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

November 2, 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*
- **Jatin Shah, MD,** *Executive Vice President, Chief Medical 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, including expected increases in total annual sales 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; the commercial opportunity for XPOVIO; 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 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 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. 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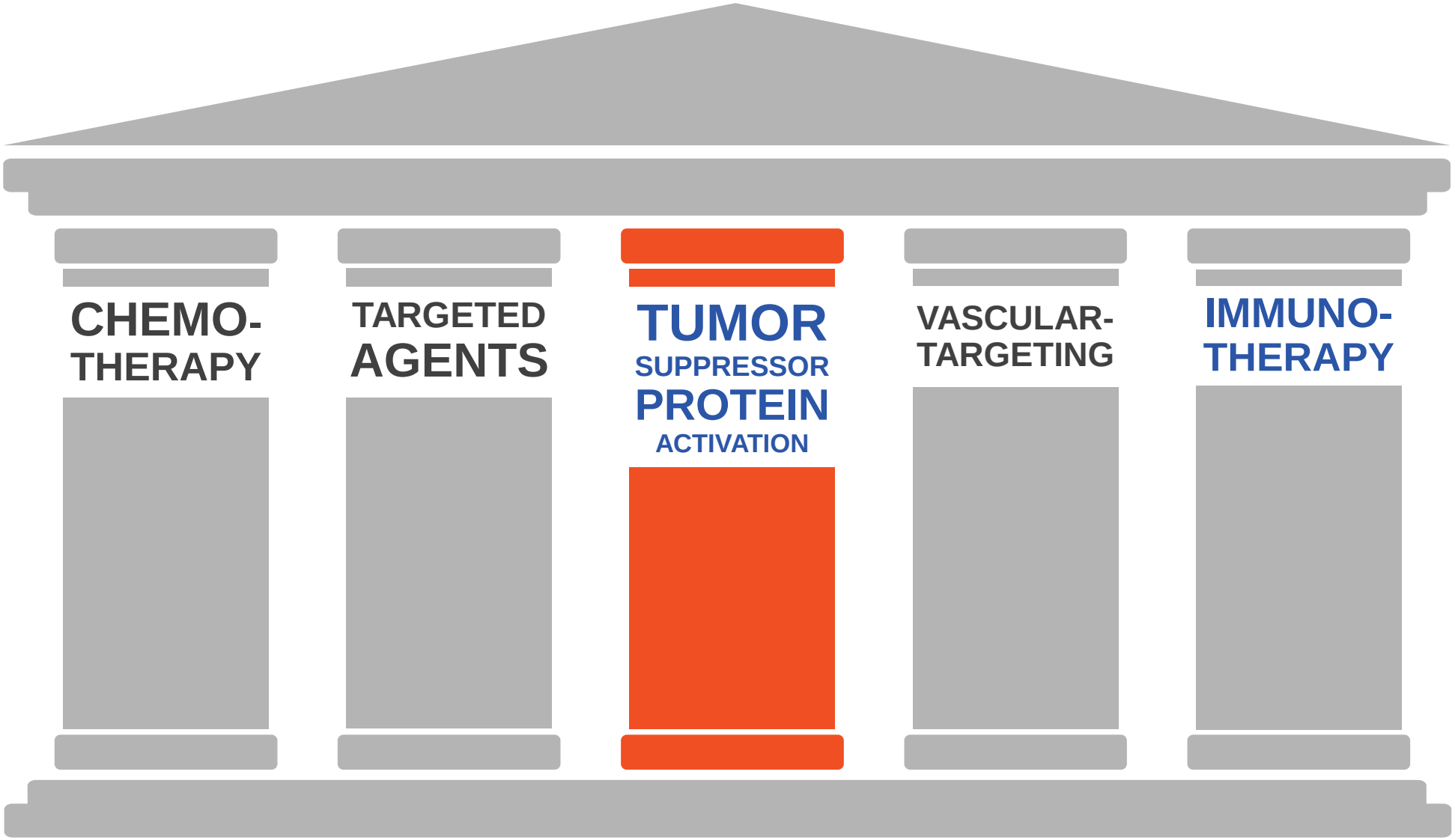
Core Pillars of Cancer Drug Therapy



Harnessing the body's own natural defense mechanisms

Karyopharm Near and Medium-Term Corporate Goals

Next 1-2 Years
(2021-2022)

- Increasing impact on the lives of patients battling cancer
- U.S. XPOVIO approval in 2nd line multiple myeloma in 2021 and subsequent significant increase in total annual sales[1]
  - Increase in total sales to be largely driven by earlier use and longer duration of treatment in patients with multiple myeloma
- Initial approval(s) and commercial launch of XPOVIO in Europe and other international markets[1]
- First U.S. launch of XPOVIO in a solid tumor indication[1]
- Continued clinical development for XPOVIO, eltanexor, and KPT-9274 in additional cancer indications

Next 3-5 Years
(2023-2025)

- Increasing impact on the lives of patients battling cancer
- Additional indication approvals for XPOVIO, including in solid tumors, across U.S. and international markets[1]
- Meaningful revenue contributions from royalties and milestones on international XPOVIO sales[1]
- Continued pipeline expansion for XPOVIO, eltanexor, and KPT-9274
- XPO1 inhibition established as a core therapeutic approach in cancer therapy

[1] Subject to regulatory submission and/or approval(s)

Solid Tumor Update: SEAL Phase 3 Positive Top-Line Results:

Top-Line Phase 3 Data

- Study met primary endpoint with significant increase in progression-free survival in patients with unresectable dedifferentiated liposarcoma following at least two prior therapies
- Hazard ratio=**0.70**; p=**0.023**
- Safety profile consistent with previous clinical studies with fewer hematologic and infectious adverse events as compared to selinexor studies in patients with multiple myeloma and diffuse large B-cell lymphoma
- Full data to be presented in an oral presentation at the Connective Tissue Oncology Society (CTOS) Annual Meeting on November 20, 2020

Strategic Implications

- Significant advance in the treatment of patients with dedifferentiated liposarcoma
- Potential to be first oral treatment available
- Positive pivotal data in liposarcoma demonstrates XPOVIO's substantial potential across multiple solid tumors, representing a major advance for the development and commercial potential of XPOVIO in oncology
  - Consistent with other, earlier stage positive results from ongoing XPOVIO studies in diseases such as endometrial cancer, GBM, melanoma, lung cancer, and others
- Represents entry point for XPOVIO into solid tumor treatment landscape; 9 of top 10 most common and fatal forms of cancer are solid tumors

Innovation with a Purpose: Demonstrate Meaningful Activity in Difficult to Treat Patient Populations and Then Expand, Dramatically

Significant Growth Opportunities

Foundational Beginnings

2nd Line+ multiple myeloma in combination with standard of care drugs

- **BOSTON Study** (Phase 3)
- **STOMP Study** (Phase 1b/2)
- **Selinexor + Pomalidomide + Dexamethasone**
  (Phase 3 expected to start in 2021)

STORM Study
- Penta-refractory MM
- Positive top-line data: 2018
- FDA Approval: 2019

Multiple Myeloma

1

2nd Line+ DLBCL in combination with standard of care drugs

- **XPORT-DLBCL-030** (Phase 2/3)
- **XPORT-DLBCL-025** (Phase 1/2)

SADAL Study
- 3rd line+ DLBCL
- Positive top-line data: 2018
- FDA Approval: 2020

DLBCL

2

Broad utility across numerous solid tumor indications

- **Endometrial Cancer** (Phase 3)
- **GBM** (Phase 1/2)
- **Lung Cancer** (Phase 1)
- **CRC** (Phase 1)
- **Melanoma**
  (Phase 1/2 expected to start in 2021)

SEAL Study
- 3rd line+ dedifferentiated liposarcoma
- Positive top-line data: 2020

Solid Tumors

3

Another Record Quarter for XPOVIO Sales and Key Development Milestones Achieved

Commercial Update

- Q3 2020 XPOVIO net sales of **$21.3M** marking **highest quarterly sales** since launch
- XPOVIO Q3 2020 net sales increase of **15% vs. Q2 2020** driven primarily by increase in new multiple myeloma patients and initial diffuse large B-cell lymphoma (DLBCL) prescriptions
- Initial DLBCL commercial launch **progressing well** with two-thirds of early prescriptions coming from community-based physicians

Pipeline / Clinical Data Update

- Phase 3 SEAL study **meets primary endpoint with significant increase in progression-free survival** in patients with unresectable dedifferentiated liposarcoma (**Hazard Ratio=0.70, p=0.023)**
- sNDA for expanded multiple myeloma indication **assigned March 19, 2021 PDUFA date**
- Additional clinical data **submitted to EMA** in support of MAA in Europe (based on STORM study) and additional information request received from CHMP
- **Encouraging data** from ongoing selinexor studies in patients with solid tumors presented at European Society for Medical Oncology Virtual Congress Conference

Corporate Development and Balance Sheet

- Sharon Shacham, Founder, President, and CSO wins EY Entrepreneur of the Year® 2020 New England Award
- Christy J. Oliger appointed to Board of Directors
- Ended Q3 2020 with **$304.2M** in cash and investments; cash runway expected to be sufficient to fund planned operations into the second half of **2022**

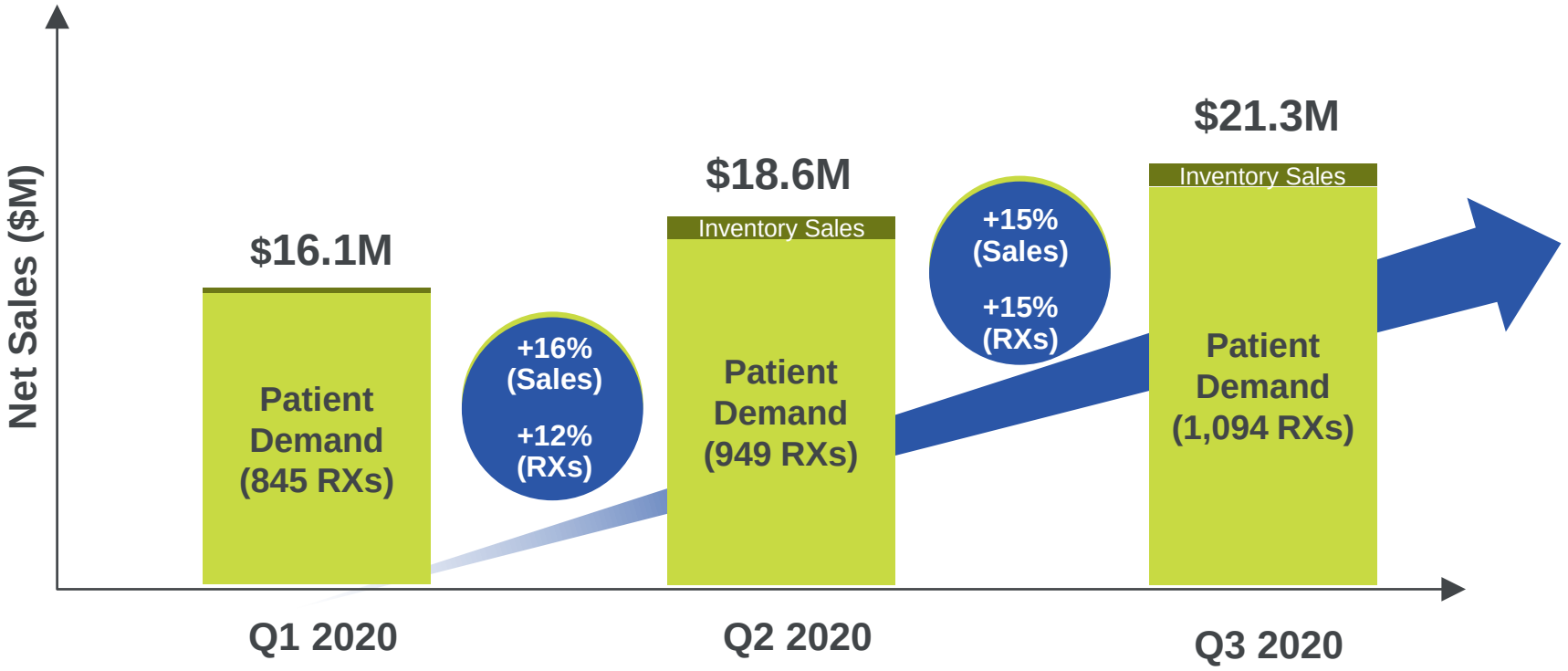
Most Impactful Features of XPOVIO for Physicians Treating Patients with Relapsed Refractory Multiple Myeloma[1]

Feature	Details
1. Rapid response	Patients rapidly responded to XPOVIO combination therapy (STORM study) at a median of 4 weeks, with some responses as early as 1 week
2. Meaningful overall response rate (ORR) in challenging-to-treat populations	25.3% ORR in the challenging-to-treat STORM population is compelling, especially as 100% of patients were refractory to daratumumab and 57% had high risk cytogenetics
3. Novel mechanism of action	Overexpression of XPO1 is a key mechanism of oncogenesis; XPOVIO is the first and only FDA-approved oral XPO1 inhibitor that selectively binds to and blocks XPO1
4. Preventable, manageable, and reversible adverse reaction profile	Prophylactic treatments and dose modifications can be effective at preventing and managing most adverse reactions

[1]Karyopharm market research, July 2020, N=100.

XPOVIO 2020 Quarterly Sales and Prescription Trends

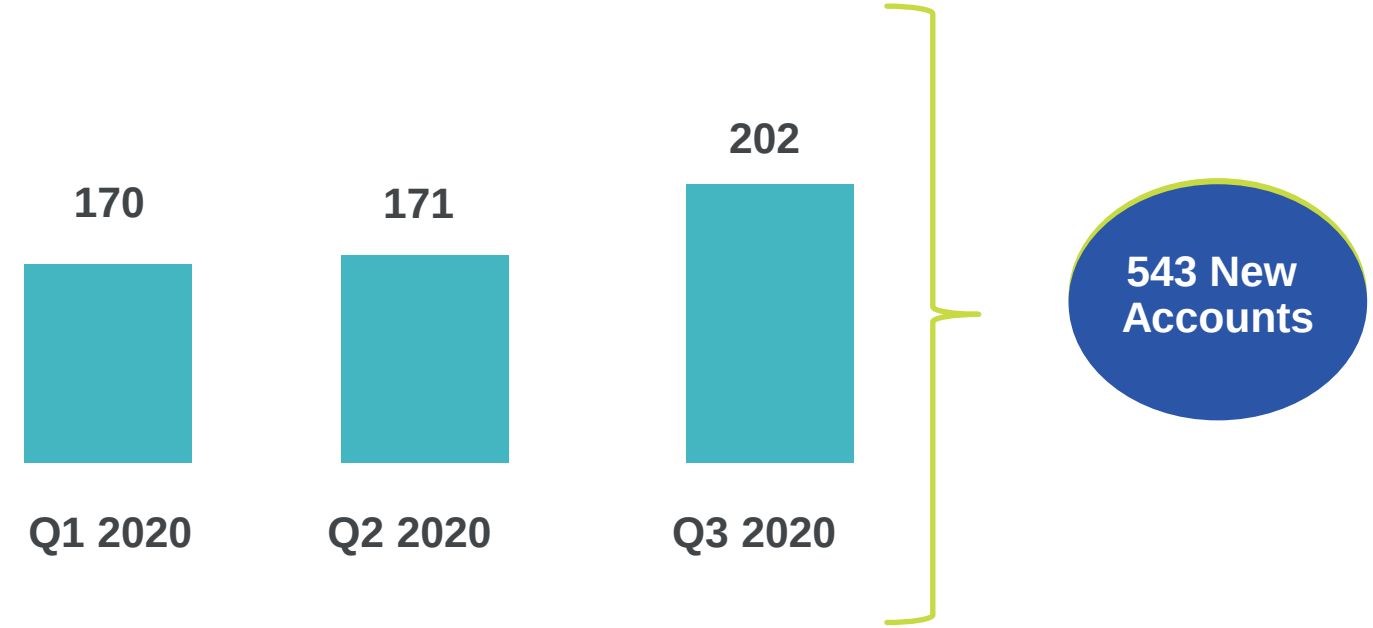
XPOVIO Product Sales and RXs in 2020



- **15% increase** in both net sales and patient demand in Q3 2020 compared to Q2 2020
- **Robust increase** in new multiple myeloma patient starts in Q3 2020 compared to Q2 2020
- Patient demand (RXs) **accelerated in Q3 2020** compared to Q2 2020
- **Majority** of RXs coming from patients with multiple myeloma with initial contributions from DLBCL

XPOVIO Prescriber Base Continues to Grow

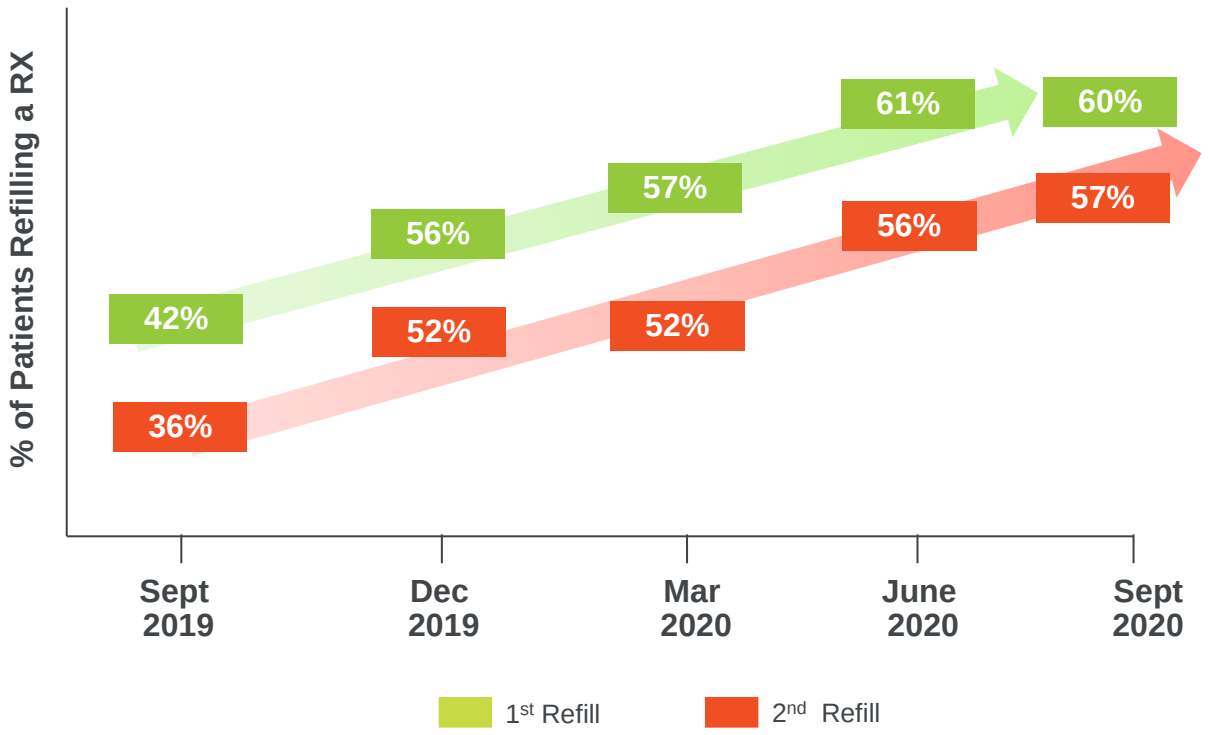
New Accounts Prescribing XPOVIO in 2020



Note: Q3 2020 includes both multiple myeloma and DLBCL treating physicians

Key XPOVIO Patient Metrics Demonstrate Positive Trends

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



Average Treatment Cycles (RXs) Per Patient =

2.9[1]

Patient Discontinuation Rate Due to Side Effects =

13%[1]

[1] Based on patient data from Karyopharm's network of specialty pharmacy providers; prescription refill rates from Sept 2019-Sept 2020, average treatment cycles per patient as of the end of Sept 2020 and discontinuation rate due to side effects YTD 2020.

Key Metrics and Insights from DLBCL Launch

Early Launch Metrics

- Two-thirds of XPOVIO DLBCL prescriptions to date have come from community-based physicians
  - 70% of all DLBCL prescriptions come from community-based physicians and 78% are also treating multiple myeloma patients
- Strong, early refill rates for those patients already eligible for 1st RX refill (~60%; similar to that seen in patients with multiple myeloma)
- Category 2A NCCN compendia listing secured within 2 weeks of approval

Physician Feedback / Early Market Dynamics

- Target physicians most attracted to XPOVIO's response rate as a single agent, oral option, and the ability to treat DLBCL patients in a completely new way
- Strong payer coverage post launch; no on-label patient denials seen to date
- Early physician feedback suggests side effect profile at 60mg 2x per week has been manageable for patients

Source: Karyopharm field reporting and market research

Regulatory Update Across Potential Future Indications

- U.S. BOSTON sNDA
  - FDA has assigned an action date of March 19, 2021 under the Prescription Drug User Fee Act (PDUFA)
  - Review process is actively progressing
  - Potential to expand multiple myeloma indication in the U.S. from penta-refractory setting to patients who have received at least one prior line of therapy
- EU (STORM, BOSTON)
  - Additional STORM data submitted in Q3 2020
  - Received further updated list of outstanding issues from the CHMP; Scientific Advisory Group to convene in the fourth quarter of 2020
  - CHMP opinion on STORM submission expected by end of 2020
  - BOSTON MAA expected to be submitted before end of 2020 (contingent upon and following receipt of CHMP's opinion)
- EU (SADAL)
  - Evaluating regulatory and market access strategy

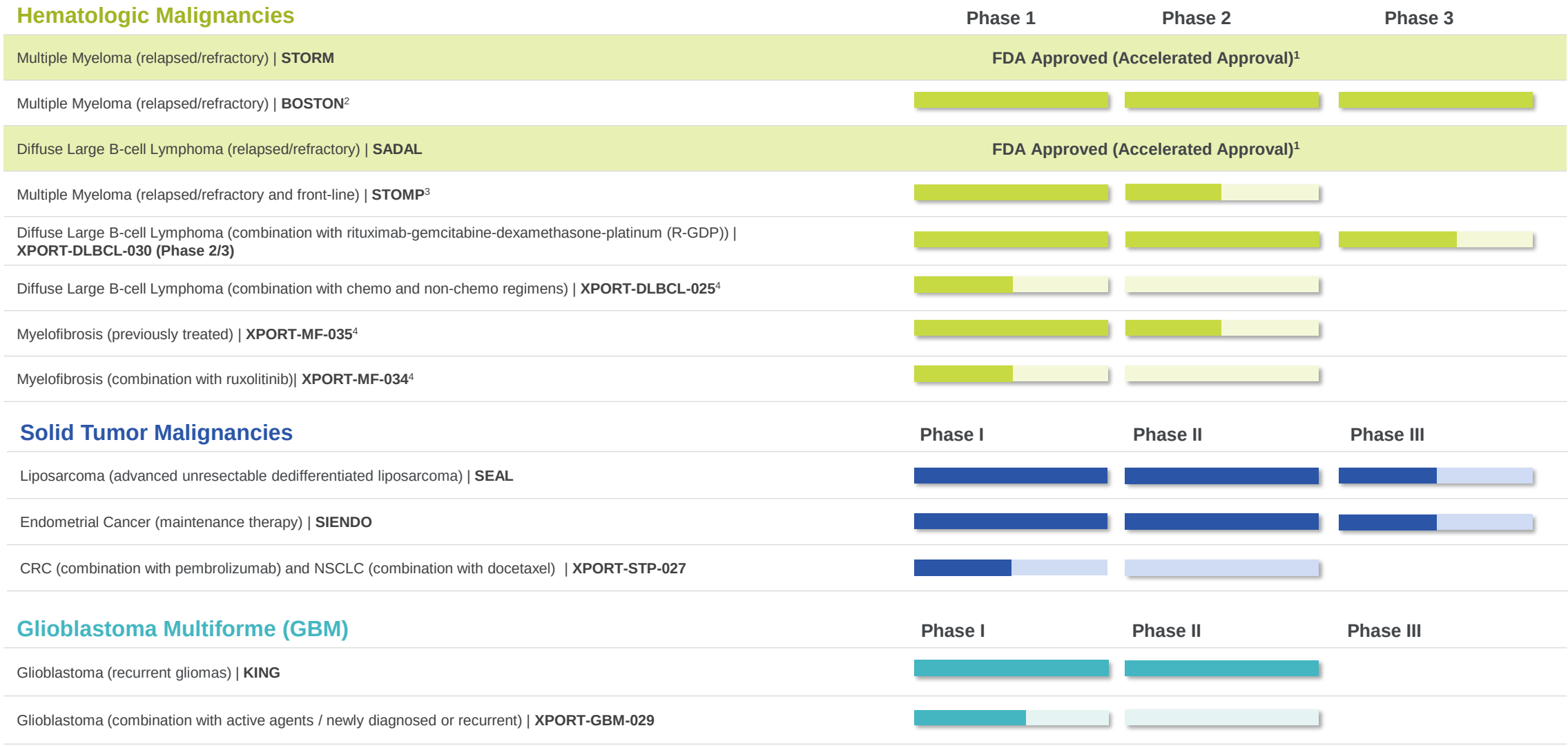
Key Future Inflection Point for Karyopharm: Potential XPOVIO Label Expansion Based on the BOSTON Study

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

	Median # of Prior Therapies	XPOVIO Dose Frequency	ORR	Median Progression Free Survival (in months)	Mean Duration of Treatment (in months)
	~6,000 Patients treated in the 4th line+ setting annually in the U.S.[5]				
STORM[1,2] Study (Penta-Refractory)	**8**	**Twice per week** (in combination with dexamethasone)	**25%**	**3.7**	**3**
	~30,000 patients treated in the 2nd and 3rd line settings annually in the U.S.[5]				
BOSTON Study[3,4] (1–3 Prior Therapies)	**2**	**Once per week** (in combination with once-weekly Velcade and dexamethasone)	**76%**	**13.9**	**10**

[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] Dimopoulos M, et al. ASCO 2020. Abstract 8501. [4] sNDA requesting expanded indication for XPOVIO based on data from the BOSTON study currently under review by FDA and assigned a March 19, 2021 PDUFA action date. [5] Karyopharm analysis based on data from Decision Resources, Kantar Cancer Impact and SEER Cancer Stat Facts, National Cancer Institute.

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] Study expected to start in 2020-2021.

Third Quarter Financial Results

Mike Mason
Chief Financial Officer

Third Quarter 2020 Financial Results

Statement of Operations	Three Months Ended Sept 30th	
	2020	2019
Total Revenue	$21.3M	$13.1M
XPOVIO Net Sales	$21.3M	$12.8M
License and Other Revenue	-	$0.3M
Total Operating Expenses	$68.4M	$52.6M
Cost of Sales	$0.4M	$1.0M
Research and Development Expense	$37.0M	$26.3M
Selling, General & Administrative Expense	$30.9M	$25.3M
Net Loss	$53.5M ($0.73 per share)	$41.4M ($0.67 per share)

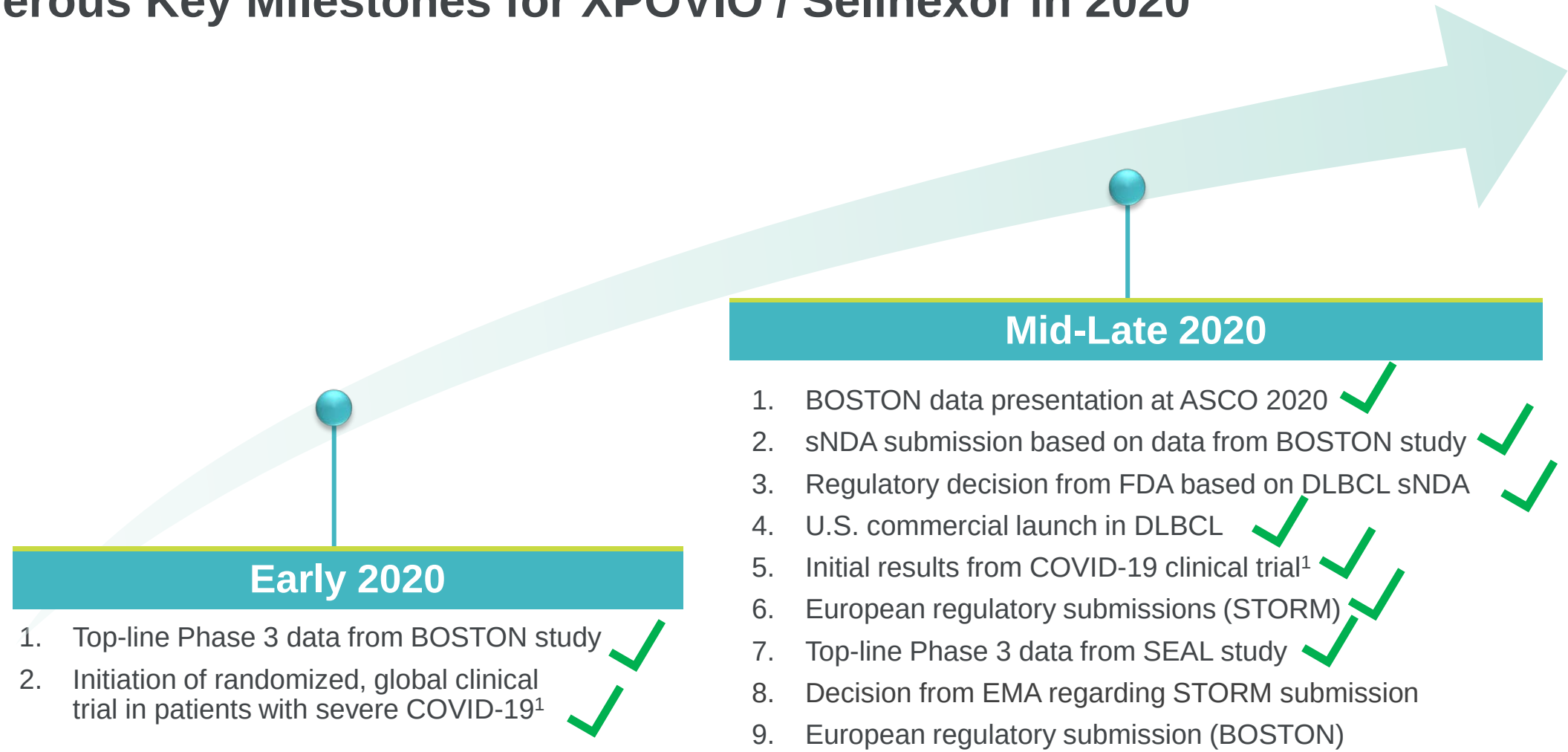
Balance Sheet and Financial Guidance

Balance Sheet	September 30, 2020	December 31, 2019
Cash, Cash Equivalents, Restricted Cash and Investments	$304.2M	$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 second half 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 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[1]

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[1]
6. European regulatory submissions (STORM)
7. Top-line Phase 3 data from SEAL study
8. Decision from EMA regarding STORM submission
9. European regulatory submission (BOSTON)
10. Start of confirmatory Phase 3 Study in DLBCL in support of accelerated approval

[1] Interim analysis indicated that the trial was unlikely to meet its pre-specified primary endpoint across the entire patient population studied and the trial has since been discontinued.

Questions?

Answers.