Karyopharm Therapeutics Presents Clinical Data on Selinexor (KPT-330) in Colorectal Cancer From Ongoing Phase 1 Study and Preclinical Data on Novel PAK4 Inhibitors at American Society of Clinical Oncology 2014 Gastrointestinal Cancers Symposium

- Data Demonstrate Preliminary Evidence of Anti-Tumor Activity of Oral Selinexor in Colorectal Cancer Patients -
- Potential Anti-Proliferative Activity of Novel PAK4 Inhibitor Seen in Preclinical Pancreatic Cancer Model -

NATICK, Mass., Jan. 22, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), 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, today announced data from two poster presentations at the American Society of Clinical Oncology (ASCO) 2014 Gastrointestinal (GI) Cancers Symposium that took place January 16-18 in San Francisco, California. The data presented included an update (as of December 16, 2013) from the ongoing Phase 1 study of oral Selinexor in solid tumors that show preliminary evidence of antitumor activity in metastatic colorectal cancer (CRC) patients. Additionally, data were presented on novel, oral p21-activated kinase 4 (PAK4) inhibitors that show anti-proliferative activity and tolerability in a preclinical pancreatic cancer model.

"We are very pleased with these preliminary results showing that single agent oral Selinexor has the potential to provide disease control in a subset of patients with heavily pretreated CRC. We are currently continuing our Phase 1 dose expansion cohorts and expect to report more data at the annual ASCO conference in June," stated Sharon Shacham, Ph.D., founder, Chief Scientific Officer and President of Karyopharm. "In addition, the preliminary preclinical data on our compounds that selectively inhibit PAK4 support our continued development of these potential therapies towards first-in-human studies."

Dr. Morten Sorensen (Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark) presented an update on 35 patients with heavily pretreated metastatic CRC (2-8 prior regimens including anti-folates, irinotecan, and oxaliplatin as well as bevacizumab, cetuximab, and/or regorafenib in many patients) whose tumors were progressing on study entry, from the ongoing Phase 1 dose escalation study in solid tumors. Patients were treated with oral Selinexor at doses ranging from 3 to 35 mg/m2. One patient had a partial response by standard RECIST (Response Evaluation Criteria In Solid Tumors) criteria and had remained on study for eight months. Eleven patients had stable disease; ten for eight weeks or longer with four of those ten patients (11%) demonstrating stable disease for over 25 weeks. Two patients were not evaluable for response, and 21 had progressive disease at first evaluation.

Adverse events associated with Selinexor in the Phase 1 study were primarily Grade 1 or 2, and were reduced or eliminated with standard supportive care. Clinically significant grade 3 or 4 adverse events were uncommon, and were reversible with supportive care and dose adjustment. Cumulative toxicities were rare, and no major organ dysfunction was noted. The most common adverse events were GI in nature including nausea (71%), vomiting (57%), anorexia (51%), weight loss (46%), taste alterations (49%), and diarrhea (26%). Grade 1/2 fatigue occurred in 49% of patients. Grade 1/2 blurred vision occurred in 20% of patients with no objective findings except for worsening of pre-existing cataracts in one patient, which was considered possibly related to Selinexor. Grade 3 hyponatremia (26%) was usually associated with dehydration, and grade 3 fatigue (23%) was rapidly reversible with supportive care and dose adjustment. Myelosuppression was uncommon with the most common form being grade 3/4 thrombocytopenia, which was reversible and not associated with bleeding.

Results supporting the possible mechanism of action of Selinexor in heavily pretreated CRC patients were also reported, as well as dose- and time-dependent pharmacodynamics analyses. Several of the patients in the study underwent pretreatment and on-treatment tumor biopsies. Microscopic analyses of the tumor lesions that shrunk, as detected by CT scan, showed that Selinexor induced nuclear localization of the tumor suppressor proteins p53 and/or FOXO1, reductions in proliferation rates as assessed by Ki67 staining, and increased apoptosis levels. In addition, in many of the tumor biopsies, malignant tumor cells were replaced by non-proliferative stromal (connective) tissue. Regarding pharmacodynamics, results presented in the patients with CRC showed that Selinexor induced a dose- and time-dependent increase in XPO1 messenger RNA in circulating

white blood cells, and that the effects lasted 24-48 hours. There was a trend to higher levels of XPO1 mRNA in patients who achieved stable disease or partial responses.

Dr. Sorensen commented, "This cohort of heavily pretreated patients with advanced CRC has received as many as eight prior regimens, each with several anti-cancer agents. These are incredibly sick patients with tumors that are growing on study initiation so we are excited about these early data with single-agent oral Selinexor. We look forward to obtaining additional data from cohorts at higher doses and from combination studies of oral Selinexor with already available anti-cancer agents."

Dr. Asfar Azmi (Wayne State University, Detroit, Michigan) presented data from a preclinical model of pancreatic cancer using some of Karyopharm's highly selective covalent allosteric inhibitors of PAK4. These compounds induced the death of pancreatic cancer cells in vitro, and showed preliminary tolerability in mouse studies, with efficacy models ongoing.

Dr. Azmi noted, "We are quite intrigued with the data we have generated to date in preclinical models of pancreatic cancer - one of the most difficult cancers to treat. Karyopharm's novel oral PAK4 inhibitor may represent a new approach to the treatment of this and other cancers, and we look forward to continuing work on these compounds."

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound that is undergoing Phase 1 studies in patients with advanced hematologic malignancies (NCT01607892), solid tumors (NCT01607905), and sarcomas (NCT01896505). Selinexor functions by blocking 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. It is believed that this leads to the selective induction of apoptosis in cancer cells, while largely sparing normal cells.

About Karyopharm

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 blocking XPO1, preventing the export of various proteins out of the nucleus. SINE compounds have shown biological activity in models of cancer, autoimmune disease, certain viruses, and wound-healing. Karyopharm was founded by Dr. Sharon Shacham and is located in Natick, Massachusetts.

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 SINE compounds and PAK4 inhibitors, 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), PAK4 inhibitors or any other drug candidate 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, 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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