Karyopharm Publishes Preclinical Data in Nature Demonstrating Selinexor's Potential in KRAS-Mutant Non-Small Cell Lung Cancer (NSCLC)

- Nuclear Transport Machinery Identified as a Necessary and Universal Driver of KRAS-mutant Cell Survival -
- Inhibition of the Nuclear Export Protein XPO1 Promoted Apoptosis across a Panel of Aggressive NSCLCs -

NEWTON, Mass., Sept. 29, 2016 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that preclinical data describing XPO1 inhibition with selinexor (KPT-330), the Company's lead, oral Selective Inhibitor of Nuclear Export / SINE™ compound, in a KRAS-mutant non-small cell lung cancer (NSCLC) model, were published online in Nature. The paper, titled, "XPO1 Dependent Nuclear Export is a Druggable Vulnerability in KRAS-mutant Lung Cancer," discusses preclinical results supporting selinexor's potential as a new therapeutic strategy for patients with highly aggressive and difficult to treat KRAS-mutant NSCLC.

In the manuscript, scientists from the University of Texas Southwestern Medical Center and Karyopharm demonstrated that KRAS-mutant NSCLC cells are addicted to Exportin 1 (XPO1) and that inhibition with selinexor induced robust cellular apoptosis of these malignant cells, both in vitro and in vivo.

"We are honored to collaborate with Dr. Michael White at UT Southwestern Medical Center on this important research. The KRAS gene is known to play an important role in cell division, differentiation and apoptosis," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "This research provides an improved understanding of the role of XPO1 nuclear transport in KRAS-mutant NSCLC and recognizes the potential for therapeutic intervention utilizing an XPO1 inhibitor such as selinexor in certain patient sub-types that can be identified through genomic screening. Beyond NSCLC, these findings could have implications in other KRAS-driven malignancies, including in patients with KRAS mutant colorectal cancer."

"Many of the most lethal human cancers harbor oncogenic mutant KRAS proteins, and this observation, combined with new detection methods to identify somatic KRAS mutant alleles in patient samples, has led to intensive efforts to develop drugs that inhibit KRAS activity," said Erkan Baloglu, PhD, Senior Director, Discovery and Early Development Program Lead at Karyopharm, and co-author of the paper. "However, advances have been hindered by several factors, including druggability of key pathway members and the swift development of acquired-drug resistance to otherwise effective targeted therapies. These data show the dependence of KRAS-mutant NSCLC cells on XPO1-mediated nuclear export, suggesting that XPO1 inhibition could provide a promising new therapeutic strategy for a considerable cohort of patients with lung cancer when coupled with genomics-guided patient selection and observation."

"Very importantly, this study also reveals potential predictive markers of response to selinexor and XPO1 inhibition," said Yosef Landesman, PhD, Senior Director, Head of Scientific Affairs at Karyopharm and co-lead author of the paper. "Those markers are genes from two central cellular pathways: The NFκB pathway that controls inflammation and tumorigenesis, along with the Hippo signaling pathway that controls organ size, cell proliferation and apoptosis."

As a result of this research, Karyopharm Therapeutics is evaluating the potential for a clinical trial of selinexor in patients with KRAS mutant NSCLC.

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. This reinitiates and amplifies their tumor suppressor function and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 1,700 patients have been treated with selinexor and it is currently being evaluated in several mid- and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in combination with low-dose dexamethasone (STORM) and backbone therapies (STOMP), and in acute myeloid leukemia (SOPRA), diffuse large B-cell lymphoma (SADAL), and liposarcoma (SEAL), among others. Karyopharm plans to initiate a pivotal randomized Phase 3 study of selinexor in combination with bortezomib (Velcade®) and low-dose dexamethasone (BOSTON) in patients with multiple myeloma in early 2017.

Additional Phase 1, Phase 2 and Phase 3 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 and related 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). In addition to single-agent and combination activity against a variety of human cancers, SINE™ compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm, which was founded by Dr. Sharon Shacham, currently has several investigational programs in clinical or preclinical development. 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), 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, including with respect to the need for additional clinical studies; 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, which was filed with the Securities and Exchange Commission (SEC) on August 4, 2016, 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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