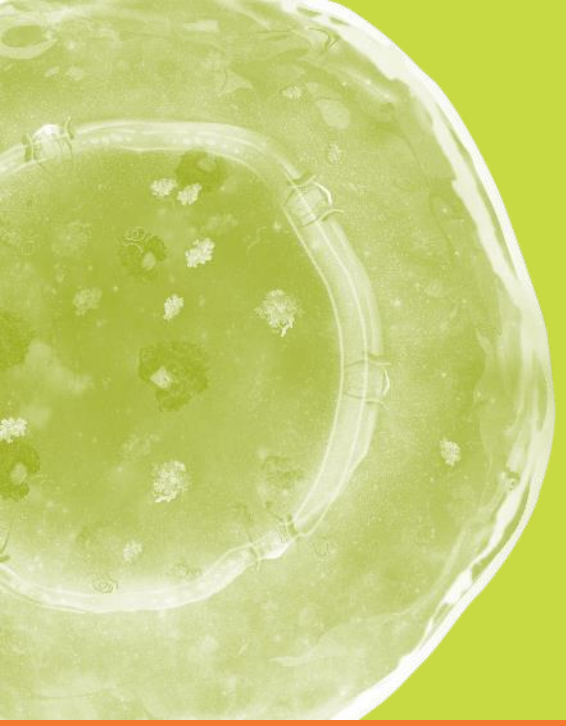
Karyopharm® Therapeutics

40th Annual J.P. Morgan Healthcare Conference

January 2022

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 preliminary financial information for fourth quarter and full year 2021; guidance on its expected cash runway and 2022 research and development expenses; expectations to provide annual revenue guidance during Q1 2022; expectations and plans relating to XPOVIO or any of its drug candidates, if approved, 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, if approved, and the commercial performance of XPOVIO; submissions to, and the review and potential approval of selinexor or any of its other drug candidates 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 and eltanexor. 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 presentation could also be affected by risks and uncertainties relating to a number of other factors, including the following: the risk that the COVID-19 pandemic could disrupt Karyopharm's business more severely than it currently anticipates, including by negatively impacting sales of XPOVIO, interrupting or delaying research and development efforts, impacting the ability to procure sufficient supply for the development and commercialization of selinexor or other drug 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 September 30, 2021, which was filed with the Securities and Exchange Commission (SEC) on November 3, 2021, and in other filings that Karyopharm may make with the SEC in the future. Any forward-looking statements contained in this presentation speak only as of the date hereof, and, except as required by law, Karyopharm expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. Karyopharm regularly uses its website to post information regarding its business, drug development programs and governance. Karyopharm encourages investors to use www.karyopharm.com, particularly the information in the section entitled "Investors," as a source of information about Karyopharm. References to www.karyopharm.com in this presentation are not intended to, nor shall they be deemed to, incorporate information on www.karyopharm.com into this presentation by reference. 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. Karyopharm only promotes XPOVIO for its approved indications.



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

Karyopharm® Therapeutics

Passionately driven in its mission to positively impact lives and defeat cancer

Expanding on myeloma foundation

Expecting opinion on MAA in 2L+ in 1H22; pursuing additional 2L+ indications

Near-term opportunity in solid tumors

SIENDO recruitment complete; top-line Phase 3 results in endometrial cancer in 1Q22

Focused clinical pipeline

Pursuing approvals in MDS and myelofibrosis over the next 3-4 years

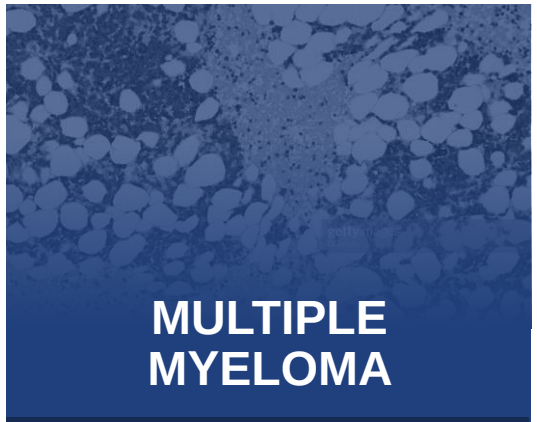
Strong executive leadership

Ability to achieve commercial and development excellence to execute corporate objectives

Well-capitalized

Cash runway into early 2024

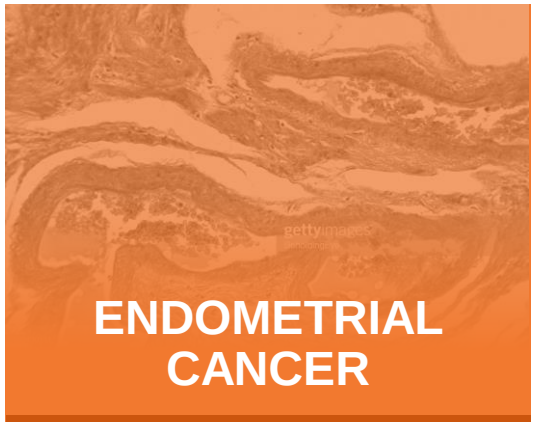
Prioritized and targeted core programs focused on areas of high unmet need driving continued and sustained innovation across our pipeline



MULTIPLE MYELOMA

~40,000 patients (2L+)[1,5]

Growing adoption of approved regimens and generating data for novel combinations in 2L+



ENDOMETRIAL CANCER

~14,000 frontline patients[2,5]

Potential to be first and only treatment post chemotherapy in the maintenance setting

MYELODYSPLASTIC SYNDROMES

~15,000 intermediate to high risk patients[3,5]

Potential to improve survival in HMA-refractory MDS

MYELOFIBROSIS

~5,000 MF patients[4,5]

Potential to improve patient outcomes in JAKi-refractory MF

Opportunity to expand into additional lines of therapy in all four core indications

1. Kantar Cancer Impact. **2.** Sorbe, B et al. Int J Gynecol Cancer 2008. **3.** Clarivate/DRG Epidemiology Data. **4.** https://my.clevelandclinic.org/health/diseases/15672-myelofibrosis. **5.** Annual U.S. incidence.

Progressing Focused Pipeline Across Cancers With High Unmet Needs

	Regimen	Indication	Study Name	Early Stage	Mid Stage	Late Stage	Commercial
XPOVIO® (selinexor)	w/dexamethasone	Multiple myeloma (penta-refractory)	STORM				
	w/bortezomib + dexamethasone	Multiple myeloma (2L+)	BOSTON				
	monotherapy	DLBCL (R/R)	SADAL				
SELINEXOR	w/R-GDP	DLBCL (R/R)	XPORT-DLBCL-030[1]				
	monotherapy	Endometrial cancer (maintenance therapy)	SIENDO				
	w/pomalidomide + dexamethasone	Multiple myeloma (2L+)	XPORT-MM-031[2,3,4]				
	w/carfilzomib	Multiple myeloma (relapsed/refractory)	STOMP				
	monotherapy	Myelofibrosis (previously treated)	XPORT-MF-035				
	w/ruxolitinib	Myelofibrosis (treatment naïve)	XPORT-MF-034[5]				
ELTANEXOR	monotherapy	Myelodysplastic syndromes (refractory)	KCP-8602-801				
	+ hypomethylating agents	Myelodysplastic syndromes (treatment naive)	KCP-8602-801				

hematologic cancer solid tumor cancer Coming soon

1. XPORT-DLBCL-030 is a Phase 2/3. **2.** Versus elotuzumab, pomalidomide, and dexamethasone. **3.** Study expected to dose first patient in 1Q22. **4.** Sponsored by European Myeloma Network. **5.** XPORT-MF-034 is a Phase 1/2.

MULTIPLE MYELOMA

Selinexor Improves Outcomes for Patients with Relapsed Multiple Myeloma

What is Multiple Myeloma?

- Cancer of the plasma cells and the **second most common blood cancer** in the world[1]
- Malignant plasma cells produce a paraprotein (an inactive antibody known also as M-protein) that adversely affects bone marrow, bones, and kidneys

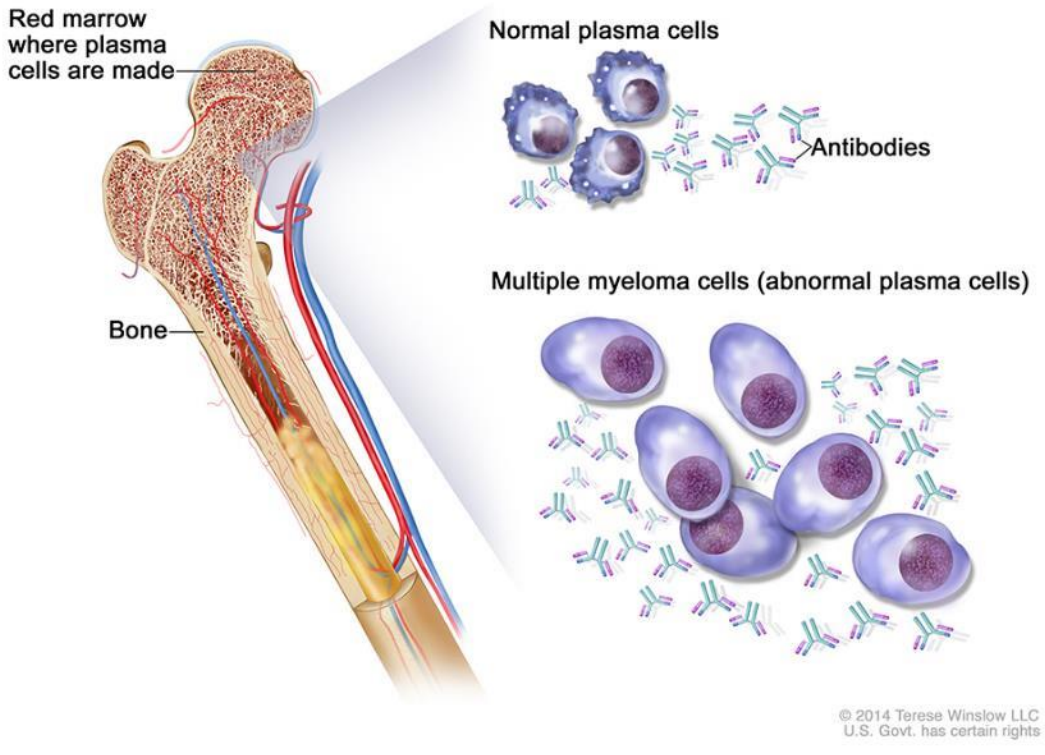
Treatment Landscape

- Following first line progression, **treatment decisions are based on physician and patient choice** rather than clear treatment guidelines
- Current standard of care is to **switch drug classes** once a regimen stops responding

Opportunity and Unmet Need

- Retrospective analyses of currently approved combination regimens demonstrate **poor outcomes for patients with multiple myeloma refractory to prior daratumumab (anti-CD38 mAb)** treatment, including low ORRs and short PFS
- **25%** patients have multiple myeloma with high-risk cytogenetics and poorer outcomes with currently available therapies[3]

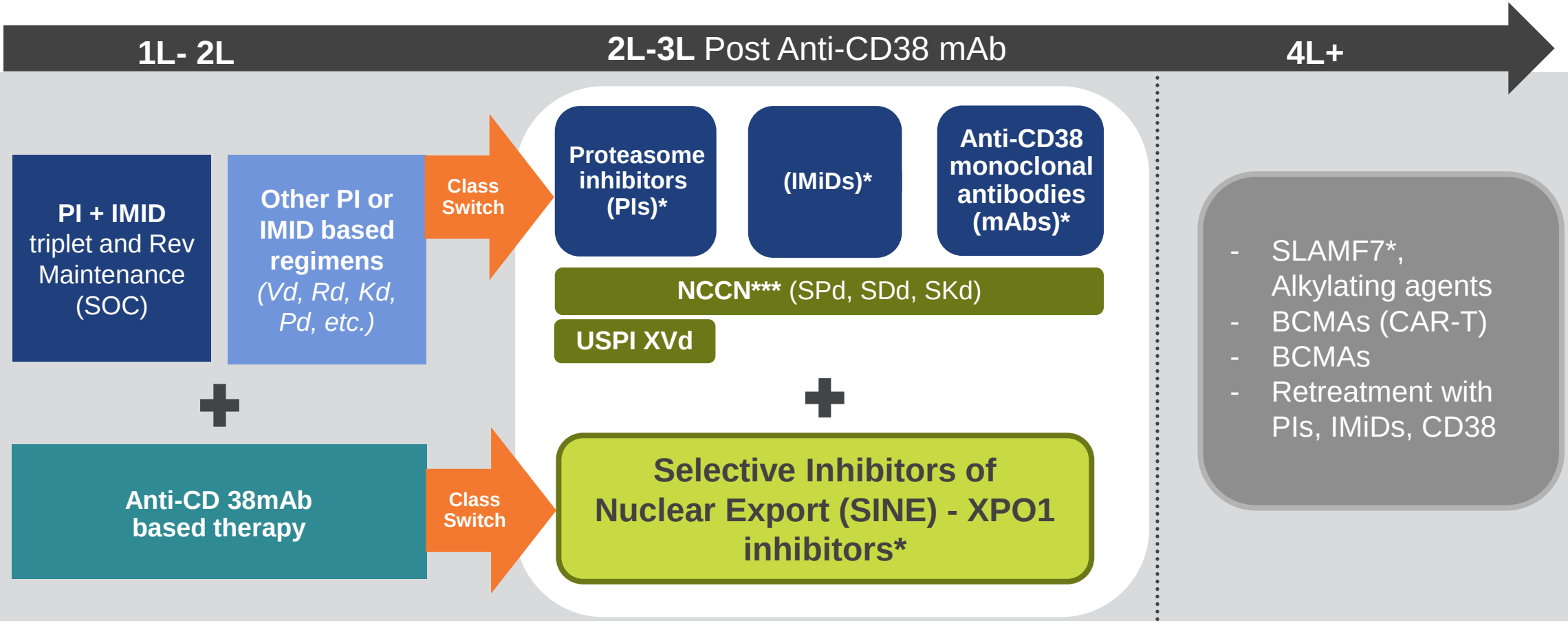
Affects ~40,000 patients in the US in 2L+[2]



1. International Myeloma Foundation. What is Multiple Myeloma? https://www.myeloma.org/what-is-multiple-myeloma. Accessed November 2021. **2.** Kantar Cancer Impact. **3.** Am J Hematol. 2020;95:548–567

Clarity of Sequencing with XPOVIO-based Regimens Post Anti-CD38mAb in the 2L and 3L Settings of RRMM

XPOVIO provides a mechanistic switch and maintains full optionality to future regimens.



Combinations other than XVd and Xd will not be promoted by Karyopharm, but may be considered for future indication updates

* +dexamethasone
*** NCCN Guideline inclusion for SPd, SDd and SKd

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

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

Approval Date: July 2019	Approval Date: Dec 2020	Ongoing/Completed
1st approval in MM **Dose:** 160 mg (80 mg twice weekly)	**2nd approval in MM** **Dose: 100 mg once weekly**	**Phase 1/2 study in MM** **Dose range: 6**0-100 mg once weekly
Xd STORM	**XVd** BOSTON	**SPd, SKd, SDd** STOMP
Phase 2b, single-arm, open-label, multicenter study	**Phase 3, 2-arm, active comparator-controlled, open-label, multicenter study**	**Phase 1/2, open-label, multicenter study**
Patients with penta-refractory MM	After at least 1 prior therapy in MM	Patients with RRMM (dose escalation/expansion)

IN THE BOSTON STUDY

- **65% of patients in the XVd arm had an XPOVIO dose reduction (126/195 patients) vs 35% of those without a dose reduction (69/195)**
- **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 selinexor in combination with other MOAs across multiple triplet and quadruplet regimens, including XVd.
MM=multiple myeloma; MOA=mechanism of action; RRMM=relapsed or refractory multiple myeloma.

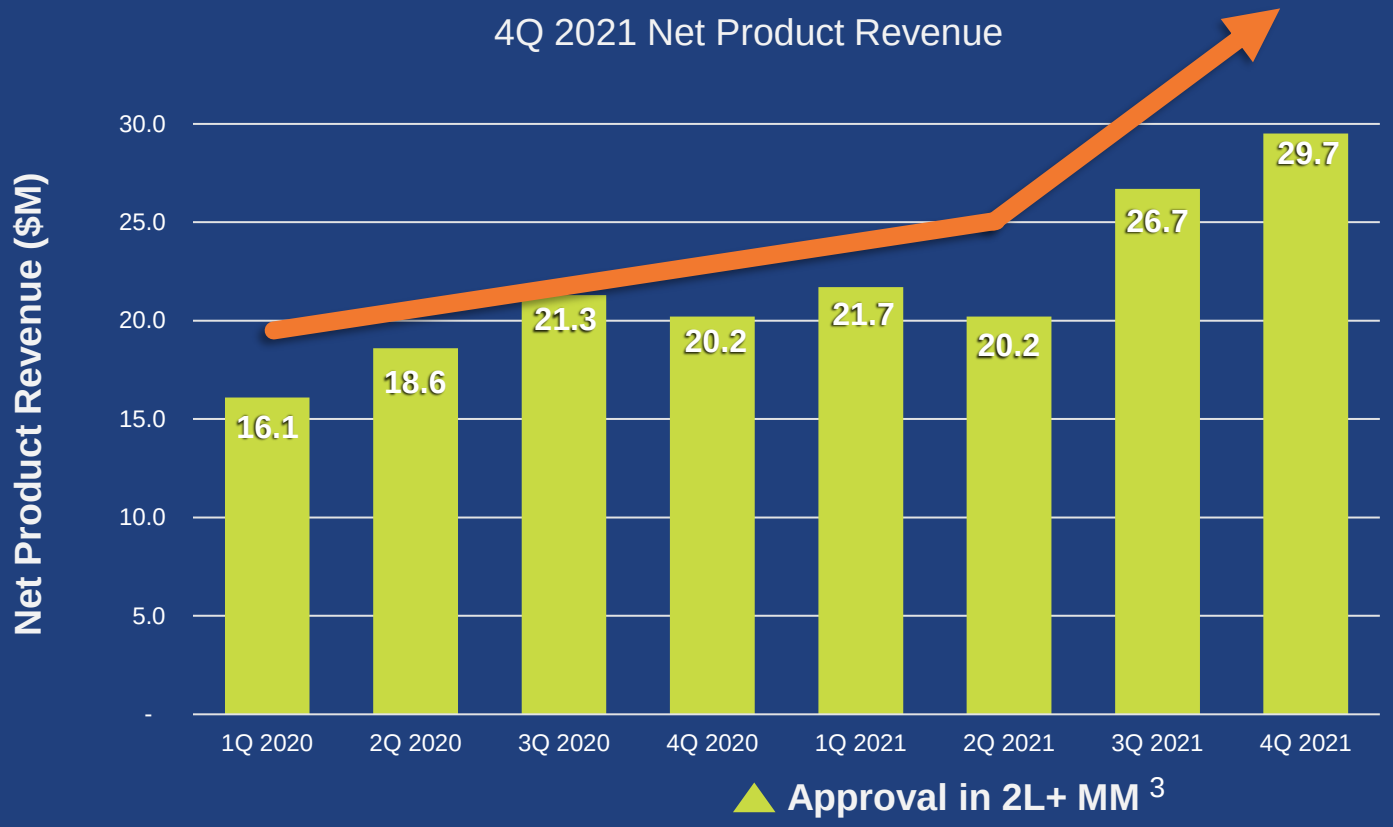
Combinations other than XVd and Xd are not promoted by Karyopharm, but may be considered for future indication updates

XPOVIO Launch Update: 4Q 2021

Accelerated Growth in 2L+

~$29.7M[1]

4Q 2021 Net Product Revenue



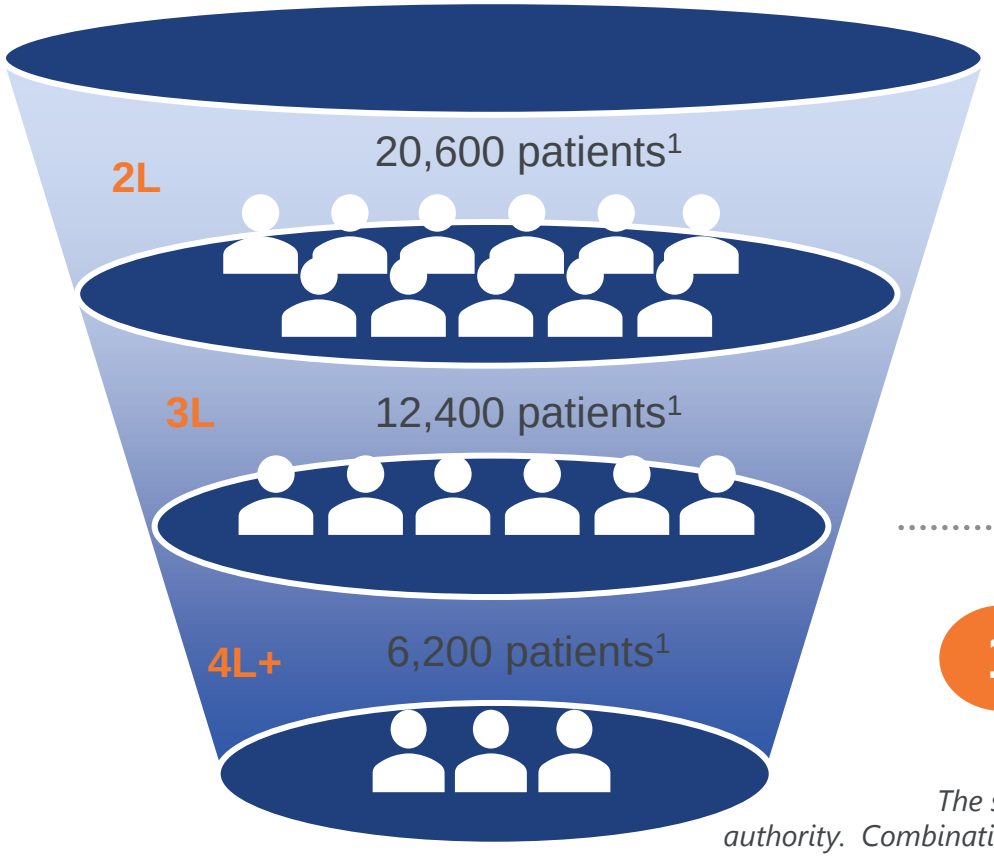
4Q 2021 Highlights

- Net product revenue up 48% year-over-year and 11% quarter-over-quarter[1]
- Sustained product demand quarter-over-quarter despite COVID impact
- Increased uptake in 2L to 4L; fastest growing MM therapy used in 3L regimens[2]
- Continued increase in breadth and depth of use of XPOVIO
- Building confidence in community and continued positive shift in Intent to Prescribe metrics

1. Based on preliminary unaudited estimate. 2. Komodo Health Claims Data Jan-Dec 2021. 3. Approval of 2L+MM in December 2020.

Striving to be a Standard of Care in 2L+, Driving Sustainable and Long-Term Growth

~40,000 US patients/year in 2L+[1]



Karyopharm's focus

2

XVd

BOSTON approval in 2L+ (Dec 2020)

3

XPd

Advancing all-oral triplet into Phase 3 targeting 2L+

1

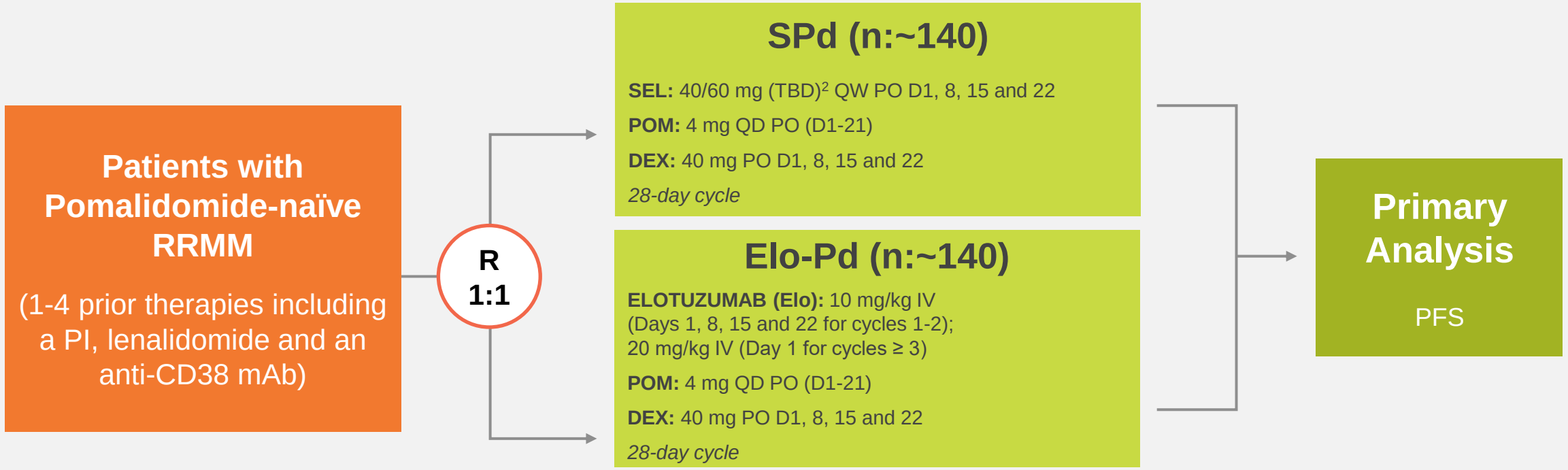
Xd

STORM approval in 4L+ (July 2019)

The safety and efficacy of SPd has not been established and has not been approved by the FDA or any other regulatory authority. Combinations other than XVd and Xd are not promoted by Karyopharm but may be considered for future indication updates.

1. Kantar CancerMPact

Phase 3 Study Evaluating Selinexor, Pomalidomide and Dexamethasone (SPd) in Patients with Previously Treated Multiple Myeloma[1]



Expect to dose first patient in 1Q 2022

Top-line data expected 2024

1. XPORT-MM-031; 2. Final dosing for Selinexor arm to be determined following interim analysis of data from first 60 patients

Ongoing Progress With Global Selinexor Access

Europe

- MAA validated and under review by CHMP for 2L+; expect review to be completed in 1H22

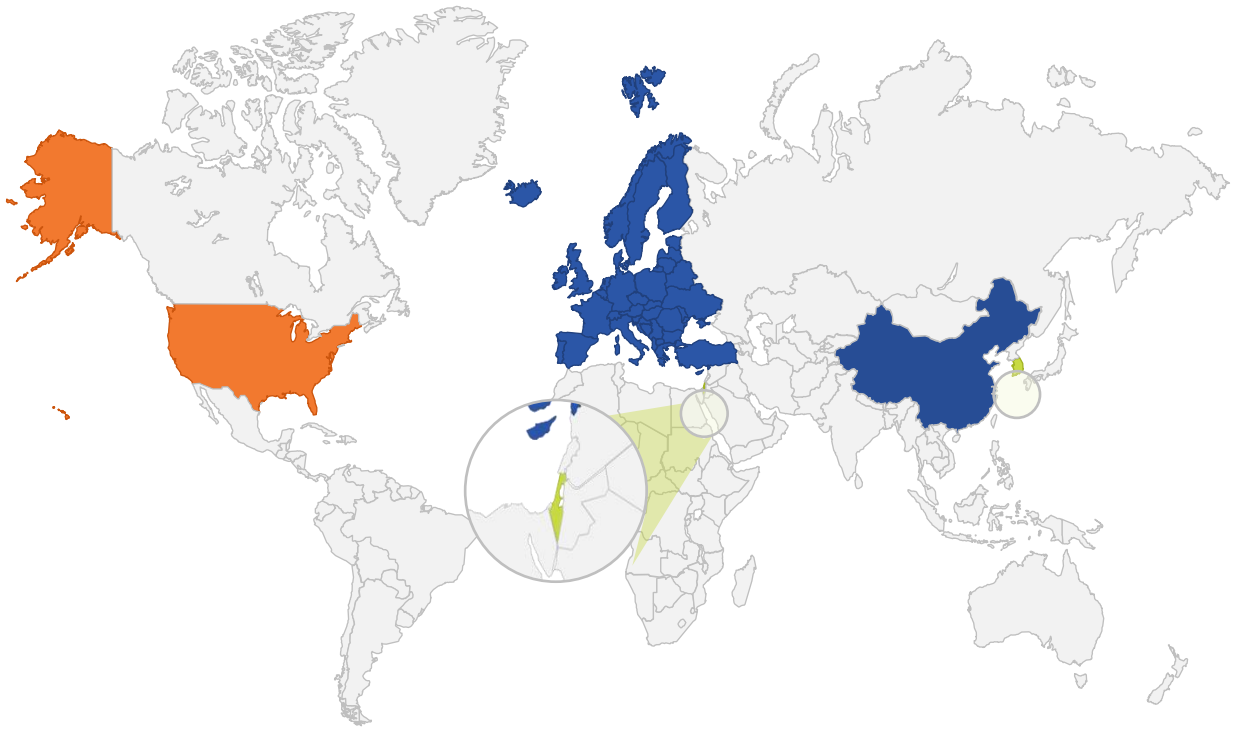
Asia

- Antengene received conditional approval in China for penta-refractory multiple myeloma

- NDAs submitted by Antengene in multiple additional Asia Pacific markets including Hong Kong, Australia, Singapore and Taiwan[1]

Canada

- NDS in 2L+ filed by Forus Therapeutics and accepted for review by Health Canada



2L+ multiple myeloma and R/R DLBCL

Penta-refractory multiple myeloma

Penta-refractory multiple myeloma and R/R DLBCL[2]

1. Antengene press release dated June 4, 2021. **2.** Approved in Israel and South Korea.

Selinexor in Multiple Myeloma: Key Takeaways

1. **Continued strong net product revenue growth**
2. **Driving adoption of XPOVIO-based combinations for 2L+ where an effective new class of therapies is needed**
3. **Critical need for efficacious, novel combinations post anti-CD38 with the ability to combine with PIs and IMiDs**
4. **Pursuing approvals in additional settings, including with the all-oral regimen XPd**

ENDOMETRIAL CANCER

Selinexor Has the Potential to Extend Remission in Patients with Advanced or Metastatic Endometrial Cancer

What is Endometrial Cancer?

- Arises from the endometrium, the layer of cells that form the lining of the uterus.

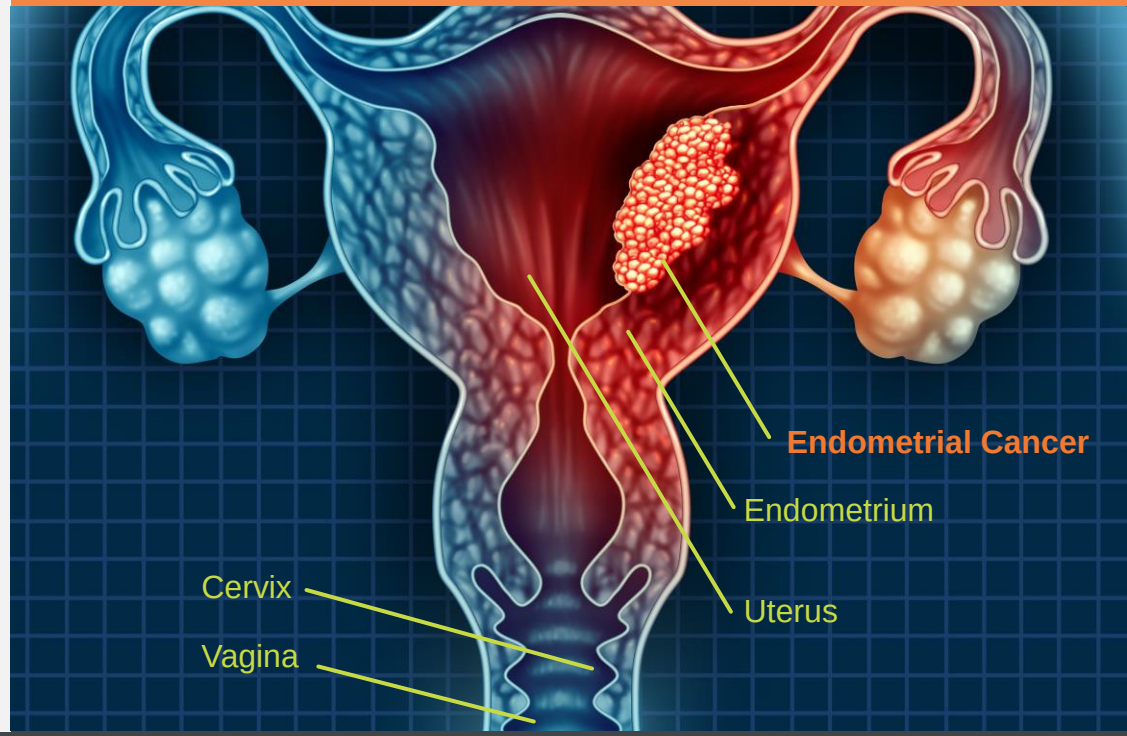
Treatment Landscape

- First-line treatment is chemotherapy (taxane plus platinum), where response rates (CR or PR) can be as high as 67%[1]
- Following chemotherapy, NCCN Guidelines® recommend “watch and wait” until disease relapses[2]

Opportunity and Unmet Need

- Prognosis is poor, with **progression expected within 4-6 months** for patients responding to first-line chemotherapy treatment
- No SoC or FDA-approved agent for maintaining response in EC post-systemic treatment to prevent or delay progression to later lines of treatment

The most common gynecological cancer in the US[3]



The safety and efficacy of selinexor in endometrial cancer has not been established and has not been approved by the US FDA or any other regulatory authority.

1. Sorbe, B et al. Int J Gynecol Cancer. 2008). **2.** National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Uterine Neoplasms. v4.2021. September 3, 2021; www.nccn.org. **3.** www.hopkinsmedicine.org/health/conditions-and-diseases/endometrial-cancer.

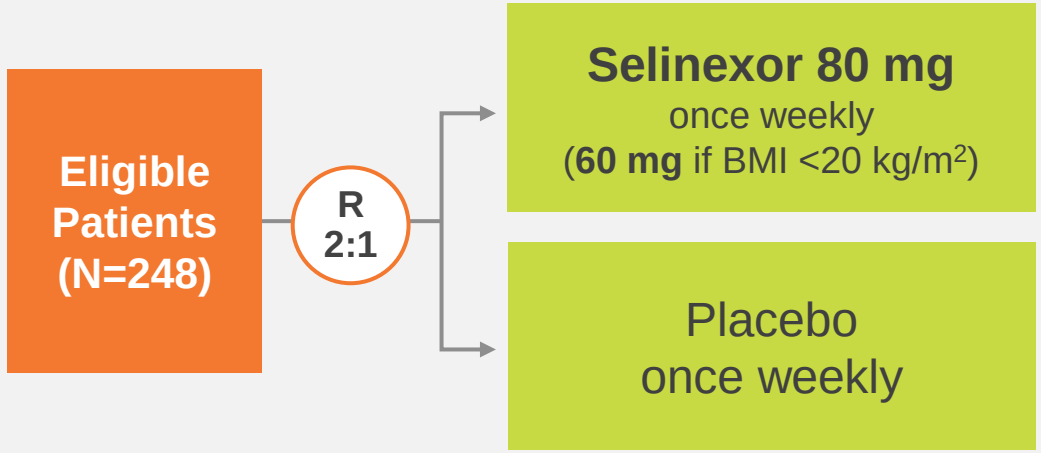
SIENDO Study Design:

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

- The trial is powered to show a HR of 0.60 with the estimated median PFS improvement of 67%, from 4.5 months for placebo to 7.5 months for Selinexor

Completed recruitment December 2021

Top-line data expected in 1Q 2022

Selinexor Could be the First Approved Drug for the Maintenance of Advanced Endometrial Cancer, with the Potential to Extend Remission

Growing Market Opportunity

- Most common gynecologic cancer in the U.S with ~66K cases[1]
- Addressable market will grow with new and more effective therapies over time[2]
- ~14,000 frontline patients receiving chemotherapy with a growing addressable patient population in maintenance setting[3]

Competitively Well-positioned

- No approved drug therapies post chemotherapy in the maintenance setting to prolong response
- Promising results in a Phase 2 study (Vergote, 2019) in patients with progressing endometrial cancer (2L and later)

Critical Success Factors

- Deliver clinically significant results from SIENDO and rapidly engage FDA with sNDA
- Establish once-weekly oral EC maintenance as SoC vs. “watch and wait” approach
- Leverage established field and access capabilities
- Engage opinion leaders and patient advocacy

1. SEER / NCI Cancer Stat Facts. 2020. https://seer.cancer.gov/statfacts/html/corp.html. **2.** Decision Resources. **3.** Epic Oncology (Incidence, 1st/ 2nd line treated); epic Oncology physician survey 2019. **3.** Sorbe, B et al. Int J Gynecol Cancer 2008.

Selinexor in Endometrial Cancer: Key Takeaways

1. **Addressing significant unmet need for maintenance therapy with a growing number of patients**

2. **Well-positioned to be the first and only treatment post chemotherapy in the maintenance setting that has the potential to extend time in response and remission**

3. **Top-line Phase 3 SIENDO data expected early 2022, followed by rapid sNDA submission**

MYELODYSPLASTIC SYNDROMES

Eltanexor Has the Potential to Improve Survival in HMA Refractory Myelodysplastic Syndromes

What is Myelodysplastic Syndrome (MDS)?

- Blood-forming cells in marrow become abnormal and create immature blood cells that are not able to function properly

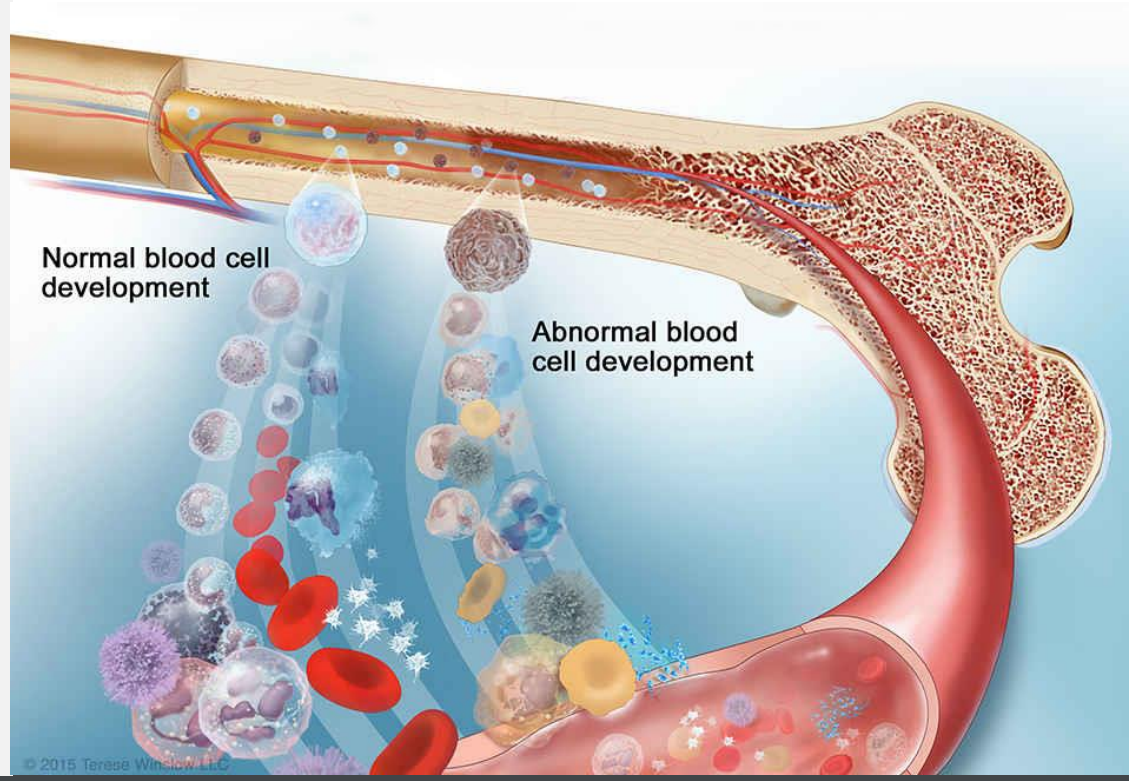
Treatment Landscape

- Hypomethylating agents (HMA) are the current standard of care for patients with newly diagnosed, higher-risk MDS
- Approximately 50% of patients respond; responses typically last <2 years[2]

Opportunity and Unmet Need

- Prognosis in HMA-refractory disease is poor, with an **expected survival of 4-6 months**[3,4]
- No currently approved therapies for HMA-refractory disease

~15,000 patients diagnosed with intermediate-to-high risk MDS each year in the US[1]



1. Clarivate/DRG Myelodysplastic Syndromes Landscape & Forecast (Nov 2020). **2.** Gil-Perez A. Ther Adv Hematol. 2019 doi:10.1177/2040620719847059.. **3.** Jabbour E, Cancer. 2010;116(16):3830-4. **4.** Prébet T. J Clin Oncol. 2011;29:3322-7. **5.** Clarivate/DRG Myelodysplastic Syndromes Landscape & Forecast (Nov 2020).

Single-agent Eltanexor Demonstrated Robust Activity with an ORR of 53% Among Patients With HMA Refractory MDS in a Phase 1 Study[1]

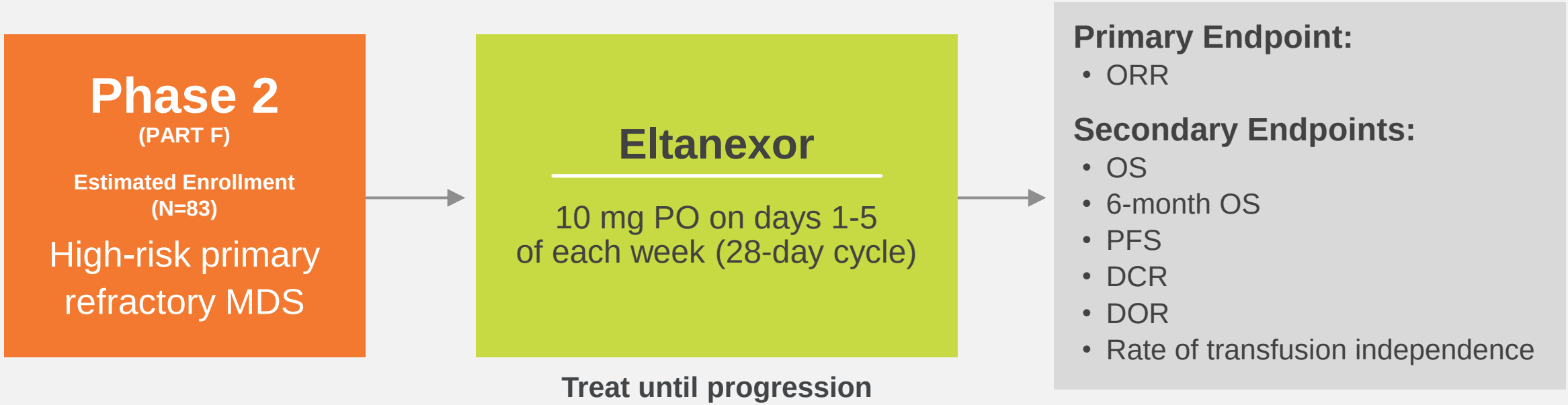
- No approved drugs and historical overall survival (OS) 4-6 months in patients with HMA-refractory MDS
- **Single-agent eltanexor demonstrated median OS of 9.9 months**
- **Single-agent eltanexor demonstrated 53% ORR**

	Total N=15
Overall Response Rate (mCR + HI)[2,3]	**53%**
Median treatment duration (weeks, all patients)	13.0
Median time to response (weeks)	8.4
Median duration of response (weeks)	19.2

The Grade 3/4 AEs across all patients were anemia (40%), leukopenia (20%), thrombocytopenia without bleeding (20%), decreased appetite/weight (20%), neutropenia (40%): no febrile neutropenia, 1 case of sepsis.
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.
No severe bleeding events — which is the corresponding clinical outcome for thrombocytopenia (as you have febrile neutropenia and sepsis as the clinical outcome for neutropenia.

1. Lee, Sangmin, et al. EHA 2021. 2. mCR = complete response without marrow recovery. 3. HI = hematologic improvement.

Phase 2 Expansion of the Ongoing Phase 1/2 Study of Single-Agent Eltanexor in HMA Refractory MDS



First patient dosed Sept 2021

Top-line data expected 1H 2023

DCR, disease control rate; DOR, duration of response; MDS, myelodysplastic syndrome; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PO, by mouth; Karyopharm Therapeutics Inc. Clinical Study Protocol. Version 7.0. KCP-8602-801.

Eltanexor in MDS: Key Takeaways

1. **Addressing significant unmet need for patients with HMA-refractory MDS**
2. **Single-agent eltanexor showing robust responses and survival in HMA-refractory MDS with the potential to be the first approved new class of therapy**
3. **Phase 2 study ongoing in patients with HMA-refractory MDS; top-line data expected 1H 2023**
4. **Initiated eltanexor in combination with HMAs in Phase 1 in frontline MDS**

MYELOFIBROSIS

Selinexor Has the Potential to Improve Patient Outcomes in JAKi Refractory Myelofibrosis

What is Myelofibrosis (MF)?

- Type of bone marrow cancer that disrupts body's normal production of blood cells.
- Causes extensive scarring in bone marrow, leading to severe anemia that can cause weakness and fatigue

Treatment Landscape

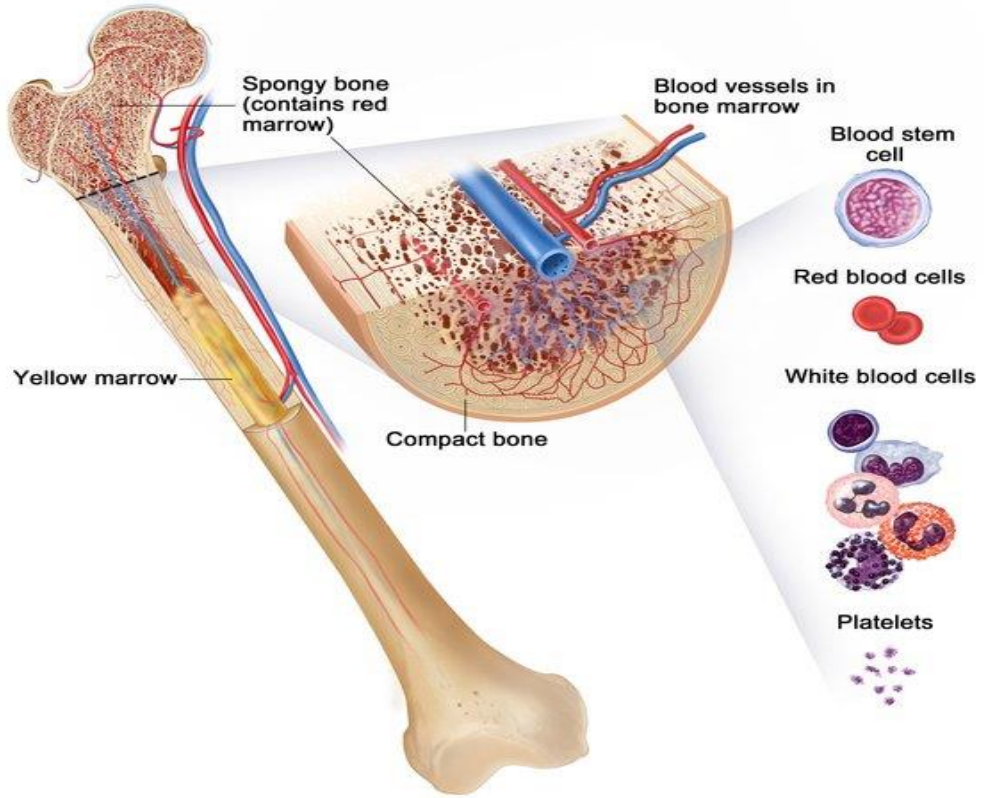
- Ruxolitinib is the standard of care for patients with newly diagnosed MF and it has resulted in splenic and clinical responses up to 4 years for primary responders
- Approximately 40% of patients respond[2]

Opportunity and Unmet Need

- Prognosis in ruxolitinib-refractory disease is poor, with an **expected median survival of ~14 months**[3]
- No other class of therapies other than JAK inhibitors

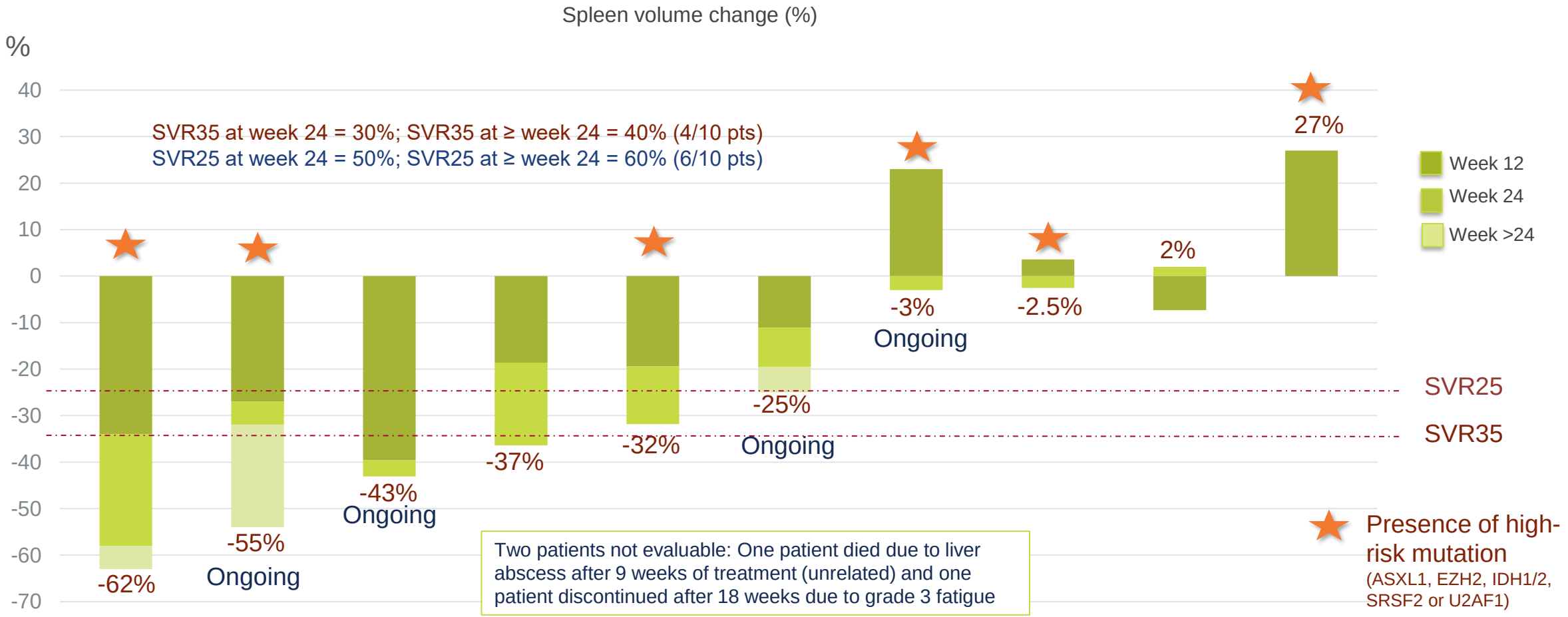
The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the US FDA or any other regulatory authority.

It is estimated that ~5,000 cases of MF occur in the US annually[1]



1. https://my.clevelandclinic.org/health/diseases/15672-myelofibrosis. **2.** https://www.jakafi.com/myelofibrosis/high-risk-treatment. Accessed Nov 2021. 3. Newberry KJ , et al. Clonal evolution and outcomes in myelofibrosis after ruxolitinib discontinuation. Blood . 2017;130:1125–1131; Palandri F, et al. Life after ruxolitinib: reasons for discontinuation, impact of disease phase, and outcomes in 218 patients with myelofibrosis. Cancer . 2019;26:1243–1252; Kuykendall AT, et al. Between a rux and a hard place: evaluating salvage treatment and outcomes in myelofibrosis after ruxolitinib discontinuation. Ann Hematol . 2018;97:435–441.

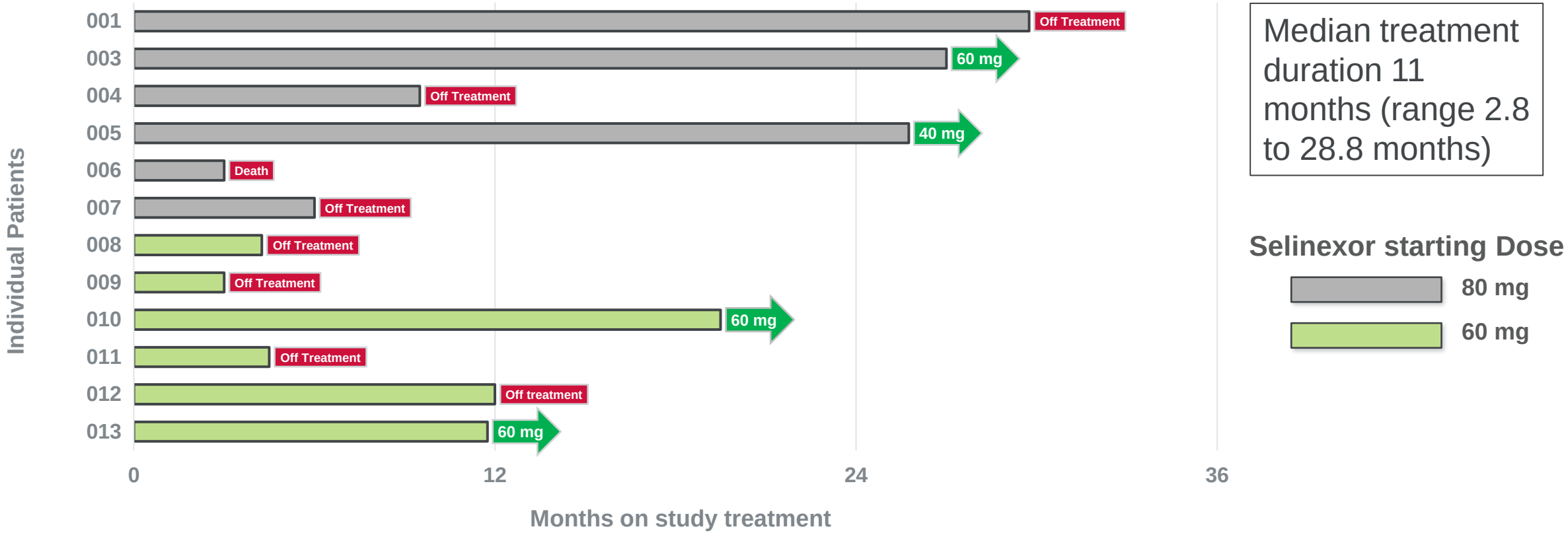
Single-Agent Selinexor Resulted in Sustained Spleen Responses in Refractory MF Patients[1]



The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the US FDA or any other regulatory authority.

1. Tantravahi, et al. ASH 2021.

Single-Agent Selinexor Resulted in Durable Responses with Long Term Therapy Documented Beyond Two Years[1]



Median treatment duration 11 months (range 2.8 to 28.8 months)

Selinexor starting Dose

80 mg

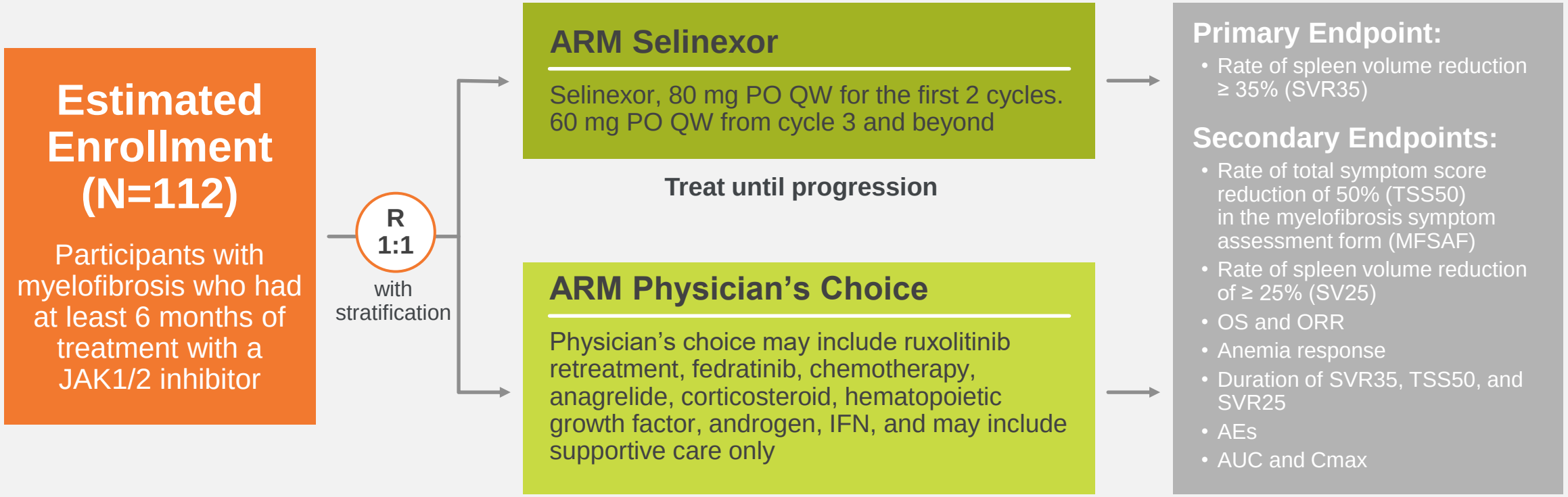
60 mg

Eight pts (70%) discontinued Selinexor due to: progression (n=2; 1 spleen size progression and 1 AML), changed to another clinical trial (n=2), death (n=1), and toxicity (n=3; 1 fatigue and 2 weight loss)

The safety and efficacy of selinexor in myelofibrosis not been established and has not been approved by the US FDA or any other regulatory authority.

1. Tantravahi, et al. ASH 2021.

A Company-sponsored Phase 2 Study Evaluating Single-Agent Selinexor Versus Physician's Choice in Previously Treated MF



First patient dosed December 2021

Top-line data expected 2H 2023

AEs, adverse events; AUC, area under the curve; Cmax, maximum concentration; DCR, disease control rate; DOR, duration of response; IFN, interferon; MDS, myelodysplastic syndrome; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PO, by mouth; QW, once weekly; Therapeutics Inc. Clinical Study Protocol. Version 7.0. KCP-8602-801.

Selinexor in Myelofibrosis: Key Takeaways

1. **Addressing significant unmet need for patients with JAKi-refractory MF**
2. **Single-agent selinexor showing robust responses in JAKi-refractory disease with the potential to be the first approved new class of therapy**
3. **Phase 2 study ongoing in patients with previously treated MF; top-line data expected 2H 2023**
4. **Initiated selinexor in combination with JAKi in Phase 1 in frontline MF**

PARTNERSHIPS, FINANCIAL HIGHLIGHTS AND MILESTONES

Strategic Partnerships Driving Expansion of Our Global Footprint

Commercial Partnerships Serving Key Global Markets

NEXPOVIO® (selinexor) NOW PARTNERED in Europe, Asia Pacific, and other key global territories

The MENARINI Group

Exclusively licensed rights to NEXPOVIO in European Union, the UK, Switzerland, CIS Countries and Latin America

- Karyopharm received upfront payment of $75M
- Eligible to receive up to an additional $202.5M in future milestones (based on regulatory and sales performance), plus tiered double-digit royalties on net sales ranging from the mid-teens to the mid-twenties
- Menarini to co-fund 25%, up to a maximum of $15M per calendar year, of Karyopharm's global R&D expenses each year from 2022 to 2025

ANTENGENE

AsiaPac

the MENARINI group

EU & LatAm

NEOPHARM

Israel

FORUS THERAPEUTICS

Canada

Large Ex-US Opportunity to Treat Multiple Myeloma and Endometrial Cancer

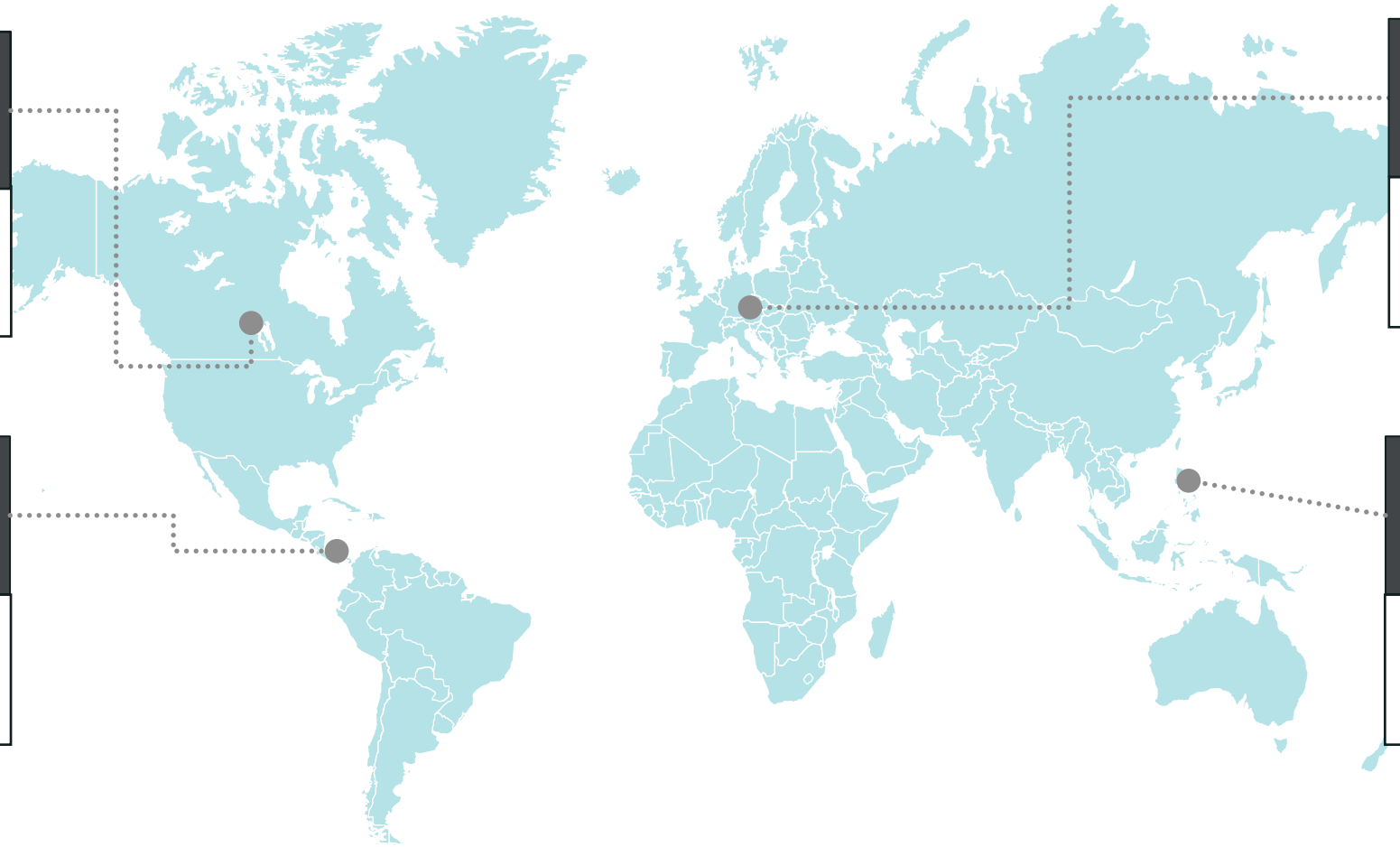
For Patients with Multiple Myeloma (2L+) and Endometrial Cancer (Maintenance Therapy)

Canada
MM: 3,300[1]
Endometrial: 2,500[5]

FORUS THERAPEUTICS

LatAm
MM: 12,000[3]
Endometrial: 11,000[5]

the MENARINI group



EU
MM: 30,700[2]
Endometrial: 17,000[5]

the MENARINI group

APAC
MM: 14,000[4]
Endometrial: 10,500[5]

ANTENGENE

Sources: **1.** Myeloma Canada **2.** Decision Resource Group **3.** Epic Oncology. 4 Extrapolated from Incidence Rate. 5. Extrapolated from Decision Resource Group

Financial Snapshot

$209.3M

CASH, EQUIVALENTS & INVESTMENTS
30-Sept-2021

Early 2024

EXPECTED CASH RUNWAY

~$98.3M

NET PRODUCT REVENUE 2021[1]

75.5M

SHARES OUTSTANDING
27-Oct-2021

- Expect to provide 2022 annual product revenue guidance during Q4/FY Earnings Call in February 2022
- 2022 R&D expense expected to decrease by ~15% compared to 2021

1. Preliminary unaudited estimate.

Upcoming Milestones for 2022 and 2023

MULTIPLE MYELOMA

- Leverage commercial capabilities and increase US XPOVIO sales (2022)
- Dose first patient in Phase 3 study evaluating selinexor + pomalidomide + dex (Q1 2022)
- EMA decision on MAA in 2L+ based on BOSTON study[1] (1H 2022)

ENDOMETRIAL CANCER

- Report top-line Phase 3 selinexor SIENDO data (Q1 2022)
- Submit sNDA (1H 2022)
- Conduct pre-launch activities (2022)
- Potential approval and launch as a maintenance therapy (1H 2023)

MYELODYSPLASTIC SYNDROMES

- Report preliminary Phase 1 eltanexor data in combination with HMA in frontline MDS (2022)
- Report top-line Phase 2 eltanexor data in HMA-refractory MDS (1H 2023)

MYELOFIBROSIS

- Report top-line Phase 1 data in combination with JAKi in treatment naïve MF (2H 2022)
- Report top-line Phase 2 selinexor data in previously treated MF (2H 2023)

1. Approval of the BOSTON study will fulfill the confirmatory study requirement for STORM conditional approval.

Karyopharm® Therapeutics

Thank you!

APPENDIX