Phase 2b STORM Data Evaluating Selinexor in Patients with Penta-Refractory Multiple Myeloma Presented at the Society of Hematologic Oncology 2018 Annual Meeting

-- Oral Selinexor Achieves 26.2% Overall Response Rate and Duration of Response of 4.4 Months in Overall Study Population; Responses Typically Occurred Within 1 Cycle (4 Weeks) of Treatment --
-- Median Survival of 8.6 Months in All Patients; Median Survival of 15.6 Months in Patients with MR or Better --
-- Commercial Preparation Underway; New Drug Application Submitted to FDA --
-- Management to Host Conference Call Tomorrow, September 14, 2018 at 8:00 a.m. ET --

NEWTON, Mass., Sept. 13, 2018 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that updated clinical data from the Phase 2b STORM (Selinexor Treatment of Refractory Myeloma) study evaluating selinexor, the Company's lead, oral Selective Inhibitor of Nuclear Export (SINE) compound, in heavily pretreated patients with penta-refractory multiple myeloma, were presented during an oral session at the Society of Hematologic Oncology (SOHO) 2018 Annual Meeting on September 13, 2018, in Houston. Sundar Jagannath, MD, Director of the Multiple Myeloma Program, Professor of Medicine (Hematology and Medical Oncology) at Tisch Cancer Institute at Mount Sinai School of Medicine, and principal investigator of the STORM study, presented the data in a session entitled, "Phase 2b Results of the STORM Study: Oral Selinexor plus Low Dose Dexamethasone (Sd) in Patients with Penta-Refractory Myeloma."

"The additional Phase 2b clinical results presented today are very encouraging for the patients suffering from penta-refractory multiple myeloma and their families. Most notably, the overall response rate (ORR) for patients treated with oral selinexor and dexamethasone (dex; Sd) was 26.2% with median duration of response (DOR) of 4.4 months based on the Independent Review Committee (IRC) assessment, along with a median overall survival (OS) across the entire study of 8.6 months," said Dr. Jagannath. "Of particular significance, for the nearly 40% of patients who had a minimal response (MR) or better, the median survival was 15.6 months, which provided the opportunity for a meaningful clinical benefit for patients on the STORM study with advanced penta-refractory myeloma that is difficult to treat."

Dan Vogl, MD, MSCE, Assistant Professor of Medicine at the Hospital of the University of Pennsylvania, commented, "The results from the Phase 2b STORM study showed that selinexor resulted in a meaningful clinical benefit in this heavily pretreated patient population. This includes patients treated with the most modern combination therapies and most exciting experimental therapies. For example, the overall response rate was 29.1% in patients who had previously been treated with daratumumab combination regimens, and the two patients on the STORM study who had previously received investigational CAR-T cell therapy both achieved partial responses on selinexor and dexamethasone. These results provide further evidence that selective inhibition of nuclear export could be an effective strategy for myeloma therapy and of selinexor's potential to be a new option for patients with penta-refractory multiple myeloma."

"Patients with highly resistant myeloma have very few treatment options available, which underscores the urgent need for the advancement of therapies with novel mechanisms, like selinexor," said Sharon Shacham, PhD, Founder, President and Chief Scientific Officer of Karyopharm. "The 26.2% ORR from the STORM study is particularly meaningful considering that 96% of the patients had myeloma refractory to Kyprolis®, Pomalyst® and Darzalex®, and nearly 70% of patients had disease that was confirmed to be refractory to all five of the standard of care myeloma drugs, Revlimid®, Velcade®, Pomalyst®, Kyprolis®, and Darzalex®. These results reinforce the potential of selinexor in this difficult to treat patient population. Following our recent submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for selinexor with low dose dexamethasone, we are making great strides in building our key commercial capabilities as we prepare for a potential initial market launch, which could be as early as the first half of 2019. We also remain on track to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in the first quarter of 2019 for conditional approval in the same disease indication."

Karyopharm has submitted an NDA to the FDA, with a request for accelerated approval for oral selinexor with low dose dexamethasone as a new treatment for patients with penta-refractory multiple myeloma. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. The Company also plans to submit a MAA to the EMA in the first quarter of 2019 with a request for conditional approval. In parallel, Karyopharm is conducting the pivotal, randomized Phase 3 BOSTON study evaluating selinexor in combination with the proteasome inhibitor Velcade® and dex (SVd) for the treatment of patients with multiple myeloma who have had one to three prior lines of therapy. The Company expects to complete enrollment in the BOSTON study by the end of 2018, with top-line data anticipated in 2019. Assuming a positive outcome, Karyopharm plans to use the results from the BOSTON study to support an application for full approval of selinexor in relapsed/refractory multiple myeloma. Development of selinexor in other disease indications, including diffuse large B-cell lymphoma, liposarcoma, endometrial cancer and other malignancies remains

on track.

Phase 2b STORM Results

These clinical results are from Part 2 of the international, multi-center, single-arm Phase 2b STORM (Selinexor Treatment of Refractory Myeloma) study, which enrolled 122 heavily pretreated patients (median of seven prior treatment regiments) with penta-refractory myeloma. Each patient started 80mg oral selinexor twice weekly in combination with low-dose dexamethasone (dex; 20mg twice weekly). Patients with penta-refractory myeloma have previously received the two proteasome inhibitors (PIs), Velcade® (bortezomib) and Kyprolis® (carfilzomib), the two immunomodulatory drugs (IMiDs), Revlimid® (lenalidomide) and Pomalyst® (pomalidomide), and the anti-CD38 monoclonal antibody Darzalex® (daratumumab), as well as alkylating agents, and their disease is refractory to glucocorticoids, at least one PI, at least one IMiD, Darzalex and their most recent therapy.

For the STORM study's primary objective, oral selinexor achieved a 26.2% ORR, which included two stringent complete responses (sCRs), six very good partial responses (VGPRs) and 24 partial responses (PRs) in these patients with penta-refractory myeloma. The two sCRs were negative for minimal residual disease, one at the level of 1x10-6 and one at 1x10-4; this is particularly significant in this penta-refractory population. The ORR in patients who had previously received Darzalex® combination therapy (n=86) was 29.1%. The Disease Control Rate for patients who had achieved stable disease or better was 78.6%. All responses were confirmed by an IRC. Median progression-free survival (PFS) was 3.7 months and the median DOR was 4.4 months (range <1 to 9.9 months). Median OS across the study was 8.6 months. Median OS in the ~40% of patients with at least a MR on selinexor + dex was 15.6 months compared to a median OS of 1.7 months in patients whose disease progressed or were not evaluable ($p<0.0001$). The short median OS of patients with no response to selinexor is consistent with the lack of available effective therapies for the very heavily pretreated population who entered the study.

Across the relevant patient population, side effects of oral selinexor were generally predictable and often managed with dose adjustments and/or supportive care, with safety results that were consistent with those previously reported from Part 1 of this study (Vogl et al., J Clin Oncol, 2018) and from other selinexor studies. As anticipated, the most common non-hematologic treatment-related adverse events (AEs) were largely Grade 1/2 and included fatigue (70%), nausea (69%), anorexia (52%) and weight loss (47%). The most common Grade 3/4 AEs were cytopenias (thrombocytopenia (54%) and anemia (29%)) and were generally not associated with clinical sequelae. No significant major organ toxicities were observed, and bleeding and infection rates were low.

Conference Call Information

Karyopharm will host a conference call tomorrow, Friday, September 14, 2018, at 8:00 a.m. Eastern Time, to discuss the Phase 2b STORM clinical data presented at the SOHO 2018 Annual Meeting. The call will feature recognized myeloma experts Drs. Sundar Jagannath and Dan Vogl, along with members of the Karyopharm executive leadership team. To access the conference call, please dial (855) 437-4406 or (484) 756-4292 (international) at least five minutes prior to the start time and refer to conference ID: 8474737. The call will also be webcast live on the Company's website, http://www.karyopharm.com. An audio recording of the call will be available under "Events & Presentations" in the "Investors" section of Karyopharm's website approximately two hours after the event.

About Selinexor

Selinexor 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 2,600 patients have been treated with selinexor. In April 2018, Karyopharm reported positive top-line data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with penta-refractory multiple myeloma. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm has submitted a New Drug Application to the U.S. Food and Drug Administration, with a request for accelerated approval for oral selinexor as a new treatment for patients with penta-refractory multiple myeloma. The Company also plans to submit a Marketing Authorization Application to the European Medicines Agency in early 2019 with a request for conditional approval. Selinexor is also being evaluated in several other 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), as a potential backbone therapy in combination with approved therapies (STOMP), in diffuse large B-cell lymphoma (SADAL), liposarcoma (SEAL), and an investigator-sponsored study in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or planned, including multiple studies in combination with approved therapies in a variety of tumor types to further inform Karyopharm's clinical development priorities for selinexor. Additional clinical trial information for selinexor is available at www.clinicaltrials.gov.

Further Information About Potential Accelerated Approval for Selinexor in Multiple Myeloma

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 overall response rate. 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 multiple myeloma, accelerated approval carries a high regulatory threshold. Consistent with its general guidance, the FDA has noted to the Company its preference for randomized studies geared toward full approval, which the Company has undertaken with the ongoing pivotal, Phase 3 BOSTON study, and has reminded the Company that accelerated approval requires patients to have exhausted all available approved therapies. FDA's Fast Track designation is available to therapeutics treating an unmet medical need in a serious condition; the Company has received Fast Track designation from the FDA specifically for the population treated in the STORM trial. In light of this recognition that the STORM patient population represents an unmet medical need and the positive top-line data reported, the Company believes that the STORM study should support its request to the FDA for accelerated approval.

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 submissions to regulatory authorities, including the anticipated timing of such submissions, and the potential availability of accelerated approval pathways, the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor, and the plans for commercialization. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that regulators will agree that selinexor qualifies for accelerated approval in the U.S. or conditional approval in the E.U. as a result of the data from the STORM study in patients with penta-refractory myeloma or that any of Karyopharm's drug candidates, including selinexor, will successfully complete necessary 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, 2018, which was filed with the Securities and Exchange Commission (SEC) on August 7, 2018, 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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Source: Karyopharm Therapeutics Inc.

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