Karyopharm Reports Third Quarter 2023 Financial Results and Highlights Recent Company Progress

– Achieved Third Quarter 2023 Total Revenue of $36.0 Million and U.S. XPOVIO® (selinexor) Net Product Revenue of $30.2 Million –

– Maintains Full Year 2023 Total Revenue Guidance of $145 Million to $160 Million, Including U.S. XPOVIO Net Product Revenue Guidance of $110 Million to $125 Million –

– Strong SVR and TSS Durability Observed from Phase 1 Study of Selinexor 60mg and Ruxolitinib in JAK Inhibitor (JAKi)-Naïve Myelofibrosis Patients, with No SVR or TSS Progressions Observed [1] *–*

– Announced Clinical Trial Collaboration with Bristol Myers Squibb to Evaluate Novel CELMoD™ Agent CC- 92480, Mezigdomide in Combination with Selinexor in Patients with R/R Multiple Myeloma Progressing After T-cell Immunotherapies –

– Conference Call Scheduled for Today at 8:00 a.m. ET –

NEWTON, Mass., Nov. 2, 2023 /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, 2023, and highlighted select corporate milestones and progress on its key clinical development programs.

"We are strongly positioned for our next stage of growth driven by our focused and rapidly advancing late-stage pipeline with evolving data including impressive durability data observed with selinexor 60mg in combination with ruxolitinib in patients with myelofibrosis as well as the substantial progression-free survival observed in patients with *TP53* wild-type endometrial cancer," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "Our commercial organization continues to perform with resilience amidst an increasingly competitive multiple myeloma landscape, focusing on fueling growth in the community and expanding use of selinexor in the earlier lines."

Third Quarter 2023 and Recent Highlights

XPOVIO Commercial Performance

- Achieved U.S. net product revenue of $30.2 million for the third quarter of 2023, compared to $32.0 million U.S. net product revenue in the third quarter of 2022.
- Net XPOVIO revenue continued to be adversely impacted year over year by increased utilization of the KaryForward Patient Assistance Program (PAP), resulting from multiple myeloma foundation closures[2] and higher gross-to-net driven by increased 340B discounts and Medicaid rebates, as compared to the third quarter of 2022. During the third quarter of 2023, new patient starts within the PAP normalized, although the impact from refills remained.
- Total demand for XPOVIO was adversely impacted by 3% year over year, largely due to increasing competitive pressures seen in the later lines in the academic setting.
- Continued shift in earlier lines with more than 60%[3] of all XPOVIO new starts in the second to fourth line, representing approximately 20% year over year growth.
- The National Comprehensive Cancer Network® (NCCN) Clinical Practice Guidelines elevated XPOVIO in combination with bortezomib (Velcade®) and dexamethasone (XVd) to a preferred and category 1 regimen for lenalidomide refractory patients with relapsed or refractory multiple myeloma who have received one-to-three prior lines of therapy in the September 2023 Clinical Practice Guidelines in Oncology.

R&D Highlights

Myelofibrosis

- Data from the Phase 1 study evaluating the safety and efficacy of once-weekly selinexor in combination with ruxolitinib in patients with JAKi-naïve myelofibrosis (NCT04562389) on durability of response is being presented today at the 15th International Congress on Myeloproliferative Neoplasms. As of the August 1, 2023 data cut-off date, all patients treated with 60mg selinexor and who achieved ≥35% reduction in spleen volume (SVR35) at week 24 (n=11), continued to remain in radiographic response[1]. In addition, all of the 7 patients who achieved TSS50 at Week 24 remained in response as of the data cut-off[1]. The maximum duration of follow-up was 78 weeks with a median duration of 32 weeks for SVR35 durability, and a maximum duration of follow-up was 64 weeks with a median duration of 51 weeks for TSS50 durability.

Endometrial Cancer

- The Phase 3 SIENDO study (NCT03555422) manuscript was published in the *Journal of Clinical Oncology*.
- Long term exploratory subgroup analysis of the pre-specified subgroup of patients with advanced or recurrent *TP53* wild-type endometrial cancer from the SIENDO study was presented as an encore oral presentation at the 24th European Gynaecological Oncology Congress (ESGO) in September.
- Presented pre-clinical data from patient derived cancer models at the 2023 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics that suggest *TP53* wild-type status may predict sensitivity to exportin 1 (XPO1) inhibitors selinexor and eltanexor in multiple cancer types, including endometrial, ovarian, kidney, liver, esophageal, lung, pancreatic and bladder, and that sensitivity was similar for both eltanexor and selinexor. These data support the importance *of TP53* wild-type status with XPO1 inhibition in endometrial cancer.

Multiple Myeloma

- The Company entered into a clinical trial collaboration and supply agreement with Bristol Myers Squibb (BMS) to evaluate BMS' proprietary investigational cereblon E3 ligase modulator (CELMoD™) agent mezigdomide in combination with selinexor in patients with relapsed/refractory multiple myeloma progressing after T-cell immunotherapies. This trial will evaluate mezigdomide in combination with selinexor doses of either 40mg or 60mg plus dexamethasone in patients who have prior exposure to immunomodulatory drug agent, proteasome inhibitors, and anti-CD38 monoclonal antibody treatment. All patients must have received at least two prior lines of therapy, and either have progressed after or are not eligible to receive CAR-T or bispecific antibody treatment. Under the terms of the agreement with BMS, Karyopharm will sponsor the trial as a new arm of its Phase 1b/2 STOMP trial and BMS will supply the study's clinical drug mezigdomide.

Third Quarter 2023 Financial Results

Total Revenues: Total revenue for the third quarter of 2023 was $36.0 million, compared to $36.1 million for the third quarter of 2022.

Net product revenue: Net product revenue for the third quarter of 2023 was $30.2 million, compared to $32.0 million for the third quarter of 2022.

License and other revenue: License and other revenue for the third quarter of 2023 was $5.8 million, compared to $4.1 million for the third quarter of 2022. The increase was primarily due to an increase in revenue for the reimbursement of development-related expenses from the Menarini Group.

Cost of sales: Cost of sales for the third quarter of 2023 was $0.9 million, compared to $1.0 million for the third quarter of 2022. Cost of sales reflects the costs of XPOVIO units sold and third-party royalties on net product revenue.

Research and development (R&D) expenses: R&D expenses for the third quarter of 2023 were $35.6 million, compared to $31.4 million for the third quarter of 2022. The increase was primarily due to higher clinical trial costs related to the advancement of our three pivotal Phase 3 programs.

Selling, general and administrative (SG&A) expenses: SG&A expenses for the third quarter of 2023 were $30.8 million, compared to $34.6 million for the

third quarter of 2022. The decrease was primarily due to a decrease in consulting, professional and other costs as a result of more focused commercial-related activities due to lower headcount.

Interest income: Interest income for the third quarter of 2023 was $2.8 million, compared to $0.7 million for the third quarter of 2022, due to higher average interest rates on investments.

Interest expense: Interest expense for the third quarters of both 2023 and 2022 was $6.1 million.

Net loss: Karyopharm reported a net loss of $34.5 million, or $0.30 per share, for the third quarter of 2023, compared to a net loss of $36.3 million, or $0.45 per share, for the third quarter of 2022.

Cash position: Cash, cash equivalents, restricted cash and investments as of September 30, 2023 totaled $209.2 million, compared to $279.7 million as of December 31, 2022.

2023 Financial Outlook

Based on its current operating plans, Karyopharm reiterates its guidance for full year 2023 as follows:

- Total revenue expected to be in the range of $145 million to $160 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 expected to be in the range of $110 million to $125 million.
- Non-GAAP R&D and SG&A expenses*, which exclude stock-based compensation expense, expected to be in the range of $240 million to $255 million.
- The Company continues to expect 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 be sufficient to fund its planned operations into late 2025.

* Karyopharm has not reconciled the full year 2023 outlook for non-GAAP R&D and SG&A expenses to full year 2023 outlook for GAAP R&D and SG&A expenses because Karyopharm cannot reliably predict without unreasonable efforts the timing or amount of the factors that substantially contribute to the projection of stock compensation expense, which is excluded from the full year 2023 outlook for non-GAAP R&D and SG&A expenses.

Non-GAAP Financial Information

Karyopharm uses a non-GAAP financial measure, non-GAAP R&D and SG&A expenses, to provide operating expense guidance. Non-GAAP R&D and SG&A expenses exclude stock-based compensation expense. Karyopharm believes this non-GAAP financial measure is useful to investors because it provides greater transparency regarding Karyopharm's operating performance as it excludes non-cash stock compensation expense. This non-GAAP financial measure should not be considered a substitute or an alternative to GAAP R&D and SG&A expenses and should not be considered a measure of Karyopharm's liquidity. Instead, non-GAAP R&D and SG&A expenses should only be used to supplement an understanding of Karyopharm's operating results as reported under GAAP.

Conference Call Information

Karyopharm will host a conference call today, November 2, 2023, at 8:00 a.m. Eastern Time, to discuss the third quarter 2023 financial results and financial outlook for 2023 and to provide other business highlights. To access the conference call, please dial (888) 349-0102 (local) or (412) 902-4299 (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, http://investors.karyopharm.com/events-presentations. 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 to be approved for the treatment of cancer. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein XPO1. XPOVIO is approved in the U.S. and marketed by Karyopharm in multiple oncology indications, including: (i) in combination with VELCADE® (bortezomib) and dexamethasone (XVd) in patients with multiple myeloma after at least one prior therapy; (ii) in combination with dexamethasone in patients with heavily pre-treated multiple myeloma; and (iii) in patients with diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy. XPOVIO (also known as NEXPOVIO® in certain countries) has received regulatory approvals in a growing number of ex-U.S. territories and countries, including Europe, the United Kingdom, China, South Korea 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 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 guidance on its 2023 total revenue, 2023 U.S. net product revenue and 2023 non-GAAP R&D and SG&A expenses; Karyopharm's expected cash runway; expectations with respect to commercialization efforts; the ability of selinexor or eltanexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma, myelodysplastic neoplasms and other diseases; 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 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; 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, 2023, which was filed with the Securities and Exchange Commission (SEC) on August 2, 2023, 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.

References:

[1] For SVR 35: Events defined as less than or equal to 35% spleen volume reduction from baseline and more than 25% increase in spleen volume from Nadir, assessed radiographically. For TSS50: Events defined as a total symptom score that is equal to or exceeds the baseline value. As of August 1, 2023 data cut off.

[2] Four multiple myeloma foundations provide financial support to Medicare patients with multiple myeloma

[3] Based on Komodo claims data analysis, accessed in September 2023

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,	
	2023	2022	2023	2022
Revenues:				
Product revenue, net	$ 30,207	$ 32,009	$ 86,955	$ 89,319
License and other revenue	5,802	4,136	25,331	34,175
Total revenue	36,009	36,145	112,286	123,494
Operating expenses:				
Cost of sales	911	980	3,456	3,345
Research and development	35,553	31,359	99,369	117,730
Selling, general and administrative	30,805	34,645	101,193	110,752
Total operating expenses	67,269	66,984	204,018	231,827
Loss from operations	(31,260)	(30,839)	(91,732)	(108,333)
Other income (expense):				
Interest income	2,750	658	8,423	1,025
Interest expense	(6,073)	(6,114)	(17,615)	(19,111)
Other income (expense), net	89	16	(145)	(70)
Total other expense, net	(3,234)	(5,440)	(9,337)	(18,156)
Loss before income taxes	(34,494)	(36,279)	(101,069)	(126,489)

Income tax provision	(12)	(45)	(193)	(296)
Net loss	$ (34,506)	$ (36,324)	$ (101,262)	$ (126,785)
Net loss per share—basic and diluted	$ (0.30)	$ (0.45)	$ (0.89)	$ (1.60)
Weighted-average number of common shares outstanding used in net loss per share—basic and diluted	114,401	80,210	114,033	79,153

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

	September 30, 2023	December 31, 2022
Assets		
Cash, cash equivalents and investments	$ 208,315	$ 277,967
Restricted cash	926	1,697
Accounts receivable	37,923	47,086
Other assets	22,796	31,422
Total assets	$ 269,960	$ 358,172
Liabilities and stockholders' deficit		
Convertible senior notes	$ 170,702	$ 170,105
Deferred royalty obligation	132,479	132,718
Other liabilities	67,175	72,005
Total liabilities	370,356	374,828
Total stockholders' deficit	(100,396)	(16,656)
Total liabilities and stockholders' deficit; 114,523 and 113,213 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively	$ 269,960	$ 358,172

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Elhan Webb, CF, Senior Vice President, Investor Relations, 617.658.0600 | elhan.webb@karyopharm.com, or Media: Stacy Nobles, Head of Corporate Communications, 617.658.0540 |stacy.nobles@karyopharm.com

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