Karyopharm Reports First Quarter 2025 Financial Results and Announces New Data in Myelofibrosis that Further Suggests Selinexor May Lead to Meaningful Spleen Volume Reduction, Symptom Improvement, Hemoglobin Stabilization and Disease Modification

– New Randomized Phase 2 Monotherapy Data from XPORT-MF-035 Trial in a Hard-to-Treat Patient Population Further Strengthens Conviction in Selinexor's Potential in Combination with Ruxolitinib in JAKi-Naïve Myelofibrosis in Ongoing Phase 3 SENTRY Trial –

– Phase 3 SENTRY Trial Passed Planned Futility Analysis; Trial is Approximately 80% Enrolled with Target Enrollment Expected in June/July 2025 –

– Demand for XPOVIO® (selinexor) Increased 5% in the First Quarter of 2025 Compared to the First Quarter of 2024; Total Revenue was $30.0 Million; U.S. XPOVIO® Net Product Revenue of $21.1 Million was Adversely Impacted by a $5.0 Million Increase in the Product Return Reserve due to Atypical Returns of Expired 80 mg and 100 mg Units –

– Reaffirms Full-Year 2025 Total Revenue Guidance of $140 Million to $155 Million, Including U.S. XPOVIO Net Product Revenue Guidance of $115 Million to $130 Million –

– Company is Exploring Various Alternatives to Extend Cash Runway –

– Conference Call Scheduled for Today at 4:30 p.m. ET –

NEWTON, Mass., May 12, 2025 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today reported financial results for the first quarter ended March 31, 2025 and highlighted progress on key clinical development programs.

"We are pleased that our Phase 3 SENTRY trial in patients with JAKi-naïve myelofibrosis has passed its pre-specified futility analysis and continues as planned without modifications. Our conviction in this trial is further strengthened by our new data in hard-to-treat myelofibrosis patients where we observed spleen volume reduction, symptom improvement, hemoglobin stabilization and evidence of disease modification with selinexor monotherapy, addressing all four hallmarks of the disease," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "The outcomes that we have observed from our multiple pre-clinical and clinical trials continue to suggest that selinexor may be additive, if not synergistic, when combined with ruxolitinib in JAKi-naïve myelofibrosis patients. This combination holds the potential to be a much needed, new standard of care for patients with myelofibrosis."

First Quarter 2025 Highlights

XPOVIO Commercial Performance

- Demand for XPOVIO increased 5% in the first quarter of 2025 compared to the first quarter of 2024, with demand growth in both the community and academic settings.
- U.S. net product revenue was $21.1 million in the first quarter of 2025 compared to $26.0 million in the first quarter of 2024. Net product revenue in the first quarter of 2025 was impacted by a $5.0 million increase in the product return reserve due to atypical returns of expired 80 mg and 100 mg units from clinics and hospitals that had purchased these units following the 2020 approval by the U.S. Food and Drug Administration of XPOVIO® 100 mg in combination with bortezomib and dexamethasone. The majority of XPOVIO® that is prescribed today are 40 mg and 60 mg doses, and the Company expects product returns will revert to historical levels in future quarters.
- Expanded global patient access for selinexor is translating into growth in royalty revenue from Menarini, Antengene and other international partners. Royalty revenue increased 57% to $1.7 million in the first quarter of 2025 compared to the first quarter of 2024.

Research and Development (R&D) Highlights

Myelofibrosis

- The Phase 3 SENTRY trial (XPORT-MF-034; NCT04562389) continues as planned without any modifications following a pre-specified futility analysis conducted by the independent Data Safety and Monitoring Board. The trial is now approximately 80% enrolled. SENTRY is evaluating 60 mg once-weekly selinexor in combination with ruxolitinib compared to ruxolitinib plus placebo and is targeting 350 patients for enrollment.
- Data from the XPORT-MF-035 (NCT04562870) Phase 2, randomized, open-label trial of selinexor versus physician's-choice (PC) in hard-to-treat patients with heavily pretreated myelofibrosis indicated signs of single-agent clinical activity with selinexor, including spleen volume reduction, hemoglobin stabilization, symptom improvement and evidence of disease modification. Patients were randomized 1:1 to either selinexor monotherapy or PC. Selinexor was administered at 80 mg weekly for the first two cycles and then decreased to 60 mg weekly from cycle 3 onwards. An optional crossover was available for PC treated patients if they met predefined spleen progression criteria. In total, 12 patients were randomized to the selinexor arm and 12 patients to the PC arm; 6 patients crossed over from PC to selinexor. Inclusive of crossover, spleen volume reduction of 25% or more (SVR25) at anytime was achieved in 8/12 (67%) efficacy evaluable selinexor treated patients versus 3/8 (38%) efficacy evaluable patients treated with PC. Spleen volume reduction of 35% or more (SVR35) at anytime was observed in 4/12 (33%) efficacy evaluable patients treated with selinexor versus 1/8 (13%) efficacy evaluable patients treated with PC. Patients treated with selinexor had higher mean hemoglobin levels throughout the study duration and lower rates of red blood cell transfusions than those treated with PC. In addition, data on key cytokines that are relevant to myelofibrosis pathogenesis, symptom development, and anemia including IL-6, IL-8, TNFa, and hepcidin, demonstrated greater reductions at week 4 compared to baseline in patients treated with selinexor than patients treated with PC. Most common (≥25% overall) treatment emergent adverse events (TEAEs) in the randomized arms were decreased weight (selinexor: 50%; PC: 50%), anemia (25%; 58%), asthenia (42%; 25%), nausea (33%; 25%), thrombocytopenia (33%; 25%) and upper respiratory tract infection (25%; 33%). Most common (≥15% in any arm) Grade 3+ TEAEs were anemia (17%; 58%), cardiac failure (0%; 17%), decreased appetite (17%; 0%) and nausea (17%; 8%). No treatment discontinuations due to TEAEs were observed in the selinexor arm. In 2023, Karyopharm decided to stop enrollment at 24 patients in this trial to focus resources on the Phase 3 SENTRY trial.
- The Company continues to enroll patients into the 60 mg cohort of the Phase 2 SENTRY-2 trial of selinexor monotherapy in JAKi-naïve patients with moderate thrombocytopenia (XPORT-MF-044; NCT05980806).

Endometrial Cancer

- Enrollment continues in the Phase 3 XPORT-EC-042 (NCT05611931) trial evaluating selinexor as a maintenance-only therapy following systemic therapy versus placebo in patients with *TP53* wild-type advanced or recurrent endometrial cancer. The Company expects to report top-line data from this event-driven trial in mid-2026.

Multiple Myeloma

- Enrollment of approximately 120 patients in the Phase 3 XPORT-MM-031 trial (EMN29; NCT05028348) was completed in the fourth quarter of 2024. The trial is being conducted in collaboration with the European Myeloma Network and is evaluating the all-oral combination of selinexor 40 mg, pomalidomide and dexamethasone (SPd40) in patients with previously treated multiple myeloma who received an anti-CD38 in their immediate prior line of therapy. The Company expects to report top-line data from this event-driven trial in the first half of 2026.

Anticipated Catalysts and Operational Objectives in 2025

Myelofibrosis

- Announce completion of target enrollment (N=350) of the Phase 3 SENTRY trial evaluating selinexor in combination with ruxolitinib in JAKi-naive myelofibrosis patients in June/July 2025.
- Report preliminary data on a subset of participants in the 60 mg cohort from the Phase 2 SENTRY-2 trial evaluating selinexor as a monotherapy in patients with JAKi-naïve myelofibrosis with moderate thrombocytopenia in 1H 2025.
- Report top-line results from the Phase 3 SENTRY trial in late 2025/early 2026.

Multiple Myeloma

- Maintain the Company's commercial foundation in the increasingly competitive multiple myeloma marketplace and drive increased XPOVIO revenues.
- Continue global launches and regulatory 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.

Endometrial Cancer

- Continue to enroll patients into the Phase 3 XPORT-EC-042 trial of selinexor as a maintenance monotherapy for patients with *TP53* wild-type advanced or recurrent endometrial cancer.

2025 Financial Outlook

Based on its current operating plans, Karyopharm expects the following for full year 2025:

- Total revenue to be in the range of $140 million to $155 million. Total revenue consists of U.S. XPOVIO net product revenue and license, royalty and milestone revenue earned from partners.
- U.S. XPOVIO net product revenue to be in the range of $115 million to $130 million.
- R&D and selling, general and administrative (SG&A) expenses to be in the range of $240 million to $255 million, which includes approximately $20 million of estimated non-cash stock-based compensation expense.
- The Company expects that its existing cash, cash equivalents and investments, and the revenue it expects to generate from XPOVIO net product sales, as well as revenue generated from its license agreements, will fund its planned operations into early first quarter of 2026.[1]

[1]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 fund its operations into early fourth quarter of 2025. The Company is exploring various alternatives to extend its cash runway, which may not result in the consummation of any transaction.

First Quarter 2025 Financial Results

Please note: All share amounts and per share amounts in this press release have been adjusted to reflect a 1-for-15 reverse split of our common stock, which we effected on February 25, 2025.

Total revenue: Total revenue for the first quarter of 2025 was $30.0 million, compared to $33.1 million for the first quarter of 2024.

Net product revenue: Net product revenue for the first quarter of 2025 was $21.1 million, compared to $26.0 million for the first quarter of 2024. The decrease in net product revenue was due to an increase in the gross-to-net provision, primarily related to atypical product returns recorded in the first quarter of 2025, resulting in a $5.0 million increase in the product return reserve.

License and other revenue: License and other revenue for the first quarter of 2025 was $9.0 million, compared to $7.1 million for the first quarter of 2024. The increase was attributable to timing of revenue recognition for the reimbursement of development-related expenses from Menarini.

Cost of sales: Cost of sales for the first quarter of 2025 was $1.3 million, compared to $1.9 million for the first quarter of 2024. Cost of sales reflects the costs of XPOVIO units sold and the costs of products sold to our partners.

R&D expenses: R&D expenses for the first quarter of 2025 were $34.6 million, compared to $35.4 million for the first quarter of 2024. The decrease was due to a reduction in personnel costs, partially offset by increased clinical trial activity related to our myelofibrosis trial.

SG&A expenses: SG&A expenses for the first quarter of 2025 were $27.4 million, compared to $29.5 million for the first quarter of 2024. The decrease was primarily due to the realization of previously implemented cost reduction initiatives.

Interest income: Interest income for the first quarter of 2025 was $1.0 million, compared to $2.2 million for the first quarter of 2024. The decrease in interest income was due to a lower cash and investments balance quarter-over-quarter.

Interest expense: Interest expense for the first quarter of 2025 was $11.0 million, compared to $5.9 million for the first quarter of 2024. The increase was related to the term loan and convertible debt that were issued in the second quarter of 2024.

Other income: Other income for the first quarter of 2025 was $19.8 million due to recurring non-cash fair value remeasurements which related to the refinancing transactions that were completed in the second quarter of 2024. The Company had immaterial other income in the first quarter of 2024.

Net loss: Karyopharm reported a net loss of $23.5 million, or $2.77 per basic and diluted share, for the first quarter of 2025, compared to a net loss of $37.4 million, or $4.85 per basic and diluted share, for the first quarter of 2024. Net loss included non-cash stock-based compensation expense of $3.6 million and $5.0 million for the first quarters of 2025 and 2024, respectively.

Cash position: Cash, cash equivalents, restricted cash and investments as of March 31, 2025 totaled $70.3 million, compared to $109.1 million as of December 31, 2024.

Conference Call Information

Karyopharm will host a conference call today, May 12, 2025, at 4:30 p.m. Eastern Time, to discuss the first quarter 2025 financial results, the financial outlook for 2025 and to provide other business updates. To access the conference call, please

dial (800) 836-8184 (local) or (646) 357-8785 (international) at least 10 minutes prior to the start time and ask to be joined into the Karyopharm Therapeutics call. A live audio webcast of the call, along with accompanying slides, will be available under "Events & Presentations" in the Investor section of the Company's website. An archived webcast will be available on the Company's website approximately two hours after 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 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 adult patients with multiple myeloma after at least one prior therapy; (ii) in combination with dexamethasone in adult patients with heavily pre-treated multiple myeloma; and (iii) under accelerated approval in adult 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 guidance on its 2025 total revenue, 2025 U.S. net product revenue and 2025 R&D and SG&A expenses; 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 Annual Report on Form 10-K for the year ended December 31, 2024, which was filed with the Securities and Exchange Commission (SEC) on February 19, 2025, 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.

KARYOPHARM THERAPEUTICS INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(unaudited)
(in thousands, except per share amounts)

	Three Months Ended March 31,	
	2025	**2024**
Revenues:		
Product revenue, net	$ 21,054	$ 26,006
License and other revenue	8,961	7,120
Total revenue	30,015	33,126
Operating expenses:		
Cost of sales	1,301	1,911
Research and development	34,618	35,425
Selling, general and administrative	27,352	29,549
Total operating expenses	63,271	66,885
Loss from operations	(33,256)	(33,759)
Other income (expense):		
Interest income	1,000	2,156
Interest expense	(10,994)	(5,884)
Other income, net	19,824	196
Total other income (expense), net	9,830	(3,532)
Loss before income taxes	(23,426)	(37,291)
Income tax provision	(36)	(71)
Net loss	$ (23,462)	$ (37,362)
Basic and diluted net loss per share	$ (2.77)	$ (4.85)
Weighted-average number of common shares outstanding used to compute basic and diluted net loss per share	8,470	7,700

KARYOPHARM THERAPEUTICS INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(unaudited)
(in thousands)

	March 31, 2025	**December 31, 2024**
Assets		
Cash, cash equivalents and investments	$ 69,941	$ 108,712
Restricted cash	340	338
Accounts receivable	35,243	30,766
Other assets	22,187	24,602
Total assets	$ 127,711	$ 164,418
Liabilities and stockholders' deficit		
Convertible senior notes due 2025	$ 24,459	$ 24,426
Convertible senior notes due 2029	59,635	68,345
Senior secured term loan	95,197	94,603
Deferred royalty obligation	73,499	73,499
Other liabilities	80,805	89,562
Total liabilities	333,595	350,435
Total stockholders' deficit	(205,884)	(186,017)

Total liabilities and stockholders' deficit; 8,568 and 8,413 shares issued and outstanding at March 31, 2025 and December 31, 2024, respectively	$ 127,711	$ 164,418

SOURCE Karyopharm Therapeutics Inc.

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