Karyopharm Initiates Third Registration-Directed Clinical Trial of Oral Selinexor (KPT-330)

NEWTON, Mass., Dec. 11, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the initiation of the SADAL study, (Selinexor and Dexamethasone in Aggressive Lymphoma), a registration-directed, Phase 2b study of Selinexor (KPT-330), in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL). This randomized, multi-center study of Selinexor, one of the company's novel, oral Selective Inhibitor of Nuclear Export/SINE™ compounds, is being evaluated as a single agent in combination with dexamethasone for supportive care and is expected to enroll approximately 200 patients in approximately 90 sites worldwide. Karyopharm has received Orphan Drug Designation from the U.S Food and Drug Administration (FDA) and European Medicines Agency (EMA) for Selinexor for the treatment of patients with DLBCL.

This open-label Phase 2b study will evaluate the safety and efficacy of high dose (100 mg) versus mid dose (60 mg) Selinexor in combination with low dose (8-12 mg) dexamethasone for supportive care, each given orally to approximately 200 patients (100 per arm) with relapsed/refractory DLBCL. Overall response rate (ORR) is the primary endpoint. The study is expected to take approximately two years to complete and is intended to support accelerated regulatory approval. This study was designed in consultation with the FDA and on the basis of data from Karyopharm's ongoing Phase 1 study of Selinexor in patients with advanced hematologic malignancies. In that ongoing Phase 1 study, as of December 1, 2014, data from heavily pretreated patients with relapsed/refractory DLBCL and other types of non-Hodgkin's lymphoma (NHL) show:

- median duration of response (DOR) of approximately 7 months for Selinexor in patients with NHL;
- a 40% ORR in aggressive B-cell NHL, including four of 10 partial responses (PRs), in patients treated with high-dose (≥ 60 mg/m2 equivalent to &#62 100 mg) Selinexor, and a 37% ORR, including four complete responses (CRs) and three PRs, in patients treated with mid-dose (20-50 mg/m2 equivalent to ~60mg) Selinexor; and
- anti-tumor activity across DLBCL subtypes, including 36% and 40% ORRs in patients known to have the Germinal Center B-Cell like (GCB) or non-GCB subtypes, respectively, as well as a 50% ORR (1 CR, 1 PR) in four patients with "double-hit" DLBCL.

"This study in DLBCL is the third registration-directed study initiated for Selinexor this year. In June we initiated a registration-directed study evaluating Selinexor in patients with acute myeloid leukemia and in November we initiated a registration-directed study evaluating Selinexor in patients with Richter's Transformation," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "We are very encouraged by the responses and durability demonstrated to-date in patients with DLBCL and look forward to continuing to evaluate Selinexor in this patient population. Our goal is to accelerate development of Selinexor in severe hematologic indications with great unmet need while simultaneously broadening the scope of our development efforts in other hematologic and solid tumor indications."

About Diffuse Large B-Cell Lymphoma

Diffuse large B-cell lymphoma (DLBCL) is the most common form of non-Hodgkin lymphoma (NHL), accounting for up to 30 percent of newly diagnosed cases in the United States, with about 25,000 new cases per year. DLBCL is an aggressive type of NHL marked by rapidly growing tumors in the lymph nodes, spleen, liver, bone marrow, or other organs. Currently, DLBCL is initially treated with chemotherapy (with or without radiation). Some patients whose disease becomes refractory/relapse following chemotherapy may be eligible for stem cell transplant (with or without high-dose chemotherapy). Overall, about 60% of patients with DLBCL are cured, but the remainder have limited treatment options and eventually succumb to their disease.

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 550 patients have been treated with Selinexor in Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Karyopharm has initiated three registration-directed clinical trials of Selinexor, one in older patients with acute myeloid leukemia, one in patients with Richter's Transformation and one in patients with diffuse large B-cell lymphoma (DLBCL). At least one additional registration-directed clinical trial in a hematologic or solid tumor indication is also planned for the first half of

2015. Additional Phase 1 and Phase 2 studies are ongoing or currently planned, including multiple investigator-sponsored studies of Selinexor in combination with one or more approved therapies. 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 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). 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, the European Medicines Agency 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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