Karyopharm's Selinexor First-in-Human Phase 1 Clinical Trial Data Published in Journal of Clinical Oncology

NEWTON, Mass., March 04, 2016 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, announced today the publication of results from a Phase 1 clinical trial of selinexor in patients with advanced solid tumors in the Journal of Clinical Oncology. This 189 patient study evaluated the safety, pharmacokinetics, pharmacodynamics, and efficacy of selinexor (KPT-330), a novel, oral small-molecule inhibitor of exportin 1 (XPO1/CRM1), and determined the recommended Phase 2 dose. Karyopharm is conducting multiple later-phase clinical trials to evaluate selinexor in hematological cancers and solid tumors and has also initiated a double-blinded, placebo-controlled, randomized Phase 2/3 study of single-agent selinexor in patients with liposarcoma (SEAL study). The Company also expects to initiate a double-blinded, randomized Phase 2/3 study of selinexor in combination with carfilzomib and low-dose dexamethasone in refractory multiple myeloma patients in mid-2016 (SCORE study).

Dr. Albiruni Razak, MB MRCPI, Medical Oncology Lead in Sarcoma at Princess Margaret Cancer Centre and Mount Sinai Hospital, and lead author for the study, commented, "We are very excited with the results of this completely novel mechanism for treating a variety of solid tumors. Selinexor showed broad and durable disease control with clear tumor shrinkage across multiple tumor types, consistent with its mechanism of re-activing tumor suppressor proteins. We look forward to additional work in multiple solid tumors, both as a single agent and in combination with existing and emerging therapies."

"This study achieved an important milestone in establishing the recommended Phase 2 dose of 60 mg given twice a week. This dosing regimen is supported by results from other early-stage selinexor clinical trials across a variety of indications, which showed that selinexor, dosed at approximately 60 mg, is associated with maximal overall response rates. We believe that this dose optimizes the therapeutic window, response rates and duration of treatment," said Sharon Shacham, PhD, President and Chief Scientific Officer of Karyopharm. "Based on these encouraging single-agent data for selinexor, including partial responses and durable stable disease for greater than four months in a variety of heavily pretreated, advanced solid tumors, we have initiated clinical studies in gynecological malignancies, glioblastoma multiforme and liposarcoma and look forward to initiating studies in combination with existing therapies and emerging therapies, such as checkpoint inhibitors."

The primary objectives of the Phase 1 dose escalation trial in solid tumors were to determine the safety, tolerability and recommended Phase 2 dose of orally administered selinexor. All patients entered the study with advanced or metastatic solid tumors after a previous treatment (median of three prior therapies) and objectively progressing on study entry. Enrolled patients had received a median of three prior therapeutic regimens. Of these patients, 157 were evaluable for response. The disease control rate, meaning an objective response of stable disease (SD) or better, was 47%. A complete response was observed in one patient with melanoma and partial responses were observed in six patients, one each with colorectal cancer (KRAS mutant), melanoma, prostate cancer, ovarian adenocarcinoma, thymoma and cervical cancer. SD was noted in 67 patients (43%), with 27 patients (17%) experiencing SD for four months or longer, which Karyopharm believes is an indication of clinically significant anti-tumor activity.

The most common treatment-related adverse events of any grade in this phase 1 study included fatigue (70%), nausea (70%), anorexia (66%), and vomiting (49%), which were generally grade 1 or 2. Most commonly reported grade 3 or 4 toxicities were thrombocytopenia (16%), fatigue (15%), and hyponatremia (13%) which were manageable with dose interruption and/or supportive care.

The maximum-tolerated dose was defined at approximately 120 mg using a twice-a-week (days 1 and 3) dosing schedule. The recommended Phase 2 dose of 60 mg given twice a week was chosen based on better patient tolerability, longer duration of therapy, and no demonstrable improvement in radiologic response or disease stabilization compared with higher doses. There was no limit to the duration of therapy, and several patients remained on therapy for longer than one year, with the longest patients on therapy for over two years without clinically significant cumulative toxicities.

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. Over 1,400 patients have been treated with selinexor in company and investigator-sponsored Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Selinexor is being evaluated in several later-phase clinical trials, including one in older patients with acute myeloid leukemia (SOPRA), one in patients with Richter's transformation (SIRRT), one in patients with diffuse large B-cell lymphoma (SADAL), one in patients with liposarcoma (SEAL) and a single-arm trial of selinexor and lose-dose dexamethasone in patients with multiple myeloma (STORM). 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 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 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 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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