Karyopharm Announces Selinexor Clinical Data to be Presented at the International Society for Influenza and Other Respiratory Virus Diseases Antiviral Group Virtual Conference on Therapeutics for COVID-19

− Encouraging Anti-Viral and Anti-Inflammatory Activity Demonstrated in a Subset of Patients in a Study of Low Dose Selinexor in Hospitalized Patients with Severe COVID-19 −
− A Case Report From a COVID-19 Patient Treated with Selinexor Now Also Published in the Annals of Case Reports -

NEWTON, Mass., Oct. 6, 2020 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq: KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced an oral presentation at the International Society for Influenza and Other Respiratory Virus Diseases Antiviral Group (ISIRV-AVG) Virtual Conference on Therapeutics for COVID-19 taking place from October 6 - 8, 2020. The presentation will feature data from a Phase 2 clinical study evaluating low dose oral selinexor in hospitalized patients with severe COVID-19 (NCT04349098).

While an interim analysis indicated that the trial was unlikely to meet its pre-specified primary endpoint across the entire patient population studied, and has since been discontinued, the results demonstrated encouraging anti-viral and anti-inflammatory activity in an important subset of treated patients. The randomized, multi-center, placebo-controlled Phase 2 study was designed to assess the activity and safety of 20mg of selinexor given orally three times a week for two weeks, a dosing level significantly lower than the U.S. Food and Drug Administration (FDA) approved dose of selinexor, marketed as XPOVIO®, to treat patients with relapsed or refractory multiple myeloma or relapsed or refractory diffuse large B-cell lymphoma.

A post-hoc analysis of 66 patients with either baseline serum lactate dehydrogenase (LDH) ≤370 U/L or D-dimer ≤600 mcg/L FEU (Low LDH/DD) showed that treatment with selinexor (n=38) compared to placebo (n=28) was associated with a significantly higher percentage of patients discharged by Day 14 (78.9% vs 57.1%; p=0.029) with a trend towards superior ≥2-point improvement in the Ordinal Scale (OSI-2) on Day 14 (78.9% vs 64.3%; p=0.095). Additionally, a positive trend was observed in patients treated with selinexor to convert to a negative COVID-19 PCR test as compared to placebo (42.1% vs 28.6%; p=0.13) and a significant reduction in IL1-RA, IL-6, IL-7, IP-10, and TNF-a levels, measurements of inflammation, was also seen within eight days of selinexor treatment ($p<0.05$). Adverse events occurred in 63.2% of patients treated with selinexor and 51.9% of patients with placebo in the subset, with similar occurrences of deaths across the treatment arms (2 vs. 1). Blood levels of LDH and D-dimer are important prognostic markers for in-hospital mortality in patients admitted for COVID-19.

"We are encouraged by the promising results observed following low dose oral administration of selinexor in hospitalized patients with severe COVID-19 and Low LDH/DD and believe they warrant the need for additional clinical studies. Additionally, we believe non-hospitalized patients with moderate COVID-19 may also benefit from this treatment regimen and should be considered for future evaluation," said Sharon

Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "We plan to continue ongoing discussions with potential clinical development partners, including U.S. and international government and academic organizations advancing COVID-19 clinical studies, to further evaluate selinexor in patients with COVID-19."

In addition to data from the Phase 2 selinexor study being presented at the ISIRV-AVG Conference, a case report from one of the clinical investigators in this trial has been published in the *Annals of Case Reports* and can be found online, here. In this case report, Marcelo Gareca, MD, an Infectious Disease specialist at Lehigh Valley Hospital, Allentown, PA, provides details of a patient with severe COVID-19 and progressive hypoxia who demonstrated marked clinical improvements following selinexor treatment without any reported adverse effects.

XPO1 inhibitors, including selinexor, have demonstrated activity against over 20 different viruses, including the RNA viruses, influenza, respiratory syncytial virus (RSV) and other common causes of respiratory infection. XPO1 inhibition has been identified in several assays as having potential activity specifically against SARS-CoV-2. One of the most important aspects of COVID-19 is the marked pulmonary inflammation with high levels of cytokines such as IL6, IL1, IFNg and others. Selinexor and other Selective Inhibitor of Nuclear Export (SINE) compounds have demonstrated potent anti-inflammatory activity through the inhibition of Nuclear Factor kB (NF-kB), leading to reductions in all of these cytokines in a variety of models, which may be particularly beneficial to hospitalized patients with COVID-19.

Details for the ISIRV-AVG oral presentation are as follows:

Title: Treatment of Severe COVID-19 with Low-Dose Selinexor: Demonstration of Anti-Viral and Anti-Inflammatory Activities in a Randomized, International, Multicenter, Placebo-Controlled Phase 2 Clinical Trial
Presenter: George F. Geils, M.D., Roper St. Francis Healthcare
Date: October 7, 2020; 10:50 EST

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 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.

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 ≥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 ≥20% of patients with DLBCL are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities in ≥15% of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in ≥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 ≥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 selinexor as a potential treatment for hospitalized patients with severe COVID-19; the design and execution of a global randomized clinical trial to study this potential application of selinexor, including the dosing regimen; and the potential anti-viral and anti-inflammatory properties of selinexor. . Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that Karyopharm will successfully complete necessary clinical development phases of selinexor in this indication; that data from a clinical trial of selinexor would support its use in treatment of hospitalized patients with severe COVID-19; that regulators will approve the use of selinexor in hospitalized patients with severe COVID-19; or that such approval will be made on an accelerated timeline. 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 reducing 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 selinexor for treatment of COVID-19 in the commercial marketplace, the timing and costs involved in commercializing selinexor for such indication or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of selinexor for such indication 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 indications 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 June 30, 2020, which was filed with the Securities and Exchange Commission (SEC) on August 4, 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.

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