Karyopharm Initiates Second Generation SINE™ Compound Clinical Trial in Multiple Myeloma

NEWTON, Mass., Jan. 19, 2016 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, announced today the initiation of a Phase 1/2 study of oral KPT-8602, a novel, second generation, small-molecule selective inhibitor of nuclear export (SINETM) protein XPO1, in patients with relapsed/refractory multiple myeloma (MM). This first-in-human study is designed to evaluate the safety, tolerability and activity of approximately eight dose levels of KPT-8602 in up to 116 patients in multiple centers in the United States and Canada. Karyopharm continues to expand its leadership in SINE-based therapies and is committed to being the world leader in nuclear transport modulation.

"We are encouraged by the preclinical profile of KPT-8602 and data presented at the 2015 American Society of Hematology annual meeting, which demonstrate that the compound can be dosed daily over five days per week in animals," said Sharon Shacham, PhD, President and Chief Scientific Officer of Karyopharm. "This dosing schedule and tolerability profile, if translated to the clinic, has the potential to yield a drug profile distinct from selinexor, Karyopharm's first-in-class, oral SINE compound. More frequent dosing provides continuous XPO1 inhibition and the potential for differentiated tolerability, efficacy, and combinability with available oncology treatments and targeted therapies. This first-in-human study represents a key expansion of our clinical pipeline and a new avenue for exploring and leveraging the mechanism for XPO1 inhibition in hematologic malignancies."

Data from several preclinical studies of KPT-8602 presented at the 2015 American Society of Hematology (ASH) annual meeting demonstrated that the compound had single-agent anti-MM activity. In addition, KPT-8602 showed synergistic activity against MM when combined with bortezomib, carfilzomib, doxorubicin, melphalan, topotecan, or VP16 as shown in proliferation and/or apoptosis assays on parental or drug-resistant cell lines, or patient derived MM samples. KPT-8602 was shown to have anti-MM activity in human tumor xenograft models as a single agent or in combination with melphalan. Promising preclinical efficacy included apparent cures in difficult murine models of AML and CLL. KPT-8602 represents a novel chemical series with pharmacological properties distinct from selinexor with more reversible binding to XPO1, similar potency in cell-based assays and substantially reduced brain penetration.

About KPT-8602

KPT-8602 is a second generation oral SINETM compound. KPT-8602 functions by binding to and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. KPT-8602 has demonstrated minimal brain penetration in animals, which has been associated with reduced toxicities in preclinical studies while maintaining potent anti-tumor effects.

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). In addition to single-agent activity against a variety of human cancers, SINE™ compounds have also shown biological activity in models of 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), KPT-8602 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2015, which is on file with the Securities and Exchange Commission (SEC) as of November 9, 2015, 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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