Investor Conference Call:
First Quarter 2020 Financial Results and Business Update

May 5, 2020

On Today's Call

Prepared Remarks

- **Michael G. Kauffman, MD, PhD,** *Chief Executive Officer*
- **John Demaree,** *Chief Commercial Officer*
- **Mike Mason, MBA,** *Chief Financial Officer*

Joining for Q&A Session

- **Sharon Shacham, PhD,** *President and Chief Scientific Officer*
- **Christopher Primiano, JD, MBA**, *Chief Business Officer & General Counsel*
- **Jatin Shah, MD,** *Executive Vice President, Chief Medical Officer*
- **Perry Monaco,** *Senior Vice President, Sales*
- **Ian Karp, MBA**, *Vice President, Investor and Public Relations*

Forward-looking Statements and Other Important Information

This presentation contains forward-looking statements within the meaning of the “safe harbor” provisions of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm’s expectations and plans relating to selinexor as a potential treatment for patients with COVID-19; the design and execution of Karyopharm’s clinical trial to study this potential application of selinexor, including the dosing regimen; the potential anti-viral and anti-inflammatory properties of selinexor; 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, including 2020 financial guidance and the sufficiency of cash to fund operatons through mid-2022. 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 Karyopharm will successfully commercialize XPOVIO, that regulators will agree that selinexor qualifies for conditional approval in the E.U. as a result of the data from the STORM study in patients with penta-refractory myeloma or accelerated approval in the U.S. based on the SADAL study in patients with relapsed/refractory DLBCL or that any of Karyopharm’s drug candidates, including selinexor and eltanexor (KPT-8602), Karyopharm’s second generation SINE compound, or KPT-9274, Karyopharm’s first-in-class oral dual inhibitor of PAK4 and NAMPT, or any other drug candidate Karyopharm is developing, will successfully complete necessary preclinical and 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. In addition, even if Karyopharm receives marketing approval for selinexor in additional indications or for any other drug candidate, there can be no assurance that Karyopharm will be able to successfully commercialize that drug candidate. Management’s expectations and, therefore, any forward-looking statements in this presentation could also be affected by risks and uncertainties relating to a number of other factors, many of which are beyond Karyopharm’s control, including the following: 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 FDA 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 diseases for which Karyopharm is currently developing its drug candidates; that the markets for multiple myeloma and DLBCL drugs will grow as predicted; Karyopharm’s ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the COVID-19 pandemic could disrupt Karyopharm’s business more severely than it currently anticipates, including by reducing 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. These and other risks are described under the caption “Risk Factors” in Karyopharm’s Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the Securities and Exchange Commission (SEC) on February 26, 2020, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this presentation are for informational purposes only and speak only as of the date hereof. Other than as is 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’s website is http://www.karyopharm.com. 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. Unless otherwise noted, this presentation contains data that are interim and unaudited based on site reports. In addition, data included in this presentation have not been updated and are as of the cutoff date for the applicable medical conference presentation. 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.

Significant Progress Made Despite Industry-Wide Challenges from the COVID-19 Pandemic

Commercial Update

- Q1 2020 XPOVIO net sales of **$16.1M** (total revenues of **$18.1M**)
- XPOVIO Q1 net sales decrease of 9% vs. Q4 2019 driven primarily by minimal channel inventory build in Q1 and **impact of COVID-19 pandemic** on new patient starts
- **>150 new** physicians / accounts prescribed XPOVIO for the first time in Q1 2020
- Achieved **leading** customer engagement in Q1 2020[1]
- XPOVIO demand **accelerated in April 2020** compared to March

Pipeline / Clinical Data Update

- **Positive** top-line BOSTON Phase 3 data announced on March 2nd
- BOSTON data selected for **oral presentation** at ASCO 2020 Virtual Scientific Program
- BOSTON sNDA submission **ahead of schedule** and expected by **end of May 2020**
- DLBCL sNDA granted **Priority Review** with June 23, 2020 PDUFA action date
- **Initiated** randomized study to evaluate low dose oral selinexor in patients with **severe COVID-19** based on strong scientific rationale and pre-clinical data

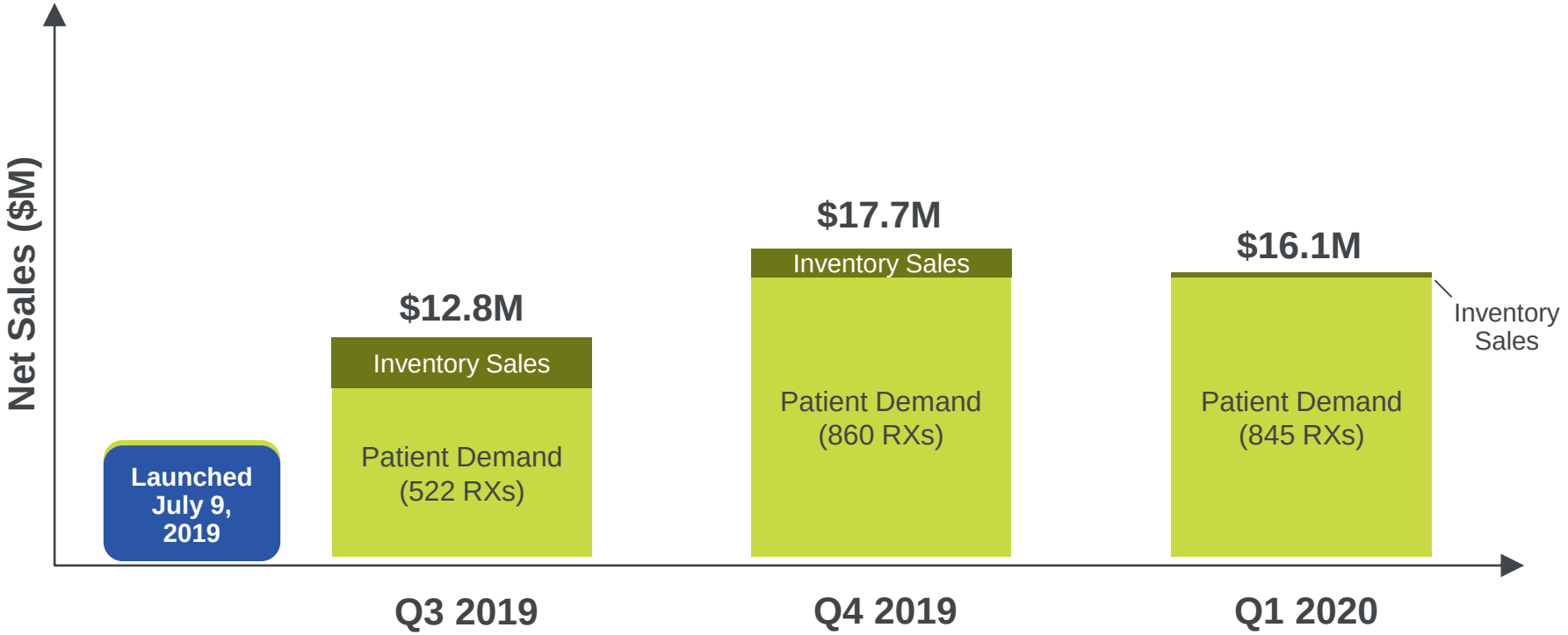
Corporate Development and Balance Sheet

- **Expanded territory rights** with Antengene to now include Australia, South Korea and additional Asian Pacific market; Karyopharm to receive **$12M** upfront and potential additional milestones / royalties
- **Reacquired commercial rights** for selinexor and eltanexor from Ono Pharmaceutical Co. in **Japan** (at no cost to Karyopharm)
- Completed common stock offering in Q1 2020 with net proceeds of **~$162M**
- Ended Q1 2020 with **~$385M** in cash and investments; cash runway now expected to be sufficient to fund planned operations into **middle of 2022**

[1] Highest sales force reach and frequency rating to target customers according to leading industry market insights provider.

XPOVIO Quarterly Sales

XPOVIO Product Sales Following Launch



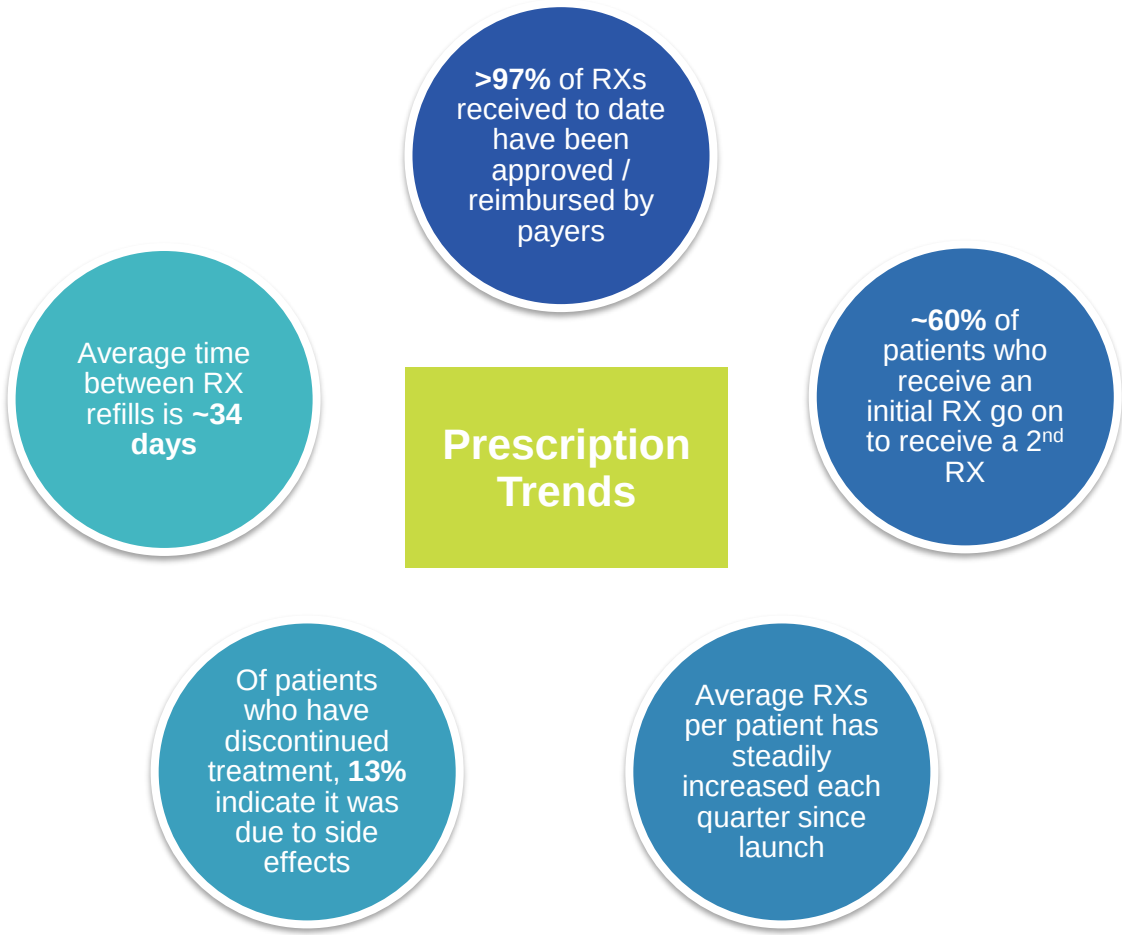
- **>2,200** prescriptions (RX) filled through March 31, 2020
- **Minimal inventory build** in distribution channel in Q1 2020
- Prescription demand **approximately flat** Q1 2020 vs. Q4 2019 primarily due to fewer than expected new patient starts which were impacted by the COVID-19 pandemic
- Average prescription refill rate **continued to grow** in Q1
- **Rx demand accelerated** in April 2020 compared to March

XPOVIO Patient Experience Continues to be Highly Positive

STORM Study[1]

- 26% overall response rate
- 39% of patients had minimal response or better
- Median duration of treatment was 9 weeks with a range of 1 week to 60 weeks (mean duration was ~12 weeks)
- 27% of patients discontinued treatment due to side effects
- Median survival of 1.7 months in patients who did not respond to XPOVIO compared to 15.6 months in patients with a minimal response or better

Real World Experience
July 2019 – March 2020[2]



[1] Chari A, et al. New England Journal of Medicine. 2019.
[2] Based on patient data from Karyopharm's network of specialty pharmacy providers.

COVID-19 Pandemic Impact on XPOVIO Commercial Market

Commercial Pressures

- Industry as a whole, including oncologists, report fewer visits for non COVID-19 patients
  - Significant impact on XPOVIO new starts in March
- Karyopharm sales force out of field territories by early March
  - Newly launched products, in general, require greater physician education before they are broadly adopted as compared to existing, more established therapies / brands

Advantages of XPOVIO as Patients and Physicians Seek to Limit Visits to the Hospital

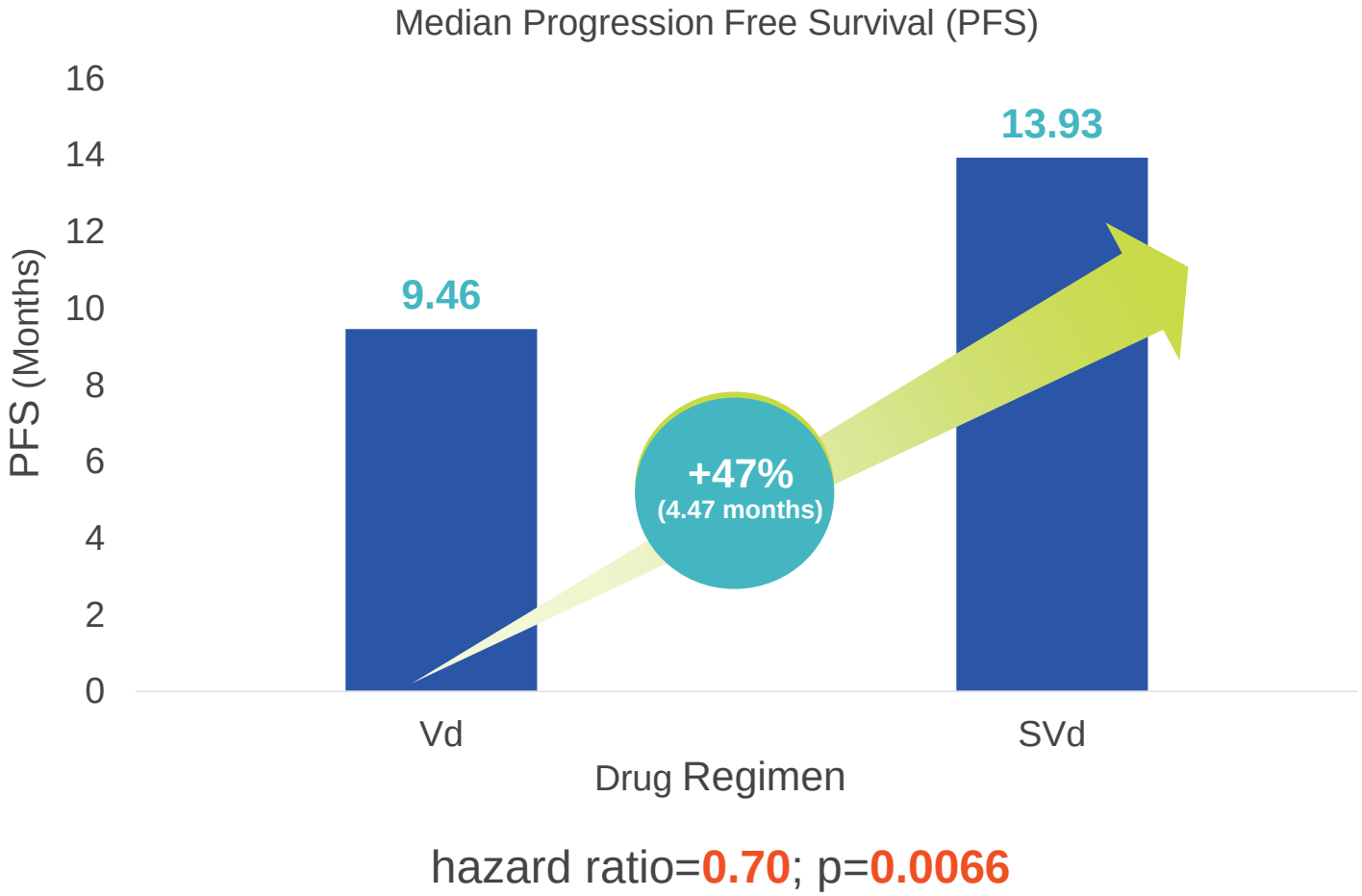
- Oral administration, delivered directly to patient's home
- Nursing support / side effect management resources available by phone
- Main supportive care agents to prevent and/or treat nausea, reduced appetite and fatigue are typically oral medicines that can also be taken at home
- Simple blood tests recommended while on XPOVIO therapy (e.g. CBC, sodium levels, etc.) can be done at local laboratory testing sites

Karyopharm is Working To Mitigate the Commercial Impact of the COVID-19 Pandemic

Key Responses

- Rapidly launched multiple digital tools to facilitate continued sales force engagement with customers
  - Extensive email campaign
  - Multiple e-detailing platforms (Zoom, Veeva Engage)
- Moved peer-to-peer programs to virtual channels to expand reach
  - Executed national webcasts
  - Planning KOL speaker vignettes
- Increasing non-personal promotion including Electronic Medical Records information at the point of diagnosis, search engine marketing and media placement
- Increased focus on physicians who have not yet prescribed XPOVIO
- Preparing for a virtual, omnichannel launch in DLBCL, pending FDA approval

Top-Line Data from the Phase 3 BOSTON Study



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
- Most frequent treatment-related adverse events (≥ grade 3) for SVd vs. Vd were thrombocytopenia, fatigue and nausea with **lower rates** of peripheral neuropathy on the SVd arm

In BOSTON Study, SVd Arm Had Lower Rates of Peripheral Neuropathy Compared to Vd Arm and Triplet-Vd Regimens Seen Across Other Phase 3 Trials

- 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 in the BOSTON study will be reported at the ASCO 2020 Virtual Scientific Program in May 2020
- The rates of PN in the SVd arm were significantly lower than in the Vd arm
- 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 50% versus 38% in Vd arm[1]
  - **OPTIMISMM Trial:** Pomalyst + Vd PN rate of 48% versus 37% in Vd arm[2]

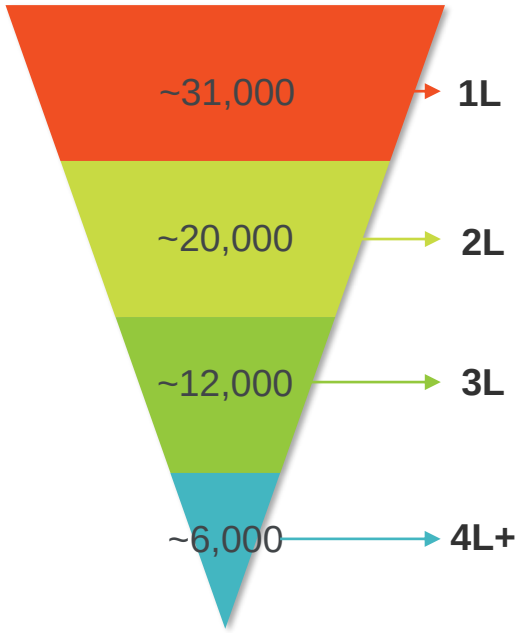
[1] Palumbo A, et. al. NEJM.2016. [2] Richardson P, et al. Lancet Oncology. 2019.

MM Patients Treated by Line of Therapy (U.S.)

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

~69,000 Patients Treated With Drug Therapy in 2019

Patients by Line of Treatment



Average Time on Therapy
++++
+++
++
+

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

Number 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

Sources: Karyopharm analysis based on data from Decision Resources, Kantar Cancer Impact and SEER Cancer Stat Facts. National Cancer Institute.

Karyopharm Initiates New Study of Low-dose Selinexor in Patients with Severe COVID-19

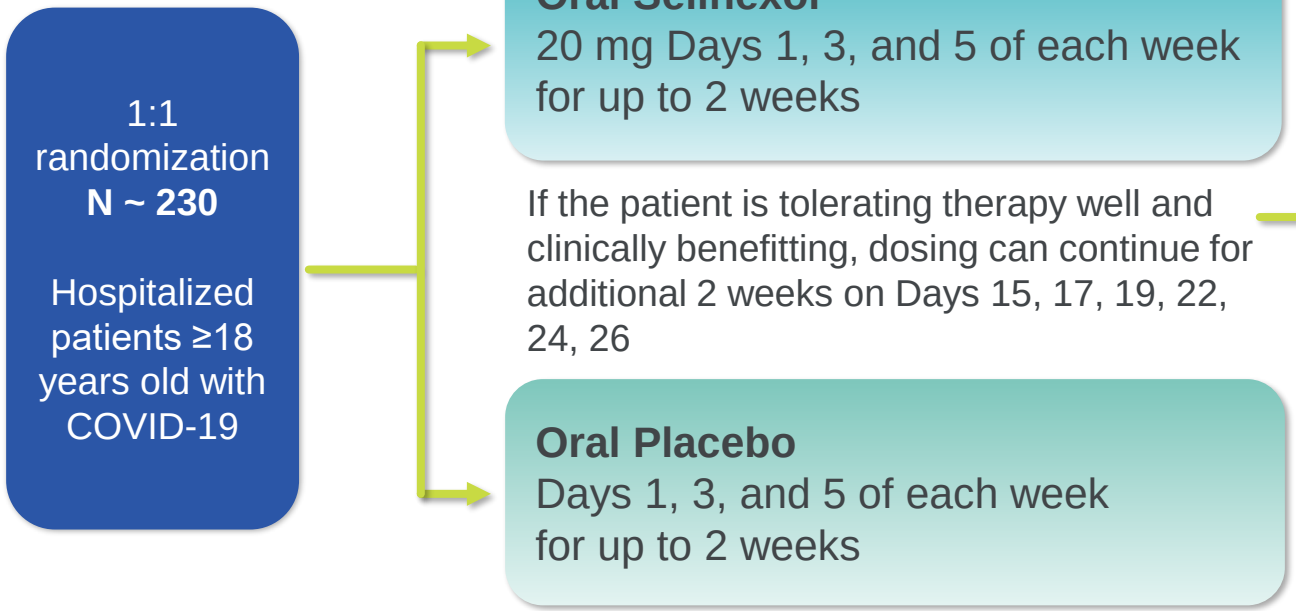
Scientific Rationale for Evaluating Selinexor in COVID-19

- XPO1 inhibitors have previously demonstrated preclinical activity against >20 viruses, including influenza, RSV and other viral respiratory infections
- XPO1 was identified as one of the host proteins with the highest number of functional connections with SARS-CoV proteins[1]
- Selinexor demonstrated potent inhibition of SARS-CoV2 propagation in monkey Vero cells inhibiting the production of new virus by 90% at a low concentration (100 nM) from cells infected with SARS-CoV2[2]
  - Additionally, even lower levels of selinexor (only 10nM) reduced the ability of the virus to infect new cells by about 99%
- Blockade of XPO1 amplifies the activities of anti-inflammatory transcription factors: IκB, PPARγ, RXRa, and others
- Verdinexor (closely related SINE compound to selinexor) treatment (low dose) delayed up to 4 days after influenza virus infection in mice showed marked anti-viral and anti-inflammatory activity and improved survival
- The severity of COVID-19, caused by SARS-CoV2, is associated with high levels of pro-inflammatory cytokines
  - Selinexor protects against LPS-induced sepsis in mice, ameliorated lung injury and reduced serum levels TNFα, IL-6 and HMGB-1

[1] Zhou Y, et. al. Cell Discovery. 2020. [2] Ralph A. Tripp, Ph.D., University of Georgia.

A Phase 2 Randomized, Single-Blind Study to Evaluate the Activity and Safety of Low Dose Oral Selinexor in Patients with Severe COVID-19 (NCT04349098)

~40 International Study Sites, ~10 countries



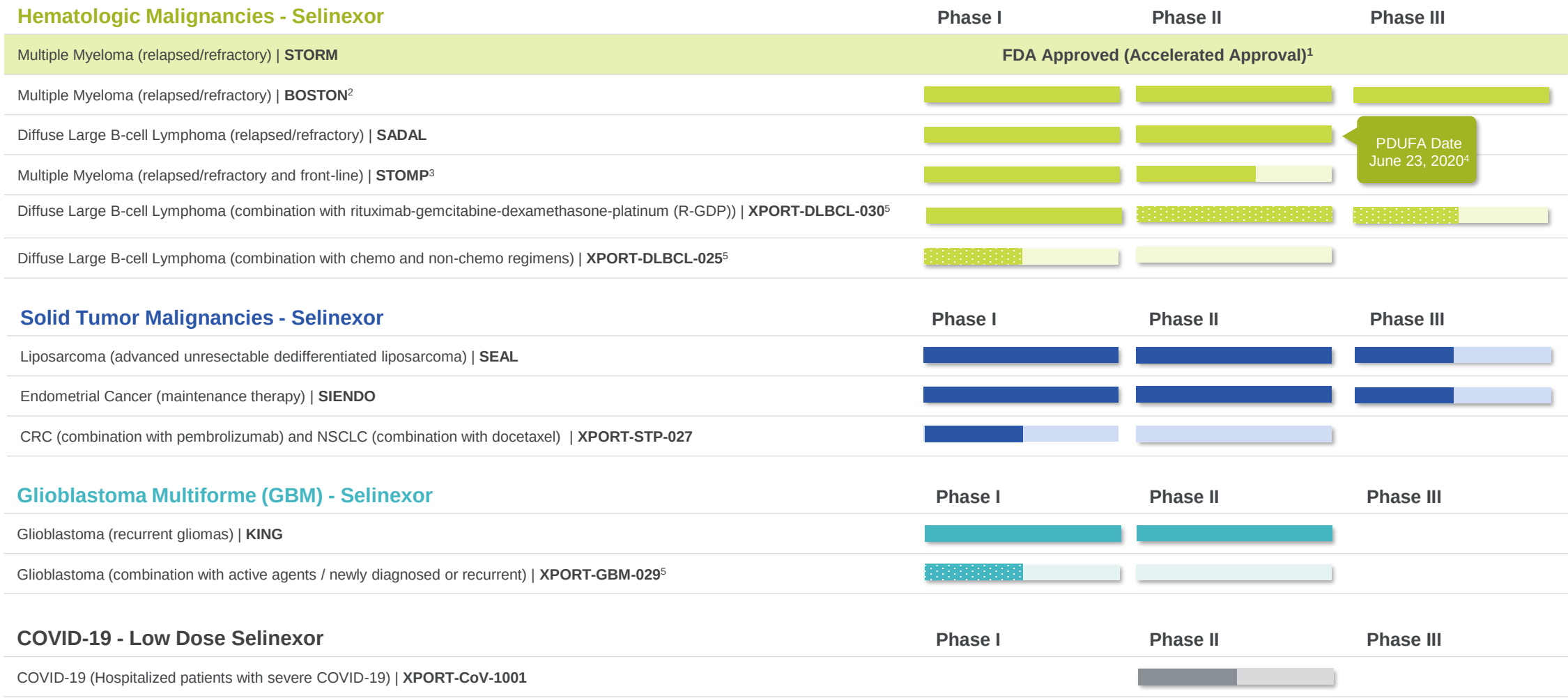
Primary endpoints: Day 14 Ordinal Scale Improvement (OSI)

Proportion of patients with at least a 2 point improvement (increase) in the Ordinal Scale from baseline (defined as the time from randomization, or lower score within 24 hours of randomization) to Day 14

Key secondary endpoints

- Time to Clinical Improvement (time from randomization or lower score within 24 hrs, to improvement of 2 points on Ordinal Scale
- Overall Death Rate on Day 28
- Rate of mechanical ventilation
- Time to mechanical ventilation

Karyopharm's Novel Pipeline | Selinexor



[1] Full Prescribing Information and Medication Guide are available at www.XPOVIO.com [2] Oral selinexor, Velcade® (bortezomib) and dexamethasone vs. Velcade and dexamethasone. [3] Oral selinexor and dexamethasone + Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade, Kyprolis® (carfilzomib) or Darzalex® (daratumumab). [4] With request for accelerated approval (U.S.). [5] Study expected to start in 2020

Karyopharm's Novel Pipeline | Eltanexor, KPT-9274 and Verdinexor

Additional Oncology Programs - Eltanexor and KPT-9274	Phase I	Phase II	Phase III
Myelodysplastic Syndromes (MDS) (single agent or in combination with hypomethylating agents)[1] Drug: Eltanexor			
Colorectal Cancer (CRC) and Prostate Cancer (PrC) Drug: Eltanexor			
Solid Tumors & AML Drug: KPT-9274			

Infectious Diseases & Autoimmune Disorders - Verdinexor	Phase I	Phase II	Phase III
Healthy Human Volunteers			
Systemic Lupus Erythematosus (SLE) | **VALOR-SLE-705**[2]			
Severe Influenza, Respiratory Syncytial Virus (RSV), HIV Inflammation, Spinal Cord Injury[2]			

[1] Study expected to start in 2020. [2] Study start pending submission and acceptance of IND.

First Quarter Financial Results

Mike Mason
Chief Financial Officer

First Quarter 2020 Financial Results

Statement of Operations	Three Months Ended March 31st	
	2020	2019
Total Revenue	$18.1M	$0.2M
XPOVIO Net Sales	$16.1M	---
License and Other Revenue	$2.1M	$0.2M
Total Operating Expenses	$65.5M	$65.1M
Cost of Sales	$0.8M	----
Research and Development Expense	$34.0M	$38.0M
Selling, General & Administrative Expense	$30.7M	$27.1M
Net Loss	$52.9M ($0.78 per share)	$66.2M ($1.09 per share)

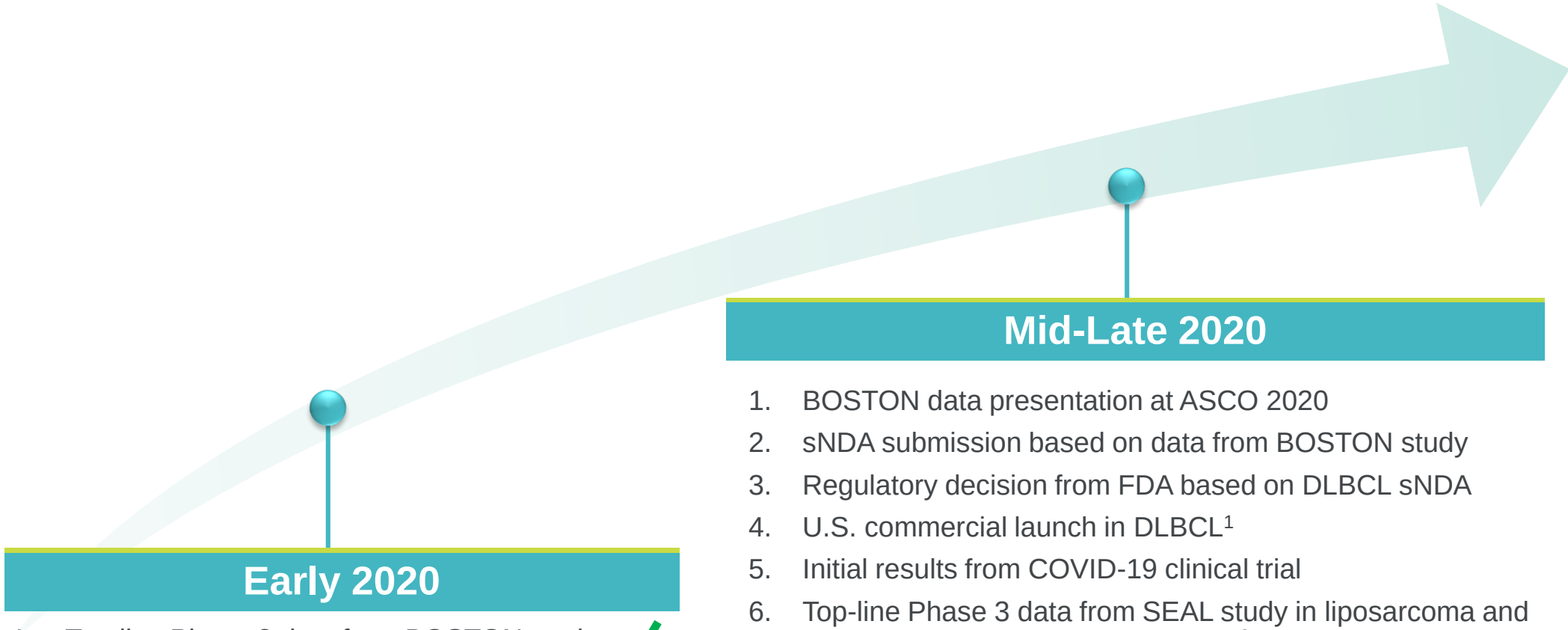
Balance Sheet and Financial Guidance

Balance Sheet	March 31, 2020	December 31, 2019
Cash, Cash Equivalents, Restricted Cash and Investments	$385.2M	$265.8M

- **XPOVIO net sales in Q2 2020 expected to be slightly higher than Q1 2020**
- **Non-GAAP R&D and SG&A expenses are expected to be at the lower end of the previously projected range of $240-260M for the full year 2020[1]**
- **Cash runway expected to be sufficient to fund planned operations into the middle of 2022**

[1] Excludes stock-based compensation expense. This outlook can only be provided on a non-GAAP basis because Karyopharm cannot reliably predict without unreasonable efforts the timing or amount of the factors that substantially contribute to the projection of stock compensation expense, which is excluded from the full year 2020 outlook for non-GAAP R&D and SG&A expenses.

Numerous Expected Key Milestones for XPOVIO / Selinexor in 2020



Early 2020

1. Top-line Phase 3 data from BOSTON study ✓
2. Initiation of randomized, global clinical trial in patients with severe COVID-19 ✓

Mid-Late 2020

1. BOSTON data presentation at ASCO 2020
2. sNDA submission based on data from BOSTON study
3. Regulatory decision from FDA based on DLBCL sNDA
4. U.S. commercial launch in DLBCL[1]
5. Initial results from COVID-19 clinical trial
6. Top-line Phase 3 data from SEAL study in liposarcoma and subsequent regulatory submissions[2]
7. Regulatory decision expected in Europe in heavily pre-treated / refractory multiple myeloma
8. Start of confirmatory Phase 3 Study in DLBCL in support of potential accelerated approval
9. U.S. commercial launch in 2nd line multiple myeloma (End of Q4 2020 to Q1 2021 depending on review timelines)[1]

[1] Subject to regulatory approval. [2] Subject to positive Phase 3 results.

Questions?

Answers.