

Karyopharm Doses First Patient in Pivotal Phase 3 BOSTON Study Evaluating Selinexor in Patients with Relapsed/Refractory Multiple Myeloma

NEWTON, Mass., June 07, 2017 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced dosing of the first patient in its pivotal Phase 3 study, named the BOSTON (Bortezomib, Selinexor and dexamethasone) study, which will evaluate selinexor (KPT-330), the Company's lead, novel, oral Selective Inhibitor of Nuclear Export (SINE™) compound, in combination with Velcade® (bortezomib) and dexamethasone (SVd), in patients with relapsed or refractory multiple myeloma (MM).

This pivotal, multicenter, randomized, open-label Phase 3 clinical trial is designed to enroll approximately 360 patients and will evaluate the efficacy and safety of selinexor in combination with SVd, compared to Velcade and low-dose dexamethasone (Vd), in patients with MM who have had one to three prior lines of therapy. Patients randomized to the selinexor arm will receive selinexor (100mg weekly), Velcade (1.3 mg/m² weekly given subcutaneously for 4 of 5 weeks) and dexamethasone (40mg weekly), which is the standard "low-dose dexamethasone" commonly used in the treatment of MM. To Karyopharm's knowledge, this is the only Phase 3 study to date to utilize once weekly Velcade dosing. The primary endpoints of the study are progression-free survival (PFS) and overall response rate (ORR), and secondary endpoints include duration of response (DOR) and overall survival (OS), among others. Importantly, the BOSTON study allows for patients on the Vd control arm to crossover to the SVd arm following objective (quantitative) progression of disease. The Company expects to include over 100 clinical sites internationally in the BOSTON study and to complete enrollment in 2018, with top-line data anticipated in 2019.

"Based on clinical and preclinical data to date, we believe that the combination of selinexor, Velcade and dexamethasone could have multiple benefits for patients," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. "The SVd regimen with once-weekly Velcade dosing utilizes 40% less Velcade and 25% less dexamethasone than the standard Vd dosing regimen. In the studies to date, the dosing schedule and regimen required fewer clinic visits for patients and had a manageable side effect profile, including rates of peripheral neuropathy, which have been significantly lower in SVd clinical data to date, compared to the historical rates of peripheral neuropathy in the standard Vd dosing regimen. We also believe that the SVd combination may resensitize myeloma cells to Velcade and other proteasome inhibitors. Clinical data to date have demonstrated a significantly higher response rate in patients who have been exposed to a proteasome inhibitor and then receive a combination of a proteasome inhibitor, selinexor and dexamethasone, compared to historical response rates with the retreatment of a proteasome inhibitor and dexamethasone alone."

"Patient dosing is now underway in our pivotal Phase 3 BOSTON study, and the initiation of this study marks an important milestone for Karyopharm," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "The design of this important study was informed by the encouraging response data and durable responses observed in the SVd combination arm of the STOMP study, including in patients whose disease is already refractory to proteasome inhibitors. Assuming a positive outcome from the BOSTON study, we intend to use the BOSTON study data to support an NDA filing for selinexor for the treatment of relapsed or refractory myeloma."

Supportive Phase 1b/2 STOMP Study Results

The BOSTON study is supported by robust clinical data from the ongoing Phase 1b/2 STOMP study, which were presented at the American Society of Hematology (ASH) 2016 annual meeting in December 2016. The data presented at ASH reflected the potential synergistic effects of the SVd combination, which achieved high response rates in patients with heavily pretreated MM. The median DOR was 7.8 months. The combination was well-tolerated with the most commonly reported adverse events being fatigue, nausea, anorexia and vomiting, which were primarily grade 1 or 2 and reversible. Grade 3 adverse events included fatigue, diarrhea, thrombocytopenia and abdominal pain and each occurred at a rate of 6% (n=1). The only Grade 4 adverse event was thrombocytopenia and occurred at a rate of 12% (n=2).

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 2,000 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 a pivotal, randomized Phase 3 study in combination with Velcade® (bortezomib) and low-dose dexamethasone (BOSTON), in combination with low-dose dexamethasone (STORM) and backbone therapies (STOMP), and in diffuse large B-cell lymphoma (SADAL), and liposarcoma (SEAL), among others. 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. Additional 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 completion of enrollment for 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 March 31, 2017, which was filed with the Securities and Exchange Commission (SEC) on May 4, 2017, 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, except as required by law, 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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