

To NASDAQ OMX Copenhagen A/S  
Announcement No. 01-09 / Copenhagen, 6 January 2009

**TopoTarget A/S**

Symbion  
Fruebjergvej 3  
DK 2100 Copenhagen  
Denmark  
Tel: +45 39 17 83 92  
Fax: +45 39 17 94 92  
CVR-nr: 25695771

[www.topotarget.com](http://www.topotarget.com)

**Belinostat moves into its first randomized trial in combination with 5-Azacytidine in the treatment of cancer patients suffering from AML or MDS**

**Copenhagen, Denmark, 6 January 2009 – TopoTarget A/S (OMX: TOPO) announces that belinostat has moved into the randomized portion of a study in patients with hematologic malignancies where patients with Myelodysplastic Syndrome (MDS) or Acute Myelogenous Leukaemia (AML) will be treated. Patients will receive treatment with belinostat + 5-Azacytidine (experimental group) or 5-Azacytidine monotherapy (control group). The study is sponsored by the Cancer Therapy Evaluation Program at the National Cancer Institute (NCI, US) under a Clinical Trials Agreement with TopoTarget for the development of belinostat.**

*"Belinostat and 5-Azacytidine open silenced genes by different routes and the combination is synergistic in several cancer models" said Professor Peter Buhl Jensen, MD and CEO of TopoTarget. "We look very much forward to see the data from this next randomized portion of the study".*

The study:

**Phase 1 Study of Belinostat (PXD101) in Combination with Azacytidine (5-AZA) for Advanced Hematologic Malignancies**

The primary objective of this study is to determine the MTD of belinostat given in combination with 5-AZA. Secondary objectives are to identify any additive or synergistic effects of the combination on pharmacodynamic parameters including apoptosis and re-expression of specific target genes, and to assess any evidence of clinical activity of the combination.

Patients are to receive 5-AZA subcutaneously on days 1-5 on a 28-day schedule, followed by belinostat by 30-minute IV infusion also on days 1-5. Doses have been escalated from 50 to 75 mg/m<sup>2</sup>/day of 5-AZA and 150 to 1000 mg/m<sup>2</sup>/day of belinostat.

Following the determination of the MTD of the combination, the study is now enrolling eighteen additional patients with myelodysplastic syndrome (MDS) or acute myelogenous leukemia (AML) who will receive treatment with either 5-AZA monotherapy (n=9) or belinostat in combination with 5-AZA (n=9).



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Pharmacodynamic endpoints will be evaluated to determine whether there is additive or synergistic activity of belinostat in combination with 5-AZA.

The study is led by Dr. Olatoyosi Odenike, Assistant Professor of Medicine, University of Chicago, Chicago, IL, USA, and investigators at the Princess Margret Hospital, Toronto, ON, Canada, and University of Wisconsin, Madison, WI, USA, will also participate in the randomized portion of the study.

Preliminary results from patients treated in the dose-escalation part of this study, i.e. all patients treated with belinostat in combination with 5-AZA, were reported at the ASCO meeting 2008 by Dr. Odenike and co-workers (Odenike, O., M. Green, R.A. Larson, et al. Proc Annu Meet Am Soc Clin Oncol. 2008; 26:A7057). At that stage efficacy of the combination was reported to be 2 complete responses, 1 partial response, and 4 patients with haematological improvement among 21 evaluable patients.

Today's announcement does not change TopoTarget's full-year financial guidance for 2008.

## TopoTarget A/S

For further information, please contact:

Ulla Hald Buhl	Telephone	+45 39 17 83 92
Director IR & Communications	Mobile	+45 21 70 10 49

## Background information

### About Belinostat

Belinostat is a promising small molecule HDAC inhibitor being investigated for its role in the treatment of a wide range of solid tumors and hematologic malignancies either as a single-agent, or in combination with other active anti-cancer agents, including carboplatin, paclitaxel, cis-retinoic acid, azacytidine and Velcade® (bortezomib) for injection. HDAC inhibitors represent a new mechanistic class of anti-cancer therapeutics that target HDAC enzymes, and have been shown to: arrest growth of cancer cells (including drug resistant subtypes); induce apoptosis, or programmed cell death; promote differentiation; inhibit angiogenesis; and sensitize cancer cells to overcome drug resistance when used in combination with other anti-cancer agents.

Intravenous belinostat is in phase III in peripheral T-cell lymphoma (PTCL) and is currently being evaluated in multiple clinical trials as a potential treatment for cutaneous and peripheral T-cell lymphomas, B-cell lymphomas, AML, mesothelioma, soft tissue sarcoma, Myelodysplastic Syndrome (MDS), and liver, colorectal, and ovarian cancers, either alone or in combination with other anti-cancer therapies. Continuous intravenous administration (CIV) is being evaluated in clinical trials in solid tumours as well as in AML. An oral formulation of belinostat is also being evaluated in a Phase I clinical trial for patients with advanced solid tumors. Several trials in the belinostat program are conducted under a Clinical Trials Agreement (CTA) under which the NCI sponsors clinical trials to investigate belinostat for the treatment of various cancers, both as a single-agent and in combination chemotherapy regimens. Furthermore TopoTarget has a Cooperative Research and Development Agreement (CRADA) with the NCI to conduct preclinical and nonclinical studies on belinostat in order to better understand its anti-tumor activity and to provide supporting information for clinical trials.

### About Azacytidine

Azacytidine is a ring analog of cytidine and has been investigated as an antileukemic agent in clinical trials since the 1970s. Azacytidine (5-Aza) is an S-phase specific agent, is incorporated into DNA methyltransferases. Early clinical trials conducted with this agent have shown that clinical responses can be achieved in refractory leukemia without



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intervening marrow aplasia, suggesting that induction of cellular differentiation may be important in mediating those responses. Inhibition of DNA methyltransferases with subsequent DNA hypomethylation and re-expression of previously silenced genes has been postulated as the clinical factor that mediates this effect on differentiation.

#### **About TopoTarget**

TopoTarget (OMX: TOPO) is an international biotech company headquartered in Denmark, dedicated to finding "Answers for Cancer" and developing improved cancer therapies. The company was founded and is run by clinical cancer specialists and combines years of hands-on clinical experience with in-depth understanding of the molecular mechanisms of cancer. TopoTarget has a broad clinical pipeline but is currently focusing on the development of belinostat which has shown proof of concept as monotherapy in treating haematological malignancies and positive results in solid tumours where it can be used in combination with full doses of chemotherapy. TopoTarget's expertise in translational research is utilizing its highly predictive in vivo and in vitro cancer models. TopoTarget is directing its efforts on key cancer targets including HDACi, NAD+, mTOR, FasLigand and topoisomerase II inhibitors. The company's first marketed product Savene<sup>®</sup>/Totect<sup>®</sup> was approved by EMEA in 2006 and the FDA in 2007 and is marketed by TopoTarget's own sales force in Europe and the US. For more information, please refer to [www.topotarget.com](http://www.topotarget.com).

#### **TopoTarget Safe Harbour Statement**

This announcement may contain forward-looking statements, including statements about our expectations of the progression of our preclinical and clinical pipeline including the timing for commencement and completion of clinical trials and with respect to cash burn guidance. Such statements are based on management's current expectations and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. TopoTarget cautions investors that there can be no assurance that actual results or business conditions will not differ materially from those projected or suggested in such forward-looking statements as a result of various factors, including, but not limited to, the following: The risk that any one or more of the drug development programs of TopoTarget will not proceed as planned for technical, scientific or commercial reasons or due to patient enrolment issues or based on new information from non-clinical or clinical studies or from other sources; the success of competing products and technologies; technological uncertainty and product development risks; uncertainty of additional funding; TopoTarget's history of incurring losses and the uncertainty of achieving profitability; TopoTarget's stage of development as a biopharmaceutical company; government regulation; patent infringement claims against TopoTarget's products, processes and technologies; the ability to protect TopoTarget's patents and proprietary rights; uncertainties relating to commercialization rights; and product liability expo-sure; We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise, unless required by law.

