Abstract for the American Association for Cancer Research 2012

Copenhagen, Denmark – February 29, 2012 – Today Topotarget A/S (NASDAQ OMX: TOPO) announced that clinical data on belinostat will be presented at the 2012 American Association for Cancer Research Annual Meeting (AACR), March 31 – April 4, 2012.

Shown below is the abstract that is now available for viewing on the AACR website (http://www.aacr.org/).

Abstract 759, Sunday, April 1, 2012 at 1.00-5.00 pm, McCormick Place West (Hall F).

Quantitation of the HDAC inhibitor belinostat (PXD-101) and metabolites in human plasma by a novel LC-MS/MS assay.

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Background:
Histone deacetylases (HDAC) are frequently deregulated in human cancers and their inhibition allows re-expression of silenced genes. Belinostat is an HDAC inhibitor with in vitro and in vivo activity in multiple malignancies, currently in phase II trials. To date, the pharmacokinetics and metabolism of belinostat have not been adequately characterized. To support an organ dysfunction study and clinical development of belinostat, we developed and validated an LC-MS/MS assay for the sensitive, accurate, and precise quantitation of belinostat and its metabolites belinostat-glucuronide, methylated-belinostat, belinostat amide, 3-ASBA, and belinostat acid in human plasma.

Methods:
The assay used 50 µL of plasma, [13C6]-belinostat and [D5]-3-ASBA as internal standards and acetonitrile (0.1% TFA) for protein precipitation. A UPLC C18 column was used with a gradient elution from 90:10 to 10:90 water-acetonitrile (0.1% formic acid) over the course of 4 min followed by re-equilibration for 3 min (7 min total run time). Flow rate was 0.5 mL/min. An ABI 4000 tandem MS/MS with ESI positive and negative ionization in MRM mode was used to detect the analytes. Bioanalytical method validation was performed based on FDA guidelines. The applicability of the assay was demonstrated by quantitating belinostat and its metabolites in plasma of a human patient sampled over the course of 24 h.

Results:
Belinostat eluted at 2.9 min, while all metabolites eluted between 2.7 and 3.6 min. The assay was linear and accurate between 30 and 5000 ng/mL for all analytes; 3 triplicate
standard curves assayed on 3 separate days displayed a CV <19% at each of 6 different calibration points (30, 100, 300, 1000, 3000, 5000 ng/mL) for belinostat and CV <29% for the metabolites. The accuracy of the assay was between 101% and 106% at 4 different QC levels (30, 100, 2500, and 4000 ng/mL) for belinostat and between 96% and 117% for metabolites, while the precision was <17% at each concentration for belinostat and <26% for metabolites. Recovery was >69% for belinostat and >64% for metabolites. Belinostat and all metabolites could be quantitated in human plasma after IV administration of belinostat over 30 min. Belinostat glucuronide appeared to be the major metabolite with up to 10-fold exposure relative to belinostat.

Conclusion:
We have developed a sensitive, accurate, and precise LC-MS/MS assay that allows quantitation of belinostat and its 5 metabolites in human plasma. UGT1A1 is responsible for glucuronidation, which appears to be a major metabolic route. This assay will be a valuable tool to assess the pharmacokinetics and metabolism of belinostat in humans, and it is being used to support clinical studies employing belinostat in multiple clinical trials.

Topotarget A/S
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Background information
About Topotarget A/S
Topotarget (NASDAQ-OMX: TOPO) is an international biopharmaceutical company headquartered in Copenhagen, Denmark, dedicated to clinical development and registration of oncology products. Topotarget focuses, in collaboration with Spectrum Pharmaceuticals, Inc., on the development in pivotal studies of its lead drug candidate, belinostat, which has shown positive results as a monotherapy treating hematological malignancies and positive results in solid tumors. Belinostat may be used in combination with full doses of chemotherapy, and is in a pivotal trial within PTCL (peripheral T-cell lymphoma). For more information, please refer to www.topotarget.com.

Topotarget A/S Safe Harbor 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 A/S 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 A/S 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 A/S’ history of incurring losses and the uncertainty of achieving profitability; Topotarget A/S’ stage of development as a biopharmaceutical company; government regulation; patent infringement claims against Topotarget A/S’ products, processes and technologies; the ability to protect Topotarget A/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.