

# Karyopharm Announces Initiation of a Phase 1 Study of Decitabine (Dacogen(R)) and Selinexor (KPT-330) in Acute Myeloid Leukemia (AML)

NATICK, Mass., April 15, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases, today announced the initiation of a Phase 1 combination trial of its novel, oral Selective Inhibitor of Nuclear Export (SINE) compound Selinexor (KPT-330) in combination with the DNA methylation inhibitor decitabine (Dacogen®) in patients with relapsed or refractory acute myeloid leukemia (AML) and in patients age ≥60 years with newly diagnosed AML. The study is being conducted at The Ohio State University Comprehensive Cancer Center under the direction of principal investigator Ramiro Garzon, MD, Associate Professor.

In this combination study, patients with relapsed and/or refractory AML or newly diagnosed AML patients ≥60 years of age ineligible for intensive chemotherapy will receive decitabine intravenously on days 1-10 and Selinexor orally twice weekly beginning on day 11 of each 31-day cycle. The primary goal of the study is to determine the maximum tolerated dose and the recommended Phase 2 dose of this combination in up to 42 patients. The secondary goal of the study is to determine the response rates and duration of leukemia control. A full description of the study is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT02093403).

Dr. Garzon stated, "We are excited to initiate this study on the combination of the novel oral SINE compound Selinexor with decitabine in patients with relapsed or refractory AML and in elderly AML patients who are not fit for intensive chemotherapy, particularly because of the limited treatment options available to this patient population. We look forward to presenting the initial results of this study later this year."

Preclinical results from Dr. Garzon's laboratory, as well as other laboratories, have shown that Selinexor, a SINE compound that covalently inhibits the nuclear export protein XPO1 (exportin 1, also called CRM1), has potent anti-AML activity *in vitro* and *in vivo*. This activity is associated with enhancement of nuclear levels of tumor suppressor proteins as well as down-regulation of oncogenic kinases such as FLT3 and c-KIT. Oral Selinexor has shown single agent anti-leukemic activity in patients with heavily pretreated, relapsed/refractory AML.

Decitabine has well described anti-AML activity, and this activity correlates with levels of the microRNA miR-29b. Interestingly, XPO1 inhibition enhances nuclear levels of miR-29b, and the combination of Selinexor and decitabine has shown synergy with good tolerability in preclinical *in vivo* models of AML.

Sharon Shacham, PhD, MBA, Karyopharm's founder, President and Chief Scientific Officer, commented, "This first combination study of Selinexor represents a significant milestone for the company as we look to broaden the scope of SINE compounds in the treatment of cancers. We are pleased to expand our relationship with Dr. Garzon and his team at The Ohio State University as we build on his preclinical work with Selinexor in combination with decitabine and its translation into the clinic."

## About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. Selinexor functions by binding with the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus, which subsequently reinitiates and amplifies their tumor suppressor function. This is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 290 patients have been treated with Selinexor in Phase 1 trials in advanced hematologic malignancies and solid tumors. Additional Phase 1 and Phase 2 studies are ongoing or currently planned and three registration-directed clinical trials in hematological indications are expected to begin enrollment during 2014. The latest clinical trial information for Selinexor is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. SINE compounds have shown biological activity in models of cancer, autoimmune disease, certain viruses, and wound-healing. Karyopharm was founded by Dr. Sharon Shacham and is located in Natick, Massachusetts.

## Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding the therapeutic potential of and potential clinical development

plans for Karyopharm's drug candidates, including the timing of initiation of certain trials and of the reporting of data from such trials. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the company's current expectations. For example, there can be no guarantee that any of Karyopharm's SINE compounds, including Selinexor (KPT-330), or any other drug candidate that Karyopharm is developing will successfully complete necessary preclinical and clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Annual Report on Form 10-K for the year ended December 31, 2013, which is on file with the Securities and Exchange Commission (SEC), and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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