Karyopharm Reports Third Quarter 2024 Financial Results and Highlights Recent Company Progress

– Achieves Third Quarter 2024 Total Revenue of $38.8 Million and U.S. XPOVIO® (selinexor) Net Product Revenue of $29.5 Million; Continued Regulatory and Reimbursement Approvals Globally –

– Following FDA Alignment, Absolute Change in Total Symptom Score (Abs-TSS) Will Replace TSS50 as a Co-Primary Endpoint in Phase 3 SENTRY Trial in JAKi Naïve Myelofibrosis (MF); Expected Top-line Data Read-out Remains on Track for 2H 2025 –

– Narrows Full-Year 2024 Total Revenue Guidance Range to $145.0 Million to $155.0 Million; U.S. XPOVIO Net Product Revenue Guidance Range to $110.0 Million to $115.0 Million; R&D and SG&A Expense Guidance Range to $255.0 Million to $265.0 Million –

NEWTON, Mass., Nov. 5, 2024 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today reported financial results for the quarter ended September 30, 2024, and highlighted select corporate milestones and progress on its key clinical development programs.

"This quarter, we delivered our third consecutive quarter of U.S. XPOVIO net product revenue growth in the highly competitive multiple myeloma marketplace. On our clinical pipeline, we are very excited with the change to our Phase 3 SENTRY myelofibrosis trial endpoints following engagement with the FDA, strengthening our confidence for a successful outcome for this trial. We continue to drive disciplined expense management and trial execution as we look forward to our next phase of growth with potential new indications in myelofibrosis and endometrial cancer," said Richard Paulson, President and Chief Executive Officer of Karyopharm.

"A significant unmet need in myelofibrosis remains, as less than half of patients achieve SVR35 with each of the approved JAKi inhibitors. I am encouraged by the Phase 1 trial which evaluated the combination of selinexor and ruxolitinib, as it shows an approximate doubling of SVR35 to 80% compared to historical JAKi monotherapy and a meaningful 18.5 point improvement in Abs-TSS at week 24 compared to baseline," said Dr. John Mascarenhas, Principal Investigator of the Phase 3 SENTRY trial, Professor of Medicine at the Icahn School of Medicine at Mount Sinai and Director of the Center of Excellence for Blood Cancers and Myeloid Disorders. "The change to Abs-TSS as a co-primary endpoint signifies a new era in the evaluation of combination therapy and reflects a growing willingness by the FDA to incorporate more sensitive methods of evaluating symptoms in trials with active comparators."

Third Quarter 2024 and Recent Highlights

XPOVIO Commercial Performance

- Achieved U.S. net product revenue of $29.5 million for the third quarter of 2024, compared to $28.0 million for the second quarter of 2024 and $30.2 million for the third quarter of 2023.
- XPOVIO net product revenue was supported by quarter-over-quarter double digit growth in demand, partially offset by higher gross-to-net quarter-over-quarter largely due to higher proportion of 340B book of business.
- Continued quarter-over-quarter demand growth with strong demand growth in the community setting, which represents approximately 60% of overall net product revenues. In the academic setting, demand for XPOVIO grew quarter-over-quarter amidst ongoing competitive pressures with continued use of XPOVIO preceding and following T-cell therapies in later lines.
- Expanded global patient access for selinexor in the third quarter of 2024 with favorable reimbursement decisions in France and Italy and additional regulatory approvals in Turkiye, South Korea, Thailand and Malaysia.

Research and Development (R&D) Highlights

Myelofibrosis

- Following recent alignment with the FDA, absolute change in total symptom score (Abs-TSS) at Week 24 will replace total symptom improvement of ≥ 50% (TSS50) as a co-primary endpoint in the pivotal Phase 3 SENTRY trial of selinexor in combination with ruxolitinib in JAKi naive myelofibrosis. Abs-TSS measures the average improvement in patient symptom scores over 24 weeks relative to the patient's baseline symptom score and is an accepted measure that has been used in

other Phase 3 clinical trials in myelofibrosis to evaluate the benefit/risk of an add-on treatment, such as selinexor, to the current standard of care. Spleen volume reduction ≥35% (SVR35) at Week 24 will remain as a co-primary endpoint. These two co-primary endpoints will be tested sequentially starting with SVR35 followed by Abs-TSS.

- Proactively increasing the total sample size of the SENTRY trial to approximately 350 patients to further increase the statistical powering. The trial continues to enroll patients with strong momentum with expected top-line data read-out remaining in the second half of 2025.

- SENTRY-2 Phase 2 trial of selinexor monotherapy in JAKi naïve patients with moderate thrombocytopenia continues to enroll patients. The Company expects to present preliminary data from this trial in late 2024 or early 2025.

Endometrial Cancer

- Long-term follow-up data from a pre-specified exploratory subgroup analysis of patients with advanced or recurrent*TP53* wild-type endometrial cancer from the SIENDO study (NCT03555422) were presented with expanded exploratory quality-adjusted time without symptoms or toxicity analysis (Q-TWiST) for the proficient mismatched repair status (pMMR) TP53 wild-type subgroup at the International Gynecological Cancer Society (IGCS) conference in October 2024. These data showed the restricted mean Q-TWiST for selinexor to be 30 months compared to 17 months for placebo, resulting in a difference of 13 months.

- Pivotal XPORT-EC-042 Phase 3 trial in TP53 wild-type endometrial cancer continues to enroll patients and is expected to read-out top-line data in early 2026.

Multiple Myeloma

- Pivotal XPORT-MM-031 (EMN29) Phase 3 trial, in collaboration with the European Myeloma Network, evaluating an oral combination of selinexor 40 mg, pomalidomide and dexamethasone (SPd) in patients with previously treated multiple myeloma now has a targeted enrollment of approximately 120 patients which leverages the positively evolving data observed with SPd 40 mg. Pending regulatory agency feedback on the updated protocol, the Company will provide guidance on the top-line data readout timeline from this trial.

2024 Financial Outlook

Based on its current operating plans, Karyopharm has further narrowed its guidance for full year 2024 as follows:

- Total revenue to be in the range of$145.0 million to $155.0 million as compared to the Company's prior guidance of $145.0 million to $160.0 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$110.0 million to $115.0 million as compared to the Company's prior guidance of $105.0 million to $120.0 million.

- R&D and selling, general and administrative (SG&A) expenses to be in the range of$255.0 million to $265.0 million, which includes approximately $20.0 million estimated non-cash stock-based compensation expense, as compared to the Company's prior guidance of $250.0 million to $265.0 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.[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 be sufficient to fund its operations into the fourth quarter of 2025.

Third Quarter 2024 Financial Results

Total revenue: Total revenue for the third quarter of 2024 was$38.8 million, compared to $36.0 million for the third quarter of 2023.

Net product revenue: Net product revenue for the third quarter of 2024 was$29.5 million, compared to $30.2 million for the third quarter of 2023.

License and other revenue: License and other revenue for the third quarter of 2024 was$9.3 million, compared to $5.8 million for the third quarter of 2023. The increase was primarily due to $6.0 million of milestone-related revenue recognized from

Menarini, which was related to reimbursement approvals for NEXPOVIO in the third quarter of 2024, partially offset by a $3.3 million decrease in revenue related to the reimbursement of development-related expenses from Menarini due to timing of reimbursement.

Cost of sales: Cost of sales for the third quarter of 2024 was $1.3 million, compared to $0.9 million for the third quarter of 2023. 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 third quarter of 2024 were $36.1 million, compared to $35.6 million for the third quarter of 2023. The increase was primarily due to an increase in clinical trial and related costs, mainly driven by increased activity in the ongoing Phase 3 SENTRY trial in myelofibrosis.

SG&A expenses: SG&A expenses for the third quarter of 2024 were $27.6 million, compared to $30.8 million for the third quarter of 2023. The decrease was primarily due to our ongoing cost reduction initiatives and lower headcount.

Interest income: Interest income for the third quarter of 2024 was $1.8 million, compared to $2.8 million for the third quarter of 2023 due to a lower cash and investments balance quarter-over-quarter.

Interest expense: Interest expense for the third quarter of 2024 was $11.4 million, compared to $6.1 million for the third quarter of 2023. The increase in interest expense was due to the Company's new term loan and new secured convertible senior notes.

Other income: Other income for the third quarter of 2024 was $3.8 million due to a non-cash gain recognized in connection with the remeasurement of embedded derivatives and liability classified common stock warrants. The Company had immaterial other income in the third quarter of 2023.

Net loss: Karyopharm reported a net loss of $32.1 million, or $0.26 loss per basic and diluted share, for the third quarter of 2024, compared to a net loss of $34.5 million, or $0.30 loss per basic and diluted share, for the third quarter of 2023.

Cash position: Cash, cash equivalents, restricted cash and investments as of September 30, 2024 totaled $133.9 million, compared to $192.4 million as of December 31, 2023.

Conference Call Information

Karyopharm will host a conference call today, November 5, 2024, at 8:00 a.m. Eastern Time, to discuss the third quarter 2024 financial results and provide business highlights. 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 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 a growing number of ex-U.S. territories and countries, including Europe, the United Kingdom, China, South Korea 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 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 2024 total revenue, 2024 U.S. net product revenue and 2024 R&D and SG&A expenses; Karyopharm's 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 June 30, 2024, which was filed with the Securities and Exchange Commission (SEC) on August 6, 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.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Revenues:				
Product revenue, net	$ 29,516	$ 30,207	$ 83,554	$ 86,955
License and other revenue	9,267	5,802	31,141	25,331
Total revenue	38,783	36,009	114,695	112,286
Operating expenses:				
Cost of sales	1,300	911	4,676	3,456
Research and development	36,134	35,553	109,930	99,369
Selling, general and administrative	27,632	30,805	88,251	101,193
Total operating expenses	65,066	67,269	202,857	204,018
Loss from operations	(26,283)	(31,260)	(88,162)	(91,732)
Other income (expense):				
Interest income	1,832	2,750	5,918	8,423
Interest expense	(11,385)	(6,073)	(26,218)	(17,615)
Gain on extinguishment of debt	—	—	44,702	—
Other income (expense), net	3,792	89	18,284	(145)
Total other income (expense), net	(5,761)	(3,234)	42,686	(9,337)
Loss before income taxes	(32,044)	(34,494)	(45,476)	(101,069)

Income tax provision	(28)	(12)	(166)	(193)
Net loss	$ (32,072)	$ (34,506)	$ (45,642)	$ (101,262)
Basic net loss per share	$ (0.26)	$ (0.30)	$ (0.38)	$ (0.89)
Diluted net loss per share	$ (0.26)	$ (0.30)	$ (0.69)	$ (0.89)
Weighted-average number of common shares outstanding used to compute basic net loss per share	125,010	114,401	120,513	114,033
Weighted-average number of common shares outstanding used to compute diluted net loss per share	125,010	114,401	126,606	114,033

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

	September 30, 2024	December 31, 2023
Assets		
Cash, cash equivalents and investments	$ 133,526	$ 191,443
Restricted cash	339	961
Accounts receivable	31,778	26,962
Other assets	23,833	21,072
Total assets	$ 189,476	$ 240,438
Liabilities and stockholders' deficit		
Convertible senior notes due 2025	$ 24,392	$ 170,919
Convertible senior notes due 2029	72,091	—
Senior secured term loan	94,109	—
Deferred royalty obligation	73,499	132,479
Other liabilities	85,032	73,246
Total liabilities	349,123	376,644
Total stockholders' deficit	(159,647)	(136,206)
Total liabilities and stockholders' deficit; 125,303 and 114,915 shares issued and outstanding at September 30, 2024 and December 31, 2023, respectively	$ 189,476	$ 240,438

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Elhan Webb, CFA, Senior Vice President, Investor Relations, 617.658.0600 | elhan.webb@karyopharm.com; Media: David Rosen, Argot Partners, 646.461.6387 | david.rosen@argotpartners.com

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