Karyopharm Presents Data Demonstrating the Potential of Nuclear Export Protein Exportin 1 (XPO1) Inhibition in the Treatment of Traumatic Brain Injury

NEWTON, Mass., April 20, 2016 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced preclinical data demonstrating the activity of its Selective Inhibitor of Nuclear Export (SINETM) compound, KPT-350, in rodent models of traumatic brain injury (TBI). These data were presented at the 2016 Annual Meeting of the American Academy of Neurology (AAN) taking place April 15-21 in Vancouver, Canada.

"In addition to its clinically-validated activity in a broad range of hematologic and solid tumor cancers, nuclear export protein Exportin 1, or XPO1, has also emerged as an attractive target for the treatment of neuro-inflammatory disorders such as traumatic brain injury," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "XPO1 is known to be upregulated in neuropathology and may mediate some of the inflammatory and neurodegenerative processes observed after TBI. By inhibiting XPO1, SINE compounds such as KPT-350 have demonstrated tolerability, brain penetrance and therapeutic activity, including neuroprotective, anti-inflammatory and anti-epileptic effects in preclinical studies. These findings warrant further evaluation of KPT-350 in neurological indications such as traumatic brain injury."

In an oral presentation titled "Functional and Imaging Studies of the Selective Inhibitor of Nuclear Export (SINE) Compound KPT-350 in a Clinically Relevant Murine Model of Traumatic Brain Injury (TBI)," Karyopharm researchers and collaborators presented data evaluating the efficacy of KPT-350 as a treatment for TBI in a murine model of closed head injury (CHI) and determined that orally administered KPT-350 improved functional outcomes, possibly by reducing cytotoxic intracellular edema.

Highlights of the data include:

- KPT-350 demonstrated improved long-term measures of physical and cognitive function relative to the vehicle or delayed treatment group.
    - Mice that received KPT-350 two hours post-CHI recovered body weight more quickly and performed better in the Rotarod test of vestibulomotor function
    - Diffusion tensor imaging studies demonstrated changes in the mean diffusivity index in several brain regions, suggesting that KPT-350 reduced cellular swelling versus vehicle

In an oral and poster presentation titled "Using the Selective Inhibitor of Nuclear Export (SINE) Compound KPT-350 to Reduce Cortical Circuit Hyperexcitability and Interneuron Cell Loss in the Controlled Cortical Impact (CCI) Model of Traumatic Brain Injury (TBI)," Karyopharm researchers and collaborators presented data evaluating the effects of orally administered KPT-350 on cortical network dysfunction in a murine model of TBI and determined that KPT-350 treatment protected mice from the damaging electrophysiological changes associated with CCI injury, suggesting a potential anti-epileptogenic effect.

Highlights of the data include:

- Following CCI-injury, brain tissues from mice treated with KPT-350 were free of seizure-associated activity, as compared with vehicle-treated mice, which showed high levels of such activity
- KPT-350 treatment normalized various measures known to correlate with aberrant brain function, such as coastline values and input-output response relationships, as compared with vehicle

About KPT-350

KPT-350, an oral SINETM compound, is an investigational new drug application-ready oral compound with preclinical data supporting potential efficacy in a number of neurological, autoimmune and inflammatory conditions. XPO1 inhibition leads to potent, multifaceted inhibition of the inflammatory mediator nuclear factor kappa-light-chain-enhancer of activated B cells, or NF-kB, a protein that plays very important roles in many types of inflammation. KPT-350 has additional important activities such as activation of proteins leading to anti-oxidant and neuroprotective properties. Preclinical data, generated mainly by Karyopharm's academic collaborators, has shown efficacy of orally-administered KPT-350 in animal models of amyotrophic lateral sclerosis, or ALS, traumatic brain injury, or TBI, multiple sclerosis, or MS, systemic lupus erythematosus, or SLE, and rheumatoid arthritis, or RA.

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 was founded by Dr. Sharon Shacham and is located in Newton, Massachusetts. 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 the timing of initiation of certain trials and of the 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 the company's current expectations. For example, there can be no guarantee that any of Karyopharm's SINE™ compounds, including KPT-350, or any other drug candidate that Karyopharm is developing 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; 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, 2015, which is on file with the Securities and Exchange Commission (SEC) as of March 15, 2016, 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 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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