

Karyopharm Receives Positive CHMP Opinion for NEXPOVIO® (selinexor) for the Treatment of Patients with Refractory Multiple Myeloma

-- European Commission Decision Anticipated by April 2021 --

NEWTON, Mass., Jan. 29, 2021 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the conditional approval for NEXPOVIO® (selinexor) 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 positive CHMP opinion is a scientific recommendation for marketing authorization and one of the final steps before the European Commission (EC) makes a decision on Karyopharm's marketing authorization application (MAA). An EC marketing authorization through the centralized procedure is valid in all 27 European Union member countries as well as the European Economic Area countries Iceland, Liechtenstein and Norway.

"We are delighted that the CHMP has adopted a positive opinion for NEXPOVIO, which could lead to Karyopharm's first regulatory approval in Europe," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "This positive opinion highlights the CHMP's recognition of the positive clinical benefit-risk profile for oral NEXPOVIO and takes Karyopharm one step closer to bringing this important medicine to European patients in need of novel multiple myeloma treatment options. We look forward to the European Commission's final decision on the NEXPOVIO MAA, which is expected by April of 2021."

The MAA is supported by data from the Phase 2b STORM study which evaluated selinexor in patients with heavily pretreated, triple class refractory multiple myeloma and published in the *New England Journal of Medicine* (Chari, et al.) in August 2019.

Karyopharm intends to submit a second regulatory filing to the EMA (Type II variation) by April 2021 based on the data from the confirmatory Phase 3 BOSTON study, which evaluated once-weekly NEXPOVIO in combination with once-weekly Velcade® and low-dose dexamethasone in patients with multiple myeloma after at least one prior therapy with the goal of further expanding the global reach of NEXPOVIO to additional patients in need of new treatment options.

About the Phase 2b STORM Pivotal Trial

The Phase 2b STORM trial (**S**elinexor **T**reatment of **R**efractory **M**yeloma) was an international, multi-center, single-arm, open-label study which enrolled 122 patients (Part 2 of the trial) with heavily pretreated, triple class refractory multiple myeloma. Patients in the trial had a median of seven previous therapeutic regimens, including a median of 10 unique antimyeloma agents.

For the study's primary endpoint, oral selinexor achieved an overall response rate of 26% (95% confidence interval [CI], 19, 35) and the trial therefore met its primary endpoint. Minimal response per IMWG criteria was observed in 16 (13%) patients and 48 patients (39%) had stable disease. All responses were adjudicated by an Independent Review Committee. The median overall survival was 8.6 months in the total population studied and 15.6 months in patients who had a minimal response or better.

Karyopharm's request for conditional approval in Europe is based upon the same patient population that served as the basis for XPOVIO's accelerated FDA approval in the U.S. Specifically, it includes the efficacy and safety data from a pre-specified sub-group analysis of 83 patients in the STORM study whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab, as the benefit-risk ratio appeared to be greater in this more heavily pre-treated population than in the overall trial population. The overall response rate in this patient population was 25.3%.

The most common adverse reactions ($\geq 20\%$) were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea and upper respiratory tract infection. In the STORM trial, fatal adverse reactions occurred in 9% of patients. Serious adverse reactions occurred in 58% of patients. Treatment discontinuation rate due to adverse reactions

was 27%.

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 Europe¹. 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 patients will eventually relapse and develop disease that is refractory to all approved 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) compound. 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. XPOVIO is approved in the U.S. in multiple hematologic malignancy indications, including in combination with Velcade® (bortezomib) and dexamethasone for the treatment of patients with multiple myeloma after at least one prior therapy, in combination with dexamethasone for the treatment of patients with heavily pretreated multiple myeloma and as a monotherapy for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. A Marketing Authorization Application for NEXPOVIO for patients with penta-refractory multiple myeloma is also currently under review by the European Medicines Agency and received a positive CHMP opinion in January 2021. Selinexor is also being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including as a potential backbone therapy in combination with approved myeloma therapies (STOMP), in liposarcoma (SEAL) and in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with 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.

For more information about Karyopharm's products or clinical trials, please contact the Medical Information department at:

Tel: +1 (888) 209-9326

Email: medicalinformation@karyopharm.com

For additional product information, including full prescribing information, please visit www.XPOVIO.com.

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 novel first-in-class drugs directed against nuclear export and related targets for the treatment of cancer and other major 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 patients with multiple myeloma after at least one prior therapy, in combination with dexamethasone for the treatment of patients with heavily pretreated multiple myeloma and as a monotherapy for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma. A Marketing Authorization Application for NEXPOVIO™ (selinexor) for patients with heavily pretreated multiple myeloma is also currently under review by the European Medicines Agency. 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 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 approval 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 and the potential availability of accelerated approval pathways; 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 agree that selinexor qualifies for conditional approval in the European Union as a result of data from the STORM study or confirmatory approval in the European Union based on the BOSTON study in 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, 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 product or product candidate. 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, 2020, which was filed with the Securities and Exchange Commission (SEC) on November 2, 2020, 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.

XPOVIO® and NEXPOVIO® are registered trademarks of Karyopharm Therapeutics Inc. Velcade® is a registered trademark of Takeda Pharmaceutical Company Limited.

References

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

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Karyopharm Therapeutics Inc., Ian Karp, Senior Vice President, Investor and Public Relations, 857-297-2241, ikarp@karyopharm.com; Media: 720 Strategies, Andrew Lee, andrew.lee@720strategies.com

<https://investors.karyopharm.com/2021-01-29-Karyopharm-Receives-Positive-CHMP-Opinion-for-NEXPOVIO-R-selinexor-for-the-Treatment-of-Patients-with-Refractory-Multiple-Myeloma?fbclid=IwAR3uSCp788RIFpCSryZ1IG03TO-LYRFXM5bZ4iHwwaa5l029VSmXKh2pzaA>