Karyopharm Announces Updated Exploratory Subgroup Analysis from SIENDO Study in Patients with Advanced or Recurrent TP53 Wild-Type Endometrial Cancer to be Presented at ASCO Plenary Series on July 25th

- *Data Provide Further Support for Company's Ongoing Phase 3 Study Evaluating Selinexor as Maintenance Therapy Following Systemic Therapy in Patients with Advanced or Recurrent TP53 Wild-Type Endometrial Cancer* -

NEWTON, Mass. , July 19, 2023 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that an updated exploratory subgroup analysis from the SIENDO study (NCT03555422) in patients with advanced or recurrent TP53 wild-type endometrial cancer will be presented at the virtual American Society of Clinical Oncology (ASCO) Plenary Series. The SIENDO exploratory subgroup data provides further support for the ongoing pivotal Phase 3 study of selinexor as a maintenance therapy following systemic therapy in patients with TP53 wild-type advanced or recurrent endometrial cancer (XPORT-EC-042; NCT05611931).

ASCO Plenary Series Program

Title: Long-term follow up of selinexor maintenance in patients with TP53wt advanced or recurrent endometrial cancer: A pre-specified subgroup analysis from the phase 3 ENGOT-EN5/GOG-3055/SIENDO study.
Presenter: Brian Slomovitz, MD, Mount Sinai Medical Center
Session Date and Time: Tuesday July 25, 2023, 3:00pm - 4:00pm (ET)

This livestream event presented by ASCO is free to register at:
https://old-prod.asco.org/meetings-education/monthly-plenary-series/program

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. The SIENDO Study (ENGOT-EN5/GOG-3055) 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). Patients 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 2:1 to receive either maintenance therapy of 80 mg of selinexor or placebo taken once per week, until disease progression or death. The primary endpoint in the study is PFS from time of randomization until death or disease progression as assessed by an investigator, and prespecified exploratory endpoints included evaluation by p53 status and other molecular subtypes. Early data was presented at European Society of Medical Oncology (ESMO) Virtual Plenary and Society for Gynecologic Oncology (SGO) meetings in 2022 and will be reported in future publications.

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.[1] 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.[2] Since 2002, the incidence of new cases and deaths from endometrial cancer have risen.[3] Risk factors include obesity, Type 2 diabetes, high-fat diets, use of tamoxifen and oral estrogens, and delayed menopause.[4] There are no approved therapies in the maintenance setting for patients with advanced or recurrent endometrial cancer. [5]

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 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 March 31, 2023, which was filed with the Securities and Exchange Commission (SEC) on May 4, 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

[1] American Cancer Society, About Endometrial Cancer: https://www.cancer.org/cancer/endometrial-cancer/about/key-statistics.html (accessed July 14, 2023)

[2] International Agency for Research on Cancer, World Health Organization. "Corpus uteri Fact Sheet." Cancer Today, 2020: https://gco.iarc.fr/today/data/factsheets/cancers/24-Corpus-uteri-fact-sheet.pdf (accessed July 14, 2023)

[3] Seer Cancer Incidence Rate Estimates, National Cancer Institute. Bethesda, MD. https://seer.cancer.gov/statistics/preliminary-estimates/ (accessed July 17, 2023)

[4] American Cancer Society, Endometrial Cancer Risk Factors. https://www.cancer.org/cancer/endometrial-cancer/causes-risks-prevention/risk-factors.html (accessed July 14, 2023)

[5] Corr B, Cosgrove C, Spinosa D, et al. Endometrial cancer: molecular classification and future treatments. *BMJ Medicine*, 2022;1:e000152.

SOURCE Karyopharm Therapeutics Inc.

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