Karyopharm Receives Conditional Marketing Authorization from the European Commission for NEXPOVIO® (selinexor) in Combination with Dexamethasone for the Treatment of Adult Patients with Relapsed and or Refractory Multiple Myeloma

-- NEXPOVIO is the First and Only Nuclear Export Inhibitor Authorized by the European Commission --
-- Second European Regulatory Filing Based on Phase 3 BOSTON Data Expected by April 2021 --

NEWTON, Mass., March 29, 2021 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that the European Commission (EC) has granted conditional marketing authorization for NEXPOVIO (selinexor), the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) medicine, 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.

Conditional marketing authorization is supported by data from the positive Phase 2b STORM study, which evaluated selinexor in adult patients with heavily pretreated, triple class refractory multiple myeloma and was published in the *New England Journal of Medicine* (Chari, et al.) in August 2019. Under the provisions of conditional approval by the EC, continued authorization for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial and is subject to additional monitoring. An EC marketing authorization through the centralized procedure (CP) is valid in all 27 European Union (EU) member countries, as well as the European Economic Area (EEA) countries of Iceland, Liechtenstein and Norway.

"NEXPOVIO represents the first and only nuclear export inhibitor authorized in Europe and we are delighted to bring this new treatment option to eligible adult patients with heavily pretreated multiple myeloma. Despite advancements in the treatment of multiple myeloma, most adult patients will eventually relapse and develop disease that is refractory to all authorized therapies, further highlighting the urgent need for new therapies with novel mechanism of actions like NEXPOVIO," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "Our first product authorization in Europe could not have been possible without the dedication of the patients, caregivers, physicians and Karyopharm employees involved in the clinical development of NEXPOVIO over the last 13 years."

"Today's authorization is an important step forward in the international expansion of selinexor, now with marketing authorization for use in Europe, Israel and the U.S.," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. "We are committed to making NEXPOVIO available in Europe initially through a Named Patient Program and are on track to submit a second European regulatory filing in April based on the positive data from the Phase 3 BOSTON study to potentially further expand NEXPOVIO to eligible adult patients in need of new treatment options."

About the Phase 2b STORM Pivotal Trial

The Phase 2b STORM trial (**S**elinexor **T**reatment **o**f **R**efractory **M**yeloma) was an international, multi-center, single-arm, open-label study which enrolled 123 adult patients (Part 2 of the trial) with heavily pretreated, triple class refractory multiple myeloma. Adult patients in the trial had a median of seven previous therapeutic regimens, including a median of 10 unique anti-myeloma 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 (n=123). 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. Among the modified intent to treat population enrolled in STORM Part 2, eighty–three (83) patients had relapse and/or refractory multiple myeloma that was refractory to two proteasome inhibitors (bortezomib, carfilzomib), two immunomodulators (lenalidomide, pomalidomide) and an anti-CD38 monoclonal antibody (daratumumab), the efficacy analysis was based on these 83 patients. A secondary efficacy endpoint included overall survival (OS), defined as the duration from start of study treatment to death due to any cause. The median OS was 8.6 months in the total population (n=123) studied and 15.6

months in adult patients who had a minimal response or better.

Karyopharm's request for conditional authorization in Europe was based upon the same patient population that served as the basis for XPOVIO's accelerated FDA approval in the U.S. The overall response rate in this patient population (n=83) was 25.3 % (95% confidence interval [CI], 16.4, 36).

The most common adverse reactions in the STORM trial (≥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 adult patients. Serious adverse reactions occurred in 58% of adult 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 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) 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. 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.

Therapeutic indication for NEXPOVIO in the EU as well as The EEA Countries of Iceland, Liechtenstein and Norway

NEXPOVIO is indicated 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.

SELECT IMPORTANT SAFETY INFORMATION
NEXPOVIO is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See www.mhra.gov.uk/yellowcard for how to report side effects.

Contraindications: Hypersensitivity to selinexor.

Special warnings and precautions for use:

Recommended concomitant treatments
Adult patients should be advised to maintain adequate fluid and caloric intake throughout treatment.
Intravenous hydration should be considered for adult patients at risk of dehydration.
Prophylactic concomitant treatment with a 5-HT3 antagonist and/or other anti-nausea agents should be provided prior to and during treatment with NEXPOVIO.

Haematology
Adult patients should have their complete blood counts (CBC) assessed at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment.

Thrombocytopenia: Thrombocytopenic events (thrombocytopenia and platelet count decreased) were frequently reported in adult patients receiving selinexor, which can be severe (Grade 3/4). Adult patients should be monitored for signs and symptoms of bleeding and evaluated promptly.

Neutropenia: Severe neutropenia (Grade 3/4) has been reported with selinexor.
Adult patients with neutropenia should be monitored for signs of infection and evaluated promptly.

Gastrointestinal toxicity: Nausea, vomiting, diarrhoea, which sometimes can be severe and may require the use of anti-emetic and anti-diarrhoeal medicinal products.

Weight loss and anorexia: Adult patients should have their body weight, nutritional status and volume checked at baseline, during treatment, and as clinically indicated. Monitoring should be more frequent during the first two months of treatment.

Confusional state and dizziness: Patients should be instructed to avoid situations where dizziness or confusional state may be a problem and to not take other medicinal products that may cause dizziness or confusional state without adequate medical advice. Patients should be advised not to drive or operate heavy machinery until symptoms resolve.

Hyponatraemia: Adult patients should have their sodium levels checked at baseline, during treatment, and as clinically indicated. Monitoring should be more frequent during the first two months of treatment.

Tumour lysis syndrome (TLS): TLS has been reported in adult patients receiving therapy with selinexor. Adult patients at a high risk for TLS should be monitored closely. Treat promptly in accordance with institutional guidelines.

Fertility, pregnancy and lactation
Women of childbearing potential/contraception in males and females: Women of childbearing potential and male adult patients of reproductive potential should be advised to use effective contraceptive measures or abstain from sexual activity to prevent pregnancy during treatment with selinexor and for at least 1 week following the last dose of selinexor.

Breast-feeding: It is unknown whether selinexor or its metabolites are excreted in human milk. A risk to breast-fed children cannot be excluded. Breast-feeding should be discontinued during treatment with selinexor and for 1 week after the last dose.

Elderly population
Patients 75 years and older had a higher incidence of discontinuation due to an adverse reaction, higher incidence of serious adverse reactions, and higher incidence of fatal adverse reactions.

Undesirable effects
Summary of the safety profile
The most frequent adverse reactions (≥30%) of selinexor in combination with dexamethasone were nausea, thrombocytopenia, fatigue, anaemia, decreased appetite, decreased weight, diarrhoea, vomiting, hyponatraemia, neutropenia and leukopenia.
The most commonly reported serious adverse reactions (≥3%) were pneumonia, sepsis, thrombocytopenia, acute kidney injury, and anaemia.

Description of selected adverse reactions
Infections: Infection was the most common non-haematological toxicity. Upper respiratory tract infection and pneumonia were the most commonly reported infections with 25% of reported infections being serious and fatal infections occurring in 3% of treated adult patients.

Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

Please see NEXPOVIO Summary of Product Characteristics and European Public Assessment Report Once Made Available by the EC

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 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.

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

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