Karyopharm Announces Positive Top-Line Data from Phase 2b STORM Study Evaluating Selinexor in Patients with Penta-Refractory Multiple Myeloma

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- Oral Selinexor Achieves 25.4% Overall Response Rate and Median Duration of Response of 4.4 Months in Patients with Penta-Refractory Myeloma -

- Company Plans to Submit a New Drug Application to the FDA in the Second Half of 2018 -

- Selinexor Continues to Demonstrate a Predictable and Manageable Tolerability Profile -

- Management to Host Conference Call Tomorrow, May 1, 2018 at 8:00 a.m. ET -

NEWTON, Mass., April 30, 2018 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported positive top-line results from the Phase 2b STORM study evaluating the Company's lead, oral Selective Inhibitor of Nuclear Export (SINE) compound selinexor in heavily pretreated patients with refractory multiple myeloma. Regarding the STORM study's primary objective, oral selinexor achieved a 25.4% overall response rate (ORR), which included two complete responses (CRs) and 29 partial (PRs) or very good partial responses (VGPRs) in these patients with penta-refractory myeloma. The median duration of response (DOR), a key secondary objective, was 4.4 months. All responses were confirmed by an Independent Review Committee (IRC). Selinexor was recently granted Fast-Track designation by the U.S. Food and Drug Administration (FDA) for this indication.

The data reported today are from Part 2 of the international, multi-center, single-arm Phase 2b STORM (**S**elinexor **T**reatment **o**f **R**efractory **M**yeloma) study, which enrolled 122 heavily pretreated patients with penta-refractory myeloma. Each patient received 80mg oral selinexor twice weekly in combination with low-dose dexamethasone (20mg twice weekly). In this study, penta-refractory is defined as patients who have previously received at least one alkylating agent, glucocorticoids, two immunomodulatory drugs (IMiDs) (Revlimid® (lenalidomide) and Pomalyst® (pomalidomide)), two proteasome inhibitors (PIs) (Velcade® (bortezomib) and Kyprolis® (carfilzomib)), and Darzalex® (daratumumab), an anti-CD38 monoclonal antibody, and whose disease is refractory to glucocorticoids, at least one PI, at least one IMiD, and Darzalex, and whose disease has progressed following their most recent therapy.

Oral selinexor demonstrated a predictable and manageable tolerability profile, 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 adverse events (AEs) were nausea, vomiting, fatigue and reduced appetite and were primarily low grade and manageable with standard supportive care and/or dose modification. The most common hematologic AEs were Grade ≥3 cytopenias and were generally not associated with clinical sequelae. Karyopharm plans to submit detailed STORM study results for presentation at an upcoming medical oncology meeting.

Paul G. Richardson, MD, Director of Clinical Research, Jerome Lipper Multiple Myeloma Center at the Dana-Farber Cancer Institute, said, "Despite numerous advances in myeloma treatment, currently available therapies are insufficient to address the increasing number of patients with highly resistant, penta-refractory myeloma, where the disease has ultimately become non-responsive to approved therapy. There is, therefore, a real urgency for new therapies with novel mechanisms of action for these patients, who have a critical unmet medical need. Selinexor's targeted inhibition of nuclear export could potentially expand the armamentarium of treatment options significantly in this important population for which no other established treatment is readily available."

"The 25.4% response rate and 4.4 month duration of response observed in the STORM study are highly compelling," stated Sundar Jagannath, MD, Director of the Multiple Myeloma Program and Professor of Medicine (Hematology and Medical Oncology) at Tisch Cancer Institute at Mount Sinai School of Medicine. "For an orally administered therapy, these new data underscore selinexor's potential to be an exciting new treatment option for these difficult-to-treat patients who have exhausted approved therapies."

Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm plans to submit a New Drug Application (NDA) to the FDA during the second half of 2018, 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 (MAA) to the European Medicines Agency (EMA) in early 2019 with a request for conditional approval. In parallel, Karyopharm is also conducting the pivotal, randomized Phase 3 BOSTON study evaluating selinexor in combination with the proteasome inhibitor Velcade and dexamethasone (SVd) for the treatment of patients with multiple myeloma who have had one to three prior lines of therapy. The Company is expecting 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 in the U.S.

"We are extremely grateful to, and thank, the patients, their families and the investigators for their important contributions to the STORM study," said Sharon Shacham, PhD, Founder, President and Chief Scientific Officer of Karyopharm. "Penta-refractory myeloma is an area of true unmet medical need as these patients have continued to progress despite receiving available therapies. We are fully committed to bringing this new, orally administered potential treatment option to patients who have no other therapy options of proven benefit. To our knowledge, oral selinexor is the most advanced agent being investigated in patients with penta-refractory myeloma and we look forward to submitting our NDA to the FDA during the second half of this year, with a submission to the EMA to follow."

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 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 recently 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 pivotal, Phase 3 BOSTON study, and has reminded the Company that accelerated approval requires patients to have exhausted approved therapies. The Company recently received Fast Track designation from the FDA, which is available to therapeutics treating an unmet medical need in a serious condition. In light of this recognition that the STORM patient population represents an unmet medical need and the positive top-line data reported today, the Company believes that the STORM study should support its request to the FDA for accelerated approval.

Conference Call Information

Karyopharm will host a conference call tomorrow, Tuesday, May 1, 2018, at 8:00 a.m. Eastern Time, to discuss the top-line Phase 2b STORM clinical data. The call will feature recognized myeloma experts Drs. Sundar Jagannath and Paul Richardson, 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: 9869309. 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 (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), thus leading to the accumulation of tumor suppressor proteins in the cell nucleus. This reinitiates and amplifies the tumor suppressor functions of these proteins and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 2,400 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 Karyopharm's clinical development priorities for selinexor. Karyopharm's composition of matter patent protection for selinexor is expected to remain in effect through at least 2032 prior to any applicable extensions (e.g., Hatch-Waxman Act, also known as the Drug Price Competition and Patent Term Restoration Act). 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, especially selinexor. 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 any of Karyopharm's drug candidates, including selinexor, will successfully complete necessary clinical development phases, that development of any of Karyopharm's drug candidates will continue or that any feedback from regulatory authorities will ultimately lead to the approval of selinexor or any of Karyopharm's other drug candidates. 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 Annual Report on Form 10-K for the year ended December 31, 2017, which was filed with the Securities and Exchange Commission (SEC) on March 15, 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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Contacts:

Investors:
Kimberly Minarovich

(646) 368-8014
kimberly@argotpartners.com

Mary Jenkins
(617) 340-6073
mary@argotpartners.com

Media:
David Rosen
(212) 600-1902
david.rosen@argotpartners.com

Primary Logo

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