. The assets are depreciated on a straight-line basis over their useful lives, which are four to ten years.

Impairment of non-current assets

In the period until a marketing approval has been obtained, the acquired research and development project is tested for impairment annually. After marketing approval has been obtained, an impairment test is performed when events or other circumstances indicate that the carrying amount may not be recoverable.

The carrying amount of other intangible assets, property, plant and equipment as well as non-current asset investments is reviewed for impairment when events or changed conditions indicate that the carrying amount may not be recoverable. Where such an indication exists, an impairment test is made. An impairment loss is recognized in the amount by which the carrying amount exceeds the recoverable amount of the asset, which is the higher of the net present value and the net selling price. In order to assess the impairment, the assets are grouped on the least identifiable group of assets that generates cash flows (cash-generating units). Impairment losses are recognized in the income statement under the same items as the associated depreciation or amortization.

Investments in subsidiaries (Parent Company)

Investments in subsidiaries are recognized and measured according to the equity method. This means that the investments are measured at the proportionate share of the companies' equity value after addition or deduction of any unamortized positive or negative goodwill, respectively, and after deduction or addition of unrealized intra-Group gains and losses.

Notes

The Parent Company's share of the subsidiaries' profits or losses after tax and after elimination of unrealized intra-Group gains and losses and with the deduction or addition of amortization of positive, or negative, goodwill is recognized in the income statement.

Subsidiaries with a negative net asset value are recognized at DKK nil, and any receivable amount from these companies is written down, to the extent it is deemed to be irrecoverable. Where the negative net asset value exceeds the amount receivable, the residual amount is recognized under provisions to the extent that the Parent Company has a legal or constructive obligation to cover the relevant company's obligations.

Net revaluation of investments in subsidiaries is transferred in connection with appropriation of the profit/loss for the year to the reserve for net revaluation according to the equity method.

Acquisitions of subsidiaries are accounted for using the purchase method. See above under consolidated financial statements.

Inventories
Inventories are measured at the lower of cost under the FIFO method and net realizable value.

The cost of goods for resale, raw materials, and consumables includes the purchase price plus transportation costs. The cost of finished goods and work in progress comprises the cost of raw materials, consumables, and other manufacturing costs incurred by a sub-supplier.

The net realizable value of inventories is calculated as the expected selling price less completion costs and costs incurred in making the sale.

Financial assets
The Group and the Parent Company classify their financial assets in the following categories:

- Loans and receivables
- Available-for-sale financial assets

Financial assets are classified according to the purpose of the acquisition. Management determines the classification on initial recognition and reevaluates this designation at every reporting date.

Loans and receivables are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. In the balance sheet, they are classified as trade receivables, other receivables and as loans.

Available-for-sale financial assets are non-derivative financial assets and are designated as short-term securities in the balance sheet.

Trade receivables
On initial recognition, trade receivables are measured at fair value and subsequently measured at amortized cost according to the effective interest method less provision for impairment based on an individual assessment.

Other receivables
On initial recognition, other receivables are measured at fair value and subsequently measured at amortized cost according to the effective interest method less write-downs for losses.

Prepayments
Prepayments comprise incurred costs relating to subsequent financial years. Prepayments are measured at amortized cost, which usually corresponds to the nominal value.

Short-term securities
The securities are easily negotiable in the established markets. Short-term securities are classified as "available for sale". Fair value equals the market price. Upon a sale, cost is measured according to the FIFO principle. Realized gains and losses (including realized exchange rate gains and losses) are recognized in the income statement as financial items. Unrealized gains and losses (including unrealized exchange rate gains and losses) are recognized directly in equity. Transactions are recognized on the trade date.

Cash and cash equivalents
Cash comprises cash holdings and bank deposits with an insignificant price risk. Cash is measured at fair value.

Notes

Equity
The share capital comprises the nominal value of the company's ordinary shares, each with a nominal value of DKK 1.

Retained earnings include amounts paid as premium compared to the nominal value of the shares in connection with the company's capital increases less external expenses, which are directly attributable to the increases of capital. The amount also includes unrealized gains and losses (including unrealized exchange rate gains and losses).

The reserve for share-based payment includes the value of recognized warrant programs measured at the fair value at the time of grant and subsequent value adjustments.

The buying and selling of own shares is recognized directly in equity. Own shares are therefore not recognized separately in the balance sheet.

Provisions
Provisions are recognised when the Group has a legal or constructive obligation as a result of a prior event on or before the balance sheet date, and it is probable that the company has to give up future economic benefits in order to repay the obligation. The provisions are measured according to an assessment of the costs required in order to repay the present obligation at the balance sheet date. Provisions which are not expected to be repaid within a year from the balance sheet date are measured at present value.

Lease commitments
Lease commitments relating to assets held under operating leases are recognized in the income statement over the terms of the contracts. Lease payments are recognized either in production costs, research and development costs, sales and distribution costs, or administrative expenses, depending on the use of the asset.

Financial liabilities
Financial liabilities, including trade payables and other payables, are initially measured at fair value. In subsequent periods, financial liabilities are measured at amortized cost, applying the effective interest method, to the effect that the difference between the proceeds and the nominal value is recognized in the income statement as financial expenses over the term of the loan.

Deferred income
The item reflects the part of revenue that has not been recognized as income immediately on receipt of payment and which concerns agreements with multiple components which cannot be separated.

Cash flow statement
The cash flow statement of the Parent Company and the Group is presented using the indirect method and shows cash flows from operating, investing, and financing activities as well as the Group's cash and cash equivalents at the beginning and the end of the financial year.

Cash flows from operating activities are calculated as the operating profit/loss adjusted for non-cash operating items, working capital changes and income taxes as well as interest paid.

Cash flows from investing activities comprise payments in connection with acquisition and divestment of enterprises and activities as well as purchase and sale of intangible assets, property, plant, and equipment as well as non-current investments.

Cash flows from financing activities comprise changes in the size or composition of the Parent Company's and the Group's share capital and related costs as well as the raising of loans, instalments on interest-bearing debt, and payment of dividends.

Cash and cash equivalents comprise cash, deposits in financial institutions, liquid securities with terms of three months or less at the date of acquisition, less short-term bank debt that forms an integral part of the Group's cash management activities.

Financial highlights and key ratios
The financial ratios have been calculated in accordance with "Recommendations & Ratios 2010", issued by the Danish Society of Financial Analysts, as set out below:

Earnings per share
Earnings per share is calculated as the net profit or loss divided by the weighted average number of outstanding ordinary shares.

Diluted earnings per share
Diluted earnings per share is calculated as the net profit or loss divided by the average number of outstanding ordinary shares adjusted for the diluting effect of issued equity instruments.

Notes

Share price at year-end
The year-end share price is determined as the average trading price (all trades) of the company's shares on the NASDAQ OMX Copenhagen stock exchange at the balance sheet date or at the most recent trading date prior to the balance sheet date.

Assets/equity
Total assets at the balance sheet date divided by total equity at the balance sheet date.

Net asset value per share
Net asset value per share is calculated as total equity at the balance sheet date divided by the number of outstanding ordinary shares at the balance sheet date.

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