

# Karyopharm Announces First Combination Data of Selinexor With Low-Dose Dexamethasone in Heavily Pretreated Multiple Myeloma Patients

NATICK, Mass., June 13, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced initial Phase 1 data from patients with multiple myeloma treated with Karyopharm's lead selective inhibitor of nuclear export (SINE), Selinexor (KPT-330), in combination with "low-dose" (20 mg twice weekly) dexamethasone. Among eight patients, the best responses were one stringent complete response (sCR), three partial responses (PRs), two minor responses (MRs), one progressive disease and one non-evaluable. Accordingly, the clinical benefit response rate (sCR+PR+MR) is 75% and the overall response rate (sCR+PR) is 50%. These new results will be reported at the 19th Congress of the European Hematology Association (EHA) in a poster presentation on Saturday, June 14th from 5:45 -7:00 PM CEST (Abstract #5580).

As part of Karyopharm's Phase 1 clinical trial of Selinexor in patients with advanced hematological malignancies, patients with multiple myeloma were treated with either single-agent Selinexor or Selinexor in combination with low-dose dexamethasone. Eight patients with multiple myeloma, whose disease was relapsed and/or refractory to all available classes of approved therapies and progressing on study entry, were treated with 45 mg/m<sup>2</sup> of oral Selinexor and 20 mg of dexamethasone, each dosed twice weekly. Patients had received a median of 5.5 prior lines of therapy. All had received prior therapy with a proteasome inhibitor and an immunomodulatory agent, while seven of the eight patients also received stem cell transplantations. Five of the six responding patients remain on study as of June 5, 2014, the data cut-off date. An additional 12 patients with multiple myeloma may be dosed with Selinexor in combination with dexamethasone in this arm of Karyopharm's ongoing phase 1 hematology study.

Adverse events in patients receiving single-agent Selinexor were generally low-grade, consistent with events observed in patients with other hematological malignancies and responsive to standard supportive care. Compared with Selinexor given alone, fewer adverse events in patients receiving Selinexor in combination with dexamethasone were reported, consistent with dexamethasone's reduction in Selinexor's main side effects of nausea, anorexia, and fatigue.

"We have observed patients with multiple myeloma receiving durable responses on Selinexor single-agent therapy. We are particularly excited to see that Selinexor with low-dose dexamethasone shows marked activity with rapid M-protein reductions and good tolerability, even in patients with disease refractory to pomalidomide and/or carfilzomib," stated Dr. Sharon Shacham, Karyopharm's Founder, President and CSO. "While we have seen safety and efficacy data to date with Selinexor as a single-agent therapy, we also believe that Selinexor may have strong synergistic potential with both existing and novel therapies."

In addition to the myeloma data, three presentations on Selinexor in acute myeloid leukemia (AML) will be given at EHA:

- An oral presentation on Sunday, June 15th from 11:15 - 11:30 AM CEST will focus on the activity of single-agent Selinexor in patients with heavily pretreated AML in the ongoing phase 1 study (Abstract #5591).
- Preclinical data from the combination of Selinexor with the FLT3 inhibitor quizartinib will be reported in a poster presented on Saturday, June 14th from 5:45 - 7:00 PM CEST (Abstract #5575).
- Preclinical data from the Ohio State University providing evidence that Selinexor restores topoisomerase II $\alpha$  (Topo II $\alpha$ ) to the nucleus and sensitizes resistant AML blasts to Topo II $\alpha$  inhibitors including adriamycin will be reported in a poster presented on Saturday, June 14th from 5:45 - 7:00 PM CEST (Abstract #5296).

Clinical and preclinical data on Selinexor in patients with double hit diffuse large B-Cell lymphoma (DLBCL) will be presented in a poster on Friday, June 13th from 5:45 - 7:00 PM CEST (Abstract #5378). New preclinical data include *in vitro* evidence of XPO1 overexpression in DLBCL cells along with cytotoxicity in DLBCL cell lines of multiple subtypes, including double hit DLBCL. Analyses of DLBCL cell lines show Selinexor can reduce cytoplasmic BCL2/BCL6 and c-MYC mRNAs, which likely contributes to Selinexor's activity in DLBCL. In the ongoing phase 1 study in patients with DLBCL treated with 3-80 mg/m<sup>2</sup> of Selinexor, responses were observed across GCB, non-GCB, and double-hit subtypes, and were also independent of prior therapies.

An additional poster presentation on Saturday, June 14th from 5:45 -7:00 PM CEST will provide results of Phase 1 and Phase 2 clinical trials of related SINE drug candidate Verdinexor (KPT-335) in spontaneous canine cancers, particularly lymphomas (Abstract #4791).

## About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. Selinexor functions by binding with 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. To date, over 300 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 are expected to begin enrollment during 2014. The latest clinical trial information for Selinexor is available at [www.clinicaltrials.gov](http://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 Natick, Massachusetts. For more information about Karyopharm, please visit [www.karyopharm.com](http://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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Source: Karyopharm Therapeutics

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