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TOPOTARGET A/S ANNOUNCES BELINOSTAT ABSTRACT AT THE 2010 ANNUAL MEETING OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY

- *Abstracts Now Available for Viewing at ASCO.org*
- *Phase 2 Study of Belinostat Monotherapy in Relapsed/Refractory PTCL demonstrated 32% Objective Response Rate*
- *Additional Information to be Provided During ASCO Annual Meeting*

Copenhagen, Denmark – 21 May 2010 – Topotarget A/S (NASDAQ OMX: TOPO) , announces that clinical data on belinostat will be presented at the 2010 Annual Meeting of the American Society of Clinical Oncology (ASCO), to be held June 4-8, 2010 at the McCormick Place Convention Center in Chicago, Illinois, as part of the ASCO proceedings.

Shown below is the summary abstract on the currently enrolling pivotal, registrational PTCL trial being conducted under a Special Protocol Assessment, as well as 4 other abstracts that are now available for viewing on the ASCO.org website (www.asco.org).

A Multicenter, Open-Label Trial of Belinostat in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma

- *Owen A. O'Connor – NYU Cancer Institute, New York, NY*
- *Pier Luigi Zinzani – University of Bologna, Bologna, Italy*

The study is a global, multicenter, single arm efficacy and safety study of belinostat monotherapy in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL) who failed at least one prior systemic therapy. Main aims are to determine objective response rate and time-related response parameters.

Belinostat is a hydroxamate, class I & II histone deacetylase inhibitor (HDACi). Pre-clinically, belinostat has a broad antineoplastic spectrum at sub-micromolar concentrations including T-cell lymphoma lines. Phase 1 and 2 trials are ongoing in multiple indications and in more than 500 patients. Belinostat treatment was safe and well tolerated, and the most common events included nausea, fatigue, and vomiting. A Phase 2 study of belinostat monotherapy in relapsed/refractory PTCL demonstrated in 19 evaluable patients an objective response rate of 32% and a median response duration of 268+ days. The results led to the present pivotal trial in PTCL as agreed with FDA under a Special Protocol Assessment.

Eligible patients have received at least one prior systemic chemotherapy and have histologically confirmed diagnosis of PTCL of one of the subtypes:

- Anaplastic large cell lymphoma (ALK-positive or negative),
- ALK-negative,
- Angioimmunoblastic T-cell lymphoma
- Enteropathy-associated T-cell lymphoma
- Extranodal NK/T-cell lymphoma
- Nasal type,
- Hepatosplenic T-cell lymphoma
- Peripheral T-cell lymphoma
- Not otherwise specified (NOS) or
- Subcutaneous panniculitis-like T-cell Lymphoma

The diagnosis should be confirmed by a positive set of T-cell markers and negativity of B-cell markers. A pathology panel will review all diagnosis specimens.

Belinostat will be administered as a 30-minute IV infusion of 1000 mg/m² on days 1-5 of every 3-week cycle until disease progression or unmanageable treatment-related toxicities.

As of January 4, 2010, 19 patients have been included in the trial. The primary study endpoint is objective response rate (ORR). The sample size was based on a 2-stage optimal design with a hypothesized ORR of p1=20% for B and a minimal or "uninteresting" ORR of p0=9%. At least 14 confirmed objective responses in 100 evaluable patients are required to confirm a 20% target response rate with an alpha of 0.05 assuming a power of 90%.

Pharmacokinetic data will be collected to explore exposure-response relationships.

Monday, June 7, 2010 – 8:00am – 12:00pm

Trials in Progress Poster Session – Special Session, Clinical trials – S Hall A2
Abstract #TPS185: An Open-Label Randomized Phase 2 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.

- Karim Fizazi – Institut de Cancerologie Gustave Roussy, Villejuif, France
- John Hainsworth – Tennessee Oncology Sarah Canon Research Institute, US

Treatment options for patients with cancer of unknown primary (CUP) are limited; carboplatin and paclitaxel combination being one of the options. Belinostat, is a hydroxamate, class I and II histone deacetylase inhibitor (HDACi) with a broad antineoplastic activity. Phase I and II trials are ongoing in multiple indications and in more than 500 patients the most common adverse events have been nausea, vomiting and fatigue. Preclinical data shows synergistic effect when combined with carboplatin and paclitaxel *in vitro* and *in vivo*. In a Phase I study for patients with pretreated advanced solid tumors, BelCaP was well-tolerated and active with objective responses seen in pancreatic and rectal cancer patients. A patient with CUP (3 prior chemotherapy regimens) had disease control during 29 months of treatment. Therefore, we are conducting a randomized Phase 2 study (N~88) of CaP with or without belinostat in CUP patients.

Randomized, global, multicenter Phase 2 trial in 19 centers. Inclusion criteria include: a confirmed diagnosis of CUP, no prior therapy, ECOG PS 0-2, age > 18 years. Eligible patients are randomized to receive either arm A or B.

- Arm A: BelCaP; belinostat as a 30-min i.v. infusion once daily (1000 mg/m²) on days 1-3,

followed by belinostat 2000mg orally once daily on days 4-5, with paclitaxel (175 mg/m²) administered 2-3 hours following belinostat on day 3 and carboplatin (AUC6) following directly after paclitaxel, up to 6 cycles. From cycle 7: belinostat 750 mg is administered orally once daily x 14 days.

- Arm B: Paclitaxel (175 mg/m²) administered day 1 and carboplatin (AUC6) following directly after paclitaxel. Cycles repeated every 3 weeks.

Primary endpoint is progression free survival (PFS) and secondary endpoints assess additional efficacy parameters and safety. Response is evaluated according to RECIST criteria. 33 patients have been randomized as of 06-Jan-2009.

Monday, June 7, 2010 – 8:00am-12:00pm

General Poster Session – Developmental Therapeutics – S Hall A2

Abstract #2585 – Phase 1 Pharmacokinetics and Metabolic Pathway of Belinostat in Patients with Hepatocellular Carcinoma.

- L. Z. Wang, et al.

Metabolic inactivation of several hydroxamic acid-derived histone deacetylase inhibitors (HDACi) involves glucuronidation. Vorinostat, a pan-HDACi, undergoes glucuronidation by UGT2B17. We studied the pharmacokinetics and metabolic pathway of belinostat (PXD101).

In vitro glucuronidation of belinostat was investigated; plasma pharmacokinetics of belinostat was studied in a phase I study in patients with hepatocellular carcinoma. Seventeen patients were treated with belinostat at escalating doses of 600 (n = 3), 900 (n = 3), 1200 (n = 6), 1400 (n = 5) mg/m² daily by intravenous infusion over 30 minutes for 5 days every 21 days; blood was drawn on day 1 before infusion, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 5 and 24 hours after the start of infusion, plasma was isolated for determination of belinostat and identification of its metabolites using LC-MS/MS. Pharmacokinetics of belinostat was studied using non-compartmental methods.

Using a panel of 12 UGT isoforms, UGT1A1 was found to be the predominant enzyme for glucuronidation of belinostat with one third of unmetabolized belinostat left after 1 h incubation at 37 °C. Belinostat glucuronide had no activity against HONE1 cell line at 10 µM, compared to an IC₅₀ of 1.59 ± 0.90 µM for belinostat. Belinostat AUC increased linearly with dose, with a mean clearance of 34.34 ± 10.56 L/h/m² and terminal half-life of 2.94 ± 0.48 h. Five metabolites in human plasma were identified. Glucuronidation was the most significant pathway of belinostat metabolism; 2 alternate biotransformation pathways involved methylation to methylated belinostat and reduction of hydroxamic group to its corresponding belinostat amide. In addition, two minor metabolites were found to be belinostat N-glucoside and belinostat acid. Belinostat glucuronide increased in levels shortly after administration, reaching the maximum concentration at 1 h from start of infusion.

Phase II biotransformation played a key role on belinostat disposition, with UGT 1A1 likely involved in the major pathway. Further studies should explore the role of common polymorphisms of UGT1A1 on belinostat disposition and pharmacodynamics.

Saturday, June 5, 2010 – 8:00am-12:00pm

General Poster Session – Leukemia, Myelodysplasia, and Transplantation – S Hall A2

Abstract #6607 – Phase 2 Study of the Histone Deacetylase (HDAC) Inhibitor Belinostat for the Treatment of Myelodysplastic Syndrome (MDS)

- Amanda Cashen, MD, et al.

Inhibition of HDAC can induce differentiation, growth arrest, and apoptosis in cancer cells. Belinostat is a potent inhibitor of both class I and class II HDAC enzymes. This Phase II study was undertaken to estimate the efficacy of belinostat for the treatment of MDS.

Adults with MDS (any WHO classification, plus at least 1 significant cytopenia if <5% bone marrow blasts) were eligible if they had ≤ 2 prior therapies for MDS, adequate renal and hepatic function, and ECOG 0-2. The primary endpoint was proportion of confirmed responses (CR, PR, and hematologic improvement [HI]) during the first 12 weeks of treatment. Patients were treated with belinostat 1000 mg/m² as a 30 min IV infusion on days 1-5 of a 21 day cycle for 4 cycles. Responding patients could receive additional cycles until disease progression or unacceptable toxicity. 21 patients were to be enrolled in the first stage, and if 3 or more responses were observed, an additional 29 would be enrolled in stage 2.

21 patients (median age, 67 years) were enrolled, and all are evaluable. Patients were a median 13.4 months from diagnosis (range, 0.3-210) and had bone marrow blasts of <5% (n=14), 5-9% (n=6), and 10-19% (n=1). 13 patients (62%) had good risk cytogenetics, and 7 (33%) had poor risk. 17 patients (81%) were transfusion dependent. Prior therapy included azacitidine (n=7) and chemotherapy (n=8). Patients were treated with a median 2.5 cycles (range, 1-8) of belinostat. There was one confirmed response – HI in neutrophils – that lasted 2.1 months, for an ORR of 5% (95% CI, 0.2-23). Median Overall Survival was 14.5 months. Median time to progression was 15.5 months. Grade 3-4 toxicities considered at least possibly related to belinostat were: neutropenia (n=10), thrombocytopenia (n=9), anemia (n=5), fatigue (n=2), febrile neutropenia (n=1), and headache (n=1). 2 patients had Grade 2 cytokine release syndrome during belinostat infusion, and 2 patients had QTc prolongation. Because the study met the stopping rule in the first stage of enrollment, it was closed to further accrual.

Although well-tolerated, belinostat does not have sufficient efficacy to warrant further investigation as a single agent in MDS. Supported by NCI N01-CM62205

About Belinostat

Belinostat (PXD 101) is a Class I and II HDAC inhibitor that is being studied in multiple clinical trials as a single agent or in combination with chemotherapeutic agents for the treatment of various hematological and solid cancers. Its anticancer effect is thought to be mediated through multiple mechanisms of action, including the inhibition of cell proliferation, induction of apoptosis (programmed cell death), inhibition of angiogenesis, induction of differentiation, and the resensitization of cells that have overcome drug resistance to anticancer agents such as platinum, taxanes and topoisomerase II inhibitors. Belinostat is the only HDAC inhibitor in clinical development with multiple potential routes of administration, including intravenous administration, continuous intravenous infusion and oral administration.

Belinostat is currently in a registrational trial, under a Special Protocol Assessment (SPA), as a monotherapy for relapsed or refractory Peripheral T-Cell Lymphoma (PTCL), an indication for which it has been granted Orphan Drug and Fast Track designation by the U.S. Food and Drug Administration. The Company currently plans to file a New Drug Application (NDA) in 2011. Belinostat is also under investigation in a randomized Phase 2 trial, as a combination therapy with carboplatin and paclitaxel, for cancer of unknown primary (CUP). Additionally, the National Cancer Institute is currently conducting several clinical trials of Belinostat in a variety of hematological and solid tumors, both as monotherapy as well as combination therapy.

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Background information

About Topotarget

Topotarget (NASDAQ OMX: TOPO) is an international biotech company headquartered in Denmark, dedicated to improve 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+, mTOR, Fas ligand and topoisomerase II. The company's first marketed product, Savene[®]/Totect[®], 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.

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 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.