Karyopharm Announces Publication of Health-Related Quality of Life Outcomes from Phase 3 SEAL Study of Selinexor in Advanced Unresectable Dedifferentiated Liposarcoma in Future Oncology

- Treatment with Selinexor Demonstrated Several Potential Clinical Advantages Compared to Placebo, Including Reduction in Pain, Longer Time to Marked Clinical Deterioration of Pain and Longer Median Time to Next Treatment -
- First Set of Clinical Data from the Phase 3 SEAL Study Published in a Peer-Reviewed Medical Journal -

NEWTON, Mass., April 19, 2021 /PRNewswire/ -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that health-related quality of life (HRQoL) data from the Phase 3 portion of the SEAL (**Se**linexor in **A**dvanced **L**iposarcoma) study were published online in *Future Oncology*. The SEAL study evaluated twice weekly, single agent selinexor, the Company's first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, versus matching placebo in patients with advanced unresectable dedifferentiated liposarcoma (DDLPS) who have experienced disease progression following at least two prior therapies. XPOVIO® (selinexor) is currently approved by the U.S. Food & Drug Administration (FDA) for the treatment of relapsed or refractory multiple myeloma and relapsed or refractory diffuse large B-cell lymphoma; XPOVIO has not been approved for the treatment of DDLPS and, therefore, its safety and efficacy for that patient population have not been established.

"The Phase 3 SEAL study suggests that selinexor has enhanced clinical activity and a manageable safety profile in patients with DDLPS, a very rare and aggressive form of cancer where there are very few treatment options available. In addition to meeting its primary endpoint with a statistically significant improvement in progression-free survival (PFS), treatment with selinexor also resulted in improvements in key quality of life parameters as compared to patients treated with placebo," said Jatin Shah, MD, Chief Medical Officer of Karyopharm. "The results highlight that the reduction in tumor growth, as measured by objective radiographic PFS, is accompanied by clinically important reductions in pain, with minimal effects on other aspects of quality of life. Since pain is one of the most devastating symptoms associated with advanced and progressing DDLPS, the significant reduction in pain, and a delay in the time to definitive deterioration reported by patients in the selinexor arm, combined with the convenience of an orally administered therapy, could represent a meaningful clinical benefit to patients."

"We are pleased to see the first set of data from the Phase 3 SEAL study now published in a peer-reviewed medical journal," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "These data continue to support our overarching development strategy to pursue additional solid tumor indications where we believe selinexor can demonstrate meaningful clinical activity both as a single agent, and more importantly, as part of future combination regimens for patients battling cancer."

The Phase 3 SEAL Study Health-Related Quality of Life Results

The published SEAL study results were based on the randomized, double blind, placebo-controlled, cross-over, Phase 3 portion of the study, which evaluated oral selinexor versus matching placebo in 285 adult patients with advanced unresectable DDLPS. The secondary endpoint of the SEAL study measured HRQoL outcomes by using the EORTC QLQ-C30 questionnaire, which was completed by 255 patients in the study. Overall, the results showed that pain scores worsened in the placebo arm compared to the selinexor arm across all post-baseline visits, though some visits were not statistically significant. The patients who received twice-weekly selinexor also reported lower rates and slower worsening of pain over time and a longer time to marked clinical deterioration of pain compared to patients treated with placebo. Median time to next treatment was also significantly longer in patients receiving selinexor compared to those receiving placebo. These results indicate that reduction in tumor growth (as measured by objective radiographic PFS) is accompanied by clinically important reduction in pain, with minimal effects on other aspects of quality of life.

About the SEAL Study

SEAL (**Se**linexor in **A**dvanced **L**iposarcoma) was 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 selinexor in patients with advanced unresectable dedifferentiated liposarcoma following at least two

prior therapies. The Phase 3 portion of the study enrolled 285 patients (2:1 randomization). Patients on the placebo arm with confirmed progressive disease were permitted to cross over to the selinexor treatment arm. The primary endpoint of the study was PFS and secondary endpoint measured HRQoL outcomes. In the study, selinexor was associated with a 30% reduction in the time to disease progression or death in the Phase 3 portion (hazard ratio (HR)=0.70; p=0.023, medians 2.83 months on selinexor compared to 2.07 months on placebo).

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%).

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 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 sarcomas.[2] 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. The safety and efficacy of selinexor for use in in patients with DDLPS has not been established; selinexor has not been approved for this use by the U.S. Food and Drug Administration (FDA) or any other regulatory agency. Karyopharm received accelerated approval of XPOVIO in July 2019 in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody. NEXPOVIO® (selinexor) has also been granted conditional marketing authorization in combination with dexamethasone for adult patients with heavily pretreated multiple myeloma by the European Commission. Karyopharm's supplemental New Drug Application requesting an expansion of its indication to include the treatment for patients with multiple myeloma after at least one prior therapy was approved by the FDA on December 18, 2020. 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 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

XPOVIO® (selinexor) is a prescription medicine approved:

- In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy (XVd).
- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti–CD38 monoclonal antibody (Xd).
- For the treatment of adult patients with relapsed or refractory diffuse large B–cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic

therapy. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

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

Adverse Reactions

- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive XVd are fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract and vomiting. Grade 3–4 laboratory abnormalities (≥10%) are thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia. In the BOSTON trial, fatal adverse reactions occurred in 6% of patients within 30 days of last treatment. Serious adverse reactions occurred in 52% of patients. Treatment discontinuation rate due to adverse reactions was 19%.
- The most common adverse reactions (≥20%) in patients with multiple myeloma who receive Xd are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea and upper respiratory tract infection. In the STORM trial, fatal adverse reactions occurred in 9% of patients. Serious adverse reactions occurred in 58% of patients. Treatment discontinuation rate due to adverse reactions was 27%.
- The most common adverse reactions (incidence ≥20%) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3–4 laboratory abnormalities (≥15%) are thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. In the SADAL trial, fatal adverse reactions occurred in 3.7% of patients within 30 days, and 5% of patients within 60 days of last treatment; the most frequent fatal adverse reactions was infection (4.5% of patients). Serious adverse reactions occurred in 46% of patients; the most frequent serious adverse reaction was infection(21% of patients). Discontinuation due to adverse reactions occurred in 17% of patients.

Use In Specific Populations
Lactation: Advise not to breastfeed.

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

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

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is a commercial-stage pharmaceutical company pioneering novel cancer therapies and dedicated to the discovery, development, and commercialization of first-in-class drugs directed against nuclear export for the treatment of cancer and other 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), is approved in the U.S. in multiple hematologic malignancy indications, including in combination with Velcade® (bortezomib) and dexamethasone for the treatment of adult patients with multiple myeloma after at least one prior therapy, in combination with

dexamethasone for the treatment of adult patients with heavily pretreated multiple myeloma and as a monotherapy for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma. NEXPOVIO® (selinexor) has also been granted conditional marketing authorization for adult patients with heavily pretreated multiple myeloma by the European Commission. 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; 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/NEXPOVIO; that regulators will grant confirmatory authorization in the European Union based on the BOSTON study in adult patients with 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/NEXPOVIO, 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/NEXPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO/NEXPOVIO or any of Karyopharm's drug candidates that receive regulatory authorization; the ability to obtain and retain regulatory authorization of XPOVIO/NEXPOVIO or any of Karyopharm's drug candidates that receive regulatory authorization; 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 authorization 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 product or product candidate. These and other risks are described under the caption "Risk Factors" in Karyopharm's Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the Securities and Exchange Commission (SEC) on February 24, 2021, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

References

[1]Livingston, 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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https://investors.karyopharm.com/2021-04-19-Karyopharm-Announces-Publication-of-Health-Related-Quality-of-Life-Outcomes-from-Phase-3-SEAL-Study-of-Selinexor-in-Advanced-Unresectable-Dedifferentiated-Liposarcoma-in-Future-Oncology