



Karyopharm Announces XPOVIO® (Selinexor) Clinical Data to be Presented at the American Society of Hematology 2019 Annual Meeting

November 6, 2019

-- Updated Results from the Pomalyst® and Kyprolis® Arms of the Phase 1b/2 STOMP Study Evaluating Selinexor in Combination with Other Approved Myeloma Therapies in Relapsed or Refractory Multiple Myeloma to be Highlighted --

-- Other Key Presentations Include New Data from the STOMP Revlimid® Arm Evaluating Selinexor in Patients with Newly Diagnosed Multiple Myeloma, Along with New Data Investigating Selinexor in Patients whose Myeloma has Progressed Following Experimental CAR-T Therapy --

NEWTON, Mass., Nov. 06, 2019 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), an oncology-focused pharmaceutical company, today announced that thirteen abstracts have been selected for presentation, including one oral presentation, at the upcoming American Society of Hematology (ASH) 2019 Annual Meeting taking place December 7-10, 2019 in Orlando. Four key abstracts to be presented at the meeting will feature clinical data for XPOVIO® (selinexor), the Company's first in class, oral SINE compound, including: updated data from the Pomalyst® (pomalidomide) and Kyprolis® (carfilzomib) arms of the Phase 1b/2 STOMP study evaluating selinexor in combination with backbone therapies in patients with relapsed or refractory multiple myeloma; new data from the Revlimid® (lenalidomide) plus selinexor arm of the Phase 1b/2 STOMP study evaluating this combination in patients with newly diagnosed multiple myeloma; and new data reporting on the use of selinexor in multiple myeloma patients whose disease has progressed following chimeric antigen receptor T-cell (CAR-T) therapy.

"We are expecting another strong presence at ASH this year with thirteen selected abstracts, including one oral presentation," said Sharon Shacham, PhD, MBA, Founder, President and Chief Scientific Officer of Karyopharm. "Of key interest will be updated data from two arms of the STOMP study; the arm investigating the all-oral regimen of selinexor and Pomalyst, and the arm investigating selinexor and Kyprolis. In both arms the response rates and safety profile remain highly encouraging. In addition, we look forward to a presentation describing new data from patients treated with selinexor-based regimens after their myeloma had progressed following experimental CAR-T therapy. Although based on a small sample size, all patients had a confirmed response when treated with selinexor/dexamethasone alone or in combination with either carfilzomib or bortezomib. As there are currently very limited data available regarding treatment options for patients whose disease has progressed following experimental CAR-T therapy, we believe these data further reinforces the therapeutic activity of selinexor in patients with advanced refractory disease."

Other abstracts at the meeting include: Encore data highlighting the previously disclosed comparison of patients in the STORM study to matched patients from the MAMMOTH study; a post-hoc analysis from the Phase 2b STORM study evaluating the efficacy and safety of XPOVIO in patients with triple-class refractory multiple myeloma with high risk cytogenetics; an additional analysis from the STORM study evaluating XPOVIO in patients with plasmacytomas; and a summary of new scientific research that identified a genetic model that predicts sensitivity to selinexor.

In addition, Phase 1/2 data evaluating eltanexor, Karyopharm's next generation SINE compound, in patients with higher-risk myelodysplastic syndrome will be presented showing encouraging activity with tolerability. Finally, data from four investigator-sponsored studies including selinexor plus ibrutinib will be featured further showing the potential for SINE technology.

Details for the ASH 2019 presentations are as follows:

Oral Presentation

Title: Selinexor, Pomalidomide, and Dexamethasone (SPd) in Patients with Relapsed or Refractory Multiple Myeloma

Presenter: Christine Chen, Princess Margaret Cancer Centre

Abstract #: 141

Session: 653. Myeloma: Therapy, excluding Transplantation: New Approaches in the Treatment of Relapsed/Refractory Plasma Cell Disorders

Date and Time: Saturday, December 7, 2019; 9:30-11:00 AM ET

Location: Orange County Convention Center, Hall E1

Poster Presentations – Company-Sponsored Studies

Title: Selinexor-Containing Regimens for the Treatment of Patients with Multiple Myeloma Refractory to Chimeric Antigen Receptor T-Cell (CAR-T) Therapy

Presenter: Ajai Chari, Icahn School of Medicine at Mount Sinai

Abstract #: 1854

Session: 653. Myeloma: Therapy, excluding Transplantation: Poster I

Date and Time: Saturday, December 7, 2019; 5:30-7:30 PM ET

Location: Orange County Convention Center, Hall B

Title: Influence of Cytogenetics in Patients with Relapsed Refractory Multiple Myeloma Treated with Oral Selinexor and Dexamethasone: A Post-Hoc Analysis of the STORM Study

Presenter: Ajay Nooka, Winship Cancer Institute, Emory University School of Medicine

Abstract #: 1872

Session: 653. Myeloma: Therapy, excluding Transplantation: Poster I

Date and Time: Saturday, December 7, 2019; 5:30-7:30 PM ET

Location: Orange County Convention Center, Hall B

Title: Safety and Efficacy of the Combination of Selinexor, Lenalidomide and Dexamethasone (SRd) in Patients with Newly Diagnosed Multiple Myeloma

Presenter: Darrell White, Dalhousie University

Abstract #: 3165

Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: A Phase 1b/2 Study of Selinexor, Carfilzomib, and Dexamethasone (SKd) in Relapsed/ Refractory Multiple Myeloma (RRMM)

Presenter: Cristina Gasparetto, Duke University Medical Center

Abstract #: 3157

Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: Response to Therapy and the Effectiveness of Treatment with Selinexor and Dexamethasone in Patients with Penta-Exposed Triple-Class Refractory Myeloma Who Had Plasmacytomas

Presenter: Andrew Yee, Massachusetts General Hospital

Abstract #: 3140

Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: A Machine Learning Approach Identifies a 30-gene Model that Predicts Sensitivity to Selinexor in Multiple Myeloma

Presenter: Alessandro Lagana, Icahn School of Medicine at Mount Sinai

Abstract #: 3101

Session: 652. Myeloma: Pathophysiology and Pre-Clinical Studies, excluding Therapy: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: Eltanexor (KPT-8602), a Second-Generation Selective Inhibitor of Nuclear Export (SINE) Compound, in Patients with Higher-Risk Myelodysplastic Syndrome

Presenter: Sangmin Lee, Weill Cornell School of Medicine

Abstract #: 2997

Session: 637. Myelodysplastic Syndromes—Clinical Studies: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: Overall Survival of Triple Class Refractory, Penta-Exposed Multiple Myeloma (MM) Patients Treated with Selinexor Plus Dexamethasone or Conventional Care: A Combined Analysis of the STORM and Mammoth Studies

Presenter: Luciano Costa, University of Alabama at Birmingham

Abstract #: 3125

Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II

Date and Time: Date: Sunday, December 8, 2019; 6:00 PM - 8:00 PM ET

Location: Orange County Convention Center, Hall B

Poster Presentations – Investigator-Sponsored Studies

Title: Selinexor in Combination with Induction and Consolidation Therapy in Older Adults with AML Is Highly Active

Presenter: Timothy Pardee, Comprehensive Cancer Center, Wake Forest Baptist Health

Abstract #: 1388

Session: 616. Acute Myeloid Leukemia: Novel Therapy, excluding

Date and Time: Saturday, December 7, 2019; 5:30-7:30 PM ET

Location: Orange County Convention Center, Hall B

Title: The Result of a Phase 1 Study of Selinexor in Combination with High-Dose Melphalan and Autologous Hematopoietic Cell Transplantation for Multiple Myeloma

Presenter: Taiga Nishihori, Moffitt Cancer Center

Abstract #: 3314

Session: 731. Clinical Autologous Transplantation: Results: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: Dual Inhibition of MDM2 and XPO1 Synergizes to Induce Apoptosis in Acute Myeloid Leukemia Progenitor Cells with Wild-Type TP53 through Nuclear Accumulation of p53 and Suppression of c-Myc

Presenter: Yuki Nishida, The University of Texas MD Anderson Cancer Center

Abstract #: 2556

Session: 604. Molecular Pharmacology and Drug Resistance in Myeloid Diseases: Poster II

Date and Time: Sunday, December 8, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: Selinexor Combined with Ibrutinib Demonstrates Tolerability and Efficacy in Advanced B-Cell Malignancies: A Phase I Study

Presenter: Deborah Stephens, Huntsman Cancer Institute, University of Utah

Abstract #: 4310

Session: 642. CLL: Therapy, excluding Transplantation: Poster III

Date and Time: Monday, December 9, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

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. In addition to receiving accelerated 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. 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), in recurrent gliomas (KING) 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 thrombocytopenia, leading to potentially fatal hemorrhage. Thrombocytopenia was reported as an adverse reaction in 74% of patients, and severe (Grade 3-4) thrombocytopenia occurred in 61% of patients treated with XPOVIO. The median time to onset of the first event was 22 days. Bleeding occurred in 23% of patients with thrombocytopenia, clinically significant bleeding occurred in 5% of patients with thrombocytopenia and fatal hemorrhage occurred in <1% of patients.

Monitor platelet counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two 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 and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

Neutropenia

XPOVIO can cause neutropenia, potentially increasing the risk of infection. Neutropenia was reported as an adverse reaction in 34% of patients, and severe (Grade 3-4) neutropenia occurred in 21% of patients treated with XPOVIO. The median time to onset of the first event was 25 days. Febrile neutropenia was reported in 3% of patients.

Obtain neutrophil counts at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Monitor patients for signs and symptoms of concomitant infection and evaluate promptly. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF). Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

Gastrointestinal Toxicity

Gastrointestinal toxicities occurred in patients treated with XPOVIO.

Nausea/Vomiting

Nausea was reported as an adverse reaction in 72% of patients, and Grade 3 nausea occurred in 9% of patients treated with XPOVIO. The median time to onset of the first nausea event was 3 days.

Vomiting was reported in 41% of patients, and Grade 3 vomiting occurred in 4% of patients treated with XPOVIO. The median time to onset of the first vomiting event was 5 days.

Provide prophylactic 5-HT3 antagonists and/or other anti-nausea agents, prior to and during treatment with XPOVIO. Manage nausea/vomiting by dose interruption, reduction, and/or discontinuation. Administer intravenous fluids and replace electrolytes to prevent dehydration in patients at risk. Use additional anti-nausea medications as clinically indicated.

Diarrhea

Diarrhea was reported as an adverse reaction in 44% of patients, and Grade 3 diarrhea occurred in 6% of patients treated with XPOVIO. The median time to onset of diarrhea was 15 days.

Manage diarrhea by dose modifications and/or standard anti-diarrheal agents; administer intravenous fluids to prevent dehydration in patients at risk.

Anorexia/Weight Loss

Anorexia was reported as an adverse reaction in 53% of patients, and Grade 3 anorexia occurred in 5% of patients treated with XPOVIO. The median time to onset of anorexia was 8 days.

Weight loss was reported as an adverse reaction in 47% of patients, and Grade 3 weight loss occurred in 1% of patients treated with XPOVIO. The median time to onset of weight loss was 15 days.

Monitor patient weight at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Manage anorexia and weight loss with dose modifications, appetite stimulants, and nutritional support.

Hyponatremia

XPOVIO can cause hyponatremia; 39% of patients treated with XPOVIO experienced hyponatremia, 22% of patients experienced Grade 3 or 4 hyponatremia. The median time to onset of the first event was 8 days.

Monitor sodium level at baseline, during treatment, and as clinically indicated. Monitor more frequently during the first two months of treatment. Correct sodium levels for concurrent hyperglycemia (serum glucose >150 mg/dL) and high serum paraprotein levels. Treat hyponatremia per clinical guidelines (intravenous saline and/or salt tablets), including dietary review. Interrupt and/or reduce dose, or permanently discontinue based on severity of adverse reaction.

Infections

In patients receiving XPOVIO, 52% of patients experienced any grade of infection. Upper respiratory tract infection of any grade occurred in 21%, pneumonia in 13%, and sepsis in 6% of patients. Grade ≥ 3 infections were reported in 25% of patients, and deaths resulting from an infection occurred in 4% of patients. The most commonly reported Grade ≥ 3 infections were pneumonia in 9% of patients, followed by sepsis in 6%. The median time to onset was 54 days for pneumonia and 42 days for sepsis. Most infections were not associated with neutropenia and were caused by non-opportunistic organisms.

Neurological Toxicity

Neurological toxicities occurred in patients treated with XPOVIO.

Neurological adverse reactions including dizziness, syncope, depressed level of consciousness, and mental status changes (including delirium and confusional state) occurred in 30% of patients, and severe events (Grade 3-4) occurred in 9% of patients treated with XPOVIO. Median time to the first event was 15 days.

Optimize hydration status, hemoglobin level, and concomitant medications to avoid exacerbating dizziness or mental status changes.

Embryo-Fetal Toxicity

Based on data from animal studies and its mechanism of action, XPOVIO can cause fetal harm when administered to a pregnant woman. Selinexor administration to pregnant animals during organogenesis resulted in structural abnormalities and alterations to growth at exposures below those occurring clinically at the recommended dose.

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 (incidence $\geq 20\%$) are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.

The treatment discontinuation rate due to adverse reactions was 27%; 53% of patients had a reduction in the XPOVIO dose, and 65.3% had the dose of XPOVIO interrupted. The most frequent adverse reactions requiring permanent discontinuation in 4% or greater of patients who received XPOVIO included fatigue, nausea, and thrombocytopenia. The rate of fatal adverse reactions was 8.9%.

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

About Eltanexor (KPT-8602)

Eltanexor (KPT-8602) is a second generation oral SINE compound. Eltanexor functions by binding to and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. Eltanexor has demonstrated minimal brain penetration in animals, which has been associated with reduced toxicities in preclinical studies while maintaining potent anti-tumor effects.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq: KPTI) is an oncology-focused pharmaceutical company 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 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 FDA in July 2019 in combination with dexamethasone as a treatment for patients with heavily pretreated multiple myeloma. A Marketing Authorization Application for selinexor is also currently under review by the European Medicines Agency (EMA). 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 relating to XPOVIO for the treatment of patients with heavily pretreated multiple myeloma, commercialization of XPOVIO or any of its drug candidates, 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, 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 accelerated or conditional approval in the U.S. or EU, respectively, based on 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 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: 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, 2019, which was filed with the Securities and Exchange Commission (SEC) on November 4, 2019, 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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Kyprolis® is a registered trademark of Onyx Pharmaceuticals, Inc.

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