

# Karyopharm Therapeutics Announces Multiple Presentations on Selective Inhibitors of Nuclear Export (SINE) in Solid and Hematologic Malignancy Models and Spontaneous Canine Cancers at the American Association of Cancer Research (AACR) Meeting

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Karyopharm Therapeutics Inc., a leader in the new field of nuclear transport modulators, announces nine presentations covering its Selective Inhibitors of Nuclear Export (SINE), oral small molecule CRM1 antagonists, at the AACR meeting on March 31 – April 4, 2012, in Chicago. The presentations are being made by academic collaborators studying the use of Karyopharm's novel SINE, along with Karyopharm scientists, for the treatment of prostate, pancreatic, melanoma, colorectal, non-Hodgkin's lymphoma (NHL), and Ph<sup>+</sup> acute leukemias. In addition, in a late breaking abstract, Dr. Cheryl London of Ohio State University will present the use of SINE compounds to treat spontaneous chemotherapy resistant canine lymphomas.

Dr. William Senapedis of Karyopharm will make an oral presentation in Experimental and Molecular Therapeutics Session 25 (Room W185 McCormick Place West Level 1) on Monday April 2, 2012, between 3:00 and 5:00 PM, entitled "KPT-SINE (Selective Inhibitors of Nuclear Export) induce apoptosis in colon cancer cells in vitro and in vivo through nuclear localization of Tumor Suppressor Proteins (TSPs)" (Abstract 2943).

In our first reports of activity in spontaneous chemotherapy-resistant tumors in larger animals, Dr. Cheryl London of Ohio State University will present "Preliminary results of a phase I study of the novel CRM1 inhibitors KPT- 276 and KPT-335 in dogs with spontaneous cancer" on Tuesday, April 3, 2012 in the Poster Section: Late- Breaking Research: Clinical Trials (8:00 AM – 12:00 PM), Hall F (Section 40).

All other poster presentations will take place on Monday, April 2, 2012, 8:00AM-12:00 noon in Hall F, Experimental and Molecular Therapeutics 12.

Drs. Giovanni Gravina and Claudio Festuccia of University of L'aquila, Italy, will present "Selective inhibitors of nuclear export (SINE) activate multiple tumor suppressor pathways and kill prostate cancer cells across multiple genotypes in vitro and in vivo" (Abstract 1841; Section 30).

Drs. Asfar Azmi and Ramzi Mohammed of Wayne State University will present two posters: "CRM-1 as a potential therapeutic target in pancreatic cancer" (Abstract 1815; Section 30) and "Novel small molecule CRM-1 inhibitor for Non Hodgkin's Lymphoma" (Abstract 1825; Section 30).

Drs. Roberto Fragomeni and James Cusack of Massachusetts General Hospital will present "Potent

anticancer activity against both BRAF-mutant and BRAF wild-type melanoma cell lines using a novel CRM1 nuclear export inhibitor” (Abstract 1914; Section 34).

Drs. Christopher Walker and Danilo Perrotti of the Ohio State University will present “Nuclear export (karyopherin) inhibitors: A novel therapeutic strategy for treating Philadelphia-positive (Ph+) acute leukemias” (Abstract 3839; Section 32).

Dr. Dilara McCauley of Karyopharm will present “Selective inhibitors of nuclear export (SINE) induce multiple tumor suppressor proteins (TSP) activity and show single agent antitumor effect and synergy with Bcl-2 antagonist in non-small cell lung cancer” (Abstract 1831; Section 30).

Dr. Yosef Landesman of Karyopharm will present a poster, “Pharmacokinetic (PK) / pharmacodynamic (PDn) and efficacy relationship of selective inhibitors of nuclear export (KPT-SINE)” (Abstract 3775; Section 30).

Karyopharm’s founder and Chief Scientific Officer Dr. Sharon Shacham commented, “We are very pleased to share the results of our continuing collaborative and internal work on the mechanisms of action and anti-tumor activity of SINE compounds in the treatment of a variety of malignant conditions. We are encouraged by their activity in dogs with naturally occurring and chemotherapy refractory tumors, and we are on track to bring our first in class, oral clinical candidate into Phase 1 studies this year.”

About Karyopharm Therapeutics Inc.

Karyopharm is a privately held oncology company headquartered in Natick, Massachusetts, focused on the development of modulators of nuclear transport as novel therapies for cancer, inflammatory and other diseases. Drs. Sharon Shacham, Michael Kauffman, Ronald DePinho, and Giulio Draetta founded the company in 2009. The nuclear transport machinery plays an integral role in the regulation of many molecules involved in a broad spectrum of human and animal disease, and drug discovery has been enhanced with the recent determination of the 3-dimensional structure of the nuclear pore complex. Karyopharm is developing novel selective inhibitors of nuclear export (SINE) for the treatment of cancer, autoimmune diseases and HIV. These SINEs act by forcing the nuclear localization of key tumor suppressor and growth regulatory proteins causing the selective death of cancer cells while sparing normal cells. The Karyopharm platform, utilizing rapid chemical optimization with integrated computational/in silico rational drug design, has yielded multiple novel active small molecule SINEs, which have shown potent activity in animal models of cancer. Additional programs focused on other aspects of nuclear export, as well as nuclear import, have been initiated.

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