FDA Approval of XPOVIO® (Selinexor) as a Treatment for Patients with Multiple Myeloma After At Least One Prior Therapy

December 18, 2020
On Today’s Call

**Prepared Remarks**
- Ian Karp, MBA, Senior Vice President, Investor and Public Relations
- Michael G. Kauffman, MD, PhD, Chief Executive Officer
- John Demaree, MBA, Chief Commercial Officer

**Joining for Q&A Session**
- Sharon Shacham, PhD, MBA, President and Chief Scientific Officer
- Mike Mason, MBA, Chief Financial Officer
This presentation 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 and plans relating to XPOVIO for the treatment of patients with relapsed or refractory multiple myeloma or relapsed or refractory diffuse large B-cell lymphoma; commercialization of XPOVIO or any of its drug candidates and the commercial performance of XPOVIO; submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the Company's regulatory strategy, the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities and the potential availability of accelerated approval pathways; the expected design of the Company's clinical trials; 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 confirmatory approval in the E.U. based on the BOSTON study in patients with multiple myeloma 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: 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 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 indications 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, 2020, which was filed with the Securities and Exchange Commission (SEC) on November 2, 2020, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this presentation 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. Karyopharm regularly uses its website to post information regarding its business, drug development programs and governance. Karyopharm encourages investors to use www.karyopharm.com, particularly the information in the section entitled "Investors," as a source of information about Karyopharm. References to www.karyopharm.com in this presentation are not intended to, nor shall they be deemed to, incorporate information on www.karyopharm.com into this presentation by reference. Other than the accelerated approval of XPOVIO, selinexor, eltanexor, KPT-9274 and verdinexor are investigational drugs that have not been approved by the FDA or any other regulatory agency, and the safety and efficacy of these drugs has not been established by any agency.

XPOVIO® (selinexor) is a registered trademark of Karyopharm Therapeutics Inc. Any other trademarks referred to in this presentation are the property of their respective owners. All rights reserved.
XPOVIO® (selinexor) Now Approved In Significantly Expanded Multiple Myeloma (MM) Patient Population

Now approved for adult patients with multiple myeloma as early as first relapse

XPOVIO is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Full Prescribing Information and Medication Guide available at www.XPOVIO.com

XPOVIO (selinexor) package insert

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Safety Highlights from the XPOVIO Prescribing Information\(^1\)

- No Black Box Warnings
- No Contraindications
- Patient Medication Guide

Monitoring Instructions and Recommended Concomitant Treatments
- Monitor complete blood count (CBC) with differential, standard blood chemistries, body weight, nutritional status, and volume status at baseline and during treatment as clinically indicated. Monitor more frequently during the first three months of treatment.
- Patients advised to maintain adequate fluid and caloric intake throughout treatment. Consider intravenous hydration for patients at risk of dehydration.
- Provide prophylactic antiemetics. Administer a 5-HT3 receptor antagonist and other anti-nausea agents prior to and during treatment with XPOVIO.
- Recommended XPOVIO dosage reductions and dosage modifications for adverse reactions are included in the Prescribing Information.

Warnings and Precautions
- Thrombocytopenia
- Neutropenia
- Gastrointestinal Toxicity
- Hyponatremia
- Serious Infection
- Neurological Toxicity
- Embryo-Fetal Toxicity
- Cataract

\(^1\) XPOVIO (selinexor) package insert

Full Prescribing Information and Medication Guide available at www.XPOVIO.com
Approximately 33,000 MM Patients Treated in the 2\textsuperscript{nd} and 3\textsuperscript{rd} Line Settings and 6,000 in the 4\textsuperscript{th} Line+ Setting Where XPOVIO is Now Approved for Use

2020 U.S. MM Epidemiology

~32,000
(>95\% treated)

1L

~2,4\% YoY growth

20,600

2L

~2,4\% YoY growth

12,400

3L

~2,4\% YoY growth

6,200

4L+

~4,3\% YoY growth

~130K total prevalence
~60,000 patients not on treatment / in long-term remission

Sources: Decision Resources used for growth rates for treated patients and overall prevalence; Kantar Cancer Impact; SEER; Cancer Facts and Figures 2020
Study Design and Clinical Data from BOSTON Study Helps Position XPOVIO for Future Expanded Use

Select Differences Between the STORM and BOSTON Studies
Evaluating XPOVIO in Patients with Multiple Myeloma

<table>
<thead>
<tr>
<th>Study</th>
<th>Median # of Prior Therapies</th>
<th>XPOVIO DOSE FREQUENCY</th>
<th>Overall Response Rate (ORR)</th>
<th>Median Progression Free Survival (in months)</th>
<th>Mean Duration of Treatment (in months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STORM(^{1,2})</td>
<td>8</td>
<td>Twice per week</td>
<td>25%</td>
<td>3.7</td>
<td>3</td>
</tr>
<tr>
<td>(Penta-Refractory)</td>
<td></td>
<td>(in combination with dexamethasone)</td>
<td></td>
<td></td>
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<tr>
<td>BOSTON Study(^3)</td>
<td>2</td>
<td>Once per week</td>
<td>76%</td>
<td>13.9</td>
<td>10</td>
</tr>
<tr>
<td>(1–3 Prior Therapies)</td>
<td></td>
<td>(in combination with once-weekly Velcade(^{®}) and dexamethasone)</td>
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1 STORM study provided the basis for XPOVIO’s approved indication in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least 4 prior therapies and whose disease is refractory to at least 2 proteasome inhibitors (PI), at least 2 immunomodulatory agents (IMiD), and an anti-CD38 monoclonal antibody (mAb). 2 XPOVIO Prescribing Information and Chari et al., NEJM. August 2019. 3 Grosicki S, et al. Lancet. 2020.
Once-weekly, oral XPOVIO + Vd delivered an early and sustained PFS advantage versus twice-weekly Vd\(^1\)

Kaplan-Meier Curve for progression-free survival (PFS)\(^{1,a}\)

Time (months)

<table>
<thead>
<tr>
<th>Probability of progression-free survival</th>
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<tbody>
<tr>
<td>1.00</td>
</tr>
<tr>
<td>0.75</td>
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<tr>
<td>0.50</td>
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<tr>
<td>0.25</td>
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</tbody>
</table>

- Selinexor, bortezomib, and dexamethasone: median 13.9 months (95% CI, 11.7, not reached)
- Bortezomib and dexamethasone: median 9.5 months (95% CI, 7.6, 10.8)

Hazard ratio (HR) is based on stratified Cox's proportional hazard regression modeling, p-value based on stratified log-rank test.

\(^a\) According to the International Myeloma Working Group [IMG Uniform Response Criteria for Multiple Myeloma], as assessed by an Independent Review Committee (IRC). XVd=XPOVIO\(^6\) with Velcade\(^8\) (bortezomib) and dexamethasone and Vd=Velcade\(^8\) and dexamethasone.

30% reduction in risk of progression or death\(^1\)

Hazard ratio: 0.70 (96% CI 0.5-0.93), \(p=0.0075\)

\(^1\) XPOVIO (selinexor) package insert

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Responses Were Longer and Deeper on XVd Compared to Vd

Responses observed with oral, once-weekly XPOVIO + Vd were rapid and durable versus twice-weekly Vd:\(^1\)

- **Median time to response**: 1.4 months (once-weekly XPOVIO + Vd) vs 1.6 months (twice-weekly Vd)
- **Median duration of response**: 20.3 months (once-weekly XPOVIO + Vd) vs 12.9 months (twice-weekly Vd)

Depth of response observed with once-weekly XPOVIO + Vd was significant versus twice-weekly Vd (\(p=0.0082\)):\(^1\)

- **Once-weekly XPOVIO + Vd**: ORR: 76.4%
  - PR: 32%
  - VGPR: 28%
  - sCR + CR: 17%

- **Twice-weekly Vd**: ORR: 62.3%
  - PR: 30%
  - VGPR: 22%
  - sCR + CR: 10%

\(^1\) XPOVIO (selinexor) package insert. \(^2\) Grosicki et al. The Lancet. 2020.
Adverse Reactions\textsuperscript{1}

- The most common adverse reactions (≥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 (≥10%) are thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia

\textsuperscript{1} XPOVIO (selinexor) package insert

Full Prescribing Information and Medication Guide available at www.XPOVIO.com
Key Messaging for Expanded Indication in Multiple Myeloma

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<tr>
<th>Unmet Need</th>
<th>In MM, treating with different mechanisms as early as possible may be vital for success</th>
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<tr>
<td>Efficacy &amp; Duration</td>
<td>Weekly XPOVIO + Vd conferred a <strong>rapid and sustained PFS benefit</strong>. And patients achieved a <em>clinically significant durable response</em> with once-weekly XPOVIO + Vd regardless of cytogenetics, renal impairment, or prior therapeutic exposure</td>
</tr>
</tbody>
</table>
| Mechanism of Action | XPOVIO is the first and only FDA-approved oral XPO1 inhibitor that *gets to the cell’s nucleus which leads to cell cycle arrest and apoptosis* in cancer cells  
  - First new mechanism approved since 2016 for the treatment of MM in patients who received at least 1 prior therapy  
  - XPOVIO has a strong synergistic effect with proteasome inhibitors, leading to cancer cell death |
| Dosing | The **oral, once-weekly** XPOVIO + once-weekly Vd combination offers a high-efficacy regimen while potentially reducing the burden for in-office Velcade® treatment |
| Safety | XPOVIO + Vd offers a **manageable safety profile** for a broad range of patients |
Specific Patient Types that Physicians May Find Particularly Appealing for the XPOVIO + Vd Regimen in the 2nd Line+ Settings

• Received Revlimid® and Darzalex® in the front-line setting and are Velcade®-naïve following first relapse
• Received only a short course of Velcade® in the front-line setting prior to stem cell transplant
• Have high-risk disease and/or cytogenetic abnormalities
• Have renal dysfunction
• Prefer a once weekly oral drug and once-weekly injection rather than IV infusions or more frequent visits to the clinic
• Might benefit from a drug with a completely novel mechanism of action, synergistic with a proteasome inhibitor