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**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)

## **First patient dosed in TopoTargets randomized BelCaP study in CUP (Carcinoma of Unknown Primary site)**

*- Randomized phase II study of belinostat in combination with carboplatin and paclitaxel (BelCaP) compared to carboplatin and paclitaxel initiated in solid tumors (Carcinoma of Unknown Primary site; CUP) -*

Copenhagen, Denmark – 16 April 2009 – TopoTarget A/S (OMX: TOPO) has announced that the first patient has been dosed in 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 CUP. The study aims to demonstrate the efficacy of belinostat in solid tumors in a randomized setting. Approximately 44 patients will be randomized to each group, in total 88 patients.

“We are proud to collaborate with key CUP opinion leaders both in the US and in Europe on this trial aimed to improve the progression free survival of patients suffering from CUP. We have previously demonstrated very promising results in platinum-resistant ovarian cancer when adding full dose belinostat to the combination of carboplatin and paclitaxel - the so-called BelCaP combination. Carboplatin and paclitaxel is also a first time standard of care in CUP and we can now directly evaluate the effect of adding belinostat” says professor Peter Buhl Jensen, CEO of TopoTarget.

Carcinoma of Unknown Primary site (CUP) represents a solid tumor type that is defined by the presence of metastases (where the cancer has spread to other parts of the body) at first presentation for which a primary site cannot be determined after defined diagnostic procedures.

### The study:

An open-label randomized phase II trial of belinostat (PXD101) in combination with carboplatin and paclitaxel (BelCaP) compared to carboplatin and paclitaxel in patients with previously untreated Carcinoma of Unknown Primary site. Patients will be randomized to treatment within either of two study groups:

Group A: belinostat (1000 mg/m<sup>2</sup>) administered as a 30 minute IV infusion once daily on days 1, 2 and 3, followed by belinostat 2000 mg (flat dose) administered orally once daily on days 4 and 5,

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every 3-weeks, in combination with paclitaxel (175 mg/m<sup>2</sup>) administered as an IV infusion following the infusion of belinostat on cycle day 3, and carboplatin (AUC 6) administered as an IV infusion directly after the paclitaxel administration on cycle day 3.

Group B: paclitaxel (175 mg/m<sup>2</sup>) administered as an IV infusion directly followed by carboplatin (AUC 6) administered as an IV infusion on cycle day 1 of a 3-weekly cycle.

Approximately 44 patients will be randomized to each group (in total 88 patients). Patients will be treated in three week cycles for up to 6 cycles of chemotherapy containing treatment unless there is disease progression or treatment-related toxicities that are not manageable with dose-reduction schemes or by appropriate supportive measures. After 6 cycles of treatment, patients in Group A will continue treatment on belinostat monotherapy at a dose of 750 mg (flat dose) administered orally once daily on days 1 to 14, every 3-weeks until disease progression or treatment-related toxicities. Patients in Group B will stop chemotherapy treatment after 6 cycles. Patients with documented progressive disease will be taken off study treatment at time of progression and may be offered 2nd line treatment.

Toxicity will be monitored continuously during study treatment and 30 days following last study drug administration. Safety will be assessed by adverse events and laboratory tests, graded according to the NCI CTC. Survival follow-up will be carried out every 3 months for the initial 2 years, and then every 6 months until 5 years from the start of study treatment.

The purpose of the trial is to provide an estimate of the hazard ratio of treatment effect, with the primary study endpoint being progression free survival (PFS), due to the combination of belinostat with carboplatin and paclitaxel (BelCaP).

### **TopoTarget A/S**

For further information, please contact:

Peter Buhl Jensen	Telephone	+45 39 17 94 99
CEO	Mobile	+45 21 60 89 22

### **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.

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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 Carcinoma of unknown primary site (CUP)**

Carcinoma of Unknown Primary site (CUP) represents a group of cancers that are defined by the presence of metastases at first presentation for which a primary site remains unknown at final diagnosis. It accounts for approximately 2-4% of all cancer diagnoses (Greco 2005). The Surveillance, Epidemiology, and End Results (SEER) estimates for 2007 that 32,100 patients (2.2% of all diagnoses of malignancy) in the United States will be diagnosed with "other and unspecified primary sites" (ACS 2007). European cancer registries indicate similar incidence rates for CUP as in the US.

#### **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, and is in phase III in PTCL. 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.