JP Morgan Healthcare Conference 2020

Michael G. Kauffman, MD, PhD, *Chief Executive Officer*

January 14, 2020

Forward-looking Statements and Other Important Information

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm's expectations relating to XPOVIO® for the treatment of patients with heavily pretreated multiple myeloma; the therapeutic potential of and potential clinical development plans and commercialization for Karyopharm's drug candidates, including the timing of initiation of certain trials, of the reporting of data from such trials, of the submissions to regulatory authorities and of potential commercial launches; the potential availability of accelerated approval pathways; the potential size of the markets for multiple myeloma drugs and multiple myeloma drugs for treatment of patients with relapsed multiple myeloma; the potential size of the markets for diffuse large B-cell lymphoma (DLBCL) drugs and DLBCL drugs for treatments of patients with relapsed and/or refractory DLBCL; and Karyopharm's strategic and financial plans and expectations, as well as financial projections for Karyopharm. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that Karyopharm will successfully commercialize XPOVIO, that regulators will agree that selinexor qualifies for conditional approval in the E.U. as a result of the data from the STORM study in patients with penta-refractory myeloma or accelerated approval in the U.S. based on the SADAL study in patients with relapsed/refractory DLBCL or that any of Karyopharm's drug candidates, including selinexor and eltanexor (KPT-8602), Karyopharm's second generation SINE compound, or KPT-9274, Karyopharm's first-in-class oral dual inhibitor of PAK4 and NAMPT, or any other drug candidate Karyopharm is developing, will successfully complete necessary preclinical and clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in Karyopharm's drug candidate portfolio will result in stock price appreciation. In addition, even if Karyopharm receives marketing approval for selinexor in additional indications or for any other drug candidate, there can be no assurance that Karyopharm will be able to successfully commercialize that drug candidate. Management's expectations and, therefore, any forward-looking statements in this presentation could also be affected by risks and uncertainties relating to a number of other factors, many of which are beyond Karyopharm's control, including the following: the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the FDA and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; unplanned cash requirements and expenditures; development of drug candidates by Karyopharm's competitors for diseases for which Karyopharm is currently developing its drug candidates; that the markets for multiple myeloma drugs will grow as predicted; 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 September 30, 2019, which was filed with the Securities and Exchange Commission (SEC) on November 4, 2019, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this presentation are for informational purposes only and speak only as of the date hereof. Other than as is required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. Karyopharm's website is http://www.karyopharm.com. Karyopharm regularly uses its website to post information regarding its business, drug development programs and governance. Karyopharm encourages investors to use www.karyopharm.com, particularly the information in the section entitled "Investors," as a source of information about Karyopharm. References to www.karyopharm.com in this presentation are not intended to, nor shall they be deemed to, incorporate information on www.karyopharm.com into this presentation by reference. Unless otherwise noted, this presentation contains data that are interim and unaudited based on site reports. In addition, data included in this presentation have not been updated and are as of the cutoff date for the applicable medical conference presentation. Other than the accelerated approval of XPOVIO, selinexor, eltanexor, KPT-9274 and verdinexor are investigational drugs that have not been approved by the FDA or any other regulatory agency, and the safety and efficacy of these drugs has not been established by any agency.

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Karyopharm's Vision of Becoming a Leading Oncology-Focused Biopharmaceutical Company

Novel Science & Mechanism of Action

- Nuclear export dysregulation is increasingly recognized as playing a fundamental role in oncogenesis
- XPOVIO® (selinexor) is the 1st and only FDA approved XPO1 inhibitor with few direct competitors in development

Emerging Myeloma Leadership

- XPOVIO U.S. accelerated approval and commercial launch in July 2019
- Highly encouraging launch metrics and product sales in 1st six months on the market
- Top-line data from Phase 3 BOSTON trial evaluating XPOVIO in combination with Velcade® in 2nd line multiple myeloma expected in early 2020

Potential for Broad Impact Across Cancer Types

- sNDA submission in lymphoma (DLBCL) on Dec 23, 2019[1]
- Two ongoing Phase 3 studies in solid tumors: liposarcoma and endometrial cancer
- Two additional drug candidates in earlier clinical development: eltanexor and KPT-9274
- Additional clinical development in other high unmet need cancers

All programs developed in-house with patent protection on XPOVIO out to 2032+

[1] With request for accelerated approval (U.S.).

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2019 was a Landmark Year for Karyopharm with a Strong Year-End Finish

Commercial Update

- **July 3rd** FDA accelerated approval of XPOVIO
- Full year 2019 XPOVIO sales of **$30-31 million** ($17-18M in Q4)[1]
- **>550** physicians / accounts prescribed XPOVIO in first 6 months
- **~1,400** XPOVIO prescriptions fulfilled through December 31st

Pipeline / Clinical Data Update

- BOSTON Phase 3 top-line data on-track, expected **early 2020**
- DLBCL sNDA submitted **Dec 2019**
- **New England Journal of Medicine** publication of STORM data
- **22** presentations at ASH 2019
- MAA decision in Europe expected in **early 2020**

Balance Sheet

- Entered into royalty agreement with Healthcare Royalty Partners for up to **$150 million**
- Ended Q3 2019 with **~$270 million** in cash, cash equivalents, restricted cash and investments
- Cash runway expected to be sufficient to fund planned operations into **middle of 2021**

[1] Based on preliminary unaudited sales data; Karyopharm press release, 1/13/20.

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XPOVIO® (selinexor) Received Accelerated Approval by the FDA in July 2019

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 ongoing, randomized Phase 3 BOSTON study evaluating selinexor in combination with Velcade® (bortezomib) and low-dose dexamethasone will serve as the confirmatory trial.

- XPOVIO is the **first** and **only** nuclear export 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

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

[1]XPOVIO Prescribing Information.

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Safety Highlights from the XPOVIO Prescribing Information[1]

- Warnings and Precautions
  - Thrombocytopenia
  - Neutropenia
  - Gastrointestinal Toxicity
  - Hyponatremia
  - Infections
  - Neurological Toxicity
  - Embryo-Fetal Toxicity
- No Black Box Warnings and No Contraindications
- Patient Medication Guide
- Monitoring Instructions and Recommended Concomitant Treatments
  - Monitor complete blood count (CBC), standard blood chemistry, and body weight at baseline and during treatment as clinically indicated. Monitor more frequently during the first two cycles of treatment
  - Patients are 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 concomitant treatment with a 5-HT3 antagonist and/or 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

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

[1]XPOVIO Prescribing Information.

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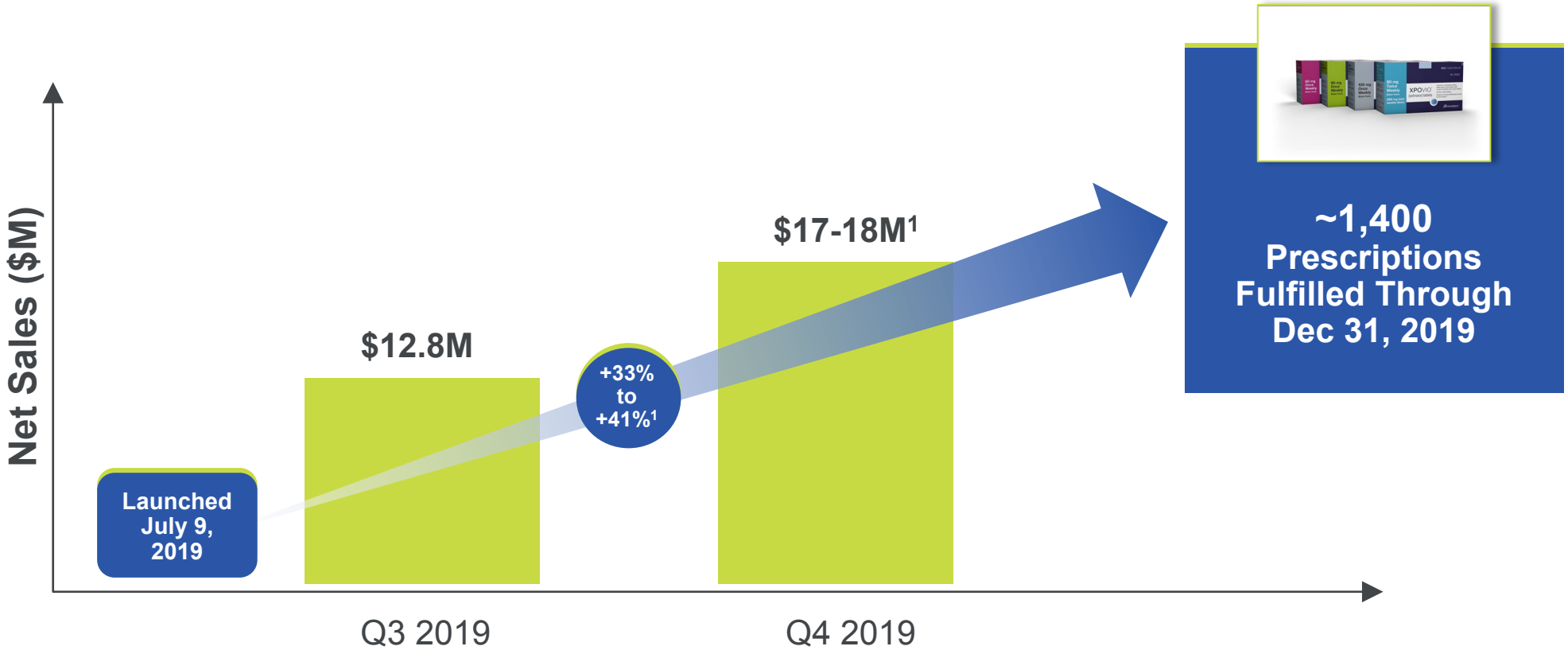
Strong XPOVIO Sales Growth Following FDA Approval

XPOVIO Product Sales Following Launch



[1] Based on preliminary unaudited sales data; Karyopharm press release, 1/13/20.

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Encouraging XPOVIO Metrics in First Six Months Post Commercial Launch

Select Prescription Metrics[1]

>550	~60% / ~40% Split	29-33 days	160 mg per week
• # of unique prescribers and prescribing accounts	• % of RXs covered by Medicare or Medicaid compared to commercial payers[2]	• Average # of days between prescription and subsequent refill[2]	• Most frequently prescribed dose for both new RXs and refills

[1] Data on file at Karyopharm through Dec 31, 2019. [2] Based on prescriptions fulfilled through Karyopharm's specialty pharmacy provider network.

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Feedback and Insights from Myeloma-Treating U.S. Physicians Surveyed in October 2019 (Less than 4 months Post Launch) (n=121)

Awareness of XPOVIO

1. ~90% aided and 50% unaided awareness of XPOVIO
2. ~50% are knowledgeable about the term “XPO1 Inhibitor”
3. ~90% recall one or more branded XPOVIO message

Attitudes and Perceptions

1. ~80% believe in aggressively treating multiple myeloma (MM) patients to maximize survival across all lines of therapy
2. >60% believe XPOVIO is a good option for patients with penta-refractory disease
3. Novelty of mechanism of action, clinical data, and oral administration are the key drivers of XPOVIO usage, to date

Source: Karyopharm market research, Oct 2019.

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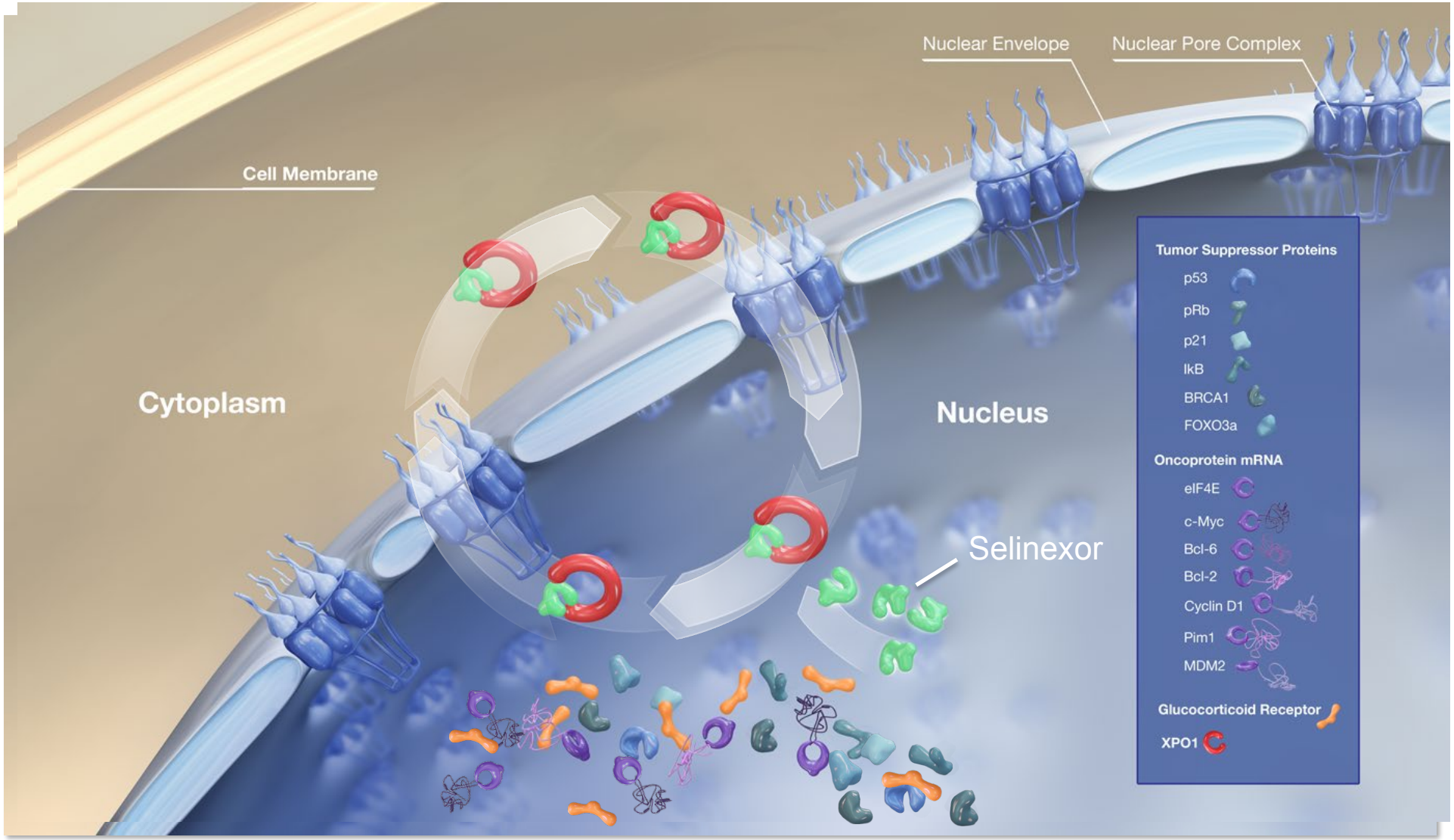
XPOVIO (Selinexor) Clinical Data Overview

- Multiple Myeloma
- Diffuse Large B-Cell Lymphoma

XPOVIO / SINE 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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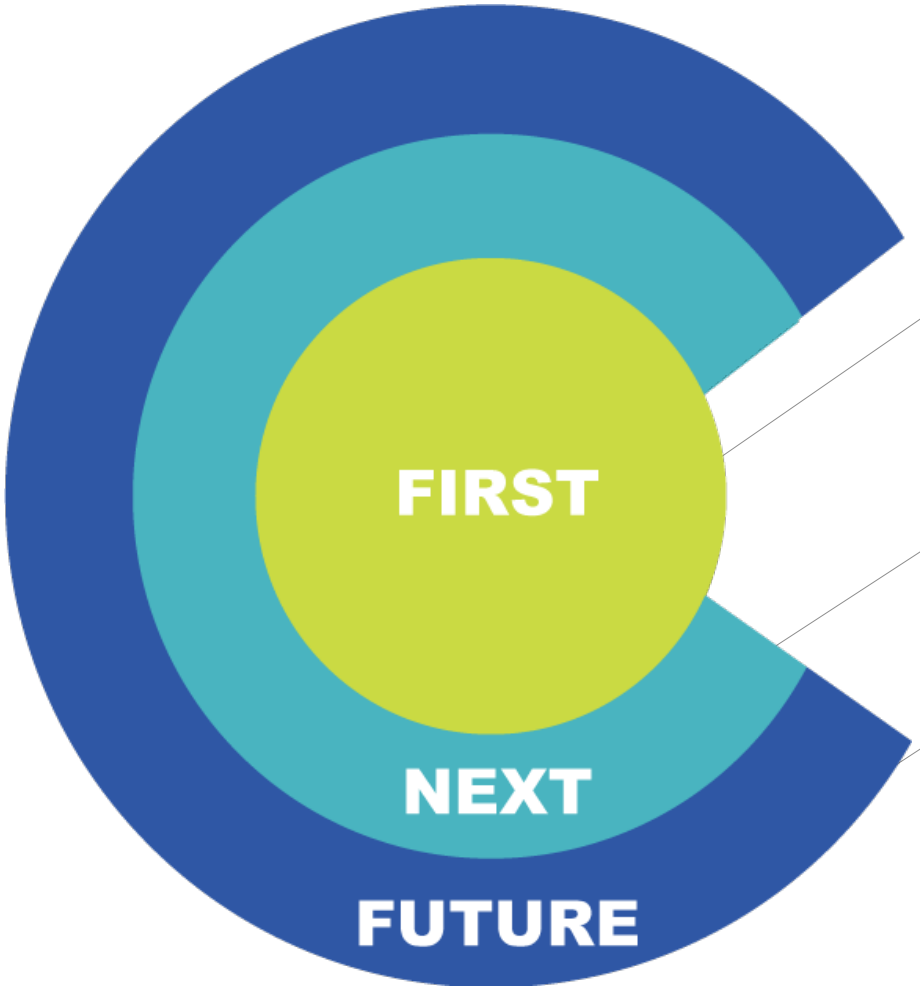
Planned XPOVIO (selinexor) Development Strategy in Multiple Myeloma



Phase 2b STORM study[1] addressing patients with heavily pretreated relapsed refractory multiple myeloma

- Disease refractory to PIs, IMiDs and Darzalex®
- Highest unmet medical need in multiple myeloma

Pivotal Phase 3 BOSTON study addressing patients with relapsed or refractory disease following 1-3 prior lines of therapy

- Selinexor combined with once-weekly Velcade® and low-dose dexamethasone

Phase 1b/2 STOMP as a potential backbone therapy in combination with standard approved therapies

- Selinexor and low-dose dexamethasone combined with Revlimid®, Pomalyst®, Velcade®, Kyprolis® or Darzalex®
- Future Phase 2/3 studies in combination for labeling

1. The accelerated approval of XPOVIO was based upon the efficacy and safety in a prespecified subgroup analysis of the 83 patients in STORM 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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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%

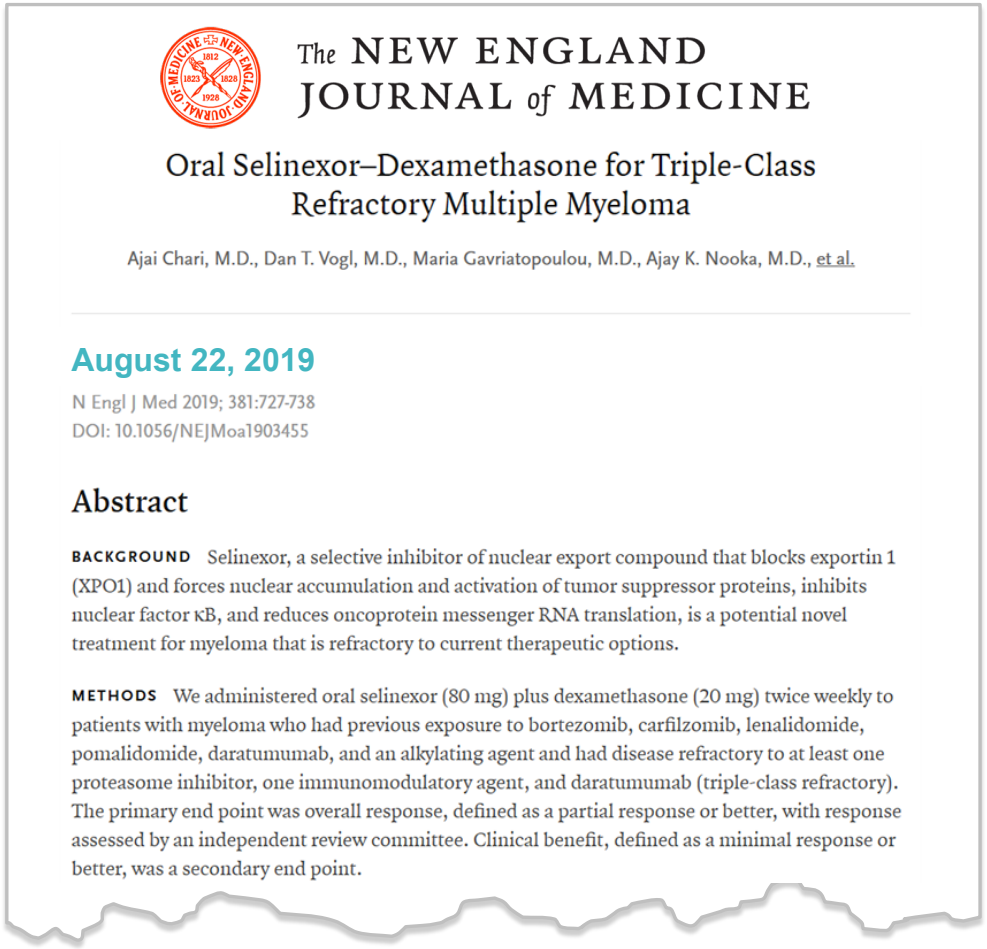
Overall Response Rate (ORR)

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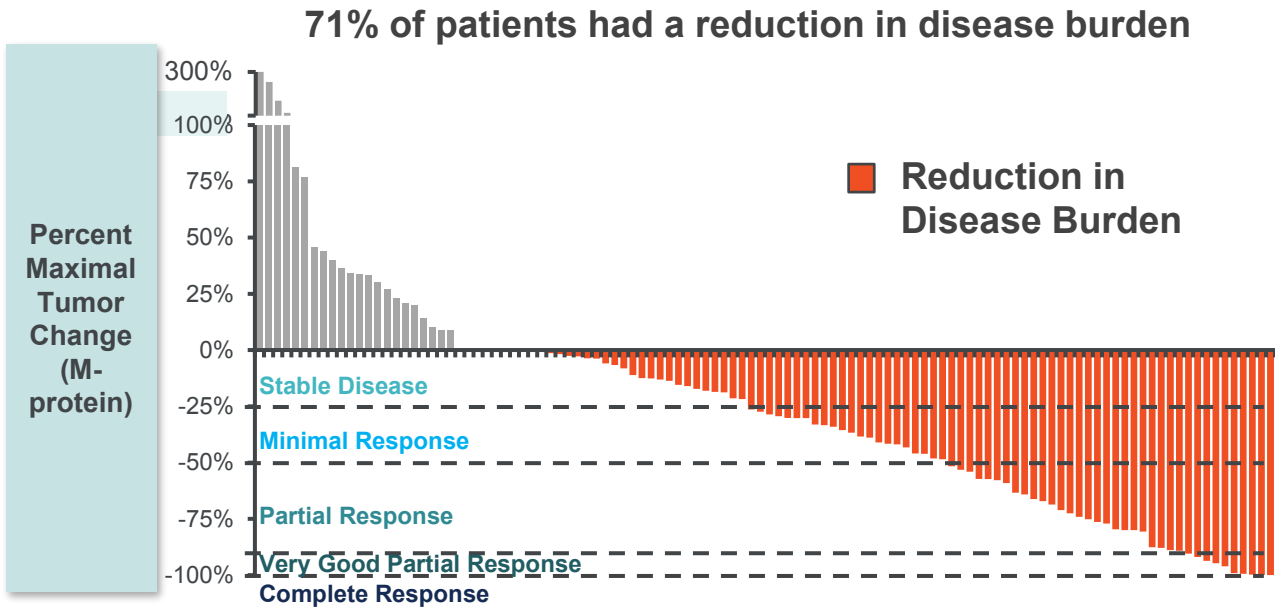
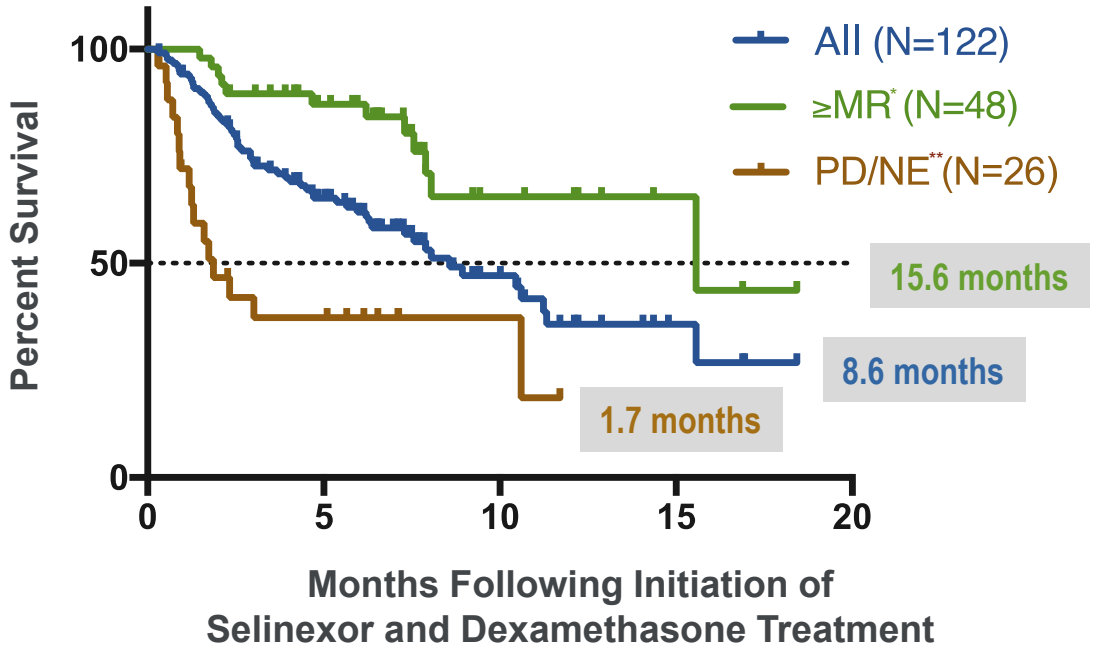
Additional Efficacy Data from Part 2 of STORM (n=122)[1]

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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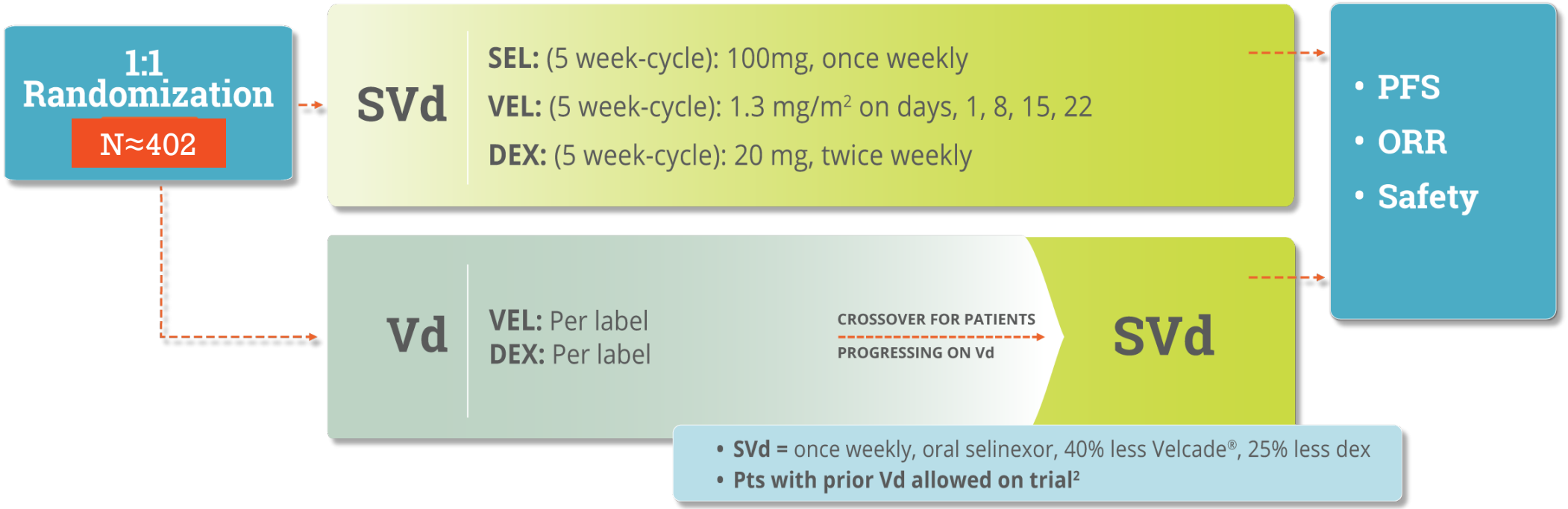
BOSTON[1]: A Phase 3 Study as 2nd Line+ Treatment in Myeloma

Top-line data expected in early 2020[3]



Ongoing randomized, open-label clinical trial evaluating ***once weekly*** selinexor and Velcade® (bortezomib) plus low-dose dex versus standard ***twice-weekly*** Velcade® plus low-dose dex in patients with relapsed or refractory MM, who have had 1-3 prior lines of therapy

[1] **Bo**rtezomib, **S**elinexor and dexame**t**has**on**e [2] Pts must have achieved ≥PR, and completed proteasome inhibitor therapy at least 6 months prior. [3] Pending PFS events.

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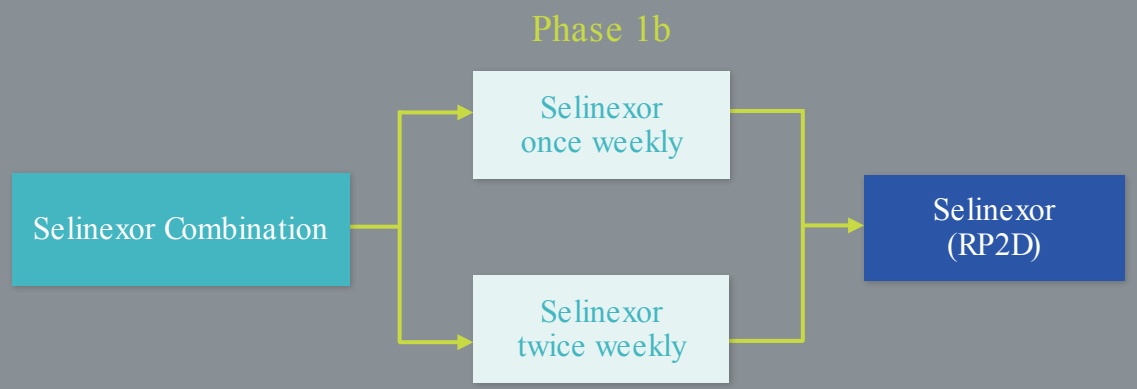
STOMP: Study Overview & Objectives

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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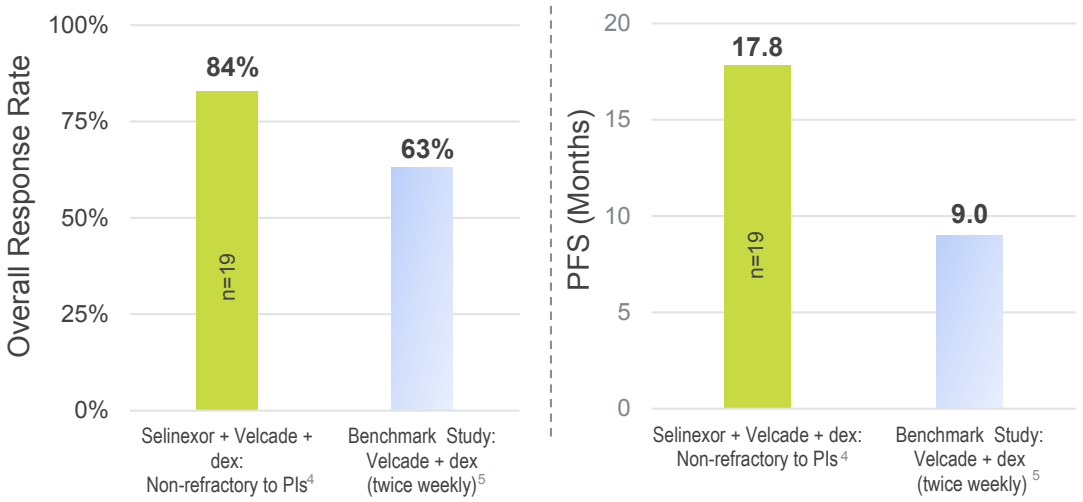
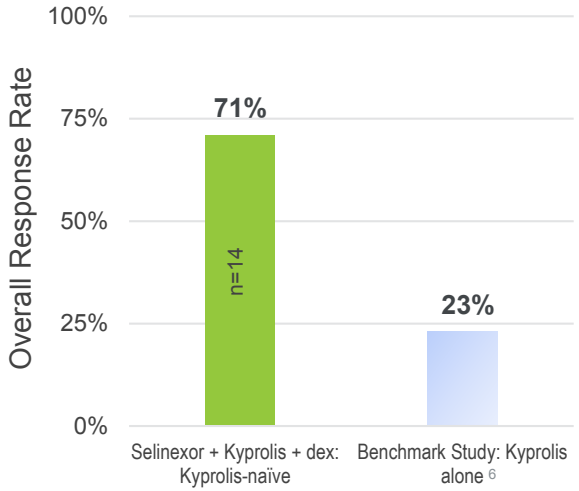
STOMP[1]: A Phase 1b/2 Study in Myeloma

In combination with a proteasome inhibitor

Selinexor + Velcade® + dex (SVd)[2]
(n=19 "BOSTON" Type Patients)



Selinexor + Kyprolis® + dex (SDd)[3]
(n=14 / Median of 4 prior regimens)



Safety:

- AEs consistent with those reported from other selinexor studies
- Most common Grade 1/2 AEs were constitutional symptoms (e.g. nausea, fatigue, anorexia)
- Most common Grade 3/4 AEs were cytopenias (e.g. thrombocytopenia, neutropenia, anemia)
- In the selinexor + Velcade+ dex arm (SVd), peripheral neuropathy across all patients was Grade 1/2 and limited to six patients (14%)[7]

Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies[8]

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 for Velcade and Kyprolis is to highlight that the clinical results from STOMP reported to date strongly support ongoing / additional clinical investigation of selinexor in combination regimens.

[1] **S**elinexor and Backbone **T**reatments **o**f Multiple **M**yeloma **P**atients. [2] Bahlis NJ, et al. Blood 2018. [3] Gasparetto C, et al. ASH 2019. Abstract 122902. [4] Patient population eligible for Phase 3 BOSTON study. [5] Dimopoulos MA et al., Lancet 2016. [6] Kyprolis Package Insert; Study PX-171-003 A1. [7] Five of six had prior Velcade exposure. [8] Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).

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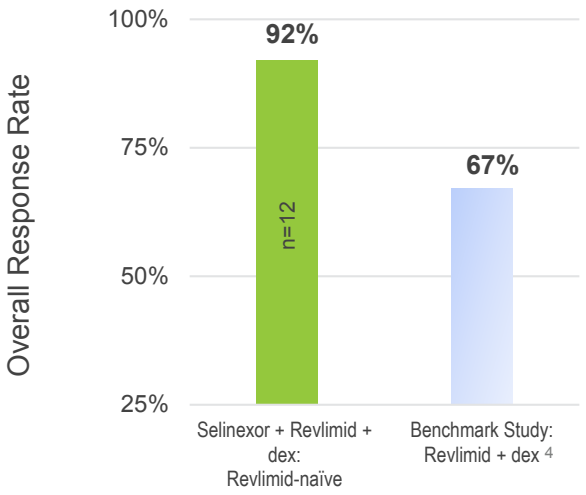
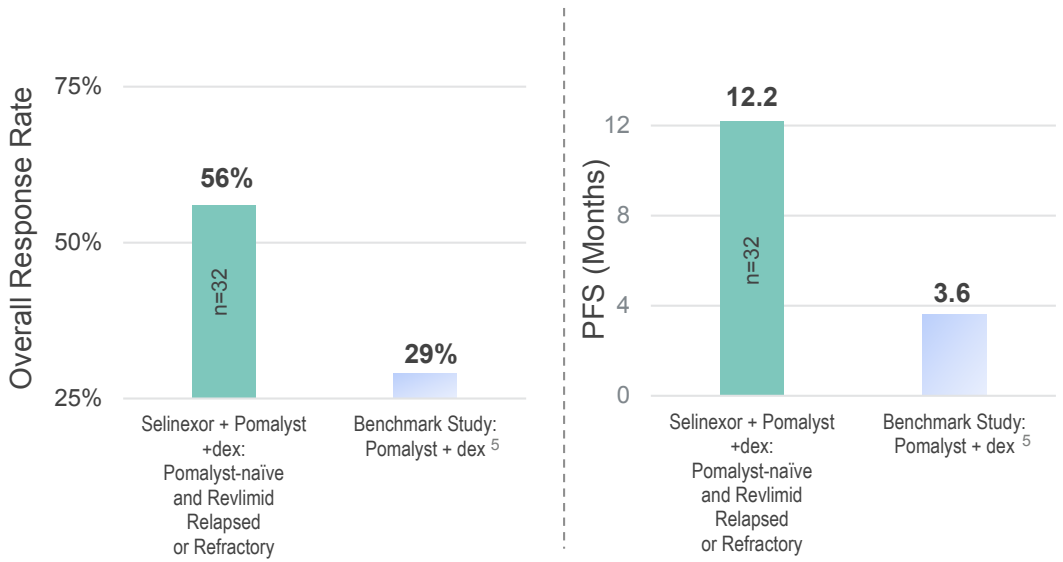
STOMP[1]: A Phase 1b/2 Study in Myeloma

In combination with immunomodulatory drugs

Selinexor + Revlimid® + dex (SRd)[2]
(n=20 ≥ 2nd Line)



Selinexor + Pomalyst® + dex (SPd)[3]
(n=46 / Median of 4 prior regimens)



Safety:

- AEs consistent with those reported from other selinexor studies
- Most common Grade 1/2 AEs were constitutional events (e.g. nausea, fatigue, anorexia)
- Most common Grade 3/4 AEs were cytopenias (e.g. thrombocytopenia, neutropenia, anemia)
- **Exploring frontline setting:** Initiated new ***all oral*** arm evaluating selinexor + Revlimid® + dex in newly diagnosed patients

Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies[6]

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 for Revlimid and Pomalyst is to highlight that the clinical results from STOMP reported to date strongly support ongoing / additional clinical investigation of selinexor in combination regimens.

[1] **S**elinexor and Backbone **T**reatments **o**f Multiple **M**yeloma **P**atients. [2] White D, et al. IMW 2019. Abstract 353. [3] Chen C, et al. ASH 2019. Abstract 141. [4] Stewart et al. NEJM 2015. [5] Pomalyst Package Insert. [6] Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).

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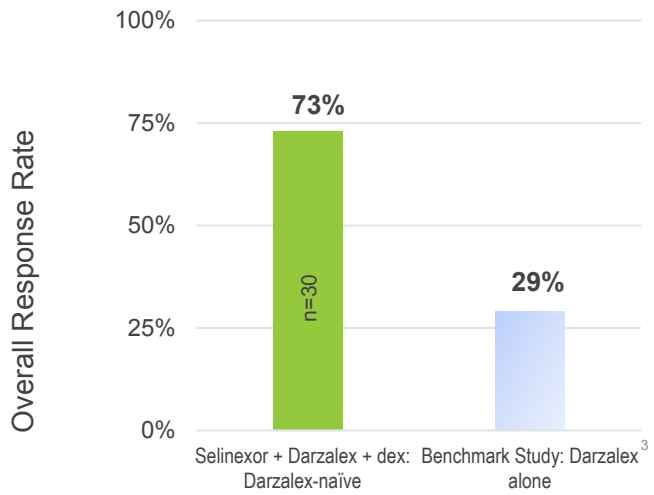
STOMP[1]: A Phase 1b/2 Study in Myeloma

In combination with an anti-CD38 mAb

Selinexor + Darzalex® + dex (SDd)[2]
(n=32 / Most Triple/Quad Refractory)



Safety:

- AEs consistent with those reported from other selinexor studies
- Most common Grade 1/2 AEs were constitutional symptoms (e.g. nausea, fatigue, anorexia)
- Most common Grade 3/4 AEs were cytopenias (e.g. thrombocytopenia, neutropenia, anemia)

Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies[4]

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 for Darzalex is to highlight that the clinical results from STOMP reported to date strongly support ongoing / additional clinical investigation of selinexor in combination regimens.

[1] **S**elinexor and Backbone **T**reatments **o**f Multiple **M**yeloma **P**atients. [2] Gasparetto C, et al. EHA 2019. Abstract S1606. [3] Lonial et al., Lancet 2016. [4] Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).

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

- *Enrollment completed and top-line data reported at ASH 2018 and Updated at ICML 2019*
- *Fast Track designation granted by FDA*
- *sNDA submitted on Dec 23, 2019*

N=127

Relapsed or Refractory or Transformed DLBCL

- For patients after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell
- Includes patients with 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[1,2]

Selinexor 60mg twice weekly (n=127)

OVERALL RESPONSE RATES

All Patients	**28.3%** (n=127)	**CRs 10.2%[3] PRs 18.1%**
Genetic Subsets	**33.9%** GCB (n=59)	**20.6%** non-GCB (n=63)

Note:5 additional patients had an unclassified subtype of which 1 had a CR and 2 had PRs

ADDITIONAL ENDPOINTS

Durability of Response

- Median DOR was **9.2** months
- Most responses at first scan (**~2** months)

Overall Survival

- All patients (n=127) = **9.0** months
- Patients with CR or PR (n=36) = **Not Yet Reached**
- Patients with Progressive Disease or No Response (n=80) = **4.1** months

Safety:

- Most common treatment related non-hematologic AEs were fatigue, nausea and anorexia, primarily Grade 1/2, and most were manageable with dose modifications and/or supportive care
- Most common Grade 3/4 AEs were thrombocytopenia, anemia, and neutropenia, and most were also manageable with dose modifications and/or supportive care

[1] Per Lugano Classification (Cheson, 2014); as adjudicated by an Independent Central Radiological Review Committee [2] Kalakonda N, et al. ICML 2019. Abstract 031. [3] CR rate included in sNDA is 11.8% as two additional patients achieved a CR since data was presented at ICML.

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XPOVIO: A Growing Body of Safety Data

- Side effects of dosing regimens utilized in key Phase 2 and 3 trials (e.g., BOSTON, STORM, STOMP, SADAL and SEAL) were generally consistent across studies and often managed with dose adjustments or supportive care, particularly when used once weekly in combination regimens
- Major organ toxicities were not prominent in clinical studies
- No clinically significant cumulative toxicities in clinical studies
- Combination regimens have demonstrated additive or synergistic activity in studies with potential to re-sensitize malignancies to prior therapies with predictable and manageable tolerability profile

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Karyopharm and XPO1 Data Presented at ASH 2019

Overview

- **22 total abstracts presented**
  - 1 oral presentation (SPd from STOMP study)
  - 8 company-sponsored poster presentations
  - 4 investigator-sponsored poster presentations
  - 9 additional pre-clinical and clinical studies highlighting the role of XPO1 in cancer

Highlighted Data from STORM

- ***Overall Survival of Triple Class Refractory, Penta-Exposed Multiple Myeloma (MM) Patients Treated with Selinexor Plus Dexamethasone or Conventional Care: A Combined Analysis of the STORM and MAMMOTH Studies***

Highlighted Data from STOMP

- *Selinexor-Containing Regimens for the Treatment of Patients with Multiple Myeloma Refractory to Chimeric Antigen Receptor T-Cell (CAR-T) Therapy*
- *Selinexor, Pomalidomide, and Dexamethasone (SPd) in Patients with RRMM*
- *Safety and Efficacy of the Combination of Selinexor, Lenalidomide and Dexamethasone (SRd) in Patients with NDMM*
- *A Phase 1b/2 Study of Selinexor, Carfilzomib, and Dexamethasone (SKd) in RRMM*

Highlighted Eltanexor Data

- *Eltanexor (KPT-8602), a Second-Generation Selective Inhibitor of Nuclear Export (SINE) Compound, in Patients with Higher-Risk Myelodysplastic Syndrome*

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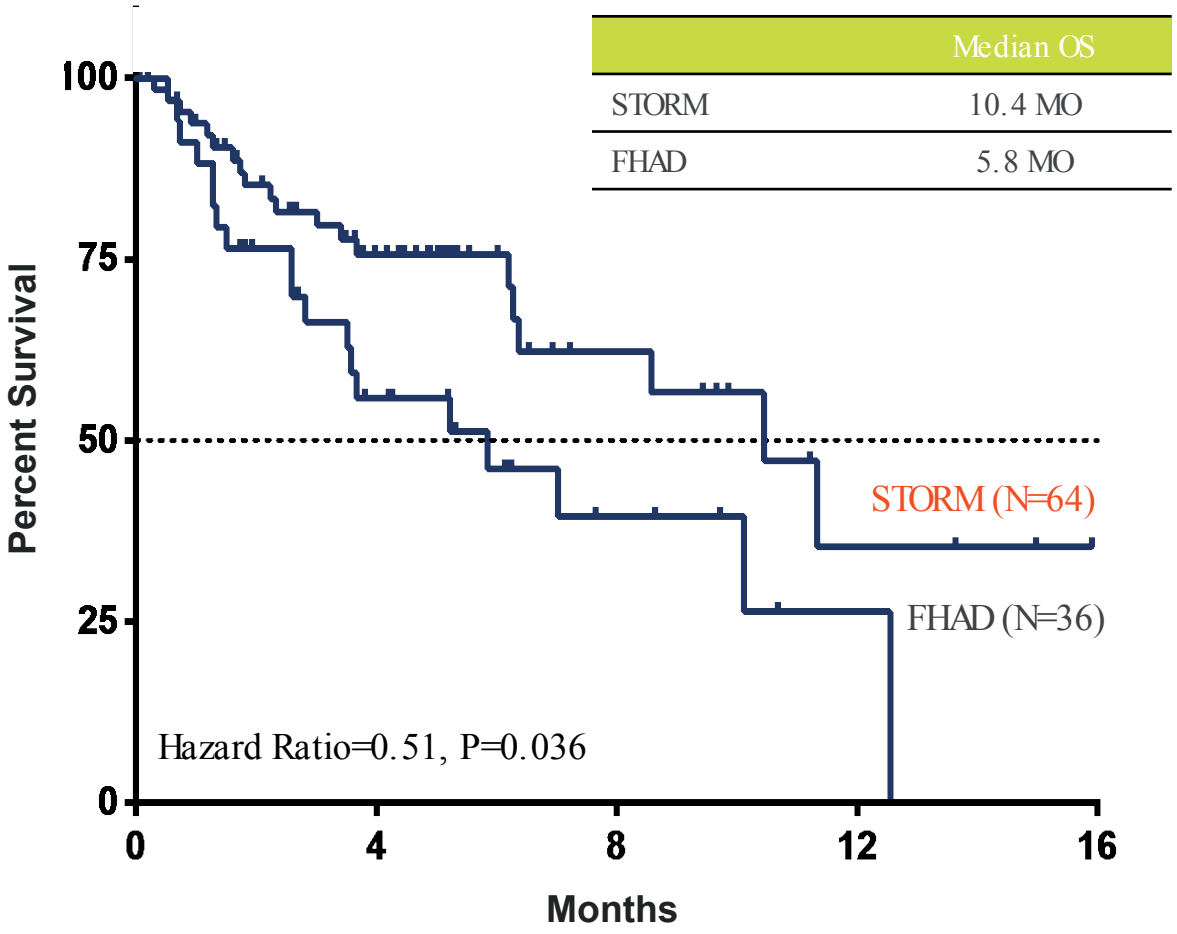
Selinexor Survival Compares Favorably with Two "Real-World" Data Sets

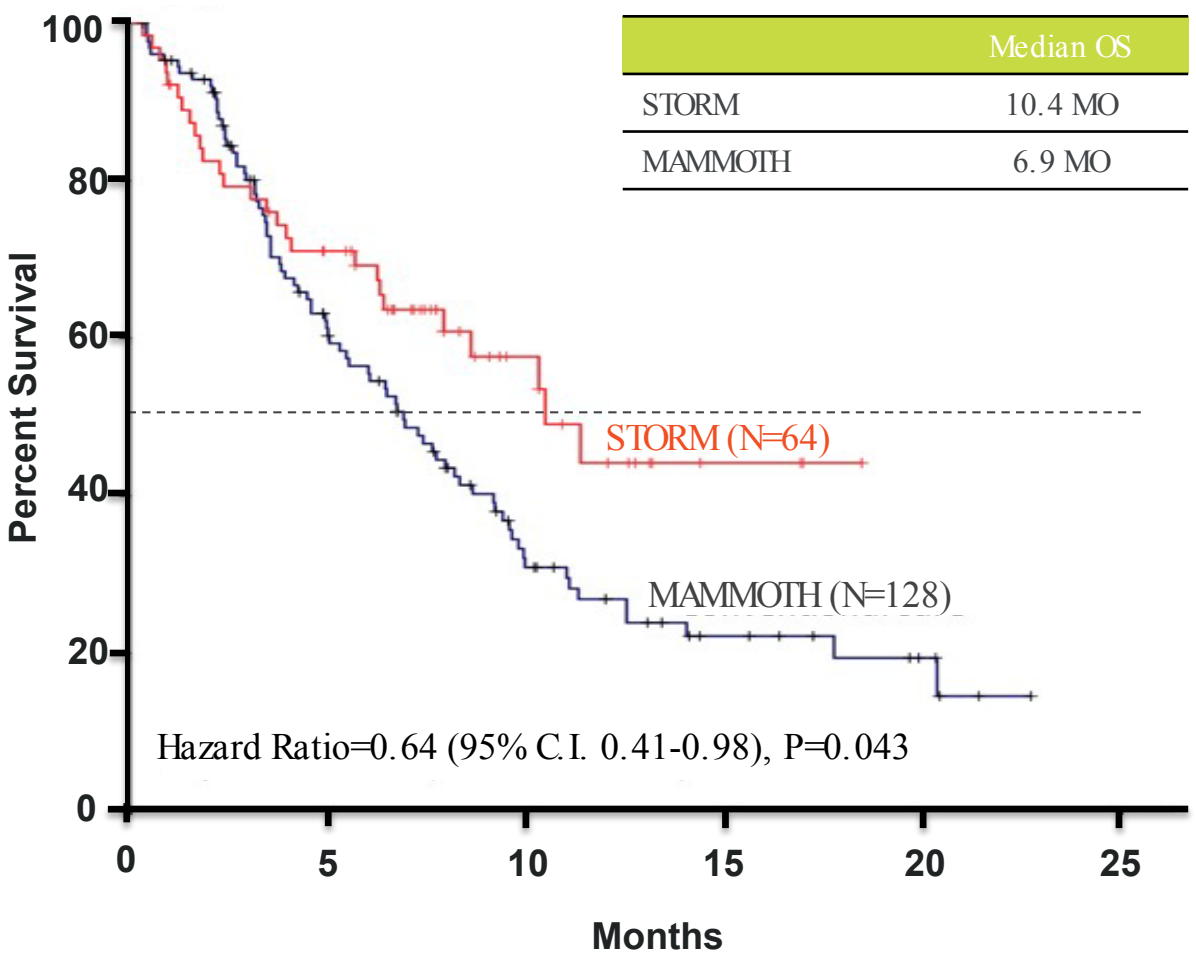
STORM vs. Flatiron Health Analytics Database (FHAD)[1]

	Median OS
STORM	10.4 MO
FHAD	5.8 MO



STORM vs. MAMMOTH (Academic)[2]

	Median OS
STORM	10.4 MO
MAMMOTH	6.9 MO



[1] Richardson P, et al., ASCO 2019. Abstract 8014. [2] Costa L, et al., ASH 2019. Abstract 3125.

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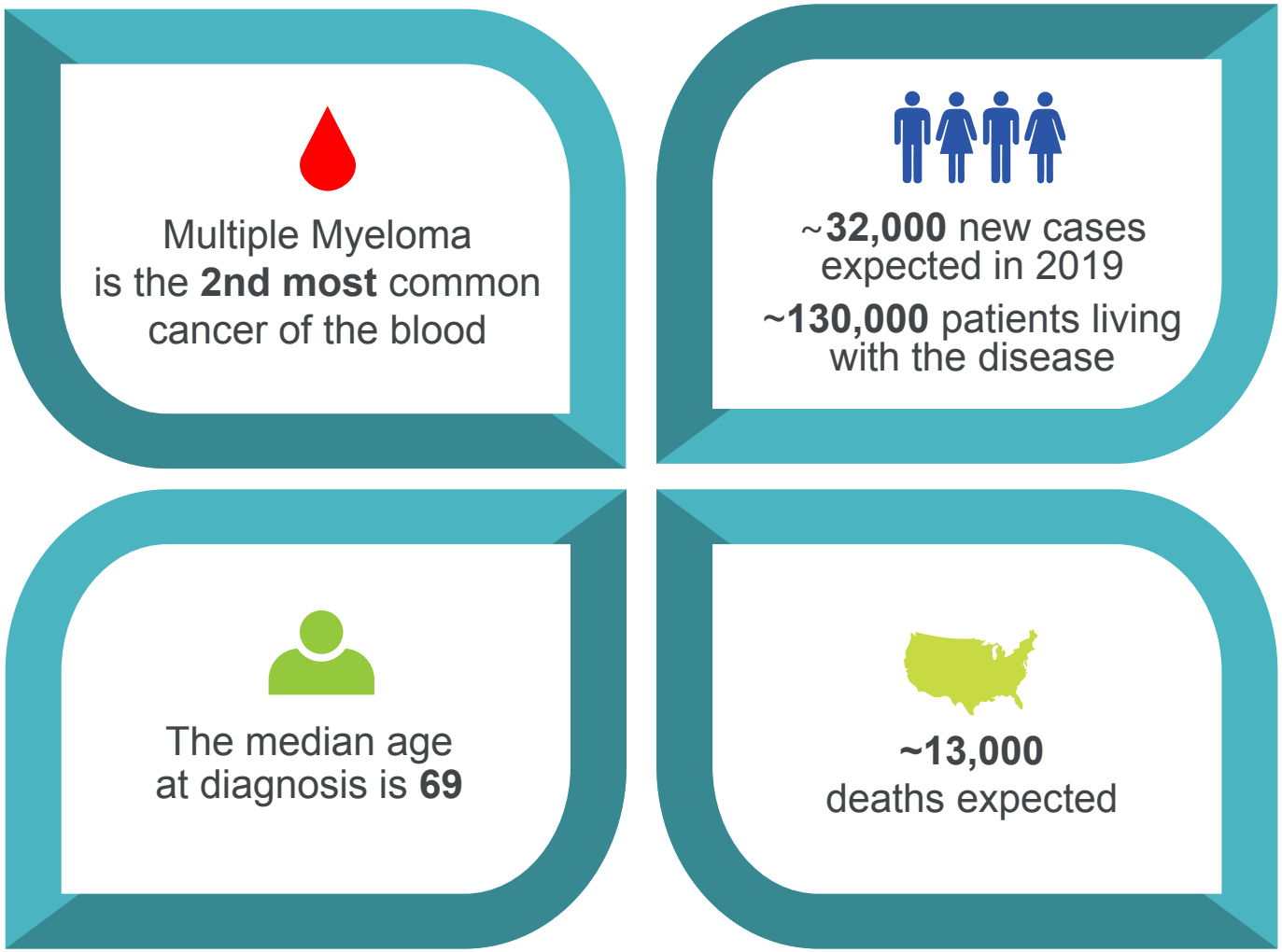
Commercial Opportunity

- Multiple Myeloma
- Diffuse Large B-Cell Lymphoma (DLBCL)

Multiple Myeloma Represents a Large Commercial Opportunity Where Patients are In Need of New Treatment Options



U.S. Statistics, 2019

Source: SEER Cancer Stat Facts, January 2019. National Cancer Institute.

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An Estimated 6,000 Patients Being Treated in the 4th Line+ Setting in the U.S.

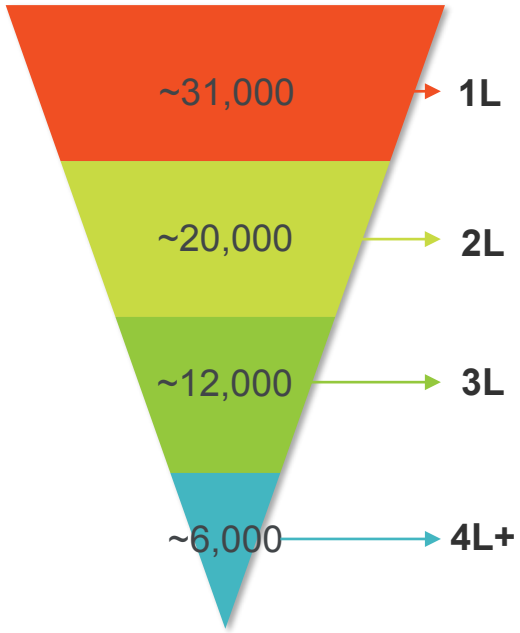
~69,000
Patients treated with drug therapy in 2019

Patients by Line of Treatment

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

# of patients with relapsed / refractory disease is growing annually by mid-single digits due to population growth and increased life expectancy as a result of newly available treatment options

Estimated U.S. Multiple Myeloma 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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Supporting a Successful XPOVIO Commercial Launch

Establish

nuclear export inhibition as a novel, fundamental approach in the treatment of multiple myeloma

Position

XPOVIO as the oral, agent of choice with a clinically meaningful efficacy profile in its approved indication

Educate

HCPs and patients on XPOVIO's side effect profile and related management strategies

Minimize

access barriers to help appropriate patients start and stay on therapy

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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]

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

[1] Based on analysis of Symphony Claims data.

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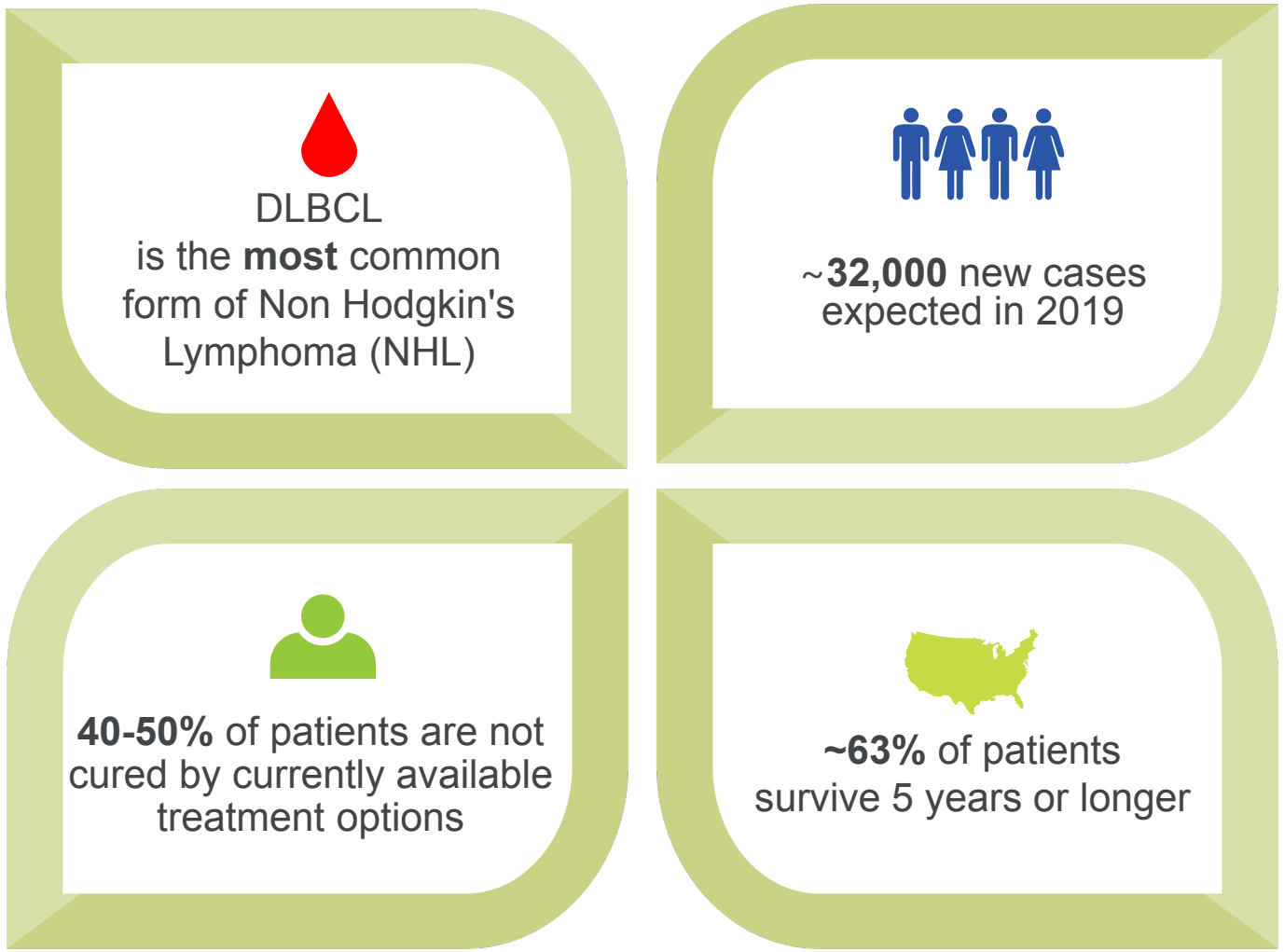
DLBCL Represents an Additional Large Commercial Opportunity Where Patients are In Need of New Treatment Options



U.S. Statistics, 2019

Sources: SEER Cancer Stat Facts, January 2019. National Cancer Institute, Decision Resources NHL and CLL Landscape and Forecast 2018, Kantar Health.

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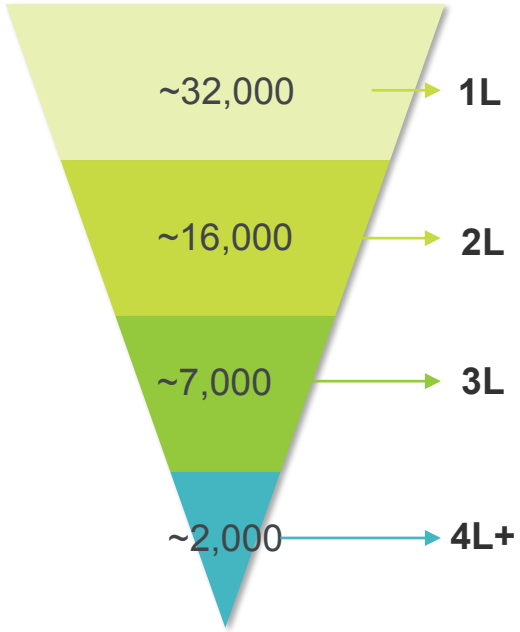
An Estimated 9,000 DLBCL Patients Being Treated in the 3rd and 4th Line+ Setting in the U.S.

~57,000
Patients treated with drug therapy in 2019

Patients by Line of Treatment

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



# of patients with relapsed / refractory disease is growing annually by low to 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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Future Opportunities and Additional Highlights

All Oral Pipeline

Hematologic Malignancies - Selinexor	Phase I	Phase II	Phase III
Multiple Myeloma (relapsed/refractory) | **STORM**	**FDA Approved (Accelerated Approval)[1]**		
Multiple Myeloma (relapsed/refractory) | **BOSTON**[2]			
Multiple Myeloma (relapsed/refractory and front-line) | **STOMP**[3]			
Diffuse Large B-cell Lymphoma (relapsed/refractory) | **SADAL**			sNDA Submitted Dec 23, 2019[4]
Diffuse Large B-cell Lymphoma (combination with rituximab-gemcitabine-dexamethasone-platinum (R-GDP)) | **XPORT-DLBCL-030**[5]			
Diffuse Large B-cell Lymphoma (combination with chemo and non-chemo regimens) | **XPORT-DLBCL-025**[5]			

Solid Tumor Malignancies - Selinexor	Phase I	Phase II	Phase III
Liposarcoma (advanced unresectable dedifferentiated liposarcoma) | **SEAL**			
Endometrial Cancer (maintenance therapy) | **SIENDO**			
CRC (combination with pembrolizumab) and NSCLC (combination with docetaxel) | **XPORT-STP-027**[5]			

Glioblastoma Multiforme (GBM) - Selinexor	Phase I	Phase II	Phase III
Glioblastoma (recurrent gliomas) | **KING**			
Glioblastoma (combination with active agents / newly diagnosed or recurrent) | **XPORT-GBM-029**[5]			

Additional Oncology Programs - Eltanexor and KPT-9274	Phase I	Phase II	Phase III
Myelodysplastic Syndromes (MDS) (single agent or in combination with hypomethylating agents[5]) Drug: Eltanexor			
Colorectal Cancer (CRC) and Prostate Cancer (PrC) Drug: Eltanexor			
Solid Tumors & Acute Myeloid Leukemia (AML) Drug: KPT-9274			

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

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Selinexor in Solid Tumor Malignancies

Selinexor in Liposarcoma

- Ongoing Phase 3 SEAL study; randomized, double-blind trial evaluating single-agent selinexor versus placebo in patients with advanced unresectable dedifferentiated liposarcoma after at least two systemic therapies
- Primary endpoint: PFS (crossover from placebo to selinexor is allowed)
- Top-line data expected in 2020
- Selinexor achieved PFS of 5.5 months versus 2.7 months for placebo in Phase 2 (n=56), HR=0.67 (RECIST v1.1)[1]

Selinexor in Endometrial Cancer

- Ongoing Phase 3 SIENDO study; transitioned to a company-sponsored trial (2019) evaluating once weekly selinexor as a maintenance therapy versus placebo in patients with endometrial cancer after first-line chemotherapy
- Achieved 45% DCR, 3 months mPFS and 8 months mOS in Phase 2 SIGN study (n=20)[2]

[1] Gounder, M, et al. ASCO 2018. Abstract 11512. [2] Vergote, I, et al. ESMO 2016. Abstract 8540.

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Financial Highlights

$270M

Cash, cash equivalents, restricted cash and investments

BALANCE SHEET
30-Sept-2019[1]

Into Middle of 2021

EXPECTED RUNWAY WITH CASH ON HAND[1]

63M

73M fully diluted

SHARES OUTSTANDING
30-Sept-2019[1]

[1] Third Quarter Financial Results, 11/4/19.

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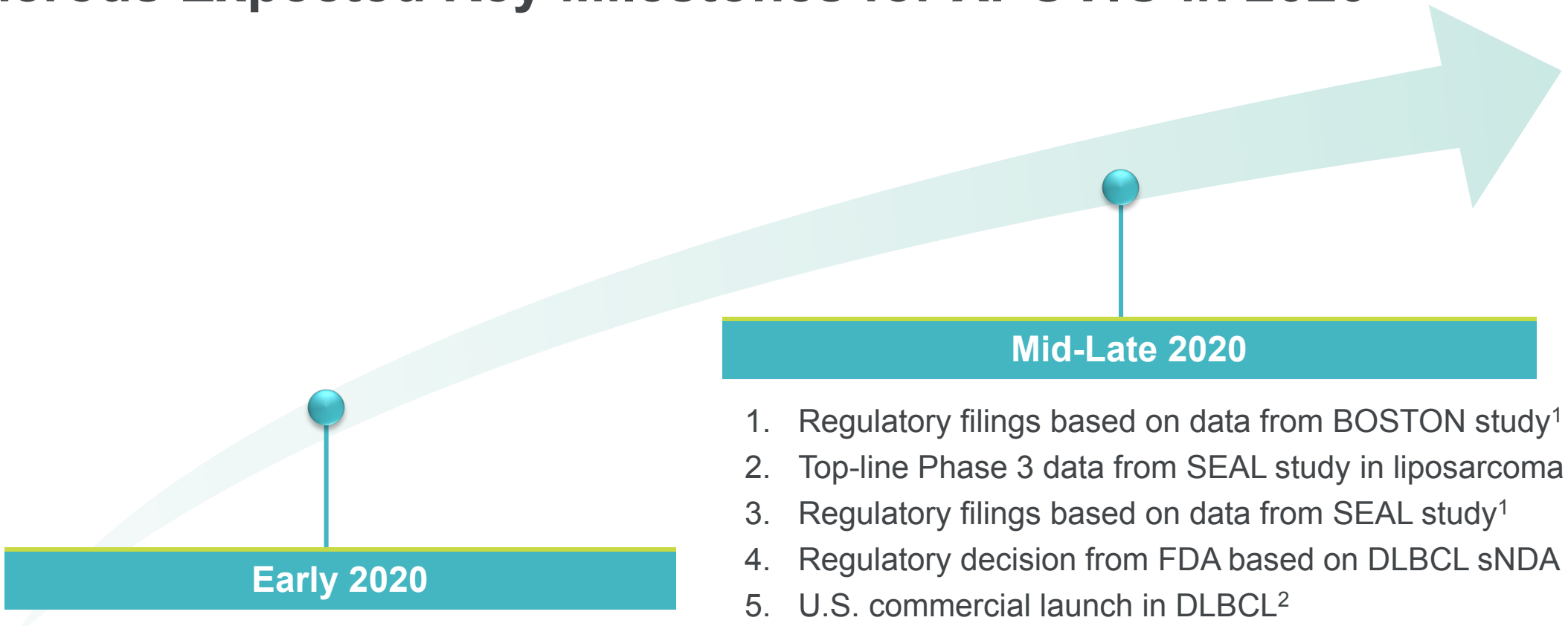
Numerous Expected Key Milestones for XPOVIO in 2020



Early 2020

1. Top-line Phase 3 data from BOSTON study
2. Regulatory decision expected in Europe in heavily pre-treated / refractory multiple myeloma

Mid-Late 2020

1. Regulatory filings based on data from BOSTON study[1]
2. Top-line Phase 3 data from SEAL study in liposarcoma
3. Regulatory filings based on data from SEAL study[1]
4. Regulatory decision from FDA based on DLBCL sNDA
5. U.S. commercial launch in DLBCL[2]
6. Start of confirmatory Phase 3 Study in DLBCL in support of potential accelerated approval
7. U.S. commercial launch in 2nd line multiple myeloma[1,2]

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

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Thank You