# Karyopharm Announces Outcome of FDA Advisory Committee Meeting Reviewing Selinexor for the Treatment of Patients with Triple Class Refractory Multiple Myeloma

February 26, 2019

NEWTON, Mass., Feb. 26, 2019 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) Oncologic Drugs Advisory Committee (ODAC) met to discuss the New Drug Application (NDA) for selinexor, a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. The NDA, which is currently under Priority Review by the FDA, is seeking accelerated approval for selinexor in combination with dexamethasone for the treatment of patients with relapsed refractory multiple myeloma who have received at least three prior therapies and whose disease is refractory to at least one proteasome inhibitor (PI), one immunomodulatory agent (IMiD), and one anti-CD38 monoclonal antibody.

The ODAC voted 8 to 5 recommending that the FDA wait for the results from Karyopharm's randomized, open-label, Phase 3 BOSTON study evaluating selinexor in patients with relapsed or refractory multiple myeloma, before making a final decision regarding approval. The BOSTON study is evaluating selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone compared to bortezomib and low-dose dexamethasone in patients with multiple myeloma who have had one to three prior lines of therapy. Importantly, in the selinexor arm of the study, both selinexor and bortezomib are administered once per week while in the control arm, bortezomib is administered at its currently indicated, twice per week schedule. Patient enrollment in the BOSTON study is now complete and top-line data are expected by the end of 2019 at the earliest, or into 2020, pending progression-free survival (PFS) events, a primary endpoint in this trial.

"While we are disappointed with ODAC's recommendation to delay the potential approval of selinexor, we plan to work with the FDA to evaluate the best path forward as they continue to review our NDA. Karyopharm remains committed to improving the outcomes of patients with cancer, including those with relapsed refractory multiple myeloma," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "Patients with triple class refractory multiple myeloma have disease which has progressed following treatment with the most effective myeloma drugs approved to date and are in desperate need of new treatment options. Karyopharm has assembled and submitted a compelling, comprehensive clinical data package to the FDA supporting the request for accelerated approval for selinexor. We are committed to working with the FDA, patients, and the myeloma community with the goal to provide selinexor as an option for those patients with no other options of known clinical benefit."

The ODAC is an independent panel of experts that evaluates data concerning the efficacy and safety of marketed and investigational products for use in the treatment of cancer and makes appropriate recommendations to the FDA. Although the FDA will consider the recommendation of the panel, the final decision regarding the approval of the product is made by the FDA solely, and the recommendations by the panel are non-binding.

Karyopharm's NDA seeking accelerated approval for oral selinexor in combination with dexamethasone as a treatment for patients with triple class refractory multiple myeloma who have received at least three prior therapies is under Priority Review by the FDA with an action date of April 6, 2019 under the Prescription Drug User-Fee Act (PDUFA).

The selinexor NDA is supported by data from Karyopharm's Phase 2b STORM ( **S**elinexor **T**reatment **o**f **R**efractory **M**yeloma) study, which evaluated selinexor and low-dose dexamethasone in 122 heavily pretreated patients with triple class refractory multiple myeloma who have been previously exposed to all five of the most commonly prescribed anti-myeloma therapies currently available. The study met its primary objective with an overall response rate (ORR) of 26.2%, which included two stringent complete responses (sCRs), six very good partial responses (VGPRs) and 24 partial responses (PRs). The most common adverse events included thrombocytopenia, nausea/vomiting, fatigue and decreased appetite. Adverse events were generally predictable and manageable with dose adjustments and treatment-emergent AEs leading to treatment discontinuation occurred in 26.8% of patients, and these were considered by the Investigator to be treatment-related in 17.9% of patients. Major organ toxicities were not prominent in this study and safety results were consistent with those previously reported from Part 1 of this STORM study (Vogl et al., J Clin Oncol, 2018) and from other selinexor studies.

The Company has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for selinexor requesting conditional approval for the treatment of patients with relapsed refractory multiple myeloma who have received at least three prior lines of therapy and whose disease is refractory to at least one PI, one IMiD, and one anti-CD38 monoclonal antibody. The selinexor MAA has been granted accelerated assessment by the EMA's Committee for Medicinal Products for Human Use.

Karyopharm will discuss ODAC's recommendation during the Company's previously-announced conference call on February 28, 2018 at 8:30 AM ET to report fourth quarter and year-end 2018 financial results. To access the conference call, please dial (855) 437-4406 (local) or (484) 756-4292 (international) at least 10 minutes prior to the start time and refer to conference ID 4246798. A live audio webcast of the call will be available under "Events & Presentations" in the Investor section of the Company's website, http://investors.karyopharm.com/events-presentations. An archived webcast will be available on the Company'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. In 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with triple class refractory multiple myeloma who have been previously exposed to all five of the most commonly prescribed anti-myeloma

therapies currently available. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm's New Drug Application (NDA) has been accepted for filing and granted Priority Review by the FDA, and oral selinexor is currently under review by the FDA as a possible new treatment for patients with triple class refractory multiple myeloma. The Company has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval and was granted accelerated assessment. Selinexor is also being studied in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). In 2018, Karyopharm reported positive top-line results from the Phase 2b SADAL study evaluating selinexor in patients with relapsed or refractory DLBCL after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. Selinexor has received Fast Track designation from the FDA for the patient population evaluated in the SADAL study. 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 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 currently 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.

**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 our expectations relating to submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the anticipated timing of such submissions and actions, 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, many of which are beyond Karyopharm's control, 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 triple class refractory myeloma or the SADAL study in patients with relapsed or refractory DLBCL 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 September 30, 2018, which was filed with the Securities and Exchange Commission (SEC) on November 8, 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.

Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited

**Contacts:**

**Investors:**
Karyopharm Therapeutics Inc.
Ian Karp
Vice President, Investor and Public Relations
857-297-2241 | ikarp@karyopharm.com

**Media:**
Argot Partners
David Rosen
212-600-1902 | david.rosen@argotpartners.com

Source: Karyopharm Therapeutics Inc.