Karyopharm Reports Positive Top-Line Phase 2b STORM Results and Reviews the Planned Development Path for Selinexor in Multiple Myeloma

- Selinexor Achieves Promising Response Rates in Patients with Multiple Myeloma, Including 20.8% in Quad-Refractory and 20.0% in Penta-Refractory Disease -
- Expanding Phase 2b STORM Study to Include Approximately 120 Additional Patients with Penta-Refractory Myeloma to Support Seeking Accelerated Approval -
- Plan to Initiate Pivotal Randomized Phase 3 "BOSTON" Study in early 2017 to Evaluate Selinexor in Combination with Bortezomib and Dexamethasone versus Bortezomib and Dexamethasone in Previously Treated Myeloma Patients -
- Management to Host Conference Call Today at 8:30 a.m. ET -

NEWTON, Mass., Sept. 06, 2016 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported positive top-line results from its Phase 2b STORM study evaluating the activity of selinexor (KPT-330) in multiple myeloma (MM). Selinexor, the Company's lead, novel, oral Selective Inhibitor of Nuclear Export / SINE™ compound, is being developed for the treatment of a variety of malignancies, including MM. Karyopharm also provided an overview of the planned development path for selinexor in MM.

The Phase 2b STORM study is a single-arm clinical trial evaluating selinexor in combination with low-dose dexamethasone in heavily pretreated MM patients, meaning patients with quad-refractory disease or penta-refractory disease. Patients with quad-refractory disease have previously received two proteasome inhibitors (PIs) (bortezomib (Velcade®) and carfilzomib (Kyprolis®)) and two immunomodulatory agents (IMiDs) (lenalidomide (Revlimid®) and pomalidomide (Pomalyst®)), and their disease is refractory to at least one PI, at least one IMiD, and has progressed following their most recent therapy. Patients with penta-refractory myeloma have quad-refractory disease that is also refractory to an anti-CD38 monoclonal antibody, such as daratumumab (Darzalex™) or isatuximab.

Among the 78 evaluable patients (median seven prior treatment regimens), the overall response rate (ORR) was 20.5% based on Independent Review Committee adjudication, including very good partial responses (VGPR) and partial responses (PR). Among the 48 patients in the quad-refractory group, the ORR was 20.8%. For comparison, in a similar quad-refractory patient population, Darzalex had an ORR of 21% and isatuximab had an ORR of 20%. Among the 30 patients in the penta-refractory group, the ORR was 20.0%. Several patients remain on study, including those with VGPRs, PRs and minor responses. To the Company's knowledge, no agent has previously shown activity in this penta-refractory population. The side effect profile for selinexor was consistent with previous trials, and no new safety signals were identified. Additional data will be presented later this year.

Keith Stewart, MB. ChB., Anna Maria and Vasek Polack Professor of Cancer Research at the Mayo Clinic and lead investigator of the STORM study, said, "Although treatment of multiple myeloma has improved dramatically, eventually many patients will develop refractory disease, no longer responding to any of the immunomodulatory agents and proteasome inhibitors commonly used (quad-refractory). These patients will also eventually progress on anti-CD38 monoclonal antibodies, which we refer to as penta-refractory disease. These are clearly the patients with the highest unmet need, as they have no remaining viable treatment options. The STORM data are compelling because they demonstrate that oral selinexor achieves a 20.8% response rate in the quad-refractory group, similar to recently reported intravenous anti-CD38 therapy results in the same patient population. Selinexor also achieves an equally notable 20.0% response rate in the penta-refractory group, with the significant advantage of oral administration. We are currently unaware of any other therapy, oral or intravenous, reporting such activity in these difficult-to-treat patients who have exhausted all available therapies."

In addition to the STORM study, Karyopharm initiated the Phase 1b/2 STOMP (Selinexor and Backbone Treatments of Multiple Myeloma Patients) study to evaluate selinexor in combination with existing therapies across the broader population in MM. In the arm evaluating the combination of selinexor, bortezomib and dexamethasone, dose escalation has been completed and the recommended dose has been determined, providing a basis for the randomized Phase 3 "BOSTON" study described below.

Sagar Lonial, MD, Professor and Chair, Department of Hematology and Medical Oncology, Emory University School of Medicine and Chief Medical Officer, Winship Cancer Institute of Emory University, commented, "Myeloma continues to be an incurable blood cancer in most patients and our main goal in treating refractory disease is to induce responses and maintain them as long as possible. In addition to these new data with oral selinexor and low-dose dexamethasone, the emerging clinical data from selinexor in combination with bortezomib, including in proteasome-inhibitor refractory disease, suggests a synergistic effect and favorable safety profile. These data are quite exciting and will form the basis for future studies."

Selinexor: Multiple Myeloma Clinical Development Plans and Timelines

Based on these positive top-line STORM data and existing unmet medical need, Karyopharm plans to implement the following clinical development initiatives focusing on obtaining regulatory approval of selinexor in MM:

- Karyopharm is expanding the STORM study to include approximately 120 additional patients with penta-refractory MM. To the Company's knowledge, this will be the largest study ever undertaken in this patient population. Assuming a positive outcome and remaining unmet medical need, Karyopharm intends to use the data from the expanded STORM study to support a request that the FDA consider granting accelerated approval for selinexor in MM. The Company anticipates reporting top-line data from the expanded cohort in early 2018.

- The FDA instituted its Accelerated Approval Program to allow for expedited approval of drugs that treat serious conditions and that fill an unmet medical need based on a surrogate endpoint or an intermediate clinical endpoint thought to predict clinical benefit, like ORR. Accelerated approval is available only for drugs that provide a meaningful therapeutic benefit over existing treatments at the time of consideration of the application for accelerated approval, which the FDA has reiterated in its feedback to the Company. Particularly in disease areas with multiple available and potential new therapies, such as MM, accelerated approval carries a high regulatory threshold. Drugs approved under the Accelerated Approval Program are also typically required to be studied in randomized confirmatory trials on a post-approval basis to confirm clinical benefit. Given the number of approved and experimental therapies in development to treat MM, and consistent with its standard guidance, the FDA has recommended that the Company conduct a randomized study geared towards full approval, which the Company is planning with the BOSTON study discussed below. In addition, to the Company's knowledge, no other studies are currently being conducted in the penta-refractory patient population and no agents have shown activity in these patients. In light of this unmet medical need, the Company believes that positive data in this patient population could support accelerated approval. The FDA has stated to the Company that other therapies in MM may receive full approval prior to the potential action date on any accelerated approval request for selinexor that the Company may submit, which may prevent accelerated approval for selinexor if the FDA deems that such therapies constitute earlier lines of therapy in MM that were not administered to patients in the STORM study. Also, while the FDA has previously indicated its preference for studies that isolate the effects of individual drugs, steroids like dexamethasone are part of nearly every myeloma treatment regimen, and low-dose dexamethasone is not a single-agent treatment for MM. Other available therapies for MM, such as pomalidomide (Pomalyst®), have received accelerated approval based on studies that were conducted in combination with dexamethasone or a similar steroid. Based on these factors, the Company believes that the STORM study design and the planned expansion in the penta-refractory patient group present an opportunity for the Company to request that the FDA grant accelerated approval if data from the expansion confirm the data presented today.

- The Company also plans to initiate a pivotal randomized Phase 3 study, known as the BOSTON (Bortezomib, Selinexor and dexamethasone) study, which will evaluate selinexor in combination with bortezomib (Velcade®) and low-dose dexamethasone (SVd) compared to bortezomib and low-dose dexamethasone (Vd) in patients with MM who have had one to three prior lines of therapy. Based on data from the Phase 1b portion of the STOMP study, which was most recently presented at the 2016 European Hematology Association Annual Meeting, the Company has identified the combination dose to be used in the BOSTON study. Karyopharm expects that the study will enroll approximately 360 patients. The Company intends to seek additional FDA input on the protocol for the BOSTON study prior to commencing the trial in early 2017.

- Based in part on its plans to conduct the pivotal randomized BOSTON study to support full regulatory approval of selinexor for patients with previously-treated MM and the Company's planned expansion of STORM to support potential accelerated approval, Karyopharm will not pursue the SCORE study at this time. The SCORE study was designed to assess the combination of selinexor with carfilzomib (Kyprolis®) and low-dose dexamethasone. The ongoing Phase 1/2 investigator sponsored study evaluating selinexor in combination with carfilzomib and dexamethasone in refractory MM, including carfilzomib-refractory MM, continues to enroll patients, and updated data from this study is expected to be

presented later this year.

"Our updated clinical development plan for selinexor in myeloma reflects the strong foundation of clinical data from both the STORM and STOMP studies," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. Dr. Kauffman was instrumental in the clinical development and regulatory approvals of Velcade® and Kyprolis® in MM. "We believe this development plan provides a path to potential FDA and EMA filings for oral selinexor in MM, with the potential to support accelerated or conditional approval if the FDA or EMA, respectively, agree. We look forward to sharing the additional data from both STORM and STOMP later this year. We believe selinexor has the potential to be a much-needed oral treatment option for patients suffering with this incurable disease."

More About the Phase 2b STORM Study

The Phase 2b STORM (Selinexor Treatment of Refractory Myeloma) (NCT02336815) study is a multi-center, single-arm clinical trial evaluating selinexor in combination with low-dose dexamethasone in patients with heavily-pretreated multiple myeloma (MM), which the Company refers to as having at least quad-refractory MM. These are patients who have received bortezomib (Velcade®) and carfilzomib (Kyprolis®), each of which is a proteasome inhibitor (PI), and lenalidomide (Revlimid®) and pomalidomide (Pomalyst®), each of which is an immunomodulatory agent (IMiD), and whose disease is refractory to at least one PI, at least one IMiD, and is refractory to their most recent therapy. Prior treatment regimens must have also included an alkylating agent and a glucocorticoid. In the original version of the protocol, at least 25% of patients in this study must have had MM that is also refractory to an anti-CD38 monoclonal antibody, such as daratumumab (DarzalexTM), which the Company refers to as having penta-refractory MM. Of the 79 patients enrolled in the first cohort, 78 had measurable disease at baseline, with 48 (62%) patients classified as having quad-refractory and 30 (38%) patients classified as having penta-refractory MM.

The primary endpoint of the STORM study is overall response rate (ORR). The original trial had several secondary endpoints, including ORR in patients whose disease is relapsed/refractory to an anti-CD38 monoclonal antibody, duration of response (DOR) and clinical benefit rate (CBR). Karyopharm is now expanding the STORM study to include additional sites in the United States and Europe to enroll approximately 120 additional patients with penta-refractory MM to further evaluate the safety and efficacy of selinexor as a basis for potential regulatory submission requesting accelerated (FDA) or conditional (EMA) approval, based on ORR.

More About the Phase 1b/2 STOMP Study

The Phase 1b/2 STOMP (NCT02343042) study is a multi-arm clinical trial evaluating selinexor and low-dose dexamethasone in combination with backbone therapies bortezomib (Velcade®), pomalidomide (Pomalyst®) or lenalidomide (Revlimid®) in patients with heavily pretreated relapsed/refractory MM. Each combination is evaluated on a separate arm of the STOMP study and, within each combination, each of two treatment cohorts will receive either once weekly or twice weekly dosing of selinexor.

Data from the STOMP study was initially reported at the European Hematology Association 2016 annual meeting. As of June 8, 2016, of the 16 patients treated in the SVd combination arm, all of whom are evaluable, 11 responded (1 patient with a complete response (CR), 3 with VGPRs and 7 with PRs for an ORR of 69%). An additional three patients achieved a minor response (MR), for a CBR of 88%. Several of the patients on this selinexor, Velcade and low-dose dexamethasone (SVd) combination arm had high-risk haplotypes, including deletion of chromosome 17p, and 10 of the 16 evaluable patients had MM previously refractory to a proteasome inhibitor. Seven of these 10 patients responded (1 CR, 1 VGPR, and 5 PRs) for an ORR of 70%. An additional patient achieved an MR for a CBR of 80% in this subgroup. Overall, side effects reported in the SVd arm were similar to, or less severe than, those observed with single-agent selinexor. Karyopharm plans to submit updated data from the STOMP study for presentation at a medical conference later this year. The Company is also planning to add two additional arms to the STOMP study — one to evaluate selinexor in combination with daratumumab (Darzalex™) and the other to evaluate selinexor in combination with Pomalyst, Velcade and low-dose dexamethasone.

Conference Call Information

Karyopharm will host a conference call today, Tuesday, September 6, 2016, at 8:30 a.m. Eastern Time, to discuss the top-line Phase 2b STORM results and the planned development path for selinexor in multiple myeloma. To access the conference call, please dial (855) 437-4406 (US) or (484) 756-4292 (international) at least five minutes prior to the start time and refer to conference ID: 74213103. Accompanying slides will be available under "Events & Presentations" in the "Investor" section of Karyopharm's website, http://www.karyopharm.com, where an audio recording of the call will be available approximately two hours after the event.

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. Over 1,600 patients have been treated with selinexor in company- and investigator-sponsored Phase 1 and Phase 2 clinical trials in advanced hematologic malignancies and solid tumors. Selinexor is currently being evaluated in several mid- and later-stage clinical trials, including a Phase 2b single-arm trial of selinexor and low-dose dexamethasone in multiple myeloma (STORM), a Phase 1b/2 trial in combination with backbone therapies in multiple myeloma (STOMP), a Phase 2 trial in older patients with acute myeloid leukemia (SOPRA), a Phase 2b trial in diffuse large B-cell lymphoma (SADAL), and a Phase 2/3 trial in 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. The latest clinical trial information for selinexor is available at www.clinicaltrials.gov.

About Multiple Myeloma

Multiple myeloma (MM) is form of blood cancer that develops in the bone marrow. In multiple myeloma, normal plasma cells transform into malignant myeloma cells and produce large quantities of an abnormal immunoglobulin called monoclonal protein or M protein. The monoclonal protein produced by myeloma cells interferes with normal blood cell production. In addition, the levels of functional immunoglobulins are depressed in individuals with multiple myeloma. Although the process is not completely understood, it appears that the functional immunoglobulins made by existing, healthy plasma cells breaks down more quickly in patients with multiple myeloma than in healthy individuals. MM is the second most commonly diagnosed blood cancer after Non-Hodgkin's Lymphoma (NHL). According to SEER data from the National Cancer Institute, in the United States in 2016 approximately 30,000 new cases of MM will be diagnosed, and approximately 12,500 patients will die from the disease. Approximately 100,000 people in the United States were living with MM in 2013. According to GlobalData, the 2015 MM market was valued at approximately $11 billion and the size of the myeloma market is projected to increase to over $22 billion by 2023.

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 June 30, 2016, which was filed with the Securities and Exchange Commission (SEC) on August 4, 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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https://investors.karyopharm.com/2016-09-06-Karyopharm-Reports-Positive-Top-Line-Phase-2b-STORM-Results-and-Reviews-the-Planned-Development-Path-for-Selinexor-in-Multiple-Myeloma