

Karyopharm Reports Fourth Quarter and Full Year 2018 Financial Results and Provides Corporate Update

-- FDA Advisory Committee Votes 8 to 5 Recommending FDA Wait for the Results from the Ongoing Phase 3 BOSTON Study to Make an Approval Decision for Selinexor --

-- Company Working with FDA to Evaluate Best Path Forward as FDA Completes Its Review of Selinexor NDA; Assigned PDUFA Action Date of April 6, 2019 --

-- Conference Call Scheduled for Today at 8:30 a.m. ET --

NEWTON, Mass., Feb. 28, 2019 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today reported financial results for the fourth quarter and full year 2018 and provided a business update and an overview of recent accomplishments for selinexor, its first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound.

"Earlier this week, the U.S. Food and Drug Administration (FDA) Oncologic Drugs Advisory Committee (ODAC) voted 8 to 5, recommending that the FDA wait for the results from the ongoing Phase 3 BOSTON study before making a final approval decision regarding selinexor for the treatment of patients with triple class refractory multiple myeloma who have received at least three prior therapies," said Michael G. Kauffman, MD, PhD, Chief Executive Officer of Karyopharm. "While we are disappointed with the ODAC's recommendation, we are encouraged by the support communicated by a number of ODAC members. We intend to work closely with the FDA to evaluate the best path forward as they complete their review of our New Drug Application (NDA). We remain committed to delivering on our vision of bringing selinexor into the hands of the physicians and patients who are battling highly refractory multiple myeloma."

Fourth Quarter 2018 and Recent Events

Selinexor in Multiple Myeloma

- **FDA Advisory Committee Recommends that the FDA Should Wait for Results from the Ongoing Phase 3 BOSTON Study Before Making an Approval Decision.** On February 26, 2019, the Oncologic Drugs Advisory Committee (ODAC) of the FDA met to review data supporting Karyopharm's NDA requesting accelerated approval for selinexor. The proposed indication discussed was for selinexor in combination with dexamethasone for the treatment of patients with relapsed refractory multiple myeloma who have received at least three prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody. The FDA specifically asked the ODAC to vote on whether the committee believed the approval of selinexor should be delayed until the results from the ongoing, randomized Phase 3 BOSTON study, are available. In a vote of 8 Yes and 5 No, the ODAC recommended that the approval decision for selinexor should be delayed until the results of the BOSTON study are available. Karyopharm's NDA is under Priority Review by the FDA with an action date of April 6, 2019, under the PDUFA.

The ODAC is an independent panel of experts that evaluates data concerning the efficacy and safety of marketed and investigational products for use in the treatment of cancer and makes appropriate recommendations to the FDA. Although the FDA will consider the recommendation of the panel, the final decision regarding the approval of the product is made by the FDA solely, and the recommendations by the panel are non-binding.

- **FDA Accepts Selinexor New Drug Application and Grants Priority Review.** On October 5, 2018, the FDA accepted for filing with Priority Review Karyopharm's NDA seeking accelerated approval for selinexor, its first-in-class, oral SINE compound, as a new treatment for patients with triple class refractory multiple myeloma. The FDA also assigned a PDUFA action date of April 6, 2019.
- **Submitted Marketing Authorization Application (MAA) to the European Medicines Agency (EMA).** A MAA was submitted to the EMA on January 8, 2019 for selinexor requesting conditional approval for the treatment of patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody. Karyopharm also announced that the selinexor MAA has been granted accelerated assessment by the EMA's Committee for Medicinal Products for Human Use.
- **Updated Phase 2b STORM Data Presented at American Society of Hematology 2018 Annual Meeting (ASH 2018).** Additional results from Part 2 of the Phase 2b STORM study were highlighted in an oral presentation at ASH 2018. For the STORM study's primary objective, the overall response rate (ORR) was 26.2%, which included two stringent complete responses (sCRs), six very good partial responses (VGPRs) and 24 partial responses (PRs) in patients with triple class refractory multiple myeloma who have been previously exposed to all five of the most commonly prescribed anti-myeloma therapies currently available. The two sCRs were negative for minimal residual disease, one at the level of 1x10⁻⁶ and one at 1x10⁻⁴; this is particularly significant in this highly refractory population. The Disease Control Rate for patients who had achieved stable disease or better was 78.7%. All responses were confirmed by an Independent Review Committee. Median progression-free survival (PFS) was 3.7 months and the median duration of response (DOR) was 4.4 months. Median overall survival (OS) across the study was 8.6 months. Median OS in the approximately 40% of patients with at least a minimal response (MR) on selinexor and dexamethasone was 15.6 months compared to a median OS of 1.7 months in patients whose disease progressed or was not evaluable (p<0.0001). The short median OS of patients with no response to selinexor is consistent with the lack of available effective therapies for the very heavily pretreated population who entered the study. The most common adverse events (AEs) included thrombocytopenia, nausea/vomiting, fatigue and decreased appetite. Each patient on STORM experienced at least one AE. AEs were generally predictable and manageable with dose adjustments and/or supportive care, and treatment-emergent AEs leading to treatment discontinuation occurred in 26.8% of patients and these were considered by the Investigator to be treatment-related in 17.9% of patients. Major organ toxicities were not prominent in this study and safety results were consistent with those previously reported from Part 1 of the STORM study (Vogl et al., J Clin Oncol, 2018) and from other selinexor studies.
- **Updated Phase 1b/2 STOMP Data Presented at ASH 2018.** Two abstracts featuring clinical data from two treatment arms of the ongoing Phase 1b/2 STOMP study in patients with relapsed or refractory multiple myeloma were selected for oral and poster presentations at ASH 2018. The oral presentation highlighted updated data from the arm evaluating selinexor in combination with Darzalex® (daratumumab) and low-dose dexamethasone (SDd). In this arm, the combination demonstrated an ORR of 79% in patients with heavily pretreated, Darzalex®-naïve multiple myeloma and an ORR of 73% in the overall study population. The poster presentation described updated data from the arm evaluating selinexor in combination with Pomalyst® (pomalidomide) and low-dose dexamethasone (SPd). In this arm, the combination demonstrated an ORR of 54% in patients with Pomalyst®-naïve and Revlimid®-relapsed or -refractory multiple myeloma, with PFS of 12.2 months. The combination demonstrated an ORR of 50% in the overall study population. Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most manageable with dose modifications and/or standard supportive care.
- **Pivotal Phase 3 BOSTON Study in Progress.** Karyopharm's pivotal, randomized Phase 3 BOSTON study is progressing and in January 2019, the

Company announced the completion of enrollment in the study. Top-line data is expected at the earliest by the end of 2019 or into 2020 contingent upon the occurrence of PFS events, the primary endpoint in the study. The BOSTON study is evaluating 100mg of selinexor dosed once weekly in combination with the proteasome inhibitor Velcade® (once weekly) and low dose dexamethasone (SVd), compared to standard twice weekly Velcade and low dose dexamethasone (Vd) in patients with multiple myeloma who have had one to three prior lines of therapy. Data from the BOSTON study, if positive, would be used to support regulatory submissions to the FDA and EMA requesting the use of selinexor in second line multiple myeloma, and confirming the Company's requests for accelerated and conditional approvals, respectively, using data from the Phase 2b STORM study.

Selinexor in Diffuse Large B-Cell Lymphoma (DLBCL)

- Received Fast Track Designation from FDA for the Treatment of Patients with Relapsed or Refractory DLBCL. In addition to Orphan Drug Designation, selinexor was recently granted Fast Track designation by the FDA for the treatment of patients with diffuse large B-cell lymphoma (DLBCL) who have received at least two prior therapies and are not eligible for high dose chemotherapy with stem cell rescue or CAR-T therapy.
- Top-Line Phase 2b SADAL Data in DLBCL Presented at ASH 2018. Top-line results from the fully enrolled Phase 2b SADAL study was presented at ASH 2018. The SADAL study is designed to evaluate single agent oral selinexor 60mg for patients with relapsed or refractory DLBCL who are not eligible for stem cell transplantation. Based on the modified intention-to-treat analysis from the first 115 of 127 patients, as adjudicated by an independent central radiological committee, selinexor achieved an ORR of 29.6%. The median DOR across responding patients was 9.2 months. Patients with a complete response (CR) had a median DOR of 23.0 months and patients with a PR had a median DOR of 7.8 months. The median OS was 9.1 months for all patients in the study. As of the data cutoff date, median survival for the patients with a CR or PR was 29.7 months. The median survival for patients with best response of progressive disease or who were not evaluable for response was 3.2 months. Among the patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were gastrointestinal and constitutional symptoms, along with cytopenias; most AEs were manageable with dose modifications and/or supportive care. Based on the results from the Phase 2b SADAL study, Karyopharm plans to submit an NDA to the FDA with a request for accelerated approval for oral selinexor in this relapsed or refractory DLBCL patient population and the Company is working closely with the FDA to determine the appropriate timeline. Karyopharm is also planning to submit a MAA to the EMA with a request for conditional approval in the same indication.

Selinexor in Solid Tumors

- Ongoing Phase 3 Portion of the Phase 2/3 SEAL Study in Liposarcoma. Karyopharm previously reported results from the successful Phase 2 portion of the blinded, randomized Phase 2/3 SEAL study evaluating single-agent selinexor versus placebo in patients with previously treated, advanced unresectable dedifferentiated liposarcoma. Enrollment and dosing are currently ongoing in the Phase 3 portion of the SEAL study and, assuming a positive outcome on the primary end point of PFS, the Company intends to use the data from the SEAL study to support a NDA and a MAA submission requesting approval for oral selinexor for patients with advanced unresectable dedifferentiated liposarcoma. Top-line data from the Phase 3 portion of the SEAL study are anticipated in 2020.
- Ongoing Investigator Sponsored Phase 2/3 Trial as Maintenance Therapy in Endometrial Cancer. A randomized Phase 2/3 study of selinexor versus placebo as maintenance therapy in patients with one or two prior platinum-based treatments for advanced endometrial cancer, led by Dr. Ignace Vergote, Head of the Department of Obstetrics and Gynaecology and Gynaecologic Oncology at the Catholic University of Leuven, Belgium, is currently ongoing. Top-line data from this study are anticipated in 2020.

Corporate Updates

- Michael P. Mason Appointed Chief Financial Officer. Karyopharm announced the appointment of Michael P. Mason as Chief Financial Officer. Mr. Mason formerly served as Vice President of Finance and Treasurer at Alnylam Pharmaceuticals, Inc., a public biopharmaceutical company. He brings over 18 years of diversified financial experience to Karyopharm and has deep expertise in global financial operations and controls, financing transactions, business planning and supporting pharmaceutical product launches.

Full Year and Fourth Quarter 2018 Financial Results

Cash, cash equivalents and investments as of December 31, 2018, including restricted cash, totaled \$330.9 million, compared to \$176.4 million as of December 31, 2017.

On October 26, 2018, Karyopharm completed a private offering of \$172.5 million aggregate principal amount of 3.00% convertible senior notes due in 2025, including the full exercise of the initial purchasers' option to purchase additional notes. After deducting the initial purchasers' discounts and commissions and other offering expenses the net proceeds were \$166.9 million.

License and other revenue for the year ended December 31, 2018 was \$30.3 million, compared to \$1.6 million for the year ended December 31, 2017, primarily related to the Company's license agreements with Biogen and ONO.

For the year ended December 31, 2018, research and development expense was \$161.4 million compared to \$107.3 million for the year ended December 31, 2017. For the year ended December 31, 2018, general and administrative expense was \$48.8 million compared to \$24.9 million for the year ended December 31, 2017.

Karyopharm reported a net loss of \$178.4 million, or \$3.14 per share, for the year ended December 31, 2018, compared to a net loss of \$129.0 million, or \$2.81 per share, for the year ended December 31, 2017. Net loss includes stock-based compensation expense of \$17.3 million and \$20.4 million for the years ended December 31, 2018 and December 31, 2017, respectively.

For the quarter ended December 31, 2018, research and development expense was \$38.9 million, compared to \$34.8 million for the quarter ended December 31, 2017. For the quarter ended December 31, 2018, general and administrative expense \$18.8 million, compared to \$6.2 million for the quarter ended December 31, 2017.

Karyopharm reported a net loss of \$58.2 million, or \$0.96 per share for the quarter ended December 31, 2018, compared to a net loss of \$39.0 million, or \$0.80 per share for the quarter ended December 31, 2017. Net loss includes stock-based compensation expense of \$3.9 million and \$4.5 million for the quarters ended December 31, 2018 and December 31, 2017, respectively.

Financial Outlook

Based on its current operating plans, Karyopharm expects that its existing cash, cash equivalents and investments will be sufficient to fund its operations into the second half of 2020, which currently assumes the commercial launch of selinexor in the U.S. in the second quarter of 2019. If the FDA decides to delay its approval decision for selinexor until the BOSTON data is available, Karyopharm will re-evaluate its spending expectations for 2019. Additional key activities expected in 2019 include supporting the ongoing multiple myeloma regulatory filings for selinexor in the U.S. and Europe, progressing the pivotal Phase 3 BOSTON study in multiple myeloma and potentially submitting an NDA and MAA, in the U.S. and Europe, respectively, in DLBCL.

Further Information About Potential Accelerated Approval for Selinexor in Multiple Myeloma

The FDA instituted its Accelerated Approval Program to allow for expedited approval of drugs that treat serious conditions and that fill an unmet medical need based on a surrogate endpoint or an intermediate clinical endpoint thought to predict clinical benefit, like overall response rate. Accelerated approval is available only for drugs that provide a meaningful therapeutic benefit over existing treatments at the time of consideration of the application for accelerated approval, which the FDA has reiterated in its feedback to the Company. Particularly in disease areas with multiple available and potential new therapies, such as multiple myeloma, accelerated approval carries a high regulatory threshold. Consistent with its general guidance, the FDA has noted to the Company its preference for randomized studies geared toward full approval, which the Company has undertaken with the ongoing pivotal, Phase 3 BOSTON study, and has reminded the Company that accelerated approval requires patients to have exhausted all available approved therapies.

Conference Call Information

Karyopharm will host a conference call today, Thursday, February 28, 2019, at 8:30 a.m. Eastern Time, to discuss the fourth quarter and full year 2018 financial results, recent accomplishments, clinical developments and business plans. To access the conference call, please dial (855) 437-4406 (local) or (484) 756-4292 (international) at least 10 minutes prior to the start time and refer to conference ID 4246798. A live audio webcast of the call 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 Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport and related targets for the treatment of cancer and other major diseases. Karyopharm's SINE compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). The Company's initial focus is on seeking regulatory approval and commercialization of its lead drug candidate, oral selinexor (KPT-330). In 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with triple class refractory multiple myeloma who have been previously exposed to all five of the most commonly prescribed anti-myeloma therapies currently available. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm's New Drug Application has been accepted for filing and granted Priority Review by the FDA, and oral selinexor is currently under review by the FDA as a possible new treatment for patients with triple class refractory multiple myeloma who have received at least three prior therapies. The Company has also submitted a Marketing Authorization Application to the European Medicines Agency with a request for conditional approval and was granted accelerated assessment. Selinexor is also being studied in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). In 2018, Karyopharm reported positive top-line results from the Phase 2b SADAL study evaluating selinexor in patients with relapsed or refractory DLBCL after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. Selinexor has received Fast Track designation from the FDA for the patient population evaluated in the SADAL study. Selinexor is also being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including in multiple myeloma in a pivotal, randomized Phase 3 study in combination with Velcade® (bortezomib) and low-dose dexamethasone (BOSTON), as a potential backbone therapy in combination with approved therapies (STOMP), in liposarcoma (SEAL), and an investigator-sponsored study in endometrial cancer (SIENDO), among others. Additional Phase 1, Phase 2 and Phase 3 studies are ongoing or currently planned, including multiple studies in combination with approved therapies in a variety of tumor types to further inform Karyopharm's clinical development priorities for selinexor. In addition to single-agent and combination activity against a variety of human cancers, SINE compounds have also shown biological activity in models of neurodegeneration, inflammation, autoimmune disease, certain viruses and wound-healing. For more information, please visit www.karyopharm.com.

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 our expectations relating to submissions, to and the review and potential approval of selinexor by, regulatory authorities, including the anticipated timing of such submissions and actions, and the potential availability of accelerated approval pathways, the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor, and the plans for commercialization. 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 regulators will agree that selinexor qualifies for accelerated approval in the U.S. or conditional approval in the E.U. as a result of the data from the STORM study in patients with triple class refractory myeloma or the SADAL study in patients with relapsed or refractory DLBCL 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 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: 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; Karyopharm's ability to obtain and maintain requisite regulatory approvals and to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases in which Karyopharm is currently developing its drug candidates; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, which was filed with the Securities and Exchange Commission (SEC) on November 8, 2018, 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.

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Karyopharm Therapeutics Inc.
Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 118,021	\$ 68,997
Short-term investments	210,178	77,472
Prepaid expenses and other current assets	6,413	1,754
Restricted cash	—	200
Total current assets	334,612	148,423
Property and equipment, net	3,863	2,185
Long-term investments	2,001	29,396
Restricted cash	716	290
Total assets	\$ 341,192	\$ 180,294
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 4,332	\$ 5,665
Accrued expenses	32,493	21,445
Deferred revenue	9,362	21,921
Deferred rent	390	303
Other current liabilities	327	133
Total current liabilities	46,904	49,467
Convertible senior notes	102,664	—
Deferred revenue, net of current portion	4,532	—
Deferred rent, net of current portion	3,922	1,363
Total liabilities	158,022	50,830
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized; none issued and outstanding	—	—
Common stock, \$0.0001 par value; 100,000,000 shares authorized; 60,829,308 and 49,533,150 shares issued and outstanding at December 31, 2018 and 2017, respectively	6	5
Additional paid-in capital	857,156	625,017
Accumulated other comprehensive loss	(244) (217
Accumulated deficit	(673,748) (495,341
Total stockholders' equity	183,170	129,464
Total liabilities and stockholders' equity	\$ 341,192	\$ 180,294

(in thousands, except share and per share amounts)

	(Unaudited) For the Quarter Ended, December 31,		For the Year Ended December 31,	
	2018	2017	2018	2017
License and other revenue	\$ 206	\$ 1,534	\$ 30,336	\$ 1,605
Operating expenses:				
Research and development	38,890	34,833	161,372	107,273
General and administrative	18,771	6,153	48,847	24,870
Total operating expenses	57,661	40,986	210,219	132,143
Loss from operations	(57,455)	(39,452)	(179,883)	(130,538)
Other income (expense):				
Interest income	1,768	432	4,028	1,698
Interest expense	(2,493)	—	(2,493)	—
Other expense	(13)	(11)	(33)	(81)
Total other (expense) income, net	(738)	421	1,502	1,617
Loss before income taxes	(58,193)	(39,031)	(178,381)	(128,921)
Provision for income taxes	(17)	(9)	(26)	(63)
Net loss	\$ (58,210)	\$ (39,040)	\$ (178,407)	\$ (128,984)
Net loss per share—basic and diluted	\$ (0.96)	\$ (0.80)	\$ (3.14)	\$ (2.81)
Weighted-average number of common shares outstanding used in net loss per share—basic and diluted	60,759,500	48,644,578	56,799,699	45,899,784



Source: Karyopharm Therapeutics Inc.

<https://investors.karyopharm.com/2019-02-28-Karyopharm-Reports-Fourth-Quarter-and-Full-Year-2018-Financial-Results-and-Provides-Corporate-Update>