A Commercial-Stage Pharmaceutical Company Pioneering Novel Cancer Therapies

November 2020

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. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended Sept 30, 2020, which was filed with the Securities and Exchange Commission (SEC) on November 2, 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.

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Karyopharm at a Glance

- Commercial-stage, global pharmaceutical company with one FDA-approved drug in two indications and three additional drug candidates in clinical development
- Industry leader in targeting nuclear export dysregulation as a mechanism to treat cancer
- First drug, XPOVIO® (selinexor), received first accelerated approval from the FDA in July 2019 (penta-refractory multiple myeloma)
- Pivotal Phase 3 BOSTON study in patients with multiple myeloma following 1-3 lines of prior therapy met its primary endpoint of a statistically significant increase in progression-free survival(PFS); PDUFA date for potential label expansion: March 19, 2021
- Second FDA approval received in June 2020 for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL)
- Ongoing clinical development for selinexor and next-generation programs in earlier lines of treatment, in combination trials, and in additional tumor types across both hematologic and solid tumor malignancies
- All programs developed in-house with patent protection on lead compound to 2032+
- Numerous data read-outs and potential key milestones expected over the next 12-24 months

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Agenda

- Approved XPOVIO Indications
- Commercial and Financial Highlights
- Pipeline and Future Opportunities
- Appendix: Clinical Data
- Appendix: Commercial Insights

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XPOVIO® (selinexor) Received Accelerated Approval in Multiple Myeloma

FDA Approved in July, 2019

- XPOVIO is the **first** and **only** nuclear export / XPO1 inhibitor approved by the FDA
- XPOVIO is the **first** and **only** prescription medicine approved for patients whose multiple myeloma is refractory to proteasome inhibitors, immunomodulatory agents, and an anti-CD38 monoclonal antibody

XPOVIO is indicated 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)[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. The randomized Phase 3 BOSTON study evaluating selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone will serve as the confirmatory trial.

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

[1]XPOVIO Prescribing Information.

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XPOVIO® (selinexor) Received Accelerated Approval in RR DLBCL

FDA Approved in June, 2020

- XPOVIO is 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)

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).

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

[1]XPOVIO Prescribing Information

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Safety Highlights from the XPOVIO Prescribing Information[1]

- No Black Box Warnings
- No Contraindications
- Patient Medication Guide
- Monitoring Instructions and Recommended Concomitant Treatments
  - Monitor complete blood count (CBC) with differential, standard blood chemistries, body weight, nutritional status, and volume status at baseline and during treatment as clinically indicated. Monitor more frequently during the first three months of treatment
  - Patients advised to maintain adequate fluid and caloric intake throughout treatment. IV hydration should be considered for patients at risk of dehydration
  - Patients receiving XPOVIO should be provided prophylactic treatment with a 5-HT3 receptor antagonist and other anti-nausea agents prior to and during treatment with XPOVIO
  - Recommended XPOVIO dosage reductions and dosage modifications for adverse reactions are included in the Prescribing Information
- Warnings and Precautions
  - Thrombocytopenia
  - Neutropenia
  - Gastrointestinal Toxicity
  - Hyponatremia
  - Serious Infection
  - Neurological Toxicity
  - Embryo-Fetal Toxicity

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

[1]XPOVIO Prescribing Information

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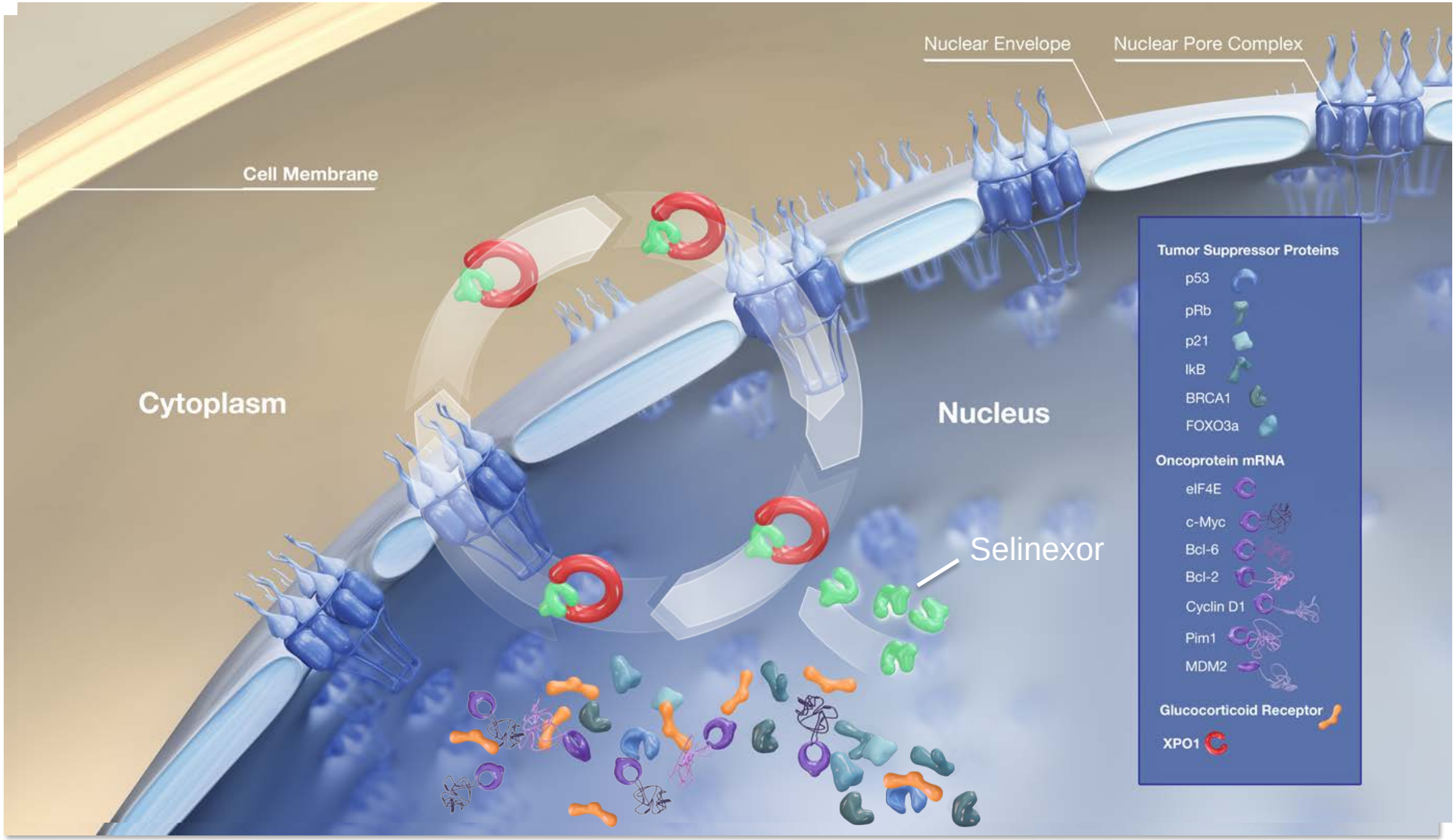
XPOVIO Leverages Unique, First-In-Class Mechanism of Action: Inhibition of XPO1[1-4]

Inhibition of XPO1 impacts tumor cells via 3 core mechanisms

1. Increases nuclear levels and activation of tumor suppressor proteins
2. Traps oncoprotein mRNA in the nucleus leading to reduced oncoprotein levels
3. Retains activated glucocorticoid receptor in the nucleus



[1] Gupta A, et al. Therapeutic targeting of nuclear export inhibition in lung cancer. J Thorac Oncol. 2017;12(9):1446-1450. [2] Sun Q, et al. Inhibiting cancer cell hallmark features through nuclear export inhibition. Signal Transduct Target Ther. 2016;1:16010.
[3] Gandhi UH, et al. Clinical implications of targeting XPO1-mediated nuclear export in multiple myeloma. Clin Lymphoma Myeloma Leuk. 2018;18(5):335-345. [4] Gravina GL, et al. Nucleo-cytoplasmic transport as a therapeutic target of cancer. J Hematol Oncol. 2014;7:85

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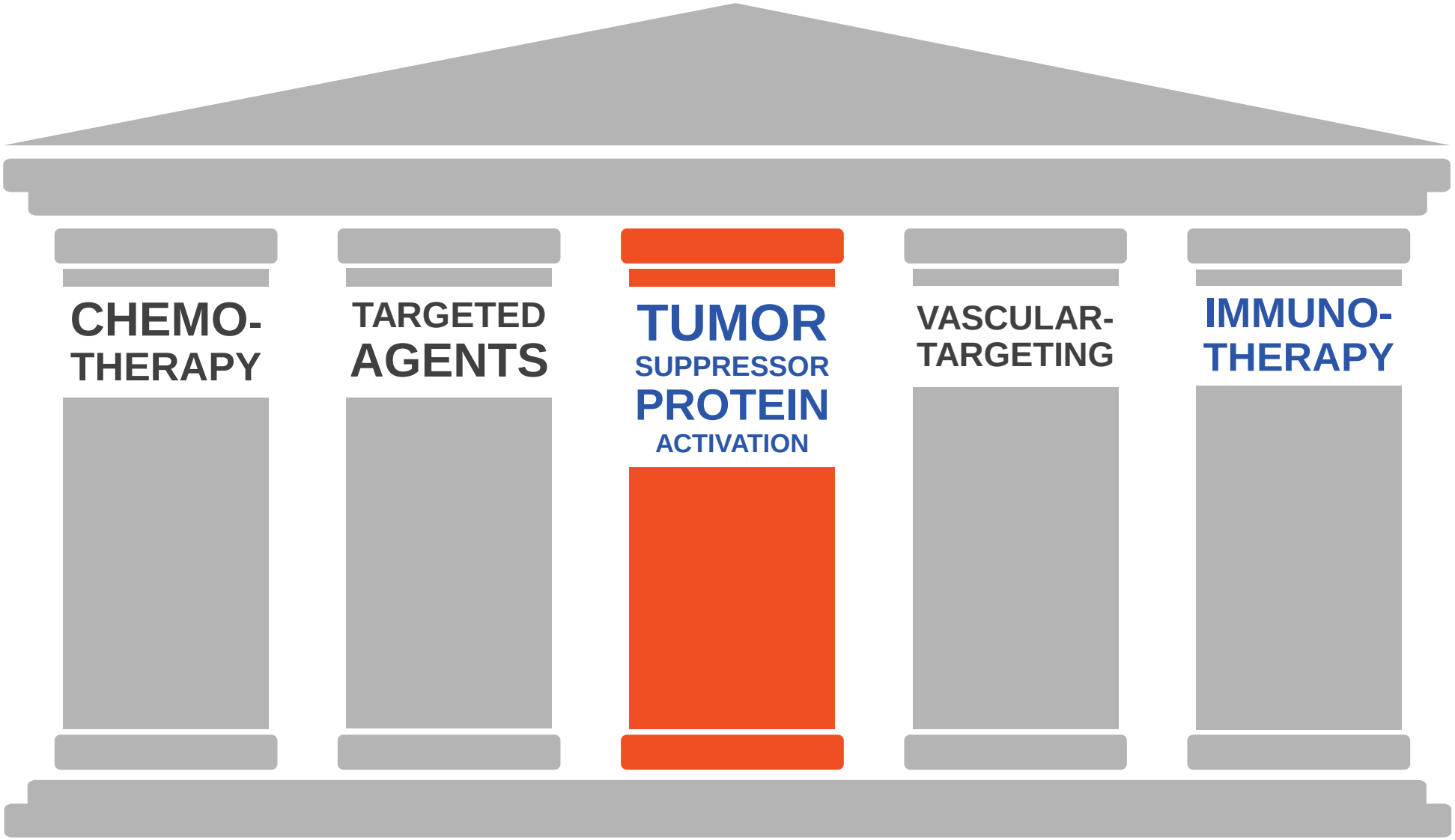
Core Pillars of Cancer Drug Therapy



Harnessing the body's own natural defense mechanisms

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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 (MM)

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

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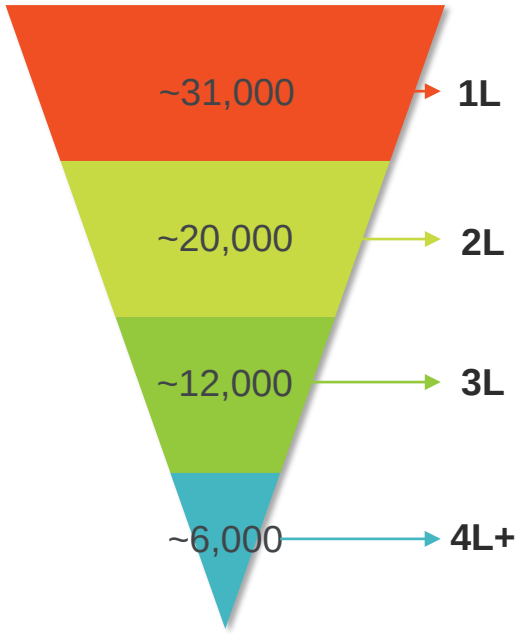
Multiple Myeloma Patients Treated by Line of Therapy (U.S.)

~69,000 Patients Treated With Drug Therapy in 2019

Patients by Line of Treatment

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



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.

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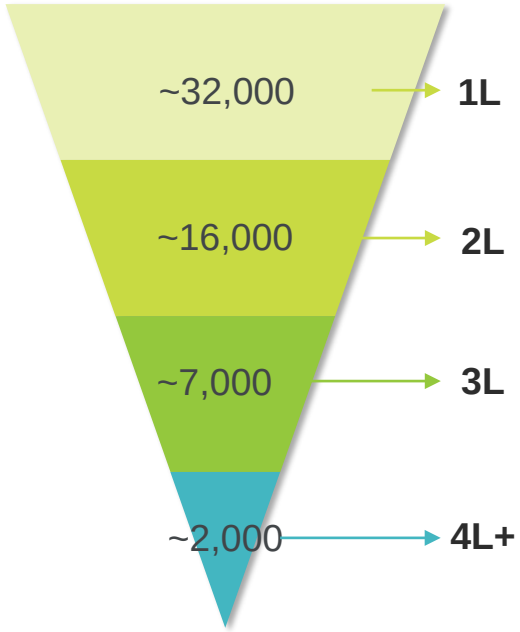
DLBCL Patients Treated by Line of Therapy (U.S.)

~57,000
Patients treated with drug therapy in 2019

Patients by Line of Treatment

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

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



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

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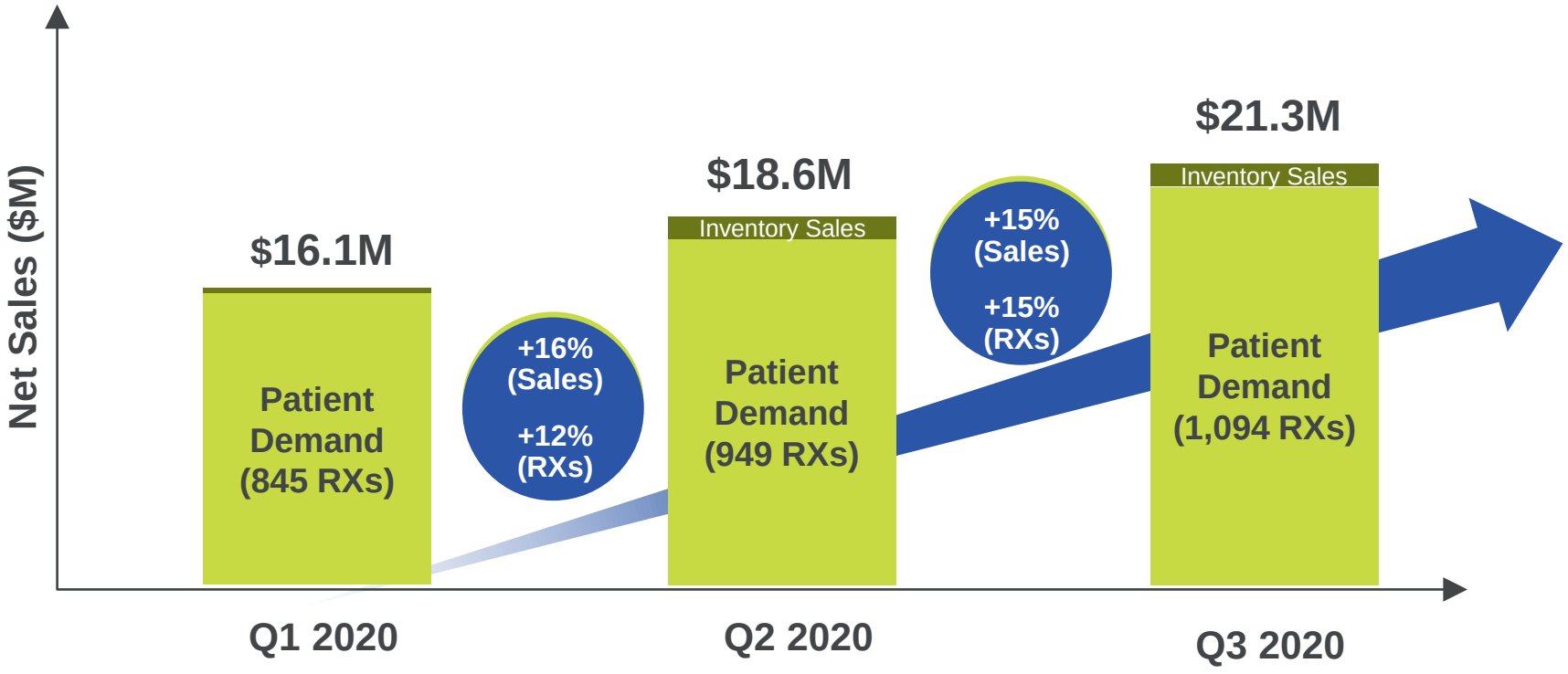
XPOVIO 2020 Quarterly Sales and Prescription Trends

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

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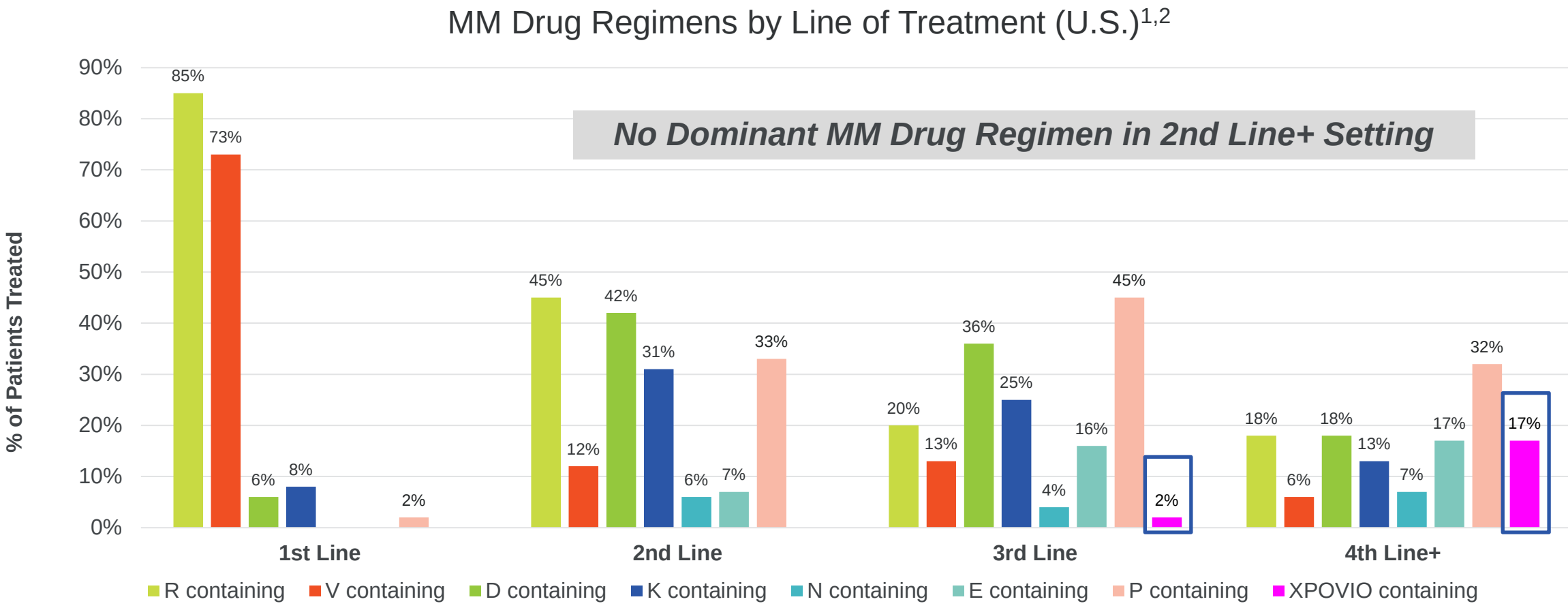
No Dominant MM Drug Regimen in 2nd Line+ Setting With Numerous Drug Combinations Used to Meet Individual Patients Needs



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®, E = Empliciti®, P= Pomalyst®

[1] Karyopharm market research (Post Launch ATU Survey Wave 2 (Mar 20), 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.

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

2019 Worldwide Sales[1]

Immunomodulatory Agents	• Revlimid®: $11B • Pomalyst®: $2.5B
Proteasome Inhibitors	• Velcade®: $1.6B • Kyprolis®: $1B
Monoclonal Antibodies	• Darzalex®: $3B

[1] EvaluatePharma, February 2020.

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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)

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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.

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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.

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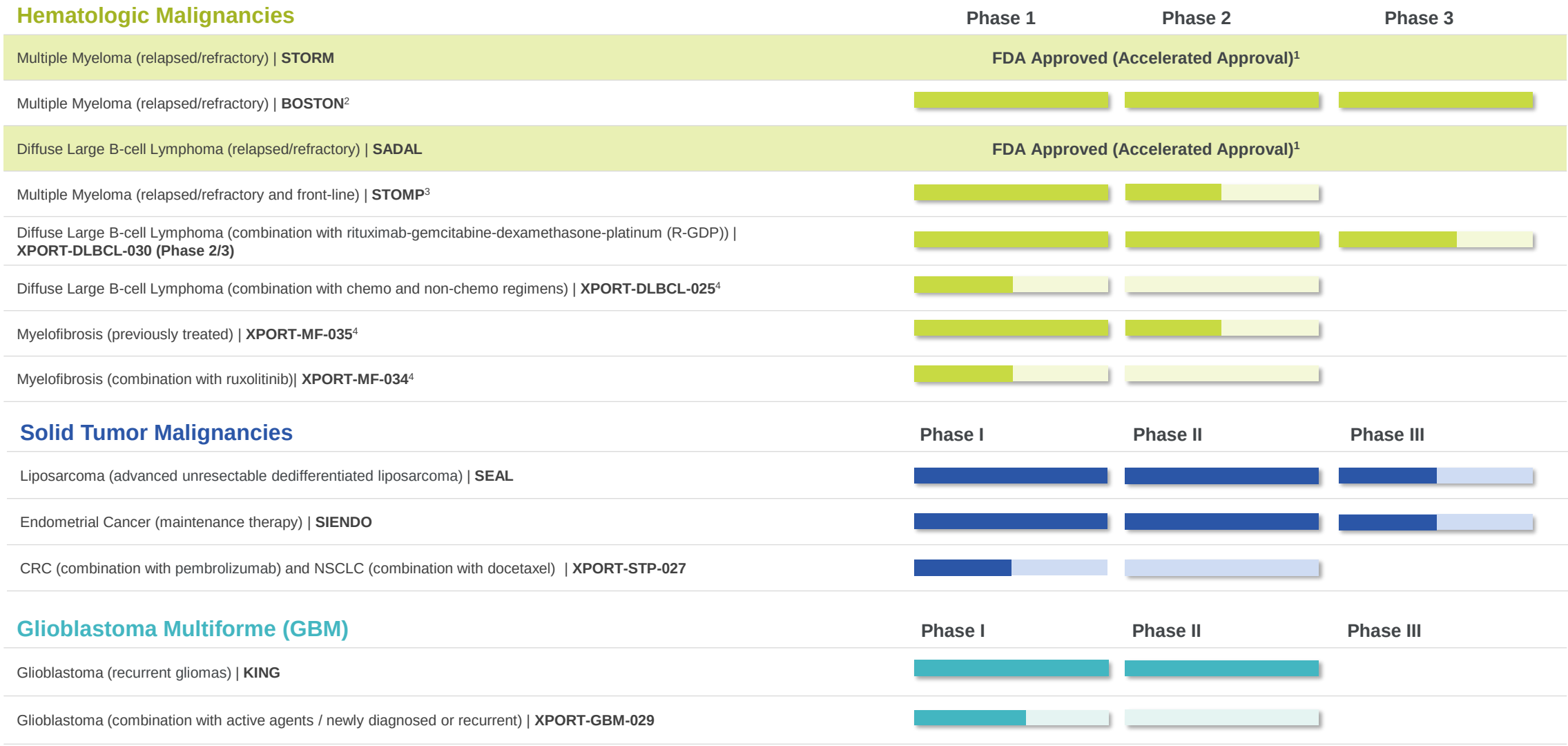
Karyopharm's Novel Pipeline | Selinexor



[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.

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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 2020-2021. [2] Study start pending submission and acceptance of IND.

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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

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Other Pipeline Programs

Eltanexor (KPT-8602)

- Oral, 2nd generation SINE compound
- Preclinical results show substantially less brain penetration versus selinexor
- Evaluated in Phase 1/2 study in myelodysplastic syndrome (MDS), colorectal cancer (CRC) and metastatic castrate-resistant prostate cancer (mCRPC)
- Reported updated data from Phase 1 portion at ASH 2017, CRC data at ESMO 2018, mCRPC data at ASCO-GU 2019 and MDS data at ASH 2019
- Additional clinical development planned in MDS
- Adverse events were generally consistent with other studies to date in >50 patients

KPT-9274

- Oral dual Inhibitor of PAK4 and NAMPT
- In Phase 1 clinical testing in advanced solid tumors
- Generally well tolerated (n=21) with early signals of anti-tumor activity
- Additional supportive preclinical research presented at ASH 2017

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Current Partnerships

Commercial partnerships to serve global markets

Antengene Corporation

Licensing partner for selinexor, eltanexor, verdinexor and KPT-9274 in China, South Korea, Taiwan, Australia and other Asia-Pacific markets, with the exception of Japan[1]

Neopharm Group

Exclusive distribution agreement for the commercialization of XPOVIO in Israel and the Palestinian Authority[2]

Europe, Japan and Other Key Markets

Seeking potential collaboration arrangements with commercial partners; analyzing potential for Karyopharm to commercialize in select European markets

Karyopharm is committed to working across the globe to bring novel therapies to patients

[1] Original transaction in May 2018 for China and some other Asian markets; territory agreement was expanded in May 2020 to include additional Asia-Pacific markets. [2] In February 2020, Karyopharm and Promedico, a fully-owned Neopharm LTD company, entered into an exclusive distribution agreement in Israel and the Palestinian Authority

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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)

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Questions?

Answers.

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STORM Study: Patients Studied in Part 2 of STORM Study Had Highly Refractory Disease and Included Patients With Significant Co-Morbidities

Key Patient Characteristics[1,2] (n=83)	
Refractory to all five of the standard of care myeloma drugs: bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab	100%
Refractory to 2 PIs, 2 IMIDs, and daratumumab	100%
Prior treatment regimens, median (range)	8 (4-18)
High-risk Cytogenetics (Includes any of del(17p)/p53, t(14; 16), t(4; 14), 1q21)	57%

Broad Enrollment Criteria

- No upper age limit (included patients > 75 years old)
- Moderate-to-severe renal dysfunction
- Hematopoietic function with up to Grade 2 cytopenia
  - ANC ≥ 1000/mm^3
  - Hemoglobin ≥ 8.5g/dL
  - Platelets ≥ 75,000/mm^3 or ≥ 50,000/mm^3 if 50% marrow plasmacytosis
- Permitted prior infections, thromboembolism, heart disease, and concomitant medications

STORM study was a single-arm clinical trial in which patients received oral XPOVIO 80 mg and dexamethasone 20 mg, twice weekly

[1]XPOVIO Prescribing Information.
[2] The accelerated approval of XPOVIO was based upon the efficacy and safety in a prespecified subgroup analysis of the 83 patients whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab, as the benefit-risk ratio appeared to be greater in this more heavily pretreated population than in the overall trial population.

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Overview of Efficacy Data for Accelerated Approval of XPOVIO (n=83)

Key Efficacy Data in Patient Population Supporting Approval (n=83)[1]

25.3%

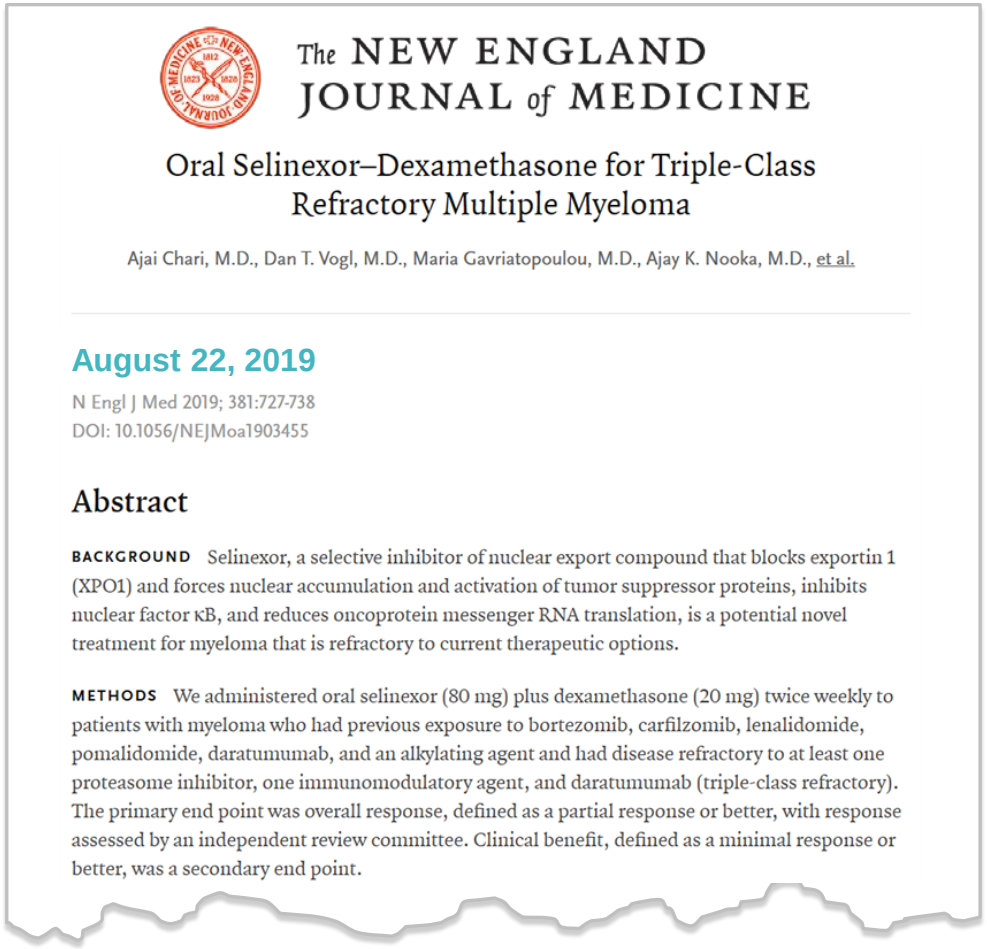
Overall Response Rate (ORR)

Including

- **1** Stringent complete response
- **0** Complete responses
- **4** Very good partial responses
- **16** Partial responses

- Median time to response: **4** weeks
- Median duration of response: **3.8** months

Full STORM results from all 122 patients published in NEJM



The NEW ENGLAND JOURNAL of MEDICINE

Oral Selinexor–Dexamethasone for Triple-Class Refractory Multiple Myeloma

Ajai Chari, M.D., Dan T. Vogl, M.D., Maria Gavriatopoulou, M.D., Ajay K. Nooka, M.D., et al.

August 22, 2019

N Engl J Med 2019; 381:727-738
DOI: 10.1056/NEJMoa1903455

Abstract

BACKGROUND Selinexor, a selective inhibitor of nuclear export compound that blocks exportin 1 (XPO1) and forces nuclear accumulation and activation of tumor suppressor proteins, inhibits nuclear factor κB, and reduces oncoprotein messenger RNA translation, is a potential novel treatment for myeloma that is refractory to current therapeutic options.

METHODS We administered oral selinexor (80 mg) plus dexamethasone (20 mg) twice weekly to patients with myeloma who had previous exposure to bortezomib, carfilzomib, lenalidomide, pomalidomide, daratumumab, and an alkylating agent and had disease refractory to at least one proteasome inhibitor, one immunomodulatory agent, and daratumumab (triple-class refractory). The primary end point was overall response, defined as a partial response or better, with response assessed by an independent review committee. Clinical benefit, defined as a minimal response or better, was a secondary end point.

[1] XPOVIO Prescribing Information.

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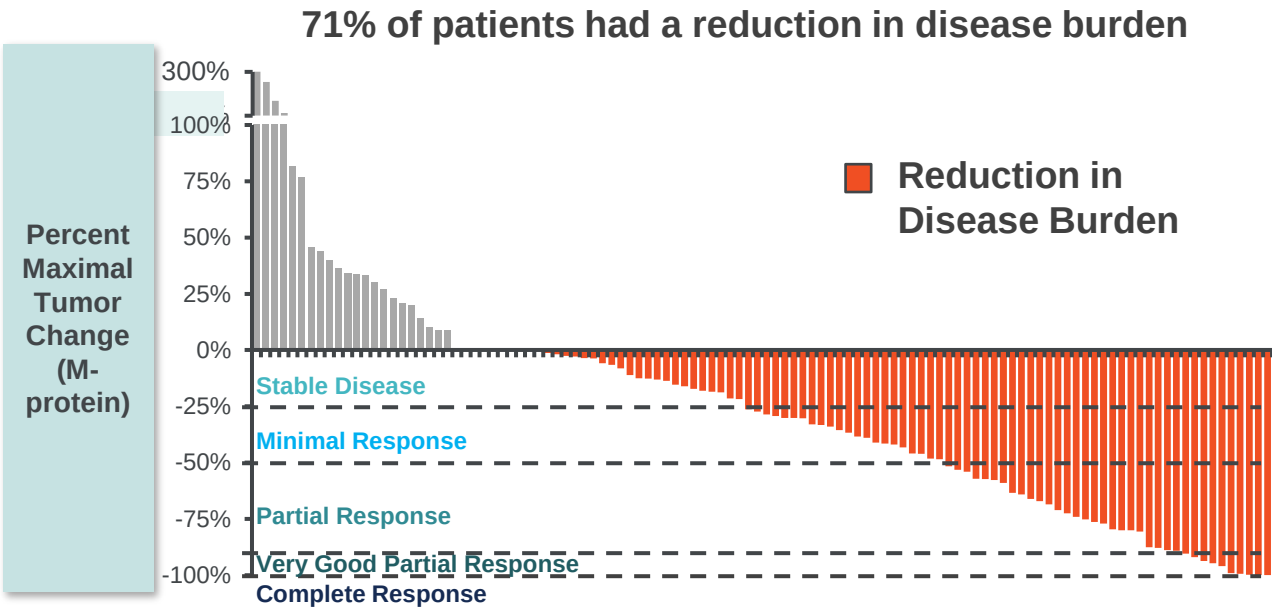
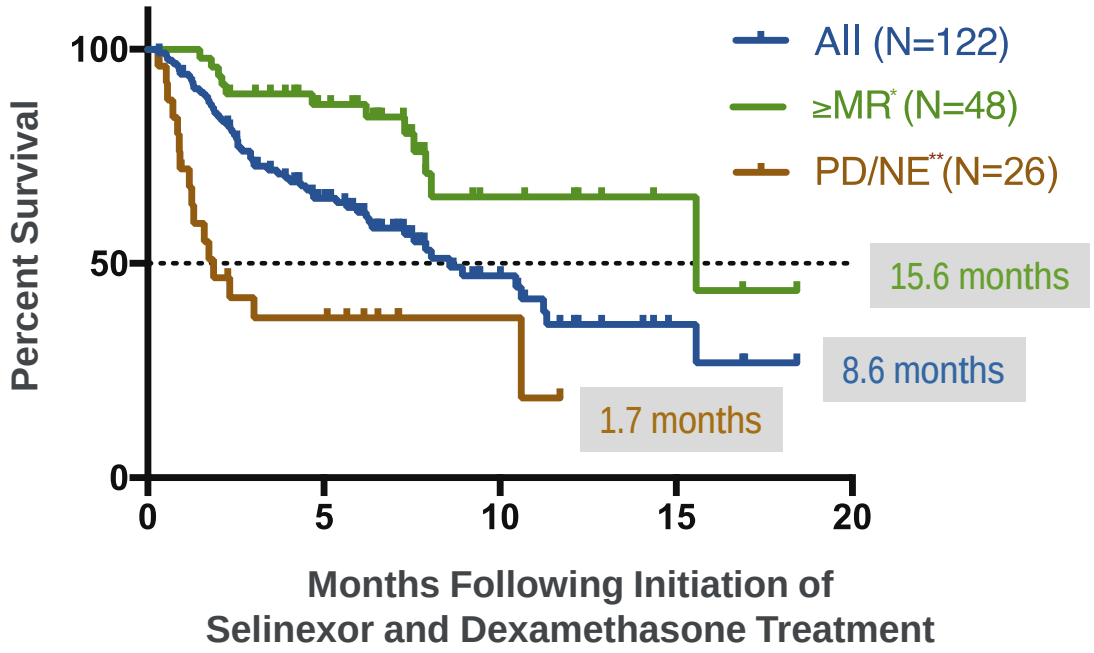
Additional Efficacy Data from Part 2 of STORM (n=122)[1]

Change in M-Protein Levels[2]



Overall Survival by Group[3]



* ≥MR = Patients had a minor response or better; at least a 25% decrease in M protein
** PD/NE = Patients had progressive disease or disease not evaluable

[1] The accelerated approval of XPOVIO was based upon the efficacy and safety in a prespecified subgroup analysis of the 83 patients whose disease was refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab, as the benefit-risk ratio appeared to be greater in this more heavily pretreated population than in the overall trial population. [2] Selinexor ODAC Presentation, February 2019. [3] Chari A, et al. New England Journal of Medicine 2019.

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Overview of Safety Data from STORM

Patients who Received XPOVIO 80 mg in Combination with Dexamethasone 20 mg on Days 1 and 3 of Every Week[1] (n=202)

- The most common adverse reactions (incidence ≥20%) were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infections
- The treatment discontinuation rate due to adverse reactions was 27%
- 53% of patients had a reduction in the XPOVIO dosage and 65.3% of patients had the dosage of XPOVIO interrupted
  - The most frequent adverse reactions requiring permanent discontinuation in 4% or greater of patients who received XPOVIO included fatigue, nausea, and thrombocytopenia
- The rate of fatal adverse reactions was 8.9%

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

[1] XPOVIO Prescribing Information.

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Rationale to Conduct the BOSTON Study

BOSTON Design

Weekly Selinexor, Velcade, and Dexamethasone (SVd) Versus Standard Twice Weekly Velcade and Dexamethasone (Vd) in Patients with Multiple Myeloma After 1-3 Prior Therapies

- 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

[1] Turner, J, et al. Oncotarget October 2016. [2] Kashyap, T, et al. Oncotarget October 2016. [2] Bahlis NJ, et al. Blood 2018.

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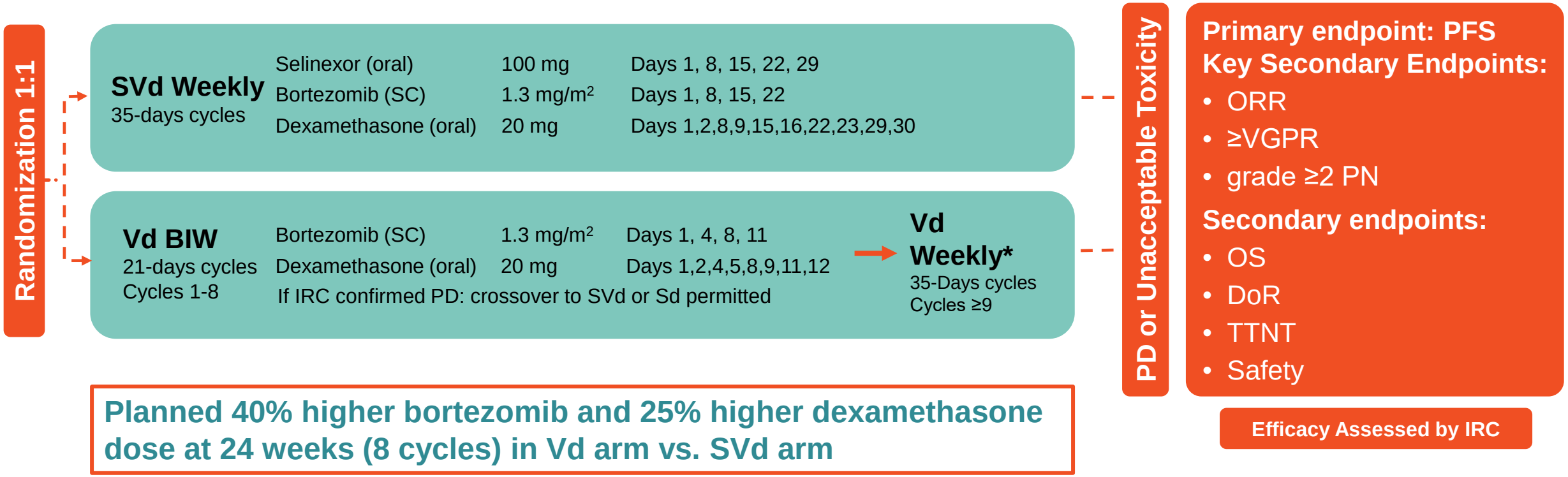
BOSTON Study: Phase 3, Global, Randomized, Open Label, Controlled Study in Patients with Multiple Myeloma who Had Received 1-3 Prior Therapies



Planned 40% higher bortezomib and 25% higher dexamethasone dose at 24 weeks (8 cycles) in Vd arm vs. SVd arm

CR= complete response, DoR = duration of response, IMWG = International Myeloma Working Group, IRC = Independent Review Committee, OS = overall survival, PD = progressive disease, PFS = progression free survival, PR = partial response, PN = peripheral neuropathy, sCR = stringent complete response, TTNT = time to next therapy, VGPR = very good partial response. PFS defined as: Time from date of randomization until the first date of progressive disease, per IMWG response criteria, or death due to any cause, whichever occurred first, as assessed by IRC. ORR: Any response ≥PR (ie, PR, VGPR, CR, or sCR) based on the IRC's response outcome assessments, according to IMWG response criteria (Kumar et al. Lancet oncology 2016). All changes in MM disease assessments were based on baseline MM disease assessments.
*Vd weekly dosing and schedule for cycles≥ 9 as per SVd arm description.

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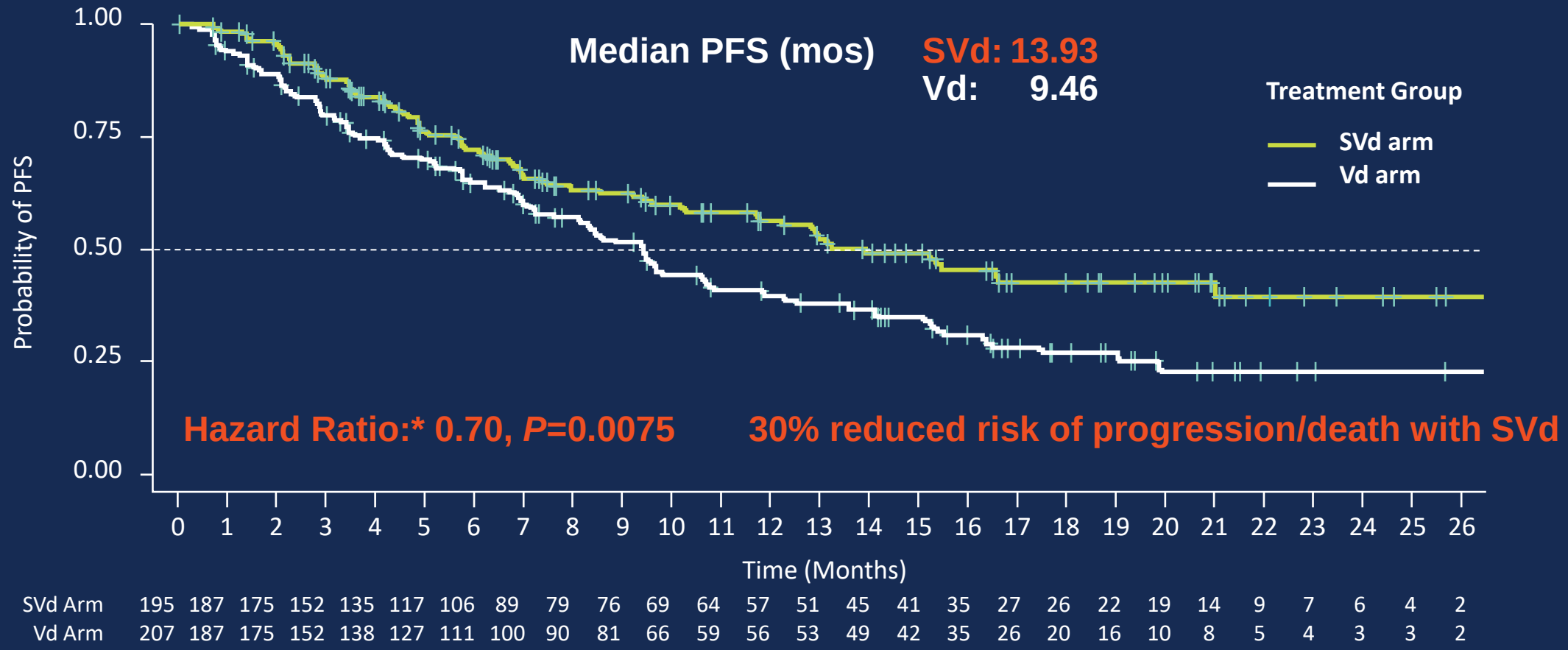
Progression Free Survival (PFS) Significantly Longer with SVd Compared to Vd

Early and Sustained PFS Benefit (Assessed by IRC)



Intention-to-treat (ITT) population N=402, Data cut-off February 18, 2020
*HR=Hazard Ratio 95% CI=0.53–0.93 one-sided *P* value

Median follow-up: 13.2 and 16.5 months in SVd and Vd arms, respectively

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

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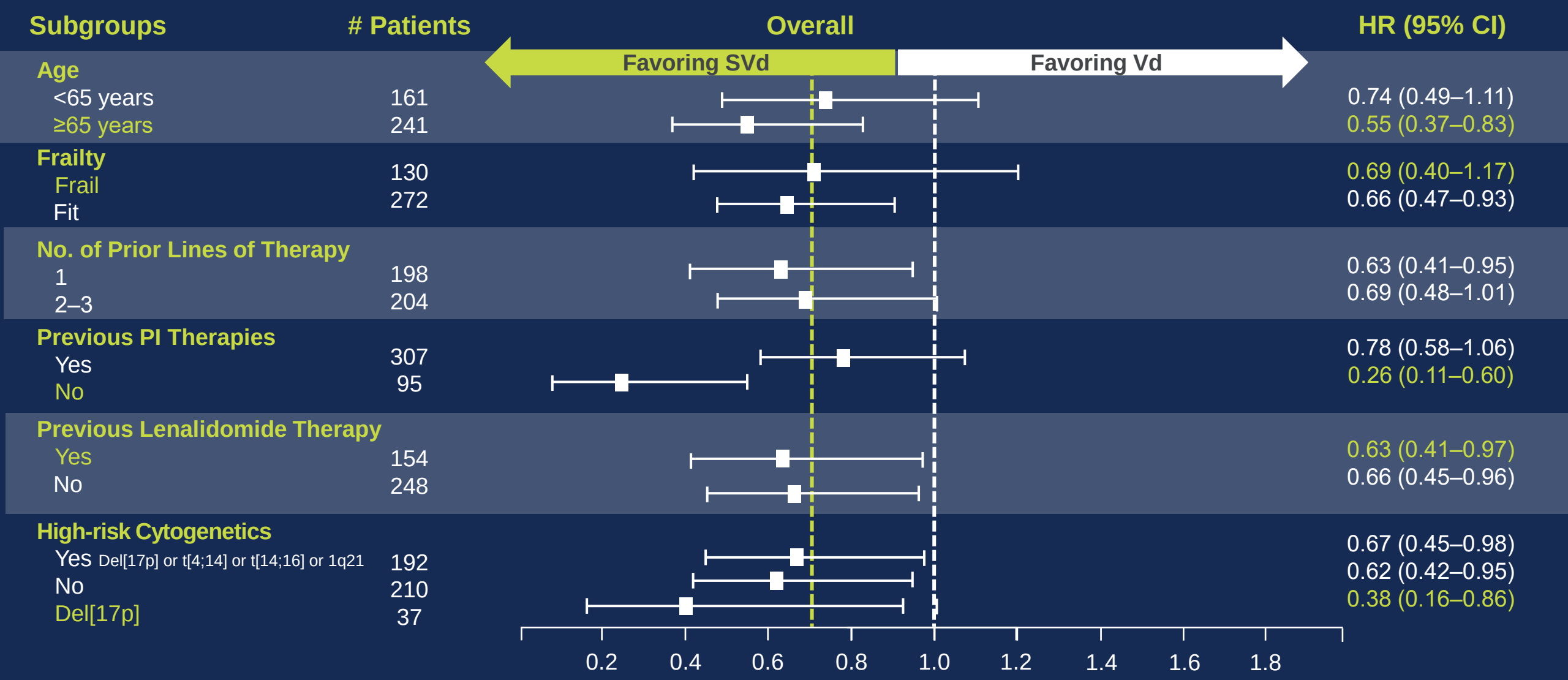
Consistent PFS Benefit for SVd Across Subgroups



HR = Hazard Ratio, Data cut-off February 18, 2020.

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

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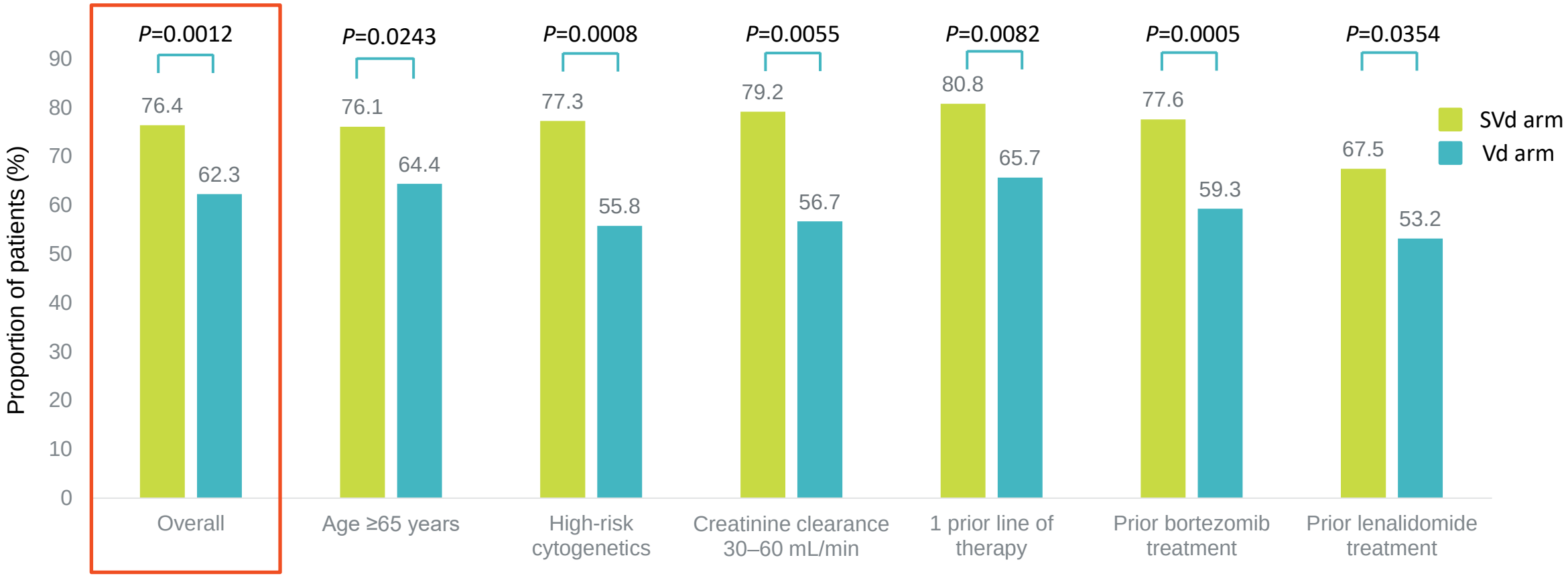
SVd Was Associated With a Significantly Higher ORR Overall and Across Patient Subgroups



One-sided P values for the Cochran-Mantel-Haenszel Test based on unstratified model. Data cut-off February 18, 2020.
ORR = Overall Response, based on Independent Review Committee's (IRC) response outcome assessments, according to IMWG response criteria (Kumar et al. Lancet Oncology 2016).
All changes in MM disease assessments were based on baseline MM disease assessments.

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

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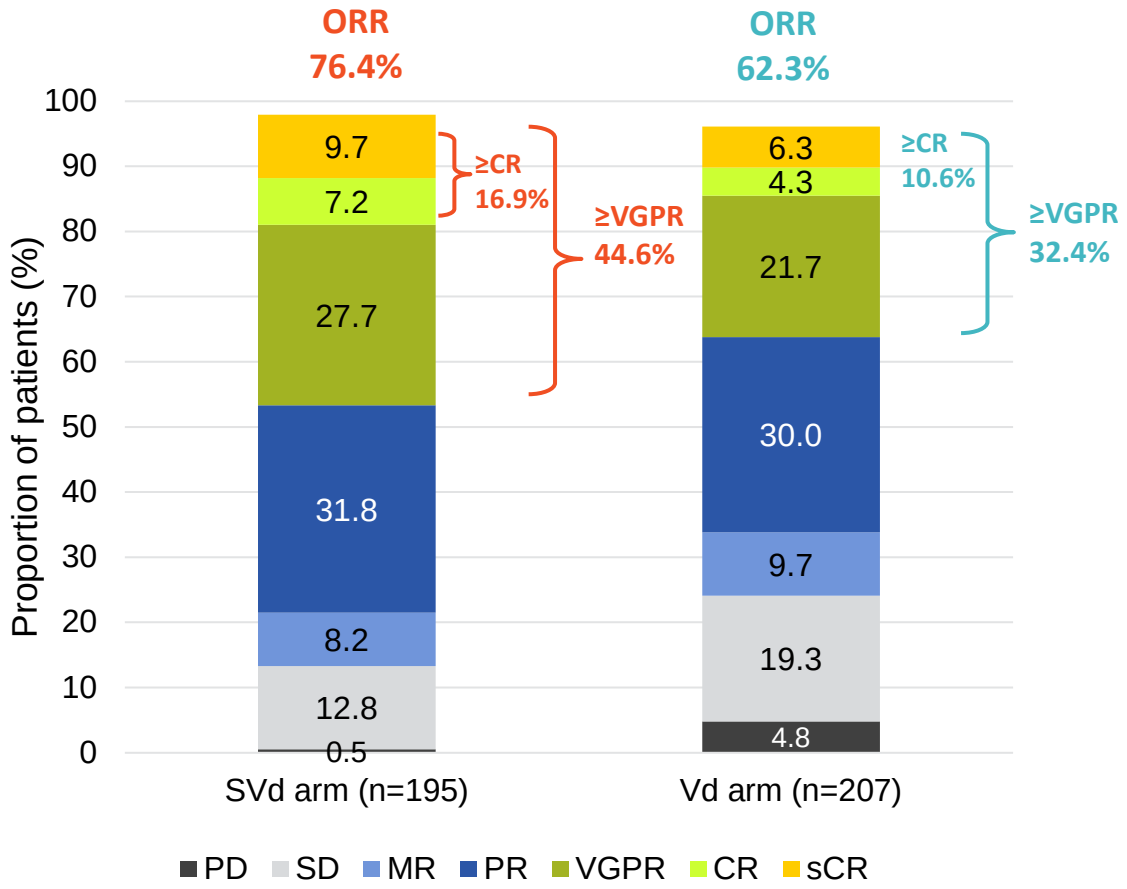
SVd Was Associated With Significantly Higher Rate of Deep Responses (≥VGPR, p=0.0082)



Longer Duration of Response with SVd

	SVd arm (n=165)	Vd arm (n=149)
Median Time to Response (months)†	1.1	1.4
Median Duration of Response (months)*	20.3	12.9

Fewer Patients with Progressive Disease: SVd (n=1, 0.5%) vs Vd (n=10, 4.8%)

CR= complete response, MR = minimal response, PD = progressive disease, PR = partial response, sCR = stringent complete response, SD = stable disease, VGPR = very good partial response. All responses assessed by an Independent Review Committee (IRC), according to the IMWG criteria (Kumar et all. Lancet Oncology 2016). †Unadjusted Time from date of randomization until first response per IMWG response criteria.
*Duration of the time interval between the first IRC-confirmed PR or better response and the first IRC-confirmed PD or death due to any cause, whichever occurred first. Data cut-off February 18, 2020.

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

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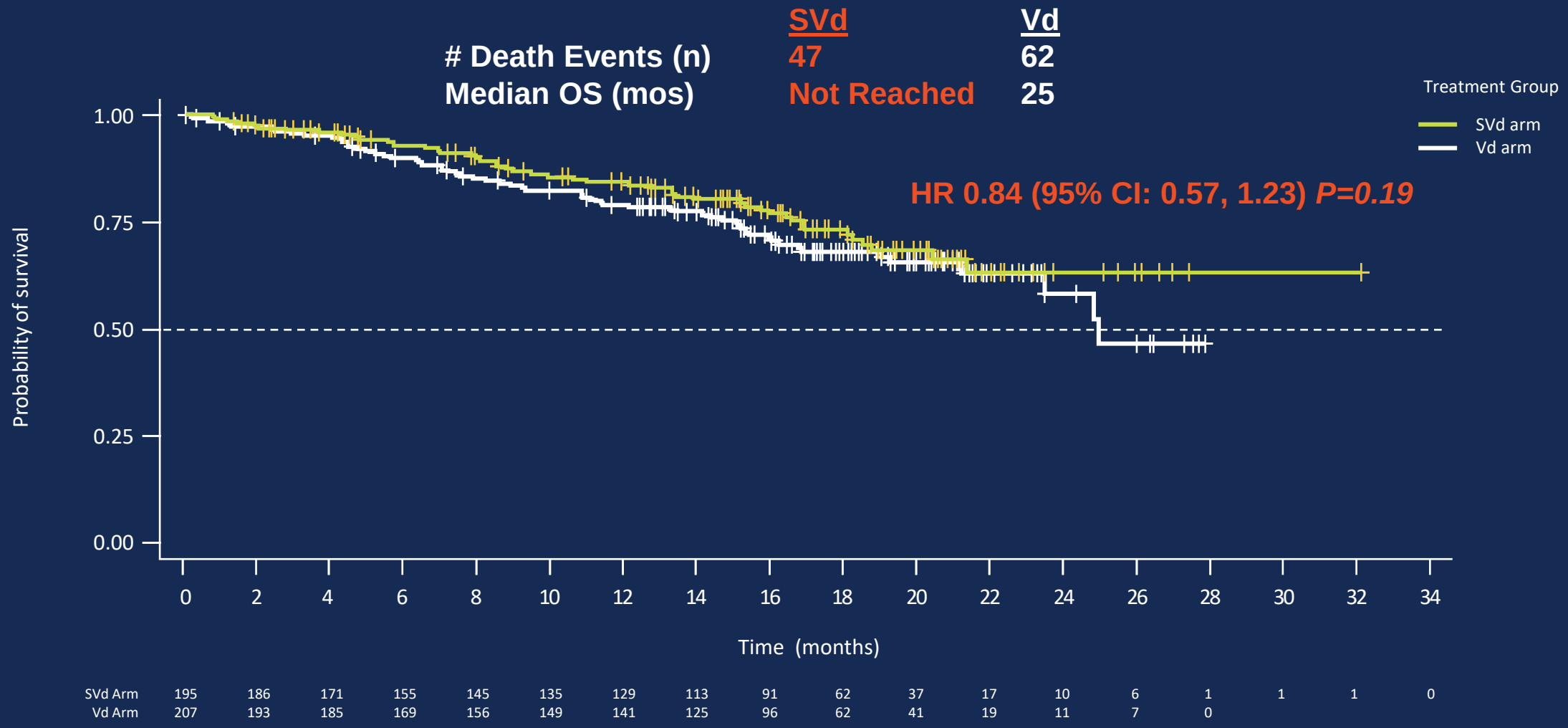
Overall Survival Interim Analysis (109 Deaths [27%])



OS = Overall Survival, Data cut-off February 18, 2020.

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

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Peripheral Neuropathy Rates were Significantly Lower with SVd than with Vd

Peripheral neuropathy was the most common adverse event (AE) leading to treatment discontinuation: 4.6% on SVd, 7.4% on Vd

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

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Selected Hematological Treatment Emergent Adverse Events (TEAEs)*

	SVd (n=195)		Vd (n=204)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematological (%)				
Thrombocytopenia	60.0†	39.5	27.0	17.2
Grade ≥3 Bleeding		2.1		1.0
Anemia	36.4	15.9	23.0	9.8
Neutropenia	14.9	8.7	5.9	3.4
Febrile Neutropenia		0.5		0.5

- Thrombopoietin receptor agonists were used to mitigate thrombocytopenia in 35 patients on SVd and 2 patients on Vd, and reduced dose interruptions and reductions
- 12 patients on SVd and 13 patients on Vd received platelet transfusions to manage thrombocytopenia

*Shown are adverse events that occurred in at least 10% of patients and had a >5% difference between treatment arms. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. For patients who crossed over, adverse events that occurred after the crossover are not included.
†Includes 3 fatal events. Data cut-off February 18, 2020.

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

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Selected Non-Hematological TEAEs*

	SVd (n=195)		Vd (n=204)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Non-hematological (%)				
Nausea	50.3	7.7	9.8	0
Fatigue	42.1	13.3	18.1	1.0
Decreased Appetite	35.4	3.6	5.4	0
Diarrhea	32.3	6.2	25.0	0.5
Peripheral Neuropathy†	32.3	4.6	47.1	8.8
Upper Respiratory Tract Infection‡	29.2	3.6	21.6	1.5
Weight decreased	26.2	2.1	12.3	1.0
Asthenia	24.6	8.2	13.2	4.4
Cataract§	21.5	8.7	6.4	1.5
Vomiting	20.5	4.1	4.4	0

*Shown are adverse events that occurred in at least 15% of patients and had a >5% difference between treatment arms. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. For patients who crossed over, adverse events that occurred after the crossover are not included. †Includes high-level term Peripheral Neuropathies NEC. ‡Includes upper respiratory infection, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis and viral upper respiratory tract infection. §Per ophthalmology exam during which 24% of patients on the SVd arm versus 8.5% of patients on the Vd arm had new-onset cataracts and worsening of cataracts on study was noted in 20.5% patients on the SVd arm versus 7.9% on the Vd arm. Data cut-off February 18, 2020.

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

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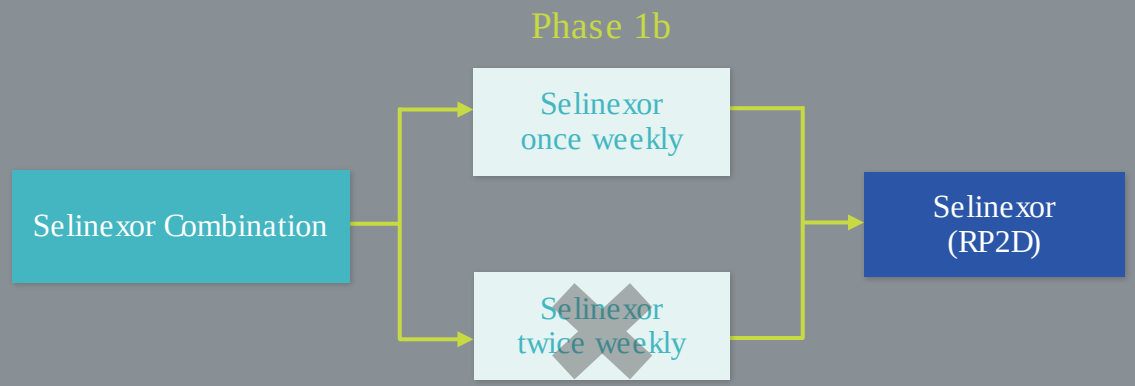
STOMP: Study Overview & Objectives

Selinexor and backbone Treatments Of multiple Myeloma Patients (STOMP): Multi-center, open-label, dose escalation (Phase 1) and expansion (Phase 2) study to assess the MTD, efficacy, and safety of selinexor in patients with RRMM

SPd Pomalidomide + Dexamethasone	**SVd** Bortezomib + Dexamethasone	**SKd** Carfilzomib + Dexamethasone
SRd RRMM Lenalidomide + Dexamethasone	**SRd NDMM** Lenalidomide + Dexamethasone	**SDd** Daratumumab + Dexamethasone



Note: MTD, maximum tolerated dose; RP2D, recommended phase 2 dose; NDMM, newly diagnosed multiple myeloma.

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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

STOMP Trial			Benchmark Data	
STOMP Triplet Regimen	**# of Patients Treated to Date**	**Efficacy Data**	**Benchmark Regimen**	**Efficacy Data**
Selinexor + Kyprolis + dex	24 (median 3 lines of prior therapy)	ORR = 71%[1]	Kyprolis + dex	ORR = 23%[5]
Selinexor + Darzalex + dex	30 (Darzalex-naïve)	ORR = 73%[2] PFS = 12.5 months[2]	Darzalex	ORR = 29%[6] PFS = 3.7 months[6]
Selinexor + Pomalyst + dex	32 (Pomalyst–naïve and Revlimid relapsed or refractory	ORR = 56%[3] PFS = 12.2 months[3]	Pomalyst + dex	ORR = 29%[7] PFS = 3.6 months[7]
Selinexor + Revlimid + dex	12 (Revlimid-naïve)	ORR = 92%[4]	Revlimid + dex	ORR = 67%[8]

Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies[9]

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.

[1] Gasparetto C, et al. ASCO 2020. Abstract 8530. [2] Gasparetto C, et al. ASCO 2020. Abstract 8510. [3] Chen C, et al. ASH 2019. Abstract 141. [4] White D, et al. IMW 2019. Abstract 353. [5] Kyprolis Package Insert; Study PX-171-003 A1
[6] Lonial et al. Lancet 2016. [7] Pomalyst Package Insert. [8] Stewart et al. NEJM 2015. [9] Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).

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SADAL[1]: A Phase 2b Study In DLBCL

FDA Approved on June 22, 2020

N=134

Relapsed or Refractory or Transformed DLBCL

- Study included patients with at least two prior multi-agent therapies and who were ineligible for transplantation
- Included patients with Germinal Center B-Cell (GCB) and non-GCB subtypes

Oral Selinexor | **60** mg

selinexor twice weekly
(4 week cycle)

[1] **S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma

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SADAL: A Phase 2b Study In DLBCL

Selinexor 60mg twice weekly (n=134*)

OVERALL RESPONSE RATES[1,2]

All Patients	29%	CRs 13% PRs 16%
Genetic Subsets	34% GCB (n=59)	21% non-GCB (n=63)

ADDITIONAL ENDPOINTS[2]

Duration of Response

- Median DOR was **9.3** months
- Most responses at first scan (**~2** months)

Overall Survival

- All patients (n=127) = **9.1** months
- Patients with CR or PR (n=36) = **Not Yet Reached**
- Patients with stable disease (n=11) = **18.3** months
- Patients with Progressive Disease or No Response (n=80) = **4.3** months

Safety:

- Most common treatment related non-hematologic adverse events (AEs) were fatigue, nausea, decreased appetite, and diarrhea, primarily Grade 1/2, and most were manageable with dose modifications and/or supportive care
- Most common Grade 3/4 AEs were thrombocytopenia, lymphopenia, neutropenia, and anemia, and most were also manageable with dose modifications and/or supportive care

[1]XPOVIO Prescribing Information. [2] Kalakonda N, et al. Lancet Haematology. 2020.
* 134 patients included in XPOVIO Prescribing Information and 127 patients included in Kalakonda N, et al. Lancet Haematology. 2020.

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Agenda

- Approved XPOVIO Indications
- Commercial and Financial Highlights
- Pipeline and Future Opportunities
- Appendix: Clinical Data
- Appendix: Commercial Insights

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Highly Experienced Team Educating the Market About XPOVIO

Customer-Facing Field Force

- ~70 sales representatives and nurse liaisons supporting commercial launch
  - **~20** average years of pharmaceutical experience
  - **~12** average years of hematology / oncology experience
  - **~5** average years of MM experience
- Experienced account management team responsible for payors and distribution partners
- Extensive patient and HCP support program anchored by KaryForward™ platform

Prescriber Base[1]

Multiple Myeloma

- ~400 accounts generate ~50% of all prescriptions
- ~1,300 accounts generate ~80% of all prescriptions
- Top accounts generally consist of larger academic institutions and multi-site community oncology practices

DLBCL

- ~3,000 physicians treat ~80% of U.S. DLBCL patients
- ~75% of targeted physicians are community-based
- >50% overlap between Karyopharm's multiple myeloma and DLBCL targets

[1] Based on analysis of Symphony Claims data.

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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.

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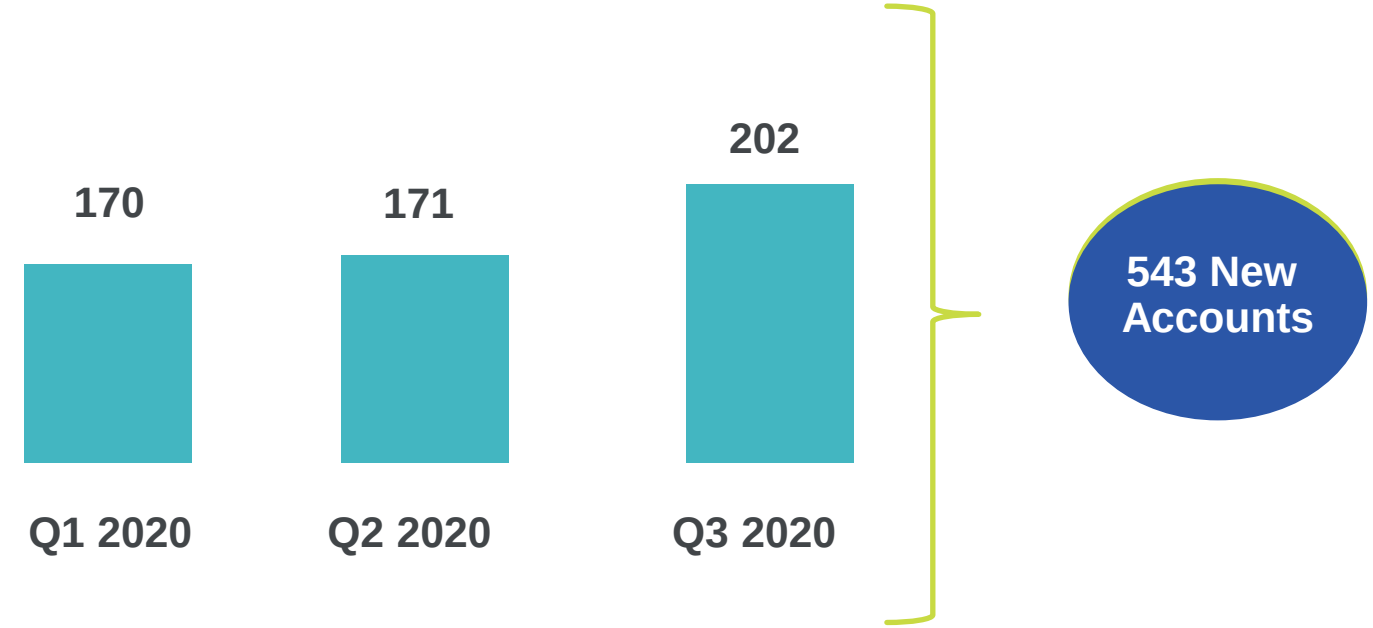
XPOVIO Prescriber Base Continues to Grow

New Accounts Prescribing XPOVIO in 2020



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

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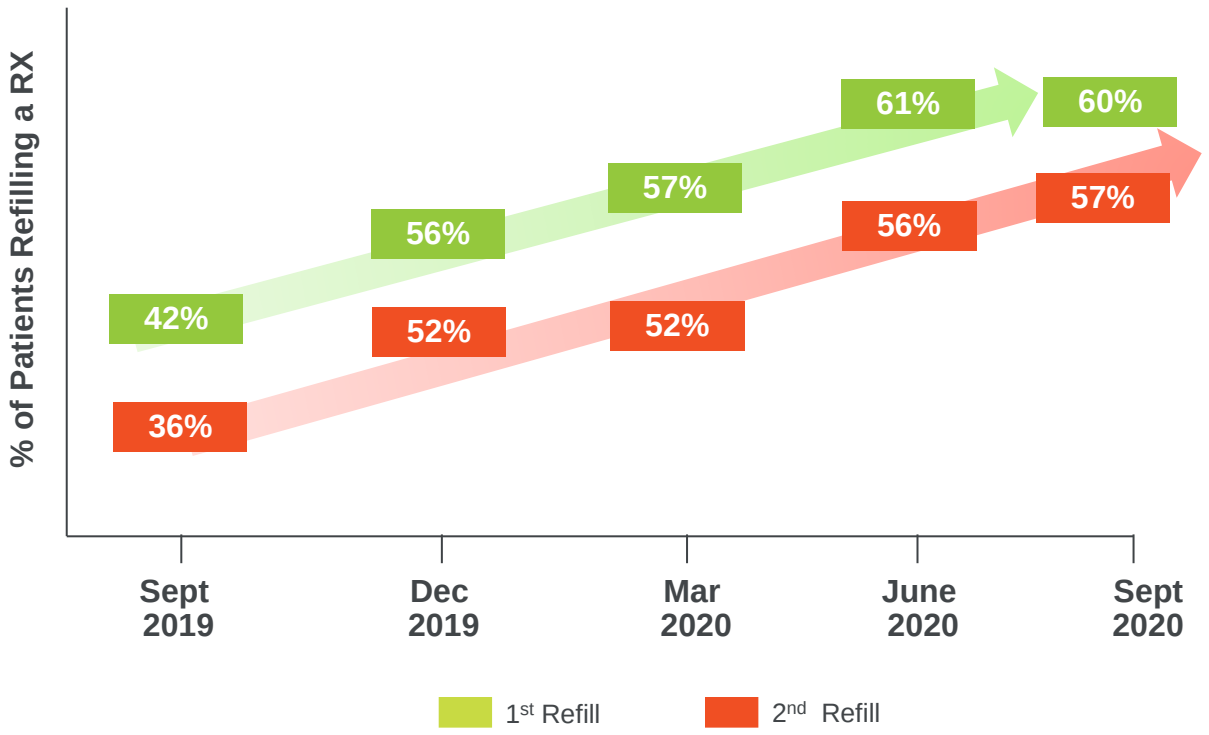
Key XPOVIO Patient Metrics Demonstrate Positive Trends

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.

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Commercial Strategy for XPOVIO in DLBCL

XPOVIO Positioning

- Successfully launch XPOVIO as the preferred DLBCL treatment option after two prior lines of therapy instead of traditional intravenous chemotherapy by educating physicians on the deep and durable efficacy achieved in clinical studies with oral, single-agent, novel, XPOVIO
- XPOVIO offers compelling efficacy with a manageable safety profile and is now:
  - **First** oral therapy approved for RR DLBCL
  - **First** single agent approved in any line of DLBCL treatment
  - **First** therapy a RR DLBCL patient can take at home

[1] Based on analysis of Symphony claims data

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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

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Key Metrics and Insights from DLBCL Launch – Q3 2020

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

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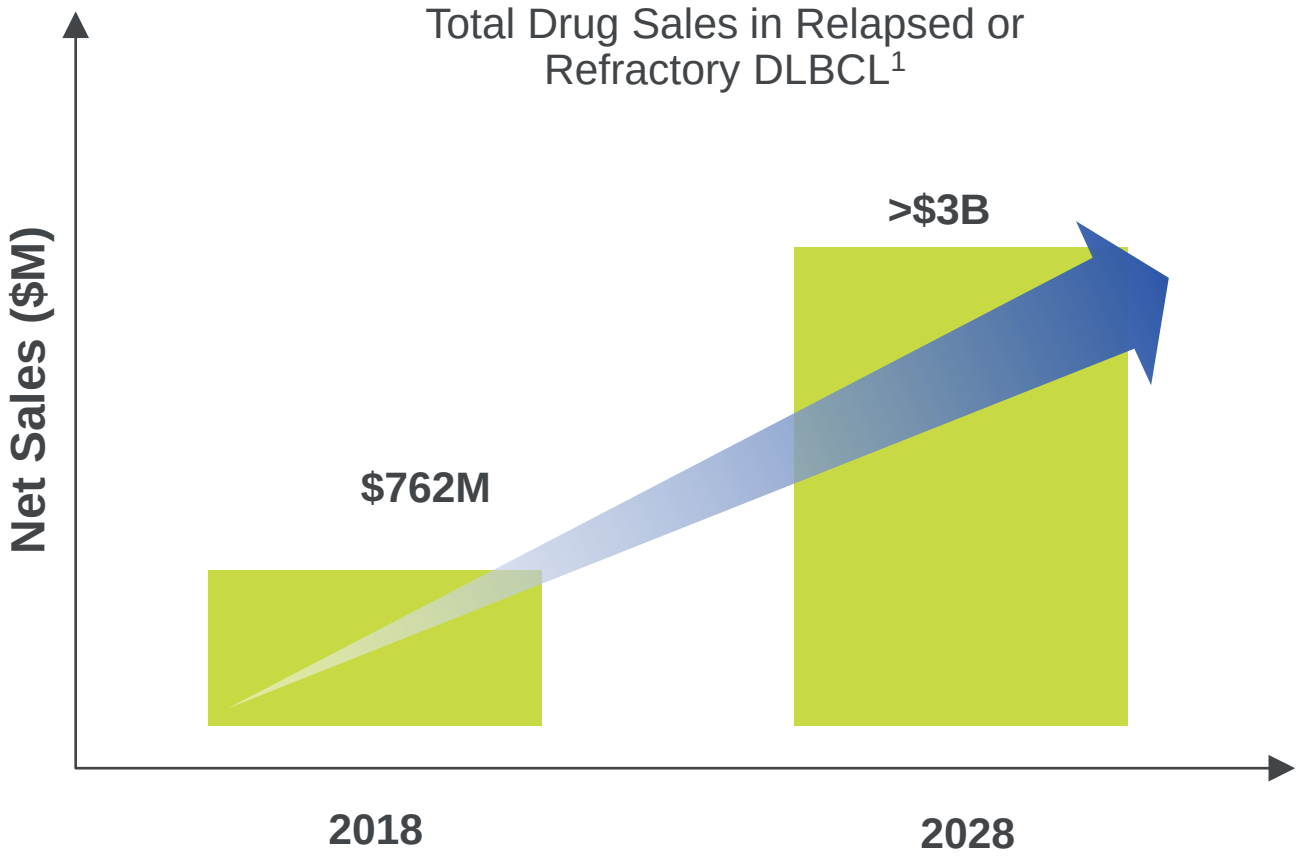
Total U.S. Drug Sales in Relapsed or Refractory DLBCL Expected to Grow from $762M in 2018 to Over $3B by 2028



[1] Decision Resources NHL and CLL Landscape and Forecast, 2019

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