Karyopharm® Therapeutics

Investor Conference Call:

Fourth Quarter and Full Year 2020 Financial Results and Business Update

February 11, 2021

On Today's Call

Prepared Remarks

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

Joining for Q&A Session

- **John Demaree**, *Chief Commercial Officer*
- **Jatin Shah, MD,** *Executive Vice President, Chief Medical Officer*
- **Stephen Mitchener**, *Chief Business Officer*
- **Ian Karp**, MBA, Senior *Vice President, Investor and Public Relations*

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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 guidance on its 2021 non-GAAP research and development and selling, general and administrative expenses; 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 or regulatory approval of drug candidates by Karyopharm's competitors for products or product candidates in which Karyopharm is currently commercializing or developing; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any of its products or product candidates. 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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.

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Q4 2020 and Recent Achievements Help Position Karyopharm For Significant Future Growth

Commercial Update

- **Expanded U.S. approval** of XPOVIO® and commercial launch (Dec 18, 2020)
- Q4 and full year 2020 XPOVIO net sales of **$20.2M** and **$76.2M**, respectively
- National Comprehensive Cancer Network® adds **three XPOVIO treatment regimens** to its clinical practice guidelines for multiple myeloma
- **>170** and **>700 new** physicians / accounts prescribed XPOVIO in Q4 and full year 2020, respectively

Pipeline / Clinical Data Update

- **Positive CHMP opinion** issued for NEXPOVIO® (selinexor) MAA in Europe based on STORM study (multiple myeloma)
- **Regulatory approval** in Israel
- **Positive Phase 3 BOSTON study** results published in the *Lancet* (multiple myeloma)
- **Positive Phase 3 Seal study** results presented at CTOS annual meeting (liposarcoma)
- **Phase 3 SIENDO study** passes planned interim futility analysis (endometrial cancer)
- **1st patient dosed** in Phase 3 confirmatory trial in DLBCL (XPORT-DLBCL-30)

Corporate Development and Balance Sheet

- Q4 and full year 2020 license revenue of **$14.9M** and $**31.9M**, respectively
- Ended Q4 2020 with **$276.7M** in cash, cash equivalents, restricted cash and investments
- Cash runway expected to be sufficient to fund planned operations into **late 2022**

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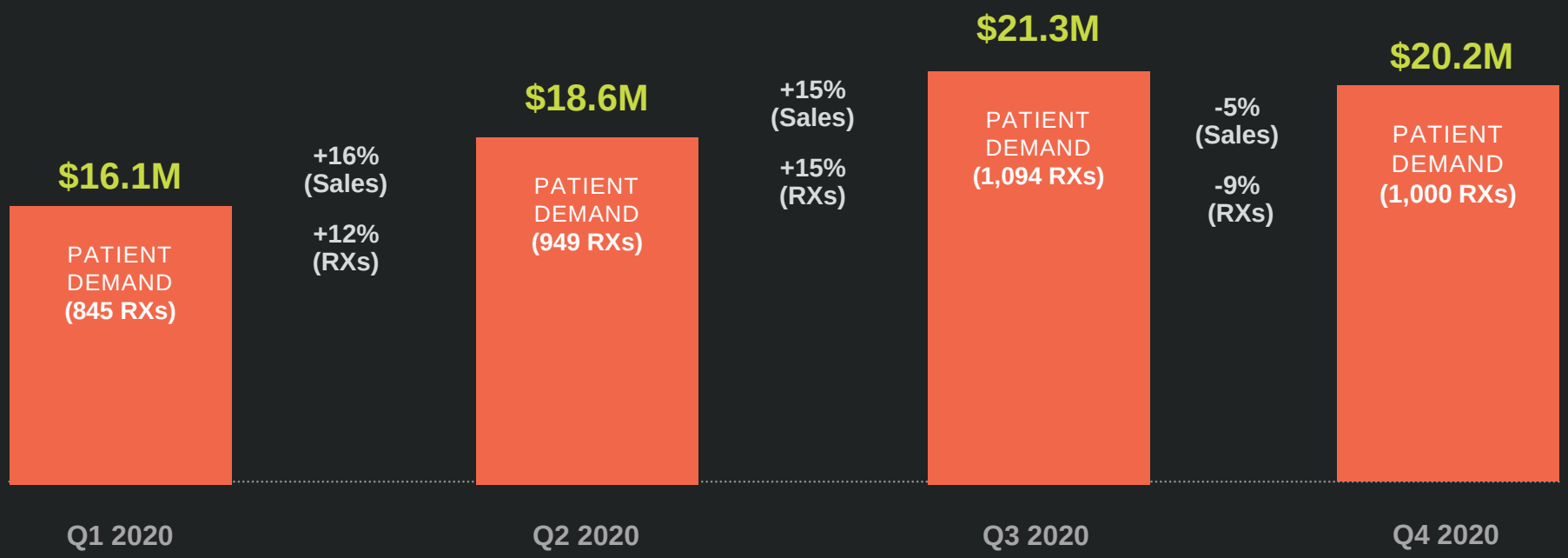
XPOVIO 2020 Quarterly Net Product Sales and Prescription (RX) Trends



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Update on Q4 2020 and Recent Sales Trends

- Q4 XPOVIO sales primarily affected by:
  1. Surge in U.S. COVID-19 cases
     - Fewer patient visits to their health care providers
     - Reduced ability of Karyopharm commercial team to access customers in-person
  2. Increased competition in the penta-refractory multiple myeloma and third line+ DLBCL patient settings
- Strong return to sales growth seen in December and January following declines in October and November of 2020
  - Positive sales momentum seen in December 2020 and January 2021 following NCCN guideline update adding three XPOVIO regimens to its treatment recommendations and the expanded XPOVIO FDA approval granted on December 18th
  - Increase in estimated new patient starts seen in December and January as compared to October and November

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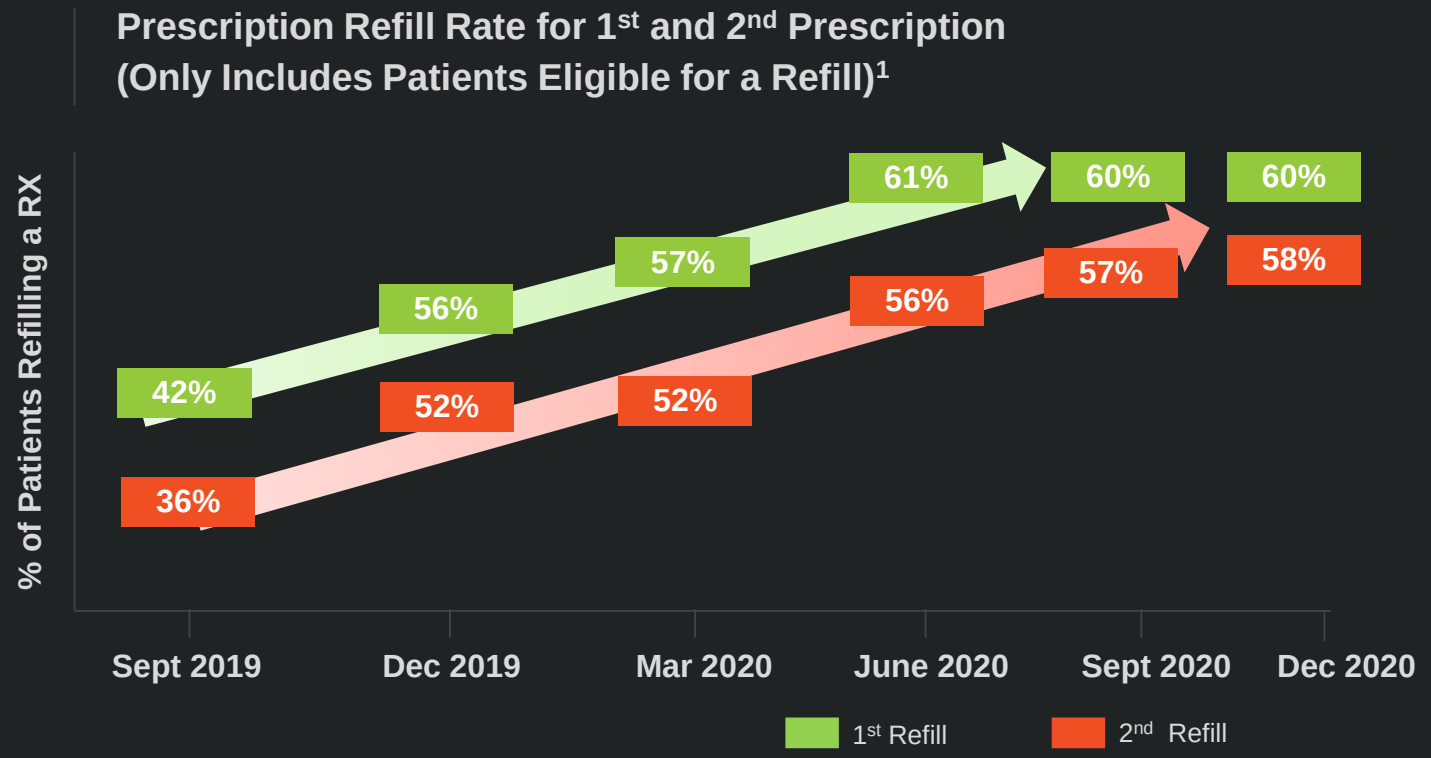
Key XPOVIO Patient Metrics in 2020



2.9[1]

Average Treatment Cycles (RXs) Per Patient

13%[1]

Patient Discontinuation Rate Due to Side Effects

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

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Status Update on Commercial Expansion in Europe

1. Positive CHMP opinion in Europe issued on January 29, 2021

- Positive opinion highlights the CHMP's recognition of the positive clinical benefit-risk profile for oral NEXPOVIO (expected brand name for selinexor in Europe)
- European Commission's final decision on the NEXPOVIO MAA expected by April 2021
- Karyopharm to submit second regulatory filing based on data from the confirmatory Phase 3 BOSTON study by April 2021

2. Selinexor added to European treatment guidelines in November 2020

- Multiple myeloma treatment guidelines developed by the European Hematology Association (EHA) and European Society for Medical Oncology (ESMO) added SVd* as a treatment option in the second line setting and Sd** for patients with triple-class refractory disease

3. Advancing partnership discussions for international markets

- Evaluating potential collaboration strategies with commercial partners for Europe and Japan
- Largest revenue opportunity in Europe to come following potential approval based on data from the BOSTON study which could occur before the end of 2021[1]

*Selinexor, Velcade®, dexamethasone
** Selinexor, dexamethasone

[1] Subject to regulatory submission and approval

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Karyopharm's Novel Pipeline | Selinexor

HEMATOLOGIC MALIGNANCIES | STUDY NAME	PHASE 1	PHASE 2	PHASE 3
Multiple Myeloma (relapsed/refractory) | **STORM**	**APPROVED[1]**		
Multiple Myeloma (relapsed/refractory) | **BOSTON[2]**	**APPROVED[1]**		
Diffuse Large B-cell Lymphoma (relapsed/refractory) | **SADAL**	**APPROVED[1]**		
Multiple Myeloma (relapsed/refractory and front-line) | **STOMP[3]**			
Diffuse Large B-cell Lymphoma (combination with rituximab-gemcitabine-dexamethasone-platinum (R-GDP)) **XPORT-DLBCL-030 (Phase 2/3)**			
Diffuse Large B-cell Lymphoma (combination with chemo and non-chemo regimens) | **XPORT-DLBCL-025[4]**			
Myelofibrosis (previously treated) | **XPORT-MF-035[4]**			
Myelofibrosis (combination with ruxolitinib)| **XPORT-MF-034[4]**			

Additional new Phase 3 study (XPORT-MM-031) evaluating XPOVIO in combination with pomalidomide and dexamethasone in patients with previously treated multiple myeloma expected to start in **2021**

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[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 2021.

Karyopharm's Novel Pipeline | Selinexor

SOLID TUMOR MALIGNANCIES | STUDY NAME	PHASE 1	PHASE 2	PHASE 3
Liposarcoma (advanced unresectable dedifferentiated liposarcoma) | **SEAL**			
Endometrial Cancer (maintenance therapy) | **SIENDO**			
NSCLC (combination with docetaxel) | **XPORT-STP-027**			
CRC (combination with pembrolizumab) | **XPORT-STP-027**			
GLIOBLASTOMA MULTIFORME (GBM) | STUDY NAME	**PHASE 1**	**PHASE 2**	**PHASE 3**
Glioblastoma (recurrent gliomas) | **KING**			
Glioblastoma (combination with active agents / newly diagnosed or recurrent) | **XPORT-GBM-029**			

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Fourth Quarter and Full Year 2020 Financial Results

Mike Mason
Chief Financial Officer

Q4 and Full Year 2020 Financial Results

Statements of Operations	Three Months Ended December 31st		Twelve Months Ended December 31st	
	2020	2019	2020	2019
Total Revenue	$35.1M	$18.1M	$108.1M	$40.9M
XPOVIO Net Sales	$20.2M	$17.7M	$76.2M	$30.5M
License and other Revenue	$14.9M	$0.4M	$31.9M	$10.4M
Total Operating Expenses	$72.2M	$61.4M	$279.9M	$230.2M
Cost of Sales	$1.1M	$1.4M	$2.7M	$2.4M
Research and Development Expenses	$37.2M	$31.6M	$150.8M	$122.3M
Selling, General & Administrative Expenses	$33.9M	$28.4M	$126.4M	$105.4M
Net Loss	$43.4M ($0.59 per share)	$48.6M ($0.76 per share)	$196.3M ($2.72 per share)	$199.6M ($3.22 per share)

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Balance Sheet and Financial Guidance

Balance sheet	December 31, 2020	December 31, 2019
Cash, Cash Equivalents, Restricted Cash and Investments	$276.7M	$265.8M

- **Non-GAAP R&D and SG&A expenses are expected to be in the range of $280-300M for the full year 2021[1]**
- **Cash runway expected to be sufficient to fund planned operations into late 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.

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Numerous Expected Key Milestones in 2021

1H 2021

1. CHMP opinion on STORM MAA ✓
2. Start of confirmatory Phase 3 Study in DLBCL in support of 2020 accelerated approval ✓
3. EMA conditional approval based on STORM data[1]
4. EMA submission of BOSTON study data (Type II variation)
5. Increased U.S. XPOVIO sales following expanded FDA approval in multiple myeloma

2H 2021

1. SIENDO Phase 3 study fully enrolled and topline data announced
2. EMA expanded approval based on BOSTON study[1]
3. Initiation of Phase 3 study evaluating XPOVIO + pomalidomide in patients with multiple myeloma
4. Initiation of Phase 2 study evaluating XPOVIO + pembrolizumab in patients with metastatic melanoma
5. Additional combination data with XPOVIO and other standard of care anti-cancer drugs to be presented at medical meetings
6. Continued, increased U.S. XPOVIO sales

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

QUESTIONS?

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