

Karyopharm Reports Positive Phase 3 SEAL Data in Oral Presentation at The Connective Tissue Oncology Society 2020 Annual Meeting

-- Twice-Weekly XPOVIO® (selinexor) Demonstrates a Statistically Significant Improvement in Median PFS (Hazard Ratio=0.70, p=0.023) in Patients with Advanced Unresectable Dedifferentiated Liposarcoma Following at Least Two Prior Therapies --

-- Results Mark the First Positive Late-Stage Data for XPOVIO in a Solid Tumor Setting, Highlighting a Major Advance for Its Future Potential in Other Solid Tumor Indications --

-- Management to Host Conference Call to Review the Data Today at 12:00 PM ET --

NEWTON, Mass., Nov. 20, 2020 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today reported it will present positive results from the Phase 3 portion of the randomized, double blind, placebo controlled, cross-over SEAL study evaluating single agent, oral XPOVIO® (selinexor) versus matching placebo in patients with liposarcoma at the Connective Tissue Oncology Society 2020 Annual Meeting (CTOS 2020). As previously reported, the SEAL study met its primary endpoint of a statistically significant increase in median progression-free survival (PFS) in patients with advanced unresectable dedifferentiated liposarcoma following at least two prior therapies.

"Dedifferentiated liposarcoma is a particularly aggressive cancer that arises in the body's fat tissue and is typically associated with high rates of metastatic recurrence and mortality. Unfortunately, there are few effective treatment options available for patients with advanced disease," said Mrinal M. Gounder, MD, Attending Physician, Sarcoma Service and Developmental Therapeutics Service, Memorial Sloan Kettering Cancer Center, and lead investigator of the SEAL study. "The data presented at CTOS 2020 demonstrated that patients treated with XPOVIO experienced a statistically significant improvement in median PFS compared to placebo in patients with at least two prior therapies. Extending PFS is an important clinical goal for these patients because the rapid progression of this disease often translates into early mortality."

"We are delighted to share these significant results from the Phase 3 portion of the SEAL study, the first, late-stage clinical data for XPOVIO in a solid tumor indication," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "We believe these data strongly support our goal of developing twice-weekly XPOVIO as an effective, convenient, novel oral therapy that can extend PFS for patients with advanced unresectable dedifferentiated liposarcoma. We are especially excited by these data because XPOVIO is the first oral therapy to show activity in patients with previously treated liposarcoma. We look forward to submitting a New Drug Application to the U.S. Food and Drug Administration (FDA) during the first quarter of 2021, requesting approval of XPOVIO to treat the patient population studied in SEAL. If approved, XPOVIO would represent the first oral, non-chemotherapy agent available for patients with dedifferentiated liposarcoma."

Results from the Phase 3 Portion of the Phase2/3 SEAL Study

The median PFS in the XPOVIO arm of the Phase 3 portion of the SEAL study was 2.83 months compared to 2.07 months in the placebo arm (hazard ratio (HR)=0.70; p=0.023). These data indicate that treatment with XPOVIO reduced the risk of disease progression or death by approximately 30%, compared to placebo. The estimated 6-month PFS survival probability was 23.9% on the selinexor arm compared to 13.9% on placebo. Additionally, the 12-month PFS survival probability was 8.4% on the selinexor arm compared to 2% on the placebo arm. Finally, 7.5% of patients on the selinexor arm had a 15% or greater reduction in their disease burden as measured by target lesion size while none of the patients on the placebo arm achieved this level of reduction. The trial allowed patients on placebo with objective progression to cross over to the XPOVIO treatment arm. The median overall survival for patients who received XPOVIO was 9.99 months compared to 9.07 months for patients who never crossed over to the XPOVIO treatment arm (HR=0.69; p=0.122).

The most common treatment-related adverse events (AEs) were cytopenias, along with gastrointestinal and constitutional symptoms and were consistent with those previously reported from other selinexor studies. Most AEs were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (81%), decreased appetite (60%), fatigue (51%), and vomiting (49%) and were mostly Grade 1 and 2 events. The most common Grade 3 and 4 treatment-related AEs were anemia (19%), hyponatremia (11%), thrombocytopenia (10%) and asthenia (10%).

XPOVIO is currently approved by the FDA as a treatment for patients with relapsed or refractory multiple myeloma and relapsed or refractory diffuse large B-cell lymphoma (DLBCL). XPOVIO is currently the only XPO1

inhibitor approved by the FDA and has been extensively tested in clinical trials across numerous cancer indications worldwide since 2012. Karyopharm has also submitted a supplemental New Drug Application (sNDA) for XPOVIO that is currently under review by the FDA for the expansion of XPOVIO's label to include XPOVIO as a treatment for patients with multiple myeloma after at least one prior line of therapy. The sNDA has been assigned an action date by the FDA of March 19, 2021 under the Prescription Drug User Fee Act. The full Prescribing Information for XPOVIO is available at www.XPOVIO.com.

Details for the oral presentation at CTOS 2020 are as follows:

Title: A Phase 2/3, Randomized, Double-Blind, Cross-Over Study of Selinexor Versus Placebo in Advanced Unresectable Dedifferentiated Liposarcoma (DDLs)

Presenter: Mrinal Gounder, MD, Memorial Sloan Kettering Cancer Center

Paper #: 20

Session: 7. Liposarcoma

Date and Time: Friday, November 20, 2020, 10:30 a.m. to 11:30 a.m. ET

Conference Call Information

Karyopharm will host a conference call today, Friday, November 20, 2020, at 12:00 p.m. Eastern Time, to discuss the results from the SEAL study. The call will feature Dr. Gounder and another recognized sarcoma expert Sant P. Chawla, MD, FRACP, Director of the Sarcoma Oncology Center, Santa Monica, CA, along with members of the Karyopharm executive leadership team. To access the conference call, please dial (877) 870-4263 (local) or (412) 317-0790 (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 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 the SEAL Study

[SEAL \(Selinexor in Advanced Liposarcoma\) is a Phase 2/3, randomized, double blind, placebo controlled, multicenter study \(NCT02606461\)](#) designed to evaluate the efficacy and safety of twice-weekly, 60mg fixed dose of XPOVIO (selinexor) in patients with advanced unresectable dedifferentiated liposarcoma following at least two prior therapies. The Phase 2 portion of the study enrolled approximately 57 patients (1:1 randomization) and the Phase 3 portion enrolled approximately 285 patients (2:1 randomization). Patients on the placebo arm with confirmed progressive disease were permitted to cross over to the XPOVIO treatment arm. The primary endpoint of the study is PFS.

About Liposarcoma

Liposarcoma is a rare type of cancer that occurs in the fat cells in the body, most often in the muscles of the limbs or abdomen. Dedifferentiated liposarcoma (DDLs) is a high grade type of liposarcoma that grows more aggressively than a low grade, well differentiated liposarcoma and is associated with poorer prognosis.¹ Liposarcoma accounts for approximately 20% of all soft tissue sarcomas². In liposarcoma, the risk of recurrence and metastasis increases with higher grade disease.³

About XPOVIO® (selinexor)

XPOVIO is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. XPOVIO functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). XPOVIO blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. Karyopharm received accelerated U.S. Food and Drug Administration (FDA) approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) 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. Karyopharm has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval of selinexor in this same RRMM indication. Karyopharm's supplemental New Drug Application (sNDA) requesting an expansion of its current indication to include the treatment for patients with multiple myeloma after at least one prior line of therapy has been accepted for filing by the FDA. In June 2020, Karyopharm received accelerated FDA approval of XPOVIO for its second indication in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. Selinexor is also

being evaluated in several other mid-and later-phase clinical trials across multiple cancer indications, including as a potential backbone therapy in combination with approved myeloma therapies (STOMP), in liposarcoma (SEAL) and 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. Additional clinical trial information for selinexor is available at www.clinicaltrials.gov.

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

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma (MM) and developed or worsened in patients with DLBCL.

Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Institute platelet transfusion and/or other treatments as clinically indicated. Monitor patients for signs and symptoms of bleeding and evaluate promptly. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection. Neutropenia and febrile neutropenia occurred in patients with MM and in patients with DLBCL.

Obtain white blood cell counts with differential at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction (AR).

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients with MM and DLBCL.

Nausea/Vomiting: Provide prophylactic antiemetics. Administer 5-HT₃ receptor antagonists and other anti-nausea agents prior to and during treatment with XPOVIO. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Administer intravenous fluids to prevent dehydration and replace electrolytes as clinically indicated.

Diarrhea: Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide standard anti-diarrheal agents, administer intravenous fluids to prevent dehydration, and replace electrolytes as clinically indicated.

Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Interrupt, reduce dose, or permanently discontinue based on severity of ARs. Provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia. Hyponatremia developed in patients with MM and in patients with DLBCL.

Monitor sodium level at baseline and throughout treatment. Monitor more frequently during the first 2 months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Assess hydration status and manage hyponatremia per clinical guidelines, including intravenous saline and/or salt tablets as appropriate and dietary review. Interrupt, reduce dose, or permanently discontinue based on severity of the AR.

Serious Infection: XPOVIO can cause serious and fatal infections. Most infections were not associated with Grade 3 or higher neutropenia. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Monitor for signs and symptoms of infection, and evaluate and treat promptly.

Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities. Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase

the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, until the neurological toxicity fully resolves. Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes. Institute fall precautions as appropriate.

Embryo-Fetal Toxicity: XPOVIO can cause fetal harm when administered to a pregnant woman.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

ADVERSE REACTIONS

The most common adverse reactions (ARs) in $\geq 20\%$ of patients with MM are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The most common ARs, excluding laboratory abnormalities, in $\geq 20\%$ of patients with DLBCL are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities in $\geq 15\%$ of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in $\geq 5\%$ were thrombocytopenia, lymphopenia, and neutropenia.

In patients with MM, fatal ARs occurred in 9% of patients. Serious ARs occurred in 58% of patients. Treatment discontinuation rate due to ARs was 27%. The most frequent ARs requiring permanent discontinuation in $\geq 4\%$ of patients included fatigue, nausea, and thrombocytopenia.

In patients with DLBCL, fatal ARs occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal AR was infection (4.5% of patients). Serious ARs occurred in 46% of patients; the most frequent serious AR was infection. Discontinuation due to ARs occurred in 17% of patients.

USE IN SPECIFIC POPULATIONS

In MM, no overall difference in effectiveness of XPOVIO was observed in patients > 65 years old when compared with younger patients. Patients ≥ 75 years old had a higher incidence of discontinuation due to an AR than younger patients, a higher incidence of serious ARs, and a higher incidence of fatal ARs.

Clinical studies in patients with relapsed or refractory DLBCL did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

The effect of end-stage renal disease ($CL_{CR} < 15$ mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

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.

Please see XPOVIO Full Prescribing Information available at www.XPOVIO.com.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development, and commercialization of novel first-in-class drugs directed against nuclear export and related targets for the treatment of cancer and other major diseases. Karyopharm's Selective Inhibitor of Nuclear Export (SINE) compounds function by binding with and inhibiting the nuclear export protein XPO1 (or CRM1). Karyopharm's lead compound, XPOVIO® (selinexor), received accelerated approval from the U.S. Food and Drug Administration (FDA) in July 2019 in combination with dexamethasone as a treatment for patients with heavily pretreated multiple myeloma. In June 2020, XPOVIO was approved by the FDA as a treatment for patients with relapsed or refractory diffuse large B-cell lymphoma. A Marketing Authorization Application for selinexor for patients with heavily pretreated multiple myeloma is also currently under review by the European Medicines Agency. 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. Karyopharm has several investigational programs in clinical or preclinical development. 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 Karyopharm's expectations and plans relating to XPOVIO for the treatment of patients with advanced unresectable dedifferentiated liposarcoma; commercialization of XPOVIO or any of its drug candidates and the commercial performance of XPOVIO; submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the Company's regulatory strategy, the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities and the potential availability of accelerated approval pathways; the expected design of the Company's clinical trials; and the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially 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; that regulators will agree that selinexor qualifies for conditional approval in the E.U. as a result of data from the STORM study or confirmatory approval in the U.S. or EU based on the BOSTON study in patients with relapsed or refractory multiple myeloma; 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 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 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 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, 2020, which was filed with the Securities and Exchange Commission (SEC) on November 2, 2020, 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

¹Livingston, J.A., et al. Role of chemotherapy in dedifferentiated liposarcoma of the retroperitoneum: defining the benefit and challenges of the standard. Sci Rep 7, 11836 (2017).

<https://doi.org/10.1038/s41598-017-12132-w>

² <https://pubmed.ncbi.nlm.nih.gov/25115417/>

³ <http://sarcomahelp.org/liposarcoma.html>

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