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## **BELINOSTAT DATA PRESENTATION AT 101<sup>ST</sup> ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH**

**Copenhagen, Denmark – 21 April, 2010 – Topotarget A/S (NASDAQ OMX: TOPO.CO) US partner, Spectrum Pharmaceuticals, Inc. (NASDAQGM: SPPI) announces belinostat pre-clinical data presented at 101<sup>ST</sup> annual meeting of the American association for cancer research**

- ***Data Suggest HDAC Inhibitors, Such as Belinostat, May Be Efficacious in the Treatment of Small Cell Lung Cancer***
- ***Results Indicate Synergy With Conventional Chemotherapy Agents***

Spectrum Pharmaceuticals, Inc. (NasdaqGM: SPPI), a commercial-stage biotechnology company with a primary focus in oncology, today announced results of a pre-clinical study conducted by the National Cancer Institute of belinostat in the treatment of small-cell lung cancer that was presented in a poster session on Wednesday, April 21, 2010 at the 101st Annual Meeting of the American Association for Cancer Research (AACR), being held at the Walter E. Washington Convention Center in Washington, DC.

"Based on the data presented today at AACR, we believe belinostat may be an effective treatment option for small-cell lung cancer," said Rajesh C. Shrotriya, MD, Chairman, President and Chief Executive Officer of Spectrum Pharmaceuticals, Inc. "While we continue to enroll patients into the 100-evaluable patient registrational trial for belinostat in peripheral T-cell lymphoma (PTCL), being conducted under a Special Protocol Assessment by the FDA, we are exploring potential clinical trial design options for the treatment of lung cancer."

### **Abstract #5372 – Synergy of Histone Deacetylase Inhibitors, Belinostat and Depsipeptide, With DNA Damaging Agents, Etoposide and Cisplatin, In Small Cell Lung Cancer Cell Lines**

Small Cell Lung Cancer (SCLC) is the most aggressive type of lung carcinoma. SCLC has a high response rate to chemotherapy, but rapid onset of drug resistance. Chemotherapeutic treatment using combinations of drugs that target different signaling pathways have demonstrated improvement in overall survival of patients with SCLC. HDAC inhibitors play a role in regulating cell cycle progression and have been suggested as potential therapeutic agents for SCLC. HDAC inhibition is believed to relax DNA, thereby allowing increased access of transcription factors to certain promoters. Likewise, these agents could increase accessibility of DNA to cytotoxic agents.

Two distinct HDAC inhibitors, belinostat and depsipeptide, were examined to determine whether they have an effect on SCLC lines and whether they could be combined with conventional chemotherapy agents etoposide and cisplatin for SCLC.

## **BELINOSTAT PRE-CLINICAL DATA PRESENTATION**

Simultaneous and schedule-dependent treatment protocols of SCLC cells with single drugs and drug combinations were used. Computational analysis of cell survival using combination index (CI) showed that HDAC inhibitors synergized with DNA damaging agents when administered simultaneously, but this effect was only additive if cells were pre-treated with HDAC inhibitors for 24 hours prior to DNA damaging agents. In addition, using DNA damaging agents 24 hours prior to HDAC inhibitors was clearly antagonistic with  $CI > 1$  for all drugs and cell lines tested.

Because of a potential use of belinostat and depsipeptide for therapy of SCLC in combination with conventional chemotherapies, the mechanisms of synergy and protection between these agents were examined. PolyADP-ribose polymerase (PARP) degradation was complete when drugs were used simultaneously, but was decreased if HDAC inhibitors were used prior to cisplatin or etoposide. The degradation of PARP enzyme prevents repair of DNA strand breaks caused by chemotherapeutic agents and thereby facilitates the programmed cell death, or apoptosis, of cancer cells. Therefore, a greater degree of PARP degradation is indicative of a greater capacity of a given anti-cancer agent or a combination of agents to induce apoptosis.

It was concluded that HDAC inhibitors synergize with DNA damaging agents only if administered simultaneously. Treatment of cells with HDAC inhibitors and DNA damaging agents induces PARP degradation. Combination of HDAC inhibitors with etoposide does not affect single stranded DNA damage. Simultaneous treatment with DNA damaging agents increases double strand DNA damage. The design of clinical trials for combination of HDAC inhibitors and chemotherapeutic agents should take into account the timing that induces maximum effect.

### **TopoTarget A/S**

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### **Background information**

#### **About TopoTarget**

TopoTarget (NASDAQ OMX: TOPO) is an international biotech company headquartered in Denmark, dedicated to finding "Answers for Cancer" and developing improved cancer therapies. TopoTarget currently focuses, in collaboration with Spectrum Pharmaceuticals, Inc., on the development in pivotal studies of its lead drug candidate, belinostat, which has shown proof-of-concept as monotherapy in treating haematological malignancies and positive results in solid tumours. Belinostat can be used in combination with full doses of chemotherapy, and is currently in a pivotal trial within PTCL (peripheral T-cell lymphoma). TopoTarget's key cancer drugs target HDAC, NAD<sup>+</sup>, mTOR, Fas ligand and topoisomerase II. 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 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

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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 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.