Karyopharm Presents Positive Combination Data for Selinexor (KPT-330) in Multiple Myeloma Patients at ASH 2014 Annual Meeting

- Selinexor Demonstrates Synergy in Combination with Approved Therapies for Multiple Myeloma -
- Durable Responses with Selinexor in Combination with Low-dose Dexamethasone in Heavily Pretreated Patients with Refractory Multiple Myeloma -
- Anti-myeloma Activity with Selinexor in Combination with Carfilzomib and Low-Dose Dexamethasone in Patients with Carfilzomib-Refractory Multiple Myeloma -

NEWTON, Mass., Dec. 8, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the presentation of positive clinical and preclinical combination data in multiple myeloma for its lead product candidate, Selinexor (KPT-330), a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound, at the 56th American Society of Hematology (ASH) Annual Meeting, held December 6-9, 2014 in San Francisco.

"We are encouraged to see the clinical response rates afforded by adding Selinexor to currently approved multiple myeloma therapies, including dexamethasone and carfilzomib," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Given the promising durability and preclinical support for synergistic activity with approved agents, we look forward to further evaluating the clinical benefits of Selinexor combination therapy in multiple myeloma."

In an ongoing Phase 1 clinical trial being conducted by Karyopharm, Selinexor in combination with low-dose dexamethasone demonstrated high rates of durable responses, including a 67% overall response rate (partial response or better) and an 89% clinical benefit rate (minimal response or better) in nine evaluable patients with heavily pre-treated and refractory multiple myeloma (one patient was not evaluable for response). Six of these patients remained on study for at least 16 weeks, including two for 28 and 43 weeks, respectively, who remained on study as of December 1, 2014. The overall median duration of response (DOR), which measures time from response to progression, is approximately 7 months.

A Phase 1/2 investigator sponsored study (IST) to evaluate tolerability and efficacy of the combination of Selinexor with the proteasome inhibitor carfilzomib (Kyprolis®) and low-dose dexamethasone (Car-Dex) is being conducted by the University of Chicago. In the first three treated patients, all of whom have myeloma refractory to carfilzomib and dexamethasone, Selinexor-Car-Dex induced one very good partial response (VGPR) and two partial responses (PR) with good tolerability. Dose escalation in this Phase 1 clinical study is ongoing.

In a related preclinical study conducted at the University of Chicago, Selinexor combined with carfilzomib induced both autophagy and apoptosis in multiple myeloma cell lines and patient samples, suggesting synergy through a combination-based priming effect. The combination had minimal effects on normal lymphocytes.

"Although early, the activity demonstrated with Selinexor in combination with carfilzomib and dexamethasone in these heavily pretreated patients with carfilzomib- and dexamethasone-refractory multiple myeloma in this ongoing clinical study is very encouraging," said Andrzej Jakubowiak, MD, PhD, Professor of Medicine, Director, Myeloma Program, University of Chicago. "Despite the advent of several new treatments for multiple myeloma, patients continue to have relapsed and refractory disease, and new agents with distinct mechanisms of action are needed."

Selinexor in combination with low-dose dexamethasone

In a poster presentation on Monday, December 8, 2014, entitled, "Selinexor Demonstrates Marked Synergy with Dexamethasone (Sel-Dex) in Preclinical Models and in Patients with Heavily Pretreated Refractory Multiple Myeloma (MM)," Karyopharm collaborators described the activity of Selinexor in combination with low-dose dexamethasone in heavily pre-treated and refractory multiple myeloma patients, including:

- Overall response rate of 67%, with one stringent complete response (sCR, 11%) and five partial responses (PR, 56%), and a clinical benefit rate of 89% in nine patients with heavily pretreated and refractory multiple myeloma treated with Selinexor in combination with low-dose dexamethasone (Sel-Dex), each dosed twice weekly at 45mg/m2 and 20mg, respectively.
- The Sel-Dex combination demonstrated reduction in nausea grades and very little weight loss compared with Selinexor alone. The most common Grade 1/2 adverse events were: nausea, fatigue, anorexia and vomiting.
- The Sel-Dex combination was also associated with an increase in time on study relative to Selinexor alone, with 66% of these nine evaluable patients remaining on study for at least 16 weeks, including two for 28 and 43 weeks, respectively, who remained on study as of December 1, 2014.
- During the dose evaluation part of the study, the 60 mg/m2 Selinexor dose was deemed intolerable in this heavily pretreated patient population. Selinexor 45 mg/m2 is the recommended future study dose.

Best Responses in Evaluable (N=9) Multiple Myeloma Patients
Oral Selinexor (45 mg/m2) and Dexamethasone (20 mg) (as of 1-Dec-2014)

Treatment	N	CBR	ORR	sCR	PR	MR	PD
Selinexor (45 mg/m2) + Low-Dose Dexamethasone (20 mg) (each 2x/week)	9	8 (89%)	6 (67%)	1 (11%)	5 (55%)	2 (22%)	1 (11%)

Selinexor in combination with carfilzomib

In a poster presentation on Saturday, December 6, 2014, entitled, "Gene Expression and Transcription Factor (TF) Activation Profiling Identifies Suppression of Multiple Myeloma (MM) Cell Survival and Chemoresistance Pathways by Inhibition of XPO1/CRM1-dependent Nuclear Export with Selinexor," Dr. Jakubowiak and colleagues at the University of Chicago described the activity of Selinexor in combination with carfilzomib and low-dose dexamethasone (Car-Dex) in patients with carfilzomib-refractory multiple myeloma in this ongoing Phase 1/2 clinical study. The group observed one very good partial response (VGPR) and two partial responses (PRs) in the first three patients with carfilzomib-refractory multiple myeloma evaluated to date. Dose escalation in this Phase 1/2 clinical study is ongoing. This study follows a

previously completed preclinical study conducted by the University of Chicago in which Selinexor in combination with carfilzomib in this patient population demonstrated a novel intracellular membrane-embedded mechanism of caspase activation suggesting a model of synergy wherein the Selinexor-carfilzomib combination promotes caspase activation, likely by induced proximity, cleavage of other caspases, and subsequent apoptosis as well as autophagy.

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 500 patients have been treated with Selinexor in Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Karyopharm has initiated two registration-directed clinical trials of Selinexor, one in older patients with acute myeloid leukemia and the other in patients with Richter's Transformation. Additional registration-directed clinical trials in hematological indications, including one in patients with diffuse large B-cell lymphoma (DLBCL) which is expected to begin in Q4 2014, are planned. 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 with 28 clinical trials involving 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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