Karyopharm Announces European Medicines Agency's Validation of its Type II Variation Marketing Authorization Application for NEXPOVIO® (selinexor) in Combination with Velcade® (bortezomib) and Dexamethasone for the Treatment of Adult Patients with Multiple Myeloma

- EMA Regulatory Decision Expected in the Fourth Quarter of 2021 -

NEWTON, Mass., April 26, 2021 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that the European Medicines Agency (EMA) has validated the Company's Type II Variation Marketing Authorization Application (MAA), which seeks to expand the currently authorized indication for NEXPOVIO® in the European Union to include, in combination with Velcade® (bortezomib) and low-dose dexamethasone, the treatment of adult patients with multiple myeloma who have received at least one prior therapy. Validation of the application confirms the submission is complete to begin the EMA's review process. The MAA is supported by the positive results from the pivotal Phase 3 BOSTON study, which evaluated once-weekly selinexor in combination with once-weekly Velcade® and low-dose dexamethasone (SVd) compared to standard twice-weekly Velcade® plus low-dose dexamethasone (Vd) in patients with multiple myeloma who have received one to three prior lines of therapy. The results of the BOSTON study were published in *The Lancet* in November 2020 and were the basis for the U.S. Food and Drug Administration approval of XPOVIO's expanded indication in December 2020.

"The submission of a Type II Variation Marketing Authorization Application based on positive data from the Phase 3 BOSTON study represents an important step towards our goal of further expanding the treatment options available to patients with multiple myeloma in Europe," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "We look forward to the EMA's review of this supplemental data, which further reinforces the broader therapeutic potential of NEXPOVIO."

In March 2021, NEXPOVIO was granted conditional marketing authorization by the European Commission in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. The new MAA will be reviewed by Committee for Medicinal Products for Human Use (CHMP), which will issue an opinion to the European Commission regarding the potential approval for the expanded indication. Karyopharm expects this review to be completed in the fourth quarter of 2021. This application is also intended to fulfill Karyopharm's obligation in the context of the conditional marketing authorization of NEXPOVIO granted in March 2021.

About Multiple Myeloma in Europe

Multiple myeloma (MM) is an incurable cancer with significant morbidity and the second most common hematologic malignancy. In 2020, there were approximately 51,000 new cases and 32,000 deaths from MM in Europe[1]. While the treatment of MM has improved over the last 20 years, and overall survival has increased considerably, the disease remains incurable, and nearly all adult patients will eventually relapse and develop disease that is refractory to all authorized anti-MM therapies. Therefore, there continues to be a high unmet medical need for new therapies, particularly those with novel mechanisms of action.

About NEXPOVIO (selinexor)

NEXPOVIO, which is marketed as XPOVIO® in the U.S., is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) medicine. NEXPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). NEXPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. NEXPOVIO (selinexor) has been granted conditional marketing authorization by the European Commission in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

For complete product information, please see the Summary of Product Characteristics that will be posted at https://ec.europa.eu/health/documents/community-register/html/h1537.htm.

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/NEXPOVIO for the treatment of adult patients with relapsed or refractory multiple myeloma and/or relapsed or refractory diffuse large B-cell lymphoma; commercialization of XPOVIO/NEXPOVIO or any of its drug candidates and the commercial performance of XPOVIO/NEXPOVIO; submissions to, and the review and potential authorization of selinexor by, regulatory

authorities, including the Company's regulatory strategy, the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities; 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. 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 Karyopharm will successfully commercialize XPOVIO/NEXPOVIO; that regulators will grant confirmatory authorization in the European Union based on the BOSTON study in adult patients with multiple myeloma; or that any of Karyopharm's drug candidates, including selinexor, 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/NEXPOVIO, 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/NEXPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO/NEXPOVIO or any of Karyopharm's drug candidates that receive regulatory authorization; the ability to obtain and retain regulatory authorization of XPOVIO/NEXPOVIO or any of Karyopharm's drug candidates that receive regulatory authorization; 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 enroll patients in its clinical trials; unplanned cash requirements and expenditures; development or regulatory authorization 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 product or product candidate. 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, 2020, which was filed with the Securities and Exchange Commission (SEC) on February 24, 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.

References

[1] World Health Organization. 2020. https://gco.iarc.fr/today/data/factsheets/cancers/35-Multiple-myeloma-fact-sheet.pdf

SOURCE Karyopharm Therapeutics Inc.

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