Karyopharm to Present Data on Oncology Pipeline at American Association for Cancer Research Annual Meeting

NEWTON, Mass., March 18, 2015 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that fourteen abstracts describing the activity of selinexor (KPT-330), the company's lead drug candidate in development for hematological malignancies and solid tumors, have been selected for presentation at the 2015 Annual Meeting of the American Association for Cancer Research (AACR) taking place April 18-22 in Philadelphia. The abstracts, which represent both company and investigator-sponsored preclinical studies, describe data related to selinexor (KPT-330), Karyopharm's first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound that inhibits exportin 1 (XPO1).

"We are pleased to be presenting such a comprehensive body of work related to Karyopharm's oncology pipeline at the AACR annual meeting," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Preclinical data to be presented on selinexor include mechanisms of drug action, specificity and molecular mechanisms leading to tumor radio-sensitization and to selective tumor and cancer stem cell killing. We will also present abstracts that expand upon the understanding of selinexor's activity in hematologic malignances, including non-Hodgkin's lymphoma, acute myeloid leukemia and multiple myeloma, and in solid tumors, including sarcoma, mesothelioma, ovarian and non-small cell lung cancers, as well as in pediatric tumors including neuroblastoma."

Mechanistic highlights include further elucidation of selinexor's selective cancer cell killing through reactivation of tumor suppressor proteins and forced nuclear retention of survivin. In addition to killing bulk cancer cells, selinexor also induces apoptosis in therapy-resistant leukemic stem cells while sparing normal hematopoietic cells. Furthermore, selinexor can inhibit the epithelial to mesenchymal transition (EMT) which is believed to play a key role in the generation of cancer stem cells. Finally, selinexor-induced inhibition of NF-kB plays an important role in its anti-tumor activity, and this action is enhanced by proteasome inhibitors.

Additionally, combination studies show that selinexor enhances the anti-tumor activity of DNA damaging agents such as radiation, alkylating agents and doxorubicin, and enhances the anti-myeloma effects of glucocorticoids.

Updated and detailed results from these studies will be presented at the conference.

The following abstracts further elucidate the impact of XPO1 inhibition in cancer:

Poster Title:	Antitumor activity of selective inhibitors of XPO1/CRM1-mediated nuclear export in diffuse malignant peritoneal mesothelioma: the role of survivin
Author:	De Cesare, Fondazione IRCCS Istituto Nazionale Tumori, Milan
Poster:	19/19
Session:	PO. MCB02.01 Cell Death Mechanisms
Date/Time:	Sunday, April 19, 1:00 - 5:00 PM
Poster Title:	Preclinical activity of selinexor, an inhibitor of XPO1/CRM1, in sarcoma
Author:	Nakayama, Dana Farber Cancer Institute
Poster:	1759/2
Session:	PO.ET02.02. Novel Agents and Mechanisms of Action
Date/Time:	Monday, April 20, 8:00 AM - 12:00 PM
Poster Title:	Single cell longitudinal studies reveal cell cycle specific effects of selective inhibitors of nuclear export (SINE)
Author:	Burke, University of Colorado
Poster:	1760/3
Session:	PO.ET02.02. Novel Agents and Mechanisms of Action
Date/Time:	Monday, April 20, 8:00 AM - 12:00 PM
Poster Title:	Pharmacodynamic and genomic markers associated with response to the XPO1/CRM1 inhibitor selinexor (KPT-330): a report from the Pediatric Preclinical Testing Program
Author:	Smith, National Cancer Institute
Poster:	1616/7
Session:	PO.CL02.01. Pediatric Cancer: Clinical Investigations/Regulatory Science Policy
Date/Time:	Monday, April 20, 8:00 AM - 12:00 PM
Poster Title:	Deconstructing protein and gene expression pathways to define the anticancer effects of XPO1 inhibition in ovarian cancer
Author:	Evans, Icahn School of Medicine at Mount Sinai

Poster: 1758/1
Session: PO.ET02.02. Novel Agents and Mechanisms of Action
Date/Time: Monday, April 20, 8:00 AM - 12:00 PM

Poster Title: F-box protein fbxl5 nuclear retention by specific inhibitors of nuclear export induces snail ubiquitination leading to reversal of EMT

Author: Muqbil, Wayne State University
Poster: 1424/6
Session: PO.TB04.03. Epithelial-Mesenchymal Transition, Mesenchymal-Epithelial Transition, and Related Behaviors
Date/Time: Monday, April 20, 8:00 AM - 12:00 PM

Poster Title: XPO1 is selinexor prime target: validation by mutating cysteine 528 on both XPO1 alleles using CRISPR/Cas9 genome editing

Author: Neggers, Rega Institute for Medical Research
Poster: 2442/7
Session: PO.CH02.01. Chemical Biology and Structure-Function Studies of Cancer Mechanisms
Date/Time: Monday, April 20, 1:00 - 5:00 PM

Poster Title: Selective inhibitor of nuclear exporter CRM1/XPO1, selinexor (KPT-330), exhibits remarkable activity against AML leukemia-initiating cells while sparing normal hematopoietic cells

Author: Etchin, Dana-Farber Cancer Institute
Poster: 4445/2
Session: PO.ET06.09. Novel Targets 1
Date/Time: Tuesday, April 21, 1:00 - 5:00 PM

Of note are the following abstracts further describing the potential role of selinexor in combination with novel and standard of care therapies across a variety of hematologic and solid tumor cancers:

Poster Title: Inhibition of exportin 1 (XPO1) by selinexor (KPT-330) synergistically suppresses growth of neuroblastoma in combination with doxorubicin or bromodomain inhibition

Author: Ranieri, Children's Hospital of Philadelphia
Poster: 501/27
Session: PO. TB08.01 Pediatric Cancer: Basic Science 1
Date/Time: Sunday, April 19, 1:00 - 5:00 PM

Poster Title: Preclinical activity in non-Hodgkin's lymphoma of selinexor, a selective inhibitor of nuclear export (SINE), is enhanced through combination with standard-of-care therapies

Author: Azmi, Wayne State University
Poster: 1756/29
Session: PO.ET06.02. Inhibitors of UPS and HSP90 Pathways and Other Targets
Date/Time: Monday, April 20, 8:00 AM - 12:00 PM

Poster Title: Selective inhibitor of nuclear export (SINE) compounds show synergistic anti-tumor activity in combination with dexamethasone in multiple myeloma

Author: Landesman, Karyopharm
Poster: 2074/22
Session: PO.MCB04.05. Oncogenes and Tumor Suppressors 2
Date/Time: Monday, April 20, 1:00 - 5:00 PM

Poster Title: Selinexor and melphalan combination therapy for the treatment of multiple myeloma

Author: Turner, Moffitt Cancer Center & Research Institute
Poster : 4434/21
Session: PO.ET04.05. Novel Mechanisms of Drug Response, Sensitivity, or Resistance 1
Date/Time: Tuesday, April 21, 1:00 - 5:00 PM

Poster Title:	Selinexor (KPT-330) radio-sensitizes non-small cell lung cancer cells in vitro and in vivo
Author:	Rashal, Karyopharm
Poster:	4490/17
Session:	PO.ET06.10. Novel Targets 2
Date/Time:	Tuesday, April 21, 1:00 - 5:00 PM

Poster Title:	Selinexor, a selective inhibitor of nuclear export (SINE), acts through NF-kB deactivation and combines with proteasome inhibitors to synergistically induce tumor cell death
Author:	Landesman, Karyopharm
Poster:	5472/24
Session:	PO.ET04.06. Novel Mechanisms of Drug Response, Sensitivity, or Resistance 2
Date/Time:	Wednesday, April 22, 8:00 AM - 12:00 PM

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound. Selinexor functions by binding with and inhibiting 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. Over 600 patients have been treated with selinexor in Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Karyopharm has initiated three registration-directed clinical trials of selinexor, one in older patients with acute myeloid leukemia (SOPRA), one in patients with Richter's transformation (SIRRT) and one in patients with diffuse large B-cell lymphoma (SADAL). Karyopharm plans to initiate a single-arm trial of selinexor in multiple myeloma in the first half of 2015 that is also intended to be registration-directed. In solid tumors, Karyopharm plans to initiate a Phase 3 pivotal trial of selinexor to treat liposarcoma during the second half of 2015. Other potential registration-directed trials in hematological and solid tumor indications are being evaluated. Additional Phase 1 and Phase 2 studies are ongoing or currently planned, including multiple studies in combination with one or more approved therapies in a variety of tumor types to further inform the company's clinical development priorities for selinexor. The latest clinical trial information for selinexor is available at 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. Karyopharm's SINE™ compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). SINE™ compounds have also shown biological activity in models of cancer, inflammation, autoimmune disease, certain viruses, and wound-healing. Karyopharm was founded by Dr. Sharon Shacham and is located in Newton, Massachusetts. For more information, please visit www.karyopharm.com.

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 PAK4 inhibitor, 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, 2014, which is on file with the Securities and Exchange Commission (SEC) as of March 13, 2015. 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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