



*An Innovation-driven Pharmaceutical Company Focused on
Improving the Lives of Patients with Cancer and Other
Major Diseases*

June 2020

Forward-looking Statements and Other Important Information

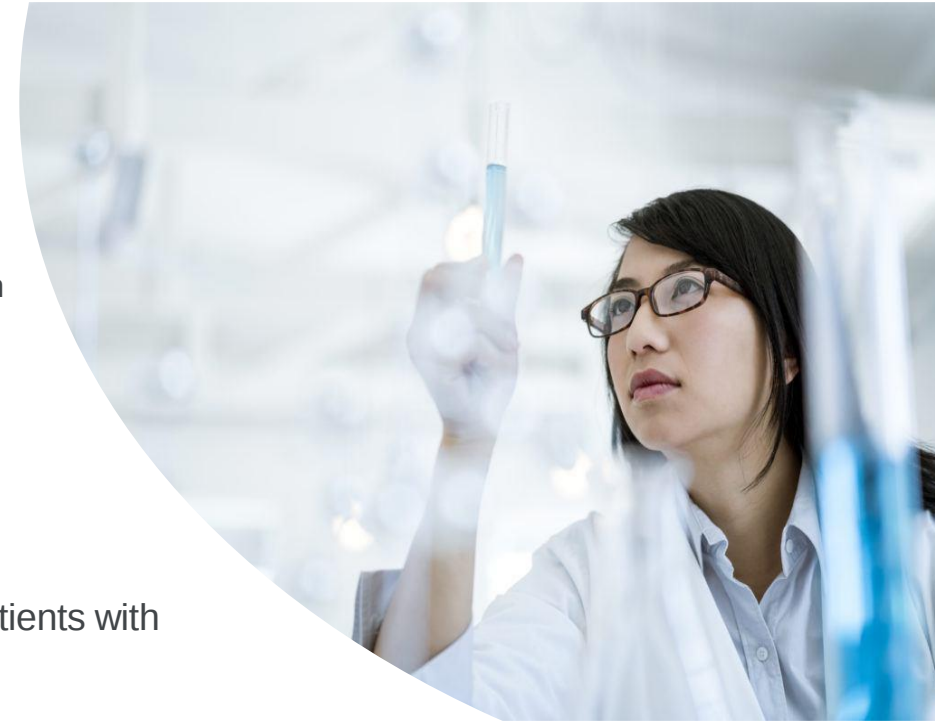
This presentation contains forward-looking statements within the meaning of the “safe harbor” provisions of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm’s expectations and plans relating to selinexor as a potential treatment for patients with multiple myeloma, diffuse large B-cell lymphoma, other types of cancer, and COVID-19; the design and execution of Karyopharm’s clinical trials to study selinexor, including the dosing regimen; the potential anti-viral and anti-inflammatory properties of selinexor; 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 treatment of patients with relapsed and / or refractory DLBCL; and Karyopharm’s strategic and financial plans and expectations as well as financial projections for Karyopharm, including 2020 financial guidance and the sufficiency of cash to fund operations through mid-2022. 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 the development or commercialization of 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: 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 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; 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 for which Karyopharm is currently developing its drug candidates; that the markets for multiple myeloma and DLBCL drugs will grow as predicted; Karyopharm’s ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the COVID-19 pandemic could disrupt Karyopharm’s business more severely than it currently anticipates, including by reducing sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients. These and other risks are described under the caption “Risk Factors” in Karyopharm’s Annual Report on Form 10-Q for the quarter ended March 31, 2020, which was filed with the Securities and Exchange Commission (SEC) on May 5, 2020, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this presentation 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.

Agenda

- Company Overview
- Multiple Myeloma
- Diffuse Large B-Cell Lymphoma (DLBCL)
- Additional Opportunities and Highlights
- Appendix: Additional Clinical Data

Karyopharm at a Glance

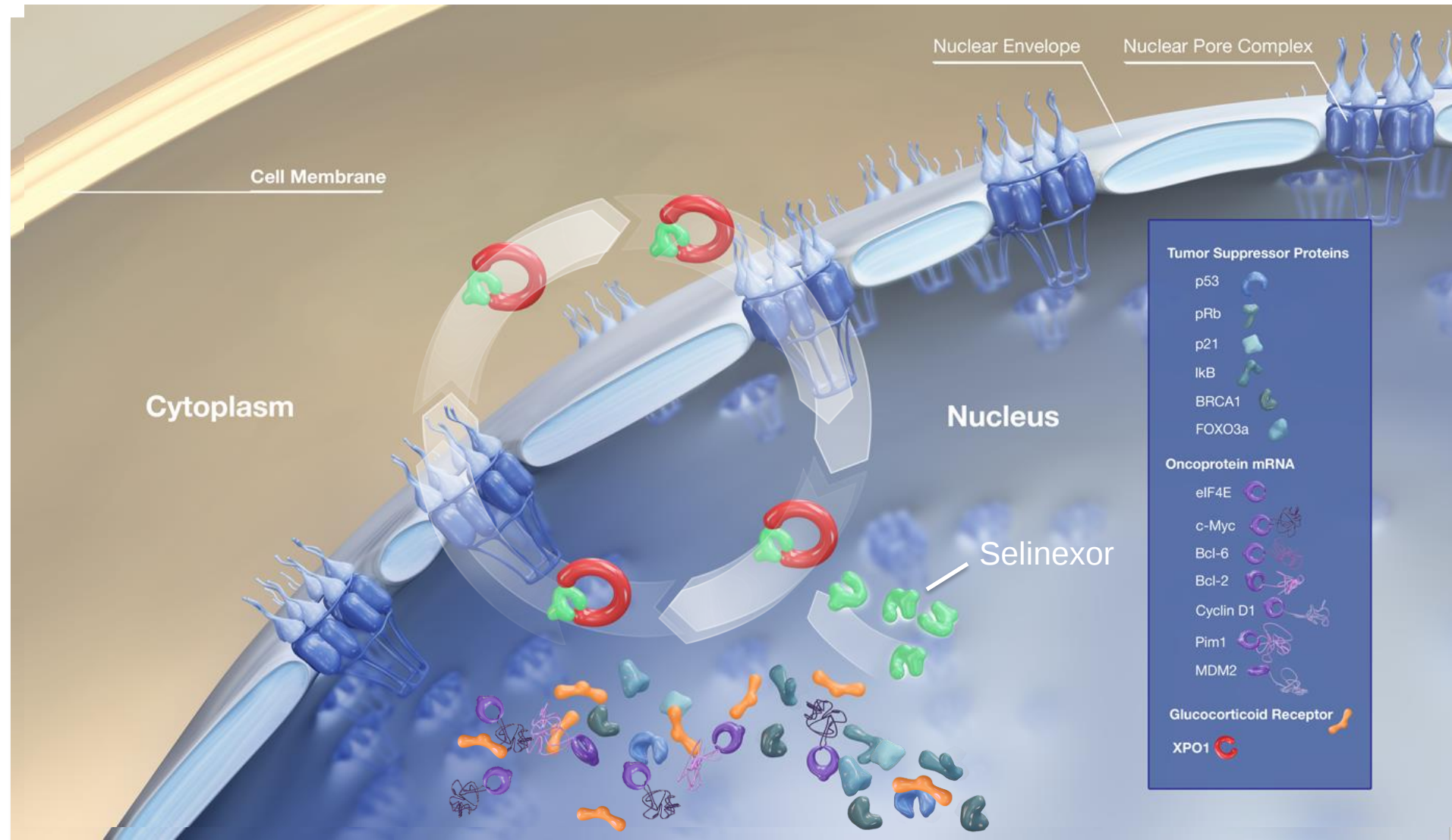
- Fully integrated, commercial-stage, global pharmaceutical company
- Industry leader in targeting nuclear export dysregulation as a mechanism to treat cancer
- First drug, XPOVIO® (selinexor), received accelerated approval from the FDA in July 2019
- Pivotal Phase 3 BOSTON study data presented at ASCO 2020 Annual Meeting; Study met primary endpoint of a statistically significant increase in progression-free survival (PFS)
 - sNDA submitted to FDA in May 2020 requesting expansion of label to include treatment for patients with multiple myeloma after at least one prior line of therapy
- MAA submitted for Europe in January 2019 with decision expected in late-2020
- sNDA in relapsed or refractory diffuse large B-cell lymphoma (DLBCL) accepted by FDA with Priority Review granted and PDUFA date set for June 23, 2020
- Recently initiated randomized, global clinical study to evaluate low dose oral selinexor in patients with severe COVID-19
- 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



XPOVIO / SINE Mechanism of Action: Inhibition of XPO1¹⁻⁴

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.

Significant Progress Made So Far in 2020



Commercial Update

- Q1 2020 XPOVIO net sales of **\$16.1M** (total revenues of **\$18.1M**)
- **>150 new** physicians / accounts prescribed XPOVIO for the first time in Q1 2020
- Achieved **leading** customer engagement in Q1 2020¹
- XPOVIO demand **accelerated in April 2020** compared to March



Pipeline / Clinical Data Update

- **Positive** top-line BOSTON Phase 3 data announced on March 2nd
- BOSTON data presented in **oral presentation** at ASCO 2020 Virtual Scientific Program
- BOSTON sNDA submitted **ahead of schedule on May 19, 2020**
- DLBCL sNDA granted **Priority Review** with June 23, 2020 PDUFA action date
- **Initiated** randomized study to evaluate low dose oral selinexor in patients with **severe COVID-19** based on strong scientific rationale and pre-clinical data



Corporate Development and Balance Sheet

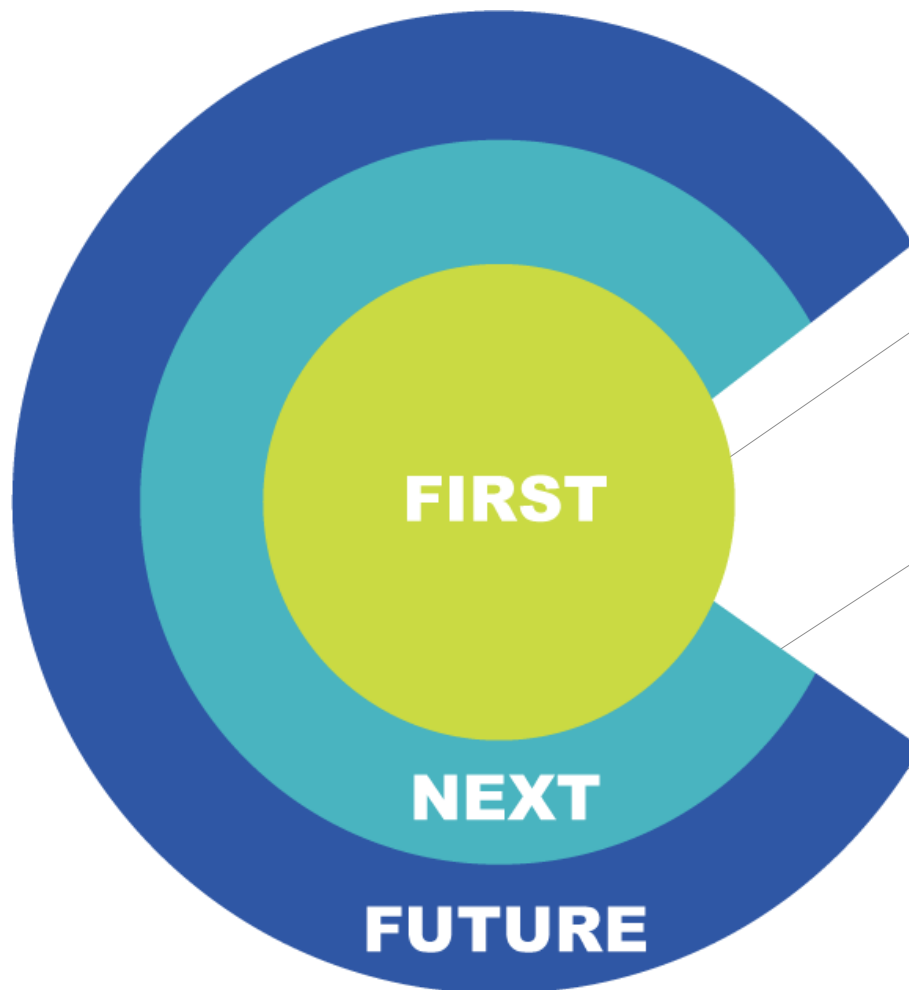
- **Expanded territory rights** with Antengene to now include Australia, South Korea and additional Asian countries; Karyopharm to receive **\$12M** upfront and potential additional milestones / royalties
- **Reacquired commercial rights** for selinexor and eltanexor from Ono Pharmaceutical Co. in **Japan** (at no cost to Karyopharm)
- Completed common stock offering in Q1 2020 with net proceeds of **~\$162M**
- Ended Q1 2020 with **~\$385M** in cash and investments; cash runway now expected to be sufficient to fund planned operations into **middle of 2022**

¹ Highest sales force reach and frequency rating to target customers according to leading industry market insights provider.

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Planned XPOVIO (selinexor) Development Strategy in Multiple Myeloma



Phase 2b STORM study¹ addressing patients with heavily pretreated relapsed refractory multiple myeloma

- Disease refractory to PIs, IMiDs and Darzalex[®]
- High 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 with approved therapies

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.

XPOVIO® (selinexor) Received Accelerated Approval by the FDA 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

¹XPOVIO Prescribing Information.

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.

Safety Highlights from the XPOVIO Prescribing Information¹

- 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

¹XPOVIO Prescribing Information.

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 Week¹ (n=202)

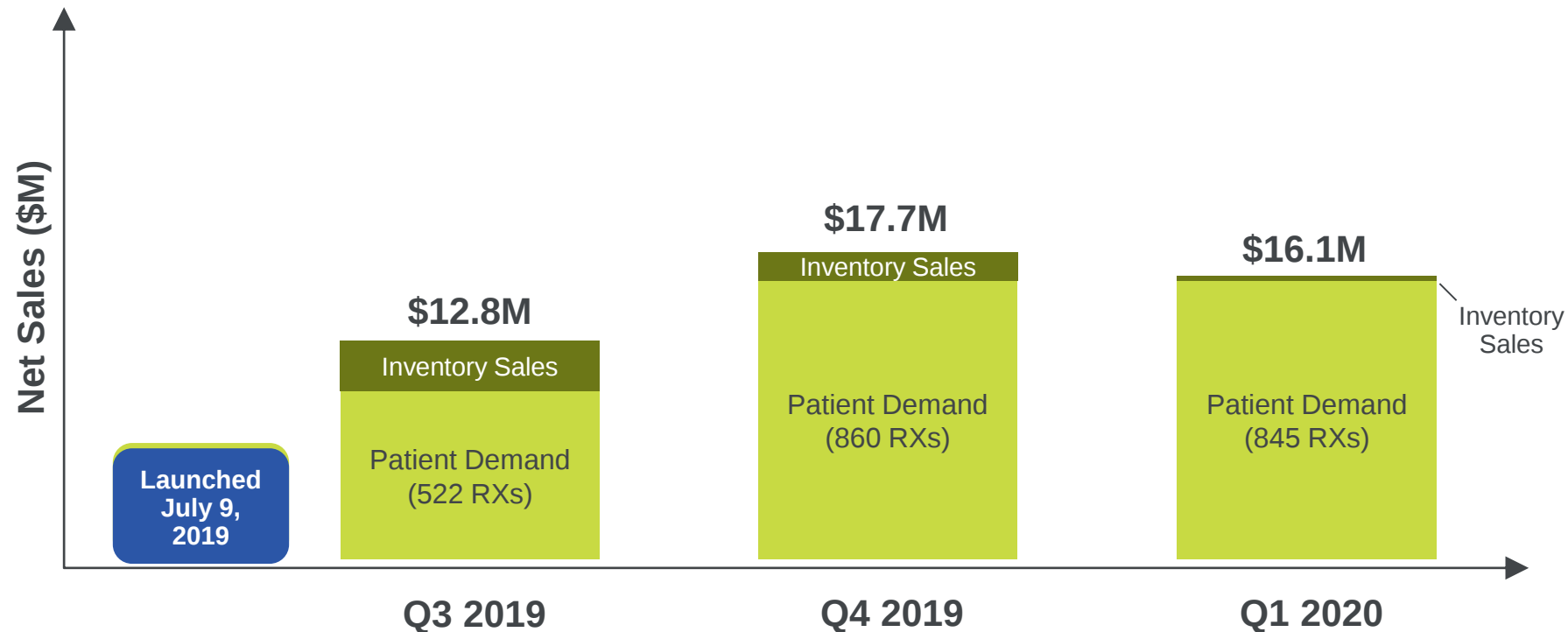
- The most common adverse reactions (incidence $\geq 20\%$) were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infections
- The treatment discontinuation rate 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.

XPOVIO Quarterly Sales

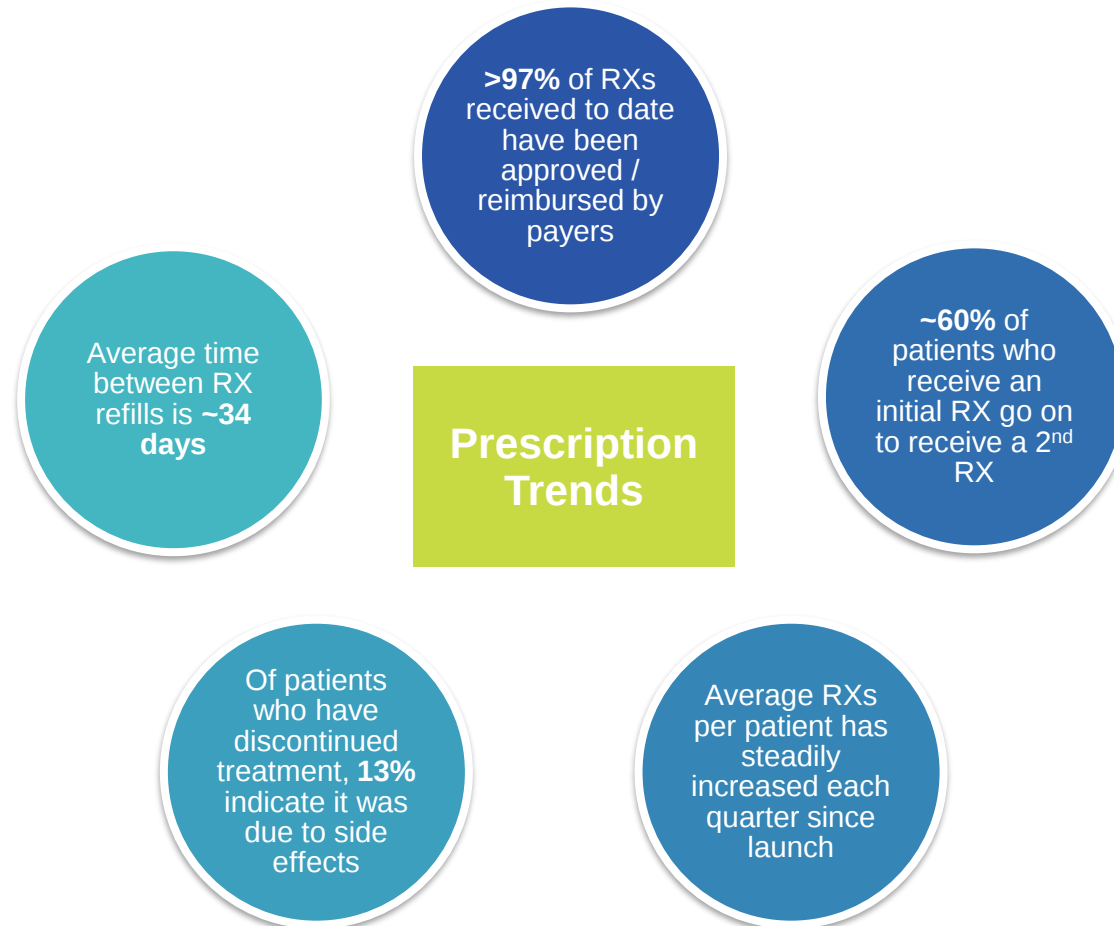
XPOVIO Product Sales Following Launch



- **>2,200** prescriptions (RX) filled through March 31, 2020
- **Minimal inventory build** in distribution channel in Q1 2020
- Prescription demand **approximately flat** Q1 2020 vs. Q4 2019 primarily due to fewer than expected new patient starts which were impacted by the COVID-19 pandemic
- Average prescription refill rate **continued to grow** in Q1
- **Rx demand accelerated** in April 2020 compared to March

XPOVIO Patient Experience Continues to be Highly Positive

Real World Experience July 2019 – March 2020²



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

Rationale to Conduct the BOSTON Study

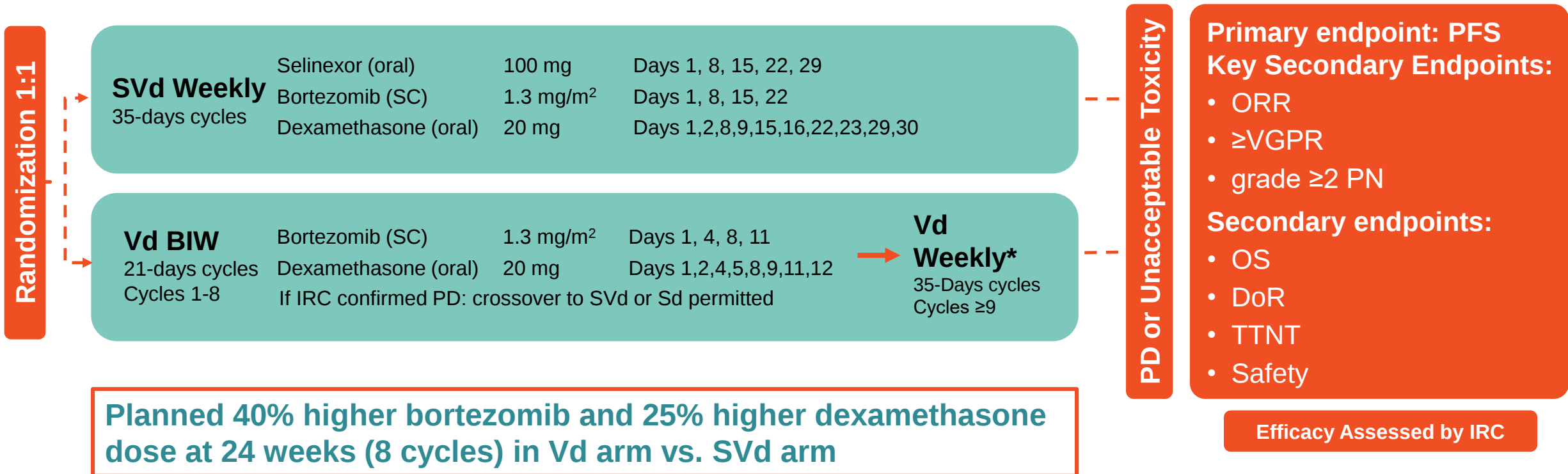
BOSTON Design

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 SVd³
- 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

¹Turner, J, et al. Oncotarget October 2016. ²Kashyap, T, et al. Oncotarget October 2016. ³Bahlis NJ, et al. Blood 2018.

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

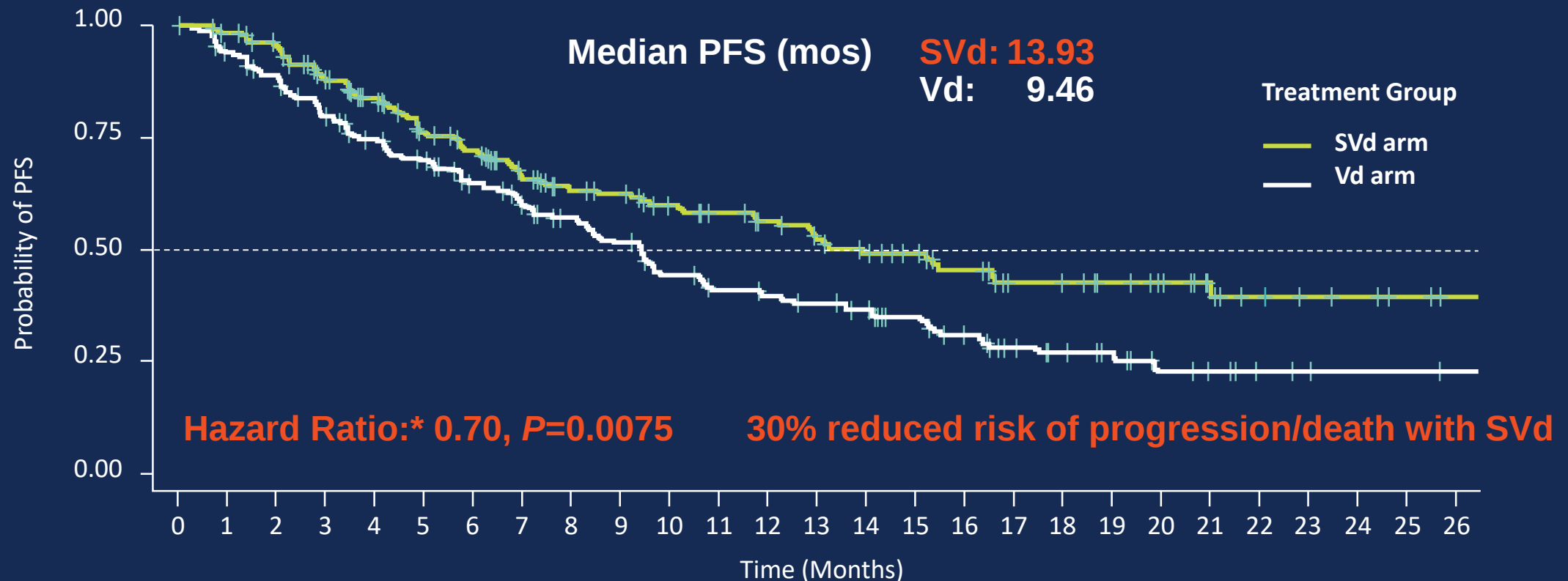


CR= complete response, DoR = duration of response, IMWG = International Myeloma Working Group, IRC = Independent Review Committee, OS = overall survival, PD = progressive disease, PFS = progression free survival, PR = partial response, PN = peripheral neuropathy, sCR = stringent complete response, TTNT = 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.

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

Early and Sustained PFS Benefit (Assessed by IRC)

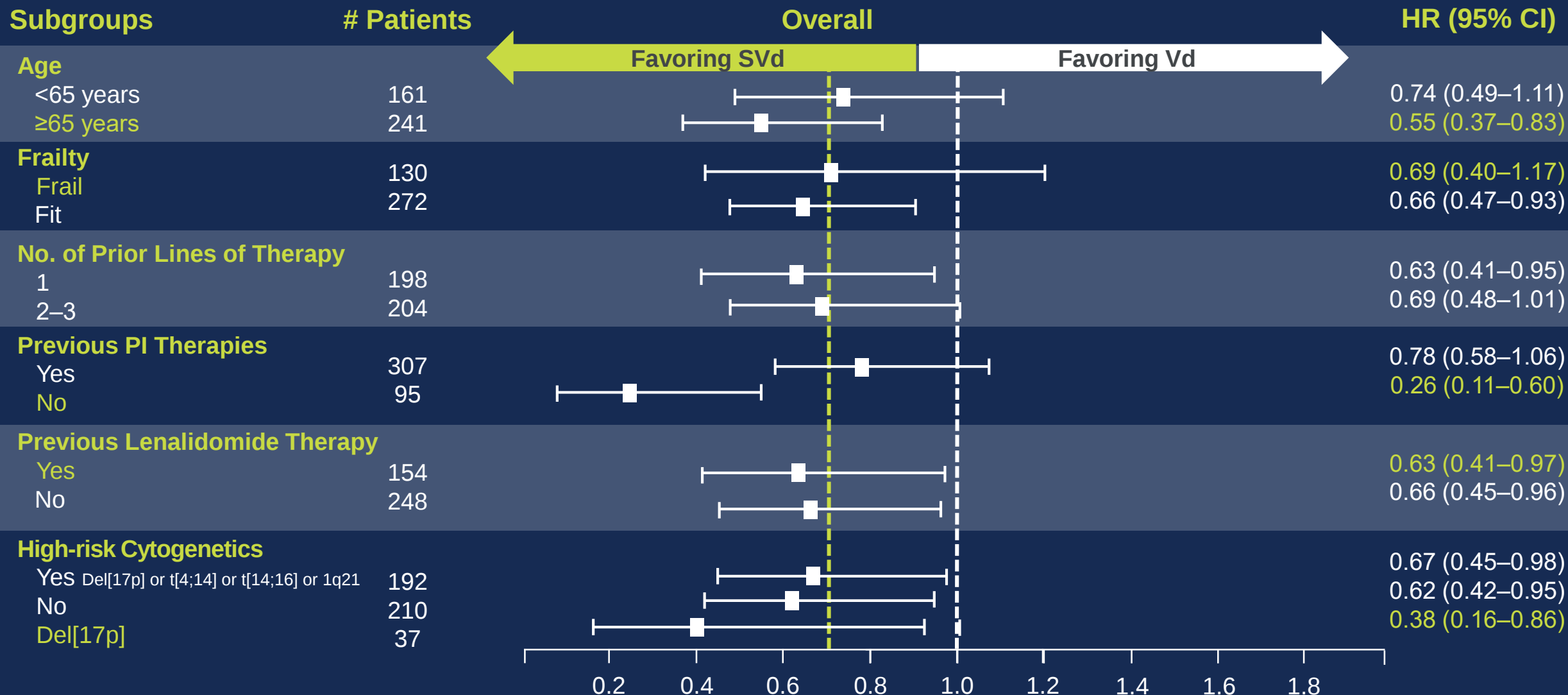


SVd Arm	195	187	175	152	135	117	106	89	79	76	69	64	57	51	45	41	35	27	26	22	19	14	9	7	6	4	2
Vd Arm	207	187	175	152	138	127	111	100	90	81	66	59	56	53	49	42	35	26	20	16	10	8	5	4	3	3	2

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

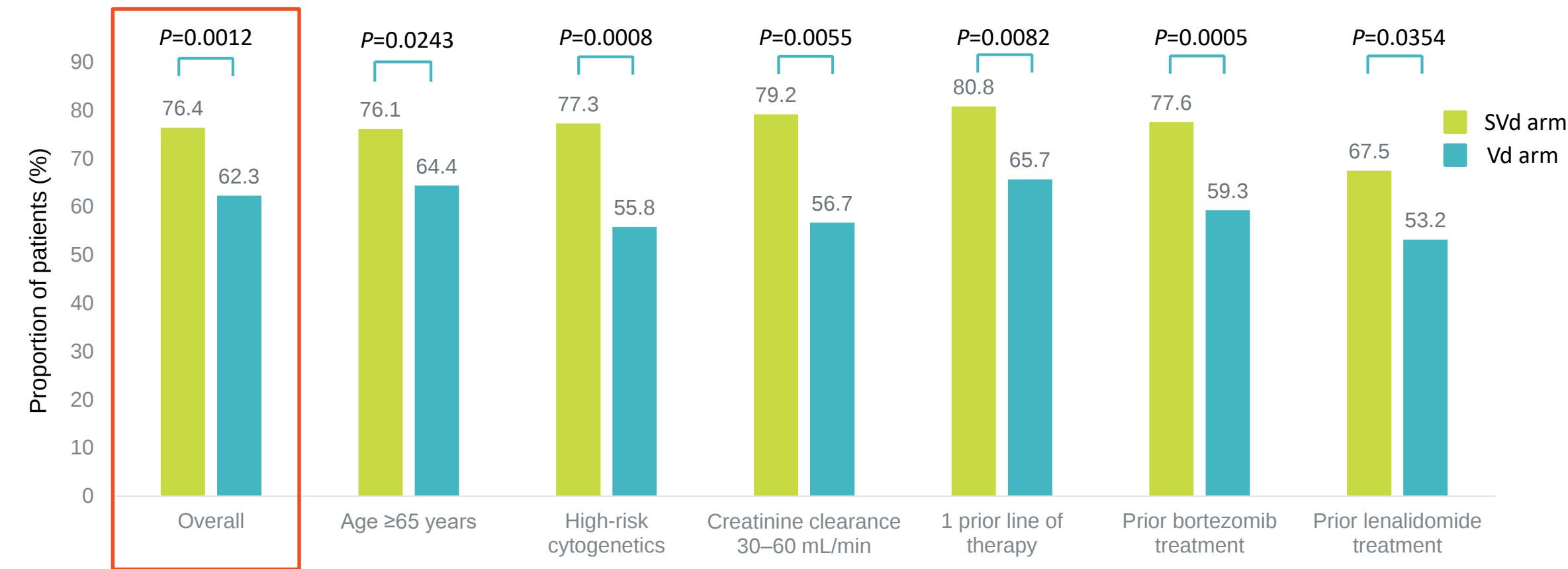
Consistent PFS Benefit for SVd Across Subgroups



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

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

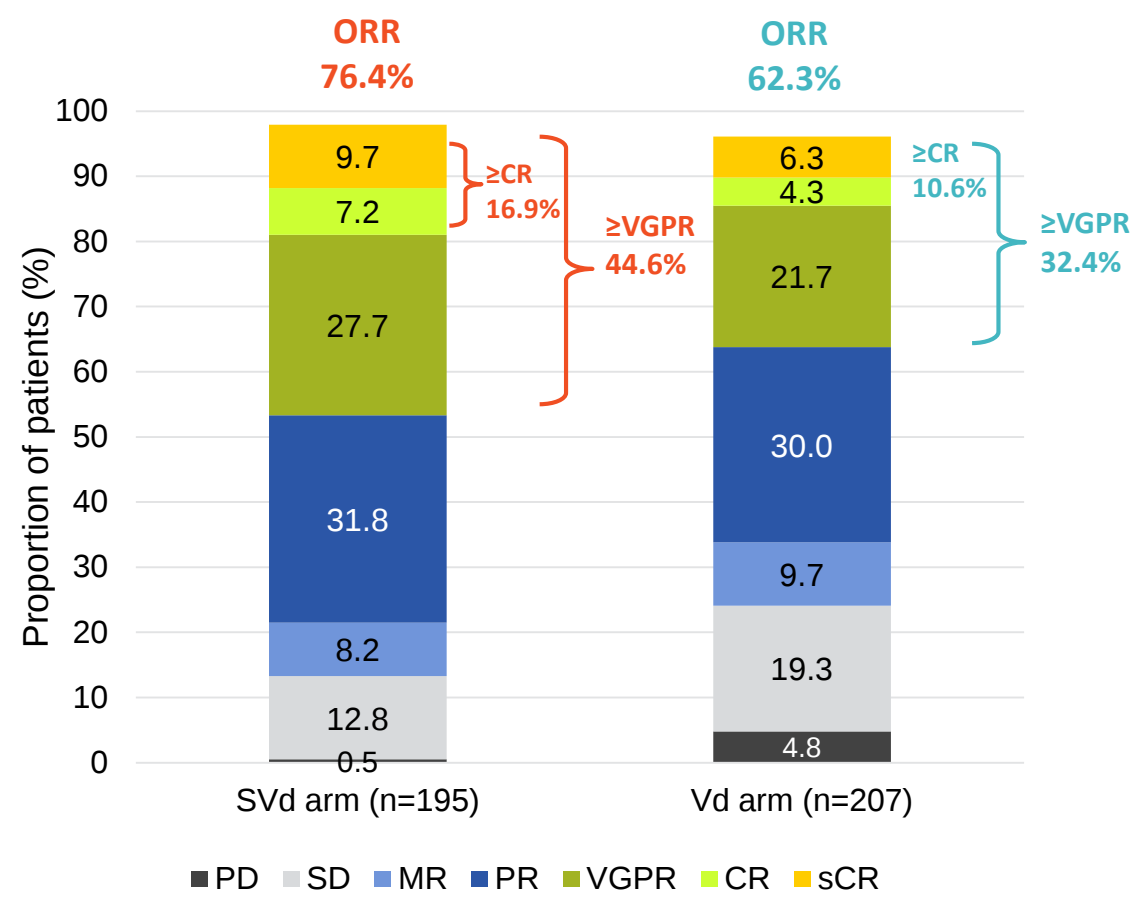
SVd Was Associated With a Significantly Higher ORR Overall and Across Patient Subgroups



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.

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



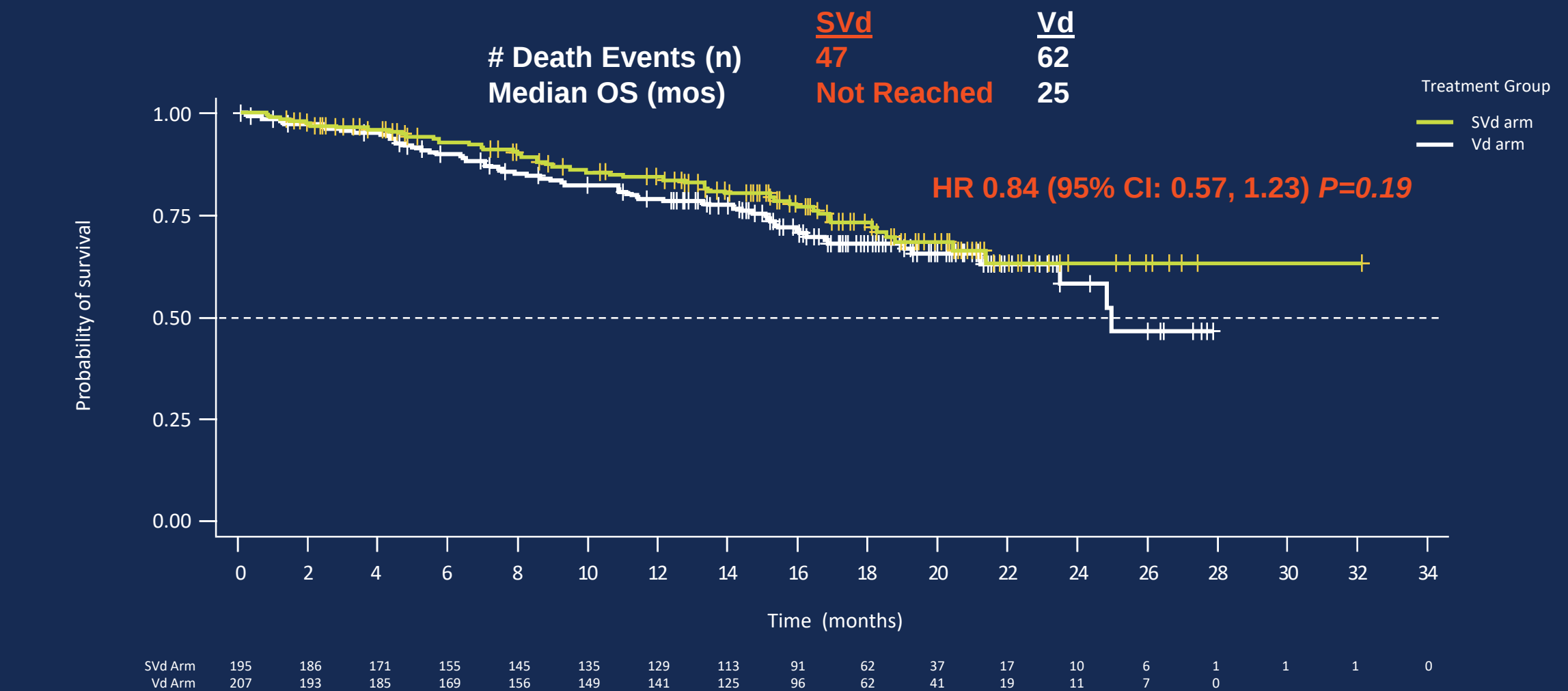
Longer Duration of Response with SVd

	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 al. 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.

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.

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

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.

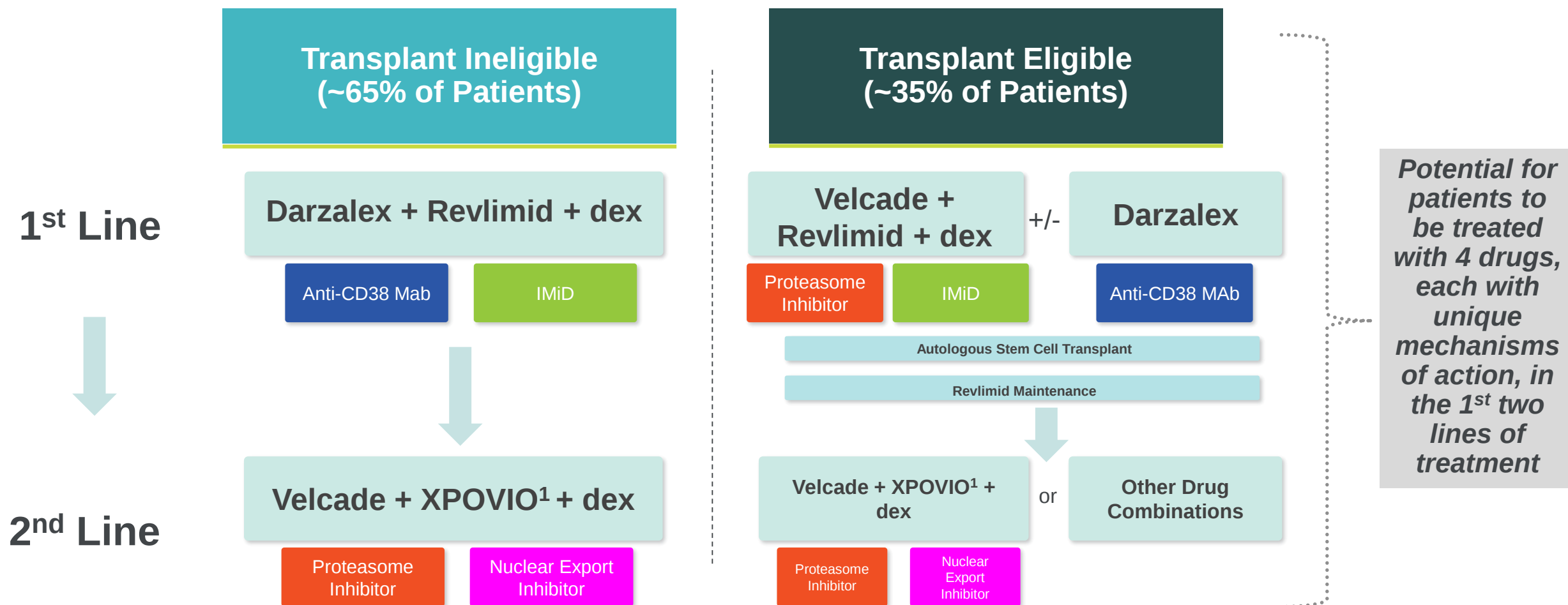
Selected Non-Hematological TEAEs*

	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 Track 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.

Expected Future Trend in 1st line Treatment May Create Significant Opportunity for XPOVIO in the 2nd line¹



¹XPOVIO is currently only approved by the FDA 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). The schematic illustrated above represents what a treatment paradigm might look like should XPOVIO be approved by the FDA as 2nd Line+ treatment in multiple myeloma in combination with Velcade and dexamethasone.

STOMP: Study Overview & Objectives

Selinexor and backbone **T**reatments **O**f multiple **M**yeloma **P**atients (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



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

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	Darzalex	ORR = 29% 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 therapies⁹

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).



Commercial Opportunity

- Multiple Myeloma

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



Multiple Myeloma
is the **2nd most** common
cancer of the blood



~**32,000** new cases
~**130,000** patients living
with the disease



The median age
at diagnosis is **69**



~**13,000**
deaths expected

U.S. Statistics, 2019

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

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 Base¹

- ~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.

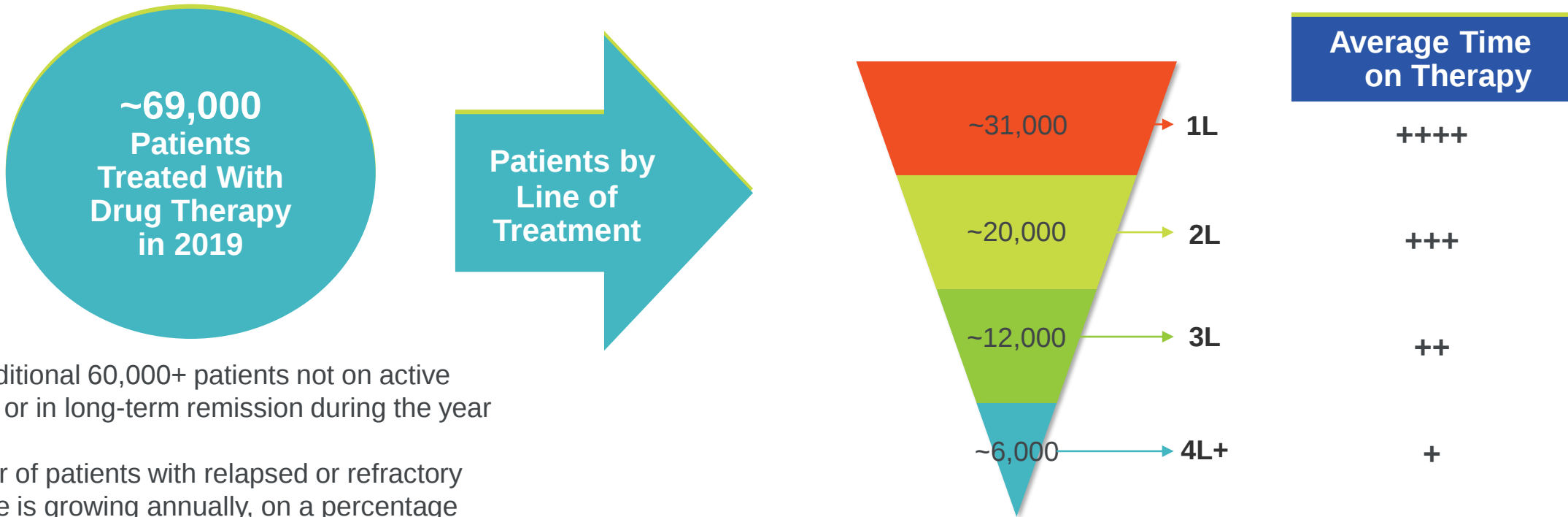
Background on the Treatment of Multiple Myeloma

- **Main classes of MM drugs used across lines of therapy include:**
 - Proteasome inhibitors (PIs): Velcade® (bortezomib), Kyprolis® (carfilzomib)
 - Immunomodulatory agents (IMiDs): Revlimid® (lenalidomide), Pomalyst® (pomalidomide)
 - Monoclonal antibodies (mAbs): Darzalex® (daratumumab), Empliciti® (elotuzumab)
 - Nuclear export inhibitor: XPOVIO® (selinexor) is the only drug in this class and is currently approved in heavily pretreated patients
- **Drugs with proven single-agent clinical activity are generally preferred by physicians, even when used in 2-4 drug-combination regimens**
 - Single agent (± steroids) activity: Revlimid®, Pomalyst®, Darzalex®, Velcade®, Kyprolis®, XPOVIO®
 - Used in combination: Alkylators, Glucocorticoids, Empliciti®
- **Velcade®, a proteasome inhibitor, is a well-established treatment for patients in early and late lines of treatment, typically in combination with dexamethasone and either an IMiD or mAb**
- **Standard Velcade® therapy is dosed twice per week and administered as a subcutaneous injection**
 - Prolonged usage is often limited due to its main adverse reaction, peripheral neuropathy, or due to acquired resistance

Patients and physicians demand new options with increasing efficacy and novel mechanisms of action

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

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

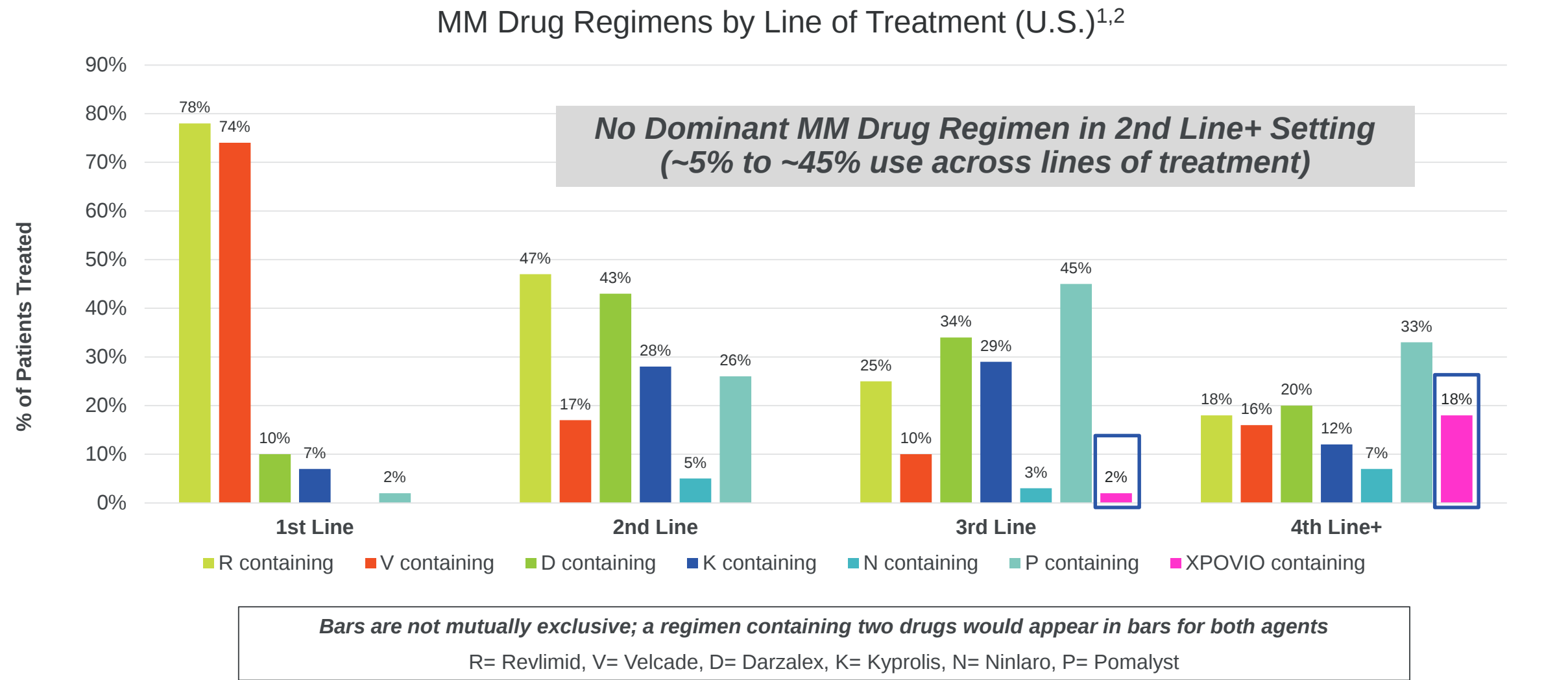


An additional 60,000+ patients not on active treatment or in long-term remission during the year

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.

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



¹ Karyopharm market research (Post Launch ATU Survey Wave 1 (Oct'19), 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.

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

2019 Worldwide Sales¹

Immunomodulatory Agents

- Revlimid: \$11B
- Pomalyst: \$2.5B

Proteasome Inhibitors

- Velcade: \$1.6B
- Kyprolis: \$1B

Monoclonal Antibodies

- Darzalex: \$3B

¹ EvaluatePharma, February 2020.

Agenda

- Company Overview
- Multiple Myeloma
- Diffuse Large B-Cell Lymphoma (DLBCL)
- Additional Opportunities and Highlights
- Appendix: Additional Clinical Data

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



DLBCL
is the **most** common
form of Non Hodgkin's
Lymphoma (NHL)



~**32,000** new cases
expected in 2019



40-50% of patients are not
cured by currently available
treatment options



~**63%** of patients
survive 5 years or longer

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.

SADAL¹: A Phase 2b Study In DLBCL

- *Enrollment completed and top-line data reported at ASH 2018 and Updated at ICML 2019*
 - *sNDA accepted by FDA with Priority Review granted*
 - *PDUFA date set for June 23, 2020*

N=127

Relapsed or Refractory or Transformed DLBCL

- Study includes patients with 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 Selinexor Against Diffuse Aggressive Lymphoma

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.

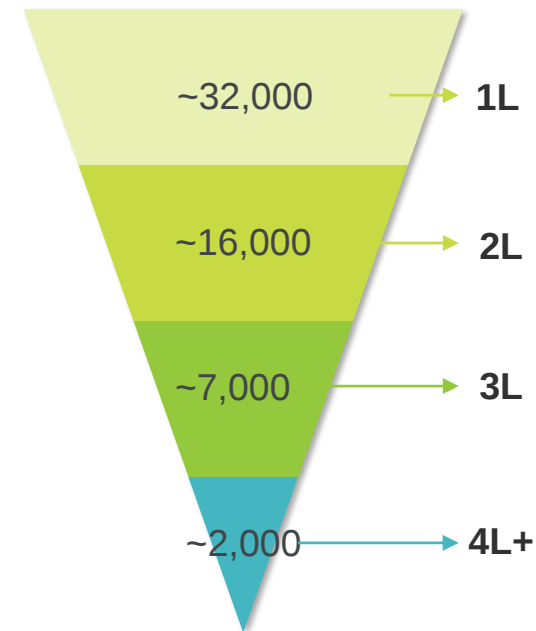
An Estimated 9,000 DLBCL Patients Being Treated in the 3rd and 4th Line+ Setting in the U.S.

~57,000
Patients treated
with drug
therapy in 2019

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

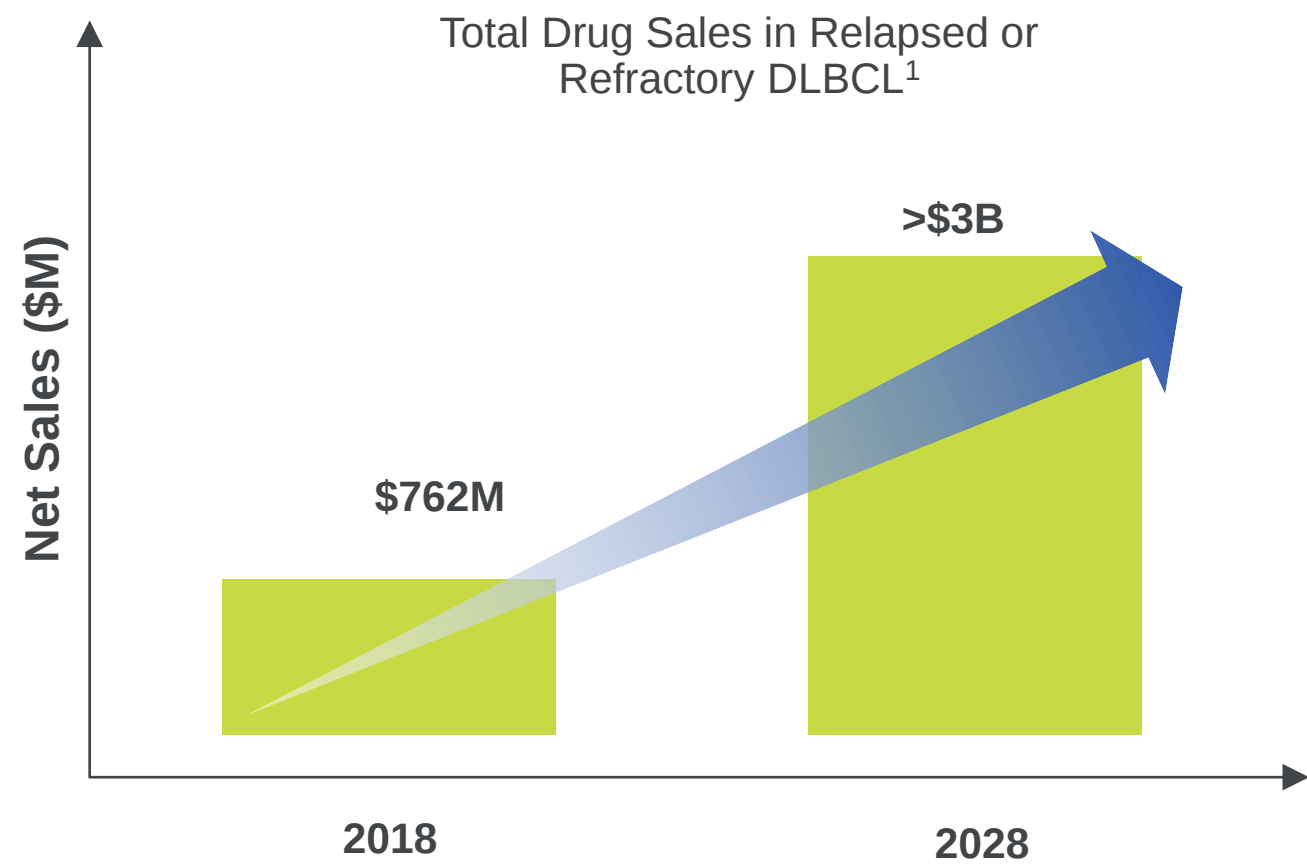


Estimated U.S. DLBCL Patients Treated by Line of Therapy, 2019



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

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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Karyopharm Initiates New Study of Low-dose Selinexor in Patients with Severe COVID-19

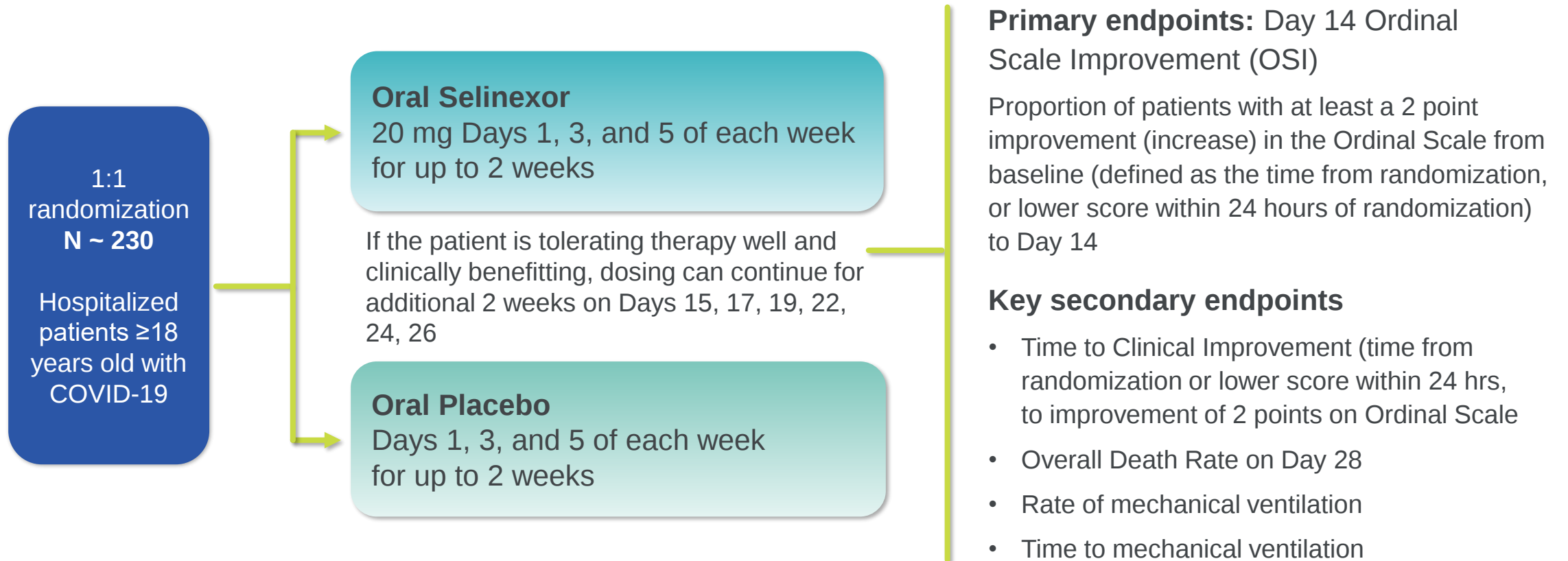
Scientific Rationale for Evaluating Selinexor in COVID-19

- XPO1 inhibitors have previously demonstrated preclinical activity against >20 viruses, including influenza, RSV and other viral respiratory infections
- XPO1 was identified as one of the host proteins with the highest number of functional connections with SARS-CoV proteins¹
- Selinexor demonstrated potent inhibition of SARS-CoV2 propagation in monkey Vero cells inhibiting the production of new virus by 90% at a low concentration (100 nM) from cells infected with SARS-CoV2²
 - Additionally, even lower levels of selinexor (only 10nM) reduced the ability of the virus to infect new cells by about 99%
- Blockade of XPO1 amplifies the activities of anti-inflammatory transcription factors: I κ B, PPAR γ , RXRa, and others
- Verdinexor (closely related SINE compound to selinexor) treatment (low dose) delayed up to 4 days after influenza virus infection in mice showed marked anti-viral and anti-inflammatory activity and improved survival
- The severity of COVID-19, caused by SARS-CoV2, is associated with high levels of pro-inflammatory cytokines
 - Selinexor protects against LPS-induced sepsis in mice, ameliorated lung injury and reduced serum levels TNF α , IL-6 and HMGB-1

¹ Zhou Y, et. al. Cell Discovery. 2020. ² Ralph A. Tripp, Ph.D., University of Georgia.

A Phase 2 Randomized, Single-Blind Study to Evaluate the Activity and Safety of Low Dose Oral Selinexor in Patients with Severe COVID-19 (NCT04349098)

~40 International Study Sites, ~10 countries



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 Japan¹

Neopharm Group

Exclusive distribution agreement for the commercialization of XPOVIO in Israel and the Palestinian Authority²

Europe, Japan and Other Key Markets

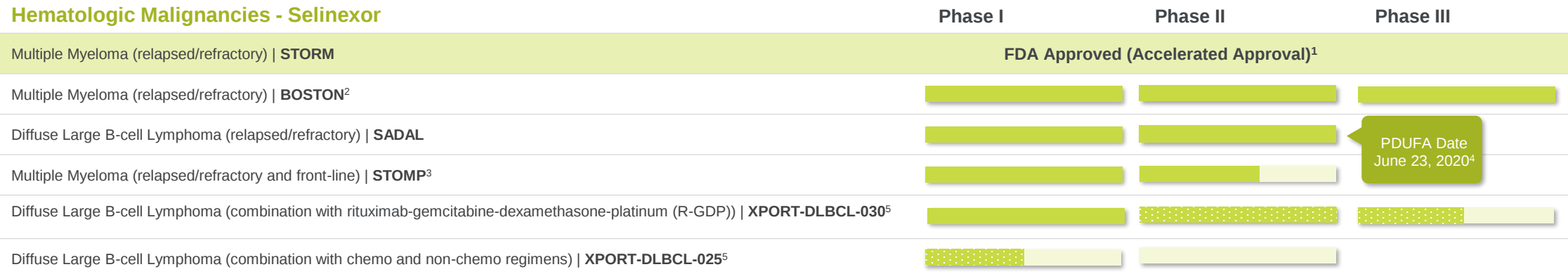
Seeking potential collaboration arrangements with commercial partners; analyzing potential for Karyopharm to commercialize in select European markets

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

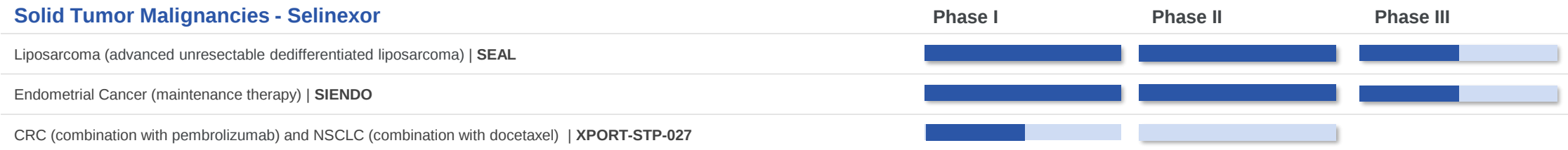
¹ Original transaction in May 2018 for China and some other Asian markets; territory agreement was expanded in May 2020 to include additional Asia-Pacific markets. ² In February 2020, Karyopharm and Promedico, a fully-owned Neopharm LTD company, entered into an exclusive distribution agreement in Israel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

Karyopharm's Novel Pipeline | Selinexor

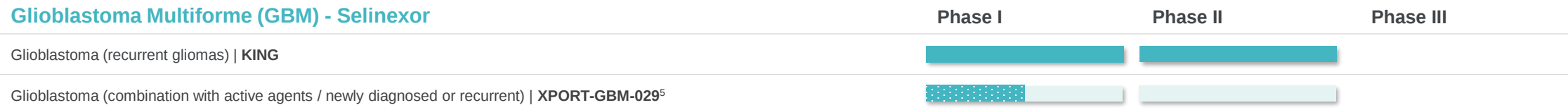
Hematologic Malignancies - Selinexor



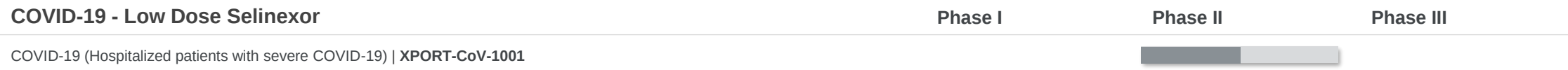
Solid Tumor Malignancies - Selinexor



Glioblastoma Multiforme (GBM) - Selinexor

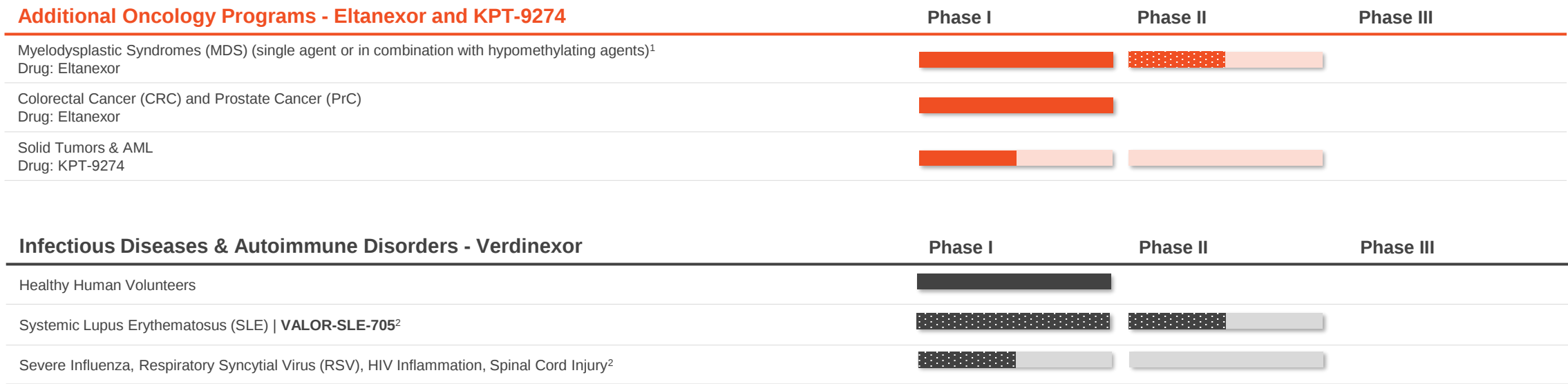


COVID-19 - Low Dose Selinexor



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 With request for accelerated approval (U.S.). ⁵ Study expected to start in 2020

Karyopharm’s Novel Pipeline | Eltanexor, KPT-9274 and Verdinecor



¹ Study expected to start in 2020. ² Study start pending submission and acceptance of IND.

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 35% DCR, 3 months mPFS and 7 months mOS in Phase 2 SIGN study (n=23)²

¹ Gounder, M, et al. ASCO 2018. Abstract 11512. ² Vergote, I, et al. Gynecologic Oncology. December 2019.

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

Financial Highlights

\$385M

Cash, cash equivalents, restricted cash and investments

BALANCE SHEET
31-Mar-2020¹

**Into
Middle of
2022**

EXPECTED RUNWAY WITH
CASH ON HAND¹

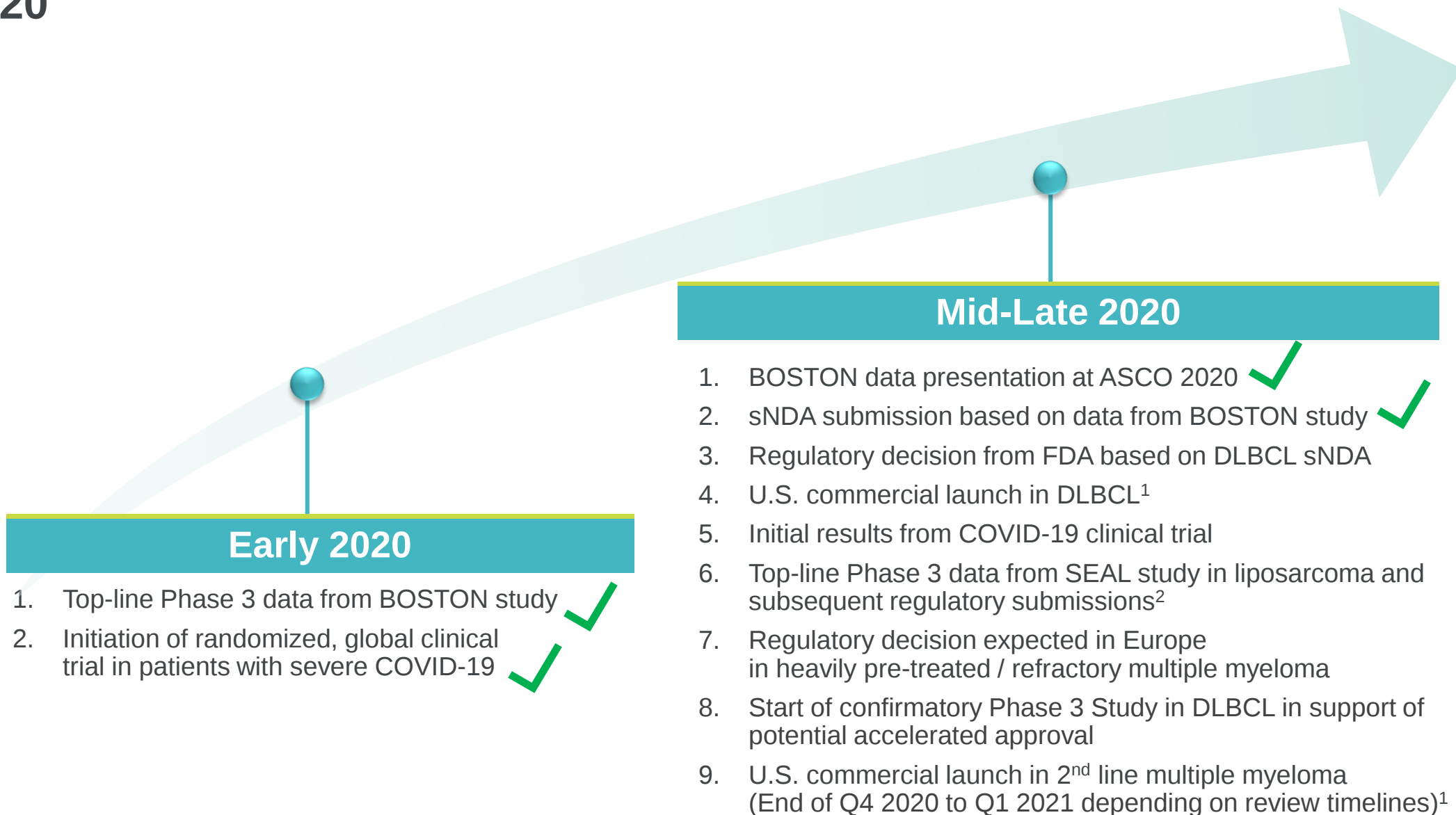
73M

86M fully diluted

SHARES OUTSTANDING
31-Mar-2020¹

¹ First Quarter Financial Results, 05/5/20.

Numerous Expected Key Milestones for XPOVIO / Selinexor in 2020



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

 Thank You



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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 $\geq 1000/\text{mm}^3$
 - Hemoglobin $\geq 8.5\text{g/dL}$
 - Platelets $\geq 75,000/\text{mm}^3$ or $\geq 50,000/\text{mm}^3$ 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

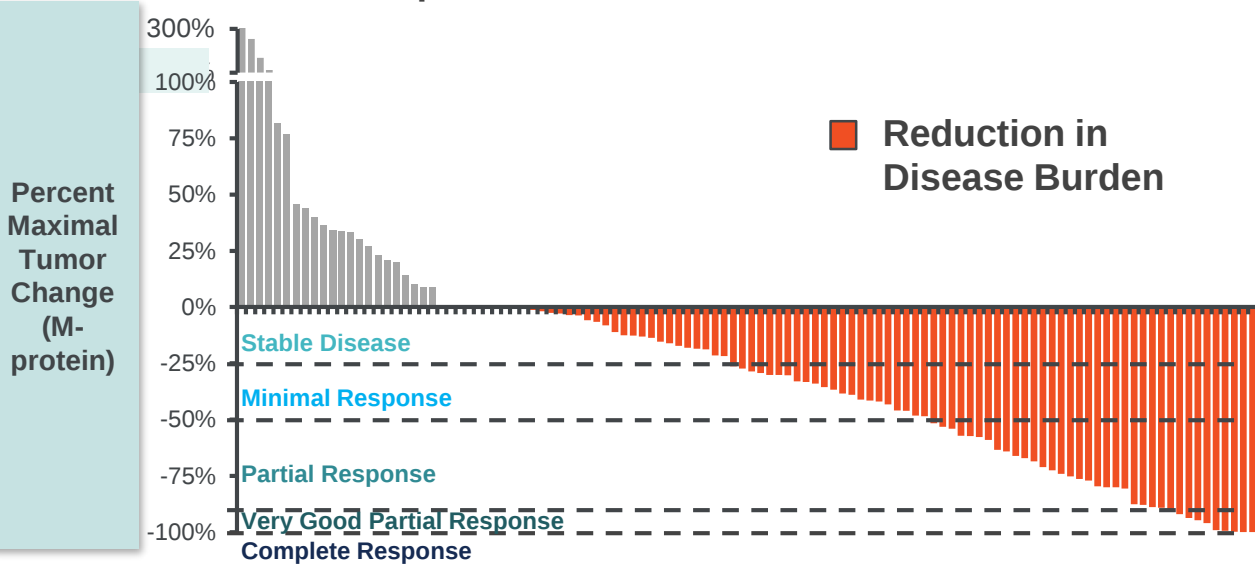
¹XPOVIO Prescribing Information.

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.

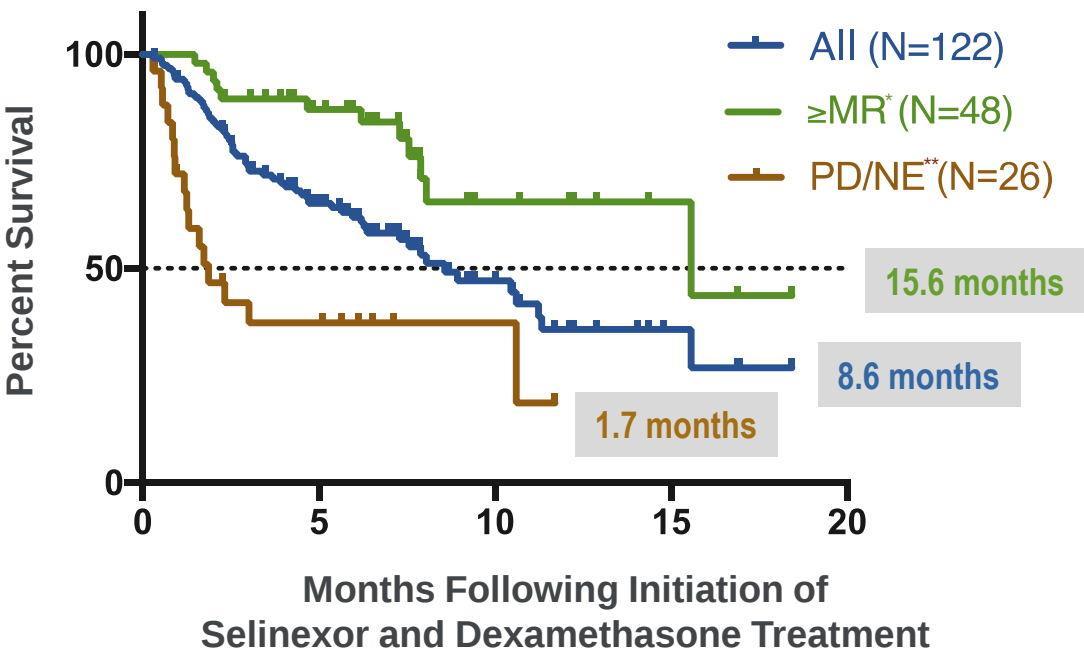
Additional Efficacy Data from Part 2 of STORM (n=122)¹

Change in M-Protein Levels²

71% of patients had a reduction in disease burden



Overall Survival by Group³



* ≥MR = Patients had a minor response or better; at least a 25% decrease in M protein

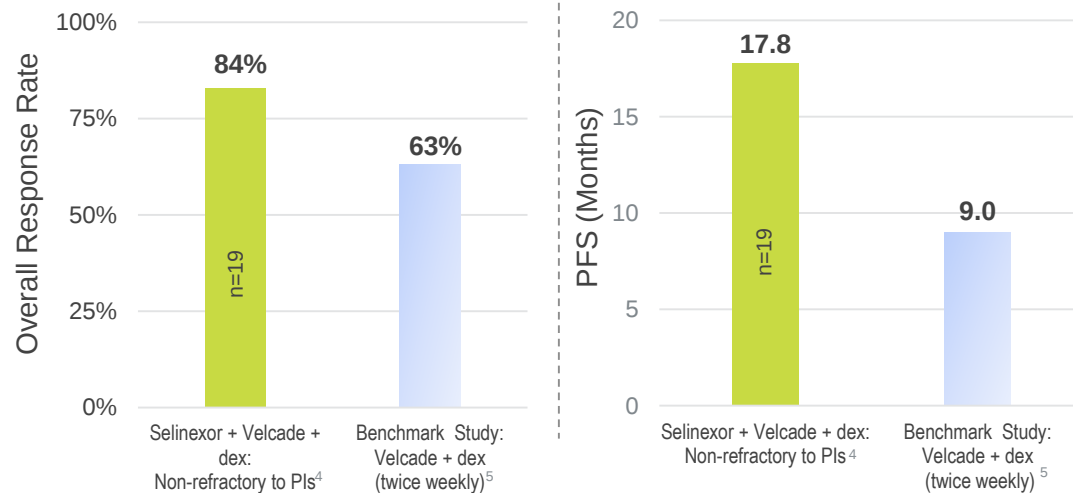
** PD/NE = Patients had progressive disease or disease not evaluable

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.

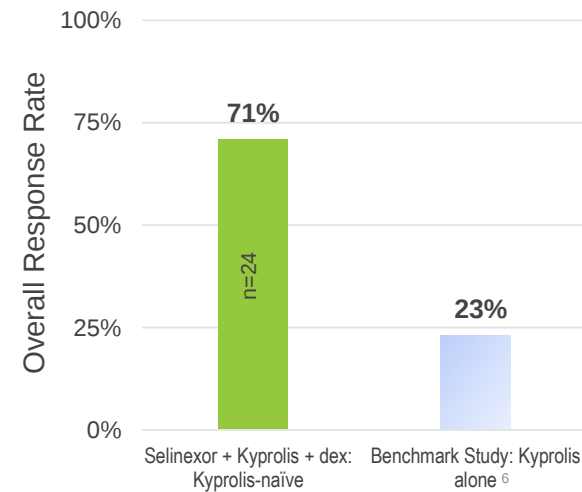
STOMP¹: A Phase 1b/2 Study in Myeloma

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)



Provides strong rationale for further clinical investigation of selinexor in combination with standard, approved therapies⁸

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.

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

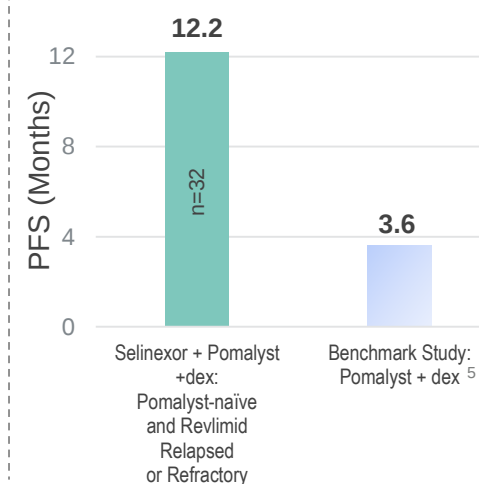
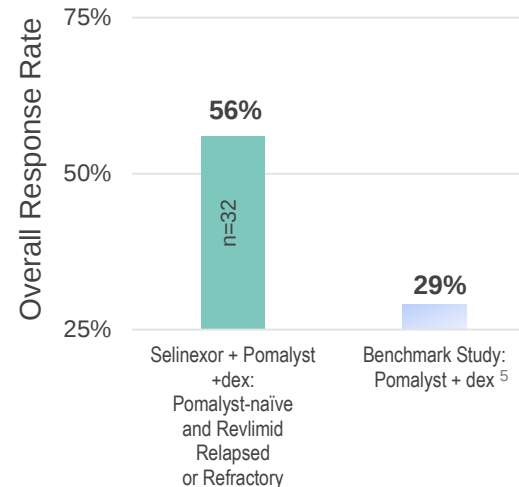
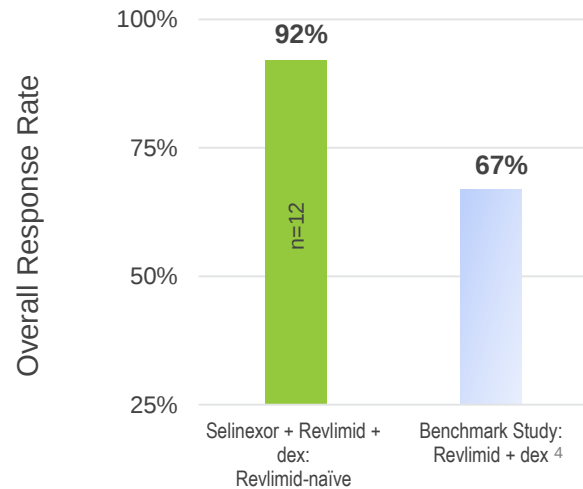
¹ Selinexor and Backbone Treatments of Multiple Myeloma Patients. ² Bahlis NJ, et al. Blood 2018. ³ Gasparetto C, et al. ASCO 2020. Abstract 8530. ⁴ Patient population eligible for Phase 3 BOSTON study. ⁵ Dimopoulos MA et al., Lancet 2016. ⁶ Kyprolis Package Insert; Study PX-171-003 A1. ⁷ Five of six had prior Velcade exposure. ⁸ Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).

STOMP¹: 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 therapies⁶

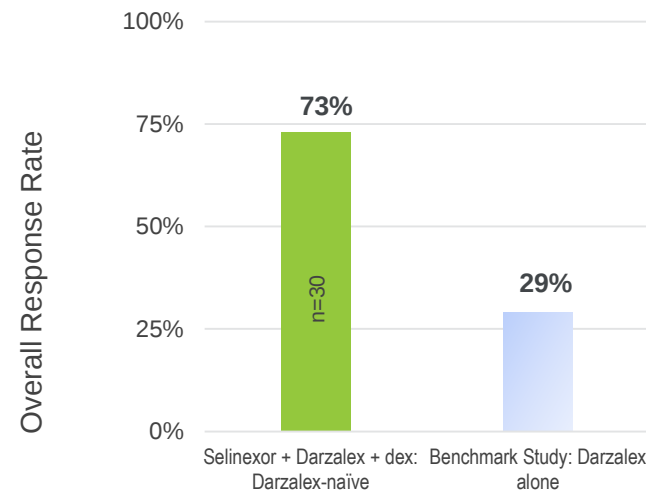
Note: The STOMP study does not include any arms studying current myeloma backbone therapies without the combination of selinexor. The purpose of displaying the “Benchmark” data above for Revlimid and Pomalyst is to highlight that the clinical results from STOMP reported to date strongly support ongoing / additional clinical investigation of selinexor in combination regimens.

¹ Selinexor and Backbone Treatments of Multiple Myeloma Patients. 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).

STOMP¹: 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 therapies⁴

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 Selinexor and Backbone Treatments of Multiple Myeloma Patients. ² Gasparetto C, et al. ASCO 2020. Abstract 8510. ³ Lonial et al., Lancet 2016. ⁴ Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade® (bortezomib), Kyprolis® (carfilzomib) or Darzalex® (daratumumab).