Karyopharm Announces Dosing of First Patient in a Phase 2 Study Investigating Oral Eltanexor in HMA Refractory Myelodysplastic Syndrome

NEWTON, Mass., Oct. 21, 2021 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced dosing of the first patient in the Phase 2 expansion of an ongoing open-label Phase 1/2 study investigating eltanexor, a novel oral, Selective Inhibitor of Nuclear Export (SINE) compound, as a single-agent or in combination with approved and investigational agents in patients with several types of hematologic and solid tumor cancers (KCP-8602-801; NCT02649790). The Phase 2 expansion is designed to evaluate eltanexor monotherapy in patients with hypomethylating agents (HMA) refractory, intermediate or high-risk myelodysplastic syndrome (MDS). The primary endpoint for this Phase 2 expansion is overall response rate (ORR) with the secondary endpoints of determining progression-free and overall survival.

Initiation of the Phase 2 expansion follows encouraging results from the Phase 1 portion of the study where single-agent eltanexor showed activity in patients with high-risk, relapsed MDS that was refractory to HMAs. In that study (Sangmin, et al. EHA 2021), eltanexor demonstrated a 53% ORR and a median overall survival of 9.9 months, comparing favorably to historical controls. At the recommended Phase 2 dose of 10 mg, eltanexor monotherapy was well tolerated with low incidence and grade of gastrointestinal events. Exacerbation of cytopenias occurred in 20-40% of patients. Based on these promising signals, the study has been expanded to include an additional 83 patients with the first patient recently dosed.

"MDS is a group of diseases characterized by ineffective production of the components of the blood due to poor bone marrow function, leading to a high risk of transformation into acute leukemia. HMAs are the current standard of care for patients with newly diagnosed, higher-risk MDS, however only 40-60% patients respond, with these responses typically lasting less than two years. As such, prognosis in HMA refractory disease is poor, with a median overall survival of four to six months. With no agents currently approved for primary HMA refractory MDS, the need for novel, efficacious agents is critical. Based on the promising signal observed in the prior Phase 1 study, we are pleased to initiate dosing in the Phase 2 expansion and look forward to updating you on the progress of this important study in the future," said Sharon Shacham, PhD, MBA, Co-Founder and Chief Scientific Officer of Karyopharm.

About Eltanexor

Eltanexor (KPT-8602) is an investigational novel SINE compound that, like selinexor, functions by binding with, and inhibiting, the nuclear export protein, XPO1, 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.

In preclinical models, eltanexor has a broad therapeutic window with minimal penetration of the blood brain barrier and, therefore, has the potential to serve as another SINE compound for cancer indications. Following oral administration, animals treated with eltanexor show lower percentage of body weight loss and improved food consumption than animals similarly treated with selinexor. This allows more frequent dosing of eltanexor, enabling a longer period of exposure at higher levels than is possible with selinexor. As a result, we believe that eltanexor represents another novel SINE compound and we are evaluating its safety, tolerability and efficacy in ongoing clinical studies.

Eltanexor is an investigational medicine and has not been approved by the United States Food and Drug Administration, Health Canada, the European Medicines Agency, or any other regulatory agency.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (NASDAQ: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development, and commercialization of first-in-class drugs directed against nuclear export for the treatment of cancer and other diseases. Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), is approved in the U.S. in multiple hematologic malignancy indications, including in combination with Velcade® (bortezomib) and dexamethasone for the treatment of adult patients with multiple myeloma after at least one prior therapy, in combination with dexamethasone for the treatment of adult patients with heavily pretreated multiple myeloma and as a

monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma. NEXPOVIO® (selinexor) has also been granted conditional marketing authorization in combination with dexamethasone for adult patients with heavily pretreated multiple myeloma by the European Commission. 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 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 Karyopharm's expectations and plans relating to XPOVIO and eltanexor for the treatment of hematologic malignancies or certain solid tumors; the expected design of the Company's clinical trials; and the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor and eltanexor. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, 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 and eltanexor, will successfully complete necessary 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 the development or commercialization of 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: the risk that the COVID-19 pandemic could disrupt Karyopharm's business more severely than it currently anticipates, including by negatively impacting sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; 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; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development or regulatory approval of drug candidates by Karyopharm's competitors for products or product candidates in which Karyopharm is currently commercializing or developing; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any of its products or product candidates. 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, 2021, which was filed with the Securities and Exchange Commission (SEC) on August 5, 2021, 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.

SOURCE Karyopharm Therapeutics Inc.

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