Karyopharm Presents Data on Oncology Pipeline at EORTC-NCI-AACR Annual Meeting

- Selinexor Synergy with DNA Damage Inducing Treatments Provides Potential for Improved Clinical Outcomes -
- XPO1 Occupancy Assay Developed to Evaluate Selinexor Binding to its Target and Predicts Drug Exposure -
- Identification of Novel Mechanism PAK4 Allosteric Modulators with Anti-Tumor Activity, Including Inhibition of Tumor Cell Growth and Induction of Apoptosis -

NEWTON, Mass., Nov. 24, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the presentation of data describing its oncology product candidates at the 26th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Barcelona, Spain held November 18 to 21, 2014. Data for its lead product candidate, Selinexor (KPT-330), a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound, described its synergistic anti-tumor activity in combination with DNA damage-inducing treatments such as anthracyclines or radiation in a non-small cell lung cancer (NSCLC) mouse model. In addition, a description of a newly developed pharmacodynamic assay designed to evaluate direct Selinexor binding to XPO1 in patients was presented. Finally, data describing the identification of novel mechanism PAK4 allosteric modulators (PAMs) and their ability to inhibit tumor cell growth and induce apoptosis were presented.

"Presentations on Karyopharm's oncology pipeline at the EORTC-NCI-AACR Annual Meeting included data highlighting key Selinexor advantages, such as synergistic activity in combination with DNA damaging agents and the development of a new pharmcodynamic assay, as well as promising data on our earlier-stage PAK4 program," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Selinexor's synergy with DNA damaging agents, such as anthracyclines and radiation in solid and hematological cancers, provide the rationale for future combination clinical studies."

In a poster entitled "Selective Inhibitors of Nuclear Export (SINE™) Block the Expression of DNA Damage Repair Proteins and Sensitize Cancer Cells to DNA Damage Inducing Agents," data demonstrated that Selinexor inhibited the DNA repair mechanisms in solid and hematological cancer cell lines and therefore, preventing the cancer cell recovery following treatment with agents that cause DNA damage, leading to increased cancer cell death. These results suggest that such a combination treatment has the potential to result in improved clinical outcomes compared to each agent alone:

- Selinexor treatment following exposure to DNA damaging agents such as doxorubicin and idarubicin inhibited the repair mechanism of DNA damage caused by these agents and resulted in synergistic Acute Myeloid Leukemia (AML) cell killing as measured by induction of PARP and Caspase 3 cleavage.
- *In vivo*, low dose Selinexor (5 mg/kg) and radiation (3 Gy) decreased xenograft tumor size of non-small cell lung cancer (A549 cell line) by 12% and 30% relative to vehicle, respectively. In contrast, combination of Selinexor and radiation resulted in an 86% tumor decrease.

In a poster presentation entitled "Quantification of Exportin-1 (XPO1) Occupancy by Selective Inhibitor of Nuclear Export / SINE™ Compounds," data demonstrated the development of a new pharmacodynamic assay that evaluate direct binding of SINE to XPO1 by measuring XPO1 occupancy. This assay can be used to correlate Selinexor dose, XPO1 binding and anti-tumor activity.

In a poster entitled "Identification of Novel Small Molecules as Selective PAK4 Allosteric Modulators (PAMs) by Stable Isotope Labeling of Amino acids in Cells (SILAC)", results of preclinical developmental studies with Karyopharm's lead PAK4 allosteric modulators (PAMs) demonstrated anti-tumor activity both in vitro and in vivo. These novel orally bioavailable small molecules showed efficacy in both solid and hematological tumor xenograft models in mice with minimal toxicity.

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound. Selinexor functions by 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 500 patients have been treated with Selinexor in Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Karyopharm has initiated two registration-directed

clinical trials of Selinexor, one in older patients with acute myeloid leukemia and the other in patients with Richter's Transformation. Two additional registration-directed clinical trials in hematological indications, one in patients with diffuse large B-cell lymphoma (DLBCL) and the other in patients with multiple myeloma, are expected to begin enrollment during the fourth quarter of 2014 and first half of 2015, respectively. At least one additional registration-directed clinical trial in a hematologic or solid tumor indication is also planned for the first half of 2015. Additional Phase 1 and Phase 2 studies are ongoing or currently planned, including multiple investigator-sponsored studies of Selinexor in combination with one or more approved therapies. 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 drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitors of Nuclear Export / 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 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, 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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