

Karyopharm Announces Results from Interim Analysis of Phase 2 SOPRA Study Evaluating Selinexor in Relapsed/Refractory Acute Myeloid Leukemia

Study Will Not Reach Statistically Significant Improvement in Primary Endpoint of Overall Survival in Patients who are Unfit for Chemotherapy and/or Transplantation; Patients Deriving Benefit to Remain on Study Clinical Development Continuing in Promising Induction and Combination Settings

NEWTON, Mass., March 02, 2017 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the results of a planned interim analysis of the Phase 2 SOPRA study evaluating single agent selinexor in relapsed/refractory acute myeloid leukemia (AML). The Company determined in concert with the study's independent Data Safety Monitoring Board (DSMB) that SOPRA will not reach statistical significance for overall survival (OS), the study's primary endpoint. However, since selinexor-treated patients that achieved a complete response (CR) showed a substantial OS benefit as compared with the physician's choice (PC) arm, Karyopharm and the DSMB agreed that patients would be permitted to continue on the selinexor arm or the PC arm, as applicable, following discussion between the patient and their treating physician. The Company plans to continue clinical development of selinexor in AML through investigator sponsored trials in multiple combination regimens, including with chemotherapy, given encouraging data to date across these settings.

SOPRA is a Phase 2 randomized study of patients 60 years of age or older with relapsed or refractory AML who were ineligible for intensive chemotherapy and/or transplantation. Patients were randomized to either receive single-agent oral selinexor 60mg twice weekly or PC. PC included best supportive care (BSC) alone, or BSC plus either azacitidine (Vidaza®), decitabine (Dacogen®), or low dose cytosine arabinoside (LD-AraC). Based on unaudited site data, SOPRA enrolled 176 patients (median of two prior regimens) in the U.S., Canada, Europe and Israel. Among patients on the selinexor arm, 13% demonstrated a CR with or without full hematologic recovery (CRI) compared to 3% of patients on the PC control arm. Some patients remained on selinexor for over one year, but this did not result in a statistically superior OS compared to the PC arm. The DSMB found no new clinically significant adverse events in the patients receiving selinexor. Importantly, rates of sepsis and febrile neutropenia (FN) were lower on the selinexor arm (sepsis 4.9%, FN 14.7%) compared to the PC arm (sepsis 6.1%, FN 36.4%). As expected, the most common selinexor-related adverse events were nausea, anorexia, fatigue, vomiting, and thrombocytopenia. Patients who have benefited from selinexor treatment on the SOPRA study have the option to continue therapy.

"SOPRA is a robust, well-conducted trial and the response rates achieved with single-agent selinexor in this heavily pretreated older population have been encouraging," said Hagop Kantarjian, MD, Chair of the Department of Leukemia, The University of Texas MD Anderson Cancer Center. "Importantly, the safety profile was as expected and the recommended Phase 2 dose was generally well-tolerated. Unfortunately, as is common in AML, the higher response rates observed with single-agent selinexor versus physician's choice did not translate into extended survival in the overall population of these frail and heavily pretreated patients."

"After performing an in-depth analysis, we and the DSMB agree that, despite the higher complete response rates observed with selinexor, the phase 2 SOPRA study evaluating single-agent selinexor in relapsed or refractory AML has not reached statistical significance for overall survival, the primary endpoint of the study," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. "While we are disappointed with the overall outcome, we are pleased that 60mg of single-agent selinexor dosed twice per week was well-tolerated and carried no increased risk of sepsis or febrile neutropenia. At Karyopharm, our primary focus remains the advancement of selinexor in relapsed or refractory multiple myeloma, where we believe we have a clear path to regulatory approval."

Dr. Kauffman continued, "Beyond myeloma, we see diffuse large B-cell lymphoma (DLBCL) and liposarcoma as high unmet need indications where selinexor has a meaningful opportunity for clinical success and where we are expecting key data readouts during 2017. We look forward to reporting top-line data from our randomized Phase 2b SADAL study evaluating single-agent selinexor in patients with relapsed or refractory DLBCL in early 2017 and top-line data from the Phase 2 portion of the randomized Phase 2/3 SEAL study evaluating single-agent selinexor in patients with advanced liposarcoma in mid-2017."

Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm, commented, "We continue to believe selinexor has potential in AML, most likely in combination with other agents in front line and later settings. We continue to explore the use of selinexor in combination with novel and standard agents through investigator-sponsored AML studies. Clinical data recently reported at the 2016 American Society of Hematology annual meeting demonstrated that selinexor in combination with certain standard therapies, including intensive chemotherapy as well as hypomethylating agents, demonstrated encouraging activity in AML in adults, both as an initial therapy and in the relapsed setting. The benefit of selinexor in combination with intensive chemotherapy will be assessed in randomized investigator sponsored trials that we

expect will begin in 2017. Furthermore, selinexor in combination with intensive chemotherapy has shown very promising responses in pediatric patients with heavily pretreated AML."

"We are deeply grateful for the support and commitment of the AML investigators and the patients and families who have taken part in or contributed to the SOPRA study," Dr. Shacham concluded.

More About the Phase 2 SOPRA Study

The Phase 2 SOPRA (Selinexor in Older Patients with Relapsed/Refractory AML) study is a randomized trial evaluating single-agent selinexor (KPT-330), Karyopharm's lead, novel, oral Selective Inhibitor of Nuclear Export / SINE™ compound, versus physician's choice in patients 60 years of age or older with relapsed or refractory AML who were ineligible for intensive chemotherapy and/or transplantation. In the SOPRA study, 176 patients with AML whose disease had relapsed after, or was refractory to, first line therapy were randomized 2:1 to receive either oral selinexor (60 mg twice per week) or one of four physician's choice (PC) therapies. Physician's choice included best supportive care (BSC) alone, or BSC plus either azacytidine (Vidaza®), decitabine (Dacogen®), or low dose cytosine arabinoside (LD-AraC). The primary endpoint of the SOPRA study was overall survival (OS), with a target of a 75% improvement in OS from 3.0 months in the PC arm to 5.2 months in the selinexor arm. SOPRA was conducted at approximately 94 sites worldwide, including sites in the U.S., Canada, Europe and Israel.

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE™ compound. Selinexor functions by binding with and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. This reinitiates and amplifies their tumor suppressor function and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 1,900 patients have been treated with selinexor and it is currently being evaluated in several mid- and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in combination with low-dose dexamethasone (STORM) and backbone therapies (STOMP), and in diffuse large B-cell lymphoma (SADAL), and liposarcoma (SEAL), among others. Karyopharm plans to initiate a pivotal randomized Phase 3 study of selinexor in combination with bortezomib (Velcade®) and low-dose dexamethasone (BOSTON) in patients with multiple myeloma in early 2017. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with one or more approved therapies in a variety of tumor types to further inform the Company's clinical development priorities for selinexor. 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 and related 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). In addition to single-agent and combination activity against a variety of human cancers, SINE™ compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. Karyopharm, which was founded by Dr. Sharon Shacham, currently has several investigational programs in clinical or preclinical development. 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), 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, including with respect to the need for additional clinical studies; 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, which was filed with the Securities and Exchange Commission (SEC) on November 7, 2016, 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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