Karyopharm® Therapeutics

A Commercial-Stage Pharmaceutical Company Pioneering Novel Cancer Therapies

JP MORGAN 2023 HEALTHCARE CONFERENCE
January 11, 2023

Richard Paulson
Chief Executive Officer

OVERVIEW

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 fourth quarter and full year 2022 financial results; Karyopharm's expected cash runway; the ability of selinexor or eltanexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, myelodysplastic neoplasms, diffuse large B-cell lymphoma, and other diseases; expectations related to future clinical development and potential regulatory submissions of selinexor or eltanexor; expectations with respect to commercialization efforts; submissions to, and the review and potential approval of selinexor, eltanexor or any of its other product 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 product 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 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 September 30, 2022, which was filed with the Securities and Exchange Commission (SEC) on November 3, 2022, 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 and eltanexor 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.

Innovation and Patient Focused

Founded in 2008, building on over a decade of research into selective inhibition of nuclear export (SINE) as a novel mechanism of action

Karyopharm® Therapeutics

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

Positioned for Next Stage of Growth

XPOVIO / NEXPOVIO
Approved in Multiple Myeloma (MM) and DLBCL[1]

- Expanded global footprint with regulatory approvals in 40 countries
- Expect total revenues to be ~$157.7m in 2022
- Moving into earlier lines of therapy in MM

Focused Clinical Pipeline with One Planned and Two Ongoing Pivotal Studies; Optimizing Dose for Efficacy and Tolerability

- Phase 3 selinexor+ruxolitinib in treatment naïve MF (planned)[2]
- Phase 3 SPd[3] in R/R MM post anti-CD38
- Phase 3 selinexor as maintenance in TP53 wildtype EC[4]

Strong Financial Position

- Cash position of ~$279m at end of 2022*
- Cash runway until late 2025

* Based on preliminary unaudited estimate

1. DLBCL approved in the U.S. under accelerated approval pathway 2. MF: myelofibrosis; pending regulatory feedback 3. selinexcor + pomalidomide + dexamethasone 4. Endometrial cancer

Key Program Accomplishments in 2022

Multiple Myeloma

Grew U.S. XPOVIO net sales by 22% to $120.4m*

- Received full marketing authorization in the EU for NEXPOVIO; Approved in 40 countries
- Commercial launches by partners ex-US
- Initiated pivotal Phase 3 study evaluating lower dose selinexor, SPd[1], an all oral regimen in R/R MM

Endometrial Cancer

Initiated pivotal Phase 3 study of selinexor as a maintenance therapy in *TP53* wild-type EC

- Partnership with Foundation Medicine to develop TP53 companion diagnostic
- Presented top-line and subgroup analysis data from SIENDO in EC

Myelofibrosis

Initial results from Phase 1 evaluating selinexor+ruxolitinib in treatment naïve MF

- Encouraging preliminary results across the three relevant endpoints of SVR35, TSS50 and hemoglobin stabilization

Myelodysplastic Neoplasms

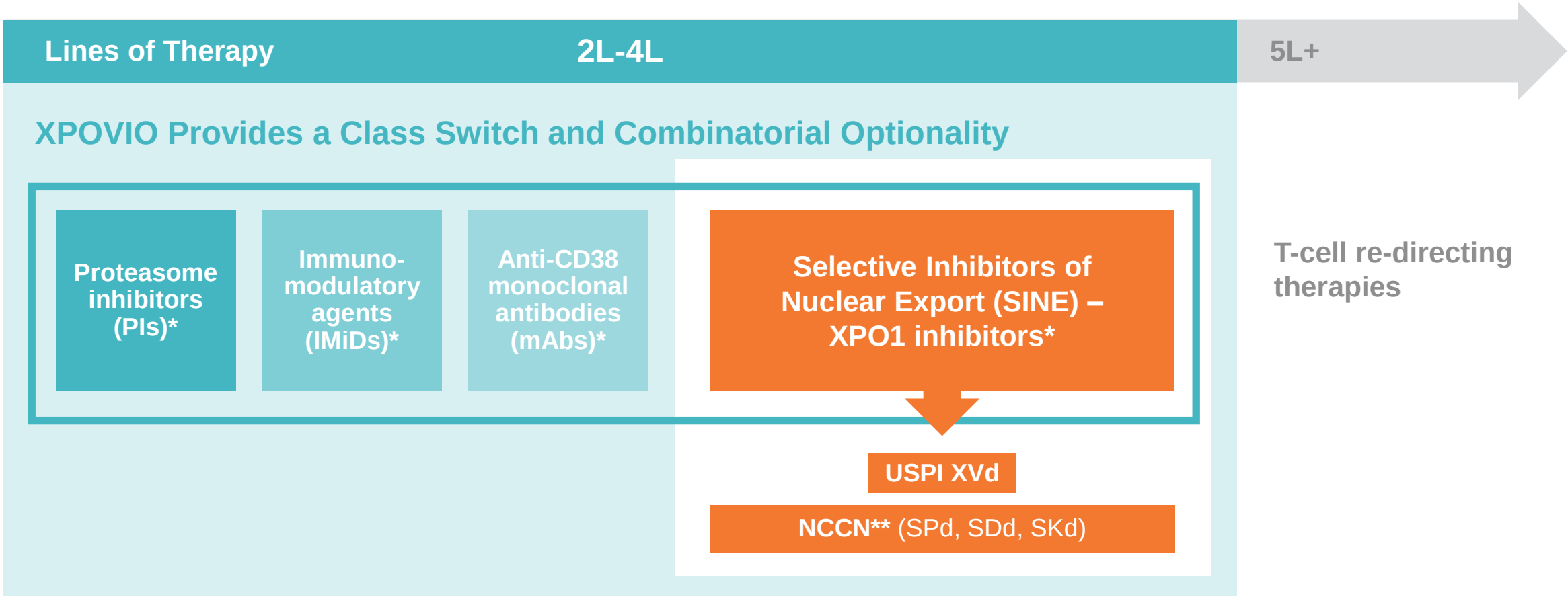
Completed recruitment for interim analysis of Phase 2 study evaluating eltanexor in high-risk relapsed/refractory MDS

- Evaluating eltanexor, second SINE compound, in patients of high unmet need

* Based on preliminary unaudited estimate;

1. Selinexor + pomalidomide + dexamethasone

XPOVIO: Novel Class of Therapy and Convenient Oral for 2L–4L RRMM post anti-CD38



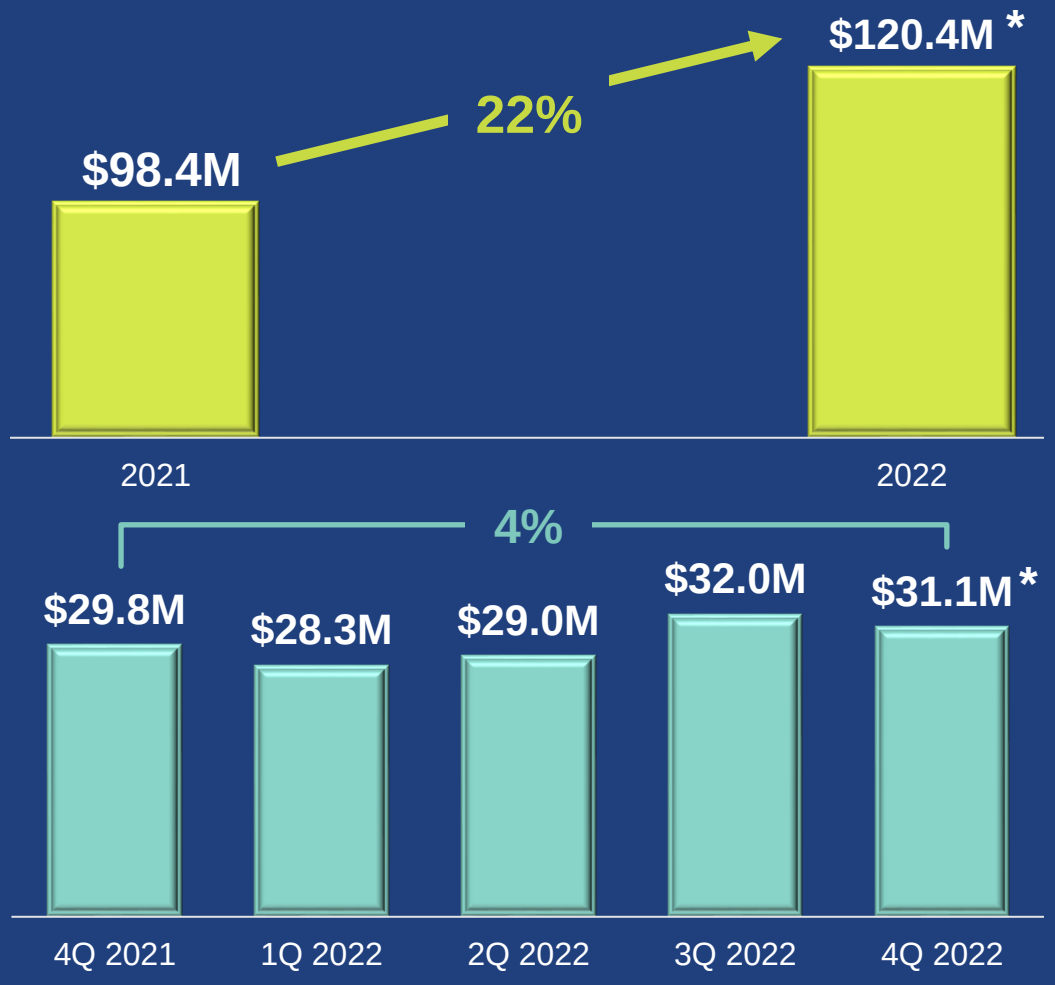
XPOVIO combinations other than XVd and Xd will not be promoted by Karyopharm, but may be considered for future indication updates.

Safety and efficacy of selinexor in combinations other than XVd and Xd have not been established and have not been approved by the US FDA or any other regulatory authority.

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

XPOVIO Update: 4Q 2022 and FY 2022

Net Product Revenue up 22% YoY Driven by Growth in 2L–4L



4Q and FY 2022 Highlights

- Continued shift into earlier lines of therapy, approaching 55% of patients in 2-4L[1], and increase in duration of therapy YoY
- Strong YoY growth in Community contributing to > 70% of selinexor revenues in Q4
- Continued improvement in perception and intent-to-prescribe data in 2-4L[2]
- Increased pressure in Academic setting due to intensifying late line competition and ongoing trials

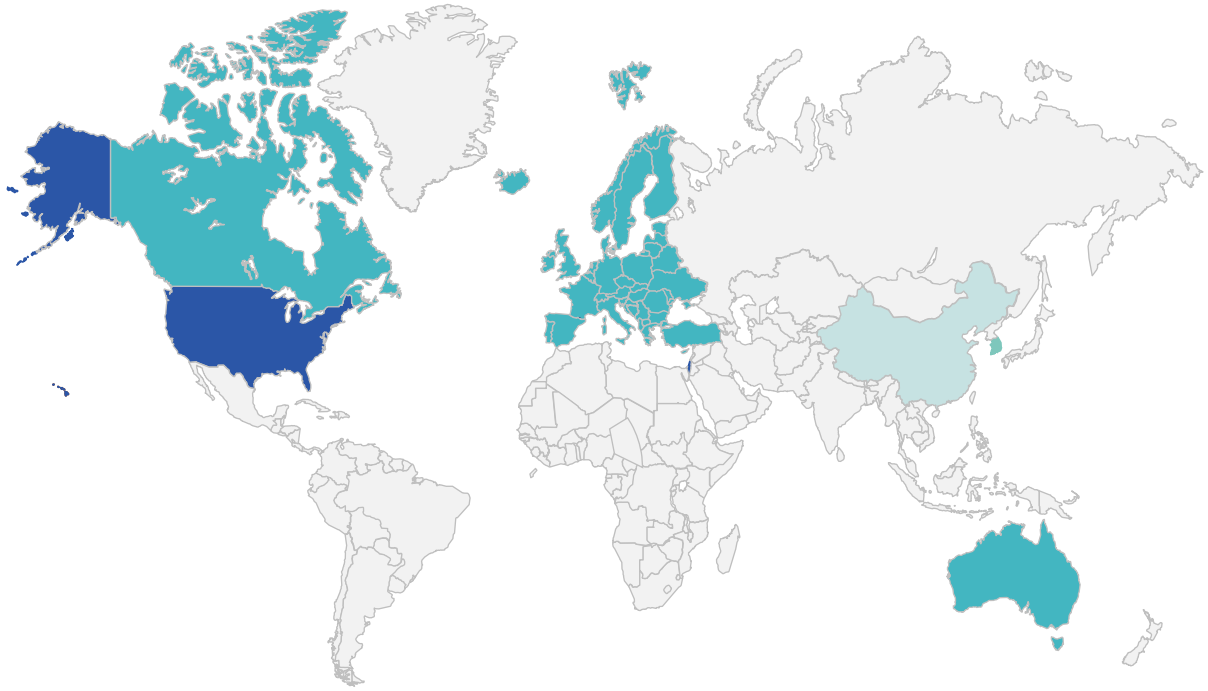
* Based on preliminary unaudited estimate

1. Based on Komodo claims analysis, assessed as of October 2022. 2. Based on internal KPTI Myeloma HCP ATU (healthcare professionals' awareness, trial and usage)

Full EMA Approval Received for NEXPOVIO® Expanding Indication to 2L+

XPOVIO® / NEXPOVIO® Now Approved in 40 Countries

Country/Region	Indication(s)	Partner
Approvals		
United States		–
Europe[1]		Menarini
UK		Menarini
Mainland China		Antengene
South Korea		Antengene
Australia		Antengene
Singapore		Antengene
Canada		Forus
Israel		Neopharm
Taiwan		Antengene



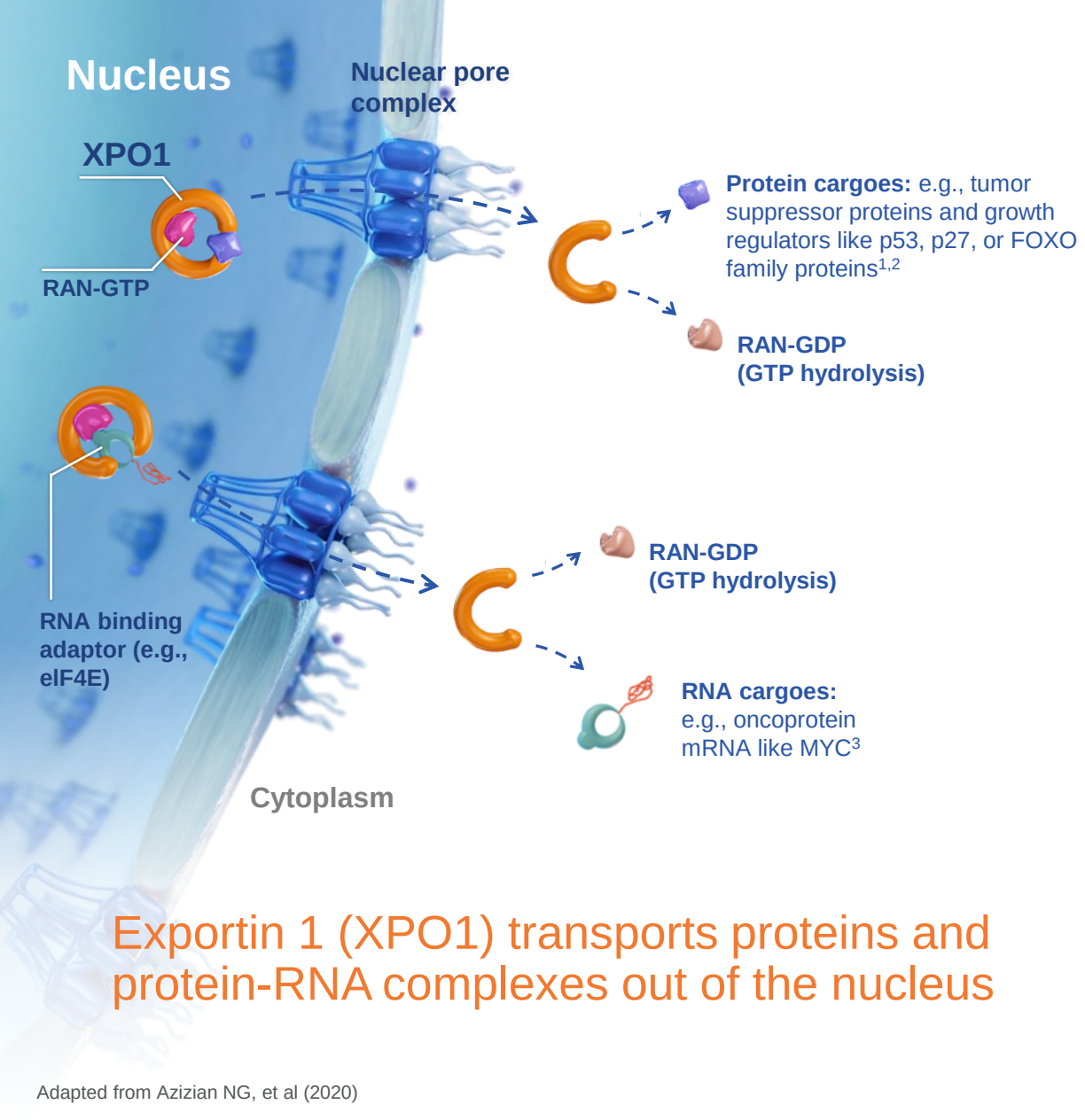
- 2L+ multiple myeloma and R/R DLBCL*
- 2L+ multiple myeloma
- Penta- or triple-class-refractory multiple myeloma and R/R DLBCL*
- Penta- or triple-class-refractory multiple myeloma

* DLBCL approved in the U.S. under accelerated approval pathway

1. The 27 countries comprising the European Union, plus Iceland, Norway, Northern Ireland and Lichtenstein.

Reshma Rangwala, MD, PhD
Chief Medical Officer

PIPELINE UPDATE



Exportin 1 (XPO1) transports proteins and protein-RNA complexes out of the nucleus

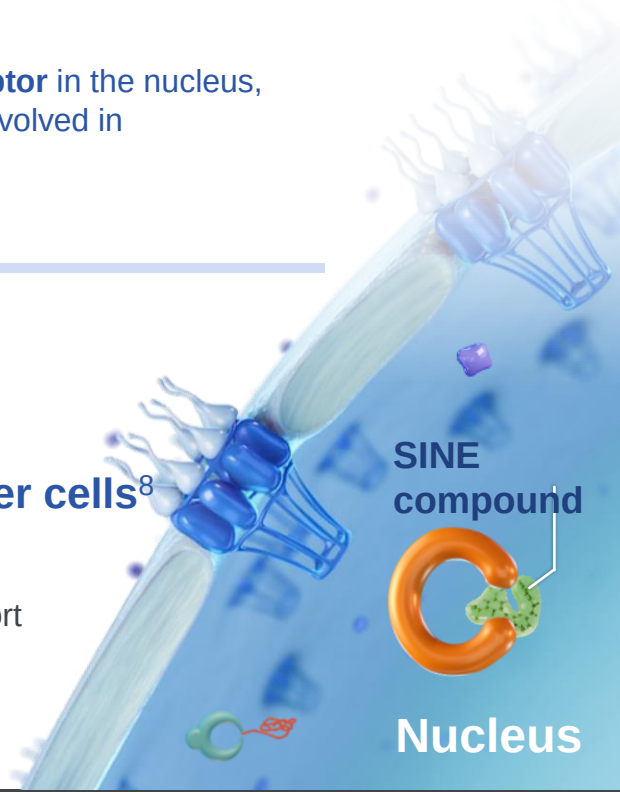
Adapted from Azizian NG, et al (2020)

Selinexor and Eltanexor (SINE compounds) selectively inhibit nuclear export by binding XPO1

1. Increases nuclear levels of **tumor suppressor proteins** and their activation[4,5]
2. Traps **oncoprotein mRNA** in the nucleus, leading to reduced oncoprotein levels[6]
3. Retains **activated glucocorticoid receptor** in the nucleus, leading to altered expression of genes involved in inflammatory pathways[7]

Reduced proliferation and **increased apoptosis of cancer cells**[8]

SINE: Selective inhibition of nuclear export



MYC, MYC proto-oncogene; eIF4E, Eukaryotic translation initiation factor 4E; FOXO, forkhead box, sub-group O; p27, cyclin-dependent kinase inhibitor 1B; p53, tumor protein 53; RAN, RAS-related nuclear protein; GDP, guanosine diphosphate; GTP, guanosine triphosphate

1. Azizian NG, et al. *J Hematol Oncol.* 2020;13(1):61. doi:10.1186/s13045-020-00903-4; 2. Das A, et al. *Exp Hematol Oncol.* 2015;4:7. doi:10.1186/s40164-015-0002-5.; 3. Culjkovic-Kraljacic B. *Cell Rep.* 2012;2(2): 207-15. doi: 10.1016/j.celrep.2012.07.007. 4. Turner JG, et al. *Biochem Pharmacol.* 2012 Apr 15;83(8):1021-32. doi: 10.1016/j.bcp.2011.12.016. 5. Azmi AS, et al. *Nat Rev Clin Oncol*. 2021 Mar;18(3):152-169. doi: 10.1038/s41571-020-00442-4. 6 Kashyap T et al, Oncotarget. 2018 Jul 20;9(56):30773-30786. doi: 10.18632/oncotarget.25637; 7. Argueta C, et al. *Oncotarget*. 2018 May 22;9(39):25529-25544. doi: 10.18632/oncotarget.25368. doi:10.1016/j.clml.2018.03.003; 8. Sun Q, et al. *Signal Transduct Target Ther*. 2016;1:16010. doi:10.1038/sigtrans.2016.10

Two Differentiated, Complementary Novel SINE Compounds

Selinexor

First novel XPO1 inhibitor

- **FDA-approved in MM and in DLBCL**[1]
- Currently being investigated in both solid tumors and hematologic malignancies[2]
- Penetrates blood-brain barrier (BBB)[3]
- Dosing: once weekly in MM (XVd), twice weekly in MM (Xd) and in DLBCL[1]
- Prioritization of clinical development in *TP53* wild type endometrial cancer and myelofibrosis

Both oral compounds have been shown to bind and inhibit XPO1.[1,2]

Eltanexor

Second novel XPO1 inhibitor

- **Investigational compound**
- Currently being investigated in relapsed/refractory (R/R) MDS[2]
- Compared to selinexor, lower BBB penetration observed in select animal models[3,†‡]
- Dosing: 5 times per week in Ph 1/2[4]
- Strong rationale for further development in both solid tumors and hematology

Focused on areas where a **highly potent** XPO1 impact is needed

Focused on areas where **continuous** XPO1 Inhibition needed

DLBCL, diffuse large B-cell lymphoma; MDS, myelodysplastic neoplasms; MM, multiple myeloma; XPO1, exportin 1.
†Assessed in three mammalian species (mouse, rat, and monkey); ‡Not a substrate of permeability glycoprotein (P-gp).
1. XPOVIO® (selinexor) [package insert]. Newton, MA: Karyopharm Therapeutics Inc; 2. Karyopharm Therapeutics. Drug pipeline. https://www.karyopharm.com/pipeline/. 3. Hing ZA, et al. Leukemia. 2016;30(12):2364-2372. doi:10.1038/leu.2016.136; 4. ClinicalTrials.gov. KCP-8602-801. https://clinicaltrials.gov/ct2/show/NCT02649790. Published August 15, 2022.

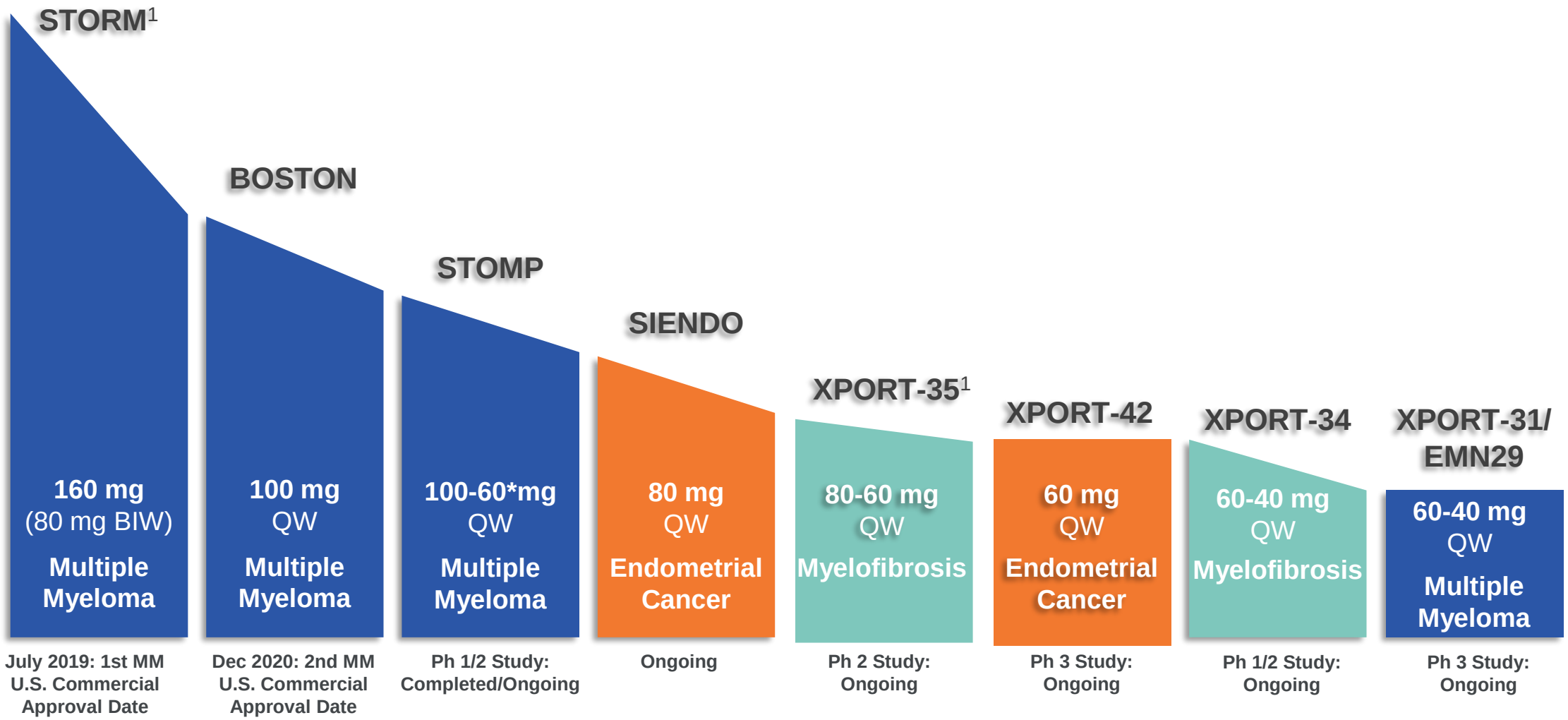
Progressing Focused Pipeline Across Cancers With High Unmet Needs

	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)	SIENDO				
	monotherapy	Endometrial cancer (maintenance; *TP53* wild-type)	XPORT-EC-042				
	w/pomalidomide + dexamethasone	Multiple myeloma (2L+)	XPORT-MM-031[2,3]				
	w/multiple approved agents	Multiple myeloma (relapsed/refractory)	STOMP[4]				
	monotherapy	Myelofibrosis (previously treated)	XPORT-MF-035				
	w/ruxolitinib	Myelofibrosis (treatment naïve)	XPORT-MF-034[5]				
ELTANEXOR	monotherapy	Myelodysplastic neoplasms (refractory)	KCP-8602-801				

hematologic cancer solid tumor cancer

1. XPORT-DLBCL-030 is a Phase 2/3. 2. Versus elotuzumab, pomalidomide, and dexamethasone.
3. EMN29 Study: Sponsored by European Myeloma Network. 4. STOMP has a total of 11 arms; enrollment complete in all arms
5. XPORT-MF-034 is a Phase 1/2.

Optimizing Selinexor Dose to Improve Patient Experience and Overall Benefit



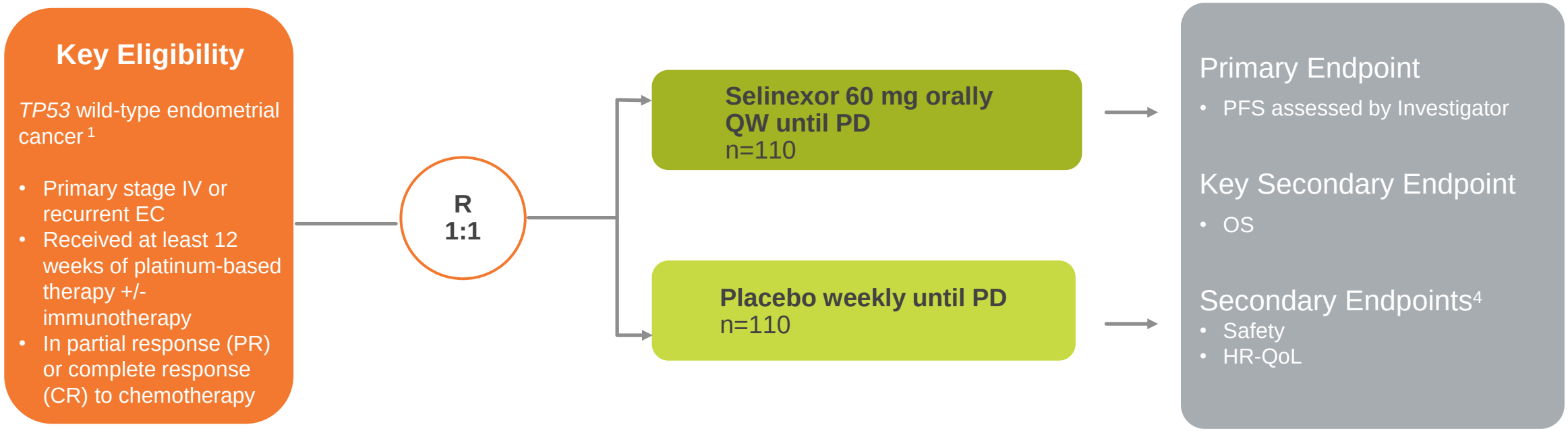
1. Following 80mg weekly * 2 cycles

ENDOMETRIAL CANCER

Initiated Global Phase 3 Pivotal Study; *TP53* Mutation Status Will Be Assessed by Companion Diagnostic Partner Foundation Medicine[1]

XPORT-EC-042 Global Phase 3, Randomized, Double-Blind, Trial of Selinexor as Maintenance Therapy for Patients with *TP53* Wild-type, Advanced or Recurrent Endometrial Cancer (N=220)

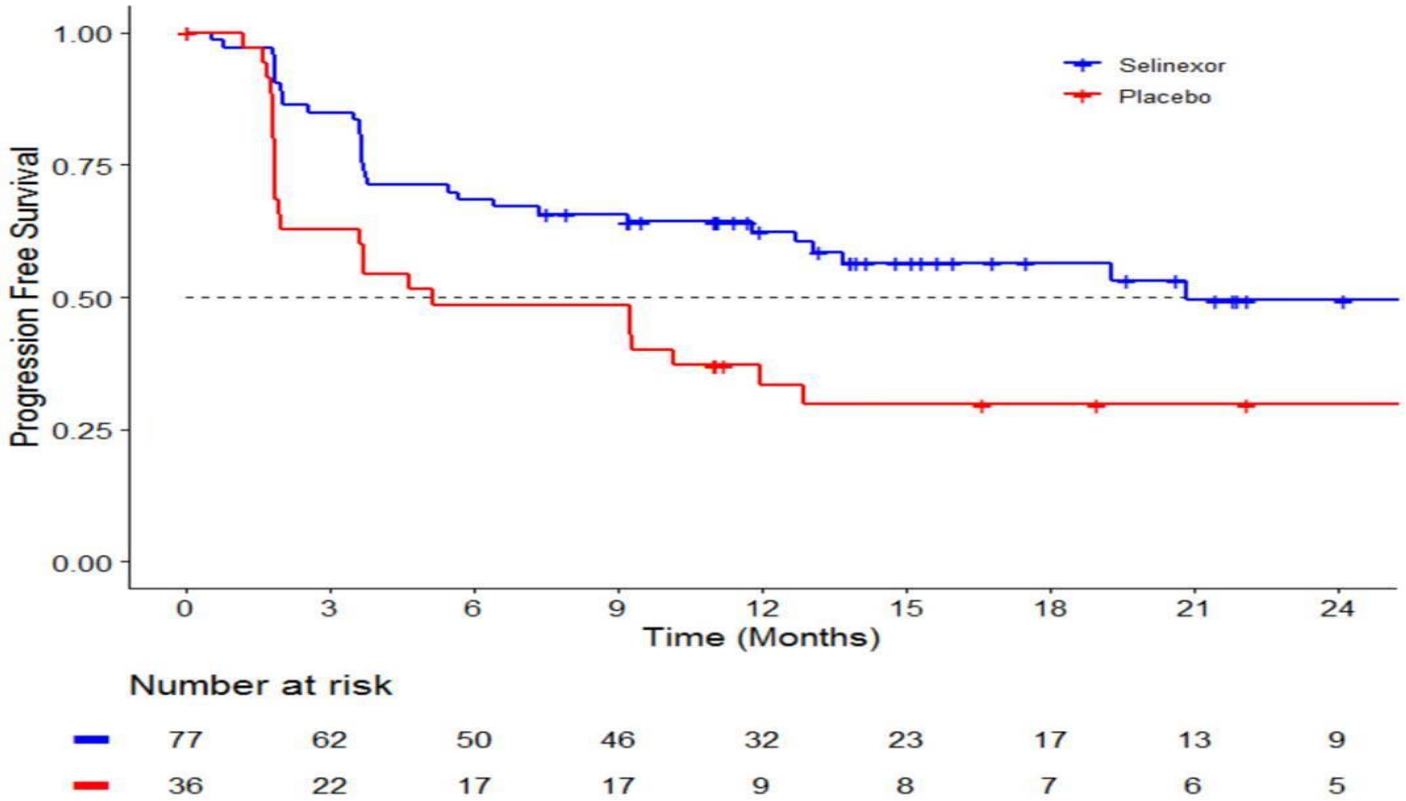
Study in Collaboration with ENGOT[2] and GOG[3]



- HR-QoL, health-related quality of life; OS, overall survival; PFS, progression-free survival; PD, progressive disease; QW, every week

1. Utilizing Foundation Medicine's tissue-based next generation sequencing test to identify *TP53* status
2. European Network for Gynaecological Oncological Trial groups; 3. Gynecologic Oncology (GOG) Foundation
4. Selected secondary endpoints

Updated Exploratory Subgroup Analysis from SIENDO Study in Patients with TP53 Wild Type Endometrial Cancer[1,2] Further Supports Rationale for Evaluating Selinexor as Maintenance Therapy



Median PFS

Selinexor (n=77): **20.8 months**

Placebo (n=36): **5.2 months**

- Most common adverse events (AE) were nausea, vomiting and diarrhea with no meaningful change in the AE profile since last data cut
- Most common Gr 3/4 AEs were neutropenia (18%), nausea (12%), thrombocytopenia (9%) and fatigue (8%). No Grade 5 events observed
- AEs were generally manageable with supportive care and dose modifications

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

1. TP53 WT/MUT status of patients under continued evaluation. 10% of patients on the selinexor arm and 7% of patients on the control arm have pending tumor TP53 status.

2. Preliminary data from pre-specified exploratory subgroup analysis as of the database cut date of November 30, 2022.

Potential for Significant Paradigm Shift for the Treatment of Women with Advanced or Recurrent *TP53* Wild-Type Endometrial Cancer

Phase 3 SIENDO study

Generated strong hypothesis in patients with *TP53* wild-type EC

Addressing a significant unmet need

Currently no FDA approved treatments in the maintenance setting

Significant market opportunity

~14K patients diagnosed with advanced and recurrent endometrial cancer in the U.S. each year[1]

~50% of these patients have *TP53* wild-type EC[2]

Supportive Mechanism of Action

Forced retention of p53 in the cell nucleus by inhibition of XPO1 allows p53 to carry out its tumor suppressor and other regulatory functions

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

1. Clarivate/DRG Endometrial Carcinoma Epidemiology Dashboard (2022 figures, pub 2020 2. “Mutated p53 portends improvement in outcomes when bevacizumab is combined with chemotherapy in advanced/recurrent endometrial cancer: An NRG Oncology study”, Leslie, Kimberly K. et al. Gynecologic Oncology, Volume 161, Issue 1, 113 – 121

MYELOFIBROSIS

Selinexor Has the Potential to Improve Patient Outcomes in Myelofibrosis

What is Myelofibrosis (MF)?

- Bone marrow cancer that disrupts body's normal production of blood cells
- Causes extensive scarring in bone marrow, leading to enlarged spleen, severe anemia and constitutional symptoms

Treatment Landscape and Unmet Need

- Ruxolitinib is the standard of care for newly diagnosed MF
  - Approximately **40% of patients respond**[2]
  - Responses last up to 4 years
  - Once patients stop responding, the median survival is **only ~14 months**[3] and 5-year survival is ~ 18%[4]
- **No other approved class of therapies** other than JAK inhibitors in the last ~ 10 years

There are ~17,000 Americans living with MF in the U.S. each year[1]

Selinexor has the potential to improve current standard of care (JAK inhibitors) in myelofibrosis

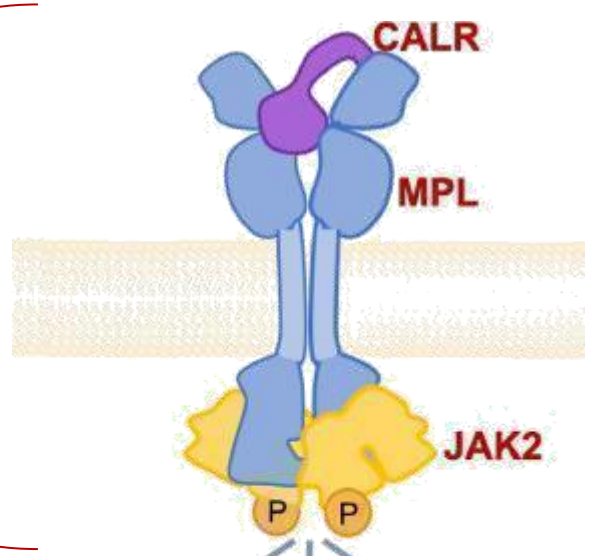
- ✓ Decrease size of spleen
- ✓ Improve constitutional symptoms
- ✓ Improve hemoglobin/anemia

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

1. Clarivate/DRG Epidemiology Data (2022 figures, pub 2019). **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. 4. Price et al. PLoS One. 2014;9(3):e902995 5. Internal assumption based on historical range of <5-30% in the literature; 30% SVR35 rate at EOC6 in patients treated with fedratinib and who received at least 3 months of prior ruxolitinib (JAKARTA-2 updated analysis, Harrison et al 2020. Am J Hematol)

Selinexor Can Inhibit Multiple Targets of the JAK/STAT Pathway, Enabling Independent Suppression of MF cells and Potentially Complementing the Function of JAKi's[1,2,3,4,5]

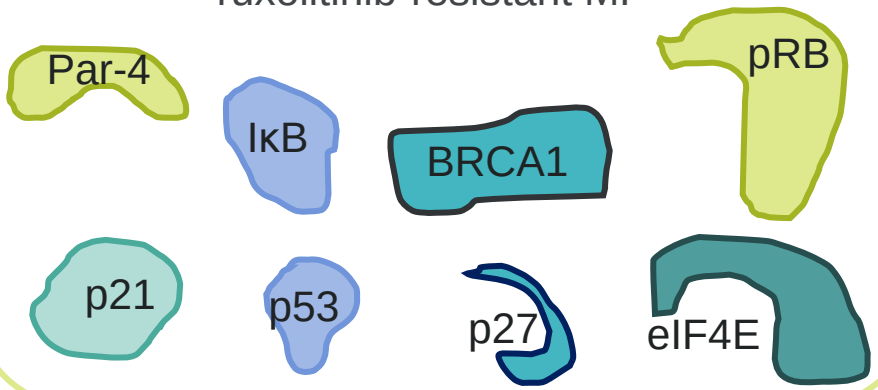
MF is driven by **upstream mutations** of *JAK2, CALR* or *MPL*



Downstream pathways are activated by the upstream mutations

The AKT, STAT and ERK pathways contain XPO1 cargo proteins

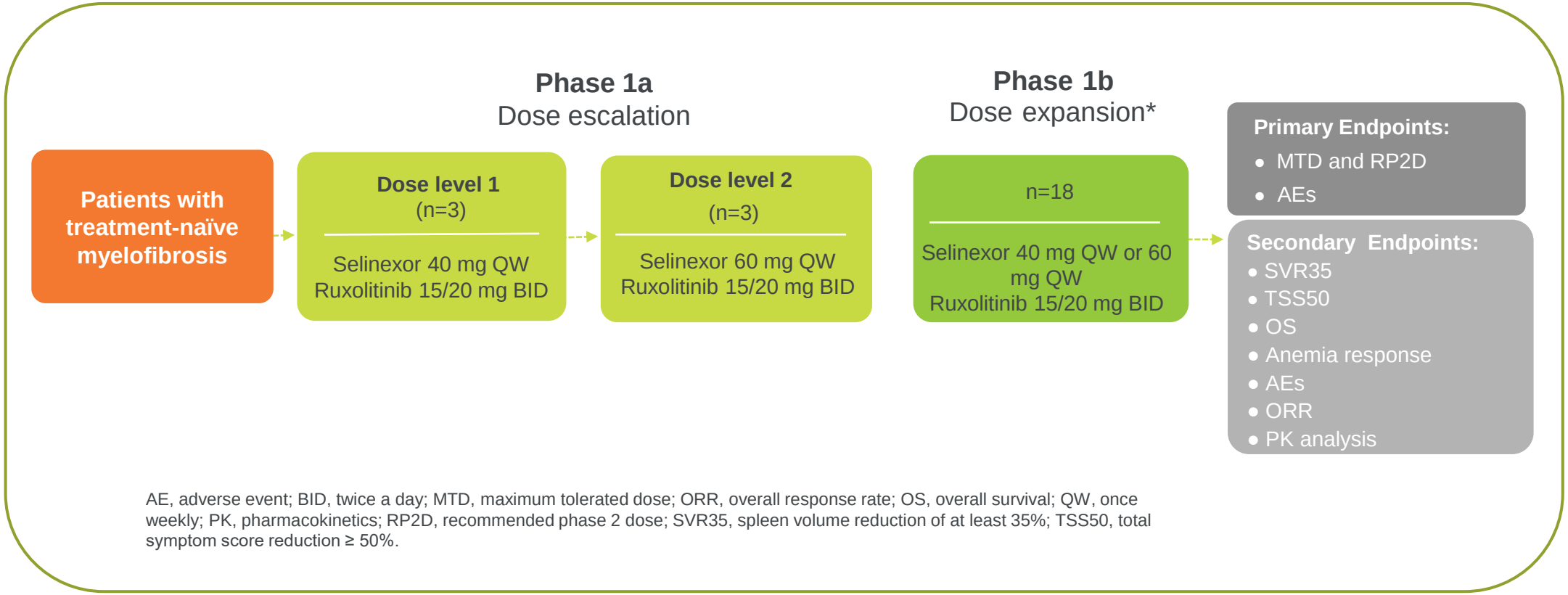
Additional XPO1 cargos proteins that regulate cell growth and survival may be important, especially in ruxolitinib-resistant MF



XPO1

1. Exp Hematol (105):2-9, Jan. 01, 2022
2. XPO1 Cargo references: https://doi.org/10.7554/eLife.11466; http://prodata.swmed.edu/LRNes/IndexFiles/namesGood.php
3. Zhong et al., Leukemia. 2014 May;28(5):1158-63 ; 4. Muqbil et al., Cancer Lett. 2016 Dec 28;383(2):309-317
5. Cheng et al., Mol Cancer Ther. 2014;13(3):675-686

Phase 1 Study (XPORT-MF-034[1]) Evaluating Selinexor in Combination with Ruxolitinib in Treatment-naïve Myelofibrosis



AE, adverse event; BID, twice a day; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; QW, once weekly; PK, pharmacokinetics; RP2D, recommended phase 2 dose; SVR35, spleen volume reduction of at least 35%; TSS50, total symptom score reduction ≥ 50%.

* Enrollment completed; 24 patients had been assigned to either a 40 mg or 60 mg once weekly dose of selinexor, in combination with ruxolitinib 15/20 mg BID (twice daily)

1. NCT04562389

Encouraging Preliminary Week 24 Data[1,2] From Evaluable Patients Across Key Efficacy Endpoints from Phase 1 Study (XPORT-MF-034) at ASH 2022

SPLEEN RESPONSES (SVR35)

92% of evaluable patients[3] (11/12) achieved SVR35 at week 24

100% of evaluable patients[3] (12/12) achieved an SVR35 at anytime

REDUCTION IN TOTAL SYMPTOM SCORES (TSS50)

67% of evaluable patients[3] (4/6) achieved TSS50 at week 24

POSITIVE IMPACTS ON HEMOGLOBIN LEVELS

57% of patients[4] (13/23) maintained stable hemoglobin (± 2g/dL) or improved hemoglobin level (>2g/dL increase) at last follow up

SAFETY AND TOLERABILITY

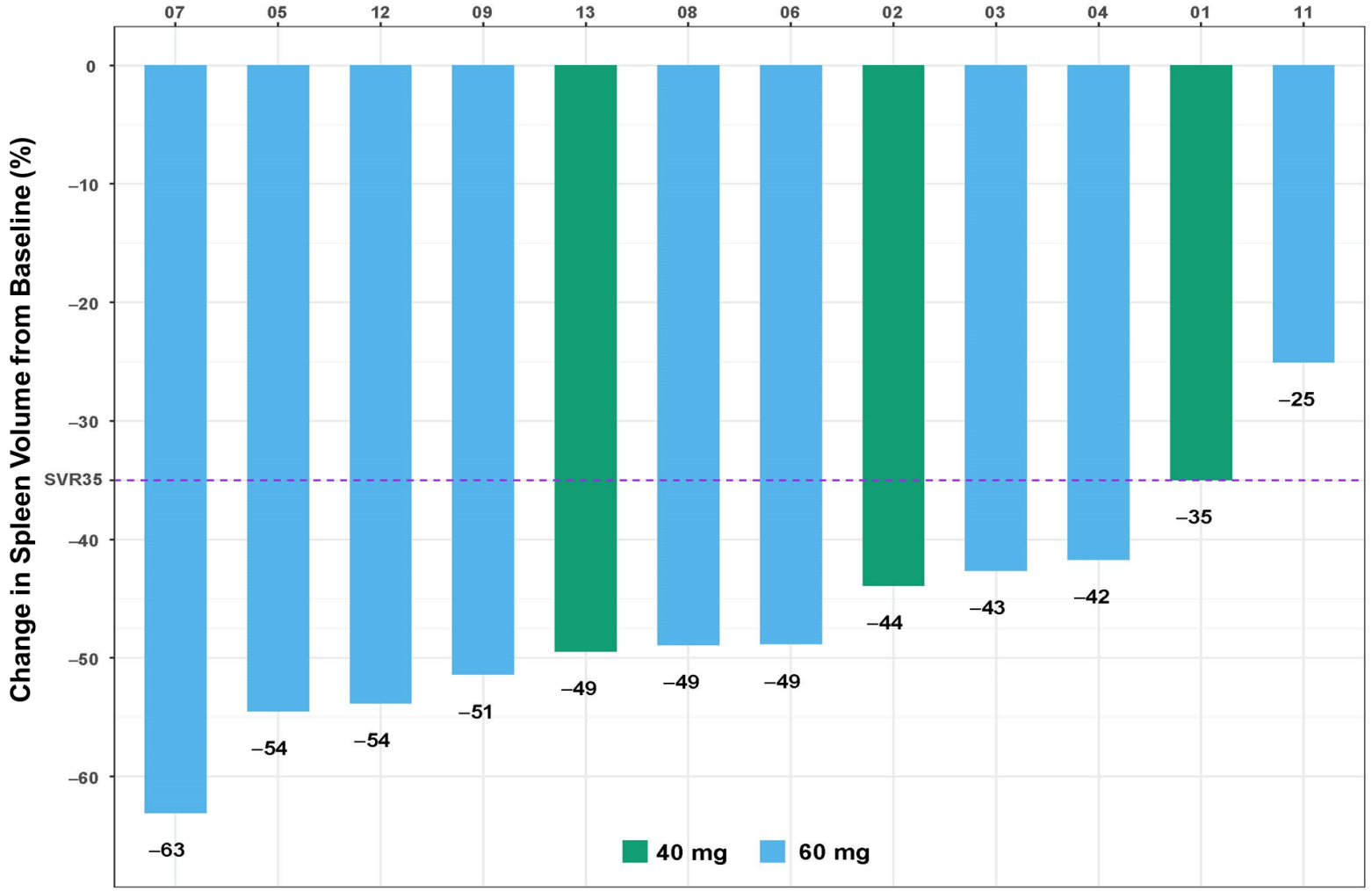
Most common TEAEs[5] (n=24):
Nausea, anemia and fatigue (majority Grade 1-2)
Most common Grade ≥ 3 TEAEs:
Anemia (38%) and thrombocytopenia (21%)

Preliminary TSS50 analysis only includes patients who filled out all their symptom evaluation forms (n=6); other 6 patients who were evaluable for SVR analysis remained on therapy. Based on symptom scores collected from patients' medical charts, an updated TSS50 analysis will be presented at a future medical congress.

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

1. Data cut from October 2022 2. Presented at ASH 2022 3. Efficacy evaluable at 24W: Patients who had a baseline efficacy evaluation and an on-treatment evaluation at 24 weeks 4. Data from 23 transfusion independent patients who had at least 8 weeks of treatment; one patient was transfusion dependent at baseline and not included in the denominator 5. Treatment emergent adverse events

At Week 24, All Evaluable Patients had Reduction in Spleen Volume Relative to Baseline



One patient received 20 mg for 3 cycles then 60 mg for 3 cycles and was included in the 40mg group for the purpose of this analysis

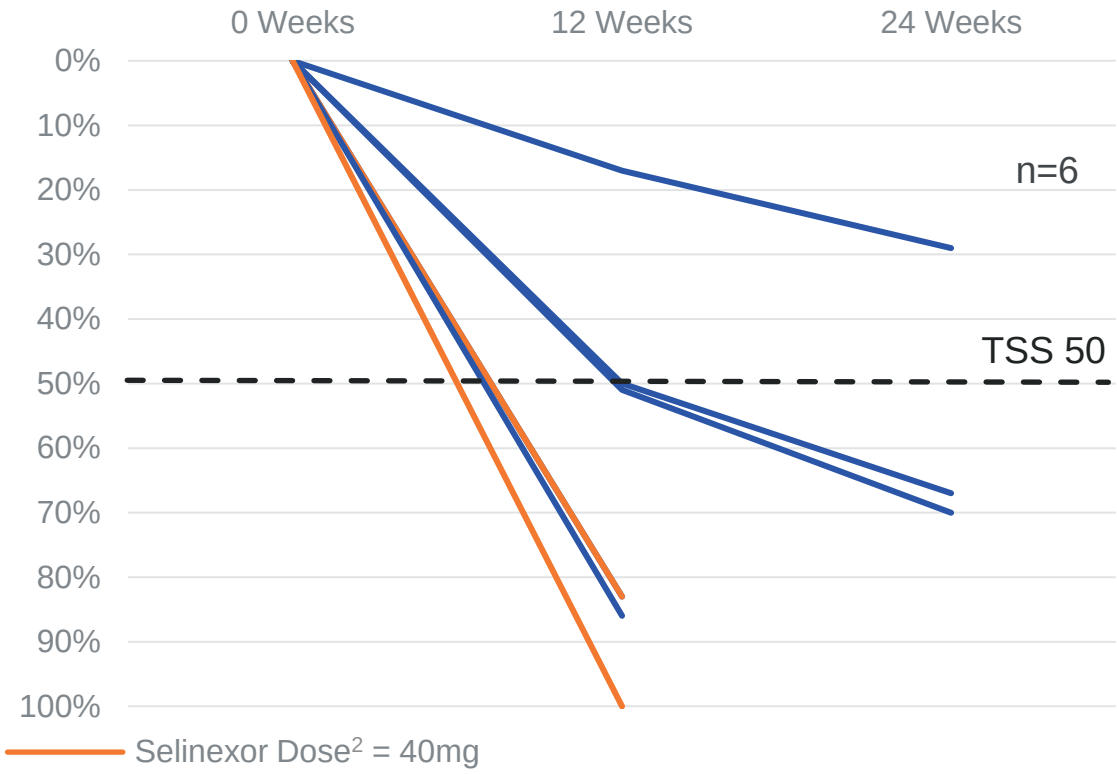
The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the U.S. FDA or any other regulatory authority.

Inhibition of XPO1 Is Potentially a Fundamental Mechanism in Myelofibrosis

Encouraging Evidence of Selinexor Activity in Retrospective, Exploratory Analysis from Phase 1 Selinexor+Ruxolitinib Study (034) in Patients with Treatment Naïve Myelofibrosis Whose Ruxolitinib Dose Was Reduced to 5mg at Cycle 1 or 2

Spleen Volume Reduction

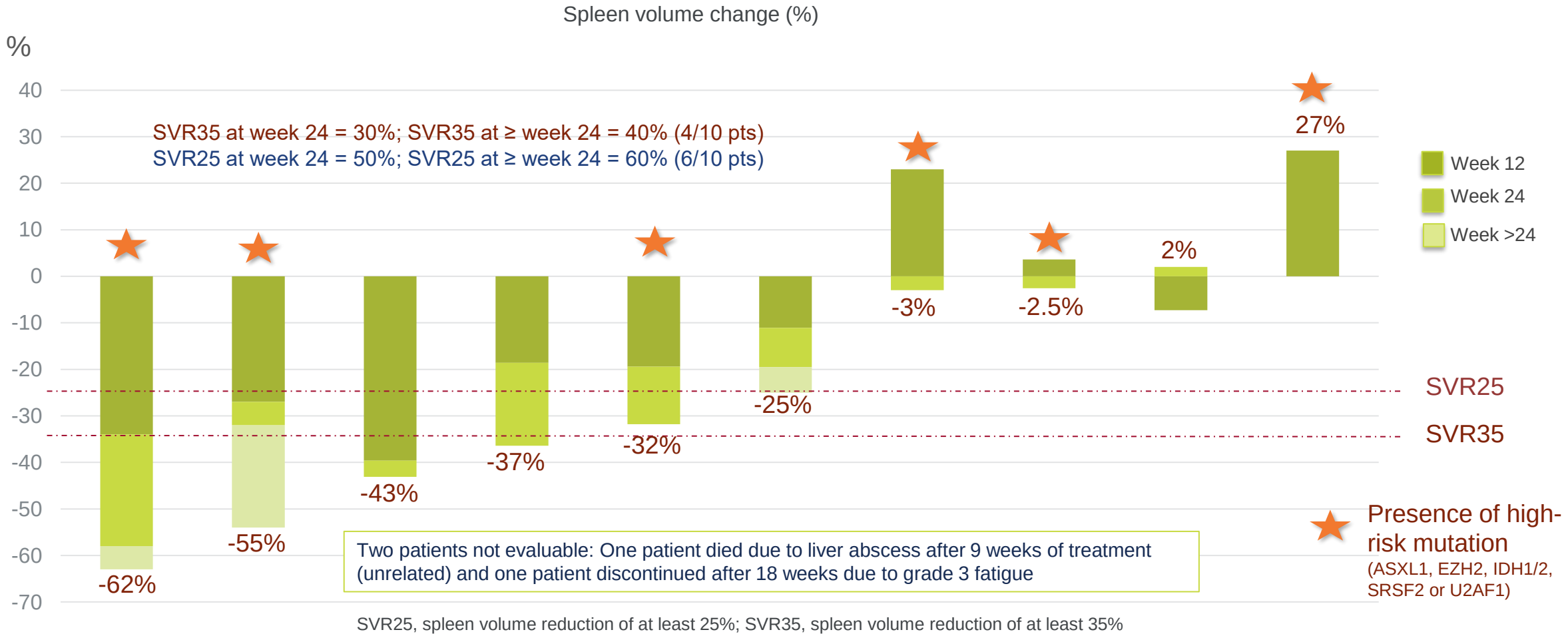
Total Symptom Score Reduction[1]



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

1. One patient with missing TSS 50 score
2. Assigned selinexor starting dose

Single-Agent Selinexor Resulted in Sustained Spleen Responses in Refractory MF Patients in Phase 2 ESSENTIAL Study[1,2]



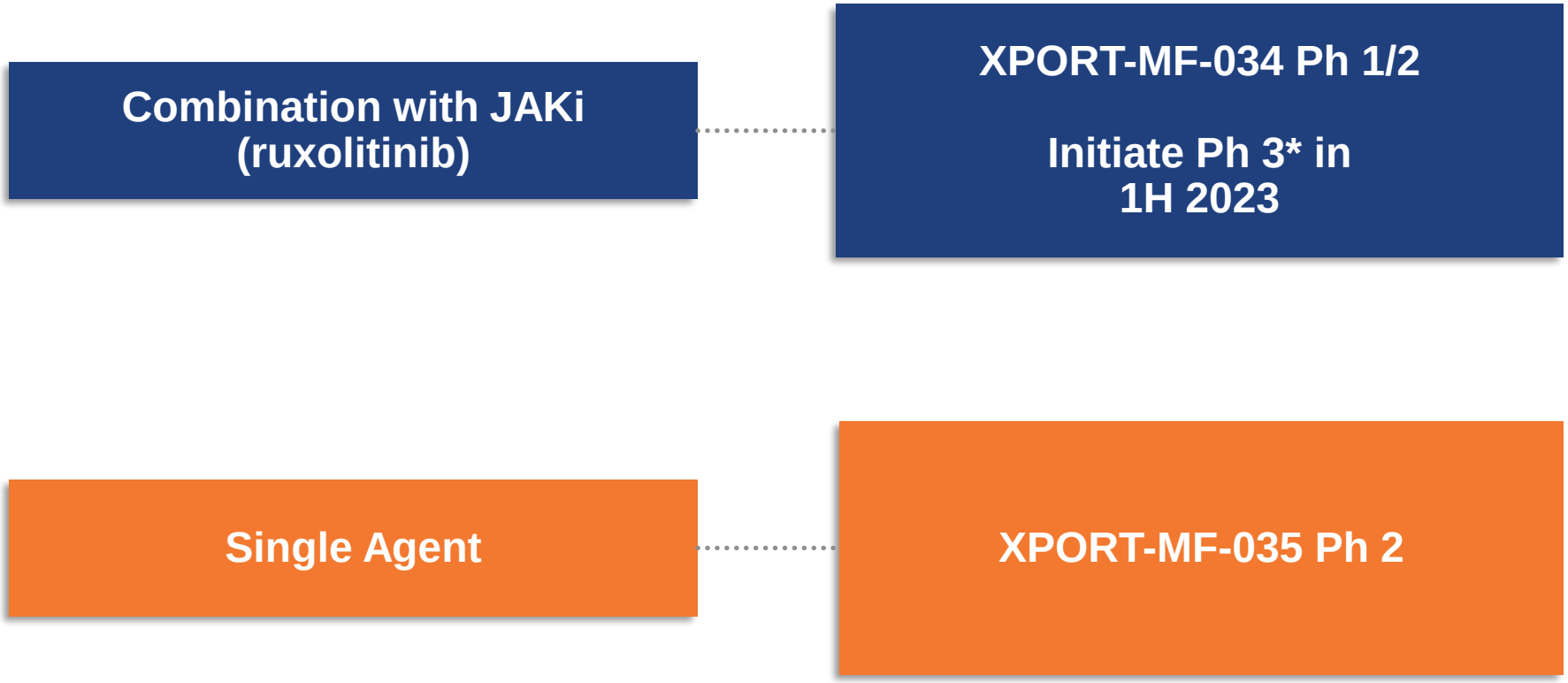
SVR25, spleen volume reduction of at least 25%; SVR35, spleen volume reduction of at least 35%

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

1. Tantravahi, et al. ASH 202 2. Data cut-off as of November 2021
2. Preliminary data cut from investigator sponsored open label trial

Initial Data Suggest That Selinexor May Have the Greatest Benefit in Treatment Naïve Myelofibrosis

Evaluating evolving data to determine optimal and efficient developmental pathway that may include monotherapy and innovative combinations



* Pending regulatory feedback

MYELODYSPLASTIC NEOPLASMS

Eltanexor Has the Potential to Improve Survival in High Risk Relapsed/Refractory Myelodysplastic Neoplasms

What is Myelodysplastic Neoplasms (MDS)?

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

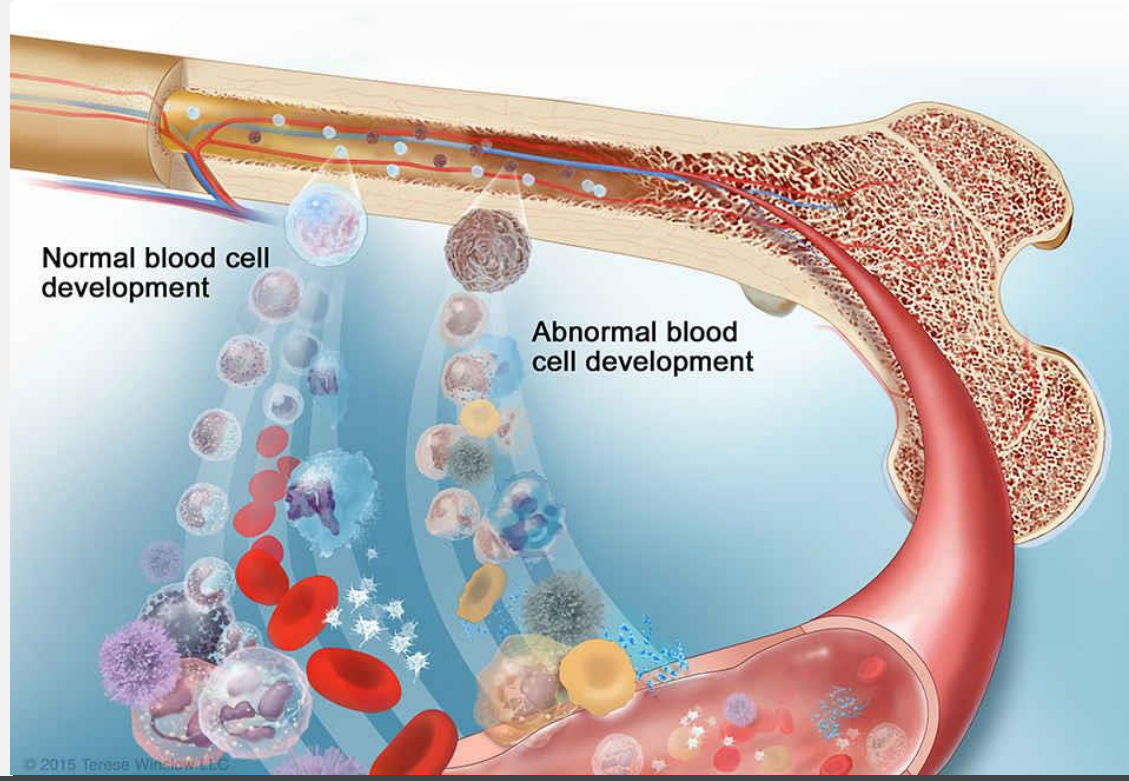
Treatment Landscape

- 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

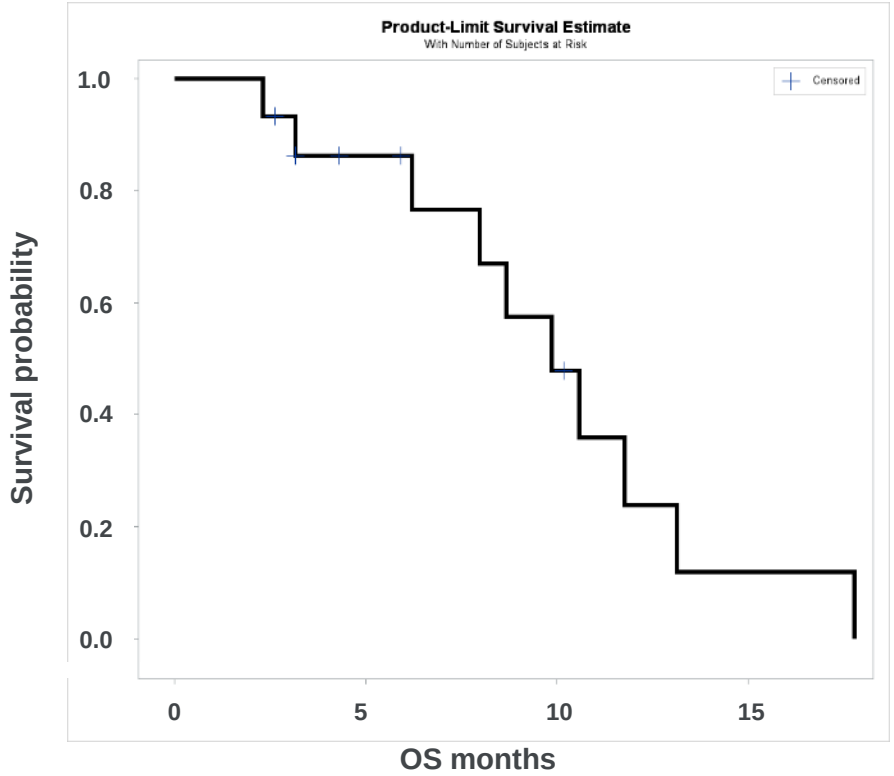
- Prognosis in relapsed/refractory disease is poor, with an **expected survival of 4-6 months**[3,4]
- No currently approved therapies for HMA-refractory disease

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



1. Clarivate/DRG Myelodysplastic-Syndrome-Epidemiology-Dashboard (2022 figures, pub 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.

Single-agent Eltanexor Demonstrated Promising Activity Among Patients With HMA Refractory MDS in a Phase 1 Study[1]



- Historical overall survival (OS) of 4-6 months in patients with relapsed/refractory MDS[3]
- **Single-agent eltanexor demonstrated median OS of 9.9 months**[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.

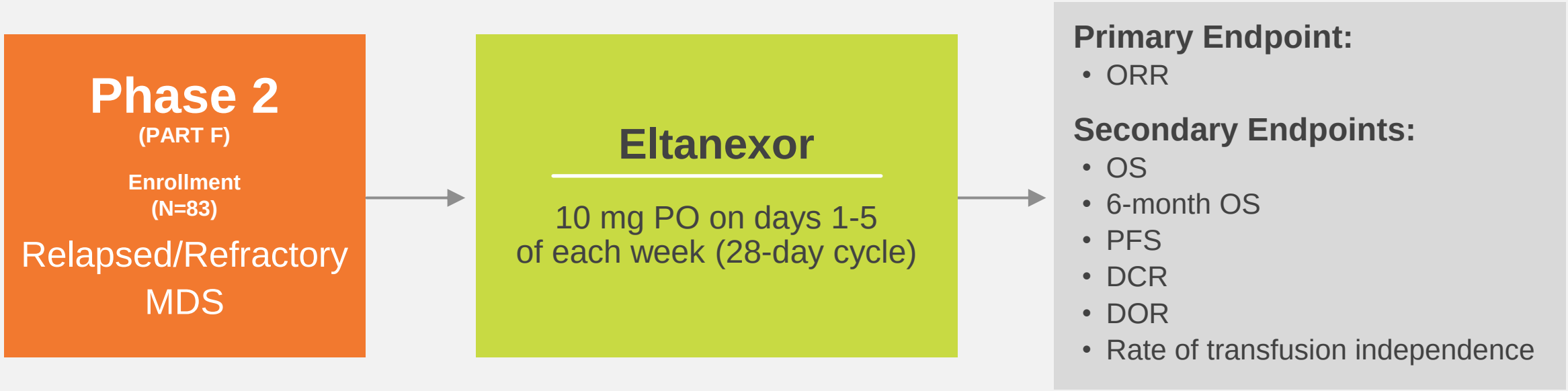
No severe bleeding events — which is the corresponding clinical outcome for thrombocytopenia (as you have febrile neutropenia and sepsis as the clinical outcome for neutropenia.)

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.

The safety and efficacy of eltanexor in MDS has not been established and has not been approved by the U.S. FDA or any other regulatory authority.

1. Lee, Sangmin, et al. ASH 2021.
2. n=15; 10 patients on 20mg eltanexor and 5 patients on 10mg eltanexor
3. Clavio M, Cancer. 2021;127(12):2015-24.

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



Data from planned interim analysis (n=30) expected in Q1 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.

FINANCIAL HIGHLIGHTS AND MILESTONES

Financial Snapshot

$279M

**CASH, EQUIVALENTS & INVESTMENTS*
31-Dec-2022[1]**

Late 2025

**EXPECTED CASH
RUNWAY**

~$157.7M

**NET TOTAL REVENUE
2022[1]**

~$120.4M

**NET PRODUCT REVENUE
2022[1]**

* Includes restricted cash

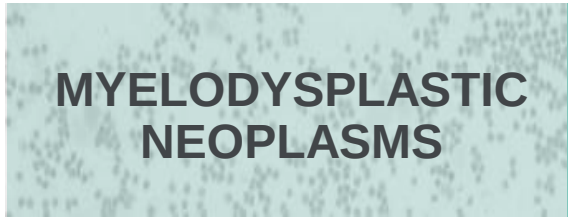
1. Preliminary unaudited estimates

Upcoming Milestones for 2023 and Beyond

- Leverage commercial capabilities and grow US XPOVIO sales (2023)
- Continuation of global launches (2023)
- Report top-line results from pivotal Phase 3 study evaluating SPd[1] (2H 2024)

- Present updated results from SIENDO study at a medical conference (2023)
- Report top-line results from pivotal Phase 3 study EC-042 in *TP53* wild-type EC (2H 2024)

- Report updated results in Phase 1 trial of selinexor+ ruxolitinib in treatment naïve MF (1H 2023)
- Initiate pivotal Ph 3 selinexor +ruxolitinib study in treatment naïve MF (1H 2023)
- Define optimal mono and innovative combo development plan (1H 2023)



- Report interim Phase 2 eltanexor data in relapsed/refractory MDS (1Q 2023) and top-line data (2024)

1. Selinexor + pomalidomide + dexamethasone

Karyopharm® Therapeutics

Thank you!