

Karyopharm Announces New Interim Phase 2 Selinexor Data in Myelofibrosis Selected for Oral Presentation at the American Society of Hematology 2021 Annual Meeting and Exposition

- **33% of Patients Who Received at Least 24 Weeks of Selinexor Treatment Achieved a Response, Defined as $\geq 35\%$ Spleen Volume Reduction (SVR) --**
- **Patients on Study had a Median Duration of 22 months of Prior JAK Inhibitor Therapy with 11 out of 12 Patients Having Disease Refractory to Ruxolitinib --**
- **Total of 17 Abstracts Selected for Presentation at the Meeting, Including Five Oral Presentations --**

NEWTON, Mass., Nov. 4, 2021 [/PRNewswire/](#) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a commercial-stage pharmaceutical company pioneering novel cancer therapies, today announced that an abstract detailing new data from a Phase 2 study evaluating selinexor, a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound, in patients with myelofibrosis (MF) previously treated with JAK inhibition has been selected for an oral presentation at the upcoming American Society of Hematology (ASH) 2021 Annual Meeting and Exposition in Atlanta, GA on December 11-14, 2021.

"JAK inhibition is the current standard of care for patients with myelofibrosis; however, patients whose disease fails treatment with ruxolitinib have a poor prognosis, with an expected survival of approximately 14 months, and there are no approved treatment options other than JAK inhibitors," said Srinivas Tantravahi, MBBS, MRCP, University of Utah Hospital and principal investigator of the Phase 2 study. "Interim results from this Phase 2 study demonstrated that once weekly single agent oral selinexor resulted in compelling spleen volume reduction rates in myelofibrosis patients who received at least 24 weeks of treatment, with 33% of those patients achieving a response, defined as $\geq 35\%$ SVR. In addition to spleen responses, there was improvement in anemia status and symptom scores in these patients. The responses were durable with the first patient on treatment for more than two years. The sustained responses and well-tolerated safety profile highlight selinexor's potential in patients with myelofibrosis who have either progressed following ruxolitinib or cannot tolerate JAK inhibition. We look forward to sharing these exciting results with the broader medical and scientific community at ASH this year."

"Once weekly, low-dose selinexor is an oral agent with a unique mechanism of action that has demonstrated strong single-agent activity in myelofibrosis patients with disease refractory to ruxolitinib," said Jatin Shah, MD, Chief Medical Officer of Karyopharm. "Importantly, there are no other classes of drug approved other than JAK inhibitors and a new class of effective drugs is a critical need for patients. Based on these encouraging data, we look forward to dosing the first patient in a new, company-sponsored Phase 2 study evaluating single-agent selinexor versus physician's choice in patients with previously treated myelofibrosis during the fourth quarter of 2021."

Results from the Phase 2 Study Evaluating Selinexor in Patients with MF Refractory or Intolerant to JAK Inhibitors

The results were based on the open label, prospective, investigator-initiated single center study in adult patients with primary or secondary MF with resistance or intolerance to JAK inhibitor therapy

(NCT03627403). Selinexor was administered orally at a dose of 80mg or 60mg once weekly to 12 patients. The primary endpoint of the study is to assess the efficacy of selinexor on SVR. Median duration of prior JAK inhibitor therapy was 22 months and 11 out of 12 patients had MF refractory to ruxolitinib.

As of the data cutoff, the median duration of treatment was 36 weeks. In the nine patients who were on treatment for over 24 weeks, SVR of $\geq 25\%$ and 35% occurred in four (44%) and three (33%) patients, respectively. The most common treatment related adverse event was weight loss (grade 2 in four patients and grade 3 in one patient). This was manageable with treatment interruption and dose reduction, except in one patient who discontinued treatment. Overall, selinexor demonstrated single-agent activity with sustained spleen responses in patients with JAK inhibitor refractory MF and long-term administration of selinexor was well tolerated. Updated data will be presented at the meeting.

Company to Host Investor Day Event

Karyopharm will host an Investor Day event on Wednesday, December 8, 2021 from 10:00 a.m. to 12:30 p.m. ET to outline its commercial and pipeline priorities and objectives. The event will feature presentations from Karyopharm management and recognized thought leaders in multiple myeloma, gynecological malignancies, and other core focus indications. The event will take place virtually and will be accessible via conference call and webcast. Full details will be made available closer to the Investor Day.

Details for the ASH 2021 abstracts are as follows:

In total, 17 abstracts were selected for presentation at the meeting, including five oral presentations and 12 posters.

Oral Presentations

Title: A Phase 2 Study to Evaluate the Efficacy and Safety of Selinexor in Patients with Myelofibrosis Refractory or Intolerant to JAK Inhibitors

Presenter: Srinivas Tantravahi, University of Utah

Abstract #: 143

Session Type: Oral Presentation

Session: Myeloproliferative Syndromes: Clinical and Epidemiological: Non-JAK Inhibitor Therapies for Myelofibrosis

Date and Time: Saturday, December 11, 2021 at 1:00 p.m. ET

Title: Transcriptomic Correlates of Response to Selinexor in Multiple Myeloma Reveal a Predictive Signature

Presenter: Paula Restrepo, Icahn School of Medicine at Mount Sinai

Abstract #: 457

Session Type: Oral Presentation

Session: Multiple Myeloma and Plasma Cell Dyscrasias: Clinical and Epidemiological: Multiple Myeloma and Waldenstrom Macroglobulinemia: Exploring Biomarkers in the Era of Personalized Medicine

Date and Time: Sunday, December 12, 2021 at 12:00 p.m. ET

Title: Enhanced p53 Activation by Dual Inhibition of MDM2 and XPO1 Disrupts MYC Transcriptional Program and Restores Sensitivity to BCL-2 Inhibition in Ven/HMA Resistant AML

Presenter: Yuki Nishida, Saga University

Abstract #: 505

Session Type: Oral Presentation

Session: Molecular Pharmacology and Drug Resistance: Myeloid Neoplasms: Novel Strategies to Overcome

Resistance to BCL-2 Inhibition

Date and Time: Sunday, December 12, 2021 at 4:30 p.m. ET

Title: Rationale for Selinexor Treatment in Daratumumab-Refractory MM Patients Identified by Paired Ex Vivo Drug Sensitivity and RNA-Seq

Presenter: Suresh Kumar Balasubramanian, Wayne State University

Abstract #: 683

Session Type: Oral Presentation

Session: Molecular Pharmacology and Drug Resistance: Lymphoid Neoplasms: Targeting Mitochondrial Survival Pathways

Date and Time: Monday, December 13, 2021 at 3:45 p.m. ET

Title: Comparison of Salvage Autologous Hematopoietic Cell Transplantation with Outcomes Following Selinexor Combinations Among Double/Triple Refractory Myeloma Patients

Presenter: Praneeth Sudalagunta, H Lee Moffitt Cancer Ctr

Abstract #: 893

Session Type: Oral Presentation

Session: Multiple Myeloma and Plasma Cell Dyscrasias: Basic and Translational: Myeloma Pathogenesis and Novel Targets

Date and Time: Monday, December 13, 2021 at 7:15 p.m. ET

Poster Presentations

Title: Efficacy and Safety of Selinexor-Containing Regimens in Patients with Multiple Myeloma Previously Treated with Anti-CD38 Monoclonal Antibodies (α CD38 mAb)

Presenter: Suzanne Lentzsch, Columbia University Irving Medical Center

Abstract #: 1651

Session Type: Poster Presentation

Session: Myeloma and Plasma Cell Dyscrasias: Clinical-Pro prospective Therapeutic Trials: Poster I

Date and Time: Saturday, December 11, 2021 at 5:30 – 7:30 p.m. ET

Title: Effects of Cytogenetic Risk on Outcomes in Multiple Myeloma Treated with Selinexor, Bortezomib, and Dexamethasone (XVd)

Presenter: Nizar Bahlis, University of Calgary

Abstract #: 1634

Session Type: Poster Presentation

Session: Multiple Myeloma and Plasma Cell Dyscrasias: Clinical and Epidemiological: Poster I

Date and Time: Saturday, December 11, 2021 at 5:30 – 7:30 p.m. ET

Title: Selinexor in Combination with Daratumumab-Bortezomib and Dexamethasone for the Treatment of Relapse or Refractory Multiple Myeloma: Initial Results of the Phase 2, Open-label, Multicenter GEM-SELIBORDARA Study

Presenter: Paula Rodríguez- Otero, Clínica Universidad de Navarra

Abstract #: 1677

Session Type: Poster Presentation

Session: Myeloma and Plasma Cell Dyscrasias: Clinical-Pro prospective Therapeutic Trials: Poster I

Date and Time: Saturday, December 11, 2021 at 5:30 – 7:30 p.m. ET

Title: Once Weekly Oral Selinexor, Pomalidomide, and Dexamethasone in Relapsed Refractory Multiple Myeloma

Presenter: Darrell White, QEII Health Sciences Center, Dalhousie University

Abstract #: 2748

Session Type: Poster Presentation

Session: Myeloma and Plasma Cell Dyscrasias: Clinical-Prospective Therapeutic Trials: Poster II

Date and Time: Sunday, December 12, 2021 at 6:00 – 8:00 p.m. ET

Title: Selinexor-Based Regimens in Patients with Multiple Myeloma after Prior Anti-B-Cell Maturation Antigen Treatment

Presenter: Muhamed Baljevic, University of Nebraska Medical Center

Abstract #: 2751

Session Type: Poster Presentation

Session: Myeloma and Plasma Cell Dyscrasias: Clinical-Prospective Therapeutic Trials: Poster II

Date and Time: Sunday, December 12, 2021 at 6:00 – 8:00 p.m. ET

Title: Single Cell RNA Sequencing of a Selinexor Clinical Trial Reveals Overexpression of Alternative Nuclear Export Pathways Associated with Resistance to Selinexor in RRMM Patients

Presenter: Yael Cohen, Tel Aviv Sourasky Medical Center

Abstract #: 2725

Session Type: Poster Presentation

Session: Multiple Myeloma and Plasma Cell Dyscrasias: Clinical and Epidemiological: Poster I

Date and Time: Sunday, December 12, 2021 at 6:00 – 8:00 p.m. ET

Title: Selinexor Enhances NK Cell Activation Against Lymphoma Cells Via Downregulation of HLA

Presenter: Matthew Blunt, University of Southampton

Abstract #: 2411

Session Type: Poster Presentation

Session: Lymphomas: Translational—Non-Genetic: Poster II

Date and Time: Sunday, December 12, 2021 at 6:00 – 8:00 p.m. ET

Title: Molecular Response Patterns in Relapsed/Refractory AML Patients Treated with Selinexor and Chemotherapy

Presenter: Piroska Klement, Hannover Medical School

Abstract #: 2369

Session Type: Poster Presentation

Session: Acute Myeloid Leukemias: Biomarkers, Molecular Markers and Minimal Residual Disease in Diagnosis and Prognosis: Poster II

Date and Time: Sunday, December 12, 2021 at 6:00 – 8:00 p.m. ET

Title: Updated Efficacy of Eltanexor Monotherapy in Patients with Higher Risk Hypomethylating Myelodysplastic Syndrome Primary Refractory to Hypomethylating Agents

Presenter: Sangmin Lee, Weill Cornell Medical College

Abstract #: 3676

Session Type: Poster Presentation

Session: Myelodysplastic Syndromes — Clinical and Epidemiological: Poster III

Date and Time: Monday, December 13, 2021 at 6:00 – 8:00 p.m. ET

Title: Clinical Outcomes in Patients with Dose Reduction of Selinexor in Combination with Bortezomib, and Dexamethasone (XVd) in Previously Treated Multiple Myeloma from the BOSTON Study

Presenter: Sundar Jagannath, Mount Sinai School of Medicine

Abstract #: 3793

Session Type: Poster Presentation

Session: Multiple Myeloma and Plasma Cell Dyscrasias: Clinical and Epidemiological: Poster III

Date and Time: Monday, December 13, 2021 at 6:00 – 8:00 p.m. ET

Title: Selinexor in Combination with R-GDP for Patients with Relapsed/Refractory B-Cell Lymphoma: SELINDA Phase Ib LYSA Study

Presenter: Marie Maerevoet, Jules Bordet Institute

Abstract #: 1411

Session Type: Poster Presentation

Session: Aggressive Lymphomas: Prospective Therapeutic Trials: Poster I

Date and Time: Saturday, December 11, 2021 at 5:30 – 7:30 p.m. ET

Title: A Phase 2/3, Multicenter Randomized Study of Rituximab-Gemcitabine-Dexamethasone-Platinum (R-GDP) with or without Selinexor in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (RR DLBCL)

Presenter: Seung Tae Lee, University of Maryland School of Medicine

Abstract #: 1420

Session Type: Poster Presentation

Session: 626. Aggressive Lymphomas: Prospective Therapeutic Trials: Poster I

Date and Time: Saturday, December 11, 2021, 5:30-7:30PM ET

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. NEXPOVIO® (selinexor) has also been granted conditional marketing authorization for adult patients with heavily pretreated multiple myeloma by the European Commission. Karyopharm's supplemental New Drug Application (sNDA) 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) 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

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 ($\geq 20\%$) 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 ($\geq 10\%$) 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 ($\geq 20\%$) 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 $\geq 20\%$) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3–4 laboratory abnormalities ($\geq 15\%$) 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 reaction 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 adult patients with relapsed or refractory diffuse large B-cell lymphoma. 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. 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 the ability of selinexor or eltanexor to treat patients with multiple myeloma, 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; that regulators will grant confirmatory approval 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 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 September 30, 2021, which was filed with the Securities and Exchange Commission (SEC) on November 3, 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.

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.

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<https://investors.karyopharm.com/2021-11-04-Karyopharm-Announces-New-Interim-Phase-2-Selinexor-Data-in-Myelofibrosis-Selected-for-Oral-Presentation-at-the-American-Society-of-Hematology-2021-Annual-Meeting-and-Exposition>