Karyopharm Announces New Preliminary Data in Overall Survival (OS) in Selinexor-Treated Patients with Advanced or Recurrent TP53 Wild-Type Endometrial Cancer as Part of Pre-Specified Exploratory Subgroup Analysis of the SIENDO Study

Long-Term Safety and Efficacy Data from SIENDO Study in the TP53 Wild-Type Exploratory Subgroup Showed Signals of Improvement in Overall Survival (OS) Regardless of Mismatched Repair Status (MMR)

Median OS Not Reached for Selinexor-Treated Patients Who are TP53 Wild-Type pMMR

NEWTON, Mass., Nov. 6, 2023 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced the presentation of updated long-term safety and efficacy data from a pre-specified exploratory subgroup analysis of the SIENDO study (NCT03555422) in patients with advanced or recurrent *TP53* wild-type endometrial cancer at the International Gynecological Cancer Society (IGCS) Annual Global Meeting in Seoul, South Korea.

The primary analysis of the Phase 3 SIENDO study of selinexor maintenance therapy in advanced or recurrent endometrial cancer showed improvements in median progression-free survival (PFS) for the intent-to-treat (ITT) population but were not clinically meaningful. However, an exploratory analysis of a pre-specified subgroup of patients with *TP53* wild-type endometrial cancer showed a promising efficacy signal.

In the exploratory subgroup analysis, 113 patients with wild-type endometrial cancer received selinexor (n=77) or placebo (n=36) as maintenance therapy. Although the survival data are immature, as of the September 1, 2023, data cut-off date, the study showed an encouraging OS signal in the *TP53* wild-type population: hazard ratio 0.76 (95% Confidence Interval [CI]: 0.36-1.59), with median OS not reached in either arm after a median follow up of 28.9 months. Similarly, encouraging preliminary OS was observed in patients with *TP53* wild-type/pMMR endometrial cancer: hazard ratio 0.57 (95% CI: 0.24-1.35), with median OS not reached in selinexor arm, and 35 months in placebo arm after median follow-up of 31.6 months , and a HR of 0.62 (95% CI: 0.06-6.81), with median OS not reached in either arm after median follow-up of 27.3 months in patients with *TP53* wild-type/dMMR endometrial cancer.

"The preliminary OS data from this exploratory subset analysis of the SIENDO study corroborate the PFS results observed, which is compelling in this novel biomarker-driven population with high unmet need," said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "These results showcase selinexor's potential as a foundational treatment for patients with *TP53* wild-type endometrial cancer. We look forward to additional data in the first half of 2025 from the company's ongoing pivotal Phase 3 trial that may support U.S. and global regulatory filings."

No new safety signals were identified as of the last data cut-off date on September 1, 2023. The most common treatment-emergent adverse events (AEs) with selinexor treatment were nausea (90%), vomiting (60%), thrombocytopenia (42%) and diarrhea (42%), the majority of which were grades 1-2. Of note, the rate of nausea in the placebo patients was 34%, vomiting 11%, and diarrhea 37%. The most common reported grade 3-4 treatment-emergent AEs included neutropenia (18%), nausea (12%), and thrombocytopenia (10%). TEAEs leading to discontinuations in the selinexor group were reported in 16% of patients.

Currently, there are no specific targeted therapies available for patients with *TP53* wild-type endometrial cancer. Advanced and recurrent endometrial cancer is associated with a poor prognosis, including limited disease control for patients who relapse after first-line systemic treatment.[1] There are about 16,000 patients diagnosed with advanced and recurrent endometrial cancer in the U.S. each year[2]. More than 50% of these patients have *TP53* wild-type cancer.[2,3] *TP53* wild-type is observed in both pMMR and dMMR populations. Recently there has been progress in potential treatment options in the dMMR subgroup with new targeted treatments; however, a large unmet need continues to exist for pMMR and for *TP53* wild-type endometrial cancer.

"Given the unmet need that remains for patients whose disease is pMMR, I'm excited by the results demonstrating an encouraging, preliminary trend in OS, coupled with signals of improvement in disease

progression," said Dr. Giovanni Scambia, oncology gynecologist at MITO and Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy. "These results highlight the potential opportunity to further personalize therapies and provide a strong rationale to further evaluate selinexor as maintenance therapy in *TP53* wild-type endometrial cancer in the ongoing Phase 3 trial".

IGCS Oral Presentation
***Title*:** Selinexor maintenance for patients with TP53wt advanced or recurrent endometrial cancer: Long-term follow up of efficacy and safety subgroup analysis of the ENGOT-EN5/GOG-3055/SIENDO study
Presenter: Giovanni Scambia, MD, MITO and Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
Session Title: **Plenary 02: Changing the Landscape of Endometrial Cancer**
***Date and Time*:** Sunday, November 5, 2023, 4:30pm - 5:30pm (GMT+9)/ 3:30am - 4:30am (ET)

IGCS Poster Presentation
***Title*:** ENGOT-EN20/GOG-3083/XPORT-EC-042 A phase 3, randomized, placebo-controlled, double-blind, multicenter trial of selinexor in maintenance therapy for patients with P53 Wild-type, advanced or recurrent endometrial carcinoma
Presenter: Brian Slomovitz, MD, Mount Sinai Medical center and Florida International University
***Date and Time*:** Sunday, November 5, 2023, through Tuesday, November 7, 2023

IGCS Industry Sponsored Symposium in Partnership with Gynecologic Oncology Group (GOG)
***Title*:** The evolving landscape in molecular-driven investigational therapies for advanced endometrial cancer
Presenters: Bradley J. Monk, MD, US Cancer Associates; Domenica Lorusso, MD, PhD, Catholic University of Rome and Fondazione Policlinico Gemelli IRCCS; Ritu Salani, MD, MS, UCLA Medical Center
***Date and Time*:** Monday, November 6, 2023, 7:15am – 8:15am (GMT+9)/ 6:15pm - 7:15pm (ET)

About the EC-042 Study
EC-042 (XPORT-EC-042; NCT05611931) is a global, Phase 3, randomized, double-blind study evaluating selinexor as a maintenance therapy following systemic therapy in patients with *TP53* wild-type advanced or recurrent endometrial cancer. The EC-042 study was initiated in November 2022 and is expected to enroll up to 220 patients who will be randomized 1:1 to receive either a 60 mg, once-weekly, administration of oral selinexor or placebo until disease progression. The primary endpoint of the study is progression free survival (PFS), as assessed by an investigator, with overall survival as a key secondary endpoint. Further, in connection with the EC-042 Study, Karyopharm entered into a global collaboration with Foundation Medicine, Inc. to develop FoundationOne®CDx, a tissue-based comprehensive genomic profiling test to identify and enroll patients whose tumors are *TP53* wild-type.

About the SIENDO Study
Karyopharm's evaluation of selinexor to treat patients with *TP53* wild-type advanced or recurrent endometrial cancer is supported by data from an exploratory subgroup analysis from its ongoing SIENDO Study, a European Network of Gynaecological Oncological Trial Groups (ENGOT)-led trial in collaboration with the Gynecologic Oncology Group (GOG) Foundation, Inc. The SIENDO Study is a multicenter, randomized, double-blinded Phase 3 study evaluating the efficacy and safety of oral selinexor versus placebo as a front-line maintenance therapy in patients with advanced or recurrent endometrial cancer following at least one prior platinum-based combination chemotherapy treatment (NCT03555422). Participants in this study with advanced or recurrent disease who had a partial response or a complete response after at least 12 weeks of taxane-platinum combination chemotherapy were randomized in a 2:1 manner to receive either maintenance therapy of 80 mg of selinexor or placebo taken once per week, until disease progression. The primary endpoint in the study was PFS from time of randomization until death or disease progression as assessed by an investigator, with the goal of the study demonstrating a HR of 0.6. In the first quarter of 2022, Karyopharm presented top-line data from the SIENDO study, including preliminary exploratory subgroup analyses. Selinexor-treated patients had a median PFS of 5.7 months compared to 3.8 months for patients on placebo in the full trial population, which was not clinically meaningful. Patients in the exploratory subgroup of *TP53* wild-type advanced or recurrent endometrial cancer treated with selinexor had a median PFS of 13.7 months compared to 3.7 months for the exploratory subgroup patients on placebo. There were no new safety signals identified, and a discontinuation rate of 10.5% due to adverse events (AEs). The most common treatment-emergent AEs in the SIENDO study of any grade were: nausea (84%), vomiting (52%), constipation (37%) and thrombocytopenia (37%). The most common grade 3 treatment-emergent AEs were nausea (10%), neutropenia (9%), thrombocytopenia (7%) and asthenia (6%).

About Endometrial Cancer
Endometrial cancer is the most common cancer of the female reproductive organs in the U.S., with approximately 66,000 new cases expected in 2023 leading to nearly 13,000 deaths.[4] In 2020, there were approximately 130,000 new cases and 29,000 deaths in Europe from endometrial cancer, while on a global scale there were 417,000 new cases and approximately 97,000 deaths.[5] Since 2002, the incidence of new cases and deaths from endometrial cancer have risen.[6] Risk factors include obesity, Type 2 diabetes, high-fat diets,

use of tamoxifen and oral estrogens, and delayed menopause.[7] There are no approved therapies in the maintenance setting for patients with advanced or recurrent endometrial cancer.[8]

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 various indications in a growing number of ex-U.S. territories and countries, including but not limited to the European Union, the United Kingdom, China, South Korea, Canada, Israel and Taiwan. XPOVIO and NEXPOVIO is marketed by Karyopharm's partners, Antengene, Menarini, Neopharm and FORUS, in China, South Korea, Singapore, Australia, Hong Kong, Germany, Austria, Israel and Canada.

Please refer to the local Prescribing Information for full details.

Selinexor is also being investigated in several other mid- and late-stage clinical trials across multiple high unmet need cancer indications, including in 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

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 was 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 an 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 Mainland China. Karyopharm has a focused pipeline targeting multiple high unmet need cancer indications, including in multiple myeloma, endometrial cancer, myelodysplastic neoplasms 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 to treat patients with endometrial cancer; and expectations related to the clinical development of selinexor and potential regulatory submissions of 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 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 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; the direct or indirect impact of the COVID-19 pandemic or any future pandemic on Karyopharm's business, results of operations and financial condition; 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 September 30, 2023, which was filed with the Securities and Exchange Commission (SEC) on November 2, 2023, 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. Any other trademarks referred to in this release are the property of their respective owners.

References

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[8] Corr B, Cosgrove C, Spinosa D, et al. *BMJ Medicine*, 2022;1:e000152.

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