Karyopharm® Therapeutics

First Quarter 2023 Financial Results & Business Update

May 4, 2023

On Today's Call

- **Welcome**
  Elhan Webb, CFA, *Senior Vice President, Investor Relations*
- **Overview**
  Richard Paulson, *President and Chief Executive Officer*
- **Commercial Highlights**
  Sohanya Cheng, *Chief Commercial Officer*
- **Pipeline Update**
  Dr. Reshma Rangwala, *Chief Medical Officer*
- **Financial Summary and Guidance**
  Michael Mason, *Chief Financial Officer*
- **Closing Remarks**
  Richard Paulson, *President and Chief Executive Officer*
- **Q&A Session**

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 2023 total revenue, 2023 U.S. net product revenue and 2023 non-GAAP R&D and SG&A expenses; 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 Annual Report on Form 10-K for the year ended December 31, 2022, which was filed with the Securities and Exchange Commission (SEC) on February 17, 2023, 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 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.

Richard Paulson
Chief Executive Officer

OVERVIEW

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
- Total revenues expected to be $145-160M in 2023
- 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* wild-type EC[4]

Strong Financial Position

- Cash position of $262M[5] at end of Q1 2023
- Cash runway until late 2025

1. DLBCL approved in the U.S. under accelerated approval pathway; 2. MF: myelofibrosis;3. selinexor + pomalidomide + dexamethasone; 4. Endometrial cancer; 5. Cash, cash equivalents restricted cash and investments

First Quarter 2023 and Recent Highlights

Expanding on Multiple Myeloma Foundation Globally

1Q 2023 U.S. XPOVIO Net Product Revenue: $28.3M consistent with 1Q 2022

- Continued YoY growth in total demand and community setting in a highly competitive market
- Net product revenue in 1Q 2023 adversely impacted by:
  - Increased use of the KaryForward patient assistance program (PAP)
  - Higher gross to net (GTN)

Continued Global Expansion of Selinexor

- Amended Menarini license agreement to add selected Middle East and Africa regions
- Received UK full marketing authorization for NEXPOVIO® in 2L+ MM

Continue to Advance Clinical Pipeline in Core Indications

Myelofibrosis (Selinexor)

- Strong efficacy and manageable tolerability with 60mg dose; Phase 1 data presented at AACR
  - 79% SVR35 and 58% TSS50 at Week 24 (ITT)
- Planning to initiate pivotal Phase 3 study in 1H 2023

MDS (Eltanexor)

- Encouraging interim efficacy data from Phase 2 study in hard-to-treat higher risk R/R MDS patient population
  - 8.7 months median overall survival (mOS)

*MDS: Myelodysplastic Neoplasms; AACR: American Association for Cancer Research; ITT: Intent to Treat; SVR35: ≥35% reduction in spleen volume; TSS50: ≥50% reduction in total symptom score; R/R: Relapsed and refractory

Sohanya Cheng
Chief Commercial Officer

COMMERCIAL HIGHLIGHTS

XPOVIO Update: 1Q 2023

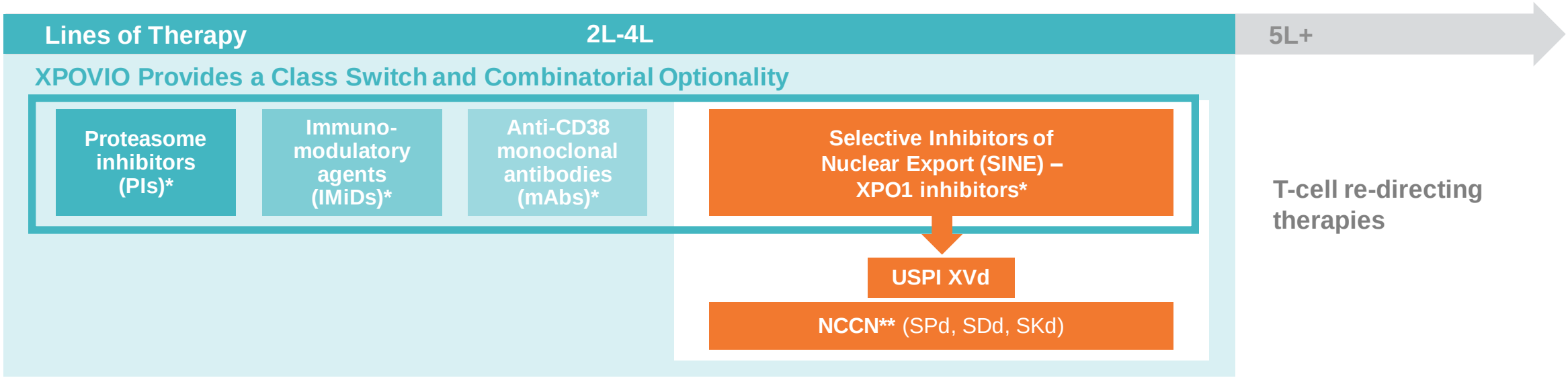
YoY Growth in Total Demand[1] of 6%; Net Revenue Adversely Impacted by Increased Utilization of PAP and Higher GTN

1Q 2023 Highlights (YoY)

- Total demand growth[1] of 6% year over year driven by the community setting which contributed ~ 70% of revenues in Q1 2023
- Sustained business in Academics despite increased competition from T-cell therapies
- Net XPOVIO revenues adversely impacted by:
  - Significant increase in utilization of PAP (free drug) due to recent lack of funding to foundations for multiple myeloma patients
  - Higher GTN driven by increased Medicare & Medicaid rebates, and 340B discounts
- Approaching 60% of new XPOVIO patients in 2-4L[2]
- Improvement in tolerability perception in 2-4L per intent to prescribe data[3]
- Net U.S. XPOVIO revenue guidance revised to $110-$125M due to expected significant increase in PAP utilization
  - In 2024, significantly fewer patients expected to utilize PAP for co-pay assistance due to IRA[4] related re-design of Part D benefits

1. Includes patient assistant program and commercial demand; 2. Based on Komodo claims data analysis, accessed in April 2023; 3. Based on internal KPTI Myeloma HCP ATU (healthcare professionals' awareness, trial and usage); 4. Inflation Reduction Act

Clear Positioning within Community & Academic Settings with XPOVIO Serving an Unmet Need as a Novel Class of Therapy and Convenient Oral Treatment for 2L–4L R/R MM Post Anti-CD38



Community setting (~70% of MM patients)

1. Broad patient population in 2-4L post-anti CD38 and patients exposed to or refractory to PIs/IMIds, in need of a novel class of therapy that is convenient, manageable and effective

Academic setting (~30% of MM patients)

2. Patients that need T-cell sparing treatment pre or post T-cell therapies
3. Patients that cannot access or do not choose a T-cell therapy e.g. elderly/frail/rural

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

Reshma Rangwala, MD, PhD
Chief Medical Officer

PIPELINE UPDATE

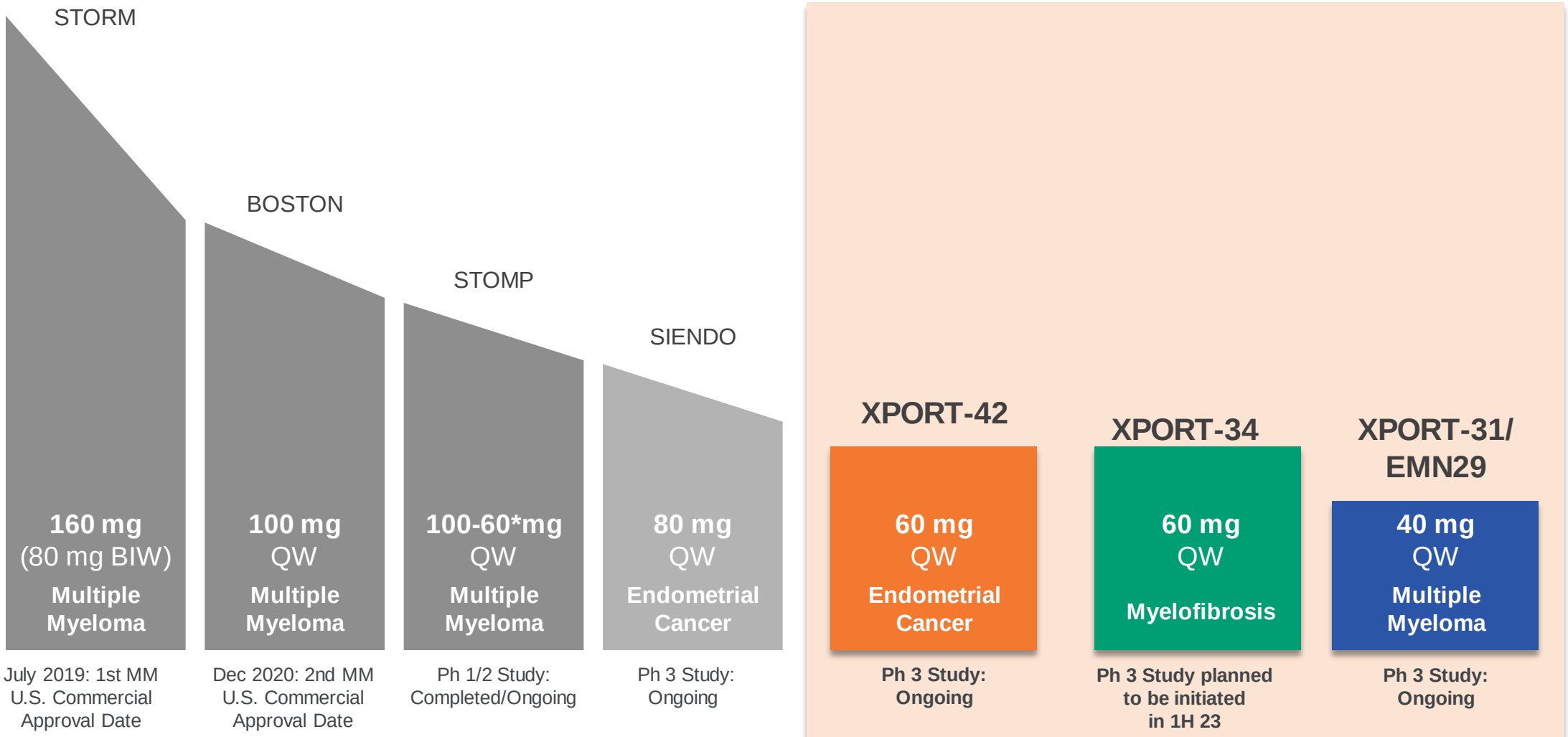
Progressing Focused Pipeline Across Cancers With High Unmet Needs

	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+; post-anti CD38)	XPORT-MM-031[2,3]				
	w/multiple approved agents	Multiple myeloma (relapsed/refractory)	STOMP[4]				
	w/ruxolitinib	Myelofibrosis (treatment naïve)	XPORT-MF-034[5]				
ELTANEXOR	monotherapy	Myelodysplastic neoplasms (relapsed/refractory)	KPT-8602-801				

hematologic cancer solid tumor cancer

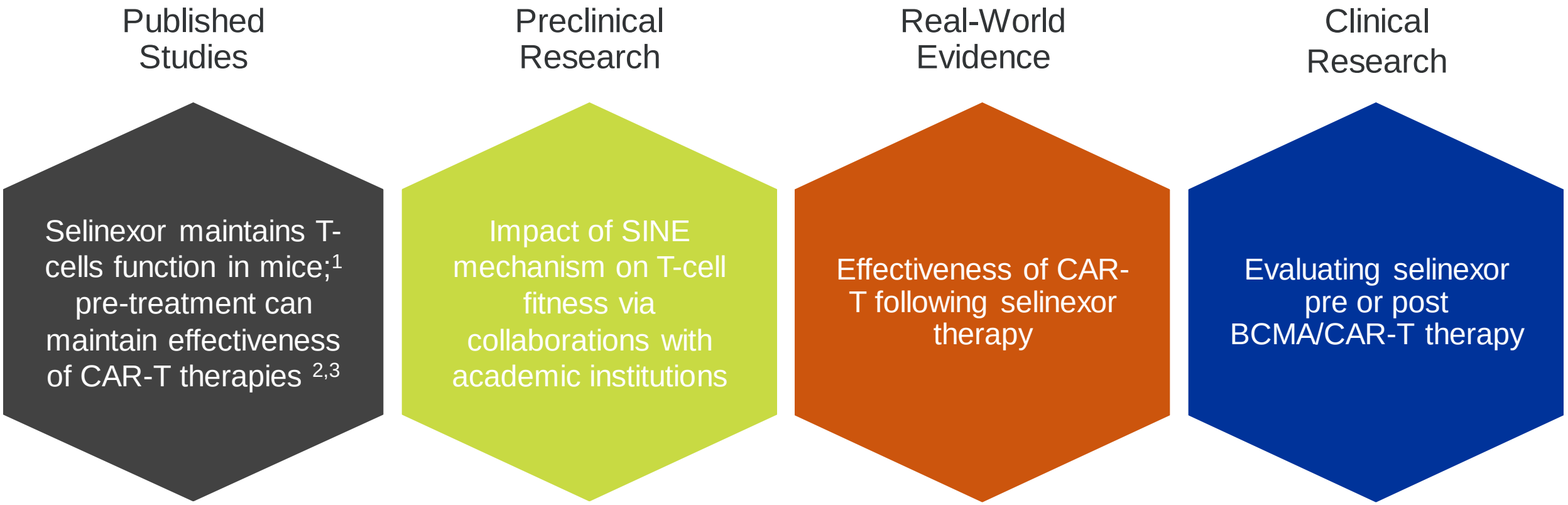
1. XPORT-DLBCL-030 is a Phase 2/3. 2. Versus elotuzumab, pomalidomide, and dexamethasone. 3. EMN29 Study: Sponsored by European Myeloma Network. 4. STOMP has a total of 11 arms, including an arm in newly diagnosed MM; enrollment complete in all arms 5. XPORT-MF-034 is a Phase 1/2. Phase 3 planned to be initiated in 1H 2023

Optimizing Selinexor Dose to Improve Patient Experience and Overall Benefit



MULTIPLE MYELOMA

Generating Evidence on the Role and Effectiveness of Selinexor pre and post T-cell Mediated Therapies



1. Tyler PM et al., Mol Cancer Ther. 2017 Mar;16(3):428-439.
2. Wang S et al., Oncol Rep. 2021 Aug;46(2):170.
3. Stadel R et al., Blood (2022) 140(Supplement 1): 7413–7414, ASH Annual Meeting 2022

MYELOFIBROSIS

XPO1, a Novel and Potentially Fundamental Mechanism in MF, has the Opportunity to Transform 1L Treatment Paradigm

Treatment Landscape and Unmet Need

~20,000 living with MF in the U.S and ~ 17,000 in EU[1]

No other approved class of therapy other than JAK inhibitors; ruxolitinib generates > $2 billion revenues annually

Significant unmet need in 1L treatment with current standard of care, ruxolitinib:

- <50% of patients achieve SVR35[2] and TSS50[2]
- ~25% of male patients achieve an SVR35 at week 24[3]
- ~23% patients who start on ruxolitinib 15 mg BID achieve an SVR35 at week 24[4]
  - ~70% patients in the real world start on ruxolitinib 15 mg BID or less[5]

Leading causes of ruxolitinib discontinuation are thrombocytopenia and anemia, which is associated with shorter survival[6,7,8]

Selinexor has the Potential to Shift the Treatment Paradigm*

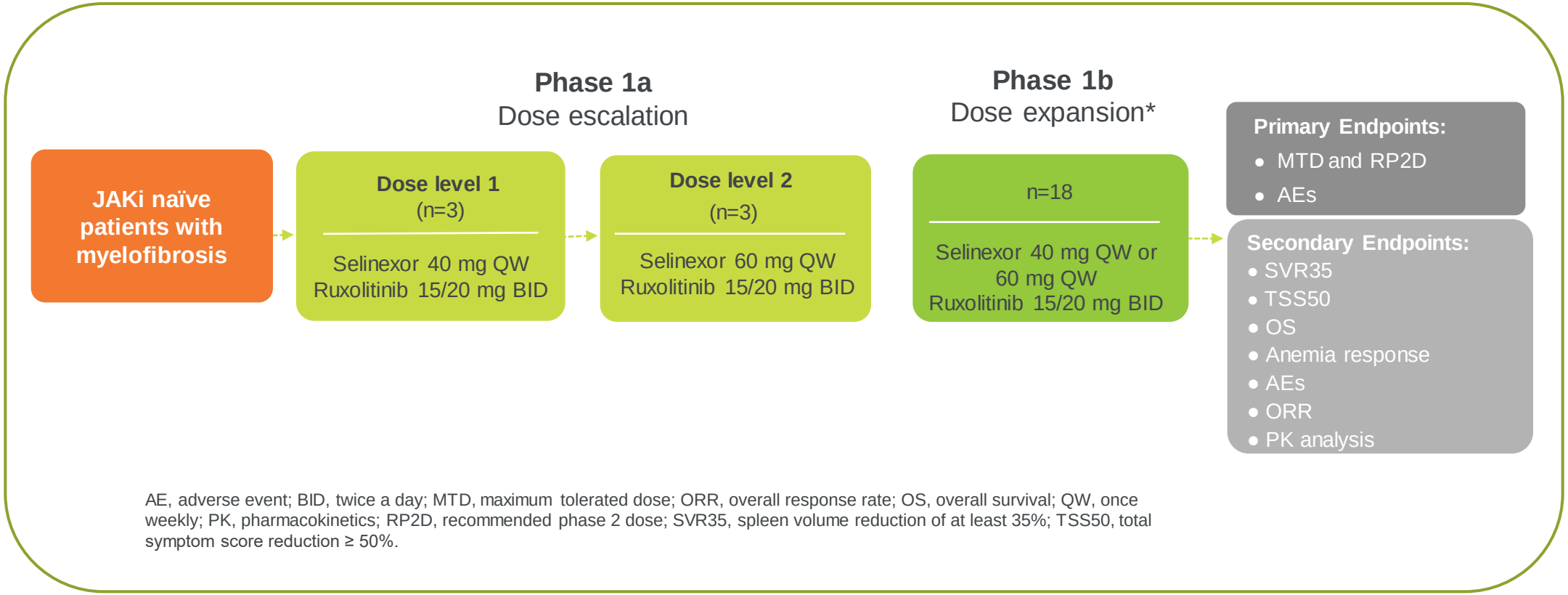
- **XPO1 inhibition is a novel and potentially fundamental mechanism in MF**
- **Synergism with ruxolitinib observed in preclinical data**[9]
- **Rapid, deep and sustained spleen response, and robust symptom improvement across all subgroups**
- **Generally tolerable and manageable side effect profile enabling sustained therapy**
- **Disease modifying with rapid normalization of platelets and maintenance of hemoglobin levels**

* Based on selinexor+ruxolitinib Ph 1 results using data cut as of February 24, 2023

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. Mehta el.al. Leuk Lyphoma 2014 Mar ;55(3):595-600 and US Census data; Clarivate/DRG Epidemiology Data (2022 figures, pub 2019). 2. Verstovsek S, et al. N Engl J Med. 2012;366(9)799-907 3. FDA multidisciplinary review of Jakafi in 2011; document no: 202192Orig1s000 4."Baseline factors associated with response to ruxolitinib: An independent study on 408 patients with myelofibrosis", Palandri et. al Oncotarget. 2017;8(45): 79073–79086.5. Passamonti et al. Future Oncology. 2022;18(18) 2217-2231. 6. Sastow D, et al. Clin Lymphoma, Myeloma Leuk. 2022;22(7):e507–20. 7. Masarova, et al. Eur J Haematol. 2018;100(3):257-263. 8. Al-Ali, et al. Hematologica. 2016;101(9):1065. 9. Yan et al. Clin Cancer Res. 2019;25(7): 2323–2335

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 (n=10) or 60 mg (n=14) once weekly dose of selinexor, in combination with ruxolitinib 15/20 mg BID (twice daily)

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. NCT04562389

Rapid, Deep and Sustained SVR35 and TSS50 Achieved with Selinexor 60 mg

		SVR35		TSS50	
Population	**Timepoint**	**Selinexor 40 mg +ruxolitinib n (%)**	**Selinexor 60 mg +ruxolitinib n (%)**	**Selinexor 40 mg +ruxolitinib n (%)**	**Selinexor 60 mg +ruxolitinib n (%)**
Efficacy Evaluable	Week 12	3/10 (30.0)	10/12[i] (83.3)	6/9[iii] (66.7)	8/10[v] (80.0)
	Week 24	**4/8[ii] (50.0)**	**11/12 (91.7)**	**4/7[iv] (57.1)**	**7/9[vi] (77.8)**
Intent-to-Treat	Week 12	3/10 (30.0)	10/14 (71.4)	6/10 (60.0)	8/12 (66.7)
	Week 24	**4/10 (40.0)**	**11/14 (78.6)**	**4/10 (40.0)**	**7/12 (58.3)**

[i] Two patients discontinued prior to Week 24.
[ii] One patient discontinued prior to week 12; one patient with missing data at week 12 who subsequently discontinued prior to week 24.
[iii] One patient with missing data
[iv] Two patients discontinued prior to Week 24 and one had missing data.
[v] One patient discontinued prior to week 12; one patient with missing data at week 12, who subsequently discontinued prior to week 24.
[vi] Two patients discontinued prior to Week 24 and one had missing data.

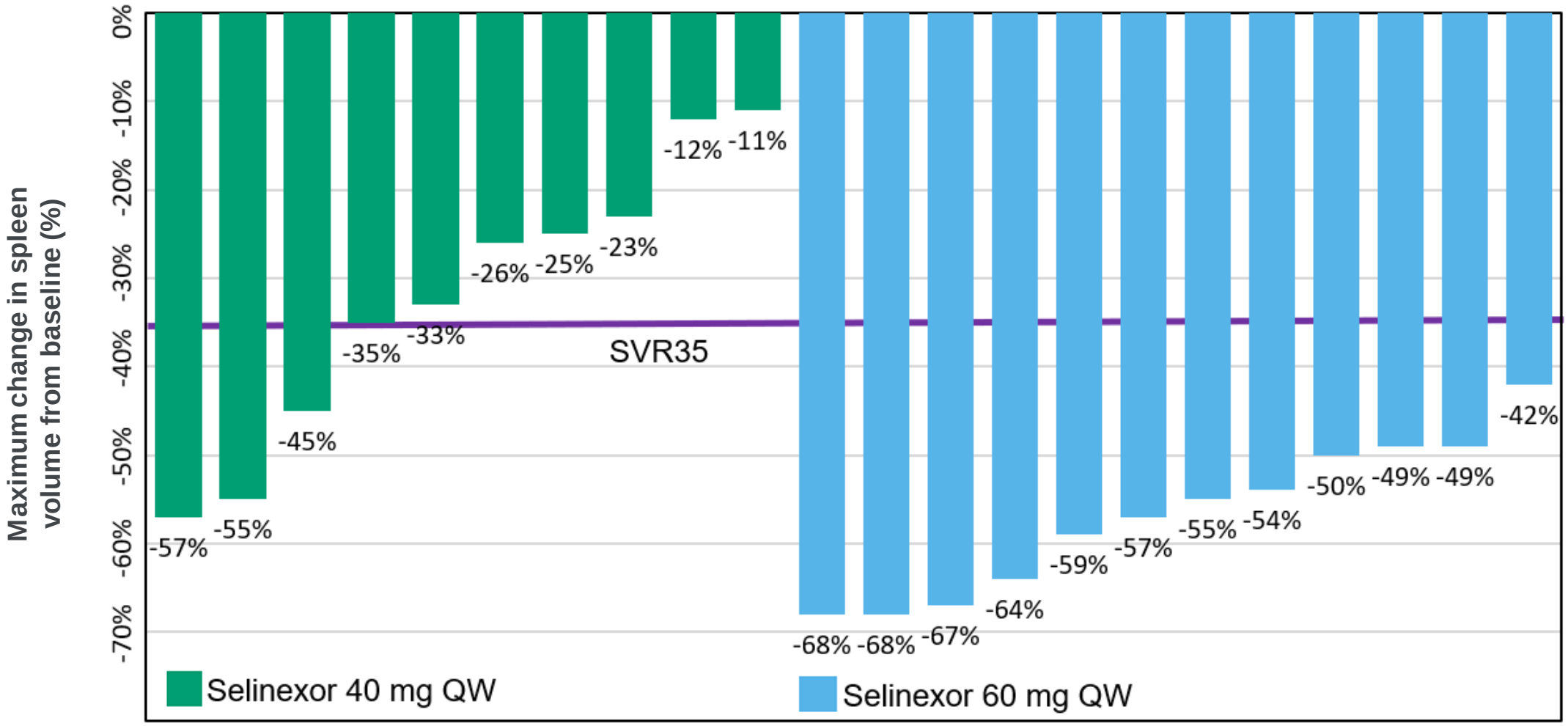
SVR35, spleen reduction volume ≥35%

TSS50, total symptom score ≥ 50. Note: Median TSS was calculated for each cycle, regardless of number of scores collected per cycle

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.

Data cut February 24, 2023

All Evaluable Patients* Treated with Selinexor 60 mg Achieved an SVR35 at Anytime



* n=12; one patient discontinued prior to week 12; one patient with missing data at week 12 who subsequently discontinued prior to week 24.

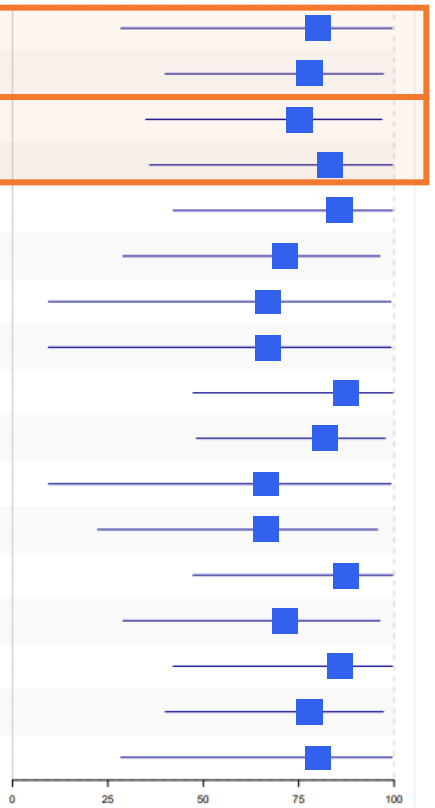
The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the U.S. FDA or any other regulatory authority.

Data cut February 24, 2023

Selinexor + Ruxolitinib Treatment Effective for All JAKi Naïve Patients, Across All Subgroups Including Males and Patients Who Started at Low Ruxolitinib Doses

SVR35* (selinexor 60 mg)

Subgroup	Total	Responder	Response Rate
Gender: Female	5	4	80 (28.4, 99.5)
Gender: Male	9	7	77.8 (40, 97.2)
Rux: 15/20 BID	8	6	75 (34.9, 96.8)
Rux: 5/10 BID	6	5	83.3 (35.9, 99.6)
MF type: Primary	7	6	85.7 (42.1, 99.6)
MF type: Secondary	7	5	71.4 (29, 96.3)
DIPSS: High Risk	3	2	66.7 (9.4, 99.2)
DIPSS: Intermediate 1	3	2	66.7 (9.4, 99.2)
DIPSS: Intermediate 2	8	7	87.5 (47.3, 99.7)
JAK2 Mutation: Mutated	11	9	81.8 (48.2, 97.7)
JAK2 Mutation: Not mutated	3	2	66.7 (9.4, 99.2)
Baseline Platelet: Platelet <= 200K	6	4	66.7 (22.3, 95.7)
Baseline Platelet: Platelet > 200K	8	7	87.5 (47.3, 99.7)
Baseline Spleen Volume: < 1800	7	5	71.4 (29, 96.3)
Baseline Spleen Volume: >= 1800	7	6	85.7 (42.1, 99.6)
Baseline TSS: < 20	9	7	77.8 (40, 97.2)
Baseline TSS: >= 20	5	4	80 (28.4, 99.5)



* Intent To Treat (ITT) population

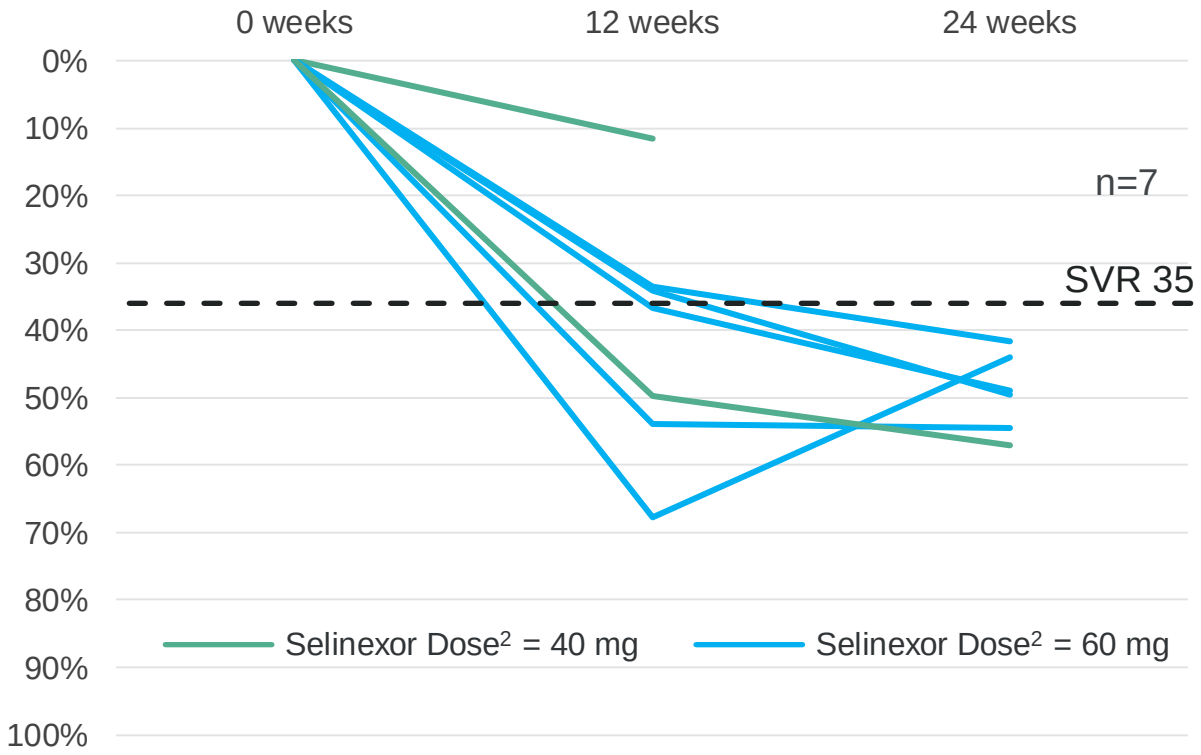
The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the U.S. FDA or any other regulatory authority.

Data cut February 24, 2023

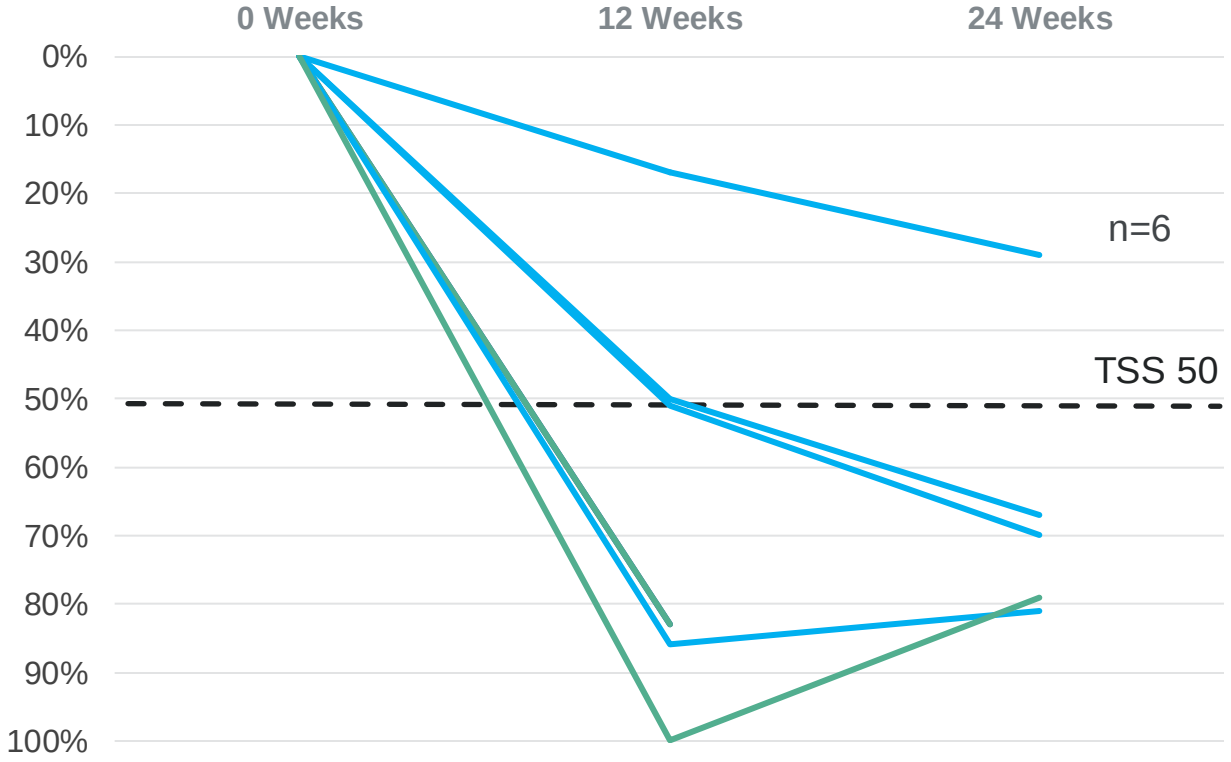
Efficacy with Selinexor in Combination with Suboptimal Dose of Ruxolitinib (5 mg) Further Supports XPO1 as a Fundamental MoA in MF

Retrospective, Exploratory Analysis from Phase 1 Selinexor + Ruxolitinib Study (034)

Spleen Volume Reduction



Total Symptom Score Reduction[1]



"Based on limited clinical data, long-term maintenance at a 5 mg twice daily dose has not shown responses and continued use at this dose should be limited to patients in whom the benefits outweigh the potential risks." Jakafi (ruxolitinib) U.S. Package Insert, January 2023

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 TSS50 score
2. Assigned selinexor starting dose

Data cut February 24, 2023

Generally Tolerable and Manageable Side Effect Profile

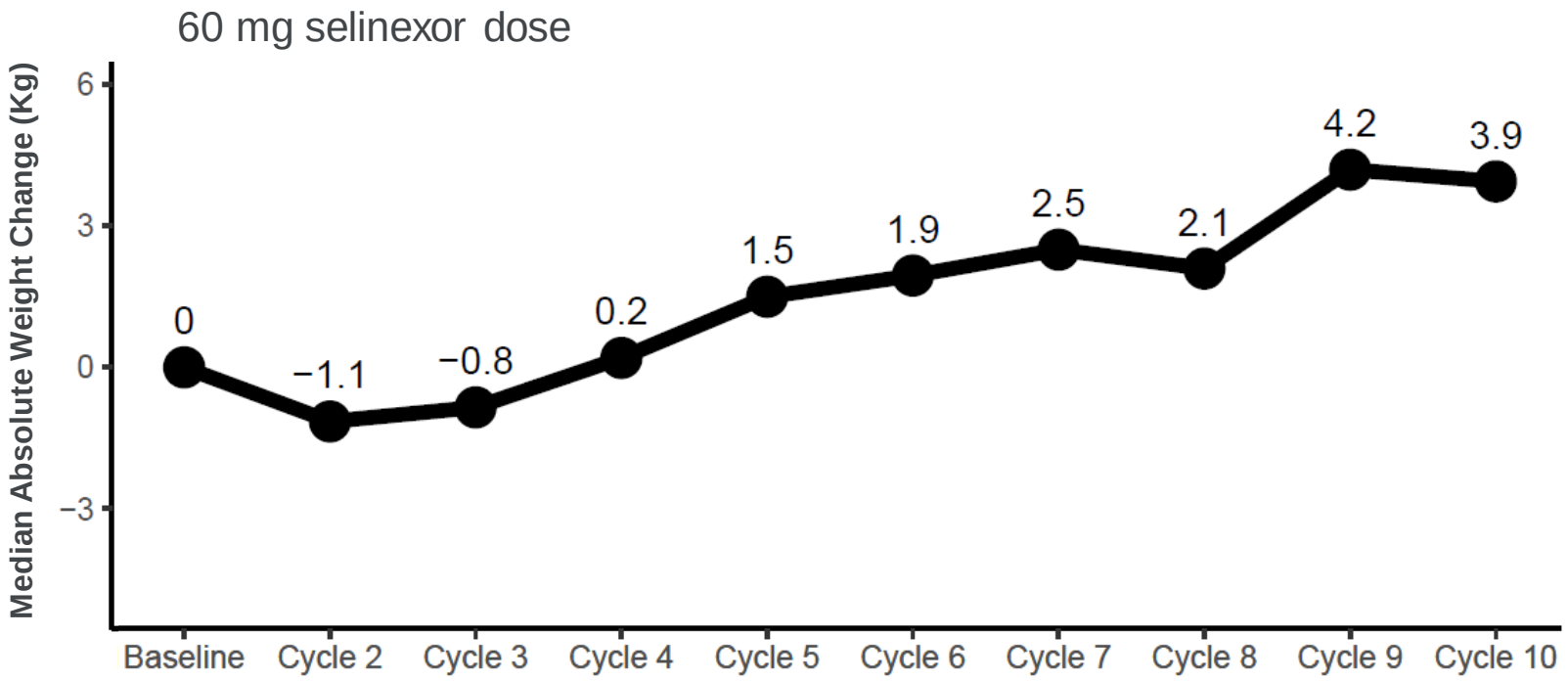
Treatment Emergent Adverse Events	Selinexor 40mg + ruxolitinib (N=10)	Selinexor 60mg + ruxolitinib (N=14)
Any grade, >25% overall		
Nausea	7 (70.0)	11 (78.6)
Anemia	4 (40.0)	9 (64.3)
Fatigue	6 (60.0)	8 (57.1)
Thrombocytopenia	4 (40.0)	9 (64.3)
Constipation	2 (20.0)	7 (50.0)
Headache	4 (40.0)	5 (35.7)
Vomiting	2 (20.0)	7 (50.0)
Neutropenia	2 (20.0)	5 (35.7)
Dyspnea	2 (20.0)	5 (35.7)
Decreased appetite	2 (20.0)	4 (28.6)
Dysgeusia	2 (20.0)	4 (28.6)
Hyponatremia	1 (10.0)	5 (35.7)
Grade 3+, >5% overall		
Anemia	3 (30.0)	6 (42.9)
Thrombocytopenia	1 (10.0)	4 (28.6)
Neutropenia	2 (20.0)	1 (7.1)
Atrial fibrillation	2 (20.0)	1 (7.1)
Back pain	0	2 (14.3)
Treatment-related adverse events leading to treatment discontinuations		
Thrombocytopenia, Grade 3	0	1 (7.1)
Peripheral Neuropathy	0	1 (7.1)

- Treatment related discontinuations due to cytopenias were low (n=1)
- 75% of nausea events were Grade 1
  - One patient experienced Grade 3 nausea (no antiemetic prophylaxis)
- In the 60mg cohort, 64% of patients received one prophylactic antiemetic
  - Amongst the subgroup who received one prophylactic antiemetic, 67% of patients experienced nausea (Grade 1 only) compared to 100% of those who did not receive prophylactic antiemetics (Grades 1-3)

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.

Data cut February 24, 2023

Patients Experienced Improved Weight with Selinexor in Combination with Ruxolitinib

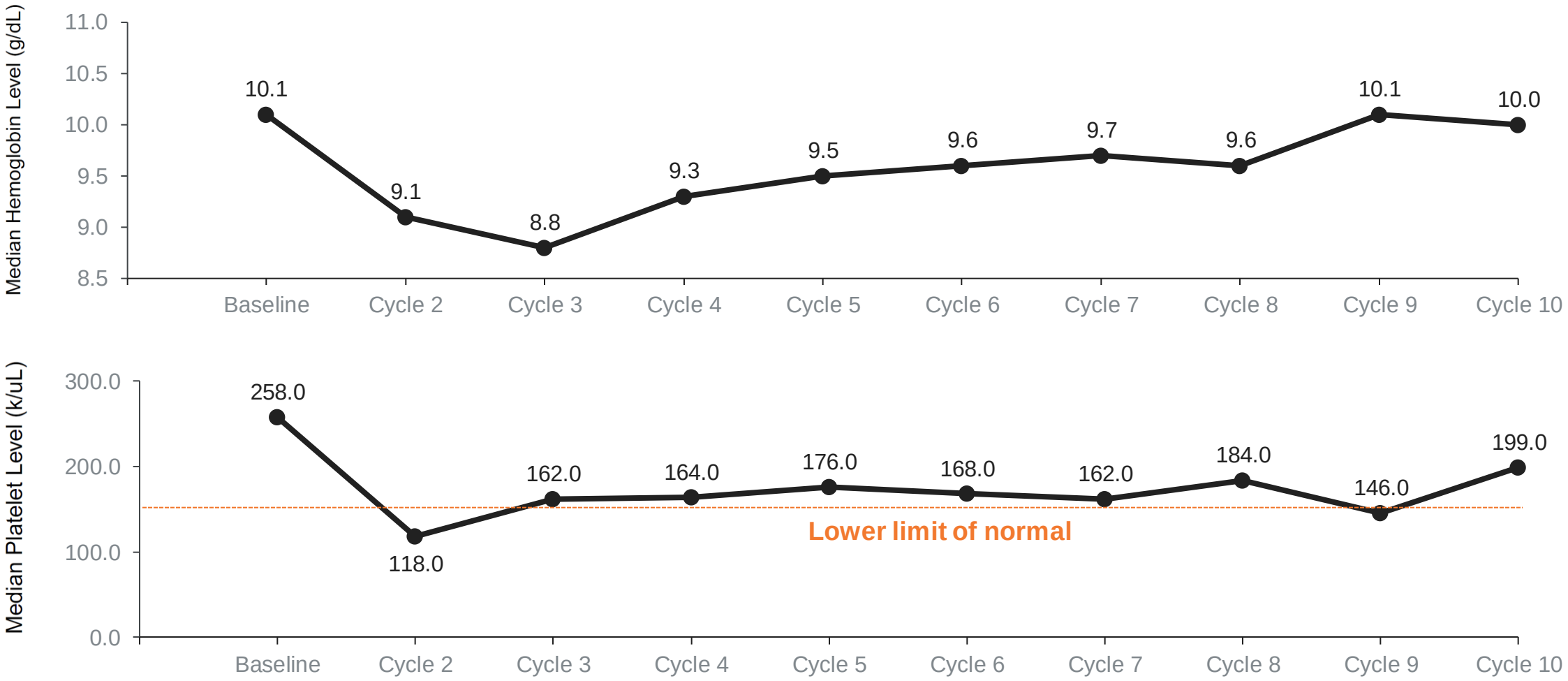


- Patients' median weight increase at Week 24 was 3 kg in the 40mg cohort and 2.5 kg in the 60mg cohort
- Despite nausea and vomiting incidence, patients generally did not experience weight loss

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.

Data cut February 24, 2023

Potential Disease Modification With Normalization of Platelets and Restoration of Hemoglobin Levels



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.

Data cut February 24, 2023

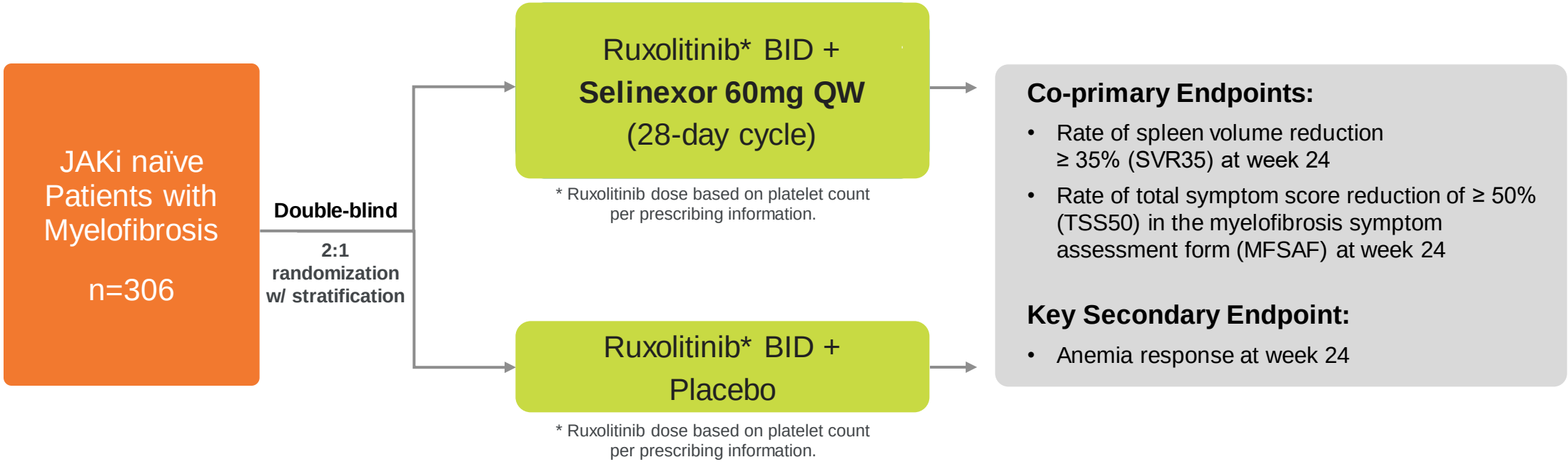
Selinexor 60 mg in Combination with Ruxolitinib Has the Potential to Transform 1L Myelofibrosis Treatment Paradigms

- **Selinexor 40 mg and 60 mg dose levels generally well tolerated and manageable allowing most patients to remain on therapy (up to 68 weeks as of data cutoff)**
  - **Only two treatment related discontinuations observed: Peripheral neuropathy (n=1) and thrombocytopenia (n=1)**
- **Rapid, deep, and sustained spleen response and robust symptom improvement in patients treated with 60 mg selinexor: SVR35: 78.6% ITT (91.7%, EE) and TSS50: 58.3% ITT (77.8%, EE) at week 24**
  - **SVR35: Observed in 100% of evaluable patients at anytime; rates consistent by gender and ruxolitinib starting dose**
  - **SVR35 and TSS50 observed amongst patients treated with suboptimal doses of ruxolitinib 5 mg**
- **Disease modification observed as evidenced by rapid normalization of platelets and restoration of hemoglobin levels**
- **Efficacy and safety data support 60 mg dose of selinexor as the recommended dose for Phase 3 study in combination with ruxolitinib**

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.

Data cut February 24, 2023

XPORT-MF-034 Phase 3 Design*



Randomization stratified by:

- Dynamic International Prognostic Scoring System (DIPSS) risk category intermediate -1 vs. intermediate -2 or high-risk
- Spleen volume <1800 cm^3 vs. >1800 cm^3 by MRI/CT scan
- Baseline platelet counts 100-200 x 10^9/ L vs. >200 x 10^9/L

*Planning to be initiated in 1H 2023

MYELODYSPLASTIC NEOPLASMS

Eltanexor Has the Potential to Improve Survival in Higher Risk Relapsed/Refractory Myelodysplastic Neoplasms (MDS)

What are Myelodysplastic Neoplasms (MDS)?

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

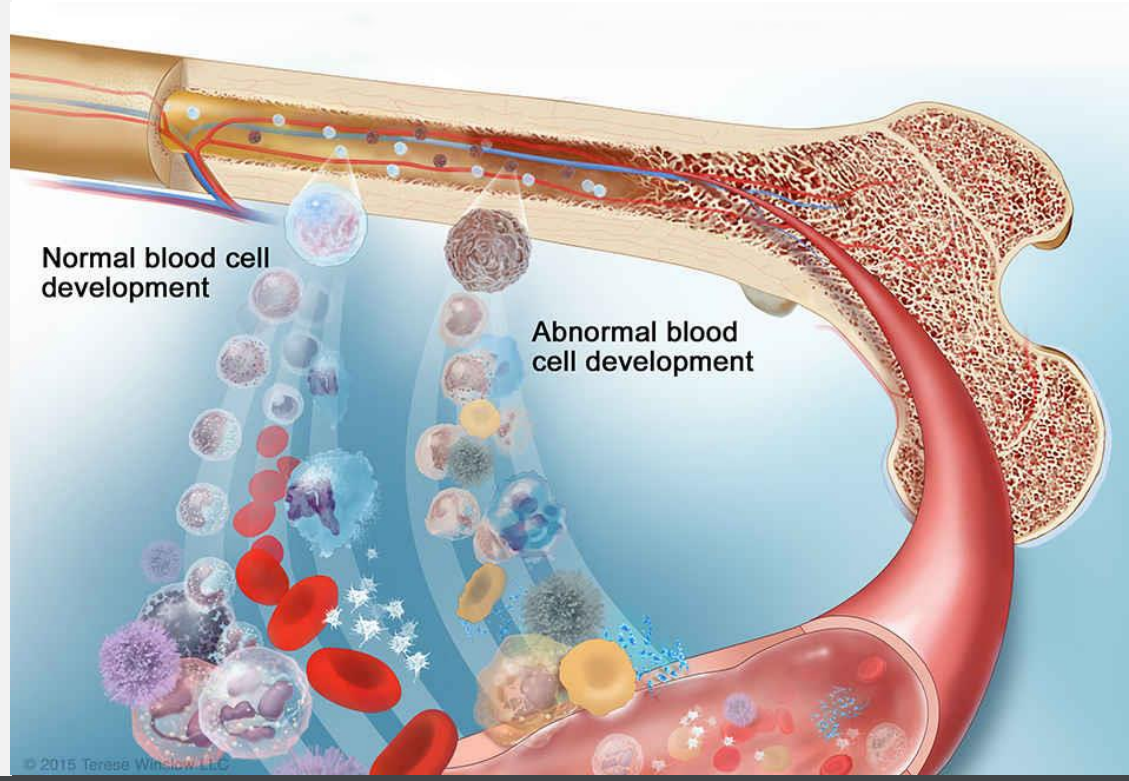
Treatment Landscape

- Hypomethylating agents (HMA) are the current standard of care (SoC) for patients with newly diagnosed, higher-risk MDS
- ~50% of 1L treated patients do not respond; for patients who achieve a response, responses last < 2 years[2]

Opportunity and Unmet Need

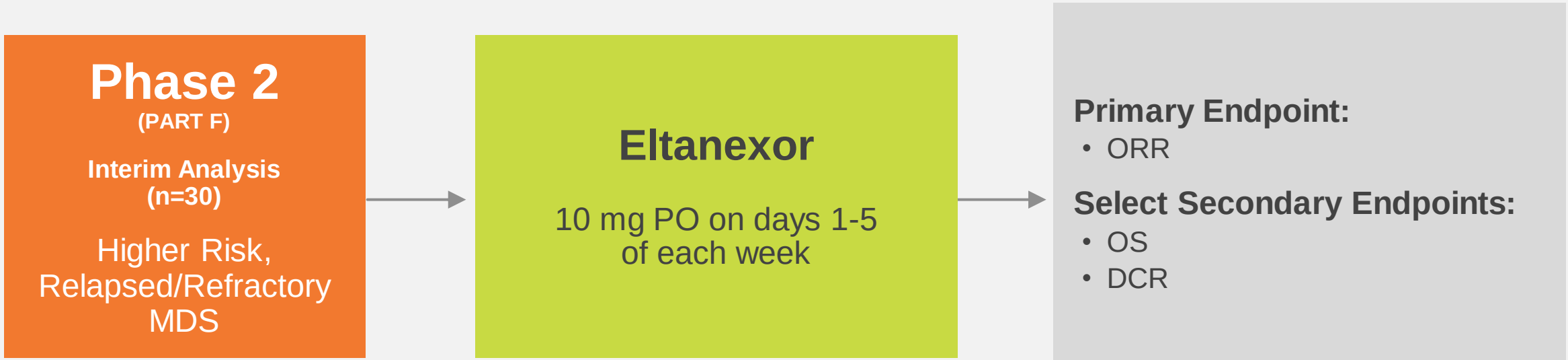
- No SoC exists for higher risk, relapsed or refractory MDS patients
- ~80% of patients treated in the community do not receive a 2L treatment
- Prognosis of higher risk relapsed/refractory disease is poor, with a median overall survival of four to six months[3,4]
- Transfusion dependence is a major problem in R/R MDS patients; transfusions impair quality of life and cause potential complications
- Critical need for novel and more effective treatment options for this patient population

~12,000 - 20,000 patients diagnosed with higher-risk MDS each year in the US[1]



1. What is MDS?," MDS Foundation, accessed April 21, 2021, https://www.mds-foundation.org/what-is-mds/
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

Phase 2 Study of Eltanexor in Higher Risk, Relapsed/Refractory MDS



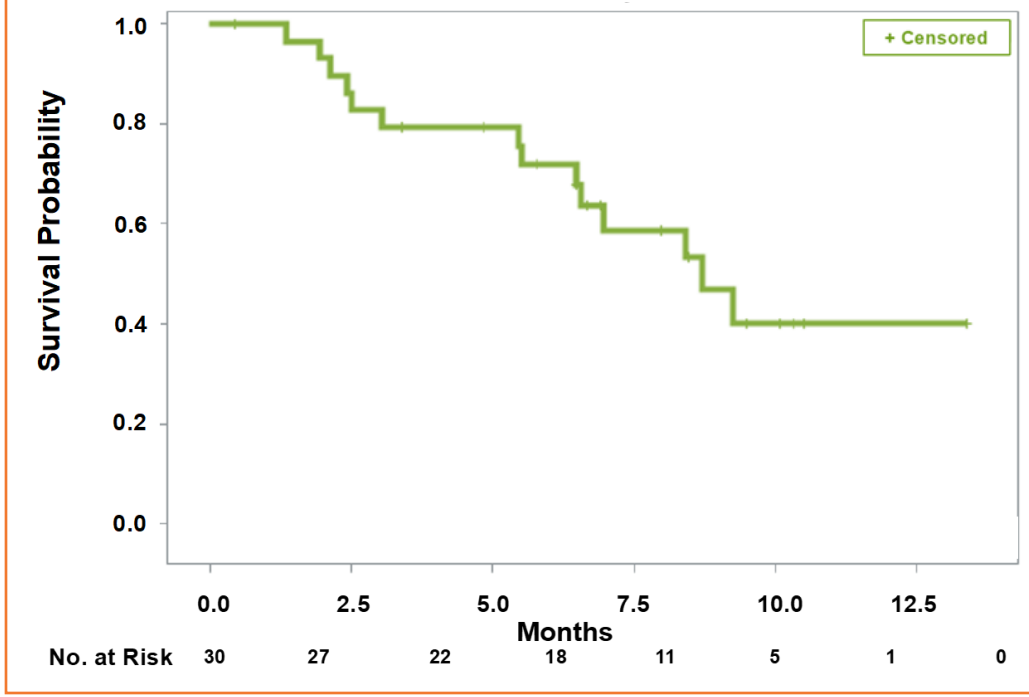
DCR, disease control rate; DOR, duration of response;; ORR, overall response rate; OS, overall survival;; PO, by mouth;.

Encouraging Efficacy Observed in Higher Risk Relapsed/Refractory MDS; a Hard-to-Treat Patient Population with Limited Treatment Options

Data from Interim Analysis (n=30)	Eltanexor (ITT)
Overall Response Rate* (ORR = mCR + HI), n (%)	8/30 (26.7)
Marrow Complete Response (mCR)	8/30 (26.7)
Hematologic Improvement (± mCR)	2/30 (6.7)
Disease Control Rate, n (%)	21/30 (70.0)
Transfusion Independence for Red Blood Cells and/or Platelets, n (%)	8/28** (28.6)

CI, confidence interval; HI, hematologic improvement; mCR, marrow complete response; NR, not reached; ORR, overall response rate as reported by Investigators
* In efficacy evaluable population: ORR: 31% and DCR: 81%
** 28 patients were RBC or platelet transfusion dependent at baseline

Median Overall Survival: 8.7 months, 95% CI (6.6, NE)



Prognosis of higher risk relapsed/refractory disease is poor, with a median overall survival of **four to six months**[1,2]

[1] Jabbour E, Cancer. 2010;116(16):3830-4. [2] Prébet T. J Clin Oncol. 2011;29:3322-7.

Generally Tolerable and Manageable Side Effect Profile

Treatment Emergent Adverse Events	Eltanexor (n=30)
Any grades, ≥20% overall	
Asthenia	14 (46.7)
Diarrhea	13 (43.3)
Nausea	10 (33.3)
Constipation	9 (30.0)
Neutropenia	9 (30.0)
Thrombocytopenia	8 (26.7)
Decreased appetite	7 (23.3)
Weight decreased	7 (23.3)
Contusion	6 (20.0)
Epistaxis	6 (20.0)
Oedema peripheral	6 (20.0)

Treatment Emergent Adverse Events	Eltanexor (n=30)
Grade 3+, ≥10%	
Neutropenia	9 (30.0)
Thrombocytopenia	8 (26.7)
Asthenia	5 (16.7)
Anemia	4 (13.3)
Febrile neutropenia	4 (13.3)
Leukopenia	3 (10.0)
Epistaxis	3 (10.0)
Fall	3 (10.0)

- There were no treatment-related AEs leading to death
- There were 3 patients that discontinued treatment due to a treatment-related AE: alanine aminotransferase (ALT) increase, aspartate aminotransferase (AST) increase, asthenia, and hemorrhagic diarrhea (increases in ALT and AST were experienced in one patient)

MICHAEL MASON
Chief Financial Officer

FINANCIAL RESULTS AND GUIDANCE

1Q 2023 Financial Results

Statements of Operations ($ millions)	1Q 2023	1Q 2022
Total Revenue	**$38.7**	**$47.7**
U.S. XPOVIO Net Product Revenue	28.3	28.3
License and Other Revenue	10.4	19.4
Total Operating Expenses	**$69.6**	**$82.3**
Cost of Sales	1.4	1.4
Research and Development Expenses	32.3	42.1
Selling, General & Administrative Expenses	35.9	38.8
Net Loss	**($34.1)**	**($41.4)**
Net Loss per share	**($0.30)**	**($0.53)**

Balance Sheet ($ millions)	March 31, 2023	Dec 31, 2022
Cash, Cash Equivalents Restricted Cash and Investments	**$261.9**	**$279.7**

Revised 2023 Financial Guidance

- Total Revenue of $145-$160M
- U.S. XPOVIO Net Product Revenue of $110-$125M
- Guidance revision primarily due to:
  - Significant increase in utilization of PAP (free drug) due to recent lack of funding to foundations for multiple myeloma patients
  - In 2024, significantly fewer patients expected to utilize PAP for co-pay assistance due to IRA related re-design of Part-D benefits
- Non-GAAP R&D and SG&A Expenses of $245-$260M[1]
- Cash runway expected to be sufficient to fund planned operations into late 2025

1. Karyopharm has not reconciled the full year 2023 outlook for non-GAAP R&D and SG&A expenses to full year 2023 outlook for GAAP R&D and SG&A expenses because Karyopharm cannot reliably predict without unreasonable efforts the timing or amount of the factors that substantially contribute to the projection of stock compensation expense, which is excluded from the full year 2023 outlook for non-GAAP R&D and SG&A expenses.

Richard Paulson
Chief Executive Officer

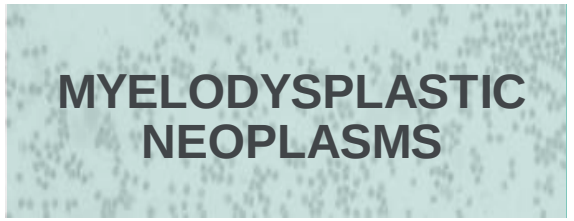
CLOSING REMARKS

Upcoming Milestones for 2023 and Beyond

- Leverage commercial capabilities and grow XPOVIO (2023)
- Continuation of global launches (2023)
- Report top-line results from pivotal Phase 3 study evaluating SPd[1] (2H 2024)
- Report data on XPOVIO pre/post T cell therapy (2H 2023-1H 2024)

- Present exploratory updated results from the *TP53* subgroup from the 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 Phase 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 higher risk R/R MDS (1H 2023) ✓
- Define development plan in higher risk R/R MDS (2H 2023)

1. Selinexor + pomalidomide + dexamethasone

Q&A SESSION