Karyopharm to Present New Selinexor Data at the 2022 American Society of Clinical Oncology Annual Meeting

– Encouraging Initial Data Observed in Phase 1/2 Study of Selinexor in Combination with Ruxolitinib in Treatment-Naïve Myelofibrosis, Including Favorable Tolerability with No Dose Limiting Toxicities and 75% of Evaluable Patients Demonstrating ≥35% Spleen Volume Reduction (SVR 35) at Week 12 –

– FDA Grants Orphan Drug Designation for Selinexor for the Treatment of Myelofibrosis –

– Exploratory Subgroup Analyses from SIENDO Trial in Patients with Endometrial Cancer Treated with Selinexor as Maintenance Therapy Identified p53 Wild-type as a Potentially Important Predictor of Efficacy, with 10-month PFS Improvement over Placebo; No Benefit Was Seen in Patients with p53 Mutant Tumors –

NEWTON, Mass., May 26, 2022 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced promising initial data from a Phase 1/2 study evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis and subgroup analyses and molecular classification data from the SIENDO study evaluating selinexor in endometrial cancer. These data, and four additional abstracts, will be presented at the 2022 American Society of Clinical Oncology Annual Meeting (ASCO 2022), being held in Chicago from June 3-7, 2022.

Results from Phase 1/2 Study Evaluating Selinexor in Combination with Ruxolitinib in Patients with Treatment-Naïve Myelofibrosis

The initial data to be presented at ASCO 2022 were based on the Phase 1 portion of the Phase 1/2 study evaluating the safety and preliminary efficacy of once-weekly selinexor in combination with standard dose ruxolitinib in patients with treatment-naïve myelofibrosis. As of May 1, 2022, 15 patients had been dosed with one of two dose levels of selinexor, 40 mg (n=3) and 60 mg (n=12), in combination with ruxolitinib 15/20 mg BID.

Seventy-five percent of evaluable patients (6 out of 8) demonstrated ≥35% reduction in spleen volume (SVR35) at week 12. Five out of 10 transfusion independent patients who had at least eight weeks of treatment maintained stable hemoglobin (± 2g/dL) or improved hemoglobin level (>2g/dL increase) at last follow up. In addition, all of the evaluable 7 patients, who had been at least 12 weeks on treatment and had complete data, experienced rapid reductions in their symptom scores with 3 of 7 patients having ≥50% reduction (TSS50) at week 12.

There were two patients who discontinued therapy in the trial: One patient discontinued after 5 months of therapy due to unrelated AEs (dizziness, atrial fibrillation, and pulmonary hypertension) and another patient discontinued after 8 weeks of therapy due to progression to AML.

The combination of selinexor and ruxolitinib was generally well-tolerated and manageable. No dose-limiting toxicities were reported at either dose level of selinexor, and the most common adverse event (AE) was nausea (40%), the majority of which were grade 1/2. Both the 40 mg and 60 mg dose levels were generally well tolerated, with the most common reported Grade 3-4 treatment-emergent AEs being thrombocytopenia (27%), anemia (20%), neutropenia (20%) and atrial fibrillation (20%). Hematologic adverse events were reversible with dose interruptions and reductions.

The trial is currently enrolling patients in the Phase 1b dose expansion part of the study.

"Despite tremendous improvements in the lives of patients with myelofibrosis with the introduction of the JAK inhibitors, there remains a significant unmet need. We are excited to develop a novel combination that may further improve outcomes for these patients," said Reshma Rangwala, MD, PhD, Chief Medical Officer of Karyopharm. "Following the promising initial results of selinexor in relapsed and refractory myelofibrosis, we are very excited with these preliminary data in treatment-naïve myelofibrosis patients in combination with ruxolitinib, with encouraging results seen across multiple measures including spleen volume reductions, improvements in symptom scores and management of anemia. We look forward to sharing these promising initial data with the broader medical and scientific community at ASCO 2022."

SIENDO Study Subgroup Analysis

A preliminary analysis of exploratory subgroups of the SIENDO study assessed four distinct molecular subtypes

in endometrial cancer using The Cancer Genome Atlas (TCGA), one of the accepted gynecologic oncology algorithms that is used to calculate prognostic risk scores. This analysis indicated that patients with p53 wild-type endometrial cancer treated with selinexor showed a median progression-free survival of 13.7 months compared to 3.7 months for patients on placebo.

"These data suggest that selinexor may provide meaningful benefit to patients with p53 wild-type endometrial cancer and reinforce the need to further evaluate selinexor's potential in a registration-enabling Phase 3 study, that we are planning to initiate in the second half of this year," added Dr. Rangwala.

Details for the ASCO 2022 selinexor presentations are as follows:

Oral Presentation

Title: Randomized phase III study of maintenance selinexor versus placebo in endometrial cancer (ENGOT - EN5/GOG-3055/SIENDO): Impact of subgroup analysis and molecular classification
Presenter: Vicky Makker, Memorial Sloan Kettering Cancer Center
Abstract #: 5511
Date and time: Tuesday, June 7, 2022, 9:48 a.m. – 10:00 a.m. EDT
Session: Clinical Science Symposium/Molecular-Based Treatment for Endometrial Cancer

Poster Presentations

Title: A phase 1, open-label, dose-escalation study of selinexor plus ruxolitinib in patients with treatment-naïve myelofibrosis
Presenter: Haris Ali, City of Hope
Abstract #: 7060
Date and time: Saturday, June 4, 2022, 9:00 a.m. – 12:00 p.m. EDT
Session: Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant

Title: Phase Ib trial of selinexor (SEL) in combination with nivolumab (NIVO) alone or nivolumab plus ipilimumab (NIVO+IPI) in patients (pts) with advanced malignancies: The renal cell carcinoma (RCC) experience.
Presenter: Omar Alhalabi, The University of Texas MD Anderson Cancer Center
Abstract #: 4551
Date and time: Saturday, June 4, 2022, 2:15 p.m. – 5:15 p.m. EDT
Session: Genitourinary Cancer–Kidney and Bladder

Title: Phase 1b study of weekly split-dose selinexor in soft tissue sarcoma (STS)
Presenter: Abdulazeez Salawu, University Health Network
Abstract #: 11563
Date and time: Sunday, June 5, 2022, 9:00 a.m. – 12:00 p.m. EDT
Session: Sarcoma

Title: Digital monitoring and assessments in patients with glioblastoma
Presenter: Yasaman Damestani, Karyopharm Therapeutics, Inc**.**
Abstract #: 2045
Date and time: Sunday, June 5, 2022, 9:00 a.m. – 12:00 p.m. EDT
Session: Central Nervous System Tumors

Title: Phase Ib study of selinexor and eribulin combination in advanced solid tumors and triple-negative breast cancer
Presenter: Blessie Elizabeth Nelson, University of Texas MD Anderson Cancer Center
Abstract #: 3108
Date and time: Sunday, June 5, 2022, 9:00 a.m. – 12:00 p.m. EDT
Session: Developmental Therapeutics–Molecularly Targeted Agents and Tumor Biology

About the SIENDO Study

The Phase 3 SIENDO study (ENGOT-EN5/GOG-3055) is a multicenter, blinded, placebo-controlled, randomized study evaluating the efficacy and safety of selinexor as a maintenance therapy following chemotherapy in patients with advanced or recurrent endometrial cancer. The study enrolled 263 patients with primary stage IV or recurrent disease who had a partial or complete response after at least 12 weeks of standard taxane-platinum combination chemotherapy. Patients were randomized 2:1 to receive either maintenance therapy of 80mg of selinexor taken once weekly, or placebo, until disease progression. The primary endpoint of the study was statistically significant improvement of progression-free survival compared to placebo. The goal of the study was to demonstrate a hazard ratio of 0.6 or better. In partnership with Karyopharm, the study was

initiated by the European Network for Gynaecological Oncological Trial (ENGOT) group. In the U.S., the collaboration includes the GOG Foundation, Inc. (GOG-F).

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 multiple myeloma, 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, which was filed with the Securities and Exchange Commission (SEC) on May 5, 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.

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