Karyopharm to Present Preclinical Data at the American Association for Cancer Research 2018 Annual Meeting

Five Posters Highlighting Selinexor Data, Including in Combinations with Zejula® (niraparib) in Ovarian Cancer and Velcade® (bortezomib) in Neuroblastoma
Two Posters Featuring Eltanexor Data in Prostate Cancer and AML; One Poster with KPT-9274 Data in Pancreatic Cancer

NEWTON, Mass., March 19, 2018 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that eight posters will be presented at the upcoming American Association for Cancer Research (AACR) 2018 Annual Meeting taking place April 14-18, 2018 in Chicago. The eight poster presentations will feature preclinical data for the Company's lead, oral Selective Inhibitor of Nuclear Export (SINE) compound selinexor, its second-generation oral SINE compound eltanexor, and its pipeline asset KPT-9274, an oral, dual inhibitor of p21-activated kinase 4 (PAK4) and nicotinamide phosphoribosyltransferase (NAMPT).

Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm commented, "Collectively, the data being presented at AACR this year continue to provide important insights that will help guide the future clinical development of selinexor, eltanexor and KPT-9274 across a wide range of malignancies, both as single agents and in combination."

Details of each of the presentations are provided below:

Selinexor

- Galinski et al. show that the combination of selinexor with bortezomib (SV) is synergistic and reduces the activity of nuclear factor kappa-B (NFkB) in aggressive neuroblastoma cell lines. These results further support observed synergies driving Karyopharm's ongoing Phase 3 "BOSTON" study of SV plus low dose dexamethasone (SVd) versus Vd, which is being studied in patients with relapsed myeloma. Furthermore, these results may lead to additional applications of the SV and/or SVd combination regimens.

  Title:Combination Treatment with Selinexor and Bortezomib for Management of Highly Aggressive Neuroblastoma
  Presenter: Basia Galinski, Albert Einstein College of Medicine
  Poster Board #: 3193/25
  Session: PO.TB08.02 - Pediatrics 2: Preclinical Therapies, Resistance, and Stem Cells
  Location: Section 7
  Date and Time:Tuesday, April 17, 2018; 8:00 AM – 12:00 PM CT

- Chang et al. show that the combination of selinexor with the PARP inhibitor Zejula® (niraparib) provide enhanced efficacy over either agent alone in preclinical models of ovarian cancer. These results support the previously reported activity of single agent selinexor in patients with ovarian and endometrial cancers in the SIGN study (ESMO, 2017), as well as the ongoing combination of selinexor with the PARP inhibitor Lynparza® (olaparib) in an investigator-sponsored study at the MD Anderson Cancer Center in Houston, Texas. Furthermore, based on these data, selinexor combinations with additional PARP inhibitors are being considered.

  Title:Enhanced Anti-Tumor Effects of Selinexor and Niraparib in Preclinical Models of Ovarian Cancer
  Presenter: Hua Chang, Karyopharm Therapeutics, Inc.
  Poster Board #: 5826/22
  Session: PO.ET01.04 - Combination Chemotherapy 2
  Location: Section 37
  Date and Time:Wednesday, April 18, 2018; 8:00 AM – 12:00 PM CT

- Wahbe et al. show that selinexor has activity against glioblastoma multiforme (GBM) cells *in vitro* and *in vivo*, supporting the previously reported and ongoing study of single agent selinexor in recurrent GBM in clinical study KING. These data also support planned investigator-sponsored studies of selinexor in combination with radiation and/or other DNA-damaging agents in this indication.

  Title:The XPO1 Inhibitor Selinexor Attenuates Global Translation and Enhances the Radiosensitivity of

Glioblastoma Cells Grown In Vitro and In Vivo
Presenter:Amy Wahba, National Cancer Institute
Poster Board #: 4444/11
Session: PO.MCB04.04 - Post-transcriptional and Translational Control of Cell Fate
Location: Section 21
Date and Time:Tuesday, April 17, 2018; 1:00 PM – 5:00 PM CT

- Additional preclinical studies with selinexor support the potential for the agent in hormone receptor positive breast cancer as well as in gastric cancer.

  Title:Combined Targeting of Estrogen Receptor Alpha and Nuclear Transport Pathways Remodel Metabolic Pathways to Induce Autophagy and Overcome Endocrine Resistance
  Presenter:Zeynep Madak Erdogan, University of Illinois at Urbana-Champaign
  Poster Board #: 3733/3
  Session: PO.EN01.02 - Steroid Receptors and Preclinical Studies of Endocrine-Related Cancers
  Location: Section 31
  Date and Time:Tuesday, April 17, 2018; 8:00 AM – 12:00 PM CT

  Title:Nuclear Exporter Protein XPO1 a Novel Prognostic and Therapeutic Target in Gastric Cancer
  Presenter: Irfana Muqbil, University of Detroit Mercy
  Poster Board #: 2491/12
  Session: PO.MCB03.03 - Nuclear Oncoproteins and Tumor Suppressor Genes
  Location: Section 21
  Date and Time:Monday, April 16, 2018; 1:00 PM – 5:00 PM CT

Eltanexor

- Preclinical studies with eltanexor support the rationale for Karyopharm's ongoing single-agent study of eltanexor in multiple indications including castration-resistant prostate cancer (CRPC) and myelodysplastic syndromes (MDS), as well as in potential future combinations of eltanexor in CRPC, MDS or acute myeloid leukemias (AML).

  Title:Selective Inhibitor of Nuclear Export (SINE) Compound, Eltanexor (KPT-8602), Synergizes with Venetoclax (ABT-199) to Eliminate Leukemia Cells and Extend Survival in an In Vivo Model of Acute Myeloid Leukemia
  Presenter:Melissa A. Fischer, Vanderbilt University School of Medicine
  Poster Board #: 1877/8
  Session: PO.ET06.04 – Experimental Agents and Combinations for Hematologic Malignancies 2
  Location: Section 38
  Date and Time:Monday, April 16, 2018; 8:00 AM – 12:00 PM CT

  Title:Down-Regulation of AR Splice Variants Through XPO1 Suppression Contributes to the Inhibition of Prostate Cancer Progression
  Presenter: Irfana Muqbil, University of Detroit Mercy
  Poster Board #: 2492/13
  Session: PO.MCB03.03 - Nuclear Oncoproteins and Tumor Suppressor Genes
  Location: Section 21
  Date and Time:Monday, April 16, 2018; 1:00 PM – 5:00 PM CT

KPT-9274

- Mpilla et al. demonstrate that PAK4-NAMPT dual inhibition with KPT-9274 has activity in preclinical models of resistant pancreatic neuroendocrine tumors.

  Title:PAK4-NAMPT Dual Inhibition as a Feasible Strategy for Treatment of Resistant Pancreatic Neuroendocrine Tumors
  Presenter: Gabriel Mpilla, Wayne State University School of Medicine
  Poster Board #: 4368/10
  Session: PO.MCB01.01 - GTPases and Their Regulators and Effectors
  Location: Section 17
  Date and Time:Tuesday, April 17, 2018; 1:00 PM – 5:00 PM CT

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 Eltanexor

Oral eltanexor 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. Eltanexor is currently being evaluated in a multi-center, open-label, dose-escalation and dose expansion Phase 1/2 clinical study to assess its safety, tolerability, and efficacy in patients with relapsed or refractory multiple myeloma, colorectal cancer, castration-resistant prostate cancer, and myelodysplastic syndrome.

About KPT-9274

KPT-9274 is a first-in-class, orally bioavailable, small molecule immunometabolic modulator that works through non-competitive dual inhibition of p21-activated kinase 4 (PAK4) and nicotinamide phosphoribosyltransferase (NAMPT). NAMPT and NAPRT (Nicotinate Phosphoribosyltransferas) are the two main pathways for production of the NAD (nicotinamide dinucleotide). About 15-30% of all solid tumors are deficient in NAPRT, making them reliant on NAMPT for NAD production. Co-inhibition of PAK4 and NAMPT is believed to lead to synergistic anti-tumor effects through suppression of ß-catenin by blocking PAK4, leading to both immune cell activation and inhibition of tumor growth, blockade of DNA repair, cell cycle arrest, and energy depletion through NAMPT inhibition, and ultimately apoptosis. KPT-9274 may therefore have both immune-activating and direct antitumor effects. Tumors deficient in NAPRT may be particularly susceptible to KPT-9274's actions. In contrast, normal cells are less sensitive to inhibition by KPT-9274 due in part to their relative genomic stability and lower metabolic demands. KPT-9274 is currently being evaluated in an open-label Phase 1 clinical study, to assess its safety, tolerability and efficacy in patients with advanced solid malignancies (including sarcoma, colon and lung cancer) or relapsed non-Hodgkin's lymphoma (NHL) following standard therapy(s).

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 drug candidates, including selinexor, eltanexor 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 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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Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited
Lynparza® is a registered trademark of AstraZeneca AB Corporation

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