



Mesothelioma Articles

CuraGen and TopoTarget Announce Initiation of NCI-sponsored Phase II Clinical Trial with PXD101 for Mesothelioma

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BRANFORD, Conn., June 20 /PRNewswire-FirstCall/ -- CuraGen Corporation (Nasdaq: CRGN - News) and TopoTarget A/S (Copenhagen Stock Exchange: TOPO) announced today the initiation of patient dosing in a Phase II clinical trial evaluating the activity of PXD101, a small molecule histone deacetylase (HDAC) inhibitor, for the [treatment of mesothelioma](#). This trial is being sponsored by the National Cancer Institute (NCI) under a Clinical Trials Agreement with CuraGen for the clinical development of PXD101.

The Phase II clinical trial is an open-label study being led by Suresh Ramalingam, M.D., Assistant Professor of Medicine at the University of Pittsburgh School of Medicine in Pittsburgh, PA. Patients with unresectable [malignant pleural mesothelioma](#), who have failed one prior line of chemotherapy, will be enrolled and receive PXD101 by intravenous infusion every three weeks. The primary endpoint for the study is response rate, with secondary endpoints evaluating safety and measuring both the time to treatment failure and survival. A total of approximately 37 patients are expected to be enrolled into this study at multiple sites across the United States.

"A significant amount of preclinical research suggests that HDAC inhibitors, including PXD101, alter the regulation of many genes, resulting in growth inhibition of human mesothelioma cells. Given the ability of HDAC inhibitors to down-regulate genes such as BCL-XL and VEGF and up-regulate cell-cycle regulating genes, including p21, we are excited to begin evaluating PXD101 as a potential treatment for this type of cancer," stated Dr. Ramalingam. "There are no proven treatment options beyond the first-line chemotherapy regimen for mesothelioma, highlighting the importance of evaluating promising therapeutics like PXD101 for this patient population."

Correlative pharmacodynamic studies will also be conducted to evaluate the potential inhibition of HDACs in mesothelioma tumor cells from patients enrolled in this trial. Evaluation of the genes regulating proliferation and apoptosis (programmed cell death), as well as acetylation of histone and non-histone proteins, will be performed.

About Mesothelioma

As many as 3,000 new cases of malignant mesothelioma are expected to be diagnosed in the United States in 2006. Mesothelioma is a type of cancer arising from the cells, known as mesothelium, with the majority of cancers beginning in the chest cavity. The incidence of mesothelioma increases with age and is rarely diagnosed in patients under 55 years old. Although environmental exposure to certain chemicals and radiation are believed to play a role in the development of mesothelioma, exposure to asbestos is believed to be the main cause of mesothelioma. The five-year survival rate for mesothelioma is approximately 10%, with an average survival of one to two years following diagnosis.

About PXD101

PXD101 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-fluorouracil (5-FU), carboplatin, paclitaxel 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.

PXD101 is currently being evaluated in multiple clinical trials as a potential treatment for multiple myeloma, T-cell lymphoma, and colorectal and ovarian cancers, either alone or in combination with anti-cancer therapies. In August 2004, CuraGen signed a Clinical

Trials Agreement with the NCI under which the NCI will sponsor several clinical trials to investigate PXD101 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 pre-clinical and non-clinical studies on PXD101 in order to better understand its anti-tumor activity and to provide supporting information for clinical trials.

About CuraGen

CuraGen Corporation (Nasdaq: CRGN - News) 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 on the companies please visit <http://www.curagen.com> and <http://www.454lifesciences.com>.

About TopoTarget

TopoTarget (CSE: TOPO - News) is a fully integrated biopharmaceutical company, headquartered in Denmark and with subsidiaries in the UK and Germany, and 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 key cancer enzyme regulators (mainly HDAC, mTOR, and topoisomerase II inhibitors) and a strong development foundation of proprietary, highly predictive cancer models has been built. TopoTarget has a broad portfolio of small molecule preclinical drug candidates and eight drugs are in clinical development, consisting of both novel anti-cancer therapeutics and new cancer indications for existing drugs. The most advanced drug candidate, Savene(tm) for extravasations is expected on the market end 2006. 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 <http://www.topotarget.com>.

Safe Harbor

This press release contains forward-looking statements including statements about the expected effects and benefits of PXD101. We caution 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 PXD101 or any other CuraGen drug development program will not proceed as planned for technical, scientific or commercial reasons or due to patient enrollment 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; CuraGen's history of incurring losses and the uncertainty of achieving profitability; CuraGen's stage of development as a biopharmaceutical company; government regulation; patent infringement claims against CuraGen's products, processes and technologies; the ability to protect CuraGen's patents and proprietary rights; uncertainties relating to commercialization rights; and product liability exposure. Please refer to CuraGen's Annual and Quarterly Reports on Forms 10-K and 10-Q for a complete description of these risks. CuraGen disclaims 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.

Contact:

Glenn Schulman, Pharm.D.
Assistant Director of Investor Relations
gschulman@curagen.com
(888) 436-6642

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