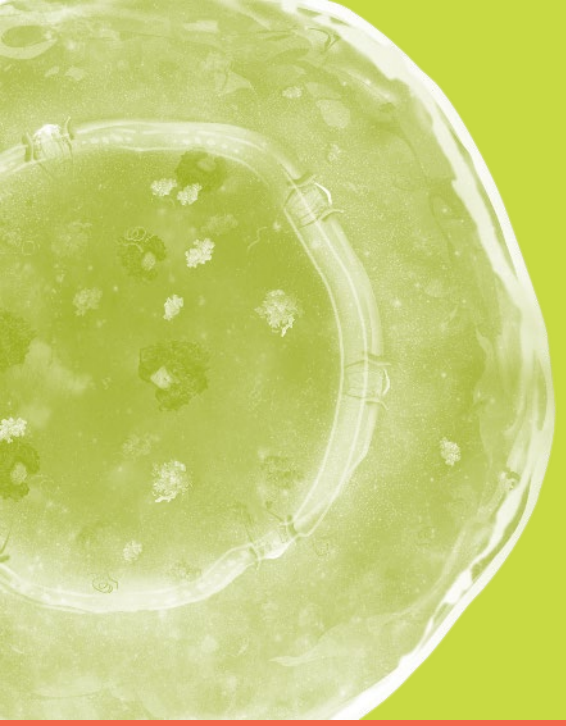
Karyopharm® Therapeutics

A Commercial-Stage Pharmaceutical Company Pioneering Novel Cancer Therapies

September 2021

Forward-looking Statements and Other Important Information

This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Karyopharm's guidance on its expected cash runway; expectations and plans relating to XPOVIO for the treatment of adult patients with relapsed or refractory multiple myeloma or relapsed or refractory diffuse large B-cell lymphoma and other hematologic malignancies and solid tumors; commercialization of XPOVIO or any of its drug candidates and the commercial performance of XPOVIO; submissions to, and the review and potential approval of selinexor by, regulatory authorities, including the Company's regulatory strategy, the anticipated availability of data to support such submissions, timing of such submissions and actions by regulatory authorities and the potential availability of accelerated approval pathways; the expected design of the Company's clinical trials; and the therapeutic potential of and potential clinical development plans for Karyopharm's drug candidates, especially selinexor. Such statements are subject to numerous important factors, risks and uncertainties, many of which are beyond Karyopharm's control, that may cause actual events or results to differ materially from Karyopharm's current expectations. For example, there can be no guarantee that Karyopharm will successfully commercialize XPOVIO; that regulators will grant confirmatory approval in the European Union based on the BOSTON study in adult patients with multiple myeloma; or that any of Karyopharm's drug candidates, including selinexor and eltanexor, will successfully complete necessary clinical development phases or that development of any of Karyopharm's drug candidates will continue. Further, there can be no guarantee that any positive developments in the development or commercialization of Karyopharm's drug candidate portfolio will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: the risk that the COVID-19 pandemic could disrupt Karyopharm's business more severely than it currently anticipates, including by negatively impacting sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other product candidates, delaying ongoing or planned clinical trials, impeding the execution of business plans, planned regulatory milestones and timelines, or inconveniencing patients; the adoption of XPOVIO in the commercial marketplace, the timing and costs involved in commercializing XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; the ability to obtain and retain regulatory approval of XPOVIO or any of Karyopharm's drug candidates that receive regulatory approval; Karyopharm's results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. Food and Drug Administration and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, including with respect to the need for additional clinical studies; the ability of Karyopharm or its third party collaborators or successors in interest to fully perform their respective obligations under the applicable agreement and the potential future financial implications of such agreement; Karyopharm's ability to enroll patients in its clinical trials; unplanned cash requirements and expenditures; development or regulatory approval of drug candidates by Karyopharm's competitors for products or product candidates in which Karyopharm is currently commercializing or developing; and Karyopharm's ability to obtain, maintain and enforce patent and other intellectual property protection for any of its products or product candidates. These and other risks are described under the caption "Risk Factors" in Karyopharm's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, which was filed with the Securities and Exchange Commission (SEC) on August 5, 2021, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. Karyopharm regularly uses its website to post information regarding its business, drug development programs and governance. Karyopharm encourages investors to use www.karyopharm.com, particularly the information in the section entitled "Investors," as a source of information about Karyopharm. References to www.karyopharm.com in this presentation are not intended to, nor shall they be deemed to, incorporate information on www.karyopharm.com into this presentation by reference. Other than the currently approved indications 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.



Leveraging the **inhibition of nuclear export** as a mechanism to treat cancer

XPOVIO® (selinexor) 20 mg tablet

APPROVED IN THE US FOR 3 INDICATIONS[1]

- Multiple myeloma as early as first relapse[2]
- Relapsed/refractory diffuse large B-cell lymphoma[3,4]

Building on myeloma foundation

Driving depth and breadth of leadership presence in myeloma

Expanding global footprint

Expect CHMP review of MAA in 2L+ to be completed in 1H22

Key phase 3 solid tumor data remains on track

SIENDO top-line results in endometrial cancer expected by year end 2021

Focused clinical pipeline

Targeting high unmet need hematological and solid tumor cancers

Well-capitalized

Cash runway into mid-2023

[1] Approved only in combination with Velcade® and dexamethasone for patients who have received at least one prior therapy. Full Prescribing Information available at XPOVIO.com [2] XPOVIO is approved in the US and Europe for the treatment of penta-refractory multiple myeloma, and in the US for second-line and higher multiple myeloma. [3] Diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. [4] This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

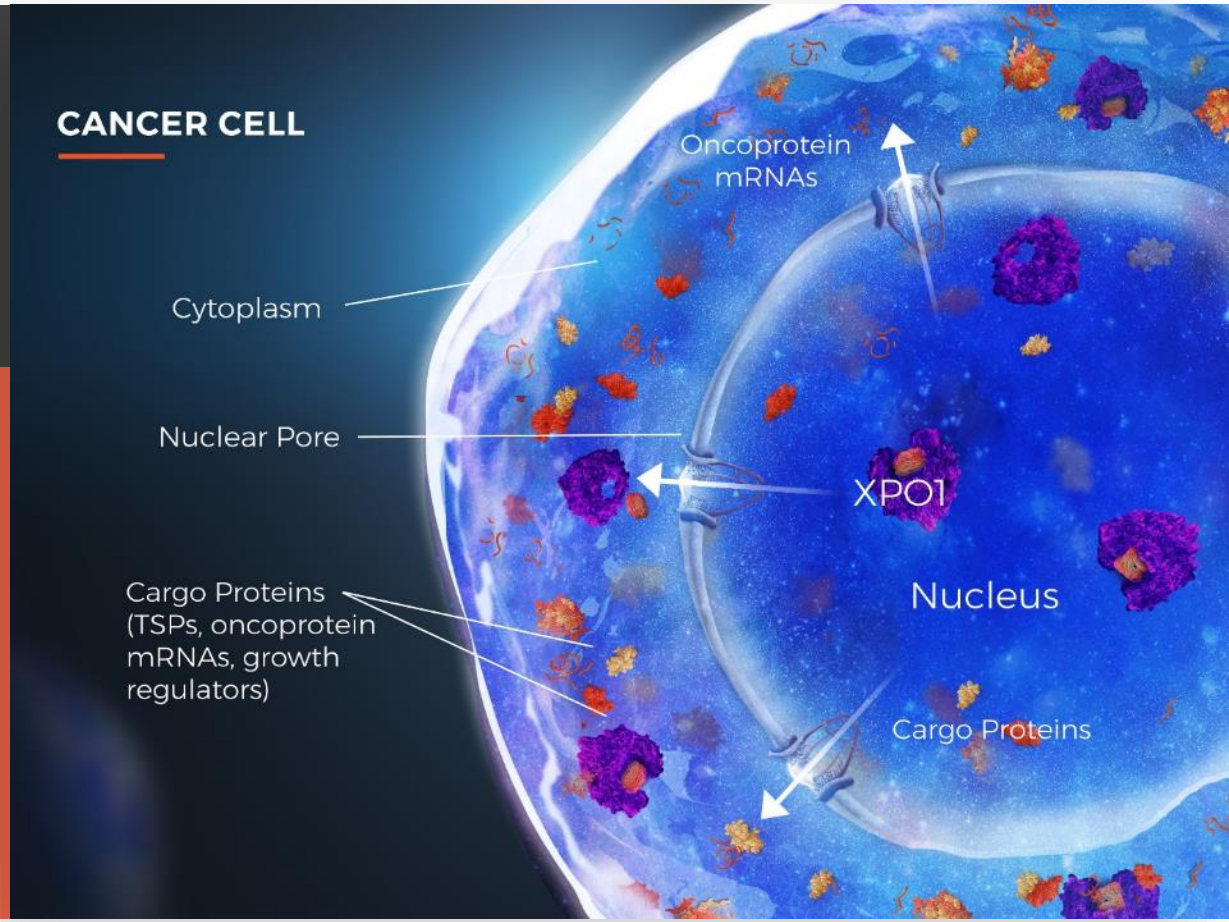
Novel XPOVIO® (selinexor) Mechanism: Only Approved, First in Class SINE that is Broadly Applicable and Foundational to Cancer Biology[1-4]

XPO1 OVEREXPRESSION

- Enables cancer cells to escape tumor suppressor proteins (TSPs), mediated cell cycle arrest, and induction of apoptosis
- Correlates with poor prognosis and drug resistance

INHIBITION OF XPO1 IMPACTS TUMOR CELLS VIA 3 CORE MECHANISMS

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



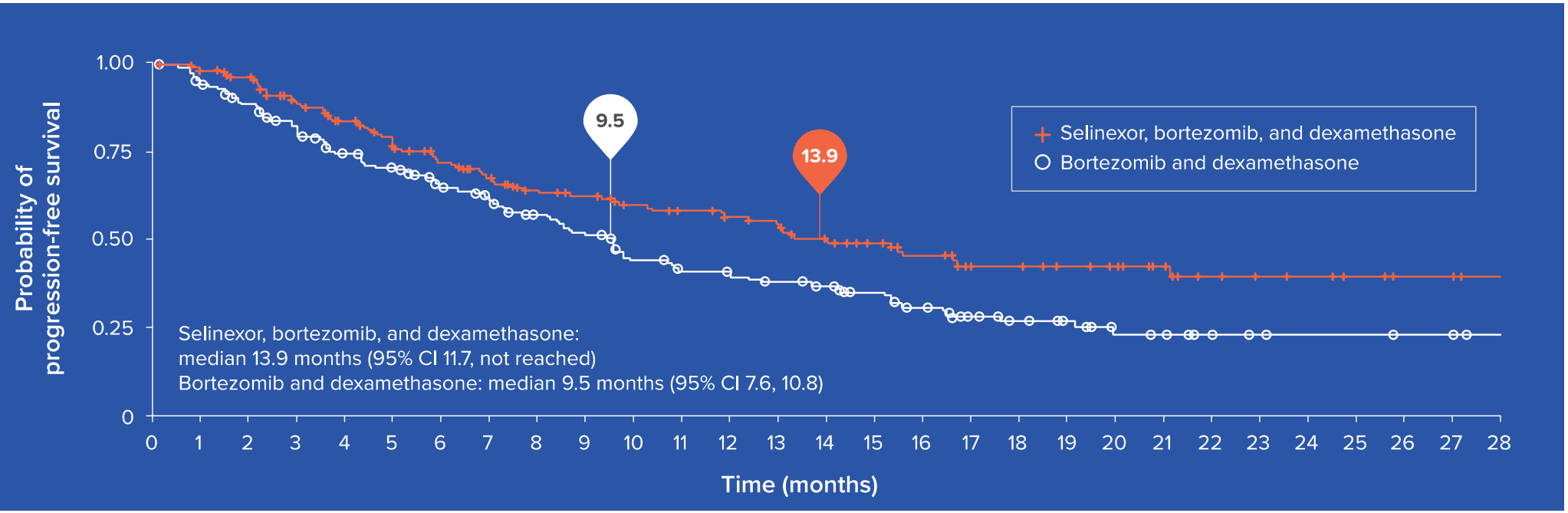
[1] Gupta A, et al. J Thorac Oncol. 2017. [2] Sun Q, et al. Signal Transduct Target Ther. 2016.
[3] Gandhi UH, et al. Clin Lymphoma Myeloma Leuk. 2018. [4] Gravina GL, et al. J Hematol Oncol. 2014

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

ONCE-WEEKLY, ORAL XPOVIO + VD DELIVERED AN EARLY AND SUSTAINED PFS ADVANTAGE VERSUS TWICE-WEEKLY Vd[1]

30% reduction in risk of progression or death[1]

Hazard ratio: 0.70
(96% CI 0.5-0.93), *p*=0.0075



Hazard ratio (HR) is based on stratified Cox's proportional hazard regression modeling, p-value based on stratified log-rank test.

*According to the International Myeloma Working Group (IMG Uniform Response Criteria for Multiple Myeloma, as assessed by an Independent Review Committee (IRC). XVd=XPOVIO® (selinexor) with Velcade® (bortezomib) and dexamethasone; Vd=Velcade and dexamethasone.

[1] XPOVIO (selinexor) package insert

Deeper and Durable Responses with XVd Compared to Vd

Responses observed with oral, once-weekly XPOVIO + Vd were rapid and durable versus twice-weekly Vd[1]

MEDIAN TIME TO RESPONSE[1]

1.4 MONTHS once-weekly XPOVIO + Vd

VS

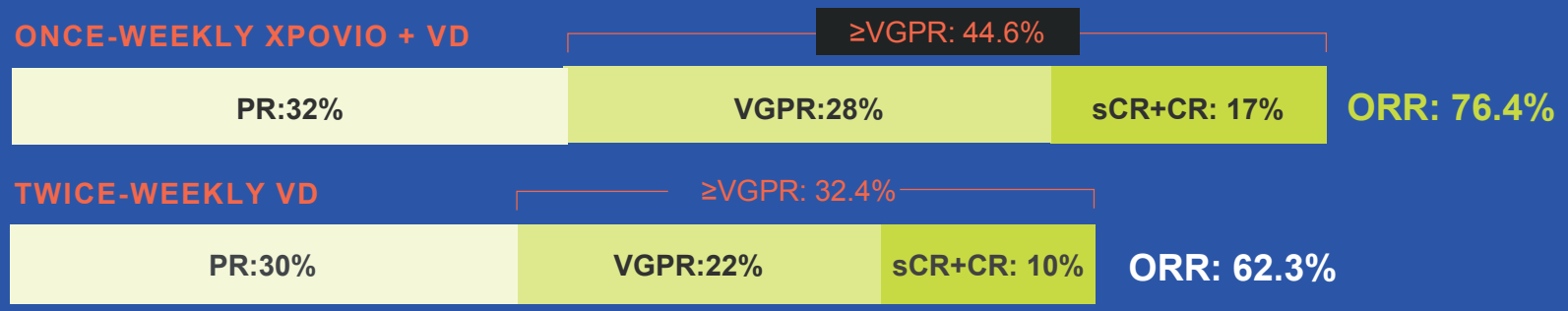
1.6 MONTHS twice-weekly Vd

MEDIAN DURATION OF RESPONSE[1]

20.3 MONTHS once-weekly XPOVIO + Vd

VS

12.9 MONTHS twice-weekly Vd



IMPROVEMENT IN ORR WAS OBSERVED ACROSS A VARIETY OF PATIENT SUBGROUPS[2]

[1] XPOVIO (selinexor) package insert [2] Grosicki et al. The Lancet. 2020.

Safety Highlights from the XPOVIO Prescribing Information[1]

No Black Box Warnings

No Contraindications

Patient Medication Guide

Warnings and Precautions

- Thrombocytopenia
- Neutropenia
- Gastrointestinal Toxicity
- Hyponatremia
- Serious Infection
- Neurological Toxicity
- Embryo-Fetal Toxicity
- Cataract

Monitoring Instructions and Recommended Concomitant Treatments

- Monitor complete blood count (CBC) with differential, standard blood chemistries, body weight, nutritional status, and volume status at baseline and during treatment as clinically indicated. Monitor more frequently during the first three months of treatment.
- Patients advised to maintain adequate fluid and caloric intake throughout treatment. Consider intravenous hydration for patients at risk of dehydration.
- Provide prophylactic antiemetics. Administer a 5-HT3 receptor antagonist and other anti-nausea agents prior to and during treatment with XPOVIO
- Recommended XPOVIO dosage reductions and dosage modifications for adverse reactions are included in the Prescribing Information

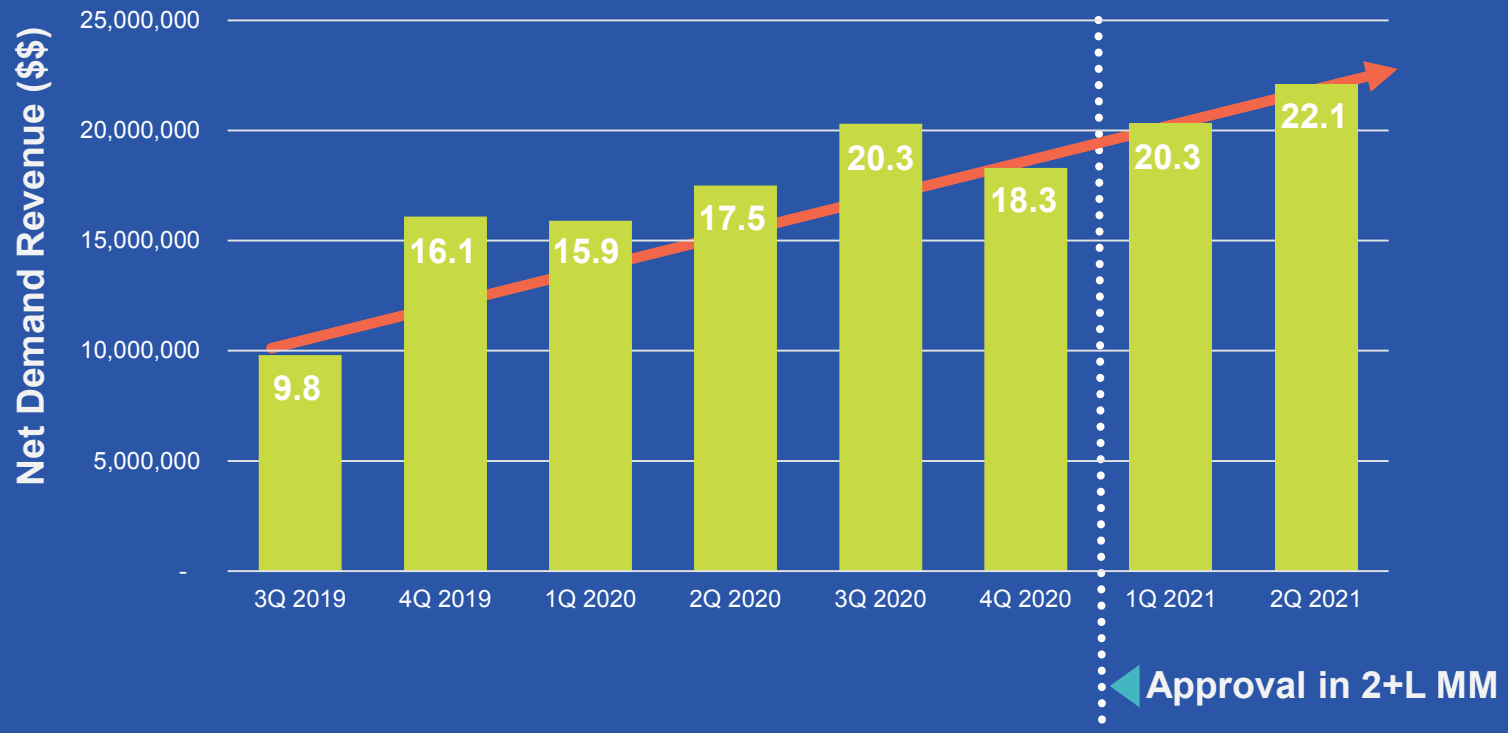
[1] XPOVIO (selinexor) package insert

XPOVIO Launch Update: 2Q 2021

Continued Progress in 2L+ Market Uptake

$22.1M
Net Demand Revenue

$20.2M
Net Product Revenue



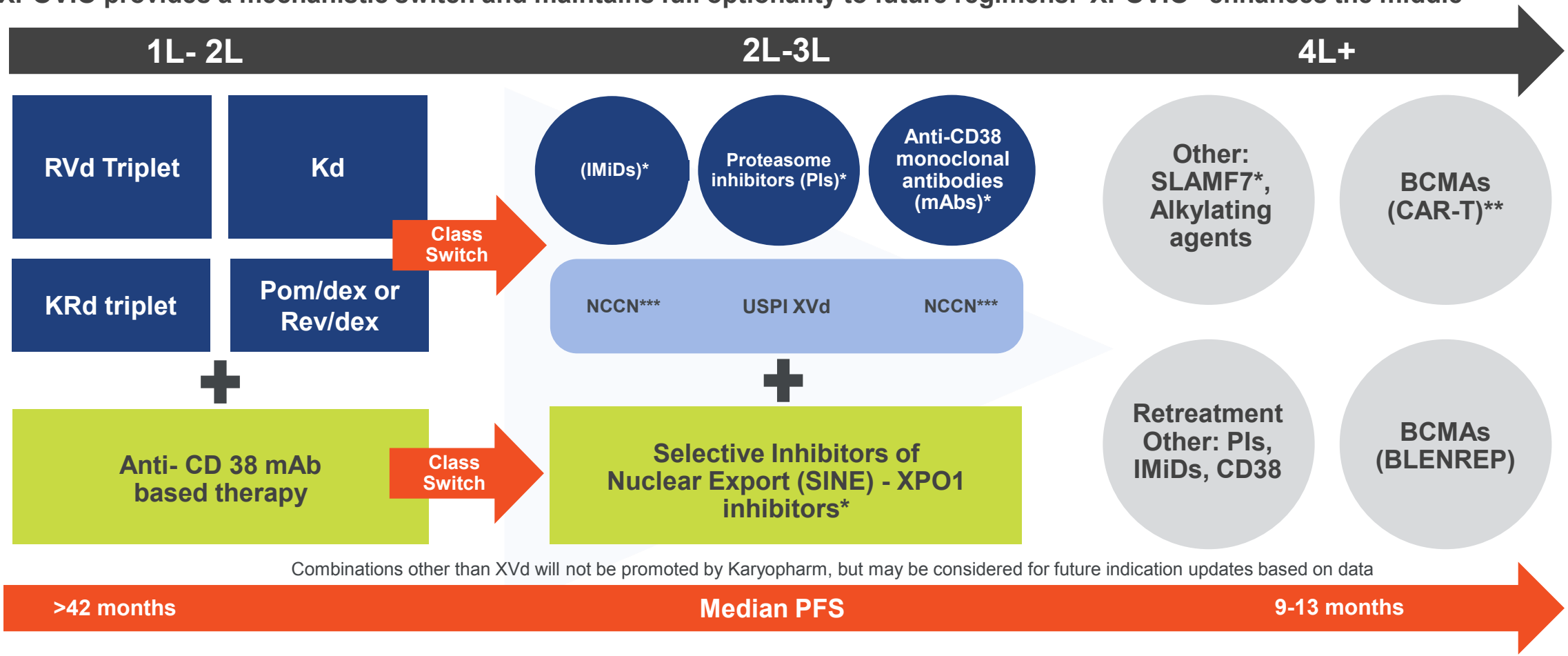
Year-to-Date Highlights

- Net demand revenue up 9% 2Q21 vs 1Q21
- Net product revenue impacted by reduction of $1.9M in channel inventory due to launch of three new strength tablets (40mg, 50mg and 60mg)
- Prescribing accounts continue to increase; up 11% 2Q21 vs 1Q21
- Introduced new launch positioning supported by data from ASCO 2021 and EHA 2021
- Rising confidence in physicians' overall perception[1]
- RXs evolving from penta-refractory to earlier lines[2]
- Preliminary data suggest patients in earlier lines staying on therapy longer[3]
- 85% of patients start on doses <160mg; 80mg and 100mg most common[4]

[1] Intent to prescribe data includes ATU assessing >100 physicians' Perceptions of Attributes for XVd by Lines of Therapy [2] BrandImpact data Jan-Jun 2021 R3M. [3] Health Payer Complete Claims data, pulled on July 20, 2021. [4] Specialty pharmacy and KaryForward data.

Applying Principles of Myeloma Treatment to Optimize Outcomes and Clarity on Sequencing: Class Switching and Early Incorporation of Different Mechanistic Approach

XPOVIO provides a mechanistic switch and maintains full optionality to future regimens. XPOVIO "enhances the middle"



* +dexamethasone

**For Academic setting: CAR-T therapy will be available for penta-refractory disease

*** NCCN Guideline inclusion for XDd and XPd

Clinical Activity of XPOVIO was Observed in Patients Previously Treated with Daratumumab-containing Regimens[1,2]

The XVd arm of the BOSTON trial showed mPFS of 13.9 months (95% CI: 11.7, NR) compared with 9.5 months (95% CI: 7.6, 10.8) in the Vd arm (N=402)[1]

PFS in patients previously treated with daratumumab in the BOSTON trial (n=17)[2,3]

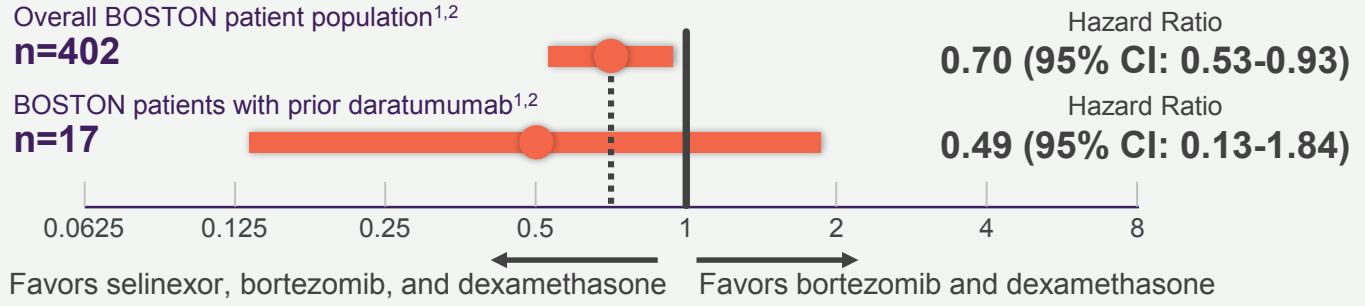
12.22 months
mPFS, XVd
(95% CI: 2.86, NR)

5.55 months
mPFS, Vd
(95% CI: 0.69, NE)

CI=confidence interval; mPFS=median progression-free survival; NE=not evaluable; NR=not reached; ORR=overall response rate; OS=overall survival; PN=peripheral neuropathy; VGPR=very good partial response.

Limitations of subgroup analyses:

- These subgroup analyses were exploratory in nature, not included in the study objectives, and do not control for type 1 error
- These subgroup analyses were not powered or adjusted for multiplicity to assess PFS across this prespecified subgroup
- These subgroup analyses are underpowered to detect clinically meaningful differences in treatment effect



IMPORTANT SAFETY INFORMATION

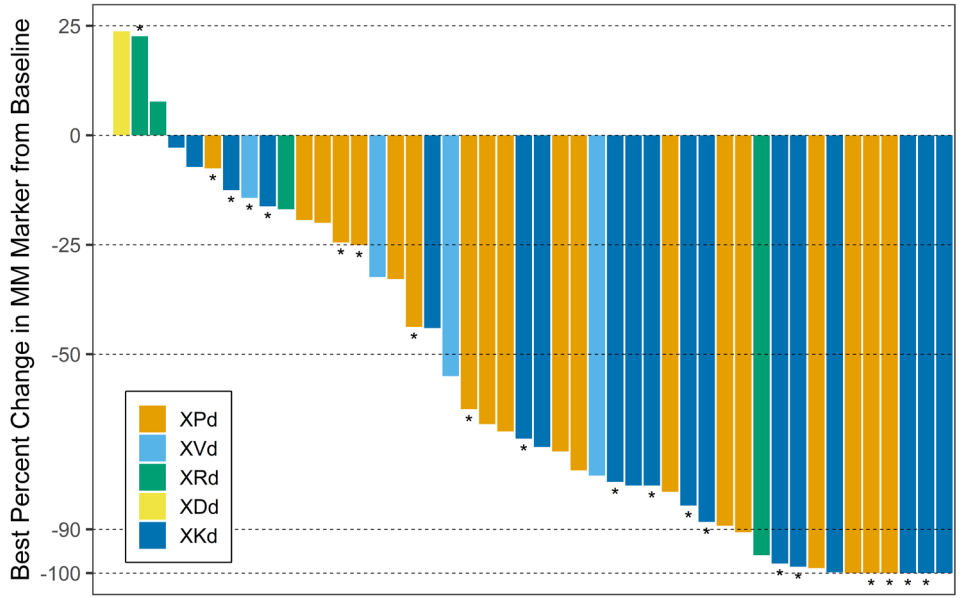
- **USE IN SPECIFIC POPULATIONS**
  No overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥65 years old had a higher incidence of discontinuation due to an adverse reaction (AR) and a higher incidence of serious ARs than younger patients. The effect of end-stage renal disease (CLCR <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

[1] XPOVIO. Prescribing information. Karyopharm Therapeutics Inc; 2021. [2] Grosicki S, et al. *Lancet*. 2020;396(10262):1563-1573. [3] Data on file. Karyopharm Therapeutics Inc. 2021.

Demonstrated Promising Response Rates with XPOVIO Based Regimens (XPd, XKd) in the STOMP Study Post Anti-CD38 mAb Treatment[1]

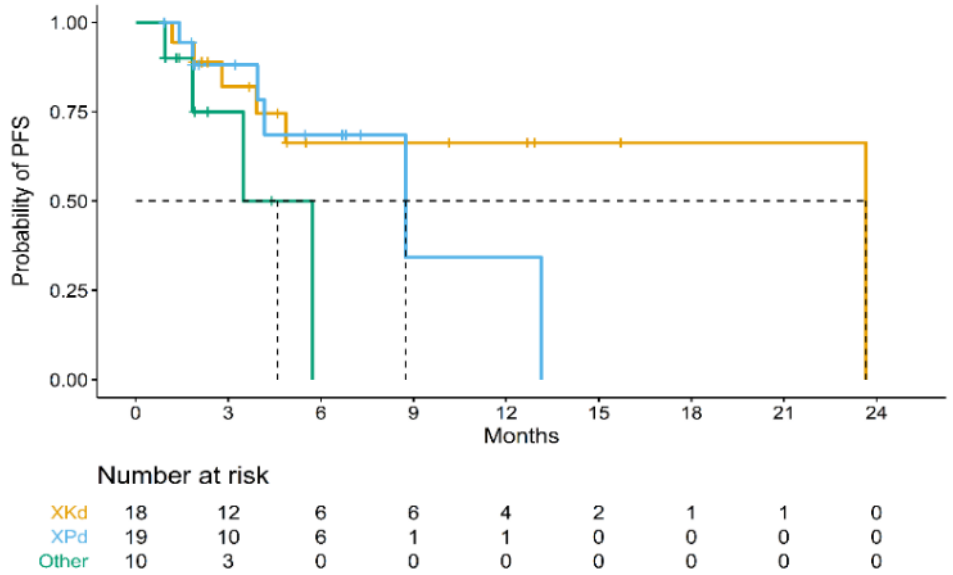
Waterfall Plot for Selinexor Triplets

Note: 1 XDd patient with +262% not shown; asterisk indicates del(17p), t(4;14), or t(14;16)



Progression-Free Survival by Selinexor Regimen

Patients previously treated with an anti-CD38 mAb



- ORR was 57.9% (11/19) in the XPd arm and 66.7% (12/18) in the XKd arm

- The safety and efficacy of XPOVIO in combination with medications other than bortezomib and dexamethasone has not been established and other combination therapies are not approved by the US FDA or any other regulatory authority

[1] Gasparetto, Cristina, et al. ASCO 2021

XPOVIO Dosing has been Continually Refined Over Time to Improve Efficacy and Patient Experience from High Dose BIW to Low Dose QW

From the STORM trial to the STOMP trial to the BOSTON trial, XPOVIO dosing has been continually refined to help optimize the patient experience

Approval Date: July 2019	Ongoing	Approval Date: Dec 2020
1st approval in MM **Dose:** 160 mg (80 mg twice weekly)	**Phase 1/2 study in MM** **Dose range:** 40-100 mg once or twice weekly	**2nd approval in MM** **Dose: 100 mg once weekly**
Xd STORM	**XVd** STOMP	**XVd** BOSTON
Phase 2b, single-arm, open-label, multicenter study Patients with penta-refractory RRMM	**Phase 1/2, open-label, multicenter study** Patients with RRMM/NDMM (dose escalation/expansion)	**Phase 3, 2-arm, active comparator-controlled, open-label, multicenter study** After 1-3 prior therapies in MM

- **65% of patients in the XVd arm of the BOSTON trial had an XPOVIO dose reduction (126/195 patients) vs 35% of those without a dose reduction (69/105)**
- **The median dosage was 80mg (range: 30-137 mg) taken once weekly**
- **Patients had their dosages reduced to mitigate adverse reactions (ARs)**

*STOMP was designed to study XPOVIO in combination with other MOAs across multiple triplet and quadruplet regimens, including XVd.
MM=multiple myeloma; MOA=mechanism of action; NDMM=newly diagnosed multiple myeloma; RRMM=relapsed or refractory multiple myeloma.

IMPORTANT SAFETY INFORMATION
No overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥65 years old had a higher incidence of discontinuation due to an adverse reaction (AR) and a higher incidence of serious ARs than younger patients. The effect of end-stage renal disease (CL_{CR} <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

XPOVIO Dosing has been Continually Refined Over Time to Improve Patient Experience

The median dosage of XPOVIO in the BOSTON trial was 80 mg (range: 30-137 mg) taken once weekly[1]

Key efficacy endpoints for patients (N=195) with and without XPOVIO dose restrictions in the BOSTON trial[2]

	With Dose Reduction	Without Dose Reduction
	XVd	XVd
n	126	69
% of ITT arm	65	35
mPFS, mo	16.62 (95% CI:12.91, NE)	9.23 (95% CI:6.77, 15.47)
ORR, %*	81.7	66.7
≥VGPR, %	51.6	31.8
mDOR, mo	Not evaluable (95% CI:13.83, NE)	12.02 (95% CI: 8.31, NE)

Limitation of subgroup analyses:

- This post hoc analysis was exploratory in nature, not included in the study objectives, and does not control for type 1 error
- This post hoc analysis was not powered or adjusted for multiplicity to assess PFS across other prespecified subgroups
- This post hoc analysis was underpowered to detect clinically meaningful differences in treatment effect

65% of patients in the XVd arm had an XPOVIO dose reduction (126/195 patients) vs 35% of those without a dose reduction (65/195 patients)[2]

*Response was evaluable in 125 of 126 patients receiving a dose modification for selinexor and 66 of the 69 patients who did not receive a dose modification for selinexor. Overall response rate is the proportion of patients who achieve a partial response or better, before IRC-confirmed progressive disease or initiating a new MM treatment or crossover.

CI=confidence interval, IRC=independent review committee; ITT=intent to treat; mDOR=median duration of response; mo=month; mPFS=median progression-free survival; NE=not evaluable; ORR=overall response rate; VGPR=very good partial response.

IMPORTANT SAFETY INFORMATION

- XPOVIO can cause severe or life-threatening hyponatremia.

[1] XPOVIO. Prescribing information. Karyopharm Therapeutics Inc; 2021. [2] Data on file. Karyopharm Therapeutics Inc. 2021.

Selinexor Supportive Care Guidelines Are Simple

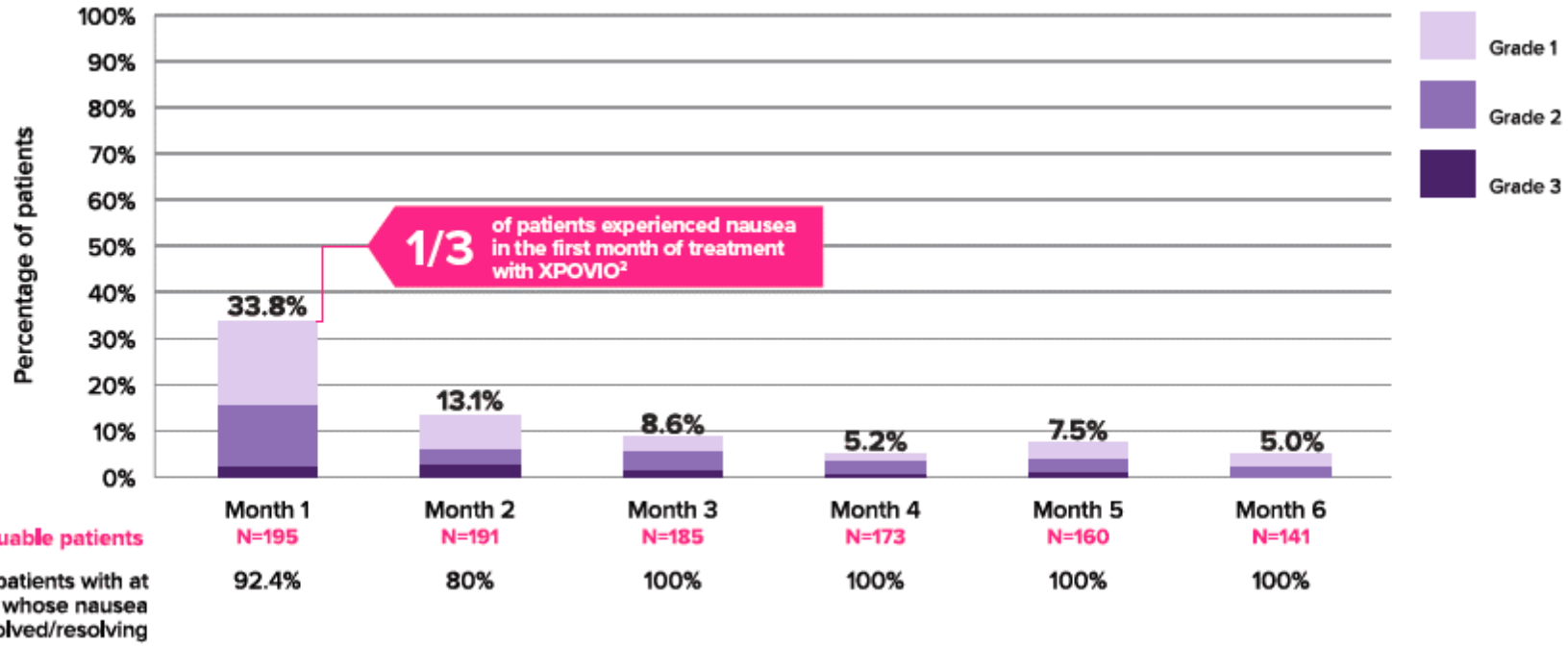
Required Prophylactic Anti-emetics: 5-HT3 Antagonists and Olanzapine	
5-HT3 Antagonist	**All patients should receive ondansetron 8 mg or equivalent, unless contraindicated, orally 1 hour before each dose of selinexor and q 8 hours for 3 days post selinexor for the first 2 cycles of the study**
	AND
Olanzapine	Olanzapine 5 mg PO or equivalent for days 1-3 post selinexor, for **the first 2 months** of the study or longer if needed.
	Or
NK-1R Antagonist	An NK1 receptor antagonist can be used together with ondansetron for the first 2 cycles or longer if needed.

- Patients may taper supportive care at treating physician's discretion after 2 cycles of therapy

Patients Tolerate Long Term XVd Well, with Greater Than 90% of Patients not Experiencing Nausea Starting in Cycle Three[1]

- Percentage of patients experiencing nausea decreased in the first month of XVd using appropriate antiemetic measures
- XPOVIO dosing in the BOSTON trial was 100mg taken orally, once weekly
- The BOSTON trial only required one anti-emetic, a 5HT3

Percentage of patients experiencing nausea events per month in the XVd arm of BOSTON trial

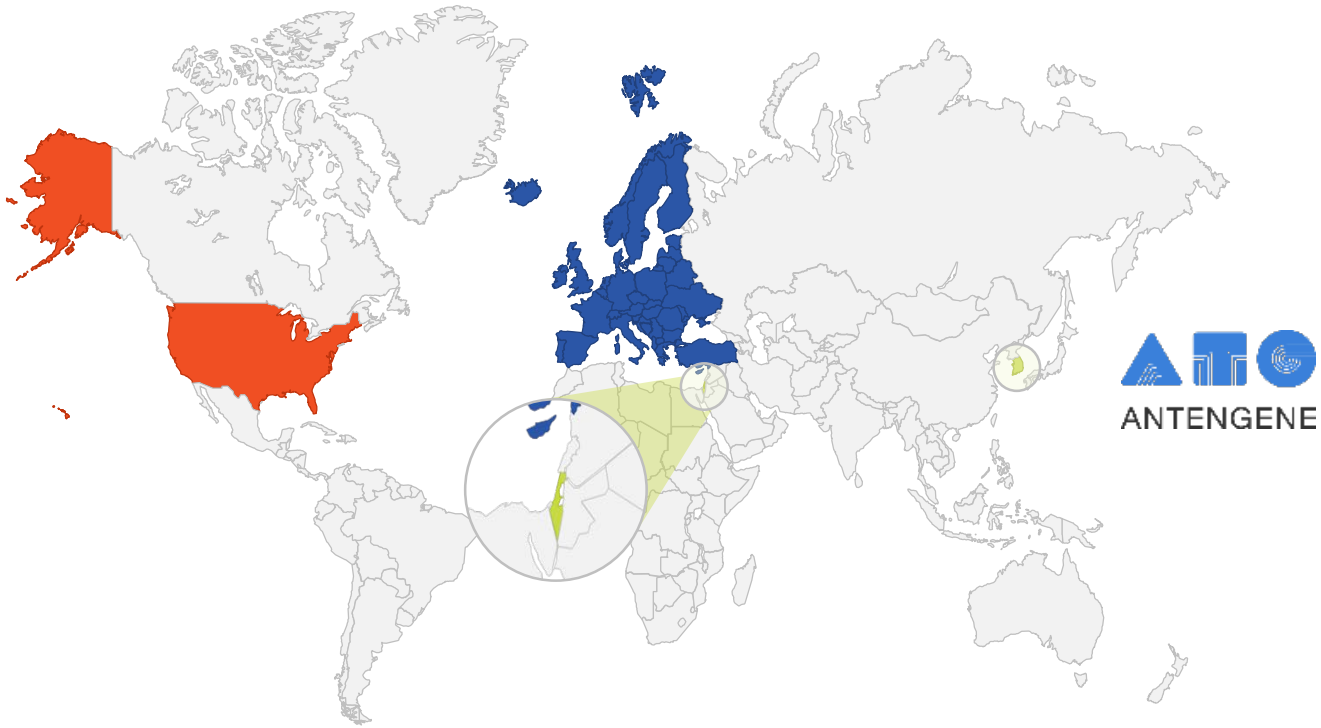


*XVd=XPOVIO + bortezomib and dexamethasone (Vd).

[1] Data on file. Karyopharm Therapeutics Inc. 2021.

Ongoing Progress with Global XPOVIO Access

- Conditional Marketing Authorization granted for NEXPOVIO® in penta-refractory multiple myeloma in the United Kingdom
- Partner Antengene secured marketing authorization for XPOVIO in penta-refractory multiple myeloma and R/R DLBCL in South Korea
- Marketing Authorization Application validated and under review by CHMP (based on Phase 3 BOSTON clinical data); Expect review to be completed in 1H22



[1] Approved in Israel and South Korea.

Advancing Focused Pipeline Across Cancers of High Unmet Need

INDICATION | STUDY NAME

PHASE 1 **PHASE 2** **PHASE 3**

HEMATOLOGICAL MALIGNANCIES

XPOVIO (selinexor)

- Multiple myeloma (previously treated; combo with pomalidomide and dexamethasone | **XPORT-MM-031**[1,2,3]
- Multiple myeloma (R/R and frontline) | **STOMP**[4]
- DLBCL (combo with R-GDP) | **XPORT-DLBCL-030**[5]
- Myelofibrosis (previously treated) | **XPORT-MF-035**[2]
- Myelofibrosis (combo w/rituximab) | **XPORT-MF-034**[6]

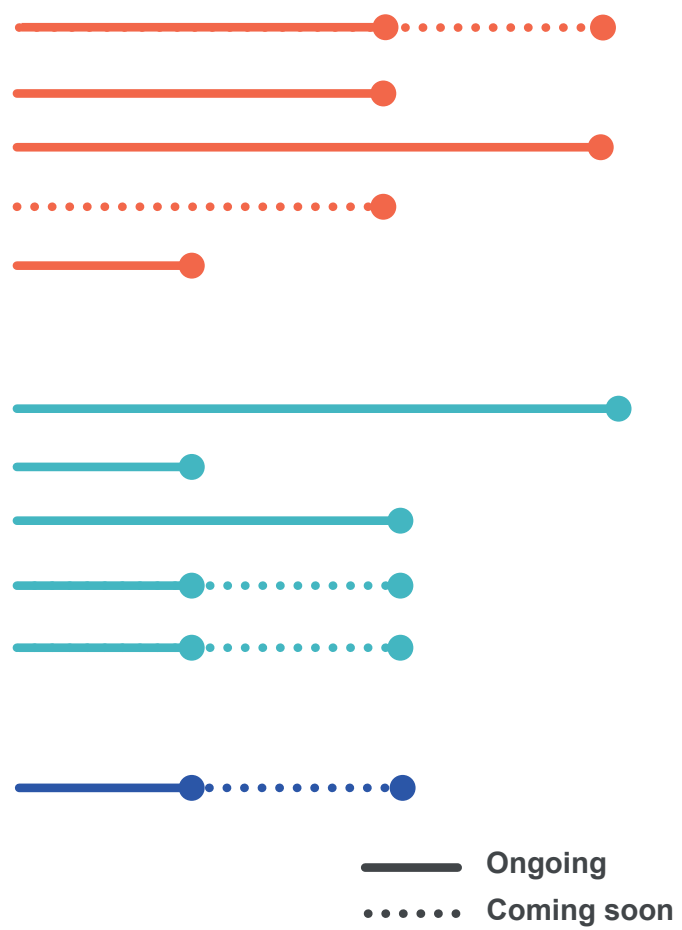
SOLID TUMORS

XPOVIO (selinexor)

- Endometrial cancer (maintenance therapy) | **SIENDO**
- Glioblastoma (newly diagnosed or recurrent; combo w/active agents) | **XPORT-GBM-029**
- Melanoma (locally advanced or metastatic) | **XPORT-MEL-033**
- CRC (metastatic w/RASm; alone or combo w/pembrolizumab) | **XPORT-CRC-041**[2,7]
- NSCLC (following checkpoint inhibitors; combo w/docetaxel) | **XPORT-NSCLC-039**[7]

ELTANEXOR

- Myelodysplastic syndromes (alone or in combo w/hypomethylating agents) | **KCP-8602-801**[2]



[1] Versus elotuzumab and pomalidomide. [2] Study expected to start in 2021. [3] Sponsored by European Myeloma Network. [4] Oral selinexor and dexamethasone + Revlimid® (lenalidomide), Pomalyst® (pomalidomide), Velcade®, Kyprolis® (carfilzomib) or Darzalex® (daratumumab). [5] XPORT-DLBCL-030 is a Phase 2/3. [6] XPORT-MF-034 is a Phase 1/2. [7] XPORT-CRC-041 and XPORT-NSCLC-039 are supported by Phase 1 data from XPORT-STP-027.

XPOVIO and ELTANEXOR IN HEMATOLOGIC CANCERS

Phase 1b/2 STOMP Study – XPOVIO Plus Pomalyst® (pomalidomide) and Dexamethasone in Relapsed/Refractory Multiple Myeloma[1,2]

Registrational Phase 3 Trial Expected to Start by Year End 2021

- This all oral XPd combination appears highly active with durable responses
- No new safety signals identified
- These data support the planned Phase 3 study evaluating XPd in RRMM with prior therapies of PIs, IMiDs and anti-CD38 mAb (XPORT-MM-031)

	N	ORR	mPFS (months)	DOR (months)
RP2D[3]	20	**65%**	Not Reached	Not Reached
Pomalyst-naïve			12.2	24.2
Prior anti-CD38 mAb	19	**58%**	8.7	7.9

The safety and efficacy of XPOVIO in combination with medications other than bortezomib and dexamethasone has not been established and other combination therapies are not approved by the US FDA or any other regulatory authority

[1] White, Darrell, et al. ASCO 2021. [2] White, Darrell, et al. EHA 2021. [3] XPOVIO (60mg QW) plus Pomalyst (4mg Days 1-21) and dexamethasone (40mg Days 1, 8, 15, 22).

Phase 1b/2 STOMP Study – XPOVIO Plus Kyprolis® (carfilzomib) and Dexamethasone in Relapsed/Refractory Multiple Myeloma[1,2]

- The XKd combination appears highly active and durable responses
- No new safety signals identified

	N	ORR	mPFS (months)
All evaluable patients	32	**78%**	15.0
High-risk cytogenetics	17	**82%**	15.0
Prior anti-CD38 mAb	12	**68%**	23.7

The safety and efficacy of XPOVIO in combination with medications other than bortezomib and dexamethasone has not been established and other combination therapies are not approved by the US FDA or any other regulatory authority

[1] Gasparetto, Cristina, et al. ASCO 2021. [2] Gasparetto, Cristina, et al. EHA 2021.

Single-agent Eltanexor Appears Active in Patients with High-risk, Relapsed MDS that is Primary Refractory to Hypomethylating Agents in Phase 1 Study[1]

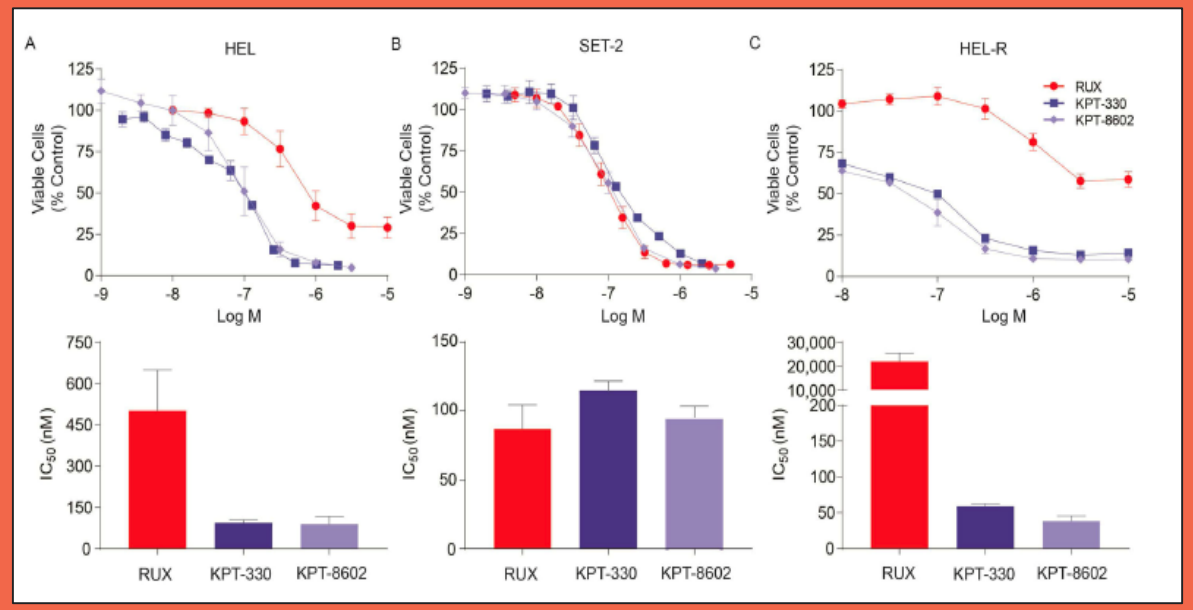
- No approved drugs and historical OS 4-6 months in HMA refractory MDS patients
- **Single-agent eltanexor demonstrated 53% ORR**
- Single-agent eltanexor demonstrated median OS of 9.9 months

	Total N=15
ORR (mCR +HI)	**53%**
Treatment duration (months)	13.0
Median time to response (months)	1.9
Median duration of response (months)	4.42

The safety and efficacy of eltanexor in myelodysplastic syndrome not been established and has not been approved by the US FDA or any other regulatory authority

[1] Lee, Sangmin, et al. EHA 2021.

Preclinical Data Supports Potential for XPOVIO in Myelofibrosis[1]



- In preclinical studies, inhibition of nuclear-cytoplasmic transport by selinexor or eltanexor reduced survival of cells expressing JAK^{2V617F}
- Potential for broad applicability in both newly diagnosed and ruxolitinib-exposed patients

- **Phase 1 data submitted to major medical meeting for presentation by the end of 2021**
- Randomized, multicenter, open-label, **Phase 2 study** (XPORT-MF-035; NCT04562870) expected **to commence by YE 2021**
- Evaluate the safety and efficacy of single-agent XPOVIO vs physician's choice in up to 112 patients with myelofibrosis who have had at least six months of prior treatment with a JAK 1/2 inhibitor
- Primary endpoint: Percentage of patients with spleen volume reduction of ≥35% from baseline and up to Week 48, as assessed by IRC
- Key secondary endpoints:
  - Safety
  - Percentage of patients with total symptom score reduction of ≥50%
  - Percentage of patients with spleen volume reduction of ≥25%
  - OS

[1] Deininger, Michael, et al. Clinical Cancer Research. April 2019.

XPOVIO IN SOLID TUMORS

Opportunity For Maintenance Therapy Post Front-line Chemotherapy

~14,000
Front-Line Patients[2]
Not including <50% recurrent disease

~67% Response Rate[3]

~9,000
Front-Line Patients Responding to Chemo

Estimated 40%–50% Treatment Rate[4]

~4,000
Est .Patients to be Treated in the Maintenance Setting
Will increase over time with effective therapies

Potential Endometrial Cancer Opportunity For XPOVIO®

Overview and Epidemiology (US)

- Most common gynecologic cancer in the U.S with **>65K** cases and **>12K** deaths in 2020[1]
- In the U.S., those diagnosed with early-stage disease generally have a good prognosis after surgery alone, however **~14K** patients each year in the front line will have advanced or metastatic disease and are treated with chemotherapy[2]

Current Treatment Paradigm

- Patients with Stage I-III disease are typically treated with surgery with or without radiation therapy (high-risk patients may also receive adjuvant chemotherapy)
- **20–30% Patients with advanced or metastatic disease typically treated with chemotherapy, commonly a taxane plus platinum**
  - Response rates (CR or PR) in the front-line setting can be as high as **67%**[3]
  - Patients then typically “watch and wait” until disease relapses
- In the second and later line settings, additional chemotherapy, immunotherapy and/or targeted agents are increasingly used
- There is currently **no drug therapy approved** in the maintenance setting, post chemotherapy in any setting

[1] SEER / NCI Cancer Stat Facts. 2020. [2] EpicOncology™ Epidemeology Database, 2020. [3] Sorbe, B et al. Int J Gynecol Cancer. 2008 [4] 40-50% treatment rate is used for illustrative purposes and informed by actual maintence therapy rates seen in the ovarian cancer marketplace (note: % of ovarian cancer patients receiving mainenance therapy in the U.S.in 2020 was 43% as per Decision Resources Ovarian Cancer Disease Landscape Foreast Report, 2021).

Selinexor Was Previously Evaluated in a Phase 2 Study in Patients with Recurrent Gynecological Malignancies (SIGN Study)[1]

Baseline Patient Characteristics (n=23)	
Previous lines of therapy (median, range)	2 (1-5)
Previous platinum agent	96%
Previous taxane	100%
Endpoints	
Disease Control Rate (% patients with PR or SD) - Defined as SD/PR ≥3 months	35%
mPFS	2.8 months

Adverse Events (AEs)
Most common AEs across all patients were nausea, fatigue, decreased appetite, vomiting, weight loss, anemia, thrombocytopenia, dysgeusia, and blurred vision and were primarily grades 1 and 2. The most common grade 3 AEs were thrombocytopenia, fatigue, anemia, nausea and hyponatremia.

The safety and efficacy of XPOVIO in combination with medications other than bortezomib and dexamethasone has not been established and other combination therapies are not approved by the US FDA or any other regulatory authority

Note: 114 total patients enrolled in SIGN study with endometrial, ovarian and cervical cancers

[1] Vergote I, et al. Gynecologic Oncology. 2019

SIENDO Study Design:

Phase 3 study evaluating once weekly selinexor as a maintenance therapy versus placebo in patients with endometrial cancer after first- or second-line chemotherapy

Eligibility

Patients who completed a single line of at least 12 weeks of taxane-platinum combination therapy for:

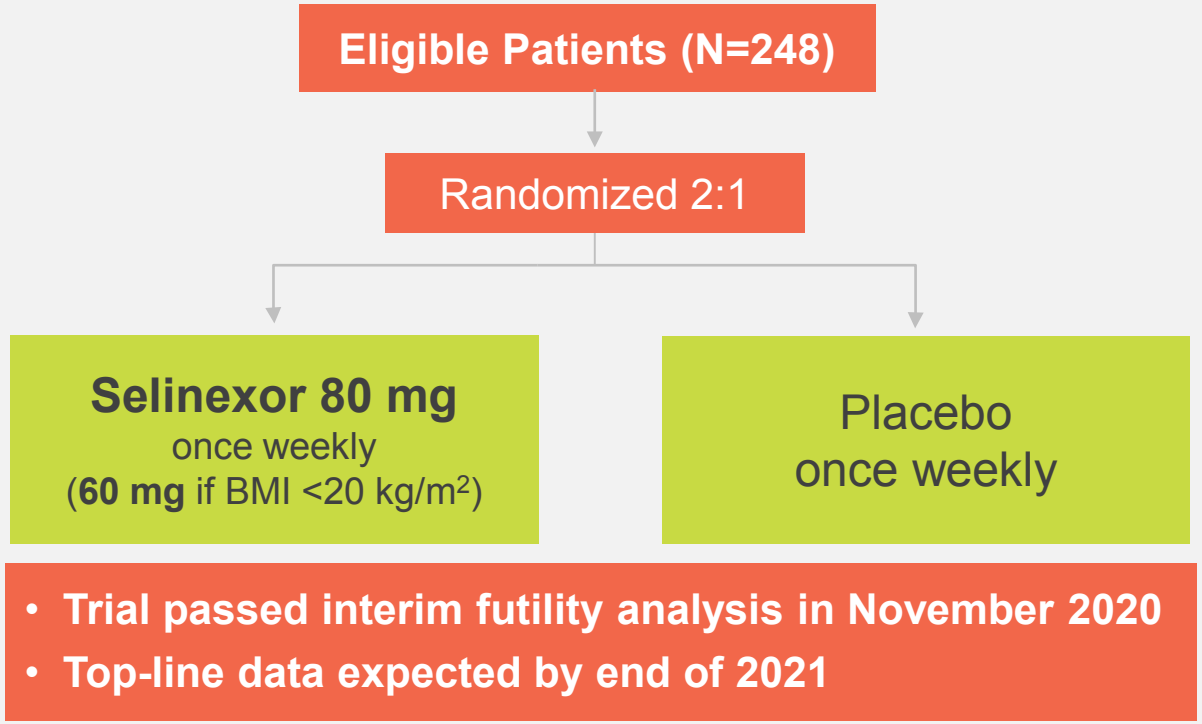
- Primary Stage IV disease
- First Relapse (i.e., relapse after primary therapy including surgery and/or adjuvant therapy for Stage I-IV disease)

Primary Endpoint

- Progression-free survival from time of randomization until death or disease progression as determined by Investigator

Statistical Design

- HR of 0.60 corresponds to a 67% increase in median PFS, assuming a median PFS of 4.5 months for placebo and 7.5 months for selinexor



- **Trial passed interim futility analysis in November 2020**
- **Top-line data expected by end of 2021**

ADDITIONAL HIGHLIGHTS AND NEXT STEPS

Financial Snapshot

$239.3M

CASH, EQUIVALENTS & INVESTMENTS
30-Jun-2021

Mid 2023

EXPECTED RUNWAY

$22.1M

Quarterly Demand Revenue
2Q 2021

75M

SHARES OUTSTANDING
30-Jun-2021

ENHANCING CAPABILITIES, EVOLVING THE ORGANIZATION AND LOOKING AHEAD TO A CATALYST-DRIVEN 2H 2021

1H 2021 Achievements

1. Increased U.S. XPOVIO sales following expanded FDA approval in multiple myeloma
2. Commenced organizational changes to enhance commercial capabilities
3. Secured $60M additional funding
4. Attained conditional marketing approval in Europe and UK for penta-refractory STORM population
5. EMA validation of BOSTON MAA (Type II variation)
6. Commenced confirmatory Phase 3 Study in DLBCL in support of 2020 accelerated approval
7. First patients dosed in two new company-sponsored trials evaluating selinexor either alone or in combination with approved agents in melanoma and myelofibrosis

2H 2021 Milestones

1. Continue to enhance commercial capabilities; continue to increase U.S. XPOVIO sales
2. Initiation of Phase 3 study evaluating XPOVIO + pomalidomide in patients with multiple myeloma
3. SIENDO Phase 3 top-line data announced
4. Planned initiation of key mid- and late-stage clinical studies in MDS, myelofibrosis, CRC and NSCLC
5. Additional combination data in hematologic and solid tumor malignancies with XPOVIO and other standard of care anti-cancer drugs to be presented at ESMO 2021 and other medical meetings
6. Host investor day to outline strategic imperative and pipeline priorities

Karyopharm® Therapeutics

Thank you!

September 2021