BELIEVERS IN THE EXTRAORDINARY

JEFFERIES GLOBAL HEALTHCARE CONFERENCE

June 5, 2024

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Karyopharm® Therapeutics

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 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, which was filed with the Securities and Exchange Commission (SEC) on May 8, 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 drug has not been established by any agency.

Richard Paulson
Chief Executive Officer

INTRODUCTION

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.

Focused, High Potential Pipeline with 3 Pivotal Studies 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 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				

hematologic cancer solid tumor cancer

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.

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)

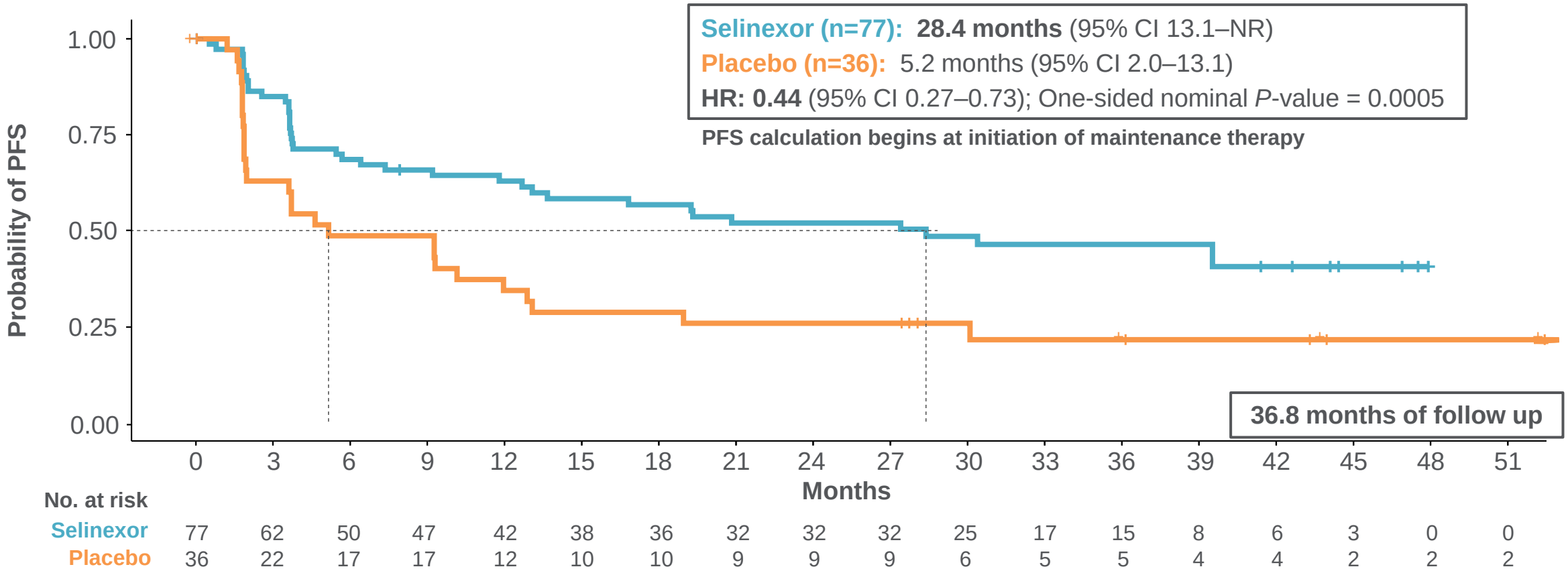
Myelofibrosis

- ❑ 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)

Well Funded With Expected Cash Runway Into End of 2025


Q&A

Long-term mPFS of 28.4 Months in *TP53*wt Subgroup

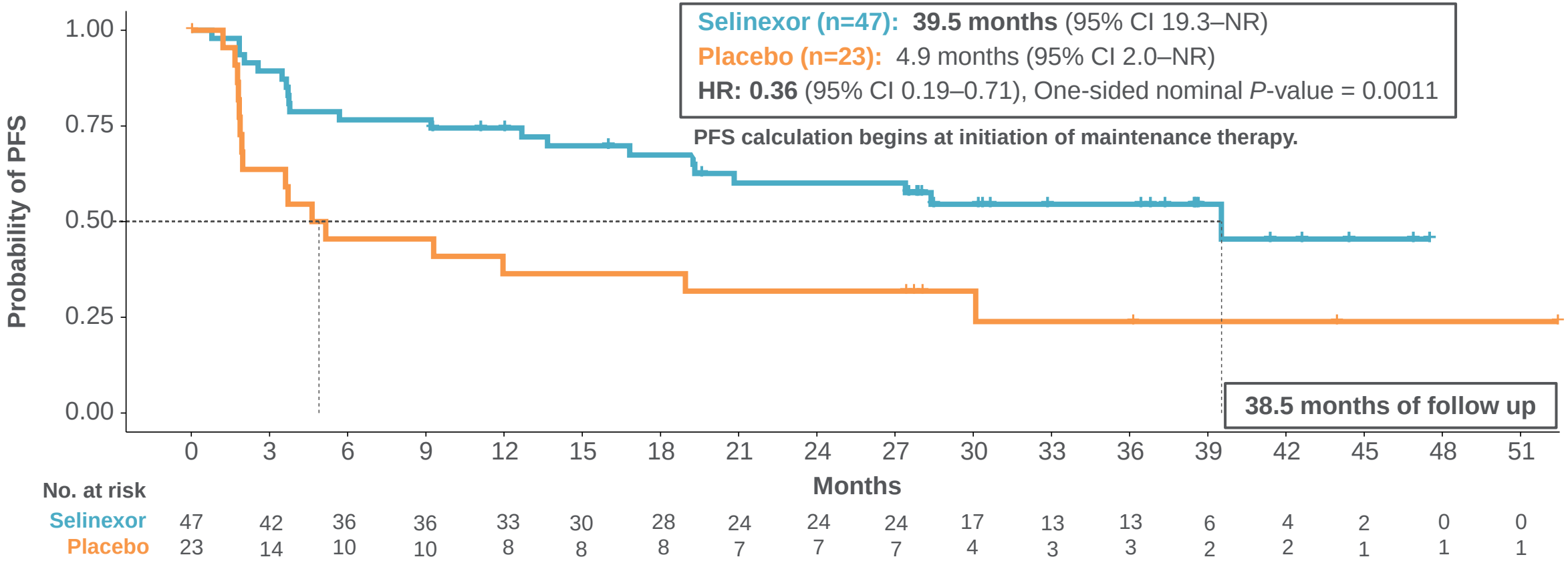


Data cutoff date: April 1, 2024

HR, hazard ratio; NR, not reached.

*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53* mutant, n=29).

Long-term mPFS of 39.5 Months in *TP53*wt/pMMR* Subgroup



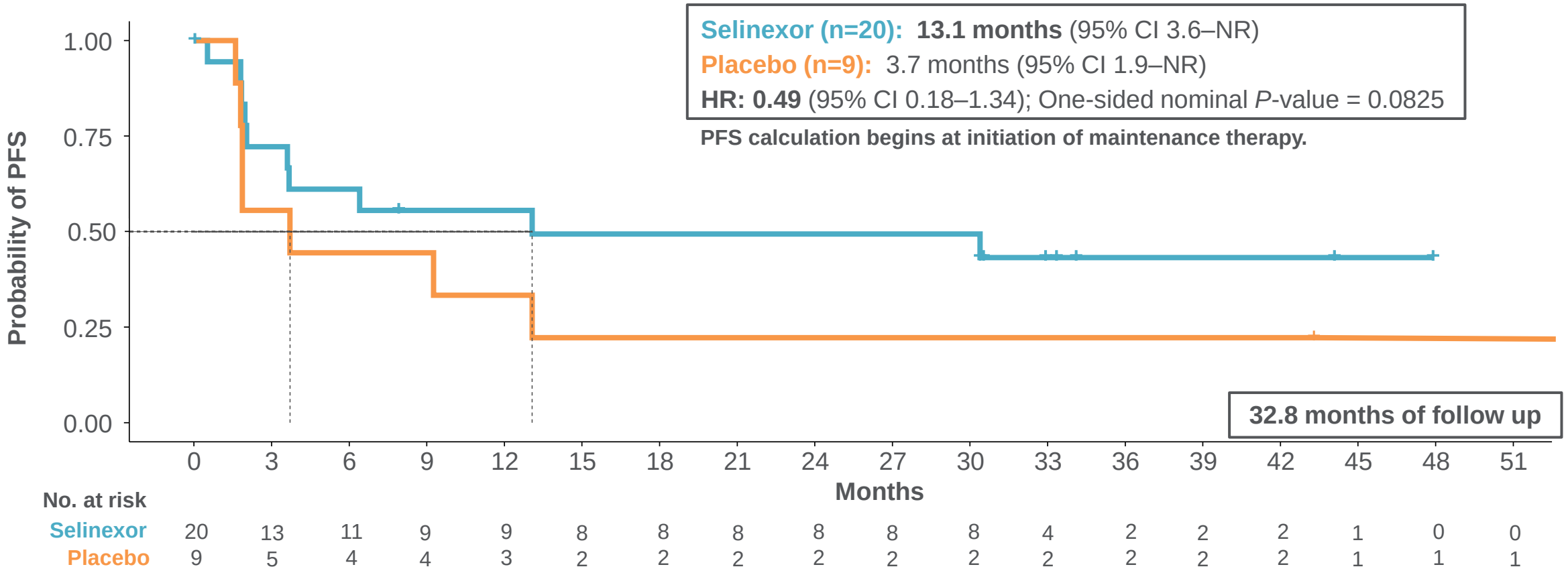
Data cutoff date: April 1, 2024

*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97; pMMR, n=164) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53*wt mutant, n=29; pMMR, n=20).

ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION® Transforming the standard of care™

Long-term mPFS of 13.1 Months in *TP53*wt/dMMR* Subgroup



Data cutoff date: April 1, 2024

*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97; pMMR, n=164) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53*wt mutant, n=29; pMMR, n=20).

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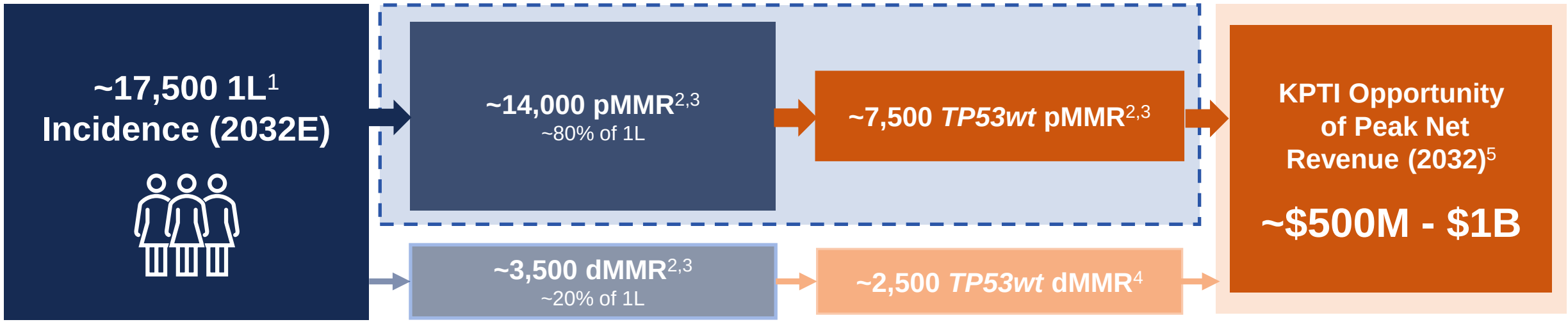
Selinexor Has Potential to be the First, Novel, Oral Maintenance Therapy to Market Targeting Patients with *TP53*wt Endometrial Cancer



Molecular classification has rapidly become the standard of care in endometrial cancer

~75%* of HCPs test for *TP53* Status

Marginal efficacy in *TP53* wt/pMMR patient population with currently available therapies

~75%* stated future intent to prescribe selinexor as maintenance therapy for *TP53* wt/pMMR patients

***Source: Double blinded physician survey conducted by leading 3rd party provider; data on file. Nov 2023. n=25 US Academic & Community HCPs**

1. Company estimates for 2032 based on Clarivate/DRG Endometrial Carcinoma Epidemiology Dashboard (2022 figures, pub 2020) 2. Mirza, M et al. (2023, October 2024). 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. 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 4. Vergote I, et al J Clin Oncol. 2023;41(35):5400-5410 5. 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