Karyopharm Reports New and Updated Selinexor Combination Data from the Phase 1b/2 STOMP Study at the European Hematology Association 2019 Annual Meeting

In this arm of the Phase 1b/2 STOMP study, oral selinexor (dosed once weekly) is being evaluated in combination with Kyprolis (56mg/m² or 70mg/m² once weekly) and low dose dexamethasone (orally, 40mg once weekly or 20mg twice weekly) in patients with relapsed refractory MM who have received at least two prior therapies, which can include previous treatment with a proteasome inhibitor (PI), one or more immunomodulatory drugs (IMiDs: Revlimid, Pomalyst) or Darzalex. All patients on the study had previously received both PIs and IMiDs. The following table is a summary of the efficacy results:

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>ORR</th>
<th>CR</th>
<th>VGPR</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (Kyprolis-naive)</td>
<td>9</td>
<td>7 (78%)</td>
<td>2 (22%)</td>
<td>5 (56%)</td>
<td>2 (22%)</td>
</tr>
</tbody>
</table>

Key: ORR=Overall Response Rate (CR+VGPR+PR); SD= Stable Disease
1 Responses were adjudicated according to the International Myeloma Working Group criteria
2 Based on interim unaudited data

Among the 9 patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (67%), fatigue (44%), hyperglycemia (44%), anorexia (33%) and vomiting (33%), and were mostly Grade 1 and 2 events. As expected, the most common treatment-related Grade 3 and 4 AEs were hematologic AEs and included thrombocytopenia (78%), leukopenia (33%), anemia (22%) and neutropenia (22%). Dose limiting toxicities, including Grades 3 and 4 thrombocytopenia, Grade 3 pneumonia and Grade 3 vomiting, were observed in patients receiving selinexor 80mg and Kyprolis 70mg/m² and selinexor 100mg and Kyprolis 56mg/m². No DLTs were reported in the selinexor 80mg and Kyprolis 56mg/m² cohort, and therefore, confirmation of the recommended Phase 2 dose (RP2D) is ongoing with this dosing regimen.

Updates on Phase 1b/2 STOMP Study: SDD and SPd

Selinexor plus Darzalex and Low-dose Dexamethasone (SDD)

In this arm of the Phase 1b/2 STOMP study, oral selinexor (dose escalated using either 100mg once weekly or 60mg twice weekly) is being evaluated in combination with Darzalex (16mg/kg intravenously once weekly) and low dose dexamethasone (dexamethasone (dex, orally, 40mg once weekly or 20mg twice weekly) in patients with relapsed or refractory MM who received at least three prior lines of therapy, including a PI and an IMiD, or patients with MM refractory to both a PI and an IMiD. The following table is a summary of the updated efficacy results:

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>ORR</th>
<th>VGPR</th>
<th>PR4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darzalex naive</td>
<td>30</td>
<td>22 (73%)</td>
<td>11 (37%)</td>
<td>11 (37%)</td>
</tr>
<tr>
<td>All</td>
<td>32</td>
<td>22 (69%)</td>
<td>11 (34%)</td>
<td>11 (34%)</td>
</tr>
</tbody>
</table>

Key: ORR=Overall Response Rate (VGPR+PR); PR= Partial Response
1 Responses were adjudicated according to the International Myeloma Working Group criteria
2 Based on interim unaudited data
3 Two patients were not evaluable for response as they withdrew consent prior to disease follow up
4 Two unconfirmed PRs

Despite the heavily pretreated nature of the patients in the study, with 100% of the patients having dual- (PI and IMID)-refractory disease, only one patient (3%) did not have at least a minimal response. Median progression-free survival (PFS) has not been reached. Among patients with at least a PR, the median time on treatment was 7.7 months, while the median time on study for all evaluable patients was 4.8 months. Median time to response was 1.0 month. Based on published data, the expected ORR for Darzalex therapy without selinexor in the Darzalex-naive population is ~29%. Thus, the ORR of 73% continues to provide a basis for further evaluation of the SDD combination.

Among the 31 patients evaluated for safety as of the data cutoff date, the most common treatment-related AEs were cytopenias, along with gastrointestinal and constitutional symptoms; most were manageable with dose modifications and/or standard supportive care. The most common non-hematologic treatment-related AEs were nausea (67%), fatigue (44%), anorexia (33%) and vomiting (33%), and were mostly Grade 1 and 2 events. As expected, the most common treatment-related Grade 3 and 4 AEs were hematologic AEs and included thrombocytopenia (78%), leukopenia (33%), anemia (22%) and neutropenia (22%). Dose limiting toxicities, including Grades 3 and 4 thrombocytopenia, Grade 3 pneumonia and Grade 3 vomiting, were observed in patients receiving selinexor 80mg and Kyprolis 70mg/m² and selinexor 100mg and Kyprolis 56mg/m². No DLTs were reported in the selinexor 80mg and Kyprolis 56mg/m² cohort, and therefore, confirmation of the recommended Phase 2 dose (RP2D) is ongoing with this dosing regimen.
Selinexor 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.

About Selinexor

Note: As reported previously by Karyopharm in 2017, this study did not meet its pre-specified primary endpoint.

Location: Poster Area
Date and Time: Friday, June 14, 2019
Session: Acute myeloid leukemia – Clinical
Abstract #: PF261
Lead author: Kendra Sweet
Title: A Randomized, Open-Label, Phase II Study of Selinexor Versus Physician’s Choice (PC) In Older Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

Additional selinexor presentations at EHA 2019 are as follows:

Poster Presentations

Title: Safety and Efficacy of combination of Selinexor, Daratumumab, and Dexamethasone (SDd) in Patients with Multiple Myeloma (MM) Previously Exposed to Proteasome Inhibitors and Immunomodulatory Drugs
Lead author:Cristina Gasparetto, Duke University Cancer Center
Abstract #: S1606
Session: Myeloma and other monoclonal gammopathies – Clinical
Date and Time:Sunday, June 16, 2019; 09:00 – 09:15 CEST
Location: Auditorium

Additional selinexor presentations at EHA 2019 are as follows:

Title: A Phase 1b/2 Study of Selinexor Plus Cytarabine and Idarubicin in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)
Lead author: Walter Fiedler, Hubertus Wald University Cancer Center Hamburg
Abstract #: S880
Session: Acute myeloid leukemia – Clinical
Date and Time:Saturday, June 15, 2019; 17:00 – 17:15 CEST
Location: Elicium 2

Note: As reported previously by Karyopharm in 2017, this study did not meet its pre-specified primary endpoint.

About Selinexor

Selinexor 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. In 2018, Karyopharm reported positive data from the Phase 2b STORM study evaluating selinexor in combination with low-dose dexamethasone in patients with triple class refractory multiple myeloma who have been previously exposed to all five of the most commonly prescribed anti-myeloma therapies currently available. Selinexor has been granted Orphan Drug Designation in multiple myeloma and Fast Track designation for the patient population evaluated in the STORM study. Karyopharm's New Drug Application (NDA) seeking accelerated approval has been accepted for filing and granted Priority Review by the FDA, and oral selinexor is currently under review by the FDA as a possible new treatment for patients based on data from the STORM study. The Company has also submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) with a request for conditional approval. 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), 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 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 our expectations relating to 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, the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor, and the plans for commercialization. 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 regulators will agree that selinexor qualifies for accelerated approval in the U.S. or conditional approval in the E.U. as a result of our clinical data, including the data from the STORM study or 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 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, 2019, which was filed with the Securities and Exchange Commission (SEC) on May 9, 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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Darzalex® is a registered trademark of Janssen Biotech, Inc.

Contacts:

Investors:
Karyopharm Therapeutics Inc.
Ian Karp, Vice President, Investor and Public Relations
857-297-2241 | ikarp@karyopharm.com

Media:
Argot Partners
David Rosen
212-600-1902 | david.rosen@argotpartners.com

Source: Karyopharm Therapeutics Inc.