

Karyopharm Announces Clinical Data for Selinexor (KPT-330) in Advanced Solid Tumors

- **Selinexor Demonstrates Clinical Activity in Prostate Cancer and other Solid Tumors -**
- **Data from Ongoing Phase 1 Clinical Study Presented at ESMO 2014 -**
- **Webcast Scheduled for Monday, September 29, 2014 at 4:30pm ET -**

NEWTON, Mass., Sept. 29, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, announced today the presentation of clinical data from an ongoing Phase 1 clinical study for its lead product candidate, Selinexor (KPT-330), a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound, in patients with advanced solid tumors. Data presented in patients with chemotherapy refractory, castrate-resistant prostate cancer (CRPC) treated with single-agent Selinexor showed a 60% disease control rate with maximum prostate-specific antigen (PSA) reduction ranging from 27% to 60% and duration of treatment up to 502 days. Selinexor also demonstrated early signs of clinical activity in other solid tumor indications including head and neck squamous cell carcinoma and ovarian cancer. Selinexor was shown to have manageable and predictable side effects, primarily nausea, fatigue and anorexia, which improve over time on treatment. These data were presented at the 2014 Congress of the European Society for Medical Oncology (ESMO), occurring September 26-30, 2014 in Madrid, Spain. The company will host a conference call to discuss the ESMO data on Monday, September 29, 2014 at 4:30pm ET.

"We continue to be impressed with the performance of Selinexor in advanced solid tumors," stated Dr. Sharon Shacham, PhD, President and CSO of Karyopharm. "In particular, the clinical activity and safety profile demonstrated in patients with chemotherapy refractory, castrate-resistant prostate cancer were very encouraging as these heavily pretreated patients have no other standard treatment options available. The safety and response data reported at ESMO further support our decision to proceed with Phase 2 studies in this difficult-to-treat patient population."

In an oral presentation entitled "Selinexor (KPT-330), an Oral, Selective Inhibitor of Nuclear Export (SINE) Shows Anti-Prostate Cancer (PrCa) Activity Preclinically & Disease Control in Patients (pts) with Chemotherapy Refractory, Castrate-Resistant Prostate Cancer (CRPC)", data evaluated as of September 10, 2014, demonstrated that of 15 enrolled patients, nine (60%) achieved stable disease and two (13%) had progressive disease with time to progression ranging from 31 to 502 days on study. Four patients were not evaluable for response.

"These data reveal Selinexor to be generally well-tolerated with manageable side effects and promising PSA decreases in patients with chemotherapy refractory, castrate-resistant prostate cancer," said Christopher J. Logothetis, M.D., Department Chair, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center. "Though early, these data support further studies of Selinexor in patients with treatment-resistant prostate cancer."

Karyopharm has previously announced the initiation of a Phase 2 single-agent, open-label study of Selinexor in patients with metastatic CRPC. The study, referred to as Selinexor in Hormone Refractory Indications in Prostate Cancer, or SHIP, is expected to evaluate approximately 50 patients with adenocarcinoma of the prostate with evidence for skeletal metastases on bone scan and/or CT scan. Approximately 50 qualifying patients with metastatic CRPC following at least one of the recently approved agents (enzalutamide, abiraterone or radium 223) will receive 50 mg/m² of Selinexor orally twice per week over each 28-day cycle. The study is being conducted at the MD Anderson Cancer Center lead by Drs. Christopher Logothetis and John Araujo. The primary goal of the study is to determine the disease control rate assessed according to RECIST criteria and the prevention of new bone lesions. The secondary goal of the study is to evaluate the PSA response relative to baseline. Additional studies in prostate cancer patients are planned.

In addition to data in patients with prostate cancer, Phase 1 study data was also presented that demonstrates the potential of Selinexor as a treatment for other heavily pretreated solid tumor indications, including head and neck squamous cell carcinoma and ovarian cancer. In a poster presentation entitled "Clinical Activity of the Oral Selective Inhibitor of Nuclear Export (SINE) Selinexor (KPT-330) in Patients with Head & Neck Squamous Cell Carcinoma (HN-SCC)", single-agent Selinexor was shown to stabilize disease progression in 11 (69%) of 16 heavily pre-treated patients with different types of head and neck squamous cell carcinomas. Several patients with thymic epithelial carcinomas showed durable disease shrinkage.

Based on the favorable safety profile to date and encouraging efficacy data, Karyopharm has initiated a Phase 2 single-agent study of Selinexor in patients with squamous cell carcinomas. The study, referred to as Selinexor

Treatment of Advanced Relapsed/Refractory Squamous Cell Carcinomas, or STARRS, is expected to evaluate approximately 66 patients with head and neck, lung and esophageal squamous cell carcinomas who have relapsed or have metastasis following chemotherapy. Eligible patients have received one or two prior therapies and have demonstrated progressive disease upon enrollment. Patients will receive single-agent oral Selinexor dosed twice weekly at 55 mg/m². The study will be conducted at approximately 28 sites in the United States and Canada. Disease control rate, defined as stable disease or better, is the primary endpoint.

In a second poster presentation entitled "Preclinical and Early Clinical Activity of the Oral Selective Inhibitor of Nuclear Export (SINE) Exportin 1 (XPO1) Antagonist Selinexor (KPT-330) in Patients (pts) with Platinum Resistant/Refractory Ovarian Cancer (OvCa)", Selinexor administered to seven heavily-pretreated patients with ovarian cancer was shown to induce durable disease stabilization or tumor size reduction, including one partial response, in three (60%) of five evaluable patients. Two patients (40%) experienced progressive disease and two patients withdrew consent or were not evaluable. Side effects were generally low grade and typically gastrointestinal in nature, or fatigue. These common side effects decreased over time, in part due to prophylactic use of standard supportive care. Major organ dysfunction or clinically significant cumulative toxicities have not been observed.

Karyopharm has previously announced the initiation of a Phase 2 single-agent study of Selinexor in patients with advanced gynecological malignancies. The study, referred to as Selinexor in Gynecology Neoplasms, or SIGN, is expected to evaluate approximately 63 patients with ovarian carcinoma, endometrial carcinoma and cervical carcinoma. Eligible patients have demonstrated progressive disease upon enrollment and have received at least one line of chemotherapy following relapse or, in the case of endometrial or cervical carcinomas, to treat advanced (stage IVb) disease. Patients receive single-agent oral Selinexor dosed twice weekly at 50 mg/m². The study is being conducted at approximately four sites in Europe. The primary goal of the study is to determine the disease control rate assessed according to RECIST criteria.

About the Phase 1 Study Design

This study of approximately 200 patients is an open label, multi-center study that was designed to determine the safety, tolerability and recommended Phase 2 dose of Selinexor with advanced or metastatic solid tumor cancers relapsed or refractory after multiple previous treatments and objectively progressing on study entry with no standard treatment options available. Other study endpoints include pharmacokinetics, pharmacodynamics, anti-tumor response and confirmation of recommended Phase 2 dose of Selinexor in this patient population. Patients were dosed orally between 3 mg/m² and 85 mg/m² three times weekly, twice weekly or once weekly and response evaluation was done every 2 cycles in accordance with RECIST criteria.

Webcast Information

Karyopharm will host a webcast and conference call today at 4:30 p.m. ET to discuss the data presented at ESMO. The webcast will be available on the Investors & Media section of the company's website, investors.karyopharm.com/events.cfm. To access the conference call, please dial (855) 437-4406 or (484) 756-4292 (international) at least five minutes prior to the start time and refer to conference ID 11655910. An archived webcast will be available on the Company's website approximately two hours after the event.

About Prostate Cancer

Approximately one in every seven men in North America will be diagnosed with prostate cancer during his lifetime, according to the American Cancer Society. In men, it is the most common malignancy other than skin malignancies, and the second most common cause of cancer death in North American males. Worldwide, prostate cancer ranks third in cancer incidence and sixth in cancer mortality among men. Despite the recent approvals of novel agents, the American Cancer Society estimates that over 29,000 men in the United States will die of prostate cancer in 2014, indicating the clear medical need for additional novel therapies.

About Squamous Cell Carcinomas

Squamous cell carcinoma (SCC) are uncontrolled growth of abnormal squamous cells, which comprise uppermost upper layers of skin and many other organs including the mouth, tongue, throat, larynx, and thymus, (comprising head and neck cancers), lungs, and parts of the esophagus. Non-skin related SCC are particularly difficult to treat, with few options once following initial combination chemotherapy ± anti-EGF-R antibody (i.e., cetuximab). There are approximately 42,000 head and neck, 6,000 esophageal, and more than 67,000 new lung SCC cancers diagnosed per year in the U.S. alone.

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 450 patients have been treated with Selinexor in Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Additional Phase 1 and Phase 2 studies are ongoing or currently planned and three registration-directed clinical trials in hematological indications have started enrolling patients or are expected to begin enrollment during 2014. 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 targets for the treatment of cancer and other major diseases. 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 Newton, Massachusetts. For more information about Karyopharm, 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 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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