Karyopharm Presents Positive Phase 1/2 Eltanexor Data at the American Society of Hematology 2017 Annual Meeting

– Preliminary Data Show that Eltanexor is Well Tolerated and Demonstrates Promising Activity in Multiple Myeloma —
– Expanding Program to Include Colorectal Cancer, Castration-resistant Prostate Cancer, and Myelodysplastic Syndrome —

NEWTON, Mass., Dec. 10, 2017 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced the presentation of Phase 1/2 clinical data for its novel, second-generation oral SINE compound eltanexor (KPT-8602) at the American Society of Hematology (ASH) 2017 annual meeting being held December 9-12, 2017 in Atlanta. Clinical and preclinical data for its lead, oral SINE compound selinexor, and other pipeline asset KPT-9274, an oral, dual inhibitor of p21-activated kinase 4 (PAK4) and nicotinamide phosphoribosyltransferase (NAMPT) were also presented.

"A key presentation at ASH this year features updated Phase 1/2 data showing that eltanexor is well tolerated and demonstrates promising durable activity in patients with heavily pre-treated myeloma," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "The recommended Phase 2 dose (RP2D) has now been established. We have now begun enrolling patients into expansion cohorts where we are evaluating eltanexor in patients with advanced colorectal cancer (CRC), castration-resistant prostate cancer (crPC), and myelodysplastic syndrome (MDS)."

Updated Phase 1/2 Clinical Data for Oral Eltanexor

In the poster presentation titled, "Eltanexor (KPT-8602), a Second-Generation Selective Inhibitor of Nuclear Export (SINE) Compound, in Patients with Refractory Multiple Myeloma," (Abstract #3134) Robert Frank Cornell, MD, Vanderbilt University Medical Center, presented updated clinical data from a Phase 1/2 study evaluating the efficacy, tolerability, pharmacokinetics and pharmacodynamics of oral eltanexor with or without low dose dexamethasone, in patients with relapsed or refractory MM, most with quad- or penta-refractory disease. Using a 3+3 dose escalation design, oral eltanexor (5, 10, 20, 30, 40 and 60mg) was dosed either once daily for five days per week or once every other day for three days each week for a 28-day cycle. Patients with less than a minimal response after one cycle or partial response after two cycles were permitted to add dex. In some patients, dex was added beginning on Day 1. The following table is a summary of the efficacy results:

Best Responses1 in Evaluable Patients as of 3-Nov-20172

	N3	ORR	VGPR	PR	MR	SD	CBR
Patients receiving 20 and 30mg + dex	14	5 (36%)	1 (7%)	4 (29%)	4 (29%)	4 (29%)	9 (64%)
All	34	7 (21%)	1 (3%)	6 (18%)	9 (26%)	12 (35%)	16 (47%)

Key: ORR=Overall Response Rate (VGPR+PR), MR=Minor Response, SD=Stable Disease, CBR=Clinical Benefit Rate (VGPR+PR+MR)

1Responses were adjudicated according to the International Myeloma Working Group criteria

2Based on interim unaudited data

3Five non-evaluable patients: 1 dose limiting toxicity, 2 patient decisions, 1 lost to follow up, 1 principal investigator decision

Of the 34 evaluable patients, 14 received dex with their eltanexor regimen. Objective responses correlated with longer overall survival and all patients with a VGPR or PR are still alive or censored as of November 24, 2017. Deeper and faster responses were observed when dex was started on Day 1 of Cycle 1 versus delayed dex. Among the 35 patients evaluable for M-protein, 25 patients (71%) had reductions in M-protein. The median time on treatment for the overall study population was greater than 96 days (range, 10-441).

Among the 39 patients evaluable for safety, the most common Grade 1/2 adverse events were nausea (54%), fatigue (46%), anemia (38%), diarrhea (38%), dysgeusia (33%), weight loss (33%) and neutropenia (31%). As expected in this patient population, the most common Grade 3/4 adverse events were thrombocytopenia (56%), neutropenia (26%), anemia (15%), leukopenia (15%) and hyponatremia (10%). Importantly, nausea, fatigue, diarrhea and vomiting were nearly all Grade 1, manageable and transient, and bleeding was uncommon. The maximum tolerated dose was not reached; however, dose escalation was halted as responses were achieved. Based on these data, the RP2D has been established as 20mg eltanexor dosed five times per week with 20mg dex dosed twice weekly.

Based on these results, this Phase 1/2 study is being expanded to include patients with advanced CRC, crPC, and high risk MDS. These are indications where selinexor and XPO1 inhibition has shown clear activity, but where side effects such as fatigue and anorexia were problematic for patients due to the underlying malignancies. To date, eltanexor has shown lower levels of these side effects compared to selinexor and Karyopharm believes eltanexor has the potential to control malignancies in these indications with a favorable side effect profile.

"These Phase 1/2 results show that eltanexor, both alone or in combination with dex, induces responses or disease control and is associated with prolonged survival. The combination of eltanexor and low-dose dex was well tolerated and improved the anti-cancer activity, especially if started on Day 1 of Cycle 1. The RP2D regimen has now been established and we look forward to evaluating this promising combination in patients with CRC, crPC and high risk MDS," stated Dr. Cornell.

In addition to the Phase 1/2 eltanexor data, several other abstracts describing Karyopharm's drug candidates were presented at ASH 2017, including:

Oral Presentations

Title: PAK4 Inhibition Impacts Growth and Survival, and Increases Sensitivity to DNA-Damaging Agents in Waldenstrom Macroglobulinemia (WM)
Presenter: Li Na, Dana Farber Cancer Institute
Abstract Number/Publication ID: 648

Title: Selinexor in Combination with Cladribine, Cytarabine and G-CSF for Relapsed or Refractory AML
Presenter: Geoffrey Uy, Washington University School of Medicine in St. Louis

Abstract Number/Publication ID: 816

Title: The Mechanisms by Which Mutant-NPM1 Uncouples Differentiation from Proliferation Are Reversed By Several Drugs, Enabling Rational Multi-Component Non-Cytotoxic Differentiation Therapy
Presenter: Sauntharajah Yogen, Cleveland Clinic
Abstract Number/Publication ID: 878

Poster Presentations

Title: A Phase I/II study of Selinexor (SEL) with Sorafenib in Patients (pts) with Relapsed and/or Refractory (R/R) FLT3 mutated Acute Myeloid Leukemia (AML)
Presenter: Naval Daver, University of Texas MD Anderson Cancer Center
Abstract Number/Publication ID: 1344

Title: Selective Inhibition of Nucleocytoplasmic Transport Overcomes Ruxolitinib Resistance in Myelofibrosis (MF)
Presenter: Dongqing Yan, Huntsman Cancer Institute
Abstract Number/Publication ID: 1660

Title: XPO1 Inhibition Synergizes with BCR Inhibition, Blocks Tumor Growth and Prolongs Survival in a Bioluminescent Animal Model of Primary Central Nervous System Lymphoma (PCNSL)
Presenter: Marta Crespo, Hall d'Hebron, Barcelona
Abstract Number/Publication ID: 2808

Title: Phase I/II Study of Liposomal Doxorubicin (DOX) in Combination with Selinexor (SEL) and Dexamethasone (Dex) for Relapsed and Refractory Multiple Myeloma
Presenter: Rachid Baz, H. Lee Moffitt Cancer Center and Research Institute
Abstract Number/Publication ID: 3095

Title: Selinexor maintenance is feasible and tolerable after allogeneic stem cell transplant (allo-SCT) for patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)
Presenter: Hongtao Liu, University of Chicago Medical Center
Abstract Number/Publication ID: 3312

Title: Inhibition of XPO1 by KPT-330 (Selinexor) Enhances Cell Death Induced by the BCL-2 Selective Inhibitor ABT-199 (Venetoclax) through Downregulation of Mcl-1 in Acute Myeloid Leukemia
Presenter: Daniel Luedtke, Wayne State University School of Medicine
Abstract Number/Publication ID: 3819

Title: XPO1 Inhibitor Selinexor Overcomes Ibrutinib Resistance in Mantle Cell Lymphoma (MCL) via Nuclear Retention of IκB
Presenter: Mei Ming, University of Chicago
Abstract Number/Publication ID: 3837

About Eltanexor (KPT-8602)

Eltanexor (KPT-8602) is a second generation oral SINE compound. Eltanexor functions by binding to and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. Eltanexor has demonstrated minimal brain penetration in animals, which has been associated with reduced toxicities in preclinical studies while maintaining potent anti-tumor effects.

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 2,200 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. 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. 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, eltanexor (KPT-8602) or KPT-9274, 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 September 30, 2017, which was filed with the Securities and Exchange Commission (SEC) on November 2, 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
