Karyopharm Announces Preliminary Unaudited Fourth Quarter and Full Year 2022 Revenue and Outlines 2023 Objectives

– Preliminary Unaudited Full Year 2022 Total Revenue and U.S. XPOVIO® (selinexor) Net Product Revenue Expected to be Approximately $157.7 Million and $120.4 Million, Respectively, Meeting Company's Guidance –

– Initiated Pivotal Phase 3 Study Evaluating Selinexor as a Maintenance Therapy in Women with Advanced or Recurrent TP53 Wild-Type Endometrial Cancer; Encouraging Updated Exploratory Subgroup Analysis in Patients with TP53 Wild-Type Endometrial Cancer Continues to Support Study Rationale; Partnership with Foundation Medicine to Develop TP53 Companion Diagnostic –

– Planning to Initiate Pivotal Phase 3 Study in Front-Line Myelofibrosis in 1H 2023; Report Updated Results from the Phase 1 study of Selinexor in Combination with Ruxolitinib in Patients with Treatment-Naïve MF in 1H 2023 –

– Anticipate Multiple Data Catalysts and Progress Across Multiple Myeloma, Myelofibrosis, Endometrial Cancer and Myelodysplastic Neoplasms in 2023 –

– Extended Cash Runway to Late 2025 –

NEWTON, Mass., Jan. 9, 2023 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced preliminary unaudited fourth quarter and full year 2022 total revenue and U.S. XPOVIO net product revenue estimates and outlined its 2022 achievements and 2023 objectives.

Based on preliminary unaudited financial information, Karyopharm expects total revenue, which includes license and royalty revenue from partners, to be approximately $34.2 million for the fourth quarter 2022 and approximately $157.7 million for the full year 2022, and net product revenue for XPOVIO in the U.S. to be approximately $31.1 million for the fourth quarter 2022 and approximately $120.4 million for the full year 2022, representing growth of 22% over 2021.

"In 2022, we delivered solid revenue growth with XPOVIO and made meaningful progress with our pipeline, achieving several clinical and regulatory milestones. Importantly, we solidified our financial runway to late 2025, enabling us to be well positioned to deliver the next stages of the company's growth. Moving forward in 2023, we look to continue growing our foundation in multiple myeloma, progressing our focused clinical pipeline through several important milestones, and leveraging both our commercialization and mid to late-stage clinical development expertise to deliver value for our shareholders and patients," said Richard Paulson, President and Chief Executive Officer of Karyopharm.

Key Program Highlights in 2022

Selinexor in Multiple Myeloma (MM)

- Over 20% U.S. revenue growth driven by continued progress in shifting selinexor use into earlier lines of therapy and strong growth in the community setting, accounting for approximately 70% of selinexor revenues, offsetting increased pressure in the academic setting due to intensifying late-line competition and ongoing trials.
- Selinexor is now approved in 40 countries globally, following full marketing authorization from the European Commission for NEXPOVIO® (selinexor) in combination with bortezomib (Velcade®) and dexamethasone (SVd) for the treatment of adult patients with multiple myeloma who have received at least one prior therapy, expanding the indication to 2L+.
- First patient dosed in pivotal Phase 3 study, in collaboration with and sponsored by the European Myeloma Network (EMN), evaluating an all-oral regimen of selinexor in combination with pomalidomide and dexamethasone post anti-CD38 therapy in relapsed/refractory MM.

Selinexor in Endometrial Cancer (EC)

- Initiated pivotal Phase 3 study of selinexor as a maintenance therapy following systemic therapy in patients with *TP53* wild-type advanced or recurrent endometrial cancer (EC-042; NCT03555422).
- Entered into a global collaboration with Foundation Medicine, Inc., a pioneer in molecular profiling for

cancer, to develop FoundationOne®CDx as a companion diagnostic for selinexor and to identify and enroll patients whose tumors are *TP53* wild-type in the EC-042 Phase 3 study.

Eltanexor in Myelodysplastic Neoplasms (MDS)

- Completed recruitment for the interim analysis of the Phase 2 study evaluating eltanexor in relapsed/refractory MDS.
- Received orphan drug designations by the U.S. Food and Drug Administration (FDA) and the European Commission for eltanexor for the treatment of MDS. The FDA also granted Fast Track Designation for eltanexor in MDS.

Selinexor in Myelofibrosis (MF)

- Presented encouraging preliminary data results from the Phase 1 study (XPORT-MF-034) evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve MF at the American Society of Hematology (ASH) Annual Meeting. Initial data from this study were also presented at the European Hematology Association (EHA) 2022 Hybrid Congress and ASCO.
- Received orphan drug designations from the FDA and the European Commission for selinexor for the treatment of MF.

Corporate and Financial Highlights for 2022

- Based on preliminary unaudited financial information, expect total revenue to be approximately $157.7 million, including estimated U.S. XPOVIO net product revenue of approximately $120.4 million, an increase of 22% from 2021.
- Cash, cash equivalents, restricted cash and investments as of December 31, 2022 was approximately $279.0 million, following the completion of a $165 million private placement in December 2022, extending cash runway to late 2025.
- Strengthened leadership team with several key appointments, including Reshma Rangwala, MD, PhD as Chief Medical Officer and Stuart Poulton as Chief Development Officer.

Anticipated Near-Term Catalysts and Operational Objectives in 2023

- Continue to grow our commercial foundation in the competitive multiple myeloma marketplace, driving increased XPOVIO sales.
- Additional global launches of selinexor by partners in ex-U.S. territories.
- Present data supporting optimization of selinexor dose in multiple myeloma and other key programs.
- Continue to generate data demonstrating selinexor's efficacy, combinability and tolerability in patients with multiple myeloma.
- Report interim data from the Phase 2 study evaluating eltanexor in relapsed/refractory MDS in 1Q.
- Report updated results from the Phase 1 study of selinexor in combination with ruxolitinib in patients with treatment-naïve MF in 1H. Initiate pivotal Phase 3 study in front-line myelofibrosis in 1H 2023, subject to regulatory feedback.
- Present updated subgroup analysis results in patients with TP53 wild-type endometrial cancer from the SIENDO study at a medical conference in 2023 further supporting rationale for EC-042 pivotal Phase 3 study.
- Further exploration of biomarker subsets to identify patient populations who best respond to SINE compounds.

The financial information presented in this press release may be adjusted as a result of the completion of customary quarterly and annual review and audit procedures.

Listen to the Webcast

These achievements and updates will be discussed during a webcast presentation at the 41st Annual J.P. Morgan Healthcare Conference to be held on January 11, 2023, at 1:30 p.m. Eastern Time/10:30 a.m. Pacific Time. A live webcast of the presentation and breakout session, along with accompanying slides, can be accessed under "Events & Presentations" in the Investor section of the Company's website, http://investors.karyopharm.com/events-presentations. An archived replay will be available for 30 days following the event. The presentation slides will also be available on the Company's website following the event.

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 Karyopharm's preliminary financial information for the fourth quarter and full year 2022; guidance on its expected cash runway; the ability of selinexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma, solid tumors and other diseases; expectations with respect to commercialization efforts; and expectations with respect to the clinical development plans and potential regulatory submissions of selinexor and 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 September 30, 2022, which was filed with the Securities and Exchange Commission (SEC) on November 3, 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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