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Karyopharm Therapeutics Announces Highlights From Poster Presentations on Selective Inhibitors of Nuclear Export (SINE) Compounds in Hematologic Malignancies at 2013 ASH Annual Meeting

NATICK, Mass., Dec. 7, 2013 (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 preclinical and clinical data supporting the potential of its lead oral SINE compound Selinexor (KPT-330) in patients with relapsed and/or refractory acute myeloid leukemia (AML), multiple myeloma (MM) and other hematologic malignancies presented as posters at the 2013 American Society of Hematology (ASH) Annual Meeting being held in New Orleans, LA. Selinexor inhibits Exportin 1 (XPO1, also called CRM1), preventing the exportation of tumor suppressor proteins from, and leading to their accumulation in, the nucleus, which reinitiates and amplifies their natural apoptotic function in cancer cells. Selinexor is being evaluated in both hematologic malignancies and solid tumors with registration directed trials expected to commence in two indications in the first half of 2014.

"We believe our ongoing Phase 1 dose escalation clinical study in patients with progressive, relapsed, refractory AML and MM suggest that the observed activity in preclinical models evaluating SINE compounds may translate into clinical activity. Preliminary evidence suggests that single agent oral Selinexor has the potential to control disease and to induce remissions in AML, and to induce responses and disease control in patients with MM," said Sharon Shacham, Ph.D., Founder, Chief Scientific Officer and President of Research and Development of Karyopharm. "As we continue to enroll patients in our Phase 1 clinical studies in several hematologic malignancies, we believe that we are developing a deeper understanding of the underlying mechanisms of XPO1 inhibition and the crucial role nuclear transport plays in the survival of cancer cells."

The poster presentations included additional clinical data from the ongoing Phase 1 dose escalation clinical trial of Selinexor in patients with advanced relapsed and/or refractory hematologic malignancies. In addition, preclinical data across multiple hematologic malignancies were presented at the meeting.

Phase 1 in Relapsed Acute Myeloid Leukemia (AML)

Dr. Michael Savona (Sarah Cannon Research Institute, Nashville, TN) presented results from 38 heavily pretreated, transplant-ineligible (or relapsed after transplant) patients with AML (median age 68 years). Selinexor was administered across four dose levels (16.8 — 40mg/m^2). Rates of severe (grade 3 or 4) drug-related adverse events were < 6% except for thrombocytopenia without bleeding (8%, Grade 4 only) and fatigue (8%, Grade 3 only). In 33 patients evaluable for response, complete remissions with complete (CR, N=4) or incomplete (CRi, N=1) hematologic recovery were observed (CR+CRi 15%). Two patients had partial responses (PR) and one achieved a morphologic leukemia-free state (PR+MLFS 9%). As of December 4, 2013, five patients have remained on study for at least three months, with three of them on study for at least five months with no cumulative toxicity.

Phase 1 in Relapsed/Refractory Multiple Myeloma (MM)

Dr. Christine Chen (Princess Margaret Hospital, Toronto, ON) presented data on 25 patients with heavily pretreated MM or Waldenstrom's macroglobulinemia (WM). In this study, 25 MM and three WM patients received Selinexor across seven dose levels (3 to 35 mg/m^2). Selinexor was generally well tolerated with supportive care given for anorexia and fatigue. Rates of severe (grade 3 or 4) drug-related adverse events were < 5% except for thrombocytopenia without bleeding (20%), neutropenia (not associated with infection; 14%) and hyponatremia (grade 3, 10%; no grade 4). Results from the MM patients showed prolonged disease control and responses (see Table) with five patients remaining on the therapy for over five months and two patients for over one year without clinically significant cumulative toxicity. The maximum tolerated dose (MTD) has not yet been reached, and further evaluations at 45mg/m^2 are ongoing.

Responses in MM and WM patients as of December 4, 2013 are as follows:

Diagnosis	Patients Evaluated	Partial Response (PR) (%)	Minor Response (MR) (%)	Stable Disease (SD) (%)	Progressive Disease (%)	Withdrew Consent (%)	Total PRs, MRs, and SD (%)
MM (All Doses)	25	1 (4%)	4 (16%)	15 (60%)	4 (16%)	1 (4%)	20 (80%)

MM (≥ 16.8mg/m^2)	21	1 (5%)	4 (19%)	14 (66%)	1 (5%)	1 (5%)	19 (90%)
WM	3	--	3 (100%)	--	--	--	3 (100%)

Data from preclinical studies of SINE compounds were also presented supporting the role of XPO1 inhibition in promoting cell death while sparing normal cells and further demonstrating the potential of SINE compounds as single agent or combination treatments for hematologic malignancies including non-Hodgkin lymphoma (NHL), MM, chronic myeloid leukemia (CML), AML and mantle cell lymphoma (MCL).

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitors 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. This is believed to lead 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 the 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 Selinexor, 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 Selinexor 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 which may impact management's expectations are described in greater detail in the "Risk Factors" section of the prospectus for Karyopharm's initial public offering, which is on file with the Securities and Exchange Commission, and in subsequent filings filed by Karyopharm with the Securities and Exchange Commission. 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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