

To the Copenhagen Stock Exchange  
Announcement No. 06-07 / Copenhagen 27 March 2007

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## **TopoTarget and CuraGen Initiate Phase II Trial of Belinostat (PXD101) in Combination with Velcade® for Refractory Multiple Myeloma**

**Copenhagen, 27 March 2007, TopoTarget A/S (CSE: TOPO) and CuraGen Corporation (NASDAQ: CRGN)** announced today the initiation of patient dosing in a Phase II open-label, multi-center clinical trial evaluating the efficacy and safety of intravenous belinostat (PXD101), a small molecule histone deacetylase (HDAC) inhibitor, in combination with Velcade® (bortezomib) for Injection, in multiple myeloma patients refractory to or who have rapidly relapsed from at least one previous bortezomib-containing regimen.

Based on preliminary safety results from ongoing Phase Ib trials evaluating belinostat in combination with bortezomib, TopoTarget and CuraGen have initiated this Phase II trial in multiple myeloma patients. The Phase II clinical trial is being led by James Berenson, M.D., Principal Investigator, Medical & Scientific Director at the Institute for Myeloma & Bone Cancer Research, and will be conducted at multiple sites across the U.S. Up to 35 patients are planned for study enrollment with preliminary results anticipated by the end of 2007.

"Based on our preclinical studies that showed markedly increased anti-myeloma effects when belinostat was combined with bortezomib to treat a bortezomib-resistant myeloma in immunodeficient mice, we look forward to enrolling bortezomib-resistant multiple myeloma patients into this Phase II trial and determining whether the combination can provide clinical benefit to multiple myeloma patients that have failed, or who have relapsed on bortezomib therapy," commented Dr. Berenson.

"Emerging safety results from our clinical trials that are evaluating belinostat and bortezomib have shown the combination to be generally well-tolerated. Therefore, we have initiated this Phase II study to allow relapsed and/or refractory multiple myeloma patients the ability to receive treatment with belinostat and bortezomib, and anticipate reporting preliminary results from the study by the end of the year," commented Peter Buhl Jensen, Chief Executive Officer of TopoTarget. "As data continues to be generated from our Phase II trials in ovarian cancer, colorectal cancer, and T-cell lymphomas, we look forward to presenting preliminary results during mid-2007, and remain on track to initiate a Phase III program during 2008 and advance belinostat towards registration."

In vitro studies published in the literature have shown that HDAC inhibitors and bortezomib, when combined act synergistically through independent mechanisms leading to enhanced killing of cancer cells. During the 2006 ASH Annual Meeting, preclinical results evaluating belinostat in combination with bortezomib were presented in poster entitled, "Effects of a Novel Histone Deacetylase Inhibitor, PXD101, When Used as Monotherapy or in Combination with Bortezomib on Tumor Growth in a Mouse Model of Human Multiple Myeloma." The data suggest that when mice bearing bortezomib-resistant hu-



man tumors were treated with the combination of belinostat and bortezomib, greater inhibition of both tumor growth and circulating human IgG levels were observed than when either drug was used alone, and the mice tolerated the combination well without obvious adverse effects. These results suggest that treatment with belinostat in combination with bortezomib may be an effective therapy for bortezomib-resistant multiple myeloma.

As this Phase II study of belinostat and bortezomib begins, CuraGen will close enrollment in their ongoing Phase Ib study of this combination in multiple myeloma. The NCI-sponsored trial evaluating this combination on patients with advanced solid tumors remains open for enrollment.

### **TopoTarget A/S**

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### **Background information**

#### **About Multiple Myeloma**

Multiple myeloma (MM) is a progressive cancer arising from a particular type of blood cell, called plasma cells. It is the second most prevalent blood cancer in the U.S. with nearly 50,000 individuals suffering from MM, and more than 15,000 new cases expected to be diagnosed this year. MM is characterized by excessive numbers of abnormal plasma cells in the bone marrow and the overproduction of abnormal immunoglobulins. As a result of MM, patients may develop bone lesions, anemia, elevated blood calcium levels, kidney damage, and a decreased ability to fight off infections. Despite the availability of treatments for MM, there is currently no cure for this disease.

#### **About Belinostat (PXD101)**

Belinostat is a promising small molecule HDAC inhibitor being investigated for its role in the treatment of a wide range of solid and hematologic malignancies either as a single-agent, or in combination with other active anti-cancer agents, including 5-FU, carboplatin, paclitaxel, cis-retinoic acid, azacitidine 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 currently being evaluated in multiple clinical trials as a potential treatment for multiple myeloma, T- and B-cell lymphomas, AML, mesothelioma, liver, colorectal, ovarian cancers, either alone or in combination with anti-cancer therapies. An oral formulation of belinostat is also being evaluated in a Phase I clinical trial for patients with advanced solid tumors. In August 2004, CuraGen signed a Clinical Trials Agreement with the NCI under which the NCI will sponsor several clinical trials to investigate belinostat for the treatment of various cancers, both as a single-agent and in combination chemotherapy regimens. In May 2005, TopoTarget announced the signing of 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 TopoTarget**

TopoTarget (OMX – The Nordic Exchange: TOPO) is a biopharmaceutical company, headquartered in Denmark and with subsidiaries in the UK, Germany and the USA, dedicated to finding "Answers for Cancer" and developing improved cancer therapies. TopoTarget is founded and run by clinical cancer specialists and combines years of hands-on clinical experience with in-depth understanding of the molecular mechanisms of cancer. Focus lies on highly predictive cancer models and key cancer enzyme regulators (mainly HDAC, mTOR, and topoisomerase II inhibitors) and a strong development foundation has been built. TopoTarget has a broad portfolio of small molecule preclinical drug candidates and seven drugs are in clinical development, including both novel anti-cancer therapeutics and new cancer indications for existing drugs. Savene™ is TopoTarget's first product on the market. In addition to organic growth, TopoTarget consistently looks for opportunities to strengthen and expand its activities through acquisitions and in-licensing. For more information, please refer to [www.topotarget.com](http://www.topotarget.com).

#### **About CuraGen**

CuraGen Corporation (NASDAQ: CRGN) is a biopharmaceutical company developing diverse approaches, including novel protein, antibody, and small molecule therapeutics, that aim to offer hope for patients with cancer, inflammatory diseases, and diabetes. CuraGen's strategic alliances have resulted in a deep pipeline of potential therapeutics that is being developed by the Company's experienced research and development teams. By leveraging the drug development strengths cultivated over the years, CuraGen expects to make a difference in the lives of patients by bringing forward promising therapeutics that address unmet medical needs. To further capitalize on CuraGen's extensive research and development expertise, CuraGen founded a majority-owned subsidiary, 454 Life Sciences, which has developed and is commercializing advanced technologies for the sequencing of DNA. CuraGen and 454 Life Sciences are headquartered in Branford, Connecticut. For additional information please visit [www.curagen.com](http://www.curagen.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 nonclinical 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 exposure; 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.

