

Karyopharm Presents Updated Selinexor Phase 1b/2 STOMP Myeloma Data from Multiple Combinations at the European Hematology Association 2018 Annual Meeting

-- Svd Once Weekly Demonstrates 17.8-month PFS and 83% ORR in the BOSTON Multiple Myeloma (MM) Population; 63% ORR in the Overall Study Population --

-- SDd Once Weekly Shows 82% ORR in Patients with Heavily Pretreated Darzalex-Naïve MM; 68% ORR in the Overall Study Population --

-- SPd All Oral Regimen Shows Strong Response Rates: 55% ORR in Pomalyst-Naïve and Revlimid-Relapsed or -Refractory MM with PFS of 11.6 months; 50% ORR in the Overall Study Population --

-- Initiated New STOMP Arm Evaluating All Oral Regimen of Selinexor, Revlimid and Dexamethasone (SRd) in Patients with Newly Diagnosed MM --

NEWTON, Mass., June 15, 2018 (GLOBE NEWSWIRE) -- Karyopharm Therapeutics Inc. (Nasdaq:KPTI), a clinical-stage pharmaceutical company, today announced that three posters highlighting clinical data from the ongoing Phase 1b/2 STOMP study in patients with multiple myeloma (MM) will be presented at the European Hematology Association (EHA) 2018 Annual Meeting taking place June 14-17, 2018 in Stockholm, Sweden. These three poster presentations will feature updated data from the STOMP arms evaluating selinexor, the Company's lead, novel, oral SINE compound, and dexamethasone in combination with standard approved therapies, Velcade® (bortezomib), Pomalyst® (pomalidomide) or Darzalex® (daratumumab), in patients with previously treated MM.

"The Phase 1b/2 STOMP study continues to generate important efficacy and safety data from the multiple ongoing arms evaluating selinexor and dexamethasone (dex) in combination with the standard approved therapies Velcade, Pomalyst and Darzalex in patients with multiple myeloma following at least one prior therapy," said Sharon Shacham, PhD, MBA, President and Chief Scientific Officer of Karyopharm. "Based on the positive STOMP results reported to date, we have initiated a new all-oral STOMP arm to investigate selinexor plus Revlimid® and dex in the front-line setting. Given the observed synergistic activity of selinexor with standard approved myeloma therapies, we believe oral selinexor has the potential to be a future backbone therapy in myeloma, and we look forward to elucidating its activity as part of a front-line treatment regimen."

Selinexor in Combination with Velcade and Low-dose Dexamethasone (SVd)

In the poster presentation titled, "[Selinexor combined with low dose bortezomib and dexamethasone \(SVd\) induces a high response rate in patients with relapsed or refractory multiple myeloma \(MM\)](#)," (Abstract code PS1322) Nizar Bahlis, MD, Southern Alberta Cancer Research Institute, will present updated clinical data from the SVd arm of the STOMP study. This study includes patients whose disease was proteasome inhibitor (PI) naïve, exposed or refractory, provided their disease was not refractory to Velcade as a last therapy. In this study arm, oral selinexor was dose-escalated in once-weekly (80 or 100mg) or twice-weekly (60 or 80mg) regimens. Velcade (1.3mg/m² subcutaneously) was administered once-weekly or twice-weekly. Dex was administered orally either 40mg once-weekly or 20mg twice-weekly. The following table is a summary of the efficacy results:

Best Responses¹ in Evaluable SVd Patients as of 5-Jun-2018²

Category	N3	ORR (%)	sCR	CR	VGPR	PR4	Median PFS
PI Relapsed/Naïve	19	16 (84%)	1 (5%)	3 (16%)	3 (16%)	9 (47%)	17.8 months
PI Refractory	21	9 (43%)	-	1 (5%)	4 (19%)	4 (19%)	6.1 months
All	40	25 (63%)	1 (3%)	4 (10%)	7 (18%)	13 (33%)	9.2 months
PI Relapse/Naïve, ≤3 Prior Treatments 5	18	15 (83%)	1 (6%)	3 (17%)	4 (22%)	7 (39%)	17.8 months

Key: ORR=Overall Response Rate (sCR+CR+VGPR+PR), sCR=Stringent Complete Response, CR=Complete Response, VGPR=Very Good Partial Response, PR=Partial Response

1Responses were adjudicated according to the International Myeloma Working Group criteria

2Based on interim unaudited data

3Two patients not evaluable for response: one death unrelated to myeloma and one withdrawal of consent before disease follow up

4One unconfirmed PR

5Patient population eligible for the ongoing Phase 3, randomized BOSTON study evaluating SVd versus Vd. This a subset of the PI Relapsed/Naïve, ≤3 Prior Treatments

In the PI Relapsed/Naïve population (N=19), the ORR was 84% and the median PFS was 17.8 months with similar results in the "BOSTON" population (N=18). Nearly all patients (38 of 40) had reductions in M-protein, including 33% with a ≥90% reduction. This indication of efficacy in the SVd combination, with weekly Velcade and selinexor, warranted the further evaluation of SVd versus Vd in the BOSTON study given the previously reported ORR of 60-65% and PFS of 7-9 months in the Vd regimen among similar patient populations.

Among the 42 patients evaluable for safety, adverse events were consistent with those reported previously from the SVd arm of the STOMP study, with nausea (60%), anorexia (57%), fatigue (45%), diarrhea (40%), vomiting (29%) and weight loss (24%) the most commonly reported Grade 1/2 events. Importantly, the reported peripheral neuropathy across all patients was Grade 1/2 and limited to six patients (14%), of which five had prior Velcade exposure. Grade 3/4 adverse events were also consistent with those reported previously with thrombocytopenia (45%), neutropenia (26%), fatigue (14%) and anemia (12%) being the most common. Based on the activity and tolerability observed in this study arm, the recommended Phase 2 dose (RP2D) regimen for SVd is oral selinexor (100mg once weekly), Velcade (1.3mg/m² once-weekly subcutaneously) and oral dex (40mg weekly), which represents 40% less Velcade and 25% less dex compared to the approved standard Velcade + dex (Vd) regimen. This once weekly regimen is being evaluated in BOSTON.

Dr. Bahlis commented, "These updated data from the SVd arm of the STOMP study continue to show rapid time to response, high response rates, including an 83% ORR and the emergence of complete responses, along with a 17.8-month median PFS, in patients with relapsed or refractory myeloma. The combination also continues to be well tolerated with low rates of peripheral neuropathy. Importantly, these results are being achieved with 40% less Velcade and 25% less dex than the standard approved regimen, with no overt major organ toxicities."

Selinexor in Combination with Darzalex and Low-dose Dexamethasone (SDd)

In the poster presentation titled, "[A Phase 1b study using the combination of selinexor, daratumumab, and dexamethasone in multiple myeloma patients previously exposed to proteasome inhibitors and immunomodulatory drugs](#)," (Abstract code PS1329) Cristina Gasparetto, MD, Duke University Cancer Center, will present new clinical data from the SDd arm of the STOMP study evaluating myeloma patients who received at least three prior lines of therapy, including a PI and an immunomodulatory drug (IMiD), or patients with myeloma refractory to both a PI and an IMiD. In this study arm, oral selinexor was dose escalated using either 100mg once weekly or 60mg twice weekly, with Darzalex (16mg/kg intravenously once weekly) and dex (orally, 40mg once weekly or 20mg twice weekly).

weekly).

The following table is a summary of the efficacy results:

Best Responses¹ in Evaluable SDd Patients as of 5-Jun-2018²

Category	N3	ORR	VGPR	PR4
Darzalex Naïve	17	14 (82%)	5 (29%)	9 (53%)
All	19	14 (74%)	5 (26%)	9 (47%)

Key: ORR=Overall Response Rate (VGPR+PR)

¹Responses were adjudicated according to the International Myeloma Working Group criteria

²Based on interim unaudited data

³One patient not evaluable for response withdrew consent prior to disease follow up, one patient pending response

⁴ Three unconfirmed PR

Despite the heavily pretreated nature of the patients in the study, with 100% of the patients having dual- (PI and IMiD-) refractory disease, responses occurred rapidly, with a median of one month to onset; 12 of the 19 patients remain on treatment. Based on published data the expected ORR for Darzalex therapy without selinexor in the Darzalex-naïve population is ~30%. Thus, the ORR of 82% provides a basis for further evaluation of the weekly SDd combination.

Among the 21 patients evaluable for safety, the most common Grade 1/2 adverse events were nausea (48%), fatigue (38%), diarrhea (24%), constipation (24%), and anorexia (24%). The most common Grade 3/4 adverse events were thrombocytopenia (48%), leukopenia (43%), anemia (33%), neutropenia (33%) and decreased lymphocyte count (24%). Gastrointestinal adverse events were generally manageable with supportive care. The maximum tolerated dose was not reached. Two DLTs (Grade 3 thrombocytopenia and Grade 2 fatigue) were observed in patients receiving selinexor 60mg twice weekly; both patients showed responses. Based on the preliminary tolerability and efficacy data, the RP2D of SDd is selinexor (100mg orally, once weekly), Darzalex (16mg/kg, once weekly) and dex (40mg orally, weekly).

Dr. Gasparetto commented, "These preliminary results from the SDd arm of the STOMP study show high response rates, including an 82% ORR in Darzalex-naïve patients with refractory myeloma. This combination regimen appears to be well tolerated with responses observed rapidly occurring within a median one cycle of treatment. We look forward to continuing enrollment in this treatment arm."

Selinexor in Combination with Pomalyst and Low-dose Dexamethasone (SPd)

In the poster presentation titled, "[Selinexor combined with pomalidomide and low dose dexamethasone \(SPd\) in a relapsed/refractory multiple myeloma patient population](#)," (Abstract code PF586) Christine Chen, MD, FRCP, University of Toronto, Princess Margaret Cancer Center, will present updated clinical data from the SPd arm of the STOMP study which includes patients with multiple myeloma who previously received Revlimid and a PI. In this study arm, selinexor was dosed orally either once weekly (80 or 100mg) or twice weekly (60 or 80mg) with Pomalyst (3 or 4mg orally, once daily) and dexamethasone (dex; orally, 40mg once weekly or 20mg twice weekly). The following table is a summary of the efficacy results:

Best Responses¹ in Evaluable SPd Patients as of 5-Jun-2018²

Category	N3	ORR (%)	VGPR	PR4	Median PFS
Pomalyst Naïve and Revlimid Refractory or Relapsed	22	12 (55%)	3 (14%)	9 (41%)	11.6 months
Pomalyst and Revlimid Refractory	8	3 (38%)	-	3 (38%)	4.8 months
All	30	15 (50%)	3 (10%)	12 (40%)	10.3 months

Key: ORR=Overall Response Rate (VGPR+PR)

¹Responses were adjudicated according to the International Myeloma Working Group criteria

²Based on interim unaudited data

³Four patients not evaluable for response: one death unrelated to myeloma, one non-compliance with study procedures, two withdrawal of consent before disease follow up

⁴One unconfirmed PR

Responses tended to occur rapidly with a median of one month to onset. Median PFS among all evaluable patients was 10.3 months, with a follow up of 9.4 months. The efficacy of the SPd combination warrants further clinical evaluation.

Among the 34 patients evaluable for safety, the most common Grade 1/2 adverse events were anorexia (56%), nausea (47%), fatigue (41%), weight loss (38%), diarrhea (26%) and thrombocytopenia (26%). The most common Grade ≥3 adverse events were neutropenia (56%), thrombocytopenia (32%) and anemia (29%). Gastrointestinal adverse events were generally manageable with supportive care. There were two Grade 5 treatment-related events (febrile neutropenia and intracranial hemorrhage). Six DLTs (Grade 3 fatigue, febrile neutropenia, hyponatremia, neutropenia and thrombocytopenia) were observed in patients receiving selinexor 60mg twice weekly, 80mg twice weekly and 80mg once weekly. Based on the activity and tolerability observed in this study arm, doses of oral selinexor 60-80mg once weekly are being evaluated in combination with Pomalyst (3mg orally, once daily) and low dose dex to determine the RP2D for this combination regimen.

Dr. Chen stated, "This novel, all oral regimen continues to demonstrate strong response rates, including a 55% ORR, along with an 11.6-month median PFS, in Pomalyst-naïve and Revlimid-relapsed or -refractory patients. In this STOMP arm, once-weekly selinexor has been generally well tolerated and rapidly induced durable responses in patients with PI- and Revlimid-exposed myeloma."

Details for the EHA 2018 presentations are as follows:

Company-sponsored Trials

Title: Selinexor combined with low dose bortezomib and dexamethasone (SVd) induces a high response rate in patients with relapsed or refractory multiple myeloma (MM)

Lead author: Nizar Bahlis, Southern Alberta Cancer Research Institute

Final Abstract Code: PS1322

Topic/Session Title: Myeloma and other monoclonal gammopathies – Clinical

Date and Time: Saturday, June 16, 2018; 17:30 – 19:00 CEST

Location: Poster area

Title: A Phase 1b study using the combination of selinexor, daratumumab, and dexamethasone in multiple myeloma patients previously exposed to proteasome inhibitors and immunomodulatory drugs
Lead author: Cristina Gasparetto, Duke University
Final Abstract Code: PS1329
Topic/Session Title: Myeloma and other monoclonal gammopathies – Clinical
Date and Time: Saturday, June 16, 2018; 17:30 – 19:00 CEST
Location: Poster area

Title: Selinexor combined with pomalidomide and low dose dexamethasone (SPd) in a relapsed/refractory multiple myeloma patient population
Presenter: Christine Chen, University of Toronto, Princess Margaret Cancer Center
Final Abstract Code: PF586
Topic/Session Title: Myeloma and other monoclonal gammopathies – Clinical
Date and Time: Friday, June 15, 2018; 17:30 – 19:00 CEST
Location: Poster area

Investigator-sponsored Trials

Title: A Phase II study of selinexor (KPT-330) combined with bortezomib and dexamethasone (SVD) for induction and consolidation for patients with progressive or refractory multiple myeloma; the selvedex trial
Lead author: Annemiek Broijl, Erasmus MC Cancer Institute
Final Abstract Code: PS1338
Topic/Session Title: Myeloma and other monoclonal gammopathies – Clinical
Date and Time: Saturday, June 16, 2018; 17:30 – 19:00 CEST
Location: Poster area

About Selinexor

Selinexor (KPT-330) is a first-in-class, oral Selective Inhibitor of Nuclear Export / SINE compound. Selinexor functions by binding with and inhibiting the nuclear export protein XPO1 (also called CRM1), leading to the accumulation of tumor suppressor proteins in the cell nucleus. This reinitiates and amplifies their tumor suppressor function and is believed to lead to the selective induction of apoptosis in cancer cells, while largely sparing normal cells. To date, over 2,400 patients have been treated with selinexor. In April 2018, Karyopharm reported positive top-line data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with penta-refractory multiple myeloma. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation by the U.S. Food and Drug Administration (FDA) for the patient population evaluated in the STORM study. Karyopharm plans to submit a New Drug Application (NDA) to the FDA during the second half of 2018, with a request for accelerated approval for oral selinexor as a new treatment for patients with penta-refractory multiple myeloma. The Company also plans to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in early 2019 with a request for conditional approval. 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) and as a potential backbone therapy in combination with approved therapies (STOMP), and in diffuse large B-cell lymphoma (SADAL), liposarcoma (SEAL), and an investigator-sponsored study 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 one or more 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.

About Karyopharm Therapeutics

Karyopharm Therapeutics Inc. (Nasdaq:KPTI) is a clinical-stage pharmaceutical company focused on the discovery and development of novel first-in-class drugs directed against nuclear transport 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). 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, which was founded by Dr. Sharon Shacham, currently 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 timing of submissions to regulatory authorities and the potential availability of accelerated approval pathways, 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 that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that any of Karyopharm's drug candidates, including selinexor, will successfully complete necessary clinical development phases, that development of any of Karyopharm's drug candidates will continue or that any feedback from regulatory authorities will ultimately lead to the approval of selinexor or any of Karyopharm's other drug candidates. Further, there can be no guarantee that any positive developments in 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: 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; 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 March 31, 2018, which was filed with the Securities and Exchange Commission (SEC) on May 10, 2018, 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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Revlimid® and Pomalyst® are registered trademarks of Celgene Corporation.
Darzalex® is a registered trademark of Janssen Biotech, Inc.

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