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Karyopharm Announces Successful Outcome from Phase 2 Portion of Phase 2/3 SEAL Study Evaluating Selinexor in Patients with Previously Treated Advanced Dedifferentiated Liposarcoma

— The Primary Objective of Progression-Free Survival Favored Selinexor over Placebo; Hazard Ratio of 0.60 (RECIST v1.1), Representing a 40% Reduction in Risk of Progression or Death —

— Phase 3 Portion of Study Commenced; Expanded to Include North America and Europe and Expected to Enroll Up To 222 Patients —

— Top-line Data Expected by End of 2019 —

NEWTON, Mass., Sept. 20, 2017 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported a successful outcome from the Phase 2 portion of the SEAL study evaluating the activity of selinexor (KPT-330), the Company's lead, novel, oral Selective Inhibitor of Nuclear Export / SINE™ compound, in 57 patients with previously treated, advanced unresectable dedifferentiated liposarcoma. For the SEAL study's primary endpoint of progression-free survival (PFS), oral selinexor showed superiority over placebo, achieving a hazard ratio (HR) of 0.60, representing a 40% reduction in the risk of progression or death. PFS was assessed by Independent Central Radiological Review (ICRR) based on RECIST v1.1.

In this randomized, blinded Phase 2 portion of the study, oral selinexor demonstrated an expected and manageable safety profile, primarily with nausea, anorexia and fatigue, low levels of Grade 3/4 cytopenias, and no new or unexpected safety signals identified. The majority of treatment-related adverse events (AEs) were low grade and reversible with dose modifications and/or standard supportive care. Importantly, the incidence of infections in the selinexor arm (overall 29%; Grades ≥3, 0%) was less than that reported in the placebo arm (overall 39%; Grade ≥3, 19%).

Additional efficacy assessments included PFS by World Health Organization (WHO) response criteria, effects on metabolic parameters via PET Scans, and PFS according to Choi Criteria. PFS per WHO criteria achieved a HR of 0.84; the WHO response criteria will not be included as part of the Phase 3 study objectives. Karyopharm intends to submit detailed results from the Phase 2 portion of the SEAL study for presentation at a future medical meeting.

"There are few effective treatment options for previously treated patients with recurrent dedifferentiated liposarcoma and extending PFS is an important clinical goal because the rapid progression of disease frequently results in early mortality," said Mrinal M. Gounder, MD, Attending Physician, Sarcoma Service and Developmental Therapeutics Service, Memorial Sloan Kettering Cancer Center, and Lead Investigator of the SEAL trial. "These data are promising because they show that oral selinexor is active and has the potential to prolong PFS in this patient population, with an expected and manageable safety profile. As an orally administered agent, selinexor could be a welcome addition to the liposarcoma treatment landscape and we look forward to further elucidating selinexor's efficacy and safety in the already ongoing Phase 3 portion of the SEAL study."

The Phase 3 portion of the SEAL study, which was originally initiated in North America, is ongoing and has been expanded to include Europe. In this blinded, placebo-controlled Phase 3 study, up to 222 patients are expected to be enrolled and randomized 2:1 to receive either oral selinexor, (60mg fixed dose twice weekly) until disease progression or intolerability, or placebo. Patients whose disease progresses on placebo will be permitted to cross over to the selinexor arm. The primary endpoint of the Phase 3 portion of the study is PFS (RECIST v1.1) as assessed by the ICRR. The Phase 3 study design and primary endpoint of PFS were agreed to by the U.S. Food and Drug Administration (FDA). Top-line data from the Phase 3 portion of the SEAL study are anticipated by the end of 2019. Assuming a positive outcome, these data are expected to support a New Drug Application for oral selinexor as a potential new treatment for patients with advanced dedifferentiated liposarcoma.

"Liposarcomas are difficult to treat solid tumors that arise from the body's fat tissue cells or their precursors," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Dedifferentiated liposarcoma is an aggressive form of the disease that is resistant to both standard chemotherapy and radiation and has a particularly high rate of recurrence following surgery. Most patients who progress following surgery will ultimately succumb to their disease, highlighting the significant unmet need that exists for novel therapies. The FDA has confirmed their acceptance of the

proposed Phase 3 SEAL study design, including the PFS primary endpoint, and agreed that positive results from this study could support regulatory approval in this patient population."

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 2,100 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 enrollment of certain trials and the timing of 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 Karyopharm'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, 2017, which was filed with the Securities and Exchange Commission (SEC) on August 8, 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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Contacts:

Investors:
Kimberly Minarovich
(646) 368-8014
kimberly@argotpartners.com

Gus Jenkins

(646) 351-1067
gus@argotpartners.com

Media:
Eliza Schleifstein
(917) 763-8106
eliza@argotpartners.com