Karyopharm Announces Preliminary Unaudited 2024 Revenue and 2025 Objectives

– Opportunity to Define a New Myelofibrosis Treatment Paradigm with Top-Line Data Readout from Phase 3 SENTRY Trial Evaluating Selinexor in Combination with Ruxolitinib in Patients with JAKi-Naïve Myelofibrosis Anticipated in 2H 2025; Company On Track to Complete Enrollment in 1H 2025 –

– Recently Announced Key Leadership Changes, including the Appointment ofLori Macomber as Chief Financial Officer and Brendan Strong as SVP of Investor Relations and Corporate Communications –

– Preliminary Unaudited Full Year 2024 Total Revenue and U.S. XPOVIO® (selinexor) Net Product Revenue Expected to be Approximately $145 Million and $113 Million, Respectively –

NEWTON, Mass., Jan. 13, 2025 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced preliminary unaudited fourth quarter and full year 2024 total revenue and U.S. XPOVIO net product revenue estimates and outlined its 2024 achievements and 2025 objectives.

"Our top strategic objective for 2025 is to deliver on the transformative opportunity to redefine the standard of care in myelofibrosis, with top-line results from our Phase 3 SENTRY trial on-track for the second half of this year. Our teams are focused on high-quality clinical trial execution, engaging with investigators and diligently completing enrollment in the first half of this year," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "We are excited by the potential for selinexor to be the first all-oral combination therapy in myelofibrosis and the benefit it may bring to this community. We look forward to reporting our top-line data and are preparing for a rapid launch, leveraging our demonstrated commercialization capabilities."

Key Program Highlights in 2024

Selinexor in Multiple Myeloma (MM)

- Demand for XPOVIO was consistent in 2024 versus 2023, with demand growth in the second half of 2024 in both the community setting, which represents approximately 60% of XPOVIO net product revenue, and the academic setting, offsetting a decline in demand in the first half of the year due to an intensified competitive landscape.
- XPOVIO net product revenue was impacted year-over-year by higher gross-to-net adjustments in 2024, driven primarily by increased 340B discounts and Medicare rebates.
- Expanded global patient access for selinexor in 2024 with favorable reimbursement decisions in theUnited Kingdom, France, Italy, China and South Korea and additional regulatory approvals in UAE,Kuwait, China, Malaysia, Turkey, Thailand, and South Korea in various indications, increasing the number of countries where selinexor is now approved to more than 45 countries.
- Updated clinical data on selinexor in combination with pomalidomide and dexamethasone (SPd) regimen from the Phase 2 STOMP (NCT02343042) and the Phase 2 XPORT-MM-028 (NCT04414475) trials were published in the Frontiers of Oncology Journal in May 2024. Both trials are evaluating multiple selinexor combinations, including SPd, in patients with relapsed or refractory multiple myeloma. The updated results for SPd 40 mg from these studies showed a median progression free survival of 18.4 months and a manageable safety profile with no new safety signals identified.
- Completed enrollment of the Phase 3 XPORT-MM-031 trial (EMN29; NCT05028348) of approximately 120 patients, leveraging the data published on selinexor 40 mg, pomalidomide and dexamethasone (SPd40) in 2024. The Phase 3 XPORT-MM-031 trial is being conducted in collaboration with the European Myeloma Network and is evaluating the all-oral combination SPd40 in patients with previously treated multiple myeloma who received an anti-CD38 in their immediate prior line of therapy. Pending ongoing engagement with regulatory agencies on the updated protocol and statistical plan, the Company intends to provide an update on this trial.
- Presented preclinical, translational, and real-world evidence data at multiple scientific conferences evaluating the role of XPO1 inhibition and selinexor in T-cell fitness.

Selinexor in Myelofibrosis (MF)

- Updated the co-primary endpoint on the Phase 3 SENTRY trial (XPORT-MF-034; NCT04562389) to absolute mean change in total symptom score (Abs-TSS) following alignment with the U.S. Food and Drug Administration (FDA) and proactively increased the total sample size to approximately 350 patients to further increase the statistical powering. Abs-TSS measures the average improvement in symptom scores over 24 weeks relative to the baseline symptom score. Abs-TSS is viewed by many key opinion leaders (KOLs) and patient advocacy organizations as a more accurate assessment

of symptom improvement in head-to-head clinical trials, such as SENTRY which is evaluating selinexor in combination with ruxolitinib in patients with JAK inhibitor (JAKi) naïve myelofibrosis versus ruxolitinib alone. Spleen volume reduction ≥35% (SVR35) at week 24 remains the other co-primary endpoint. These two co-primary endpoints will be tested sequentially starting with SVR35 followed by Abs-TSS.

- Hosted an investor event with leading KOLs in October 2024 to discuss the change in the co-primary endpoint in the Phase 3 SENTRY trial to Abs-TSS and highlight the strength of the data from the Company's Phase 1 trial in myelofibrosis. Data from the Company's Phase 1 trial, evaluating the combination of selinexor 60 mg plus ruxolitinib in JAKi naïve myelofibrosis patients, demonstrated that 79% of patients in the intent to treat population (n=14) achieved SVR35 and an average Abs-TSS improvement of 18.5 points in the efficacy evaluable population (n=9), at week 24 relative to baseline. Acknowledging the small sample size, these data suggest that the combination is favorable compared to historical ruxolitinib monotherapy data which indicates that less than half of patients achieve SVR35 and an Abs-TSS improvement of 11 to 14 points[1]. As of the most recent data cut off, the safety profile remained consistent and no new safety signals were identified.
- Presented pre-clinical data at the June 2024 European Hematology Association Meeting which support selinexor's potential mechanism of action targeting multiple oncogenic pathways beyond JAK/STAT. This data builds on the compelling clinical data on selinexor in myelofibrosis.

[1]Phase 3 MANIFEST trial. Rampal R, et al. ASH 2023. Oral 628; Phase 3 TRANSFORM-1 trial Pemmaraju N, et al. ASH 2023 abstract 620.

Selinexor in Endometrial Cancer (EC)

- The Company remains engaged with the FDA regarding the evolving treatment landscape in endometrial cancer and any implications this may have with respect to the Company's Phase 3 XPORT-EC-042 trial (NCT05611931). The Company intends to provide an update on its endometrial cancer program in the first quarter of 2025.

Other Pipeline Assets

- KPT-9274 (padnarsertib), a first-in-class, oral small molecule and a dual inhibitor of PAK4 and NAMPT that was discovered at Karyopharm, was granted two Rare Pediatric Disease Designations by the FDA for the treatment of Rhabdomyosarcoma (RMS) and for the treatment of Ewing sarcoma (EWS) in June 2024. The FDA further granted KPT-9274 two Orphan Drug Designations in July 2024 for the treatment of soft tissue sarcoma, which includes RMS, and for the treatment of EWS. RMS and EWS are rare cancers of the bone or soft tissue, primarily diagnosed in pediatric patients, with poor survival outcomes and high unmet need for new therapies. KPT-9274 showed tumor regressions and decreased metastatic properties in pediatric RMS and EWS pre-clinical models. Karyopharm is evaluating out-licensing and/or partnership opportunities for further advancement of this program.
- In February 2024, the Company reacquired KPT-350 and other assets, which had been sold to Biogen Inc. in January 2018 under an asset purchase agreement. KPT-350 is a clinical stage SINE compound under evaluation for neurological indications, including amyotrophic lateral sclerosis. Karyopharm intends to evaluate KPT-350 for development through a third-party.

Corporate and Financial Highlights for 2024

- Based on preliminary unaudited financial information, the Company expects total revenue, which includes license and royalty revenue from partners, to be approximately $30 million for the fourth quarter 2024 and approximately $145 million for the full year 2024, and U.S. XPOVIO net product revenue to be approximately $29 million for the fourth quarter 2024 and approximately $113 million for the full year 2024.
- Completed significant refinancing transactions and amended royalty agreement with HealthCare Royalty extending the vast majority of the Company's debt maturities into 2028 and 2029.
- Expect to deliver meaningful reductions in selling, general and administrative expense in 2024 as the Company focused its resources on research and development initiatives and overall cost optimization opportunities.
- Announced the appointment of Lori Macomber as Executive Vice President, Chief Financial Officer and Treasurer, effective January 3, 2025.
- Announced the appointment of Brendan Strong as Senior Vice President of Investor Relations and Corporate Communications, effective December 9, 2024.
- Cash, cash equivalents, restricted cash and investments as of December 31, 2024 was approximately $109 million. The Company expects that its existing cash, cash equivalents and investments, the revenue it expects to generate from XPOVIO net product sales and its license agreements and ongoing disciplined expense management and cost saving measures, will be sufficient to fund its planned operations into the first quarter of 2026.[2]

[2]Excluding re-payment of $24.5 million aggregate principal amount of the Company's remaining senior convertible notes due October 2025 (the 2025 Notes) and $25.0 million minimum liquidity covenant under the Company's senior secured term loan due 2028. Taking into account the repayment of the 2025 Notes and the minimum liquidity covenant, Karyopharm expects its cash, cash equivalents and investments will be sufficient to fund its operations into the fourth quarter of 2025.

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

Key Catalysts and Operational Objectives Anticipated in 2025

Myelofibrosis (MF)

- Announce completion of enrollment of the Phase 3 SENTRY trial evaluating selinexor in combination with ruxolitinib in JAKi naive myelofibrosis patients in 1H 2025.
- Report preliminary data on a subset of participants in the Phase 2 SENTRY-2 trial (XPORT-MF-044; NCT05980806) evaluating selinexor as a monotherapy in patients with JAKi naïve myelofibrosis with moderate thrombocytopenia in 1H 2025.
- Report topline results from the Phase 3 SENTRY trial in 2H 2025.

Multiple Myeloma (MM)

- Maintain the Company's commercial foundation in the competitive multiple myeloma marketplace and drive increased XPOVIO revenues in 2025.
- Continue global launches and reimbursement approvals for selinexor by partners in ex-U.S. territories.
- Continue to follow patients that are enrolled in the Phase 3 XPORT-MM-031 (EMN29) trial. Pending ongoing engagement with regulatory agencies on the updated protocol and statistical plan, the Company intends to provide an update on this trial.

Endometrial Cancer (EC)

- Continue to enroll patients in the Phase 3 XPORT-EC-042 trial of selinexor as a maintenance monotherapy for patients with TP53 wild type advanced or recurrent endometrial cancer. The Company remains engaged with the FDA regarding the evolving treatment landscape in endometrial cancer and any implications this may have with respect to the Company's Phase 3 XPORT-EC-042 trial. The Company intends to provide an update on its endometrial cancer program in the first quarter of 2025.

Corporate Presentation
Karyopharm will be posting an updated corporate overview presentation on its website today. The presentation will be accessible under "Events & Presentations" in the Investor section of the Company's website, http://investors.karyopharm.com/events-presentations.

About the Phase 3 SENTRY Trial
SENTRY (NCT04562389) is a pivotal, Phase 3 clinical trial evaluating a once-weekly dose of 60 mg of selinexor in combination with twice-daily ruxolitinib versus placebo plus ruxolitinib in JAKi naïve patients with platelet counts $\geq$100 x 10^9/L. Karyopharm intends to enroll approximately 350 JAKi naïve patients with myelofibrosis in this Phase 3 trial; patients are randomized 2:1 to the selinexor arm. The co-primary endpoints will be spleen volume response rate ≥ 35% (SVR35) at week 24 and the absolute mean change in total symptom score (Abs-TSS) over 24 weeks relative to baseline.

About the Phase 3 XPORT-EC-042 Study
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, 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 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 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) under accelerated approval 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, Mainland China, Taiwan, Hong Kong, Australia, South Korea, Singapore, Israel, and Canada. XPOVIO®/NEXPOVIO® is marketed in these respective ex-U.S. territories by Karyopharm's partners: Antengene, Menarini, Neopharm, and FORUS. 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

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 two 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 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 whose dedication to pioneering novel cancer therapies is fueled by a belief in the extraordinary strength and courage of patients with cancer. Since its founding, Karyopharm has been an industry leader in oral compounds that address nuclear export dysregulation, a fundamental mechanism of oncogenesis. Karyopharm's lead 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. It has also 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 indications in multiple high unmet need cancers, including in multiple myeloma, endometrial cancer, myelofibrosis, and diffuse large B-cell lymphoma (DLBCL). For more information about our people, science and pipeline, please visit www.karyopharm.com, and follow us on LinkedIn and on X at @Karyopharm.

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 2024; guidance on its expected cash runway; expectations with respect to commercialization efforts; the ability of selinexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma and other diseases; and expectations with respect to the clinical development plans 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, 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 trials, including subsequent analysis of existing data and new data received from ongoing and future trials; 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 trials; 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; substantial doubt exists regarding Karyopharm's ability to continue as a going concern; 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, 2024, which was filed with the Securities and Exchange Commission (SEC) on November 5, 2024, 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.

SOURCE Karyopharm Therapeutics Inc.

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