Karyopharm Presents Positive Clinical Data for Selinexor (KPT-330) in NHL Patients at ASH 2014 Annual Meeting

NEWTON, Mass., Dec. 8, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the presentation of positive clinical data 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. In an ongoing Phase 1 clinical trial evaluating the activity of Selinexor in patients with heavily pre-treated, progressive non-Hodgkin's lymphoma (NHL), including aggressive B-cell NHL such as diffuse large B-cell lymphoma (DLBCL), Richter's transformation, Burkitt lymphoma, mantle cell lymphoma, T-cell lymphoma and follicular/indolent lymphoma, Selinexor demonstrated a 37% overall response rate (partial response or better) and a 73% disease control rate (stable disease or better) in 52 patients who were evaluable as of December 1, 2014. Responses included five complete responses, four in patients with DLBCL and one in a patient with T-cell lymphoma, and Selinexor demonstrated a median duration of response (DOR) of approximately 7 months.

"We are extremely encouraged by the response rates, durability and tolerability observed with Selinexor in patients with advanced and progressing non-Hodgkin's lymphomas whose disease has relapsed after, or is refractory to, multiple previous regimens," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "In particular, these data further support our near-term focus on diffuse large B-cell lymphoma and Richter's transformation as part of our expedited registration strategy for hematologic malignancies."

"Patients with aggressive NHL that has relapsed after standard therapy have limited options and ultimately a minority are eligible for aggressive, curative treatment strategies such as stem cell transplantation. Patients who are ineligible for that type of treatment and those who have disease that recurs after transplant represent an area of high unmet medical need," said John Kuruvilla, MD, Division of Medical Oncology and Hematology at the Princess Margaret Cancer Center in Toronto, Canada. "Additionally, there are no therapies indicated to treat patients with Richter's transformation and these patients face an especially poor prognosis. We look forward to continuing to evaluate Selinexor in advanced NHL, particularly DLBCL and Richter's Transformation, with the goal of further improving clinical benefit and patient outcomes."

In an oral presentation on Monday, December 8, 2014, entitled, "The Oral Selective Inhibitor of Nuclear Export (SINE) Selinexor (KPT-330) Demonstrates Broad and Durable Clinical Activity in Relapsed / Refractory Non-Hodgkin's Lymphoma (NHL)," Dr. Kuruvilla described the activity of single-agent Selinexor in 52 heavily pre-treated NHL patients including:

- Overall response rate (partial response or better) of 37% (19/52) and disease control rate (stable disease or better) of 73% (38/52) in evaluable patients treated with single-agent Selinexor at doses of 3 to 80 mg/m2 taken orally once, twice, or three times each week in 28-day cycles (see Table below).
- Across all NHL types studied, responses could improve over time, with best responses including five complete responses (CR) (four in DLBCL and one in T-NHL). Eleven patients out of 52 have remained on therapy for more than 7 months (and up to 23 months) without clinically significant cumulative toxicities or major organ dysfunction.
- Clear activity was observed across all DLBCL subtypes evaluated, including a 36% overall response rate and an 82% disease control rate in 11 patients with Germinal Center B-Cell (GCB) like DLBCL and a 40% overall response rate (2 of 5) and an 80% disease control rate in patients with non-Germinal Center B-Cell (non-GCB, also called ABC)-like DLBCL. The disease control rate among four patients with "Double Hit" DLBCL was 75%; one patient achieved a CR with time on study in excess of 14 months, and a second patient with a PR on study for ~8 months.
- Selinexor treatment was generally well tolerated with supportive care and can be administered over a prolonged period. Grade 3/4 adverse events (≥5%) include thrombocytopenia (37%), neutropenia (22%), anemia (16%), fatigue (12%), leukopenia (10%) and hyponatremia (10%). The most common Grade 1/2 adverse events were: nausea (63%), anorexia (52%), fatigue (46%), and vomiting (36%) that tend to lessen in severity with supportive care and were seen less frequently following cycle 1.
- Increases in XPO1 mRNA levels, the pharmacodynamic marker for selinexor, were observed at all doses and sustained for up to 48 hours, supporting twice weekly dosing. The recommended maximal Phase 2/3 dose is 60 mg/m2 (~100mg flat dose) based on results across all Phase 1 studies.

Cancer Type	Selinexor Dose (mg/m2)	N*	ORR (%)	CR (%)	PR (%)	SD (%)	PD (%)
Aggressive B-NHL	≤ 20	4	1 (25%)	--	1 (25%)	1 (25%)	2 (50%)
(DLBCL, Transformed,	20 - 50	19	7 (37%)	4 (21%)	3 (16%)	5 (26%)	7 (37%)
FL-3b)	≥ 60	10	4 (40%)	--	4 (40%)	4 (40%)	2 (20%)
Follicular and	≤ 30	4	--	--	--	4 (100%)	--
Other Indolent NHL	≥ 35	4	2 (50%)	--	2 (50%)	1 (25%)	1 (25%)
Burkitt's Lymphoma	≥ 60	1	--	--	--	--	1 (100%)
Mantle Cell Lymphoma	≤ 30	2	1 (50%)	--	1 (50%)	1 (50%)	--
	≥ 35	1	--	--	--	--	1 (100%)
T-Cell Lymphoma	≤ 30	2	1 (50%)	--	1 (50%)	1 (50%)	--
	≥ 35	1	1 (100%)	1 (100%)	--	--	--
Richter's	≤ 30	3	1 (33%)	--	1 (33%)	2 (67%)	--
Transformation	≥ 35	1	1 (100%)	--	1 (100%)	--	--
TOTAL		52	19 (37%)	5 (10%)	14 (27%)	19 (37%)	14 (27%)

*Patients evaluable for disease response

Based on these data, Karyopharm has designed two registration-directed Phase 2 clinical trials:

- Selinexor in Relapsed/Refractory Richter's Transformation (SIRRT, NCT No. 02138786), a 50-patient single arm clinical trial that was initiated in November 2014.
- Selinexor and Dexamethasone in Aggressive Lymphoma (SADAL, NCT No. 02227251), a two arm trial in 200 patients with DLBCL following at least two prior chemoimmunotherapy regimens that is expected to begin prior to the end of 2014.

In addition, a randomized study of Selinexor in Older Patients with Relapsed AML (SOPRA, NCT No. 02088541) was initiated in mid-2014. Karyopharm

expects to initiate at least one additional registration-directed study in the first half of 2015.

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 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 for Selinexor, including 28 listed trials, 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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