Karyopharm® Therapeutics

First Quarter 2024 Financial Results & Business Update

May 8, 2024

On Today's Call

- **Welcome**
  Elhan Webb, CFA, *Senior Vice President, Investor Relations*
- **Overview**
  Richard Paulson, *President and Chief Executive Officer*
- **Pipeline Update**
  Dr. Reshma Rangwala*, Chief Medical Officer and Head of Research*
- **Commercial Highlights**
  Sohanya Cheng, *Chief Commercial Officer*
- **Financial Results 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 the anticipated benefits of and activities under the refinancing transactions, expectations for our use of proceeds from the Secured Term Loan, the expected closing date for the exchange transactions and the Company's ability to complete the exchange transactions; Karyopharm's guidance on its 2024 total revenue, 2024 U.S. net product revenue and 2024 R&D and SG&A expenses; Karyopharm's expected cash runway; beliefs about the market opportunity and annual peak revenue opportunities for selinexor; the ability of selinexor to treat patients with multiple myeloma, endometrial cancer, myelofibrosis, diffuse large B-cell lymphoma, and other diseases; expectations related to future clinical development and potential regulatory submissions of selinexor; expectations with respect to commercialization efforts; submissions to, and the review and potential approval of selinexor 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. 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, 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 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 and preclinical trials, including subsequent analysis of existing data and new data received from ongoing and future trials; 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 trials; 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; the direct or indirect impact of the COVID-19 pandemic or any future pandemic on Karyopharm's business, results of operations and financial condition; 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, 2023, which was filed with the Securities and Exchange Commission (SEC) on February 29, 2024, 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 is an investigational drug that has not been approved by the FDA or any other regulatory agency, and the safety and efficacy of this drugs has not been established by any agency.

Richard Paulson
Chief Executive Officer

OVERVIEW

Driven to Positively Impact Lives and Defeat Cancer Through Scientific Innovation

Committed to Driving Value with Next Stage of Growth

- **Novel & Differentiated Mechanism of Action**
- **Transformative Late-Stage Clinical Development Opportunities**
- **Strong Financial Position to Deliver 3 Pivotal Studies**
- **Global Commercial Presence & Approvals in over 40 Countries**
- **Potential For ~$2 Billion Annual Peak U.S. Revenues[1,2]**

1. Includes projected potential selinexor revenues in JAKi-naïve myelofibrosis, TP53 wild type endometrial cancer and multiple myeloma.
2. Annual U.S. peak revenue opportunity is not guidance, but instead represents what the Company believes to be Karyopharm's peak revenue opportunity based on internal estimates, including market research conducted for each indication.

Debt Exchange Strengthens Opportunity to Realize Multiple Phase 3 Readouts in 2025; Collective $2B+ Potential Annual Peak Revenue Opportunity[1, 2]

Topline Results:

- MM* 1H 2025
- EC 1H 2025
- MF 2H 2025

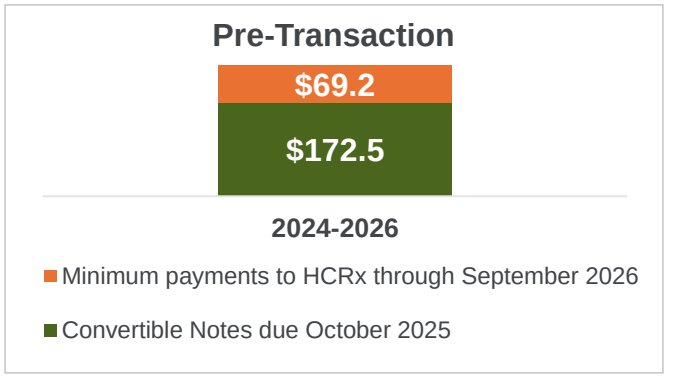
Myelofibrosis (MF) — Potential to transform 1L treatment for myelofibrosis patients with rapid, deep and sustained responses

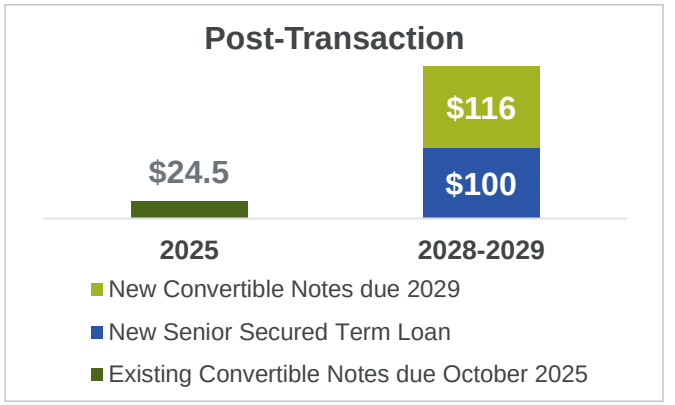
Endometrial Cancer (EC) — Potential to extend progression-free survival for *TP53* WT endometrial cancer patients

SPd[3] — Potential to address unmet need in 2L+ multiple myeloma with an all oral-triplet post anti-CD38

Current Label — Continued growth in 2L+ multiple myeloma by enabling a class switch as a novel MOA

Maturity Profile





* Multiple myeloma.

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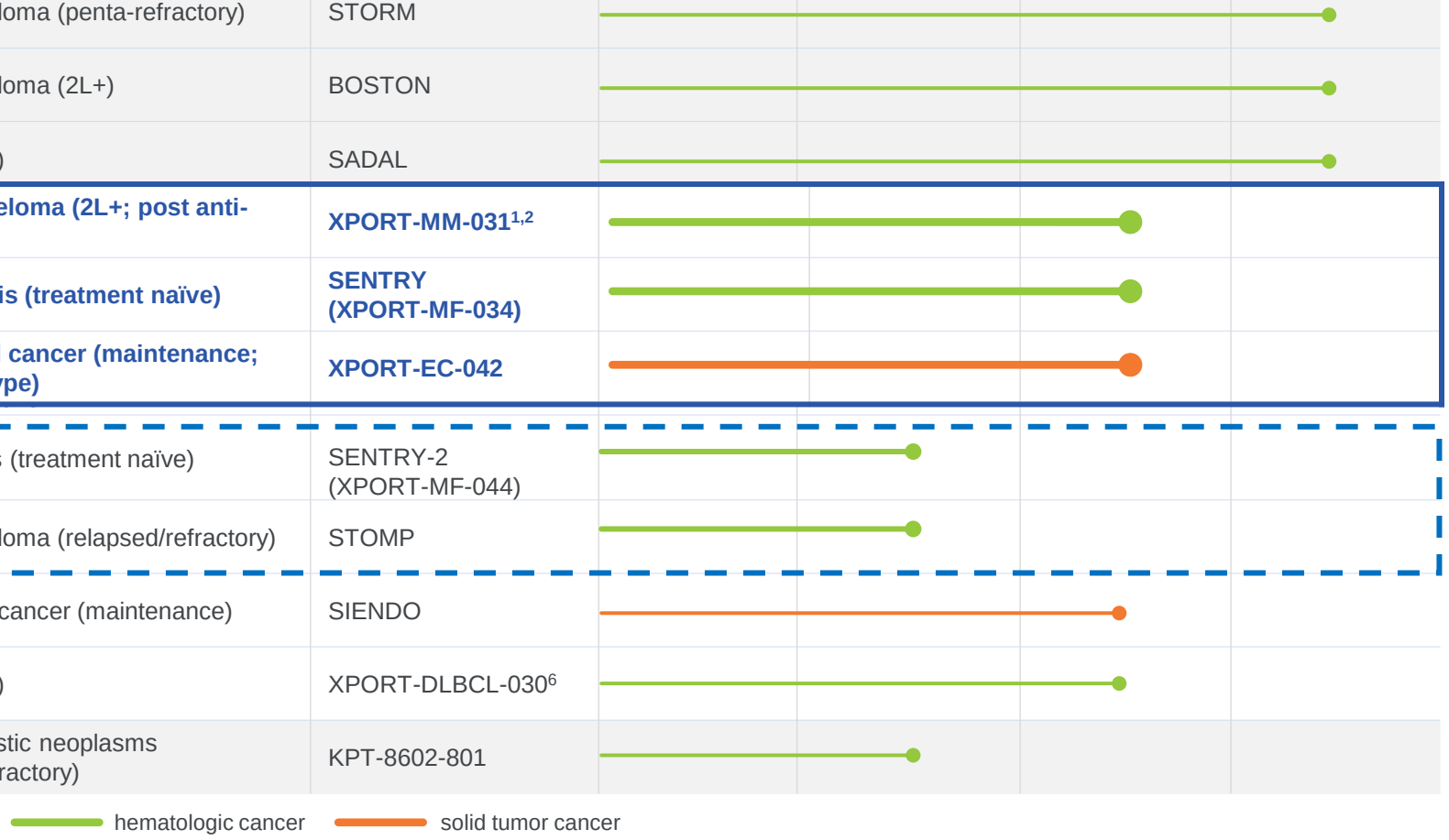
2. Annual U.S. peak revenue opportunity is not guidance, but instead represents what the Company believes to be Karyopharm's peak revenue opportunity based on internal estimates, including market research conducted for each indication.
3. Selinexor + pomalidomide + dexamethasone.

Reshma Rangwala, MD, PhD
Chief Medical Officer and
Head of Research

PIPELINE UPDATE

Focused High Potential Pipeline with 3 Pivotal Studies Across Cancers With High Unmet Needs

	Regimen	Indication	Study Name
XPOVIO® (selinexor)	w/dexamethasone	Multiple myeloma (penta-refractory)	STORM
	w/bortezomib + dexamethasone	Multiple myeloma (2L+)	BOSTON
	monotherapy	DLBCL (R/R)	SADAL
SELINEXOR Pivotal Phase 3s	**w/pomalidomide + dexamethasone**	**Multiple myeloma (2L+; post anti-CD38)**	**XPORT-MM-031[1,2]**
	w/ruxolitinib	**Myelofibrosis (treatment naïve)**	**SENTRY (XPORT-MF-034)**
	monotherapy	**Endometrial cancer (maintenance; *TP53* wild-type)**	**XPORT-EC-042**
SELINEXOR Phase 2s	Monotherapy[3] (agreement with SOBI[4])	Myelofibrosis (treatment naïve)	SENTRY-2 (XPORT-MF-044)
	w/mezigdomide[5] (clinical collaboration with BMS)	Multiple myeloma (relapsed/refractory)	STOMP
	monotherapy	Endometrial cancer (maintenance)	SIENDO
	w/R-GDP	DLBCL (R/R)	XPORT-DLBCL-030[6]
ELTANEXOR	monotherapy	Myelodysplastic neoplasms (relapsed/refractory)	KPT-8602-801



1. EMN29 Study: Sponsored by European Myeloma Network. 2. Versus elotuzumab, pomalidomide, and dexamethasone. 3. With option to add JAK inhibitors. 4. For supply of pacritinib. 5. To be initiated as an arm in the STOMP trial. 6. XPORT-DLBCL-030 is a Phase 2/3.

ENDOMETRIAL CANCER

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

Phase 3 SIENDO Study

Generated strong hypothesis in patients with *TP53* WT EC

Targeted Mechanism and Oral Treatment

XPO1 inhibition forces retention of p53 in the cell nucleus, allowing it to carry out its tumor suppressor and other regulatory functions

Addressing a Significant Unmet Need

Potential to improve treatment options for pMMR[1] (proficient mismatch repair), which represents ~80% of advanced and recurrent EC[1]

Significant Market Opportunity

~16K patients diagnosed with advanced and recurrent EC in the U.S. each year[2]

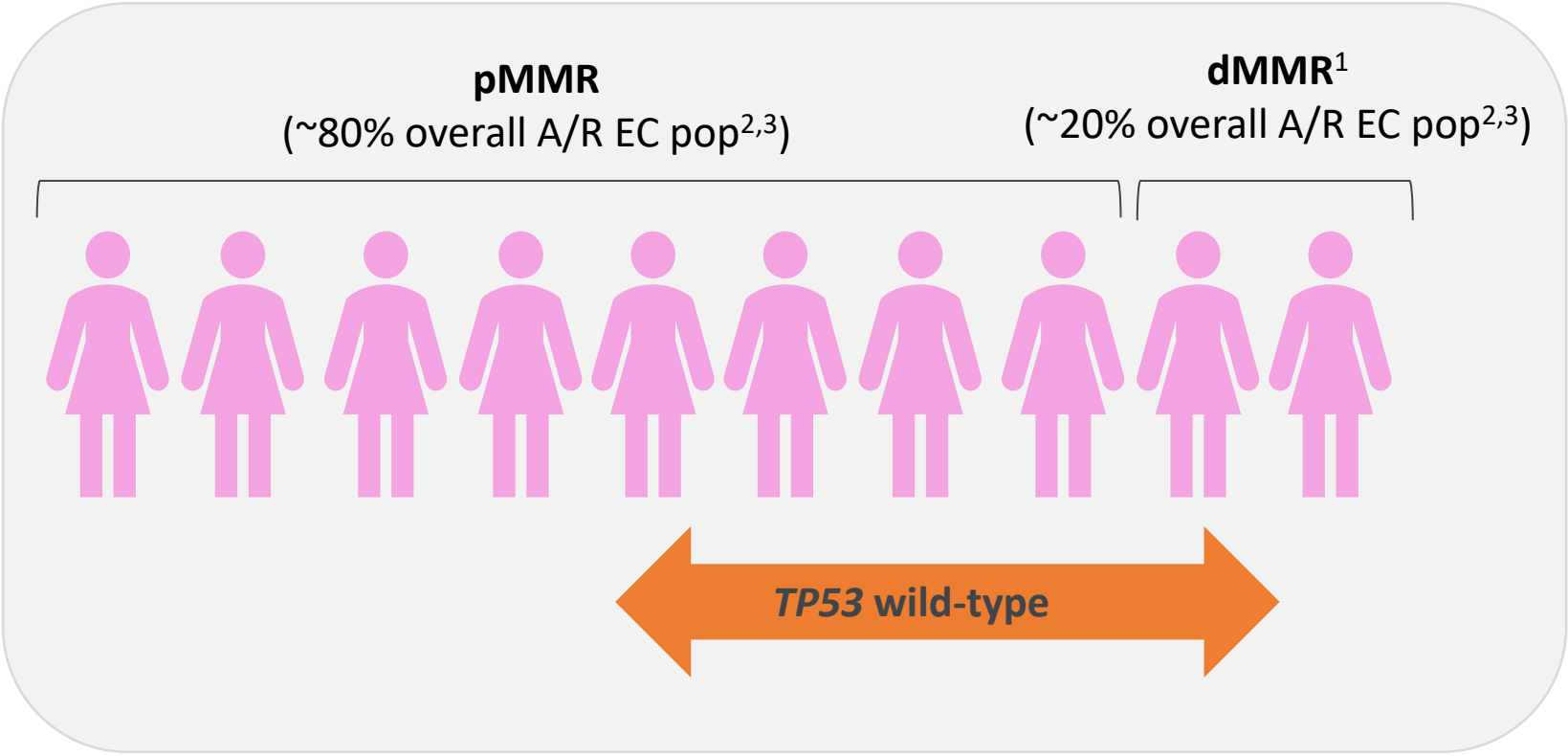
~ >50% have *TP53* WT EC, and 40-55% are *TP53* WT and pMMR[1,3]

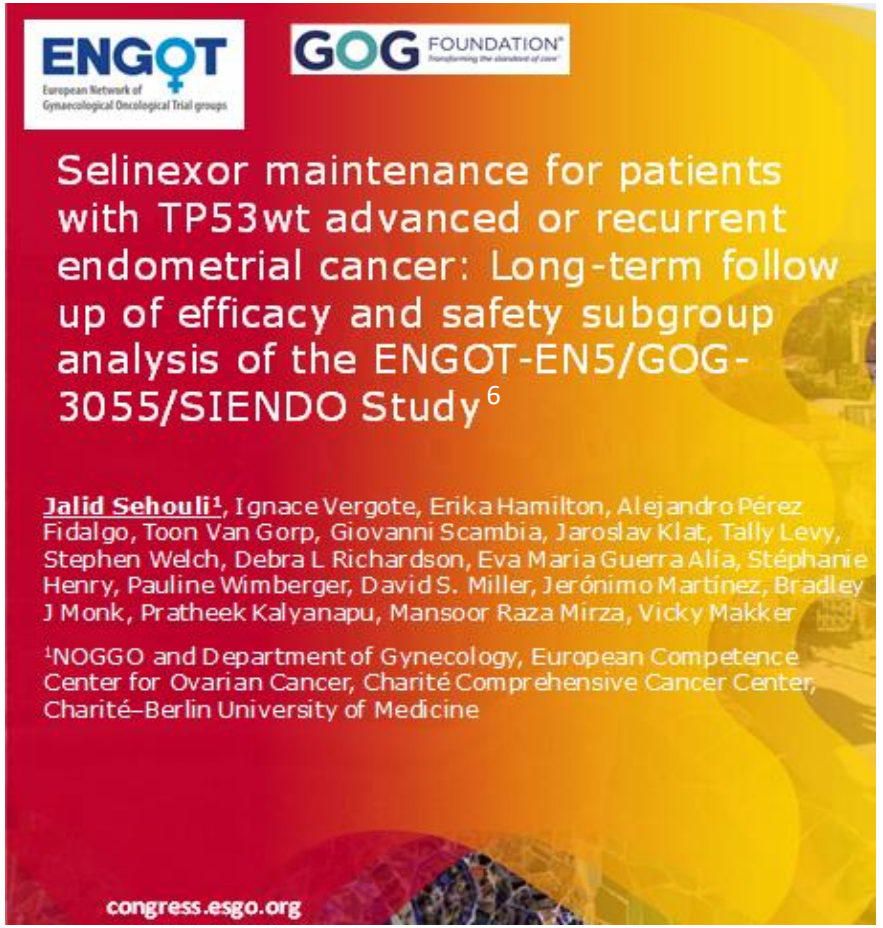
The safety and efficacy of selinexor in endometrial cancer has not been established and has not been approved by the U.S. FDA or any other regulatory authority for use in endometrial cancer.

1. Mirza, M et al. (2023, October 20-24). Dostarlimab + Chemotherapy for the Treatment of Primary Advanced or Recurrent Endometrial Cancer: Analysis of Progression Free Survival and Overall Survival Outcomes by Molecular Classification in the ENGOT-EN6-NSGO/GOG-3031/RUBY Trial. [Conference presentation]. ESMO 2023 Congress, Madrid, Spain. 2. Clarivate/DRG Endometrial Carcinoma Epidemiology Dashboard (2022 figures, pub 2020) 3. 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 3

Emerging Role of *TP53* and Importance of Molecular Profiling in the Evolving Landscape of Advanced and Recurrent Endometrial Cancer (A/R EC)

Patients Who are Both *TP53* Wild-Type AND pMMR Represent 40-55% of all A/R EC[2,3,4,5]

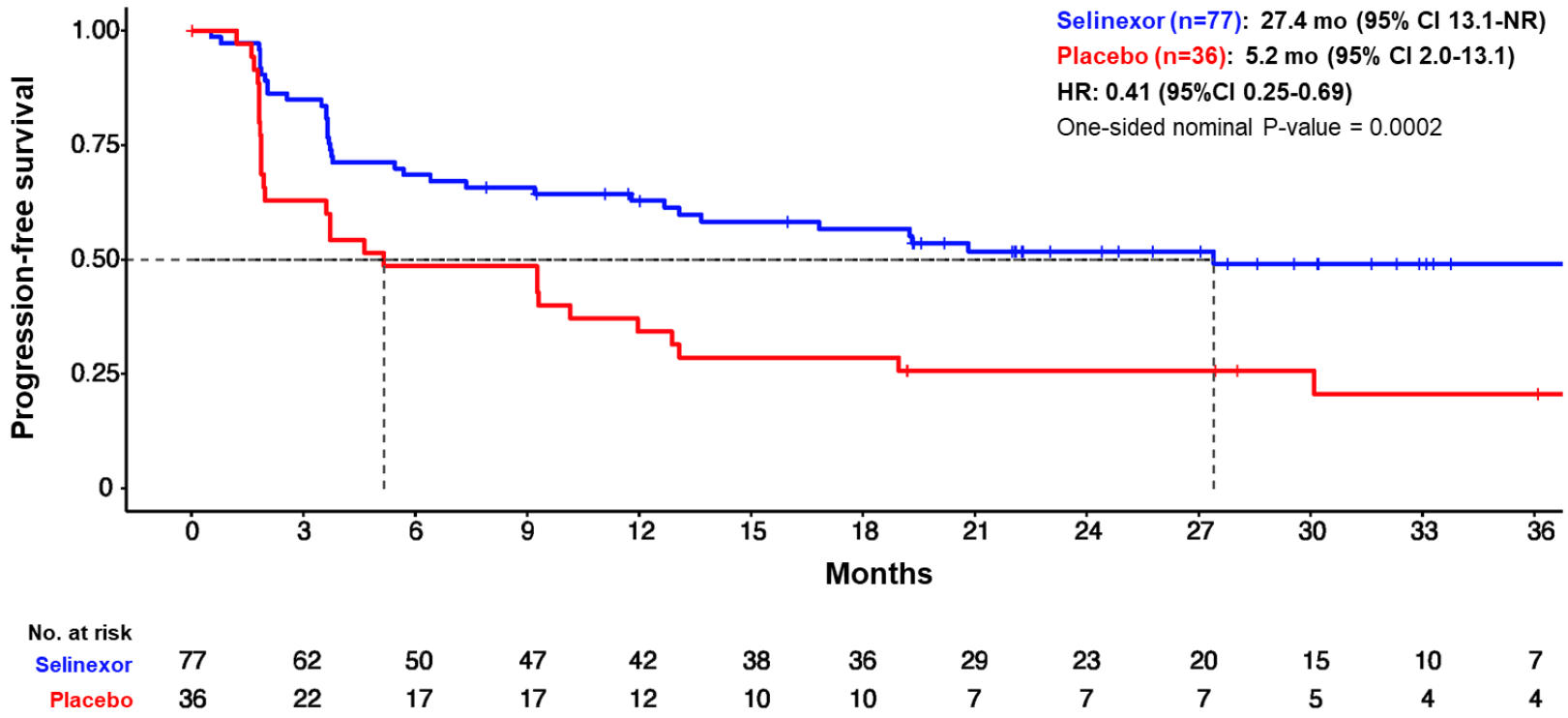




The safety and efficacy of selinexor in endometrial cancer has not been established and has not been approved by the U.S. FDA or any other regulatory authority.

1. Deficient mismatch repair. 2. Mirza, M et al. (2023, October 20-24). Dostarlimab + Chemotherapy for the Treatment of Primary Advanced or Recurrent Endometrial Cancer: Analysis of Progression Free Survival and Overall Survival Outcomes by Molecular Classification in the ENGOT-EN6-NSGO/GOG-3031/RUBY Trial. [Conference presentation]. ESMO 2023 Congress, Madrid , Spain. 3. Vergote I, et al. J Clin Oncol. 2023 Sep 5:JCO2202906.2023 Oral Selinexor as Maintenance Therapy After First-Line Chemotherapy for Advanced or Recurrent Endometrial Cancer, https://pubmed.ncbi.nlm.nih.gov/37669480/. 4. Slomovitz B et al. Presentation at American Society for Clinical Oncology Plenary Series; July 25, 2023. 5. Leslie KK, et al Gynecol Oncol. 2021 April ; 161(1): 113–121
6.Conference presentation ESGO 2024 Congress, Barcelona, Spain

Updated Data from SIENDO Study[1] Indicate Encouraging Signal of PFS Benefit with Median PFS > Two Years in *TP53* Wild-Type EC



Most common adverse events in *TP53* wt exploratory subgroup: nausea (90%, grade ≥3: 12%), vomiting (60%, grade ≥3: 3%), thrombocytopenia (42%, grade ≥3: 10%) and diarrhea (42%, grade ≥3: 4%). TEAE's leading to discontinuation 16% and death 0%.

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.

Data cut September 1, 2023

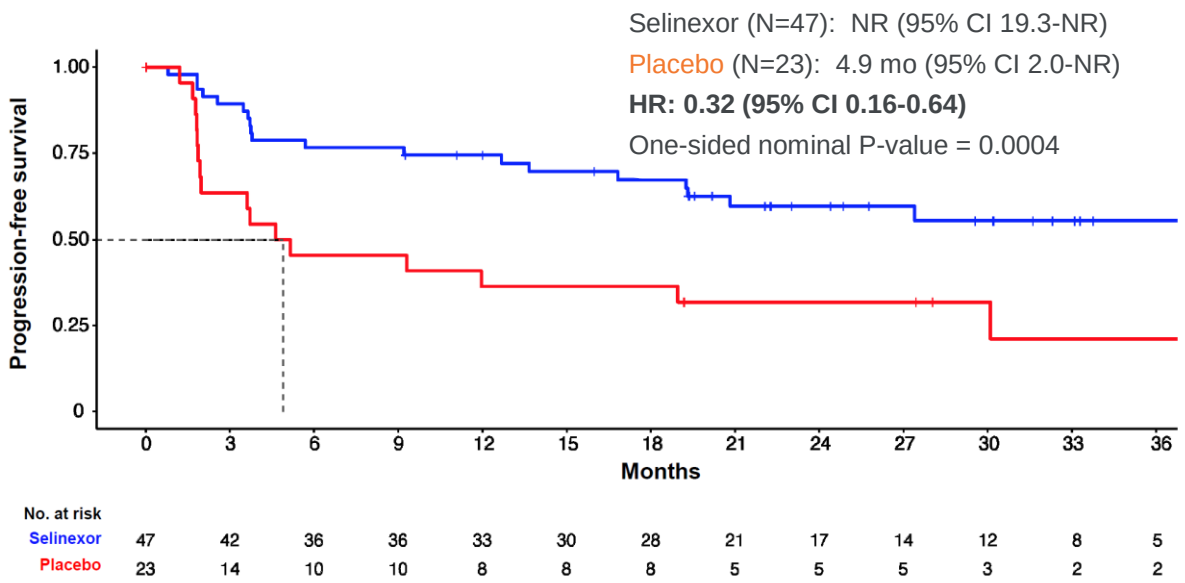
NR, not reached.

1. Pre-specified exploratory TP53wt subgroup from SIENDO trial; data presented at IGCS 2023 Annual Global Meeting and ESGO 2024 Congress

SIENDO Study: In the *TP53* WT Exploratory Subgroup, PFS Improvement Observed Regardless of MMR Status, Strongest Signal in *TP53* WT / pMMR

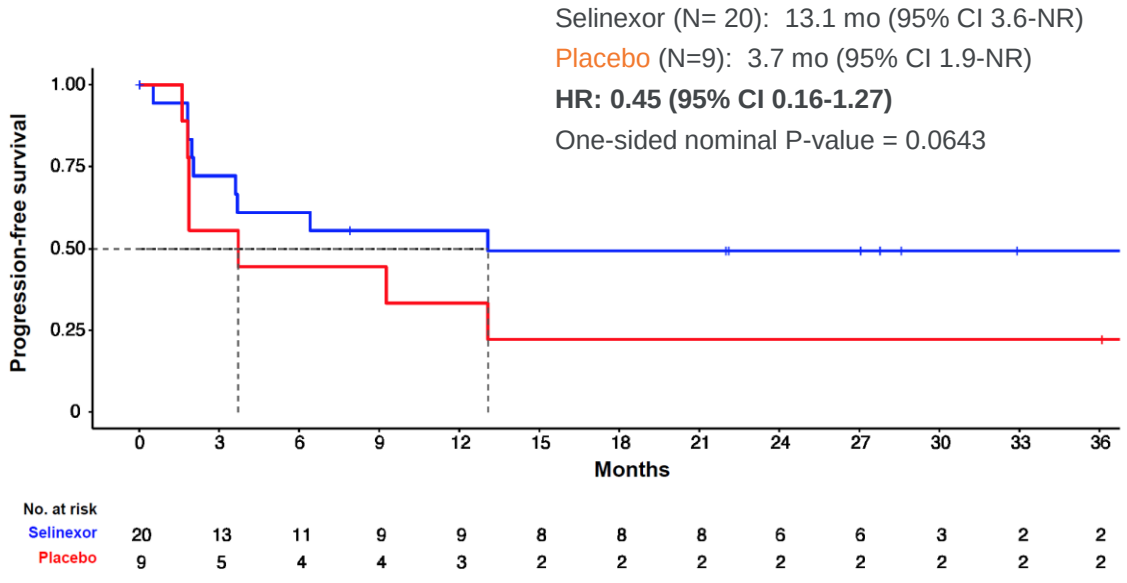
Long-Term Follow-Up[1]: PFS in *TP53* WT Exploratory Subgroup Based on MMR status

TP53 WT / pMMR (MSS)



Median follow-up: 31.6 months

TP53 WT / dMMR (MSI-H)



Median follow-up: 27.3 months

Invited to Present Updated Data Cut and New Analysis at ASCO Plenary Series Rapid Abstract Updates Oral Session

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.

Data cut September 1, 2023
NR, not reached.

1. Presented at IGCS 2023 Annual Global Meeting and ESGO 2024 Congress

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

Study is Actively Enrolling

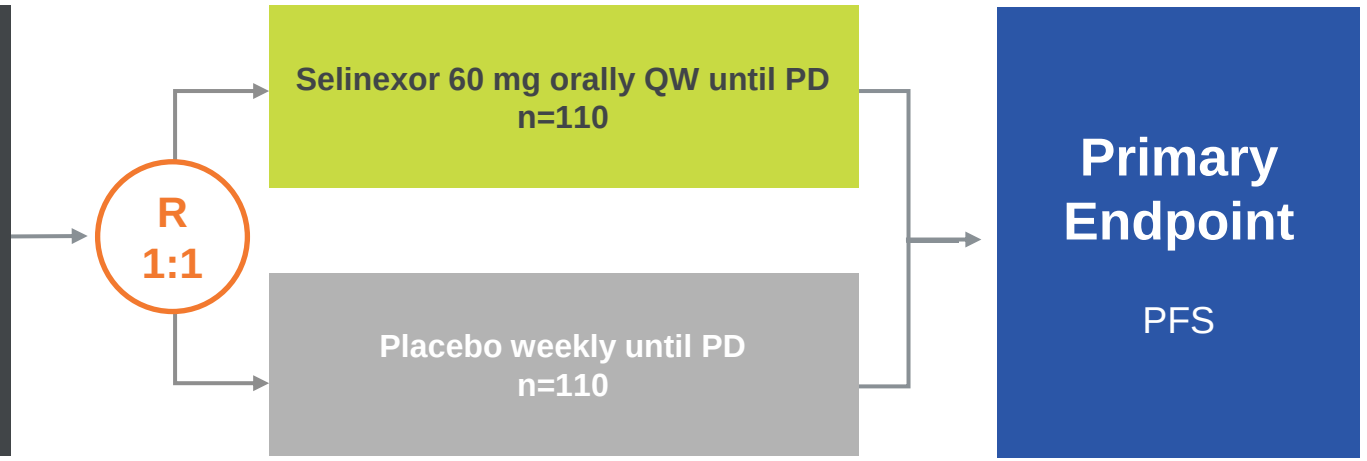
TP53 Wild-Type Status is Assessed by Companion Diagnostic Partner Foundation Medicine[1]

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

Key Eligibility

TP53 wild-type endometrial cancer [1]

- Primary stage IV or recurrent EC
- Received at least 12 weeks of platinum-based therapy +/- immunotherapy
- In partial response (PR) or complete response (CR) to chemotherapy



*NCT05611931

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.

Top-line Data in 1H 2025

PFS, progression-free survival; PD, progressive disease; QW, every week

1. Utilizing Foundation Medicine's tissue-based comprehensive genomic profiling test to identify TP53 status
2.European Network for Gynaecological Oncological Trial groups
3. Gynecologic Oncology (GOG) Foundation

MYELOFIBROSIS

Selinexor Has the Potential to Define a New Treatment Paradigm in MF*

Treatment Landscape and Unmet Need

Population living with MF:

- ~20,000 in the U.S[1]; ~17,000 in EU[1]

No other approved class of therapy other than JAK inhibitors

- Ruxolitinib generates over $1 billion[2] revenues annually in MF in the U.S.

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

- Only ~35% of patients achieve SVR35 with ruxolitinib[3]
- <50% achieve TSS50[3]

Selinexor

- ✓ **XPO1 inhibition is a novel and potentially fundamental mechanism in MF**
- ✓ **Synergism with ruxolitinib observed in preclinical data[4]**
- ✓ **Rapid, deep and sustained spleen response, robust symptom improvement and rapid, sustained cytokine reduction across all subgroups***
- ✓ **Potentially disease modifying with rapid normalization of platelets, maintenance of hemoglobin levels and rapid cytokine reduction**
- ✓ **Generally tolerable and manageable side effect profile enabling sustained therapy**

* Based on selinexor+ruxolitinib Ph 1 results, n=14; using data cut as of August 1, 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 for use in myelofibrosis.

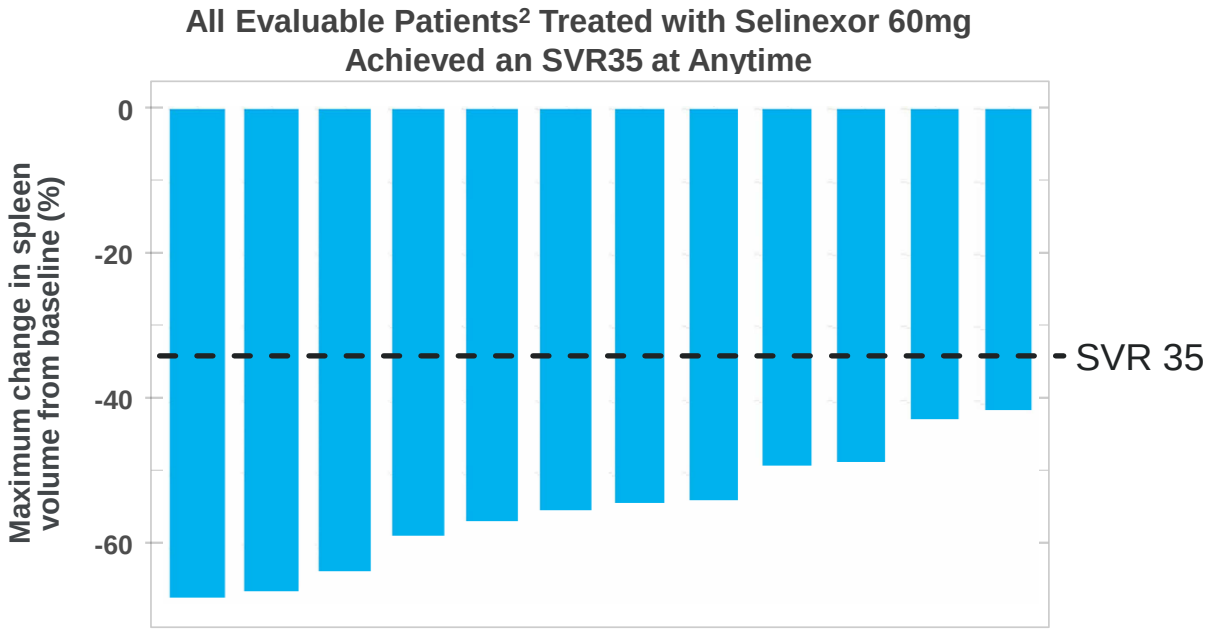
SVR 35: Spleen volume reduction ≥ 35%; TSS50: Total symptom score reduction of ≥50%

1. Mehta et.al. Leuk Lyphoma 2014 Mar ;55(3):595-600 and US Census data; Clarivate/DRG Epidemiology Data (2022 figures, pub 2019)
2. Incyte Q4 2023 Results 3. MANIFEST and TRANSFORM Phase 3 studies, ASH 2023 4. Al-Ali, et al. Hematologica. 2016;101(9):1065

Rapid and Deep SVR35 Achieved with Selinexor 60 mg + Ruxolitinib in Ph1 Trial

		SVR35
Population	**Timepoint**	**Selinexor 60mg +ruxolitinib n/N (%)**
Efficacy Evaluable	Week 12	10/12[1] (83.3)
	Week 24	**11/12 (91.7)**
Intent-to-Treat	Week 12	10/14 (71.4)
	Week 24	**11/14 (78.6)**

SVR35, spleen reduction volume ≥35%



The most common adverse events were GI side effects:

- Nausea (79%, grade ≥3: 7%), anemia (64%, grade ≥3: 43%), thrombocytopenia (64%, grade ≥3: 29%), and fatigue (57%, grade ≥3: 0%)

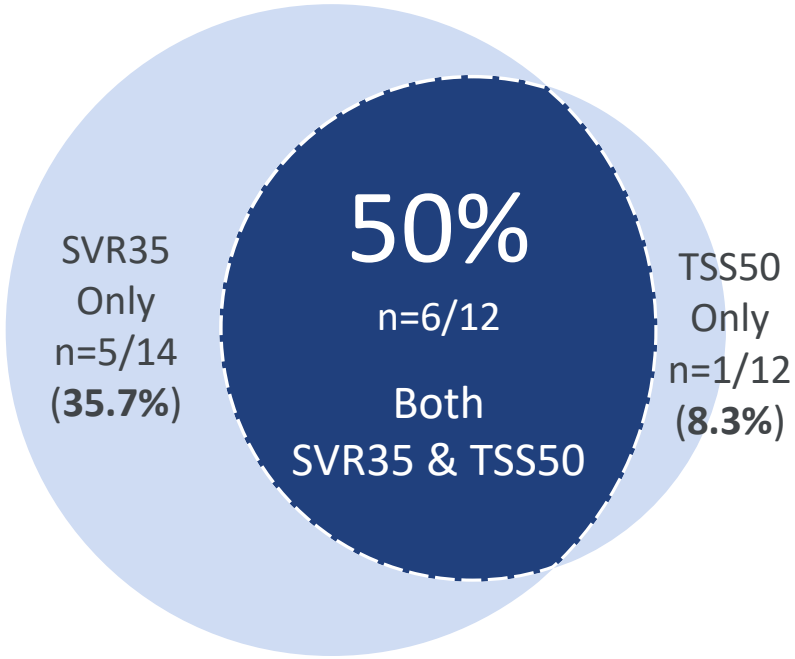
The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the U.S. FDA or any other regulatory authority for use in myelofibrosis.

Data cut August 1, 2023

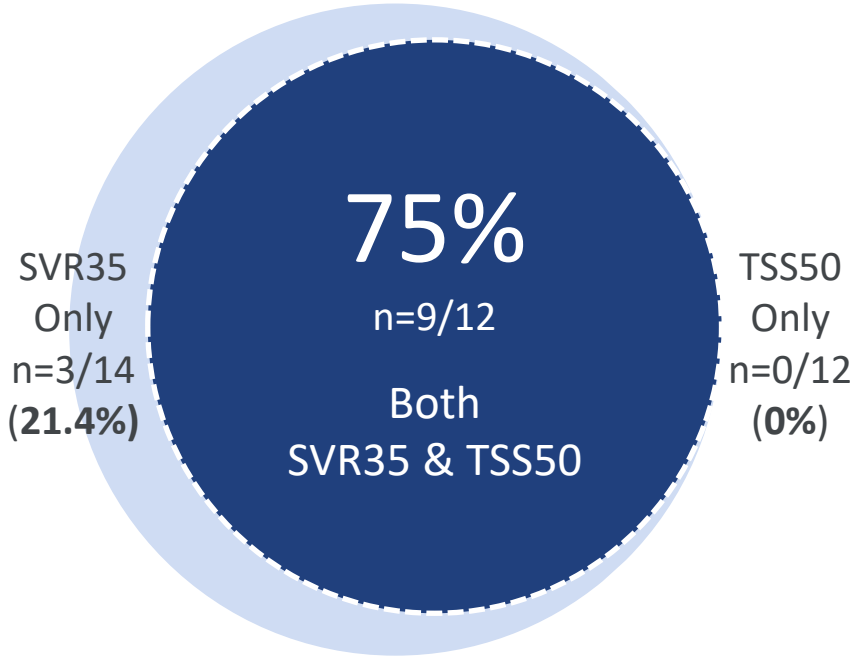
1. Two patients discontinued prior to Week 24
2. n=12; one patient discontinued prior to week 12; one patient with missing data at week 12 who subsequently discontinued prior to week 24

50% of All Patients Treated with Selinexor 60 mg + Ruxolitinib Achieved SVR35 and TSS50 at Week 24; 75% of Patients Achieved Both at Anytime

Response at Week 24



Response at Anytime



* 2 patients with no baseline symptoms (TSS = 0) were excluded from the TSS50 response and the SVR35/TSS50 dual response analyses.

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 for use in myelofibrosis.

Meaningful Improvement Observed in TSS50 and Absolute TSS with Selinexor 60 mg + Ruxolitinib at Week 24

		TSS50[1]
Population	Timepoint	Selinexor 60mg +ruxolitinib n/N (%)
Efficacy Evaluable	Week 12	8/10[3] (80.0)
	Week 24	**7/9[4] (77.8)**
Intent-to-Treat	Week 12	8/12 (66.7)
	Week 24	**7/12 (58.3)**

	Absolute TSS[2]
Timepoint	Selinexor 60mg +ruxolitinib mean (SD*)
Baseline	**27.3 (17.43)**
Week 24	**-18.5 (13.48)**

* standard deviation

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 for use in myelofibrosis.

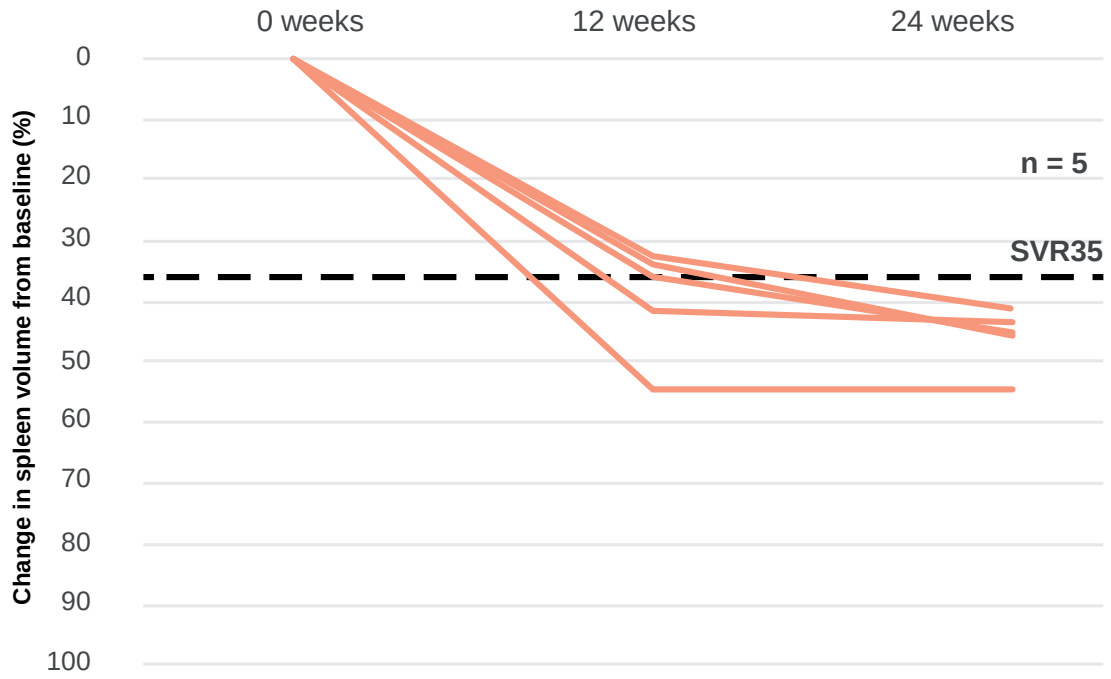
Data cut August 1, 2023

1. Proportion of patients with ≥50% reduction in TSS from baseline to Week 24 based on modified MPN-SAF TSS V.4.0
2. Average reduction in total symptom score at week 24 relative to baseline, calculated for each evaluable subject. Least square mean of the absolute TSS change was not estimated in the ITT population due to limitations in sample size
3. One patient discontinued prior to week 12; one patient with missing data at week 12, who subsequently discontinued prior to week 24
4. Two patients discontinued prior to Week 24 and one had missing data

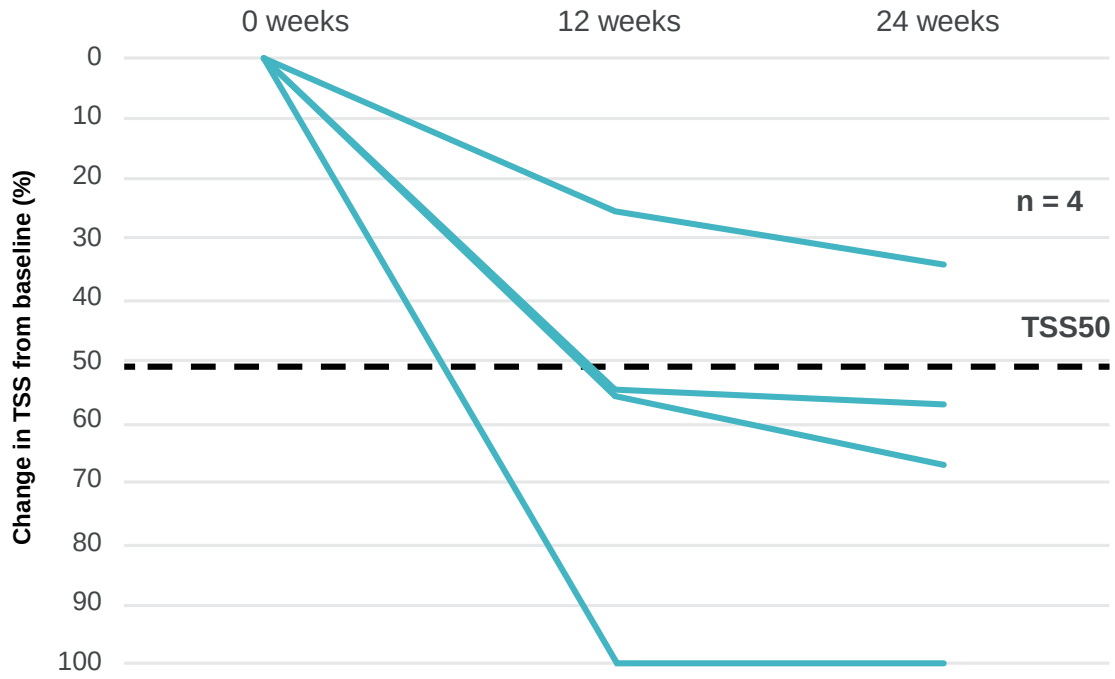
Efficacy Observed with Selinexor in Combination with Suboptimal Dose of Ruxolitinib (≤5 mg*) Further Supports XPO1 as a Fundamental MoA in MF

Retrospective, Exploratory Analysis from Phase 1 Selinexor (60 mg) + Ruxolitinib Study (034)

Spleen Volume Reduction



Total Symptom Score Reduction[1]



*Patients received ruxolitinib at ≤ 5 mg BID for at least five out of the first six cycles

"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

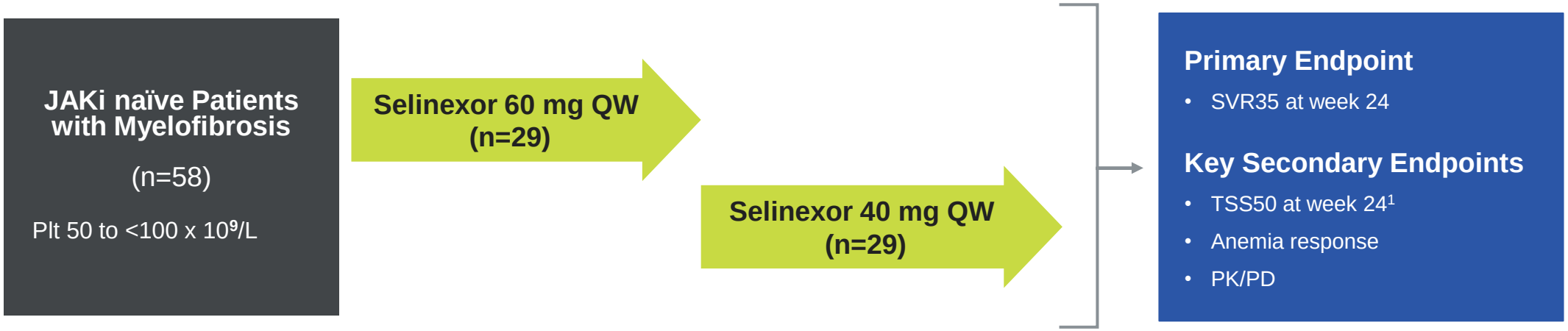
The safety and efficacy of selinexor in myelofibrosis has not been established and has not been approved by the U.S. FDA or any other regulatory authority.

Data cut August 1, 2023

1. One patient with missing TSS50 score

BID: Twice daily; MoA: Mechanism of Action; MF: Myelofibrosis

Initiated SENTRY-2 (XPORT-MF-044*) Phase 2 Trial Evaluating Selinexor As Monotherapy in JAKi Naïve MF Patients with Lower Platelet Counts



* NCT05980806

Optional Add-on Medications	
Week 12 if SVR <10%	**Week 24 if SVR <35%**
Add **ruxolitinib**[2]**:** if plt >50 x 10^9/L, and hemoglobin level is ≥ 10 g/dL	
Add **pacritinib:** if plt <50 x 10^9/L[1] sobi[4]	
Add **momelotinib**[3] if plt >50 x10^9/L hemoglobin level is <10 g/dL	

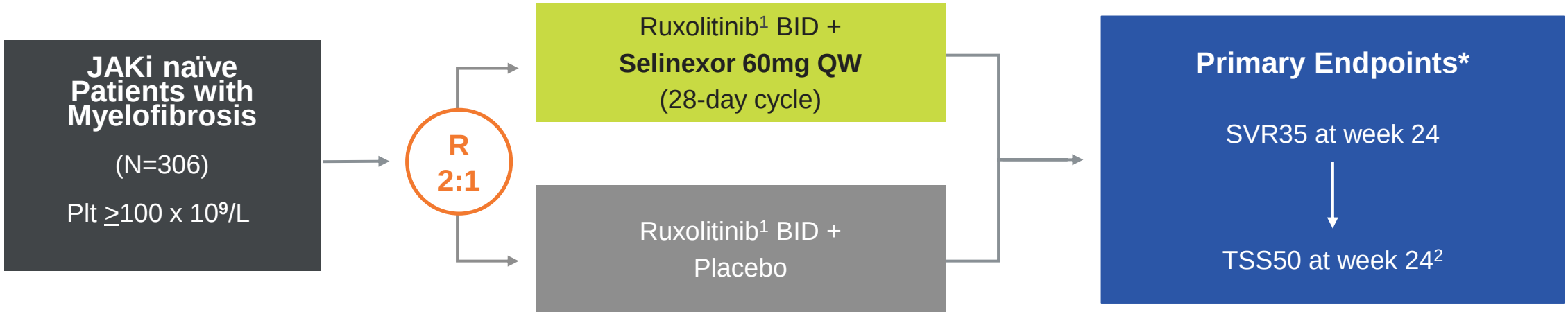
Pacritinib supply agreement with SOBI

1. Evaluated in the myelofibrosis assessment form (MFSAF) 2. Ruxolitinib dose based on platelet count per prescribing information 3.In the U.S. only 4. For supply of pacritinib

Plt: platelet; QW: Once weekly; SVR 35: Spleen volume reduction ≥ 35%; TSS50: Total symptom score reduction of ≥50%; PD: pharmacodynamic; PK: Pharmacokinetic

SENTRY (XPORT-MF-034*) Phase 3 Trial Evaluating Selinexor in Combination with Ruxolitinib in Treatment-naïve Myelofibrosis

Study is Actively Enrolling



*NCT04562389

Endpoints tested sequentially

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

Top-line Data Expected in 2H 2025

1. Ruxolitinib dose based on platelet count per prescribing information
2. Evaluated in the myelofibrosis assessment form (MFSAF)

BID: Twice daily; Plt: Platelet; QW: Once weekly; SVR 35: Spleen volume reduction ≥ 35%; TSS50: Total symptom score reduction of ≥50%

MULTIPLE MYELOMA

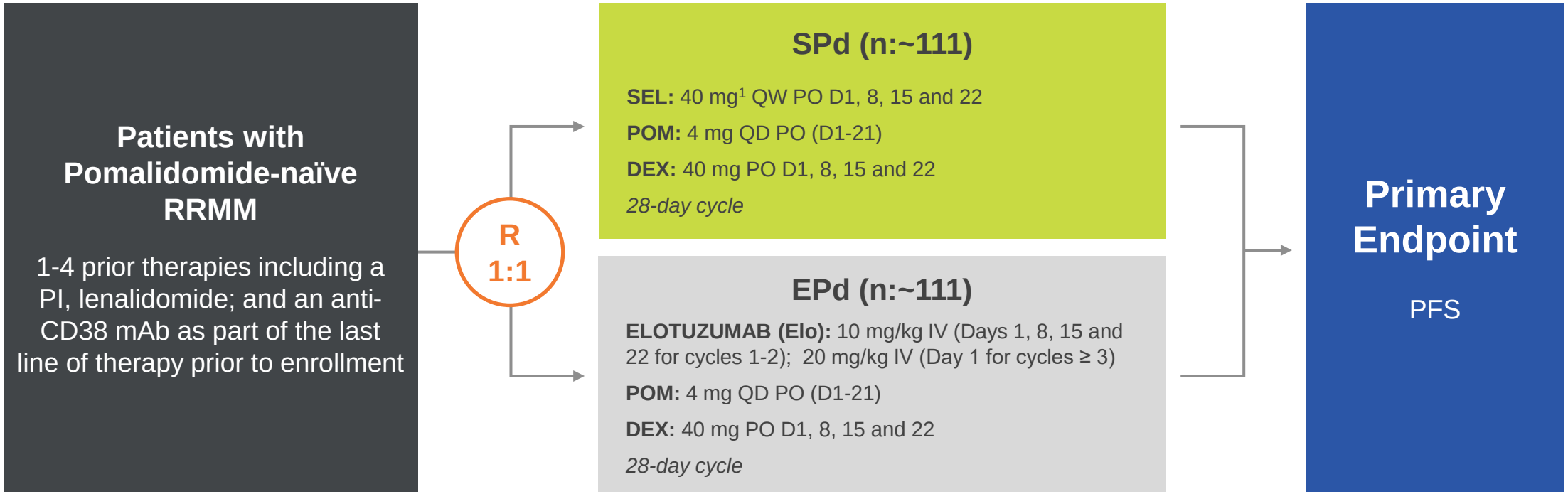
Generating Evidence on the Role and Effectiveness of Selinexor pre and post T-cell Mediated Therapies

Published Studies	Preclinical Research	Real-World Evidence	Clinical Research
Selinexor maintains T-cells function in mice;[1] pre-treatment may maintain effectiveness of CAR-T therapies [2,3]	Impact of SINE mechanism on T-cell fitness via collaborations with academic institutions	Effectiveness of CAR-T following selinexor therapy	Evaluating selinexor pre or post BCMA/CAR-T therapy

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

Phase 3 Global Study (XPORT-MM-031/ EMN29*) Evaluating SPd in Patients with Previously Treated Multiple Myeloma

Study is Actively Enrolling



*NCT05028348

The safety and efficacy of SPd has not been established and has not been approved by the FDA or any other regulatory authority

Top-line Data in 1H 2025

PI: proteasome inhibitor; mAB: monoclonal antibody

1. 40 mg selinexor dose was based upon evaluation of the safety and benefit of selinexor 40 and 60 mg doses in combo with Pd observed in the STOMP and 028 studies

Sohanya Cheng
Chief Commercial Officer

COMMERCIAL HIGHLIGHTS

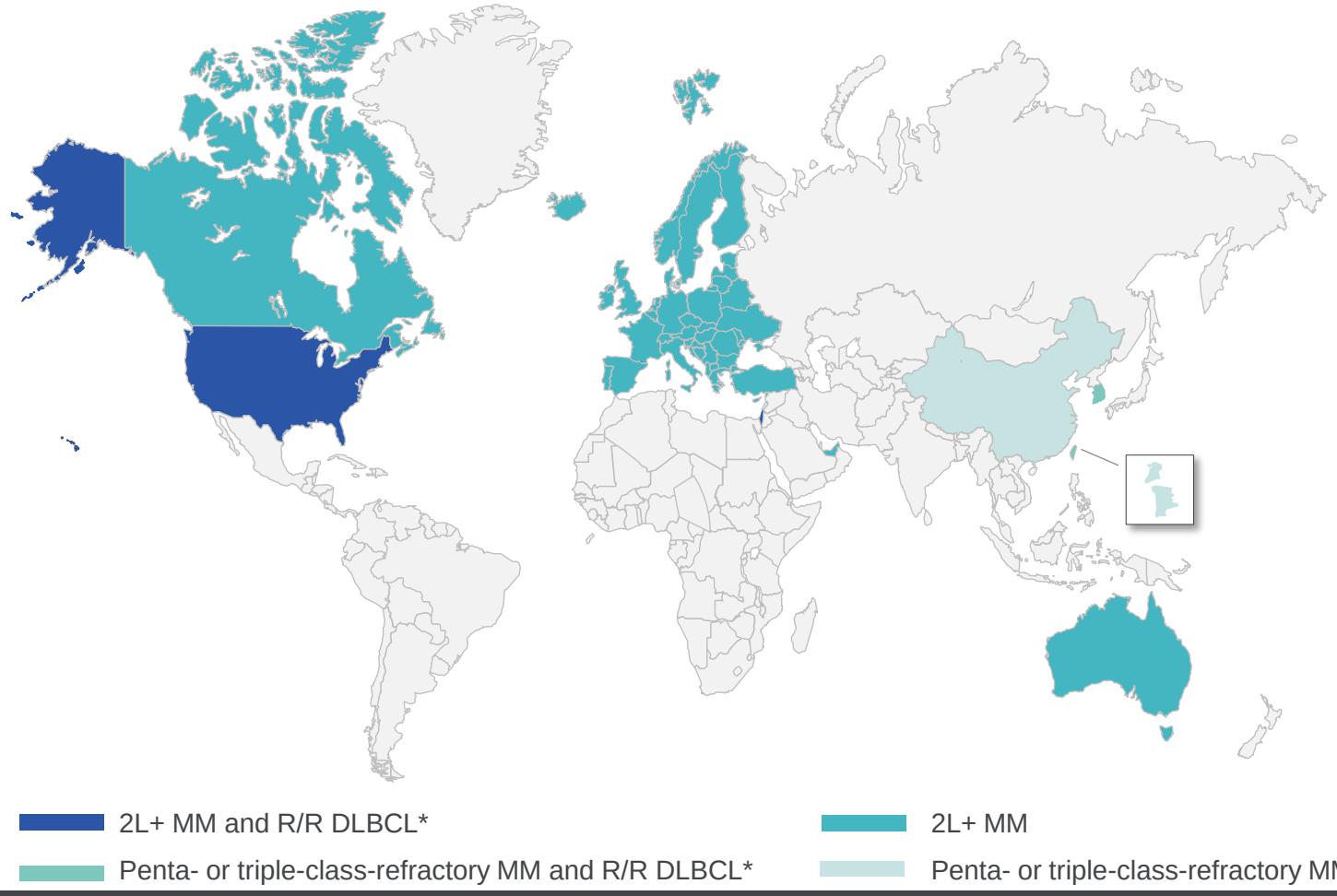
XPOVIO Net Product Revenue

1Q 2024 Highlights

- XPOVIO 1Q 24 net product revenue of $26.0M, -8% YoY and +4% QoQ, amidst increased competition
- QoQ growth in new patient starts
  - Softness in refills following lower NRx in 4Q 23
  - Higher GTN in 1Q 24, typical for first quarter of the year
- Community setting accounted for 60% of XPOVIO net revenue in 1Q 24 driven by strong NRx growth and offset by refill impact
- Academic setting XPOVIO demand grew QoQ, with increased use immediately preceding and following T cell therapies in later lines
- XPOVIO new patient mix in 2-4L stable QoQ
- Re-affirming full year 2024 XPOVIO net product revenue guidance of $100-$120M

Selinexor Approved in Over 40 Countries with Reimbursement Achieved in Key Global Markets

- Positive recommendation from NICE to expand reimbursement of NEXPOVIO in the UK for 2L+ MM in April 2024
- XPOVIO added to China's National Reimbursement Drug List (NRDL), effective as of January 1, 2024
- Reimbursement approval for NEXPOVIO in Germany in December 2023



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

FINANCIAL HIGHLIGHTS AND MILESTONES

Recent Transactions Extend Maturities into 2028 and 2029

Convertible Notes Exchange

- Extends maturity on 86% of convertible debt to 2029
  - Exchanges $148.0 million of the current $172.5 million 3% Convertible Notes due 2025 at a 25% discount to par in exchange for $111.0 million newly issued 6% Second Lien Convertible Notes due in 2029 plus warrants;
  - Issued $5.0 million New Convertible Notes to HCRx
  - Remaining $24.5 million of existing convertible notes due October 2025

New Secured Term Loan

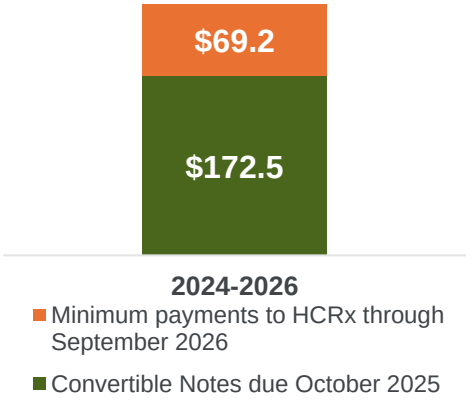
- New $100.0 million Senior Secured Term Loan due 2028 provided by the top four existing convertible note holders and HCRx

Amended HealthCare Royalty (HCRx) Agreement

- $69.2 million of the proceeds from the new Senior Secured Term Loan used to address the remaining principal portion of HCRx's $135.0 million investment
  - Eliminates potential gross-up payments to HCRx
  - Reduces royalty rate on worldwide XPOVIO net revenues and future products to 7.0% down from 12.5%

Maturity Profile

Pre-Transactions



Post-Transactions

1Q 2024 Financial Results

Statements of Operations ($ millions)	1Q 2024	1Q 2023
Total Revenue	**$33.1**	**$38.7**
XPOVIO Net Sales	26.0	28.3
License and Other Revenue	7.1	10.4
Total Operating Expenses	**$66.8**	**$69.6**
Cost of Sales	1.9	1.4
Research and Development Expenses	35.4	32.3
Selling, General & Administrative Expenses	29.5	35.9
Net Loss	**$37.4**	**$34.1**
Net Loss per share	**$0.32**	**$0.30**

Balance Sheet ($ millions)	March 31, 2024	Dec 31, 2023
Cash, Cash Equivalents Restricted Cash and Investments	**$149.3**	**$192.4**

2024 Financial Guidance

- Total Revenue of $140-$160 million
- U.S. XPOVIO Net Product Revenue of $100-$120 million
- R&D and SG&A Expenses of $260-$280 million, including estimated non-cash stock compensation of ~ $20-$25 million
- Cash runway expected to be sufficient to fund planned operations into the end of 2025*

* Excluding re-payment of the Company's remaining 2025 convertible notes and $25 million minimum liquidity covenant under the 2028 senior secured term loan

Richard Paulson
Chief Executive Officer

CLOSING REMARKS

Accelerating Innovation and Growth Strategy with Key Milestones in 2024 and 2025

Multiple Myeloma

- ❑ Leverage commercial capabilities and grow XPOVIO (2024)
- ❑ Continuation of global launches (2024)
- ❑ Report data on XPOVIO pre/post T cell therapy (2024)
- ❑ Report top line results from EMN29 trial (1H 2025)

Endometrial Cancer

- ❑ Continue to present updated exploratory results from the *TP53* subgroup from the SIENDO trial at medical conferences (2024)
- ❑ Complete enrollment in pivotal EC-042 Phase 3 trial in *TP53* wild-type EC (2H 2024)
- ❑ Report top-line results from pivotal EC-042 Phase 3 trial in *TP53* wild-type EC (1H 2025)

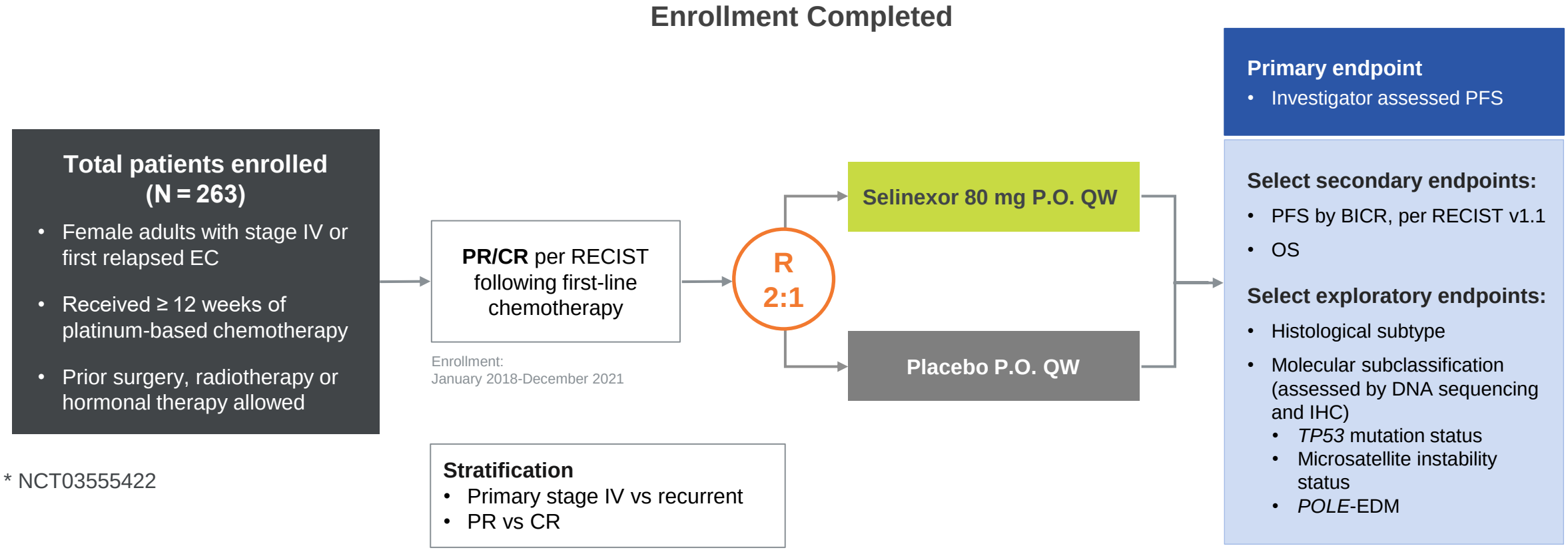
Myelofibrosis

- ❑ Report updated results from the Phase 1 trial of selinexor + ruxolitinib in treatment-naïve MF (2024)
- ❑ Report preliminary data from MF-044 Phase 2 study with single agent selinexor in JAKi naïve MF with platelet counts below 50 × 10^9/L. (2H 2024)
- ❑ Report top-line results from Phase 3 trial of selinexor + ruxolitinib in treatment-naïve MF (2H 2025)

Karyopharm® Therapeutics

APPENDIX

SIENDO*: A Randomized Double-Blind, Phase 3 Trial of Maintenance with Selinexor / Placebo after Combination Chemotherapy for Patients with Advanced or Recurrent Endometrial Cancer[1,2]



* NCT03555422

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.

BICR, blinded independent central review; CR, complete response; EDM, exonuclease domain mutation; IHC, immunohistochemistry; MSI, microsatellite instability; OS, overall survival; PFS, progression-free survival; PO, per oral; POLE, polymerase epsilon; PR, partial response; QW, once weekly; R, randomized; RECIST, response evaluation criteria in solid tumors; TP53, tumor protein 53 gene

1. Maintenance With Selinexor/Placebo After Combination Chemotherapy in Participants With Endometrial Cancer [SIENDO] (ENGOT-EN5).Updated May 30, 2023. Accessed June 26, 2023. https://www.clinicaltrials.gov/study/NCT03555422?term=NCT03555422 2. Vergote I, et al. Presentation at: European Society for Clinical Oncology Virtual Plenary; March 17-18, 2022, Abstract VP2-2022.