Phase 3 BOSTON Study Top-Line Results

March 2, 2020
On Today’s Call

Prepared Remarks

- Ian Karp, MBA, *Vice President, Investor and Public Relations*
- Michael G. Kauffman, MD, PhD, *Chief Executive Officer*

Q&A Session

- Christopher Primiano, JD, MBA, *Chief Business Officer & General Counsel*
- Mike Mason, MBA, *Chief Financial Officer*
- Perry Monaco, *Senior Vice President, Sales*
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Such forward-looking statements include those regarding Karyopharm’s expectations relating to XPOVIO® for the treatment of patients with heavily pretreated multiple myeloma; the therapeutic potential of and potential clinical development plans and commercialization for Karyopharm’s drug candidates, including the timing of initiation of certain trials, of the reporting of data from such trials, of the submissions to regulatory authorities and of potential commercial launches; the potential availability of accelerated approval pathways; the potential size of the markets for multiple myeloma drugs and multiple myeloma drugs for treatment of patients with relapsed multiple myeloma; the potential size of the markets for diffuse large B-cell lymphoma (DLBCL) drugs and DLBCL drugs for treatment of patients with relapsed and/or refractory DLBCL; and Karyopharm’s strategic and financial plans and expectations, as well as financial projections for Karyopharm. 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Multiple Myeloma Remains an Incurable Disease Where Patients are in Need of New Treatment Options

Multiple Myeloma is the 2nd most common cancer of the blood

~32,000 annual new cases
~130,000 patients living with the disease

The median age at diagnosis is 69

~13,000 deaths expected

Background on the Treatment of Multiple Myeloma (MM)

• Main classes of MM drugs used across lines of therapy include:
  ─ Proteasome inhibitors (PIs): Velcade®, Kyprolis®
  ─ Immunomodulatory agents (IMiDs): Revlimid®, Pomylast®
  ─ Monoclonal antibodies (mAbs): Darzalex®, Empliciti®
  ─ Nuclear export inhibitor: XPOVIO® (selinexor) is the only drug in this class and is currently approved in heavily pretreated patients

• Drugs with proven single-agent clinical activity are generally preferred by physicians, even when used in 2-4 drug-combination regimens
  ─ Single agent (± steroids) activity: Revlimid, Pomalyst, Darzalex, Velcade, Kyprolis, XPOVIO
  ─ Used in combination: Alkylators, Glucocorticoids, Empliciti

• Velcade (bortezomib), a proteasome inhibitor, is a well-established treatment for patients in early and late lines of treatment, typically in combination with dexamethasone and either an IMiD or mAb

• Standard Velcade therapy is dosed twice per week and administered as a subcutaneous injection
  ─ Prolonged usage is often limited due to its main adverse reaction, peripheral neuropathy, or due to acquired resistance

• Patients with newly diagnosed MM are increasingly treated with Darzalex (anti-CD38 mAb) in combination with Revlimid and dexamethasone

Patients and physicians demand new options with increasing efficacy and novel mechanisms of action
Rationale to Conduct the BOSTON Study

• Strong pre-clinical evidence of synergies when combining selinexor and a proteasome inhibitor\(^1,2\)

• Encouraging efficacy data observed in the Phase 1/2 STOMP study from 42 patients treated with SVd\(^3\)

• Current standard / indicated treatment of twice-weekly Velcade and dexamethasone is frequently reduced to once per week
  
  — Physicians commonly reduce Velcade schedule to once per week in clinical practice due to high incidence of peripheral neuropathy despite most Velcade Phase 3 trials utilizing twice-weekly dosing
  
  — Twice-weekly Velcade requires multiple visits to a physician’s office / clinic which can be particularly challenging for many patients

Randomized, open-label clinical trial evaluating **once weekly** selinexor and Velcade® (bortezomib) plus low-dose dex versus standard **twice-weekly** Velcade® plus low-dose dex in patients with relapsed or refractory MM, who have had 1-3 prior lines of therapy

1. Bortezomib, Selinexor and dexamethasone
2. Pts must have achieved ≥PR, and completed proteasome inhibitor therapy at least 6 months prior.
Top-Line Data from the Phase 3 BOSTON Study

- Study met its primary endpoint of a statistically significant increase in progression-free survival (PFS)

- 47% increase in median PFS on SVd arm versus Vd arm

- Median PFS in the SVd arm was 13.93 months compared to 9.46 months in the Vd arm, representing a 4.47 month increase in median PFS (hazard ratio=0.70; p=0.0066)

Safety

- No new safety signals in patients treated in the SVd arm
- No imbalance of patient deaths across both treatment arms
  - Fewer deaths numerically in the SVd arm
Peripheral neuropathy (PN) is amongst the most common causes of treatment limitation and discontinuation of Vd and combination Vd regimens.

The actual rates of PN on the BOSTON study will be reported at an upcoming medical meeting.

The rates of PN on SVd are significantly lower than on Vd in the BOSTON study.

Based on other recent Phase 3 trials, triplet-Vd regimens have high rates of PN (~50%) and higher than that in the Vd control arms:

- **CASTOR Trial**: Darzalex + Vd PN rate of 47% versus 38% in Vd arm\(^1\)
- **OPTIMISMM Trial**: Pomalyist + Vd PN rate of 48% versus 37% in Vd arm\(^2\)

An Estimated 20,000 Patients are Treated in the 2\textsuperscript{nd} Line and 12,000 in the 3\textsuperscript{rd} Line Settings (U.S.)

~69,000
Patients treated with drug therapy in 2019

An additional 60,000+ patients not on active treatment or in long-term remission during the year

# of patients with relapsed or refractory disease is growing annually, on a percentage basis, by mid-single digits due to population growth and increased life expectancy as a result of newly available treatment options

Estimated U.S. Multiple Myeloma Patients Treated by Line of Therapy, 2019

Drugs with Stand-Alone (± Steroid) Anti-MM Activity and Approved for 1\textsuperscript{st} or 2\textsuperscript{nd} Line Treatment have Achieved ≥$1B in Annual Sales

2019 Worldwide Sales\textsuperscript{1}

- **Immunomodulatory Agents**
  - Revlimid: $11B
  - Pomalyst: $2.5B

- **Proteasome Inhibitors**
  - Velcade: $1.6B
  - Kyprolis: $1B

- **Monoclonal Antibodies**
  - Darzalex: $3B

\textsuperscript{1}EvaluatePharma, February 2020.
No Dominant MM Drug Regimen in 2nd Line+ Setting With Numerous Drug Combinations Used to Meet Individual Patient Needs

Bars are not mutually exclusive; a regimen containing two drugs would appear in bars for both agents

R= Revlimid, V= Velcade, D= Darzalex, K= Kyprolis, N= Ninlaro, P= Pomalyst

1 Karyopharm market research (Post Launch ATU Survey Wave 1 (Oct’19), N=120). 2 Note: Patients typically receive multiple drugs in each line of therapy so many patients in 4th line and some in 3rd line will be refractory to 5 or more individual drugs.
Expected Future Trend in 1st line Treatment May Create Significant Opportunity for XPOVIO in the 2nd line

Transplant Ineligible (~65% of Patients)

**1st Line**
- Darzalex + Revlimid + dex
- Anti-CD38 Mab
- IMiD

**2nd Line**
- Velcade + XPOVIO\(^1\) + dex
- Proteasome Inhibitor
- Nuclear Export Inhibitor

Transplant Eligible (~35% of Patients)

**1st Line**
- Velcade + Revlimid + dex
- Proteasome Inhibitor
- IMiD

**2nd Line**
- Velcade + XPOVIO\(^1\) + dex
- Proteasome Inhibitor
- Nuclear Export Inhibitor

\(^1\)XPOVIO is currently only approved by the FDA 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). The schematic illustrated above represents what a treatment paradigm might look like should XPOVIO be approved by the FDA as 2nd Line\(^+\) treatment in multiple myeloma in combination with Velcade and dexamethasone.

Potential for patients to be treated with 4 drugs, each with unique mechanisms of action, in the 1st two lines of treatment.
Additional XPOVIO Triplet Regimens Indicate Additive or Synergistic Activity Compared to Benchmark Doublet Regimens

- Selinexor is currently being studied in the ongoing STOMP Phase 1b/2 trial evaluating selinexor and low-dose dexamethasone in combination with one of several standard approved myeloma therapies in patients with relapsed or refractory multiple myeloma

<table>
<thead>
<tr>
<th>STOMP Regimen</th>
<th># of Patients Treated to Date</th>
<th>Efficacy Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selinexor + Kyprolis + dex</td>
<td>14 (Kyprolis-naïve)</td>
<td>ORR = 71%¹</td>
</tr>
<tr>
<td>Selinexor + Darzalex + dex</td>
<td>30 (Darzalex-naïve)</td>
<td>ORR = 73%²</td>
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<tr>
<td>Selinexor + Pomalyst + dex</td>
<td>32 (Pomalyst–naïve and Revlimid relapsed or refractory)</td>
<td>ORR = 56%³, PFS = 12.2 months³</td>
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<tr>
<td>Selinexor + Revlimid + dex</td>
<td>12 (Revlimid-naïve)</td>
<td>ORR = 92%⁴</td>
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<table>
<thead>
<tr>
<th>Benchmark Regimen</th>
<th>Efficacy Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyprolis + dex</td>
<td>ORR = 23%⁵</td>
</tr>
<tr>
<td>Darzalex</td>
<td>ORR = 29%⁶</td>
</tr>
<tr>
<td>Pomalyst + dex</td>
<td>ORR = 29%⁷, PFS = 3.6 months⁷</td>
</tr>
<tr>
<td>Revlimid + dex</td>
<td>ORR = 67%⁸</td>
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Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies⁹

Note: The STOMP study does not include any arms studying current myeloma backbone therapies without the combination of selinexor. The purpose of displaying the “Benchmark” data above is to highlight that the clinical results from STOMP reported to date strongly support ongoing / additional clinical investigation of selinexor in combination regimens.

Next Steps

1. Data to be submitted for presentation at upcoming medical meetings

2. Submit BOSTON data to FDA as part of sNDA in Q2 2020 requesting expansion of current XPOVIO label

3. Potential to submit data to the European Medicines Agency (EMA) as part of their ongoing review of the selinexor Marketing Authorization Application (MAA)

4. Depending on FDA review time, potential U.S. commercial launch before end of 2020