Karyopharm Provides Data Update for Selinexor in Non-Hodgkin's Lymphoma and Acute Myeloid Leukemia at 2014 ASCO Annual Meeting

NATICK, Mass., May 31, 2014 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced multiple presentations of clinical data from an ongoing Phase 1 trial of its lead drug candidate, Selinexor (KPT-330), in patients with hematologic malignancies at the 2014 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL. The data indicate that first-in-class oral Selinexor showed continued evidence of anti-cancer activity as a single agent in patients with heavily pretreated Non-Hodgkin's Lymphoma (NHL) and Acute Myeloid Leukemia (AML) who had progressive disease on study entry.

Patients with relapsed and/or refractory NHL, including DLCBL and Richter's Syndrome, had a disease control rate (stable disease or better) of 74% across all doses of Selinexor; the overall response rate (ORR; partial response or better) was 28%. Responses were observed across all subtypes of NHL and independent of genetic abnormalities. Amongst 63 evaluable patients with heavily pretreated (median 3.5 prior therapies) and progressive AML, the complete response (CR) rate with or without full hematologic recovery was 11%, the ORR was 16% and the disease control rate was 49%; 16 (25%) of the 63 patients with AML were not evaluable but were included in the AML response rate calculation. Responses were observed across multiple genetic subtypes of AML. In both NHL and AML patient populations, side effects, which were generally low grade and typically gastrointestinal in nature, or fatigue, showed minimal dose response, in part due to the prophylactic use of standard supportive care. These common side effects decreased over time, permitting prolonged administration of Selinexor. Patients have remained on single agent oral Selinexor over one year. Major organ dysfunction or clinically significant cumulative toxicities have not been observed.

"We continue to be encouraged by the results and tolerability of oral Selinexor. The data presented today at ASCO further demonstrate the potential of Selinexor as a single agent for patients with relapsed or refractory hematologic malignancies who had previously progressed after available therapies," commented Sharon Shacham, Ph.D., Karyopharm's Founder, President and Chief Scientific Officer. "We have seen broad anti-cancer activity with rapid shrinkage of lymph nodes across all types of heavily pretreated NHL studied to date, including DLBCL subtypes that are often difficult to treat. We have been similarly impressed with the activity of Selinexor in patients with AML. The data further support our decision to move forward with registration-directed studies in AML, Richter's Syndrome and DLBCL."

Non-Hodgkin's Lymphoma

Dr. Martin Gutierrez from Hackensack University Medical Center, Hackensack, NJ, gave an oral presentation (Abstract #8518) with updated clinical trial data for patients with numerous NHL subtypes who were evaluated in Phase 1. Fifty-one patients, with mean prior treatment regimens of 4.1, received Selinexor orally 2-3 times per week across 10 dose levels (3 - 80 mg/m2). Grade 3/4 non-DLT adverse events (AEs) occurring in more than three patients included thrombocytopenia (20%), neutropenia (16%) and hyponatremia (6%). The most common Grade 1/2 AEs were nausea (51%), anorexia (41%) and fatigue (36%). The maximum tolerated dose was not reached, but based on biological activity and data from additional studies, the recommended Phase 2/3 dose of oral Selinexor for NHL is 60 mg/m2 twice weekly.

Single-agent anti-tumor activity was observed across all evaluated NHL subtypes with durable cancer control observed across several patients who remained on study for longer than nine months. Responses in 43 evaluable patients are shown below. Five patients had tumors deemed not evaluable and three patients had tumors pending evaluation. In patients with heavily pretreated DLBCL, bona fide responses and disease control were nearly identical across the ABC and GCB subtypes, consistent with the broad mechanism of action of Selinexor. Among four "double hit" DLBCL patients, there was one complete response, 2 patients with stable disease (43% and 45% lymph node reductions), and one progressive disease. Double hit is a particularly difficult-to-treat subtype which overexpresses the oncoproteins MYC and BCL2 or BCL6.

Best Responses in NHL/Richter's Syndrome Patients as of 13-May-2014

Cancer	N*	DCR (%)	ORR(%)	CR (%)	PR (%)	SD (%)	PD (%)	WC (%)
DLBCL	21	15 (70%)	6 (29%)	1 (5%)	5 (25%)	9 (40%)	5 (25%)	1 (5%)
Follicular	7	6 (86%)	1 (14%)	--	1 (14%)	5 (71%)	--	1 (14%)
Mantle Cell	3	2 (67%)	1 (33%)	--	1 (33%)	1 (33%)	--	1 (33%)
Transformed	3	1 (33%)	1 (33%)	--	1 (33%)	--	2 (67%)	--
T-Cell	4	3 (75%)	1 (25%)	1 (25%)	--	2 (50%)	--	1 (25%)
Richter's Syndrome	5	5 (100%)	2 (40%)	--	2 (40%)	3 (60%)	--	--
Total	43	32 (74%)	12 (28%)	2 (5%)	10 (23%)	20 (47%)	7 (16%)	4 (9%)

DCR=Disease Control Rate (CR+PR+SD), ORR=Overall Response Rate, CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease, WC=Withdrew Consent

Responses in Diffuse Large B-Cell Patients as of 13-May-2014

Type	N	DCR (%)	ORR (%)	CR (%)	PR (%)	SD (%)	PD (%)	WC (%)
GCB	11	8 (72%)	3 (27%)	1 (9%)	2 (18%)	5 (45%)	2 (18%)	1 (9%)
non-GCB	4	3 (75%)	1 (25%)	--	1 (25%)	2 (50%)	1 (25%)	--

"Data from this Phase 1 trial of Selinexor continue to show good tolerability when given with standard supportive care. There have been

durable clinical responses across a wide range of very sick patients with advanced NHL subtypes whose tumors have progressed on available agents," commented Dr. Gutierrez. "The responses in particularly hard to treat indications such as DLBCL and Richter's Syndrome are especially encouraging."

Acute Myeloid Leukemia

During a poster highlights presentation at ASCO (Abstract #7032), Dr. Karen Yee from Princess Margaret Hospital, Toronto, ON, presented data in AML patients treated with Selinexor. Sixty-five patients, most with three or more prior treatment regimens, received Selinexor orally 2-3 times per week across six dose levels (16.8 - 70 mg/m2). Grade 3/4 non-DLT AEs occurring in more than three patients included fatigue (18%), thrombocytopenia (15%), neutropenia (11%), and nausea (8%). The most common Grade 1/2 AEs were diarrhea (82%), anorexia (78%), nausea (74%), and fatigue (65%). Prolonged administration of Selinexor was feasible and there were no drug-associated deaths. Higher doses of Selinexor were associated with greater reductions in bone marrow blast counts, which were also observed across different AML subtypes. Responses in 63 patients are shown below, including sixteen patients (25%) who did not complete the first cycle of treatment and were therefore not evaluable for response, but are included in the response data. There have been no DLTs in AML patients and the maximum tolerated dose is ≥70mg/m2 twice weekly. The recommended Phase 2/3 dose of oral Selinexor for AML is 55mg/m2 twice weekly.

Best Responses in AML Patients as of 13-May-2014

N	DCR	ORR	CR	CR(i)	PR	MLFS	SD	PD	NE
63	31	10	5	2	1	2	21	16	16
%	49%	16%	8%	3%	2%	3%	33%	25%	25%

DCR=Disease Control Rate (CR+CR(i)+PR+MLFS+SD), ORR=Overall Response Rate (CR+CR(i)+PR+MLFS), CR=Complete Response, CR(i)=Complete Response Incomplete, MLFS=Morphological Leukemia Free State, SD=Stable Disease, PD=Progressive Disease, NE=Non Evaluable

The Phase 1 Clinical Trial of Selinexor in Hematologic Malignancies

Data were reported from 106 patients with NHL or AML as part of trial NCT01607892 in the dose escalation Phase 1 clinical trial. All patients entered the study with advanced hematologic malignancies relapsed or refractory after multiple previous treatments and objectively progressing on study entry. The primary objectives of the Phase 1 dose escalation trial were to determine the safety, tolerability and recommended Phase 2 dose of orally administered Selinexor. Patients were administered 8-10 doses of Selinexor from 3 - 80 mg/m2 orally in a 4-week cycle (2-3 times per week) and response evaluation was done every 1 - 2 cycles.

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.

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.

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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