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

August 4, 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*
- **Ian Karp, MBA,** Senior *Vice President, Investor and Public Relations*

Forward-looking Statements and Other Important Information

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; the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor; Karyopharm's collaboration efforts with third-parties, including the National Cancer Institute; 2020 financial expectations, including forecasted non-GAAP R&D and SG&A expenses; and expectations of the sufficiency of Karyopharm's existing cash and investments. 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 U.S. or EU based on the BOSTON study in patients with relapsed or refractory 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 presentation 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 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; 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 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, 2020, which was filed with the Securities and Exchange Commission (SEC) on May 5, 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. 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.

Progress On Karyopharm's Vision of Becoming an Oncology Leader

2013-2018

Supported the growing body of clinical data for our lead investigational compound

1. Advanced lead compound with a novel mechanism of action and broad anti-tumor activity
2. Executed a robust clinical development program with focus in 4 core cancers
3. Initiated first set of regulatory filings

2019-2020

Transition to a commercial oncology company

1. Initial commercial launch into U.S. myeloma market
2. Initial commercial launch into U.S. DLBCL market
3. Initiate and advance regulatory submissions in Europe

2021+ Future Goals

Expand commercial position, drive broader utilization and advance follow-on pipeline

1. Launch into earlier lines of myeloma and DLBCL treatment (pending regulatory approval)
2. Expand commercial sales globally
3. Advance regulatory filings in solid tumors
4. Advance follow-on pipeline programs (with increasing focus on solid tumors)

Record Quarter for XPOVIO Sales and Key Development Milestones Achieved

Commercial Update

- Q2 2020 XPOVIO net sales of **$18.6M** marking highest quarterly sales since launch (total revenues of **$33.5M**)
- XPOVIO Q2 2020 net sales increase of **16% vs. Q1 2020** driven primarily by increase in demand from multiple myeloma patients
- **~170 new** physicians / accounts prescribed XPOVIO for the first time in Q2 2020
- **DLBCL launch** commenced at end of June with initial prescriptions filled in early July

Pipeline / Clinical Data Update

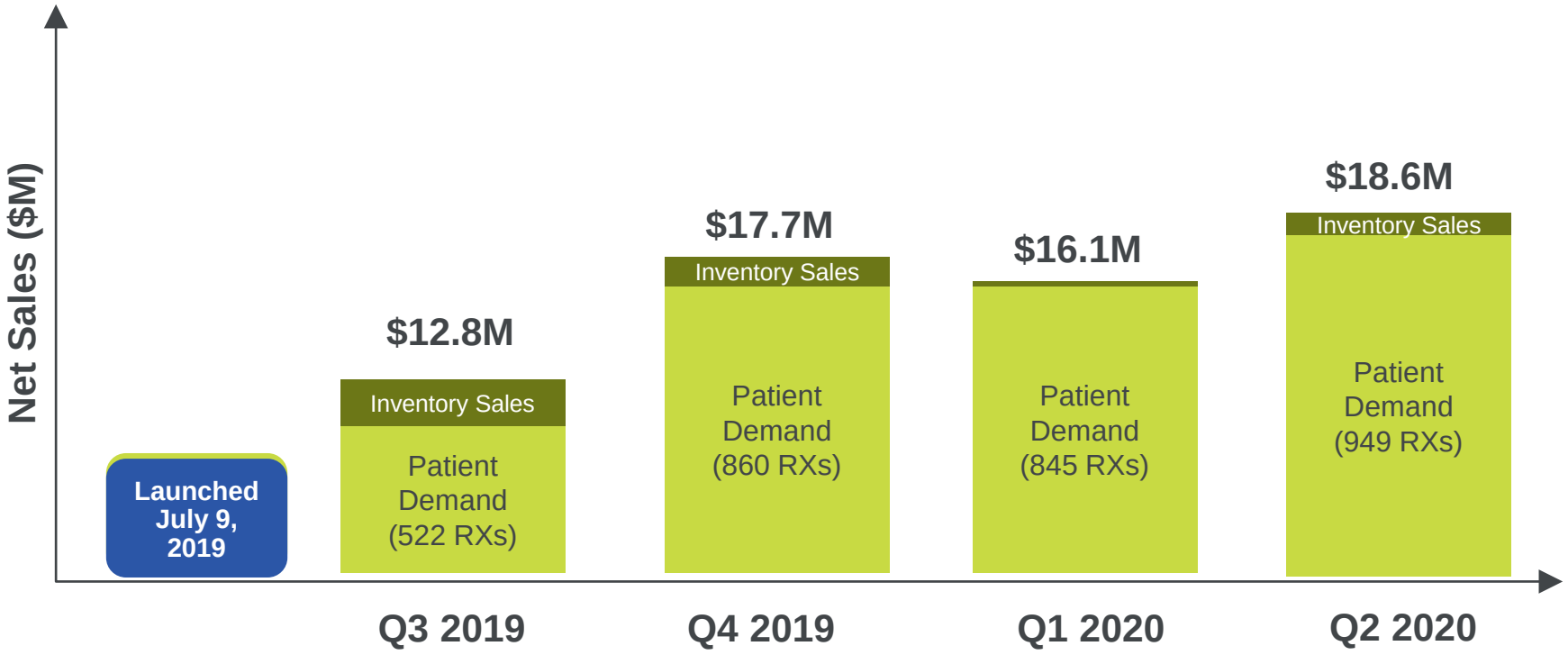
- **FDA approval** for XPOVIO in DLBCL
- **Positive BOSTON Phase 3 data** presented at ASCO 2020 Virtual Scientific Program
- sNDA for expanded indication in multiple myeloma **accepted by FDA**
- **Completion of enrollment** in Phase 3 SEAL study in liposarcoma **and initiation** of new clinical trial of selinexor in patients with glioblastoma
- Interim efficacy data from Phase 2 COVID-19 study demonstrates benefit in **patient subpopulation**; Current study to be discontinued and future development to focus on patient subpopulation

Corporate Development and Balance Sheet

- **Entered into a Cooperative Research and Development Agreement (CRADA)** with the National Cancer Institute's (NCI) Cancer Therapy Evaluation Program (CTEP) to further develop selinexor across additional tumor types
- **Recognized $12.7M** in revenue from Antengene as part of territory expansion agreement
- Ended Q2 2020 with **$348.2M** in cash and investments; cash runway expected to be sufficient to fund planned operations into **middle of 2022**

XPOVIO Quarterly Sales

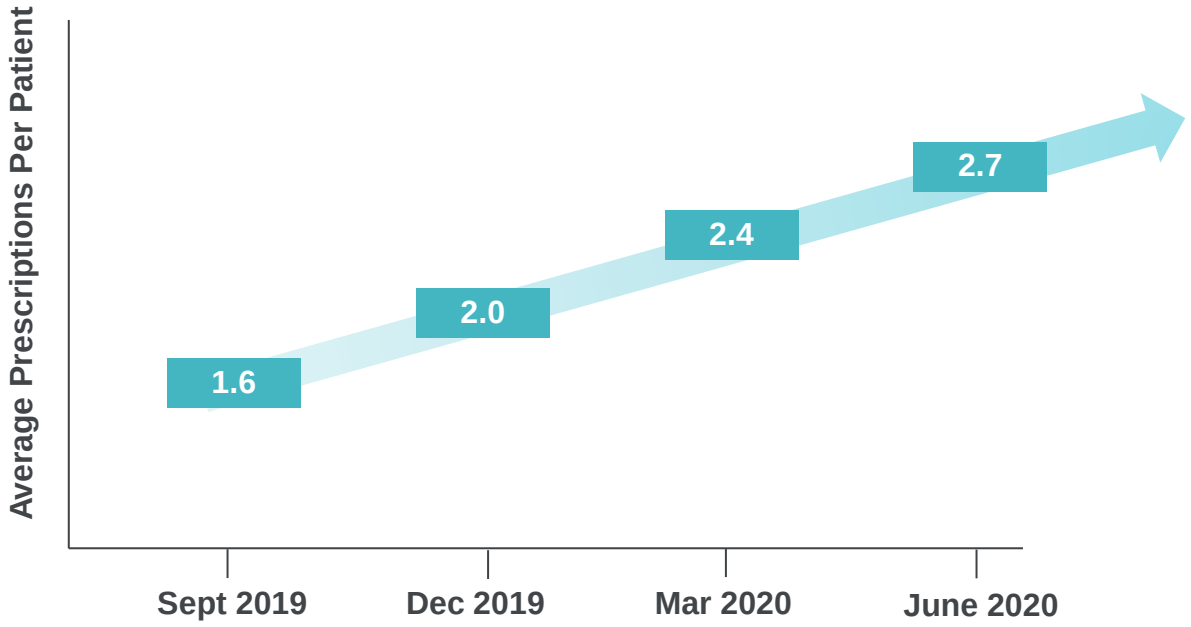
XPOVIO Product Sales Following Launch



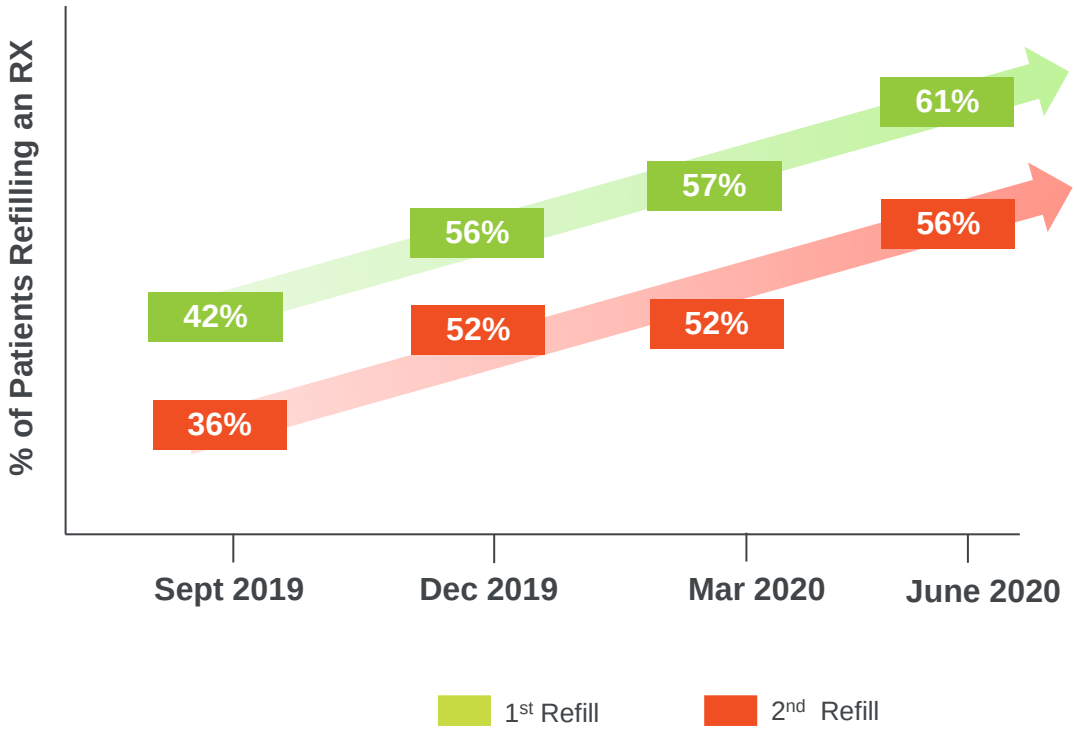
- **~3,200** prescriptions (RXs) filled from launch through June 30, 2020
- **12% increase** in prescription demand and **16% increase** in net sales in Q2 2020 compared to Q1 2020
- **Incremental inventory build** in distribution channel in Q2 to support DLBCL launch
- Q2 2020 was the **strongest quarter** to date for both net sales and patient demand

Key XPOVIO Patient Metrics Continue to Improve in Each Subsequent Quarter Since Launch

Average Treatment Cycles (RXs) Per Patient[1]



Prescription Refill Rate for 1st and 2nd Prescription (Only Includes Patients Eligible for a Refill)[1]



[1] Based on patient data from Karyopharm's network of specialty pharmacy providers.

Positive Phase 3 BOSTON Data Presented at ASCO 2020

- Once-weekly SVd significantly prolonged progression free survival (PFS) (median PFS improvement of 47%, HR 0.70, *P*=0.0075 vs Vd)
  - SVd was superior to Vd across key efficacy endpoints (PFS, ORR, ≥VGPR, and DoR) including in patients over the age of 65, those that were frail, those treated with prior lenalidomide and those with del[17p]
  - Median overall survival (OS) not reached with SVd versus 25 months with Vd
- Once-weekly dosing used in the SVd arm was associated with significantly lower rates and severity of Velcade-induced peripheral neuropathy compared with twice-weekly Vd
- Adverse events (AEs) associated with SVd were manageable and reversible
  - The most common AEs were cytopenias, along with gastrointestinal and constitutional symptoms and were consistent with those previously reported from other selinexor studies
  - Discontinuation rate due to AEs was 17% (SVd) and 11% (Vd)

BOSTON Trial Conclusions

In patients with multiple myeloma who have received 1-3 prior therapies, including prior lenalidomide or a proteasome inhibitor, once-weekly SVd offers patients an effective, convenient, IMiD-free, novel triplet regimen, requiring ~40% fewer clinic visits and reduced rate of peripheral neuropathy

Source: Dimopoulos M, et al. ASCO 2020. Abstract 8501.

Regulatory Update Across Potential Future Indications

Regulatory Update

- U.S. BOSTON sNDA
  - sNDA submitted on May 19, 2020
  - FDA accepted filing on June 17, 2020
  - FDA has assigned an action date of March 19, 2021 under the Prescription Drug User-Fee Act (PDUFA)

- EU (STORM, BOSTON)
  - Updated plan to submit additional STORM data in Q3 2020
  - BOSTON MAA expected to be submitted before end of 2020

- EU (SADAL)
  - Evaluating regulatory strategy and potential timing of future submission

XPOVIO (selinexor) Accelerated Approval by the FDA in RR DLBCL

XPOVIO is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy[1]

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

- XPOVIO is now the only single-agent, oral therapy approved for the treatment of patients with relapsed or refractory DLBCL
- XPOVIO is the first and only Nuclear Export Inhibitor approved by the FDA for use in two hematologic malignancies (multiple myeloma and DLBCL)

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

[1]XPOVIO Prescribing Information

Key Features of XPOVIO for the Treatment of Patients With RR DLBCL

Factors That Influence Treatment Choice	Key Features of XPOVIO
• Clinical efficacy	• 29% ORR[1] • 13%CR[1] • Clinically meaningful duration of response[1]
• Previous therapies / approaches	Novel mechanism of action
• Subtype and histology	Similar efficacy seen across both ABC and GCB patient sub-types
• Comorbidities • Functional status, age, frailty	Common adverse events do not include: • Peripheral neuropathy • Cardiac, liver or kidney toxicity • Opportunistic infections
• Patient preferences / logistical dynamics	• Oral route of administration taken only twice per week • Single agent, not combined with chemotherapy

[1]XPOVIO Prescribing Information

Phase 2 COVID-19 Study Demonstrates Activity in Specific Patient Subpopulation

Study Results

- Data Safety Monitoring Board (DSMB) concluded trial was likely to show a benefit in subpopulation of patients <75 years old who have a COVID-GRAM non-high risk score
  - Preliminary results indicate that in the specific subpopulation, a two-point improvement in Ordinal Score at Day 14 reached statistical significance, as did the two-point improvement in Ordinal Score by Day 28 and the rate of hospital discharge by Day 14 (all $p \leq 0.05$)
  - While rate of fatalities in the study were imbalanced in patients ≥75 years old or with a COVID-GRAM high risk score, after a detailed review, DSMB considered deaths on study were due to severe COVID-19 disease and/or underlying comorbidities without a clear contribution of selinexor
- DSMB concluded the trial, as currently designed, is unlikely to demonstrate a statistically significant efficacy benefit across the entire patient population

Next Steps

- Discontinue current study
- Further characterize specific subpopulation likely to benefit from selinexor and work with FDA to develop path forward
- Future clinical development to focus on patient subpopulation
  - Seek potential partner(s) and external funding for future development

Second Quarter Financial Results

Mike Mason
Chief Financial Officer

Second Quarter 2020 Financial Results

Statement of Operations	Three Months Ended June 30th	
	2020	2019
Total Revenue	$33.5M	$9.5M
XPOVIO Net Sales	$18.6M	---
License and Other Revenue	$14.9M	$9.5M
Total Operating Expenses	$73.8M	$51.2M
Cost of Sales	$0.4M	----
Research and Development Expense	$42.6M	$26.5M
Selling, General & Administrative Expense	$30.8M	$24.7M
Net Loss	$46.4M ($0.63 per share)	$43.4M ($0.71 per share)

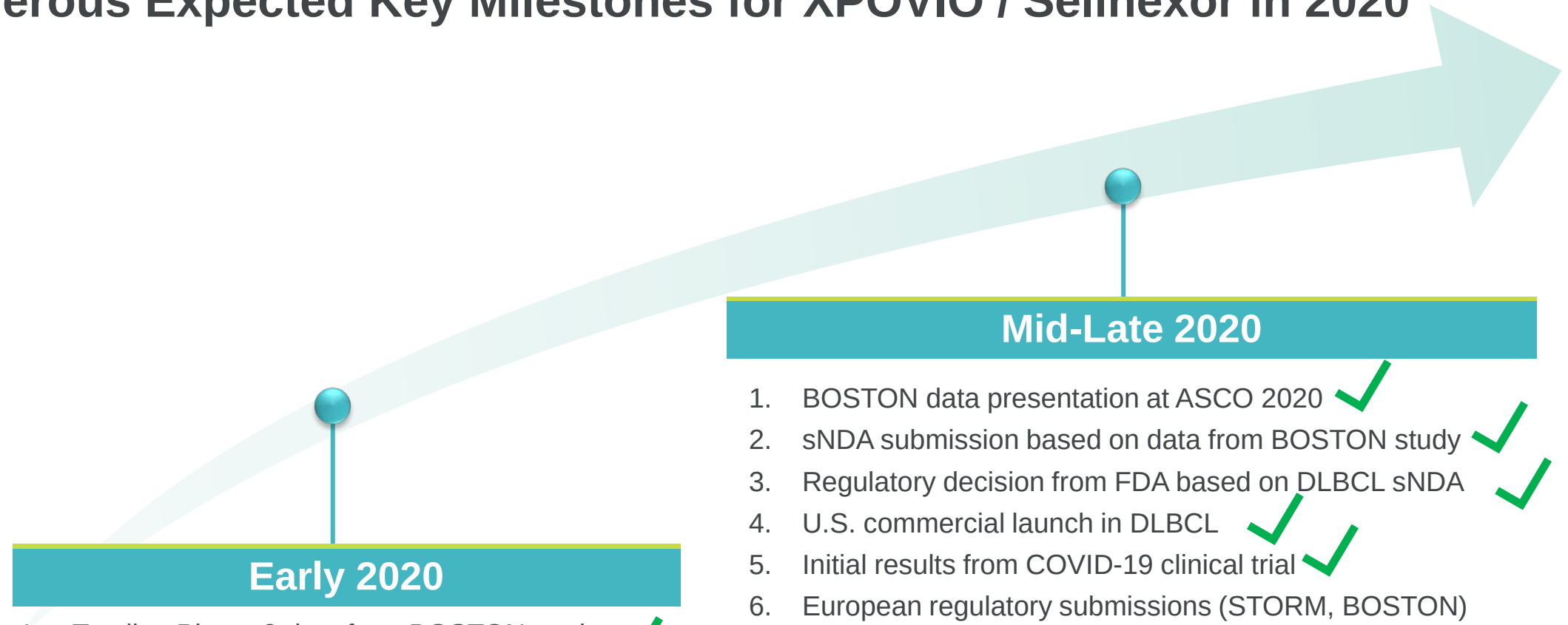
Balance Sheet and Financial Guidance

Balance Sheet	June 30, 2020	December 31, 2019
Cash, Cash Equivalents, Restricted Cash and Investments	$348.2M	$265.8M

- **Non-GAAP R&D and SG&A expenses are expected to be in the 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
5. Initial results from COVID-19 clinical trial
6. European regulatory submissions (STORM, BOSTON)
7. Top-line Phase 3 data from SEAL study in liposarcoma and subsequent regulatory submissions[1]
8. Start of confirmatory Phase 3 Study in DLBCL in support of accelerated approval

[1] Subject to positive Phase 3 results.

Questions?

Answers.