Karyopharm Reports Third Quarter 2022 Financial Results and Highlights Recent Company Progress

– Achieved Third Quarter 2022 Total Revenue of $36.1 Million, Including XPOVIO® (selinexor) Net Product Revenue of $32.0 Million, a 20 % Increase Over Third Quarter 2021–

– Initiated Phase 3 Study Evaluating Selinexor as a Maintenance Therapy in Women with Advanced or Recurrent TP53 Wild-Type Endometrial Cancer –

–Encouraging Data Observed in Phase 1 Study of Selinexor in Combination with Ruxolitinib in Treatment-Naïve Myelofibrosis, Including Activity Across Three Key Efficacy Endpoints, and a Generally Manageable Safety Profile with No Dose Limiting Toxicities. Updated Results to Be Presented at ASH –

– Company Re-Affirms Full Year 2022 XPOVIO Net Product Revenue Guidance of $120 Million to $130 Million, Total Revenue Guidance of $155 Million to $165 Million and Cash Runway into Early 2024 –

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

NEWTON, Mass., Nov. 3, 2022 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today reported business highlights and financial results for the quarter ended September 30, 2022.

"We had a highly productive third quarter executing against our key priorities which delivered strong growth in patient demand and product revenues. We also achieved an important milestone this quarter with the initiation of the pivotal Phase 3 study evaluating selinexor as a maintenance therapy in women with *TP53* wild-type endometrial cancer and anticipate sharing topline results in 2024," said Richard Paulson, President and Chief Executive Officer of Karyopharm. "Today, our abstracts were released for the American Society of Hematology (ASH) Annual Meeting, including encouraging data from the Phase 1 study evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis, which continues to demonstrate promising activity in key efficacy endpoints. We look forward to sharing further updated results from this study at the ASH meeting in December."

Third Quarter 2022 and Recent Highlights

XPOVIO Commercial Performance

- Achieved U.S. net product revenue for the third quarter of 2022 of $32.0 million, a 20% increase compared to the third quarter of 2021, driven by growth in new patient starts and refills.
- XPOVIO continued its growth in the community setting, driven by the continued shift of XPOVIO into second to fourth lines of therapy and increasing confidence in the perception of the product.
- Increased selinexor's reach with the commercial launch of NEXPOVIO by the Company's partner, Menarini Group, in Germany and Austria.

Research & Development (R&D) Highlights for Selinexor and Eltanexor

- Initiated a global, randomized, double-blind Phase 3 study evaluating selinexor as maintenance therapy for patients with *TP53* wild-type advanced or recurrent endometrial cancer. The study will utilize Foundation Medicine's tissue-based next generation sequencing test to identify and enroll patients whose tumors are *TP53* wild-type. Top-line results from the study are anticipated in 2024.
- Results from the Phase 1 study evaluating selinexor in combination with ruxolitinib in patients with treatment-naïve myelofibrosis (NCT:04562389) have been accepted for poster presentation at the ASH 2022 Annual Meeting. The data included in the abstract for ASH 2022 were based on the Phase 1 portion of the Phase 1/2 study evaluating the safety and preliminary efficacy of once-weekly selinexor in combination with standard dose ruxolitinib in patients with treatment-naïve myelofibrosis (NCT04562389). As of July 2022, 19 patients had been assigned to either selinexor 40 mg or 60 mg, in combination with ruxolitinib 15/20 mg BID. 79% (11 out of 14) and 86% (6 out of 7) of efficacy evaluable patients demonstrated ≥35% reduction in spleen volume (SVR 35) at week 12 and at week 24, respectively. 69% (9 out of 13) of efficacy evaluable patients evidenced a ≥50% reduction (TSS50) at week 12 and 65% (11 out of 17) of transfusion-independent patients who had at least eight weeks of treatment maintained stable hemoglobin (± 2g/dL) or improved hemoglobin level (>2g/dL increase) at last follow up. The data observed across both 40mg and 60mg doses demonstrate a generally manageable side effect profile with no dose limiting toxicities at either dose level in the Phase 1a dose

escalation with the most common adverse events (AEs) being nausea (58%), anemia (42%) and vomiting (42%), the majority of which were grades 1-2, and the most commonly reported grades 3-4 treatment-emergent AEs being thrombocytopenia (26%) and anemia (21%), which were reversible. Updated data from this study, including results from additional patients, will be presented at the ASH meeting in December 2022.
- The European Commission adopted the Committee for Orphan Medicinal Products opinion to designate selinexor as an orphan medicinal product for the treatment of myelofibrosis, and eltanexor as an orphan medicinal product for the treatment of myelodysplastic syndromes (MDS), in the European Union in October 2022 and July 2022, respectively.
- FDA granted Fast Track Designation for the development program of eltanexor as monotherapy for the treatment of patients with relapsed or refractory intermediate, high-, or very high-risk MDS per IPSS-R in July 2022.

2022 Financial Guidance

Based on its current operating plans, Karyopharm is maintaining its guidance for the full year 2022:

- Total revenue to be in the range of $155 million to $165 million.
- XPOVIO net product revenue to be in the range of $120 million to $130 million.
- Non-GAAP R&D and Selling, general and administrative (SG&A) expenses, excluding stock-based compensation expense, to be in the range of $250 million to $265 million.

  Karyopharm has not reconciled the full year 2022 outlook for non-GAAP R&D and SG&A expenses to full year 2022 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 2022 outlook for non-GAAP R&D and SG&A expenses.

- The Company continues to expect that its existing cash, cash equivalents and investments, and the revenue it expects to generate from XPOVIO product sales, as well as revenue generated from its license agreements, will be sufficient to fund its planned operations into early 2024.

Third Quarter 2022 Financial Results

Total Revenue: Total revenue for the third quarter of 2022 was $36.1 million, down 4% compared to $37.7 million for the third quarter of 2021.

Net product revenue: Net product revenue for the third quarter of 2022 was $32.0 million, up 20% compared to $26.7 million for the third quarter of 2021.

License and other revenue: License and other revenue for the third quarter of 2022 was $4.1 million, compared to $11.0 million for the third quarter of 2021. The decrease was primarily attributable to the recognition of $9.8 million in milestone-related revenue from Antengene Therapeutics Limited (Antengene) in the third quarter of 2021, compared to $2.4 million in royalty revenue and $1.4 million in reimbursement revenue from Menarini recognized in the third quarter of 2022.

Cost of sales: Cost of sales for the third quarter of 2022 were $1.0 million, compared to $0.6 million for the third quarter of 2021. Cost of sales includes the costs of producing and distributing XPOVIO units sold and third-party royalties on net product revenue.

R&D expense: R&D expense for the third quarter of 2022 were $31.4 million, compared to $45.8 million for the third quarter of 2021. The decrease was primarily driven by the recognition of $7.4 million of costs in connection with the acquisition of certain assets from Neumedicines Inc. in the third quarter of 2021, for which there were no similar costs in 2022. Additionally, clinical trial and related costs decreased primarily due to the prioritization of the Company's core programs in its clinical pipeline and the timing of the purchases of comparator drug used in clinical trials.

SG&A expense: SG&A expense for the third quarter of 2022 were $34.6 million, compared to $35.1 million for the third quarter of 2021.

Interest expense: Interest expense for the third quarter of 2022 was $6.1 million, compared to $8.0 million for the third quarter of 2021.

Net loss: Karyopharm reported a net loss of $36.3 million, or $0.45 per share, for the third quarter of 2022, compared to a net loss of $51.8 million, or $0.69 per share, for the third quarter of 2021. Net loss included non-cash stock-based compensation expense of $6.8 million and $7.4 million for the third quarters ended September 30, 2022 and 2021, respectively.

Cash position: Cash, cash equivalents, restricted cash and investments as of September 30, 2022, totaled $150.1 million, compared to $235.6 million as of December 31, 2021.

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 3, 2022, at 4:30 p.m. Eastern Time, to discuss the third quarter 2022 financial results and 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 various indications in a growing number of ex-U.S. territories and countries, including but not limited to the European Union, the United Kingdom, China, South Korea, Canada, Israel and Taiwan. XPOVIO and NEXPOVIO is marketed by Karyopharm's partners, Antengene, Menarini, Neopharm and FORUS in China, South Korea, Singapore, Australia, Hong Kong, Germany, Austria, Israel and Canada.

Please refer to the local Prescribing Information for full details.

Selinexor is also being investigated in several other mid- and late-stage clinical trials across multiple high unmet need cancer indications, including in endometrial cancer and myelofibrosis.

For more information about Karyopharm's products or clinical trials, please contact the Medical Information department at:
Tel: +1 (888) 209-9326
Email: medicalinformation@karyopharm.com

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Thrombocytopenia: Monitor platelet counts throughout treatment. Manage with dose interruption and/or reduction and supportive care.
- Neutropenia: Monitor neutrophil counts throughout treatment. Manage with dose interruption and/or reduction and granulocyte colony-stimulating factors.
- Gastrointestinal Toxicity: Nausea, vomiting, diarrhea, anorexia, and weight loss may occur. Provide antiemetic prophylaxis. Manage with dose interruption and/or reduction, antiemetics, and supportive care.
- Hyponatremia: Monitor serum sodium levels throughout treatment. Correct for concurrent hyperglycemia and high serum paraprotein levels. Manage with dose interruption, reduction, or discontinuation, and supportive care.
- Serious Infection: Monitor for infection and treat promptly.
- Neurological Toxicity: Advise patients to refrain from driving and engaging in hazardous occupations or activities until neurological toxicity resolves. Optimize hydration status and concomitant medications to avoid dizziness or mental status changes.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential and males with a female partner of reproductive potential, of the potential risk to a fetus and use of effective contraception.
- Cataract: Cataracts may develop or progress. Treatment of cataracts usually requires surgical removal of the cataract.

Adverse Reactions

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive XVd are fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract and vomiting. Grade 3-4 laboratory abnormalities (≥10%) are thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia. In the BOSTON trial, fatal adverse reactions occurred in 6% of patients within 30 days of

last treatment. Serious adverse reactions occurred in 52% of patients. Treatment discontinuation rate due to adverse reactions was 19%.

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive Xd are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea and upper respiratory tract infection. In the STORM trial, fatal adverse reactions occurred in 9% of patients. Serious adverse reactions occurred in 58% of patients. Treatment discontinuation rate due to adverse reactions was 27%.
- The most common adverse reactions (incidence ≥20%) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities (≥15%) are thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. In the SADAL trial, fatal adverse reactions occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal adverse reactions was infection (4.5% of patients). Serious adverse reactions occurred in 46% of patients; the most frequent serious adverse reaction was infection (21% of patients). Discontinuation due to adverse reactions occurred in 17% of patients.

Use In Specific Populations

Lactation: Advise not to breastfeed.

For additional product information, including full prescribing information, please visit**www.XPOVIO.com.**

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies. Since its founding, Karyopharm has been an industry leader in oral Selective Inhibitor of Nuclear Export (SINE) compound technology, which was developed to address a fundamental mechanism of oncogenesis: nuclear export dysregulation. Karyopharm's lead SINE compound and first-in-class, oral exportin 1 (XPO1) inhibitor, XPOVIO® (selinexor), is approved in the U.S. and marketed by the Company in three oncology indications and has received regulatory approvals in various indications in a growing number of ex-U.S. territories and countries, including Europe and the United Kingdom (as NEXPOVIO®) and China. Karyopharm has a focused pipeline targeting multiple high unmet need cancer indications, including in multiple myeloma, endometrial cancer, myelodysplastic syndromes 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 financial guidance for full year 2022; Karyopharm's expected cash runway; the ability of selinexor or eltanexor to treat patients with multiple myeloma, myelofibrosis, myelodysplastic syndromes, diffuse large B-cell lymphoma, solid tumors and other diseases; and expectations related to future clinical development and potential regulatory submissions of selinexor or eltanexor. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that Karyopharm will successfully commercialize XPOVIO or that any of Karyopharm's drug candidates, including selinexor and eltanexor, will successfully complete necessary clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in the development or commercialization of Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: the risk that the COVID-19 pandemic could disrupt Karyopharm's business more severely than it currently anticipates, including by negatively impacting sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to obtain and retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development or regulatory approval of drug candidates by Karyopharm's competitors for products or product candidates in which Karyopharm is currently commercializing or developing; and Karyopharm's ability to obtain, maintain and enforce patent

and other intellectual property protection for any of its products or product candidates. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, which was filed with the Securities and Exchange Commission (SEC) on August 4, 2022, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

XPOVIO® and NEXPOVIO® are registered trademarks of Karyopharm Therapeutics Inc. Any other trademarks referred to in this release are the property of their respective owners.

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,	
	2022	2021	2022	2021
Revenues:				
Product revenue, net	$ 32,009	$ 26,723	$ 89,319	$ 68,633
License and other revenue	4,136	10,966	34,175	14,917
Total revenues	36,145	37,689	123,494	83,550
Operating expenses:				
Cost of sales	980	589	3,345	2,660
Research and development	31,359	45,808	117,730	116,839
Selling, general and administrative	34,645	35,104	110,752	109,284
Total operating expenses	66,984	81,501	231,827	228,783
Loss from operations	(30,839)	(43,812)	(108,333)	(145,233)
Other income (expense):				
Interest income	658	98	1,025	527
Interest expense	(6,114)	(8,010)	(19,111)	(18,106)
Other income (expense), net	16	18	(70)	393
Total other expense, net	(5,440)	(7,894)	(18,156)	(17,186)
Loss before income taxes	(36,279)	(51,706)	(126,489)	(162,419)
Income tax provision	(45)	(106)	(296)	(389)
Net loss	$ (36,324)	$ (51,812)	$ (126,785)	$ (162,808)
Net loss per share—basic and diluted	$ (0.45)	$ (0.69)	$ (1.60)	$ (2.17)
Weighted-average number of common shares outstanding used in net loss per share—basic and diluted	80,210	75,461	79,153	75,065

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

	September 30, 2022	December 31, 2021
Assets		
Cash, cash equivalents and investments	$ 148,381	$ 228,615
Restricted cash	1,706	6,986
Accounts receivable	27,446	22,497
Other assets	53,703	47,207
Total assets	$ 231,236	$ 305,305
Liabilities and stockholders' deficit		
Convertible senior notes	169,894	169,293
Deferred royalty obligation	132,998	132,998
Other liabilities	68,624	82,687
Total liabilities	371,516	384,978
Total stockholders' deficit	(140,280)	(79,673)

Total liabilities and stockholders' deficit; 81,027 and 75,746 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	$ 231,236	$ 305,305

SOURCE Karyopharm Therapeutics Inc.

For further information: Investors: Elhan Webb, CFA, Senior Vice President, Investor Relations, 617.658.0600 | elhan.webb@karyopharm.com, Media: Sarah Connors, Vice President, Corporate Communications, 617.658.0600 | sarah.connors@karyopharm.com

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