The European Myeloma Network and Karyopharm Announce Dosing of First Patient in Collaborative EMN29/XPORT-MM-031 Study

- Phase 3 Study Evaluating an All Oral Regimen of Selinexor in Combination with Pomalidomide and Low-dose Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma -

ROTTERDAM, Netherlands and NEWTON, Mass., May 25, 2022 /PRNewswire/ -- The European Myeloma Network (EMN), an international collaborative network of expertise centers for multiple myeloma in Europe and Australia, and Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced the dosing of the first patient in the collaborative EMN29/XPORT-MM-031 study, a randomized, global Phase 3 study evaluating an all-oral regimen of selinexor, Karyopharm's first-in-class, oral exportin 1 (XPO1) inhibitor, in combination with Pomalyst® (pomalidomide) and low-dose dexamethasone (SPd) versus Empliciti® (elotuzumab), pomalidomide, and dexamethasone (EPd) in patients with relapsed or refractory multiple myeloma (NCT05028348//EMN29).

The Phase 3, two-arm, randomized, active comparator-controlled, open-label, multicenter study will compare the efficacy, safety, and the impact on health-related quality of life of SPd versus EPd in pomalidomide-naïve patients with relapsed or refractory multiple myeloma. Patients will have received one to four prior lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody (mAb), prior to being enrolled in the study. Final dosing for the selinexor arm at 40 mg or 60 mg will be determined following an interim analysis of data from the first 60 patients. The primary endpoint of the study is progression-free survival (PFS). The study is sponsored by the European Myeloma Network and is expected to recruit approximately 280 patients.

"Despite the progress made in treating multiple myeloma, new treatment options remain a critical need as the majority of patients will relapse and eventually stop responding to current therapies," said Reshma Rangwala, MD, PhD, Chief Medical Officer at Karyopharm Therapeutics. "We look forward to collaborating with the EMN on this important study. We have encouraging data in patients who have been treated with an anti-CD38 based regimen and we are eager to see the result in this patient population."

"We are extremely pleased to have this important study underway and look forward to further elucidating the potential of the SPd triplet regimen for Multiple Myeloma patients," added Professor Katja Weisel, Deputy Director of the University Cancer Center in Hamburg (UCCH) and principal investigator of the EMN29/XPORT-MM-031 study. "We look forward to the top-line results in 2024."

The initiation of this Phase 3 study follows encouraging data from an all-oral arm of the Phase 1b/2 STOMP study (NCT02343042) and the Phase 2 study XPORT-MM-028 (NCT04414475) in which selinexor was evaluated in combination with Pomalyst® and low-dose dexamethasone in patients with relapsed or refractory multiple myeloma who received at least two prior lines of therapy, including a PI and an IMiD.

About Multiple Myeloma

According to Clarivate Analytics, approximately 47,000 patients are diagnosed with relapsed or refractory multiple myeloma in the U.S. each year.[1] It is most frequently diagnosed in people aged 65-74 years old.[2] Despite recent therapeutic advances, there is currently no cure and most patients' disease will typically progress following treatment with currently available therapies. According to the American Cancer Society, an estimated 12,640 deaths due to multiple myeloma are expected to occur in the U.S. in 2022.[3]

About EMN

The European Myeloma Network (EMN) is an international collaborative network of expertise centers for multiple myeloma in Europe and Australia, working together with many national cooperative groups. EMN is chaired by Professor Pieter Sonneveld and Professor Mario Boccadoro. It has offices in Rotterdam, the Netherlands and in Torino, Italy. EMN has organized more than 30 international prospective trials in multiple myeloma and related diseases in collaboration with international pharmaceutical companies. EMN strongly supports translational research in its trials, focusing on modes of action of the drugs under investigation.

About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral exportin 1 (XPO1) inhibitor and the first of Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds to be approved for the treatment of cancer. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein XPO1. XPOVIO is approved in the U.S. and marketed by Karyopharm in multiple oncology indications, including: (i) in combination with Velcade® (bortezomib) and dexamethasone (XVd) in patients with multiple myeloma after at least one prior therapy; (ii) in combination with dexamethasone in patients with heavily pre-treated multiple myeloma; and (iii) in patients with diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. XPOVIO (also known as NEXPOVIO® in certain countries) has received regulatory approvals in a growing number of ex-U.S. territories and countries, including Europe, the United Kingdom, China, South Korea, Singapore and Israel, and is marketed in those areas by Karyopharm's global partners. Selinexor is also being investigated in several other mid- and late-stage clinical trials across multiple high unmet need cancer indications, including endometrial cancer and myelofibrosis. 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

XPOVIO® (selinexor) is a prescription medicine approved:

- In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy (XVd).
- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti–CD38 monoclonal antibody (Xd).
- For the treatment of adult 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. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Thrombocytopenia: Monitor platelet counts throughout treatment. Manage with dose interruption and/or reduction and supportive care.
- Neutropenia: Monitor neutrophil counts throughout treatment. Manage with dose interruption and/or reduction and granulocyte colony–stimulating factors.
- Gastrointestinal Toxicity: Nausea, vomiting, diarrhea, anorexia, and weight loss may occur. Provide antiemetic prophylaxis. Manage with dose interruption and/or reduction, antiemetics, and supportive care.
- Hyponatremia: Monitor serum sodium levels throughout treatment. Correct for concurrent hyperglycemia and high serum paraprotein levels. Manage with dose interruption, reduction, or discontinuation, and supportive care.
- Serious Infection: Monitor for infection and treat promptly.
- Neurological Toxicity: Advise patients to refrain from driving and engaging in hazardous occupations or activities until neurological toxicity resolves. Optimize hydration status and concomitant medications to avoid dizziness or mental status changes.
- Embryo–Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential and males with a female partner of reproductive potential, of the potential risk to a fetus and use of effective contraception.
- Cataract: Cataracts may develop or progress. Treatment of cataracts usually requires surgical removal of the cataract.

Adverse Reactions

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive XVd are

fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract and vomiting. Grade 3–4 laboratory abnormalities (≥10%) are thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia. In the BOSTON trial, fatal adverse reactions occurred in 6% of patients within 30 days of last treatment. Serious adverse reactions occurred in 52% of patients. Treatment discontinuation rate due to adverse reactions was 19%.

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive Xd are 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%.

- The most common adverse reactions (incidence ≥20%) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3–4 laboratory abnormalities (≥15%) are thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. In the SADAL trial, fatal adverse reactions occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal adverse reactions were infection (4.5% of patients). Serious adverse reactions occurred in 46% of patients; the most frequent serious adverse reaction was infection (21% of patients). Discontinuation due to adverse reactions occurred in 17% of patients.

Use In Specific Populations
Lactation: Advise not to breastfeed.

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

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1–888–209–9326 or FDA at 1–800–FDA–1088 or www.fda.gov/medwatch.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (NASDAQ: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies. Since its founding, Karyopharm has been the industry leader in oral Selective Inhibitor of Nuclear Export (SINE) compound technology, which was developed to address a fundamental mechanism of oncogenesis: nuclear export dysregulation. Karyopharm's lead SINE compound and first-in-class, oral exportin 1 (XPO1) inhibitor, XPOVIO® (selinexor), is approved in the U.S. and marketed by the Company in three oncology indications and has received regulatory approvals in various indications in a growing number of ex-U.S. territories and countries, including Europe and the United Kingdom (as NEXPOVIO®) and China. Karyopharm has a focused pipeline targeting multiple high unmet need cancer indications, including in multiple myeloma, endometrial cancer, myelodysplastic syndromes and myelofibrosis. For more information about our people, science and pipeline, please visit www.karyopharm.com, and follow us on Twitter at @Karyopharm and LinkedIn.

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 ability of selinexor or eltanexor to treat patients with multiple myeloma, diffuse large B-cell lymphoma, solid tumors and other diseases; and expectations related to future clinical development and potential regulatory submissions of selinexor or 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 Karyopharm will successfully commercialize XPOVIO or 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 obtain and 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 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 Annual Report on Form 10-K for the year ended December 31, 2021, which was filed with the Securities and Exchange Commission (SEC) on March 1, 2022, 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] Clarivate/DRG Market Forecast Dashboard-MM (2022 figures, pub 2020).

[2] National Cancer Institute. Cancer Stat Facts: Myeloma. https://seer.cancer.gov/statfacts/html/mulmy.html. Accessed March 2022.

[3] American Cancer Society. Key Statistics About Multiple Myeloma. https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html. Accessed May 2022.

SOURCE Karyopharm Therapeutics Inc.

For further information: Contacts: Sponsor:, EMN, info@emn.life; Investors: , Elhan Webb, CFA, Senior Vice President, Investor Relations, 617.658.0600 | elhan.webb@karyopharm.com; Media:, Karyopharm, Sarah Connors, Vice President of Corporate Communications and Patient Advocacy, 617.658.0600 | sarah.connors@karyopharm.com

---

https://investors.karyopharm.com/2022-05-25-The-European-Myeloma-Network-and-Karyopharm-Announce-Dosing-of-First-Patient-in-Collaborative-EMN29-XPORT-MM-031-Study