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MYTHIC Lunre+Camo Clinical Data Update

December 12, 2024

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Today’s agenda

1 **Introduction: About Repare**

Lloyd M. Segal
President & CEO
Repare Therapeutics

2 **Today’s Focus: Gynecologic Cancers**

Brian Slomovitz, MD
Director of Gynecologic Oncology
Mount Sinai Medical Center

3 **MYTHIC Lunresertib + Camonsertib Data**

Maria Koehler, MD, PhD
EVP and CMO
Repare Therapeutics

Paul Basciano, MD
VP, Clinical Development & Medical Affairs, Repare Therapeutics

4 **Clinical Path Forward**

Maria Koehler, MD, PhD
EVP and CMO
Repare Therapeutics

5 **Patient and Commercial Opportunity**

Phil Herman
EVP & CCO
Repare Therapeutics

6 **Conclusions, Q&A**

Lloyd M. Segal
President & CEO
Repare Therapeutics

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Introduction: About Repare

Lloyd M. Segal
President & CEO
Repare Therapeutics

Advancing pipeline of precision oncology therapeutics

Repare's mission is to apply synthetic lethal biology to bring practice-changing, precision therapies to patients who need them

Program	Tumor lesion	Drug target	Preclinical	Ph 1	Ph 2	Ph 3	Rights
Lunresertib (RP-6306)[1]	CCNE1, FBXW7 + PPP2R1A	PKMYT1	Camonsertib Combination; Chemotherapy Combinations (FOLFIRI/Gemcitabine); Debio 0123 WEE1i Combination (Debiopharm)	Today's Focus			REPARE THERAPEUTICS
Camonsertib (RP-3500)	ATM + 16 STEP[2] lesions[2]	ATR	Monotherapy NSCLC Expansion; Other Combinations (PARP Inhibitors/Gemcitabine)				REPARE THERAPEUTICS
RP-1664	TRIM37-high	PLK4	Monotherapy (LIONS)				REPARE THERAPEUTICS
RP-3467	BRCA1/2	Polθ ATPase	Monotherapy & PARPi Combo (POLAR)				REPARE THERAPEUTICS

Note: [1] Excludes ISTs. [2] Additional lesions discovered to be synthetic lethal with ATR using Repare's SNIPRx® Targeted Expansion of Patient Populations (STEP[2]) screens.

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POC achieved for registrational trial; Ph 3 EC start in 2025

We achieved POC for lunre+camo combo in EC and PROC

- Combination was effective and well-tolerated
- Clear signals, opportunity for registrational trials in both EC and PROC
- Opportunity to deliver important, new and chemo-alternative treatment options

Initiating pivotal Ph 3 randomized trial in EC in 2025

- Regulatory alignment with FDA and EMA, including accelerated approval options
- Simple Contribution of Components trial obligation, under way shortly
- PROC a de-risked life cycle opportunity, subject to capital and/or partnering

Our objectives for today:

- Set the stage for this product opportunity
- Walk you through our lunre+camo data
- Describe our planned registrational trial and supporting regulatory guidance
- Detail product opportunities longer term
- Answer your questions

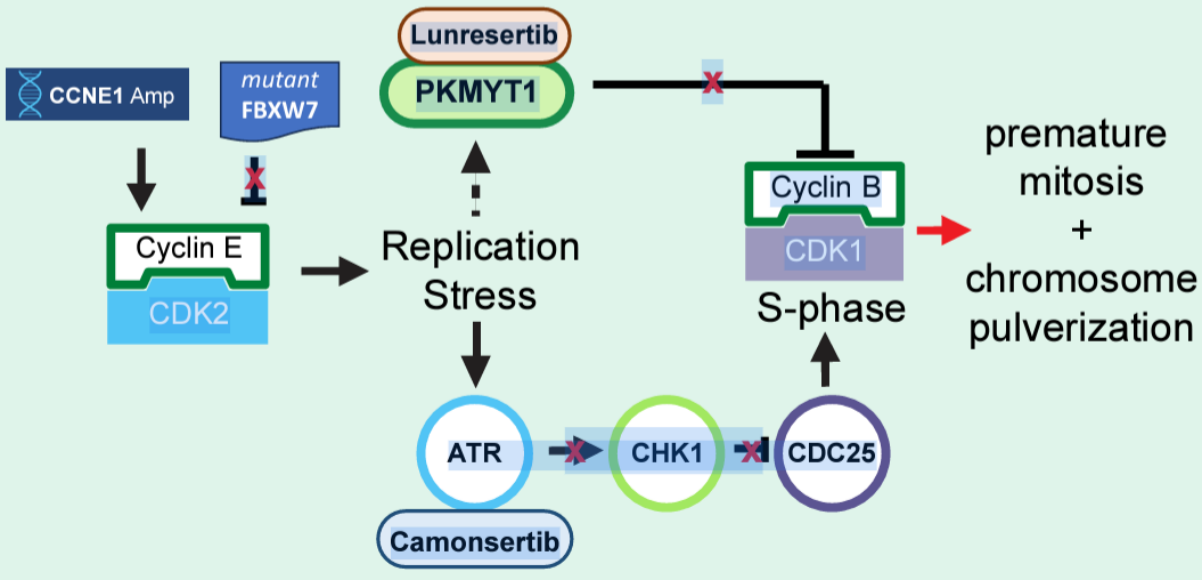
Abbreviations: POC, proof of concept.

Some key terms and abbreviations in today's discussion

Term	Abbreviation
AE	Adverse events
Camo	Camonsertib, a proprietary ATR inhibitor
EC	Endometrial cancer
ICI	Immune checkpoint inhibitor (e.g., PD-1 and PD-L1)
Lunre	Lunresertib, a proprietary PKMYT1 inhibitor
Lunre BM+	lunre-sensitizing biomarkers: CCNE1amp, mFBXW7 or mPPP2R1A
Lunre+camo	Clinical combination of lunresertib and camonsertib
MoA	Mechanism of action
OC	Ovarian cancer
PROC	Platinum-resistant ovarian cancer, a subset of OC
SOC	Current "standard of care"
TRAE	Treatment-related adverse events

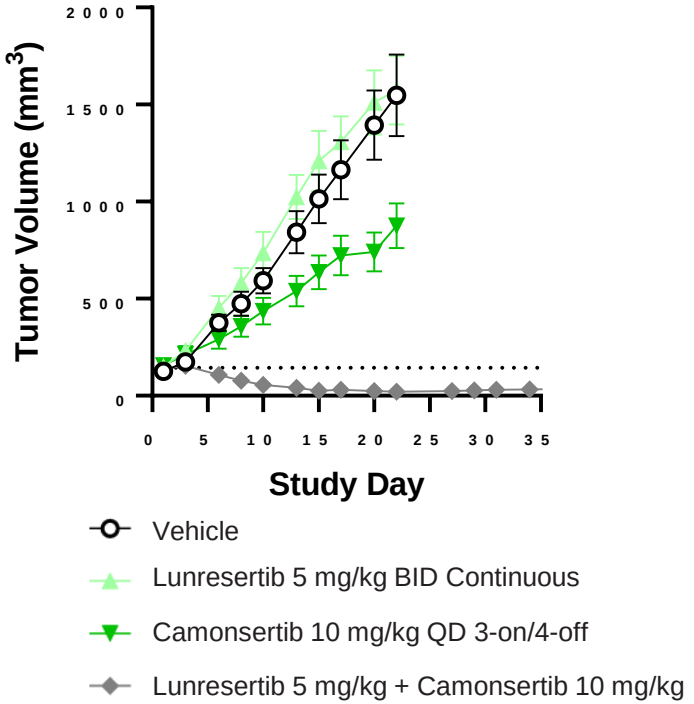
Our mechanistic rationale for lunre+camo

Lunresertib (PKMYT1i) + camonsertib (ATRi) enhance CDK1 activation and premature mitosis

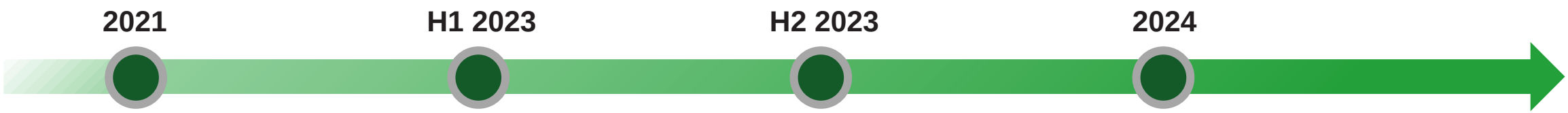


References: 1 ANE poster B057: Gallo et al. Preclinical development of PKMYT1 and ATR inhibitor combinations. ATR, ataxia telangiectasia and Rad-3 related; CDC25, cell division cycle-25; CDK, cyclin-dependent kinase; CHK1, checkpoint kinase 1; PKMYT1, protein kinase, membrane associated tyrosine/threonine 1.

Lunre+camo showed complete regressions *in vivo* (DLD1 model) FBXW7-/-



MYTHIC clinical trial: Lunre+camo background and overview



Initiated MYTHIC, first clinical trial targeting PKMYT1 inhibition

Rationale: preclinical synergies in combination

First **topline data**: monotherapy and lunre + camo combination (safety, tolerability, PK/PD, preliminary anti-tumor activity)

Established initial **RP2D**

Initiated EC and PROC **expansion cohorts**

Dose / schedule **optimized**

EC and PROC data at optimized RP2D (n=51) as of *Nov 14, 2024*

Regulatory alignment with FDA/EMA

Pivotal path forward in EC; Ph 3 preparation underway

Key achievements:

- ✓ **Achieved POC in expansion cohorts in EC and PROC**
- ✓ **Regulatory path agreed upon for Ph 3 pivotal studies**

- ✓ **Established RP2D and schedule, optimized for improved tolerability:**

  Lunre 80 mg BID + 80mg camo QD, both given 3 days, weekly or 2 weeks on/1 week off, based on hemoglobin level (**optimized dosing** with regulatory agreement)

- ✓ **Established safety and tolerability profile for lunre monotherapy and camo, FOLFIRI combinations**

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Lunre+camo today in EC and PROC

A potentially effective, well-tolerated, convenient and differentiated option

Overall

- **Encouraging efficacy in heavily pre-treated patients with adverse genomic profile and worse prognoses**
- **Promising rate of tumor responses, durable benefit**
- **Potential alternative to ADCs with improved safety and tolerability profile**
- **Clear registrational opportunities for both tumors**
- **Mirvetuximab-like opportunity for BM+ subset**

Endometrial Cancer

Strong response rate and benefit: 25.9% response rate and 24wk PFS 43%

Aiming to **define new 2L+ SOC**

Greater **unmet need** with rising incidence, mortality

PROC

Compelling response rate and benefit: 37.5% response rate and 24wk PFS 45%

Attractive **biomarker directed approach** with **differentiated tox profile**

Path forward

Focus of initial registrational trials

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Today's Focus: Gynecologic Cancers

Brian Slomovitz, MD, MS, FACOG

Director, Gynecologic Oncology
Co-Chair of Cancer Research Committee
Mount Sinai Medical Center, Miami Beach

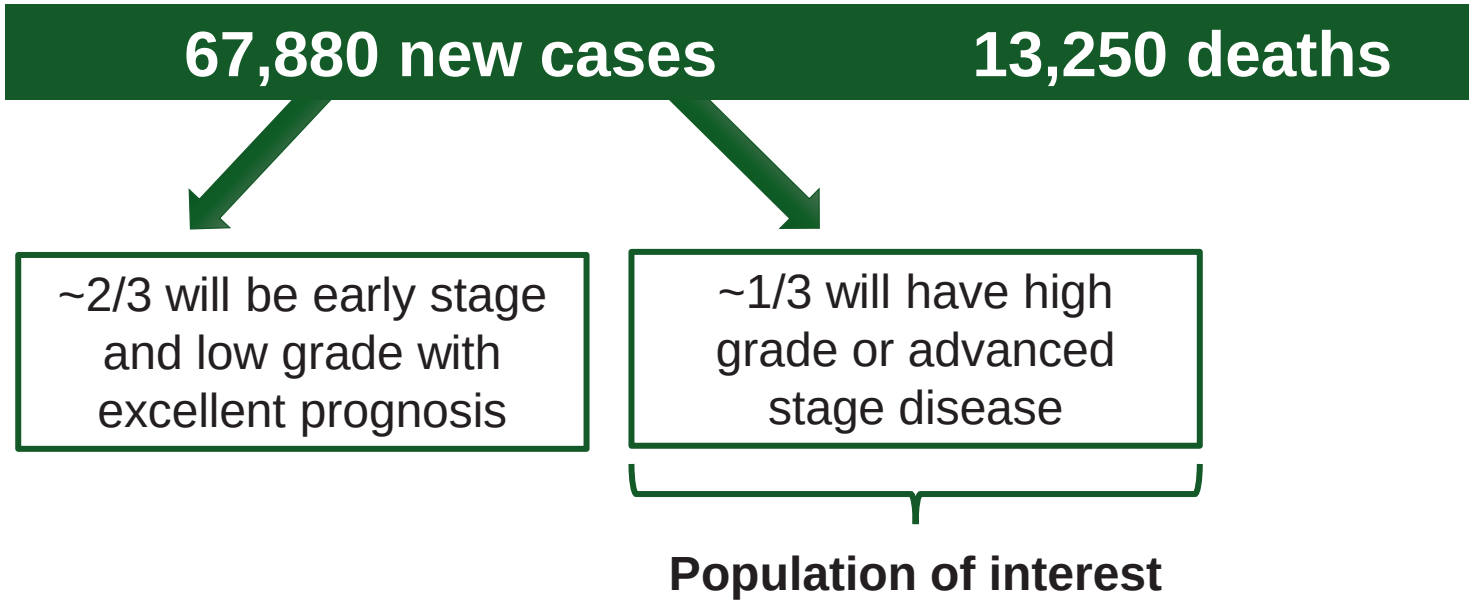
Professor, Obstetrics and Gynecology
Florida International University

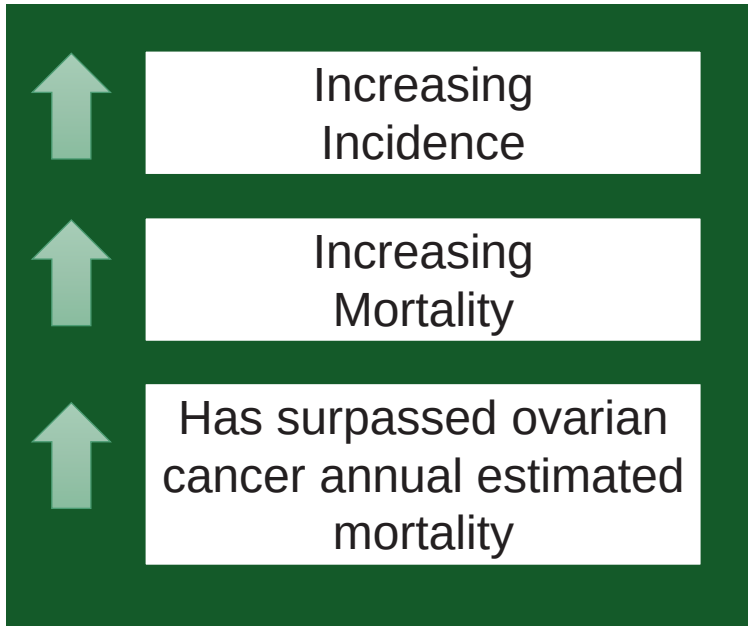
Member, Board of Directors GOG Foundation
Uterine Cancer Clinical Trial Lead, GOG Partners

Consulting / Advisory Board *for: Aadi, AstraZeneca, Clovis, Eisai, Eli Lilly, Gilead, GlaxoSmithKline, GOG Foundation, Immunocore, Incyte, MSD, Novartis, Novocure, Regeneron, and Seagen.*

Endometrial cancer in 2024

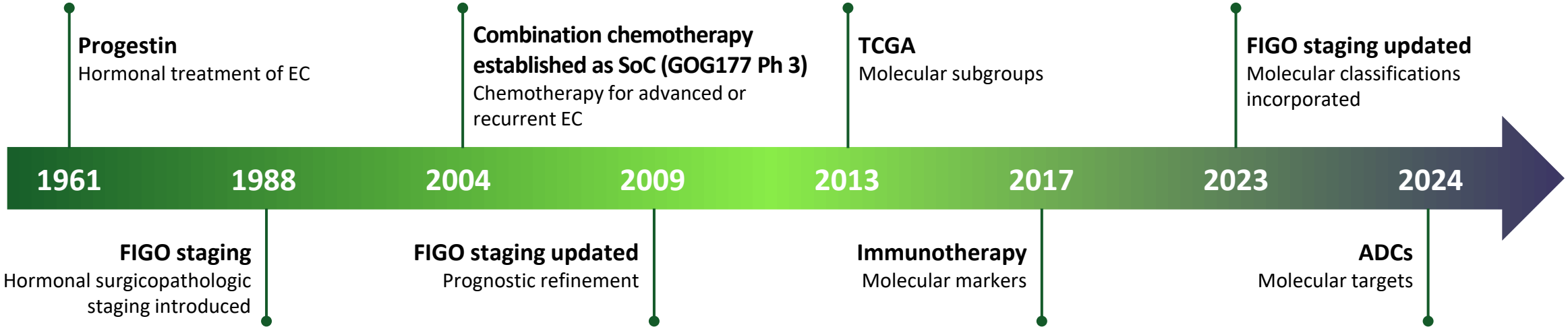
- Only gynecologic cancer with **rising incidence and mortality**
- Has now **exceeded ovarian cancer in annual estimated deaths**
- Corrected for hysterectomy rates, uterine cancer is the **2nd most common cancer** among women





References: Siegel et al. Cancer Statistics 2024
Cancer Facts & Figures 2023. American Cancer Society. Available at https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf. Accessed January 31, 2023.

Endometrial SOC has evolved to be molecularly focused



NCCN guidelines recommend molecular analysis of endometrial cancers, **including universal testing for MMR/MSI,** and considering pembrolizumab or dostarlimab for first- or second-line treatment of dMMR/MSI-H tumors; pembrolizumab + chemo or dostarlimab + chemo for first-line treatment of all adult patients; and trastuzumab-deruxtecan for previously treated unresectable or metastatic HER2-positive solid tumors.

Abbreviations: ADCs, antibody-drug conjugates; **ESGO**, European Society of Gynaecological Oncology; **ESP**, European Society of Pathology; **ESTRO**, European Society for Radiotherapy and Oncology; **FIGO**, International Federation of Gynecologists and Obstetricians; **GOG**, Gynecologic Oncology Group; **MMR**, mismatch repair; **MSI**, microsatellite instability; **SoC**, standard of care; **TCGA**, The Cancer Genome Atlas.

References: Yang S, et al. *Discov Med*. 2011;12:205-212; Haltia U-M, et al. *J Gynecol Oncol*. 2014;25:30-35; Fleming GF, et al. *J Clin Oncol*. 2004;22:2159-2166; The Cancer Genome Atlas Research Network, et al. *Nature*. 2013;497:67-73; Concin N, et al. *Int J Gynecol Cancer*. 2021;31:12-39; Berek JS, et al. *Int J Gynecol Obstet*. 2023;162:383-394; National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed September 23, 2024.

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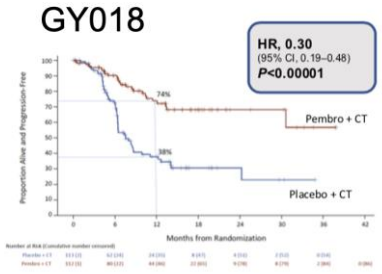
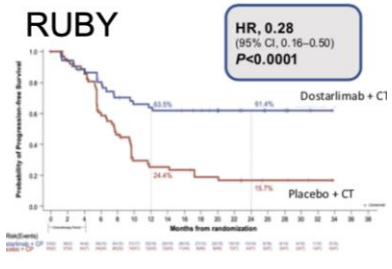
IO+Chemo: New 1st line SOC, but benefit mostly in dMMR population

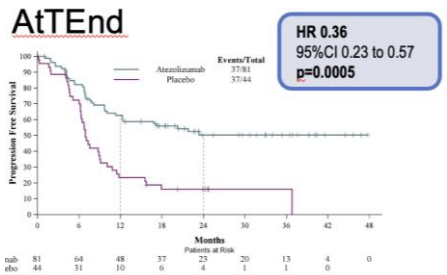
dMMR



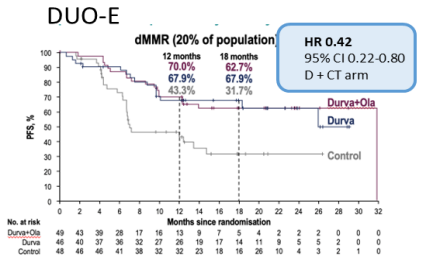
	No with events%	Median
Pembro + CT	23.2	NR (30.6-NR)
Placebo + CT	52.2	7.6 (6.4-9.9)



	No with events%	Median
Dorsta + CT	35.8	NR (11.8-NR)
Placebo + CT	72.3	7.7 (5.6-9.7)

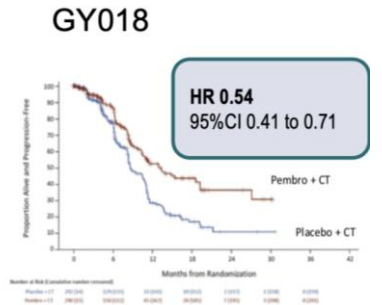


	No with events%	Median
Atezo + CT	45.7	NR (12.3-NR)
Placebo + CT	84.1	6.9 (6.2-9.0)

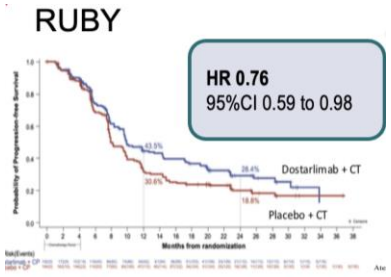


	No with events %	Median
Durva + CT	32.6	NR (NR-NR)
Durva + O + CT	37.5	31.8 (12.4-NR)
Placebo + CT	51	7.0 (6.7-14.8)

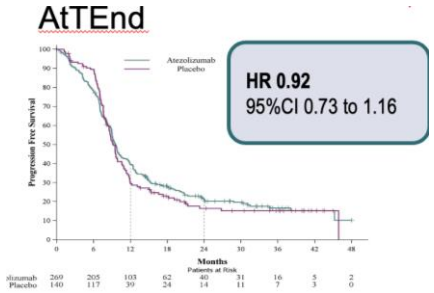
pMMR



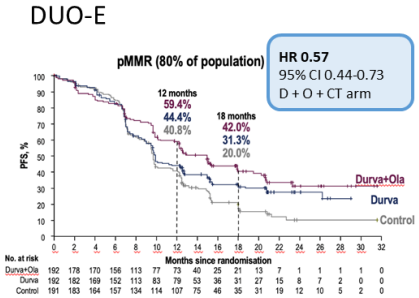
	No with events%	Median
Pembro + CT	30.6	13.1 (10.5-18.8)
Placebo + CT	45.5	8.7 (8.4-10.7)
Maturity	38.1%	



	No with events%	Median
Dorsta + CT	60.4	9.9 (9.0-13.3)
Placebo + CT	70.7	7.9 (7.6-9.8)
Maturity	65.4%	



	No with events%	Median
Atezo + CT	78	9.5 (9.0-10.4)
Placebo + CT	77	9.2 (8.5-9.9)
Maturity	78%	



	No with events %	Median
Durva + CT	64.6	9.9 (9.4-12.5)
Durva + O + CT	56.5	15 (12.4-18)
Placebo + CT	77.1	9.7 (9.2-10.1)

Impressive benefit in dMMR (<30%) tumors

Less benefit in pMMR (>70+%) tumors

MYTHIC tumors are pMMR

Approval for "all comers"

Abbreviations: **dMMR**, deficient mismatch repair; **pMMR**, proficient mismatch repair.
Note: Slide courtesy of Dr. David Tan ESMO 2023 – Revised.

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After chemotherapy + immune checkpoint inhibitor (ICI)…

The NCCN guided treatment is single agent chemotherapy…

What do I, as a gynecologic oncologist, need for my patients with endometrial cancer?

1. Treatment **solution after patients received ICI** and chemotherapy – especially pMMR
   - Lunre+camo data in pMMR to follow
   - ADCs are effective – **is there an alternative to chemo-based ADC? Where do ADCs fit?**

2. What is the optimal treatment for the specific patient I am seeing – **biomarker-based selection is critical**

3. Patients deserve good quality of life; **treatment should be well-tolerated** and, requiring, if possible, **limited monitoring so patient can enjoy their life** and healthcare system is not overwhelmed

GOG and European groups are working together to quickly bring the solutions to patients

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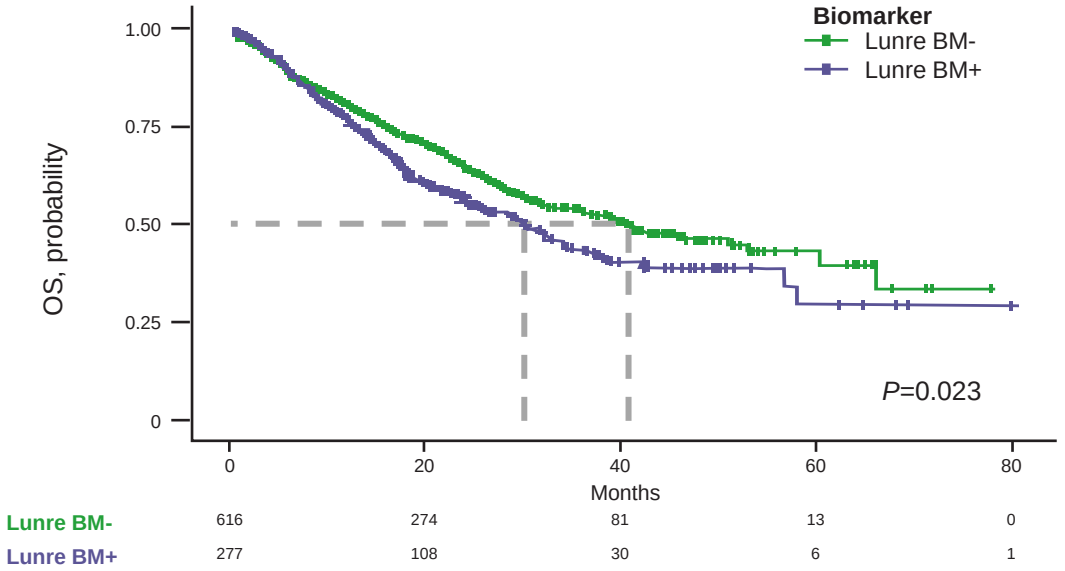
Tumors with Lunre BM+ have significantly worse outcomes

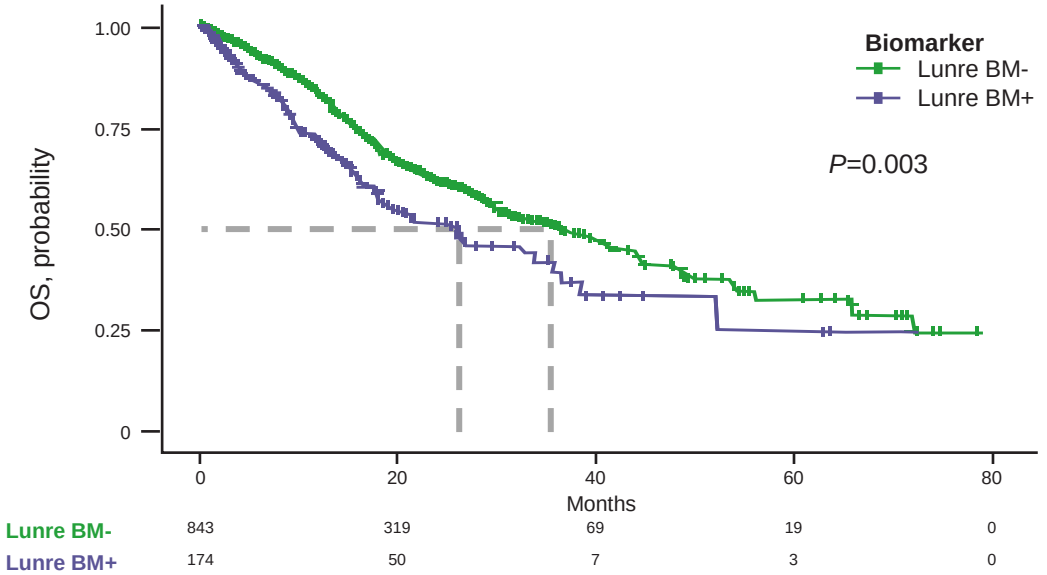
Probability of survival for a subset of 30% of patients with Lunre BM+ *(CCNE1, PPP2R1A, FBXW7)*

Endometrial Cancer[1]



Biomarker	Patients, n	mOS (95% CI), months
Lunre BM–	616	41 (31-60)
Lunre BM+	277	30 (24-38)

Ovarian Cancer[1]



Biomarker	Patients, n	mOS (95% CI), months
Lunre BM–	843	36 (30-43)
Lunre BM+	174	26 (18-38)

Abbreviation: LUNRE BM-, any genes other than Lunre BM+ specified genes **(CCNE1, PPP2R1A, FBXW7).**

References: 1. CancerMPact®, Treatment Architecture, United States, 2021; accessed 5/19/23) and lesion prevalence (TCGA). Schram AM, et al. *AACR Ovarian Cancer Research Symposium,* 2024.

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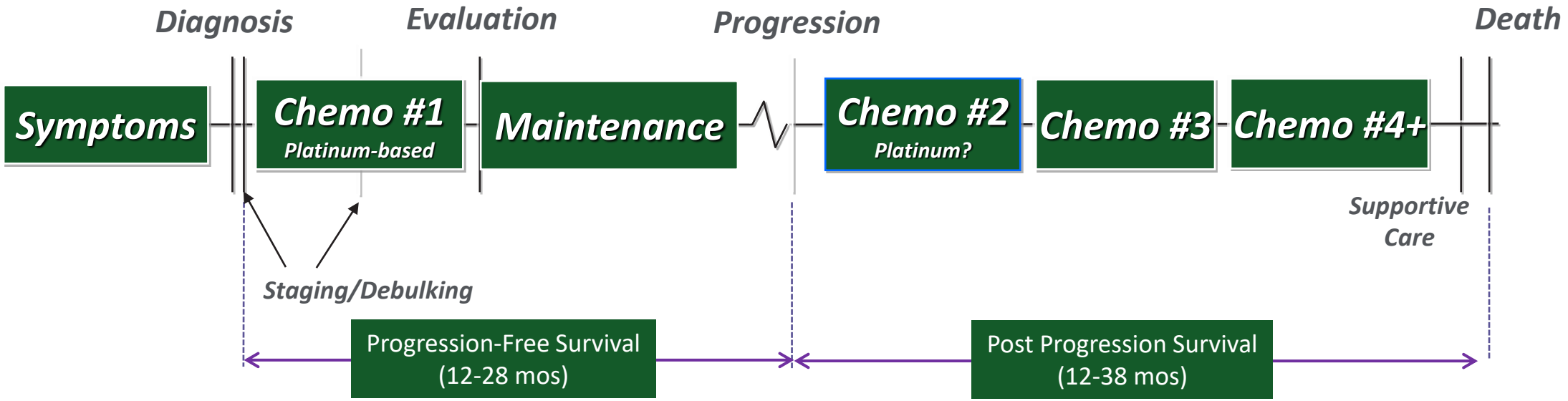
Ovarian Cancer: Natural history – we have chemotherapy…



- 19,680 women in the US will be diagnosed with ovarian cancer in 2024; 12,740 will die from the disease
- The ability to re-treat with platinum-containing chemotherapy after progression has major implications for survival
- When women become resistant to platinum treatment (PROC), median survival is only 12-18 months

Critical need for novel, well tolerated therapies

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Opportunity to meet urgent patients' needs with a chemo-free regimen

Lunre BM status is linked to significantly reduced mOS

Attractive chemotherapy-free regimen with comparable efficacy to emerging ADC is needed

We need studies applying tumor selection – the right approach that helps patients the most

Endometrial Cancer: There is no approved second line therapy after previous ICI+ chemotherapy

Ovarian Cancer: Existing therapies are insufficient to manage high-risk lunre BM+ tumors

There is no approved therapy for the Lunre BM+ tumors

Abbreviations: mOS, median overall survival.

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MYTHIC Study Data

Maria Koehler, M.D., Ph.D.
EVP, Chief Medical Officer
Repare Therapeutics

Paul Basciano, M.D.
VP, Clinical Development
& Medical Affairs
Repare Therapeutics

Overview of clinical data presentation

Overall results observed in gynecologic tumors

Endometrial cancer data

Platinum-resistant ovarian cancer data

Key perspectives on our MOA-driven response profile and our differentiation

Registrational path forward for endometrial cancer

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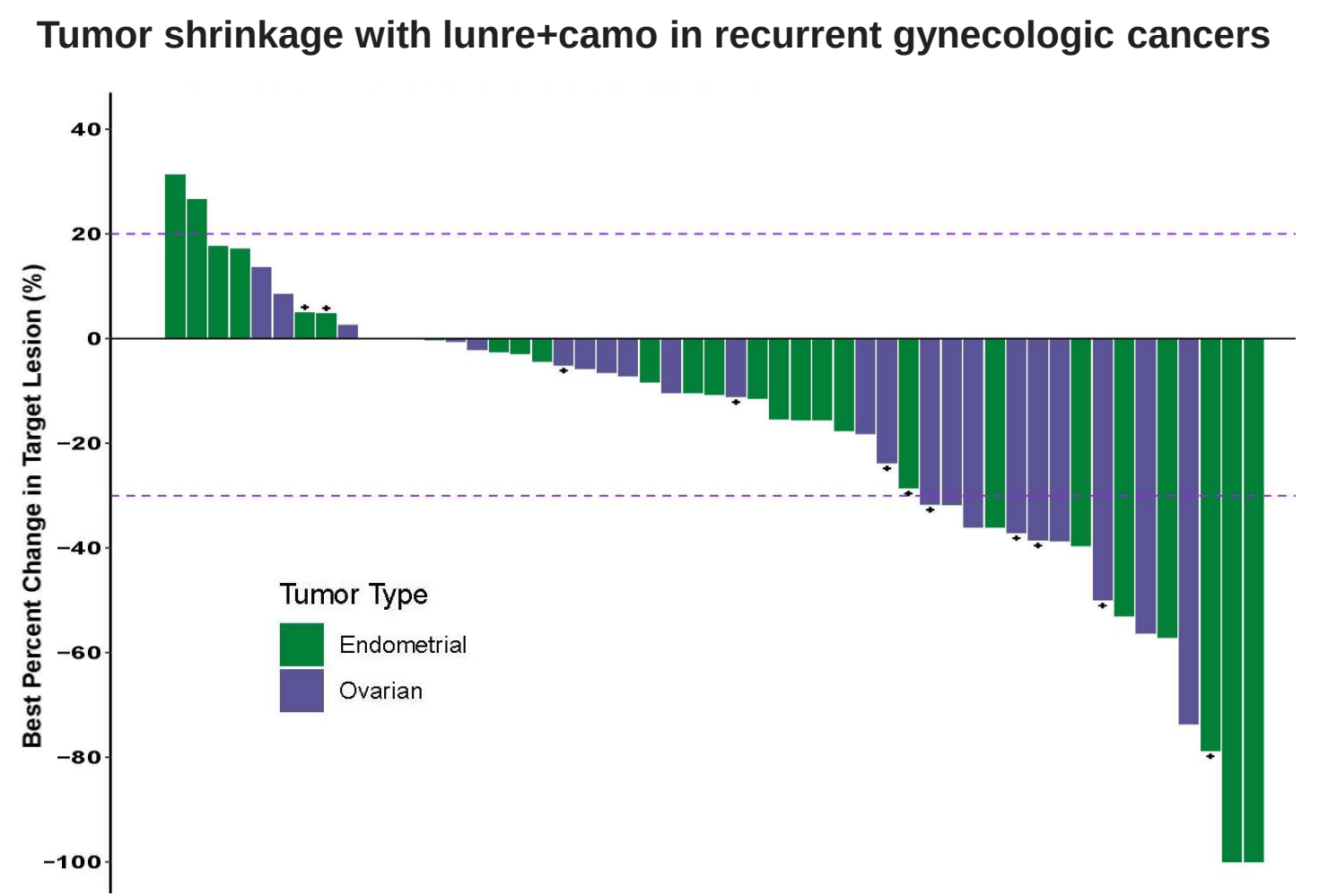
Significant overall efficacy observed with lunre+camo in gyn tumors



In efficacy-evaluable patients with EC or PROC at RP2D:

- **73%** of patients had tumor shrinkage
- **31%** (16/51) response rate (confirmed and unconfirmed)

Note: +, denotes treatment ongoing

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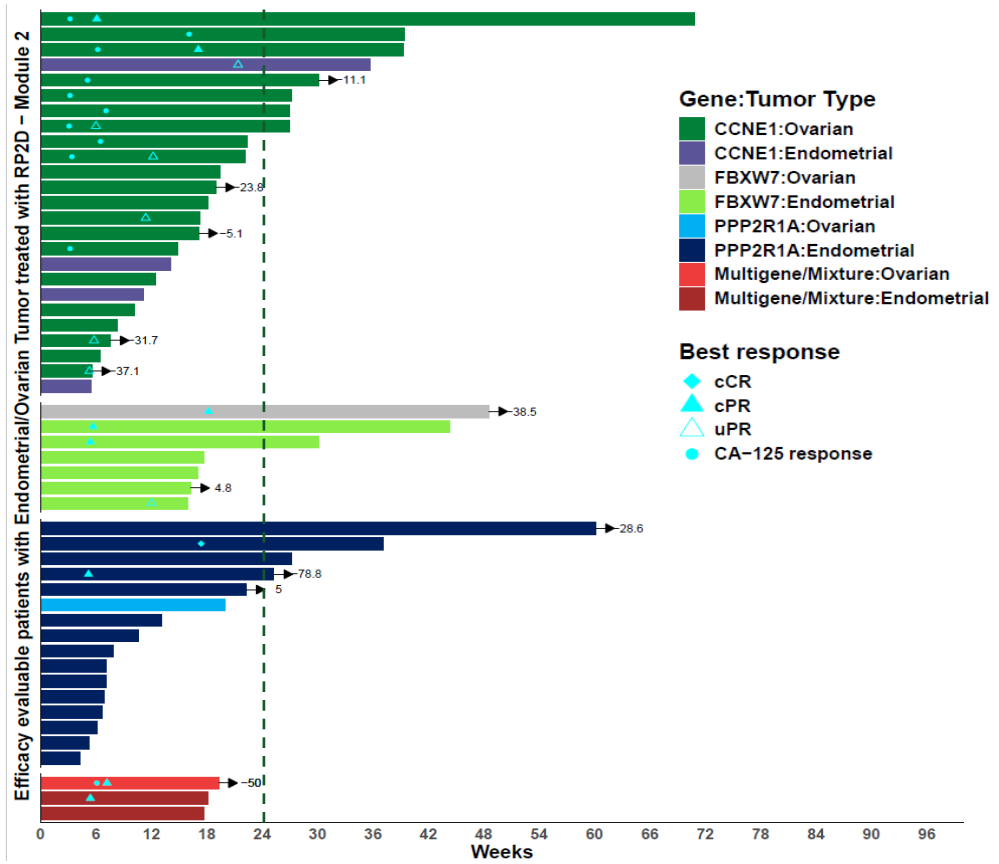
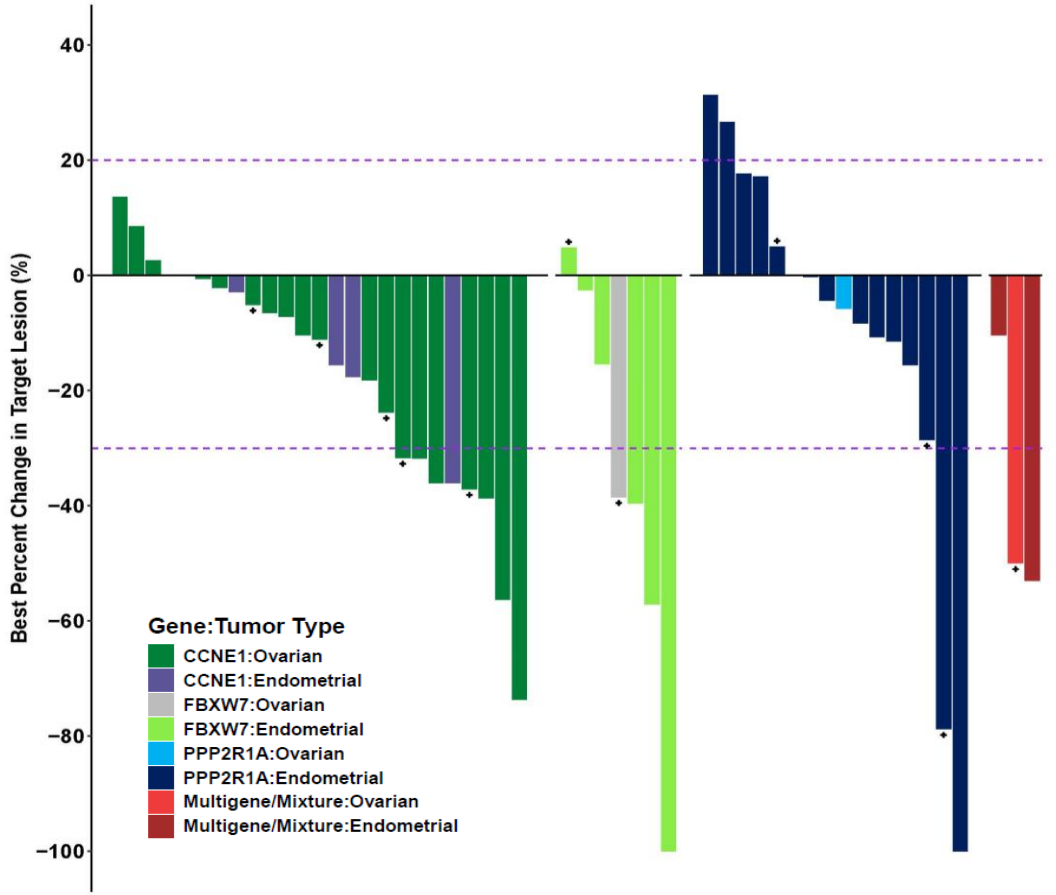
Similar efficacy seen across all BM+ subsets in PROC and EC

Duration on therapy by genomic lesion



Best degree of tumor shrinkage on therapy



Note: +, denotes treatment ongoing

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Favorable safety and tolerability vs. current and emerging treatments

Safety profile and tolerability at RP2D

TRAEs in ≥10% of patients	RP2D (all tumors; optimized dose) (N=67)		
	All Grade n (%)	Grade 3 n (%)	Grade 4 n (%)
Any Event	61 (91.0)	29 (43.3)	2 (3.0)
Anemia	49 (73.1)	18 (26.9)	0
Nausea/Vomiting	37 (55.3)	1 (1.5)	0
Rash pooled	27 (40.4)	3 (4.5)	0
Fatigue	18 (26.9)	2 (3.0)	0
Neutropenia	16 (23.9)	7 (10.4)	1 (1.5)[1]
Stomatitis	20 (29.9)	3 (4.5)	0
Decreased appetite	13 (19.4)	0	0
PPE syndrome	13 (19.4)	1 (1.5)	0
Diarrhea	10 (14.9)	0	0
WBC count decreased	11 (16.4)	1 (1.5)	2 (3.0)
Dizziness	7 (10.4)	0	0
Pyrexia	7 (10.4)	0	0

RP2D (all tumors)	N (%)
Serious TRAE	5 (7.5)
TRAE leading to dose withdrawn or therapy discontinued	2 (3.0)
TRAE Leading to death	0

- **Most frequent, on target GR3 event was anemia addressed with dose optimization based on hemoglobin level**
- **No thrombocytopenia or alopecia of any grade**
- **Rash/muco-cutaneous tox generally brief and low grade**
- **Consistent tolerability/safety profile in gynecologic patient subset**
- **FDA, EMA agreement on dose and schedule**

Median observation time for optimized dose: 15 weeks (range 1-49 weeks)

Note: 1. One patient had both Gr4 neutropenia and Gr4 WBC count decrease reported, concomitant with a viral infection and allergic reaction to cephalosporin (unrelated).

Lunre+camo potentially addresses unmet need in 2L+ EC

Patients heavily pre-treated, tumors with poor prognoses at study entry

Endometrial cancer
N=27

Heavily pre-treated patients:

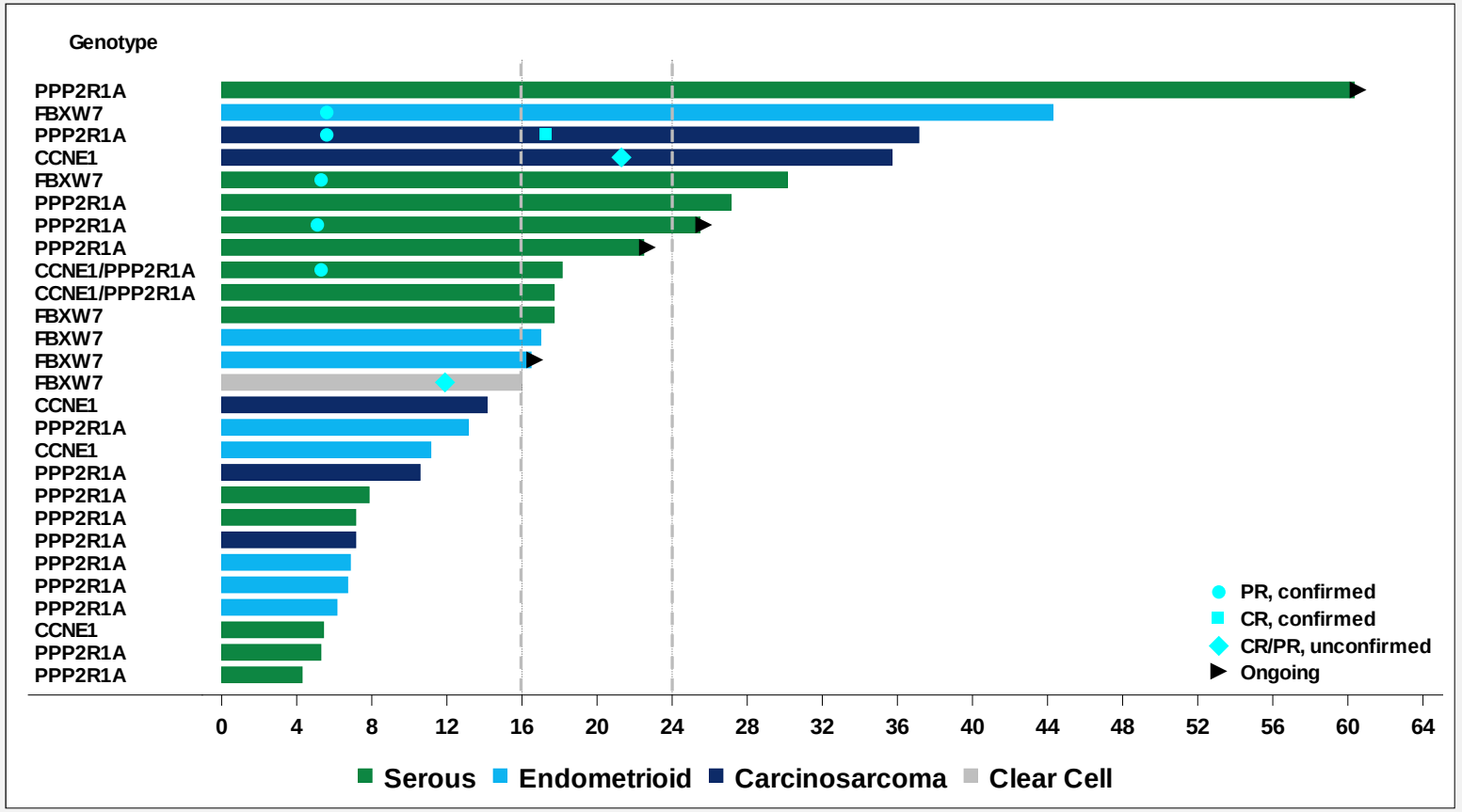
- **100% prior platinum therapy**
- **77.8% received prior ICIs**
- **59% treated as 4th line or beyond**

Age (years)	Median: 67
Racial Demographics	White: 70.4% / Black: 14.8% / Other: 14.8%
ECOG Performance Status	0: 37%, 1: 63%
Prior Therapies	Platinum: 100%, ICI: 77.8%
Lines of Therapy	3 or more: 59%
Histology	High-risk in all patients (carcinosarcoma 18.5%)
P53 Mutation	85%
MSI Status	No MSI-high detected, indicating pMMR status
Genotypes	CCNE1: 15%, FBXW7: 22%, PPP2R1A: 56%, multiple 7%

REPARE THERAPEUTICS

EC: Meaningful clinical benefit of across histological subtypes

Duration of treatment on lunre+camo



- **Progression-free rate (KM) at 24 wks is 43% (95% CI: 21-63%):**
  - Similar to emerging ADCs with comparable or less prior ICI treatment[1]
- **CBR of 48.1%**
- **Patterns of benefit reflect MOA:**
  - Long-term benefit in patients despite tumor reductions not meeting RECIST response
  - Continuous slow reductions in tumor burden and late PRs

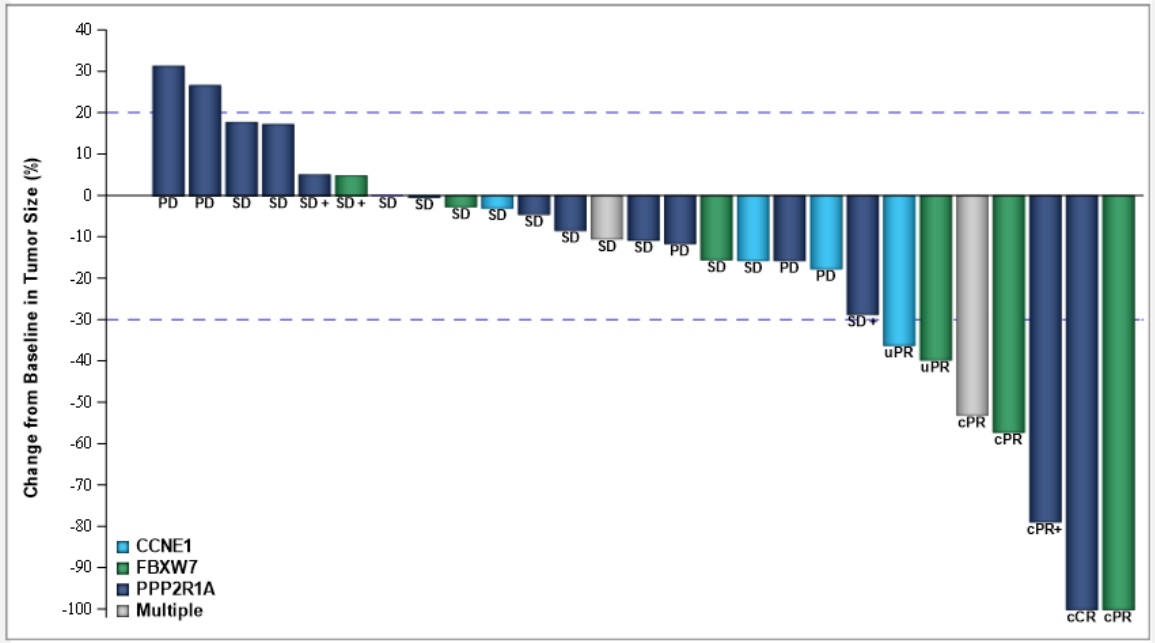
Abbreviations: KM; Kaplan Meier estimate. **CBR**, clinical benefit rate defined as having CR, PR, or at least 16 weeks treatment without PD.

Reference: 1. Bradley R. Corr et al. Efficacy and safety of sacituzumab govitecan in patients with advanced/metastatic endometrial cancer: updated results from TROPiCS-03, ESMO2024. Note that cross-trial comparisons are not based on head-to-head studies and are presented for informational purposes; no direct comparisons are being made.

REPARE THERAPEUTICS

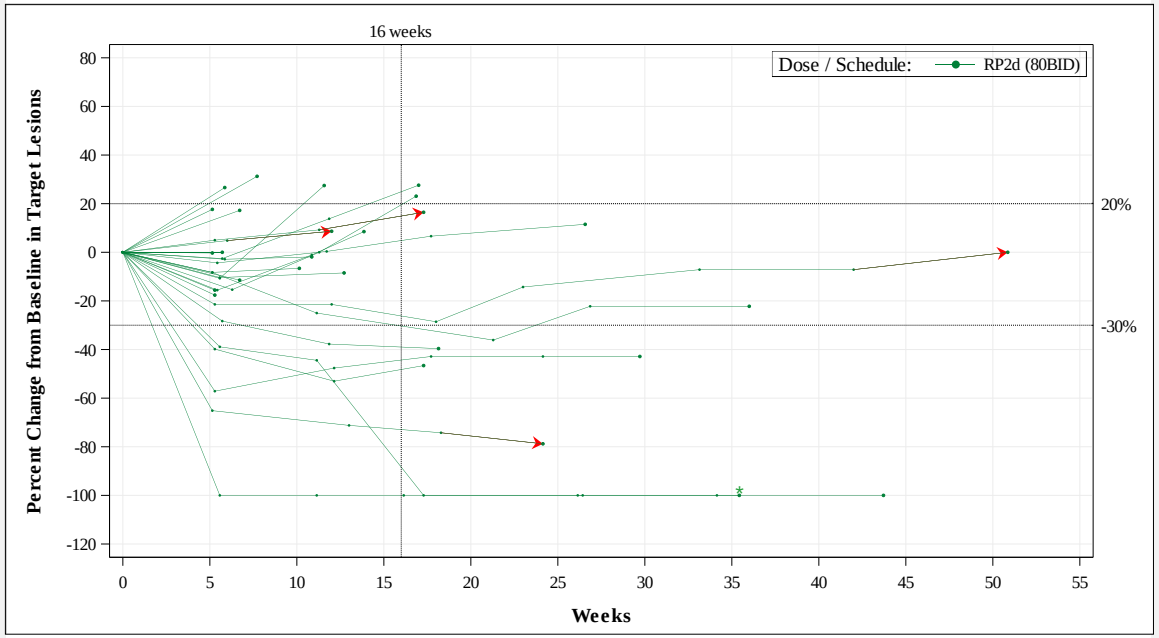
EC: Deep and durable responses across all lunre BM+ subsets

70% of patients experienced tumor shrinkage



ORR (conf.+ unconf.), %	25.9%
ORR (conf.), %	18.5%
CR	1 (3.7%)
PR	4 (14.8%)

Durable responses observed across histologies and biomarkers



Time to response (Range)	5-21 weeks

Duration of response up to ~30 weeks

Abbreviations: ORR, overall response rate**; conf.,** confirmed**; unconf.,** unconfirmed**; CR,** complete response**; PR,** partial response**; DOR,** duration of response; **PD**, progressive disease; **SD**, Stable disease.

Note: * Time of progression for one of two patients with 100% target lesion reduction

REPARE THERAPEUTICS

PROC: Lunre+camo addresses poor prognosis and chemo-resistance

Patients heavily pre-treated, tumors with poor prognostic features

PROC
Patients N=24

Heavily pre-treated patients:

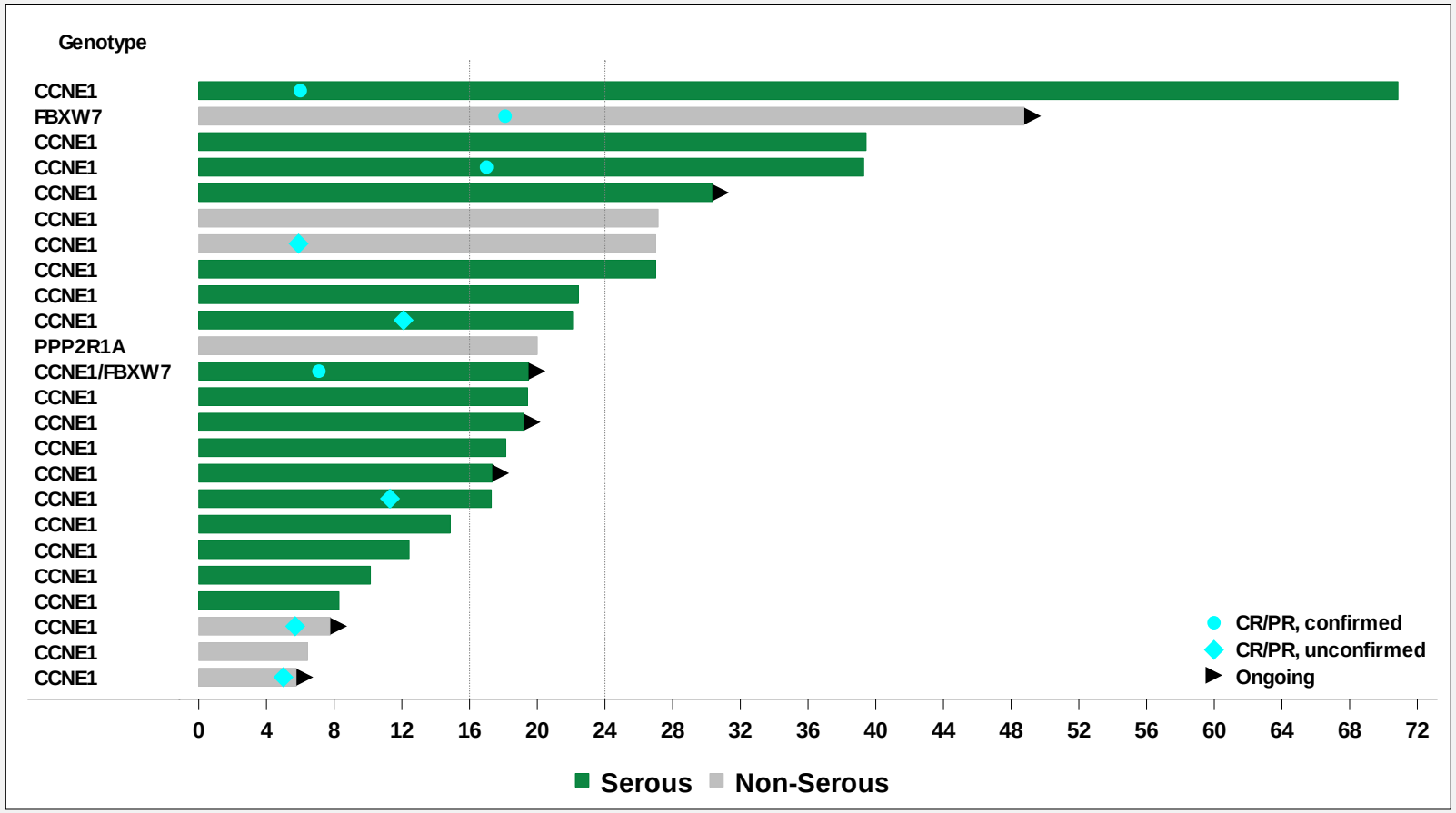
- **100% platinum-resistant or platinum ineligible**
- **45.8% received prior PARPi**
- **70.8% received prior bevacizumab**
- **54% with three or more prior lines of therapy**

Age (years)	Median: 63
Racial Demographics	White: 79.2% / Black: 4.2% / Other: 16.6%
ECOG Performance Status	0: 54.2%, 1: 45.8%
Prior Therapies	Platinum: 95.8%, PARPi: 45.8%, bevacizumab 70.8%
PROC status	Platinum-resistant/ineligible: 100%
Lines of Therapy	3 or more: 54.2%
Histology	Serous: 70.8%, Non-Serous: 29.2%
P53 Mutation	100%
Genotypes	CCNE1: 87.5%; FBXW7, PPP2R1A, CCNE1/FBXW7: 4.2% each

REPARE THERAPEUTICS

PROC: Compelling clinical benefit rate of 79% observed

Duration of treatment on lunre+camo



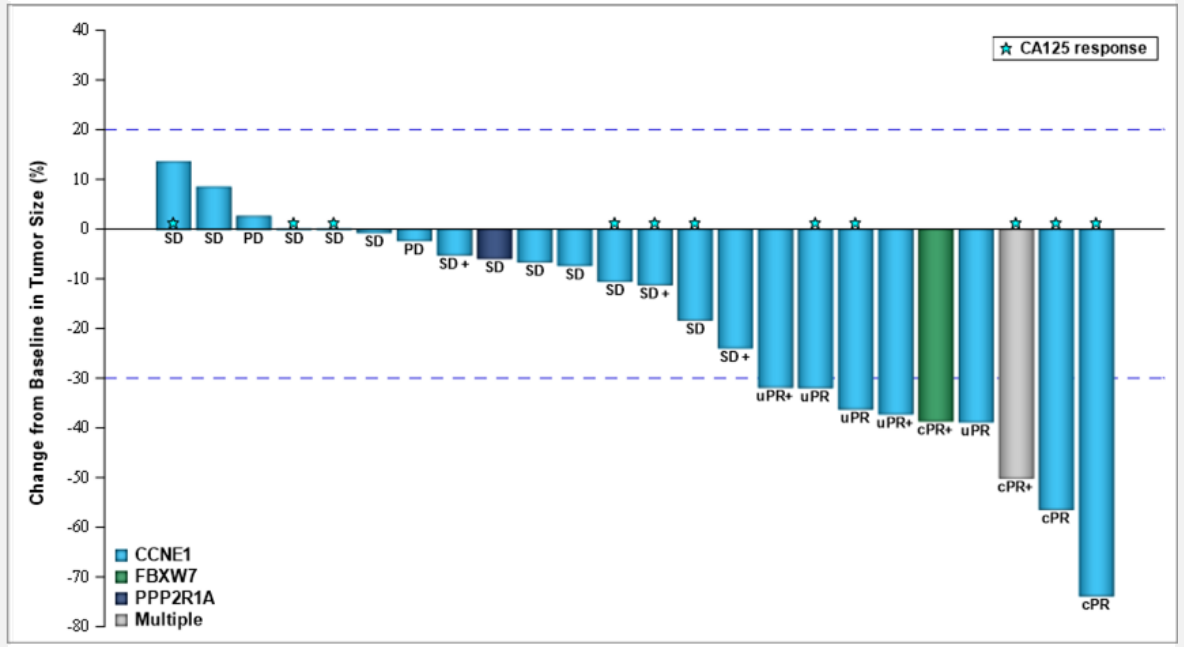
- **Progression-free rate (KM) at 24 weeks was 45% (95% CI: 22-66%)**
- **Pattern of benefit reflects unique lunre+camo MoA:**
  - Long-term benefit in patients when tumor reductions did not meet response definition
  - Continuous slow reductions in tumor burden, late and/or unconfirmed PRs
  - CA-125 responses predict clinical benefit
- **Treatment ongoing in 29% of patients; 4 additional patients with first scan pending**

CBR, %	**79%**
PFS (%) at 24-weeks (90% CI)	45% (22-66%)
TRT ongoing w/o PD, n (%)	29%

Abbreviations: CBR, clinical benefit rate defined as having CR, PR, or at least 16 weeks treatment without PD.
Note: Modified efficacy population defined as those treated patients with at least one post-baseline tumor assessment

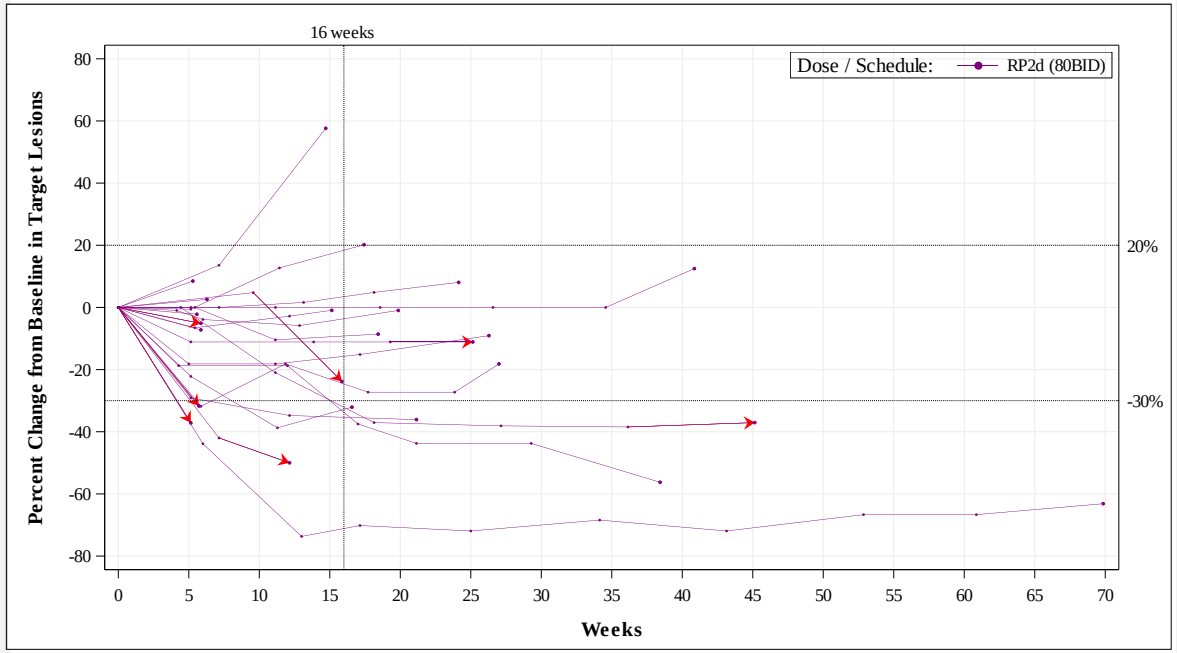
PROC: Strong efficacy in lunre BM+ tumors

75% of patients experienced tumor shrinkage



ORR (conf.+ unconf.), %	**37.5%**
ORR (conf.), %	16.7%
PR	4 (16.7%)

Durable responses observed across subtypes and genetic alterations



Time to response (Range)	**5-18 weeks**

Duration of response up to ~64 weeks

Note: +, denotes treatment ongoing

REPARE THERAPEUTICS

EC & PROC: Pattern of benefit consistent with lunre MOA

Lunre+camo combination demonstrated:

- Strong and consistent evidence of anti-tumor activity observed in both tumors despite poor prognosis of BM+ population
- Durable clinical benefit, including in patients with/without RECIST responses
  - Long stable disease with molecular response indicates drug-related effect
  - Continued tumor shrinkage, durable response
- Differentiated tolerability, predictable safety profile improves quality of life

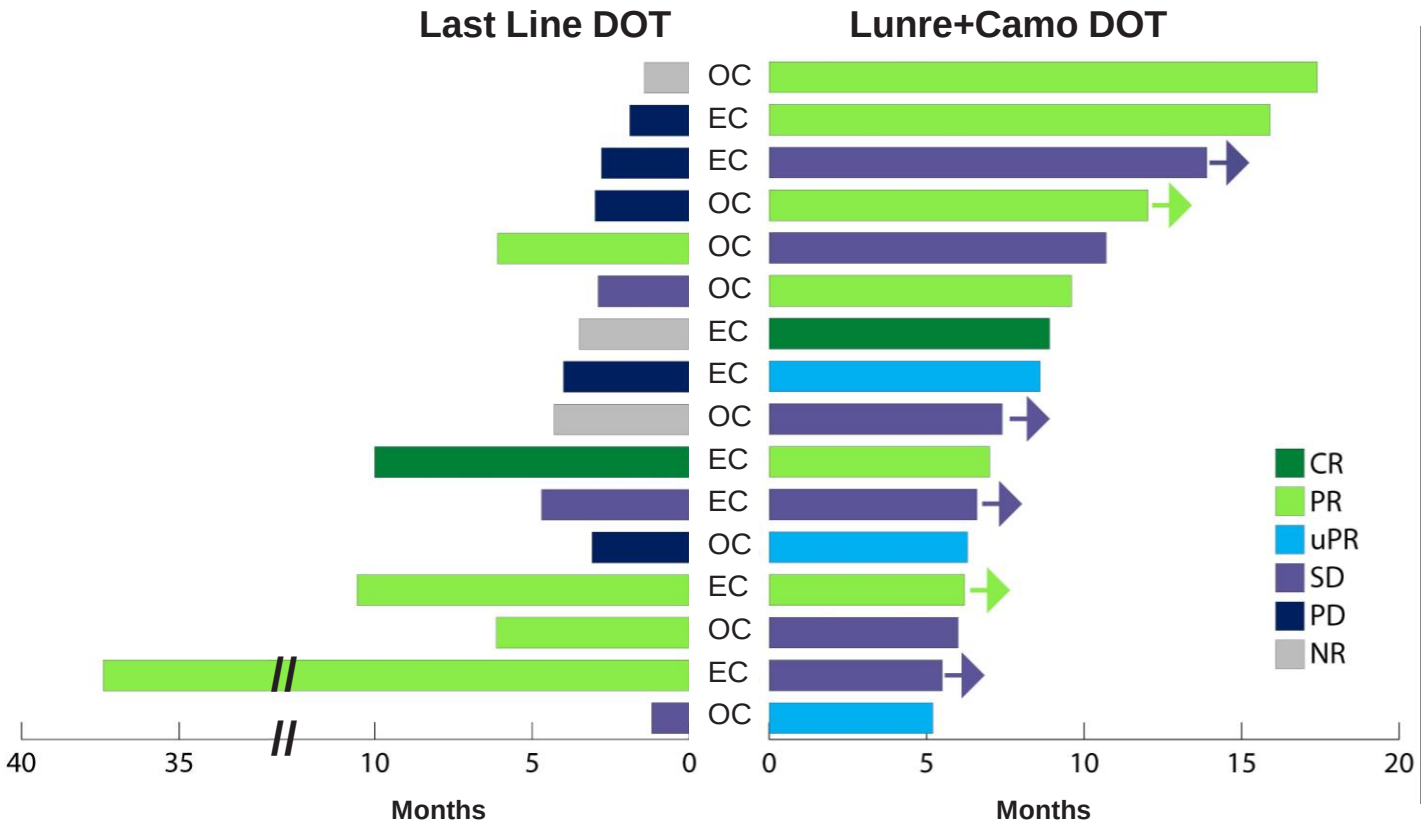
	Endometrial (N=27)	Ovarian (N=24)
Median follow-up (weeks)	20	25
Prior therapies	78% prior ICI	100% platinum resistant/ineligible
3 or more prior lines of therapy	59%	54%
P53 mutations	85%	100%
Carcinosarcoma/non-serous	19% carcinosacoma	29% non-serous
RECIST response rate (95% CI)	25.9% (11-46%)	37.5% (19-59%)
PFS at 24 weeks (KM), (95% CI)	43% (21-63%)	45% (22-66%)

REPARE THERAPEUTICS

Greater clinical benefit observed vs. prior treatments

Duration of treatment (DOT) on lunre+camo vs. previous therapy

Patients with >5mo DOT



- **Patients achieving long clinical benefit on lunre+camo had generally short treatment durations on prior therapies[1]**
  - Limited benefit of prior therapies likely associated with poor prognosis and chemoresistance of lunre BM+ tumors
  - Toxicities of prior chemotherapy further limited the clinical benefit
- **Data support benefit of lunre+camo in high-risk, high unmet need Lunre BM+ tumors**

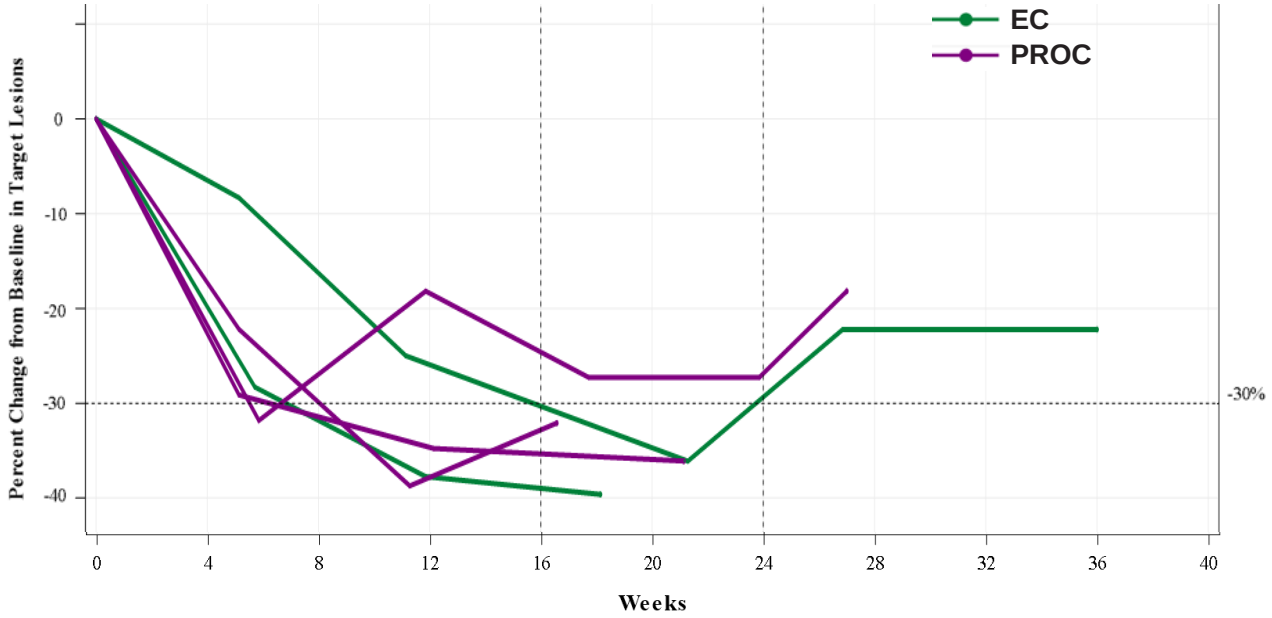
Reference: 1. https://pubmed.ncbi.nlm.nih.gov/27234642/; https://medelis.com/abstracts/the-lost-opportunity-in-phase-i-oncology-clinical-trials/.

REPARE THERAPEUTICS

Durable clinical benefit in patients with unconfirmed PRs

Tumor lesion change observed for tumors with unconfirmed PRs

EC and PROC pts with final best overall response of uPR



- **Continuous tumor burden reduction** culminating in benefit in patients with late PRs
- This **later response and benefit pattern** is expected to:
  - **Enable our planned and regulator-supported Ph 3 randomized trial primary endpoint** (PFS)
  - **Meet requirements for accelerated approval** in the context of our planned randomized trial[1]

[1]**Unconfirmed responses in randomized studies (RECIST v1.1)**
"Confirmation of response is required for trials with response primary endpoint but is no longer required in randomized studies since the control arm serves as appropriate means of interpretation of data."

Reference: EA Eisenhauer, New response evaluation criteria in solid tumors: revised RECIST guideline (version 1.1), *Eur J Cancer*. 2009 Jan;45(2):228-47.

REPARE THERAPEUTICS

Lunre+camo safety profile: Differentiation from emerging ADCs

Safety	Lunre+camo	ADCs
Dosing	▪ **Oral**	▪ **IV**
High-grade toxicities	▪ Overall Gr3/4* TRAEs: 46.3% ▪ No treatment-related deaths ▪ Predominantly manageable anemia	▪ Generally higher Gr3/4 TRAEs: ~30-70+% ▪ **Treatment-related deaths** ▪ Predominantly **neutropenia** (often high-grade)
Other toxicities	▪ Rash ▪ Fatigue	▪ Alopecia ▪ **Ocular** ▪ ILD, pneumonitis ▪ Diarrhea ▪ Fatigue
Monitoring	▪ Easily **monitorable**, **predictable** and treatable toxicities	▪ **More invasive** and **inconvenient monitoring** ▪ Increased vigilance for respiratory symptoms

Note: *, 2 Gr 4 out of 67 patients, one with neutropenia and leukopenia with concomitant viral infection and allergy to cephalosporin.

Lunre+camo: Clinical summary and development path forward

A potentially effective, well-tolerated, convenient and differentiated option

Overall

- Encouraging efficacy in heavily pre-treated patients with adverse genomic profile and worse prognoses
- Promising rate of tumor responses, durable benefit
- Potential alternative to ADCs with improved safety and tolerability
- Clear registrational opportunities for both tumors
- Mirvetuximab-like opportunity for BM+ subset

Endometrial Cancer

Strong response rate and benefit: 25.9% response rate and 24wk PFS 43%

Aiming to **define new 2L+ SOC**

Greater **unmet need** with rising incidence, mortality

PROC

Compelling response rate and benefit: 37.5% response rate and 24wk PFS 45%

Attractive **biomarker directed approach** with **differentiated tolerability profile**

Path forward

Focus on EC Pivotal trial start in 2025

- **2L+ target and robust patient need for chemo alternatives**
- **Large, growing and global unmet need**
- **EU and FDA regulatory alignment with AA option for earlier US registration**
- **Favorable competitive dynamics**

REPARE THERAPEUTICS

Pivotal development for EC supported by data and regulators

Path forward

Focus on EC Pivotal trial start in 2025

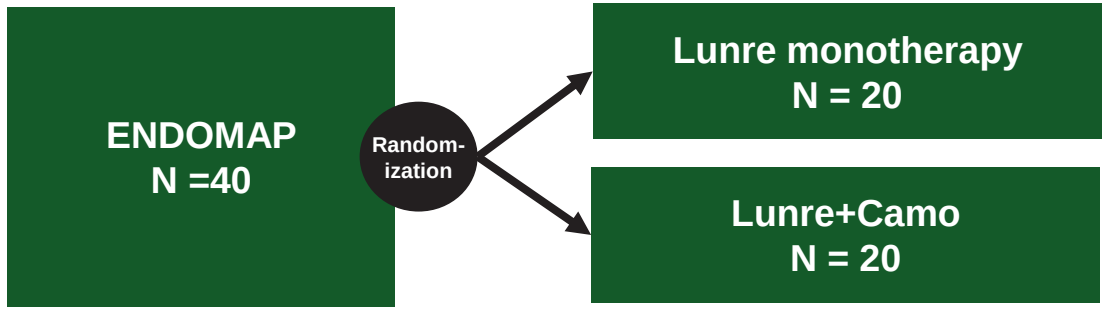
- **2L+ target and robust patient need for chemo alternatives**
- **Large, growing and global unmet need**
- **EU and FDA regulatory alignment with AA option for early US registration**
- **Favorable competitive dynamics**

Regulatory support: FDA and EMA alignment on Ph 3 registrational trial(s)

- ✓ **FDA Fast Track Designations:** Recurrent EC and PROC
- ✓ **RP2D established with** (**optimized dosing**)
- ✓ **Contribution of components (COC):** Agreement on 40-patient randomized trial with early futility analysis (N=9 per arm) agreed for both indications; EC enrollment to start Q1 2025
- ✓ **Agreement reached with FDA on key components of the Ph 3 clinical trial design including potential option for U.S. accelerated approval (AA)**

REPARE THERAPEUTICS

Efficient plan to regulatory approval: EC as lead indication



Small study to establish contribution of components

- Ph 2 study with Alliance Foundation Trials
- Submission to FDA and IRB complete
- FPI planned for Q1 2025, estimated duration ~2 yrs with early futility

Phase 3 in 2L+ EC
N ~400
Option for Accelerated Approval

Pivotal evaluation for registration

- In collaboration with Gynecological Oncology Group (GOG) in U.S. and European Network of Gynecological Oncological Trial groups (ENGOT)

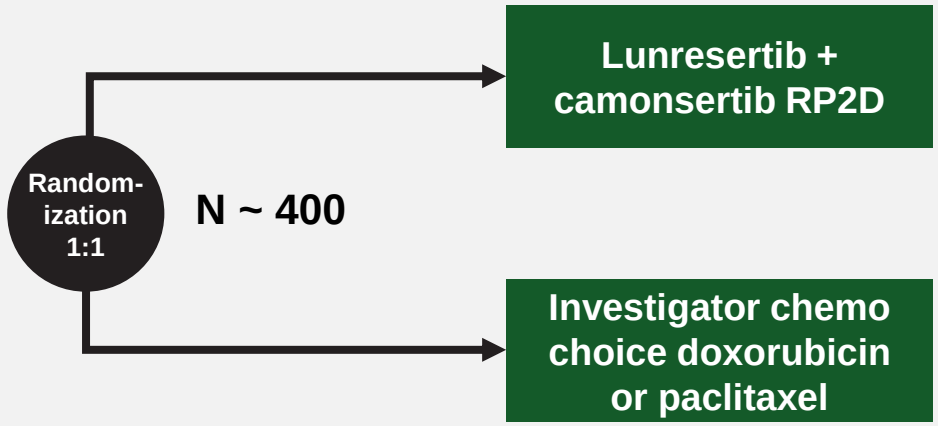
REPARE THERAPEUTICS

Ph 3 registrational trial in EC

Supporting NDA submission for potential accelerated and full approvals within one study

Eligibility criteria:

- Recurrent EC or carcinosarcoma
- Previous ICI and platinum
- At least 1 evaluable lesion
- 1-3 prior lines of therapy
- CCNE1, FBXW7 and/or PPP2R1A based on Foundation Medicine NGS diagnostic
- Previous HER2 ADC if HER2+



ORR interim analysis proposed at ~170 patients with 3 completed scans, expected H1 2027

Primary endpoints:
PFS by BICR

Key secondary:
ORR by BICR (for AA), OS

Secondary:
QOL, Safety

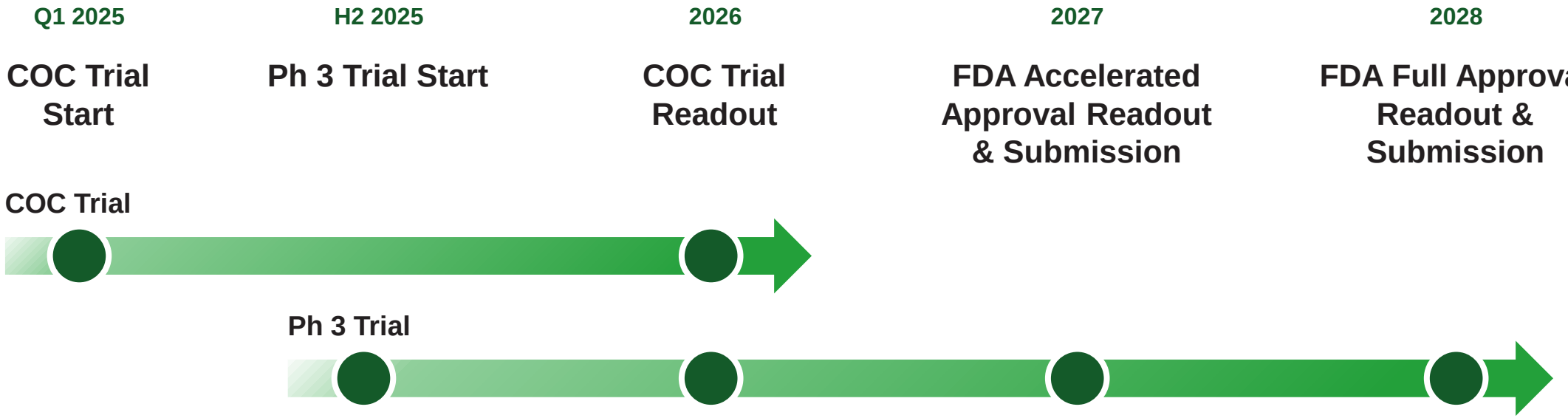
Targeted label: *Lunre+camo indicated for adult patients with CCNE1, FBXW7, PPP2R1A altered*, serous, endometroid or carcinosarcoma endometrial cancer, who have disease progression following prior systemic treatment regimens with ICI and at least one chemotherapy/ADC in any setting. Patients selected based on an FDA-approved test.

Note: BICR, Blinded Independent Central Review

REPARE THERAPEUTICS

EC as lead indication: Targeting 2028 NDA submission

Anticipated milestones starting with Q1 2025 initiation of COC trial



Patient and Commercial Opportunity

Phillip Herman
EVP, Chief Commercial and Portfolio Development Officer
Repare Therapeutics

Commercial overview: Building a strong foundation

Strong commercial opportunity

- **De-risked** opportunity in EC and PROC
- EC is our **lead indication**, with potential for **Accelerated Approval** built into design
- PROC, a future **life-cycle** opportunity
- **Clear value proposition** for lunre+camo relative to existing and emerging potential treatment options post chemo/IO

Feedback from independent market research[1]

"If you show similar outcome data, but you have something that has a better toxicity profile, I am somebody that would be open to using that drug."

-Gynecologic Oncologist

"One doctor says, 'we have a chemo you haven't tried; we guarantee it'll make you sick, but we don't guarantee you'll recover.' And another doctor says that chemo has not been shown to help with your specific cancer…There is no reason to torture myself on a 'maybe.'"

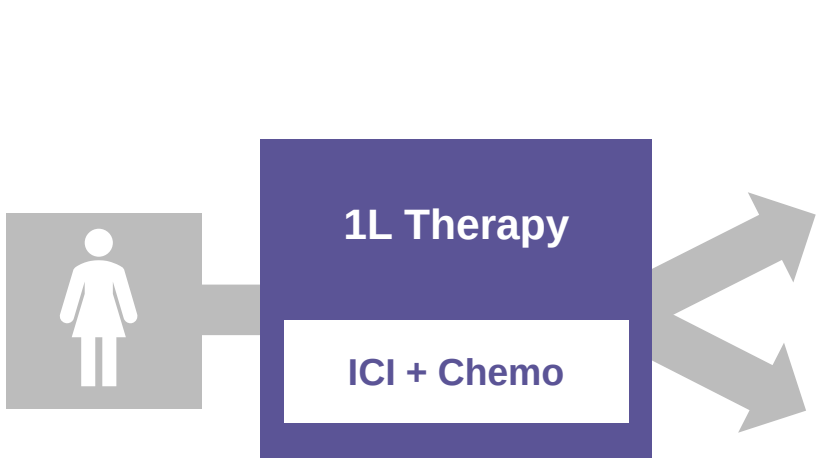
-Patient

Note: 1, Direct quotes from physician and patient feedback from Repare market research.

REPARE THERAPEUTICS

Lunre+camo combination well-positioned for success in 2L+ EC

- **New 1L standard of care will lead to majority of 2L patients having previously received ICI + chemo**
- **Limited data to support use of approved 2L options after ICI + chemo, opportunity for novel agents**



Approved 2L+ Options

Emerging Therapies: Lunre+Camo, ADCs, Other Targeted Options

Limitations of approved options:

- Little to no data post-ICI
- Chemo offers limited efficacy with AEs

Lunre+camo offers:

- Competitive and differentiated profile vs. other emerging therapies
- Biomarker-directed approach
- Convenient oral dosing

REPARE THERAPEUTICS

EC offers meaningful commercial potential as lead indication

~2.9K
Addressable 2L EC US Patients[1]

~$450M – $600M
U.S. Market Potential[2]

~$900M – $1.2B
Global Market Potential[3]

Target Label

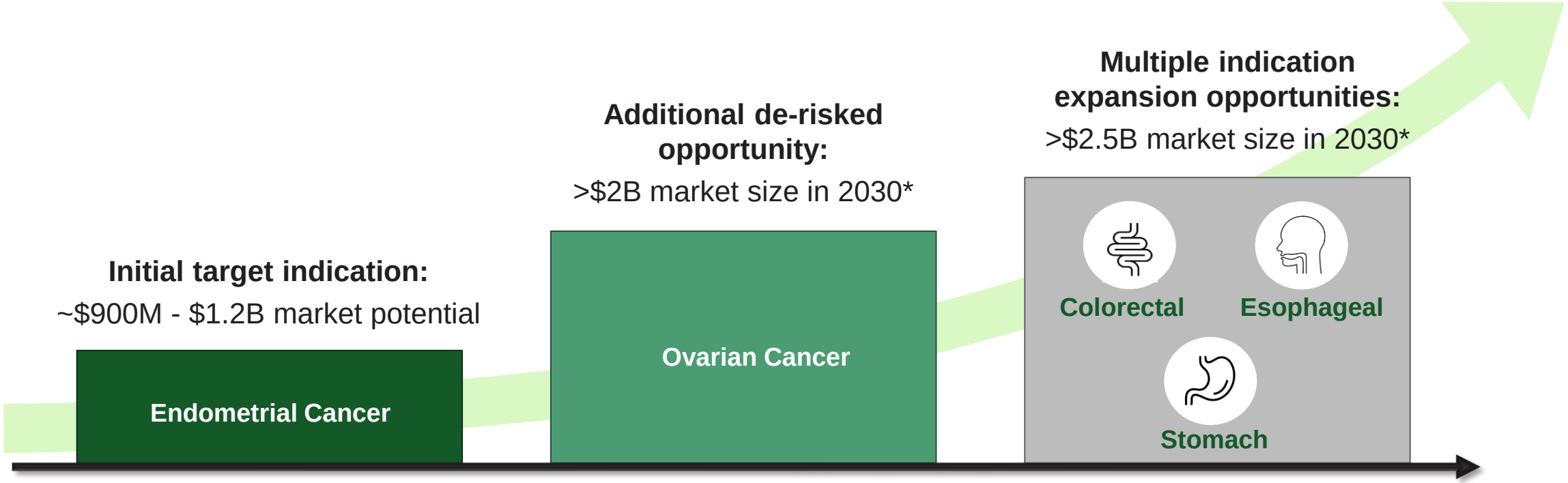
Lunre+camo indicated for adult patients with CCNE1, FBXw7, PPP2R1a altered, serous, endometroid or carcinosarcoma endometrial cancer, who have disease progression following prior systemic treatment regimens with ICI and at least one chemotherapy/ADC in any setting. Patients selected based on an FDA-approved test.

[1] Addressable patients estimated based on TCGA, GENIE and Clarivate DRG drug-treated patients. [2] Assumes net monthly pricing with 15-25% net discount. [3] Assume 2X US Potential

REPARE THERAPEUTICS

Lunre combinations offer significant market opportunity potential

Potential for multiple additional tumor types beyond EC



***Indication global sales forecast in 2030 for approved therapies and projected approved therapies (**EvaluatePharma**), 75% factor for US/EU4/UK, Lunre segment ~29% of $7B Market for Ovarian, ~16% of $16B Market across multiple indication expansion opportunities.

REPARE THERAPEUTICS

REPARE THERAPEUTICS

Closing Remarks

POC achieved for registrational trial, Ph 3 EC start in 2025

We achieved POC for lunre+camo combo in EC and PROC

- Combination was effective and well-tolerated
- Clear signals, opportunity for registrational trials in both EC and PROC
- Opportunity to deliver important, new and chemo-alternative treatment options

Initiating pivotal Ph 3 randomized trial in EC in 2025

- Regulatory alignment with FDA and EMA, including accelerated approval options
- Simple Contribution of Components trial obligation, under way shortly
- PROC a de-risked life cycle opportunity, subject to capital and/or partnering

Our objectives for today:

- ✓ Set the stage for this product opportunity
- ✓ Walk you through our lunre+camo data
- ✓ Describe our planned registrational trial and supporting regulatory guidance
- ✓ Detail product opportunities longer term
- **Answer your questions**

Abbreviations: **POC**, proof of concept.

REPARE THERAPEUTICS

Questions & Answers

Lloyd Segal
President, Chief Executive Officer
Repare Therapeutics

Phillip Herman
EVP, Chief Commercial and Portfolio Development Officer

Brian Slomovitz, MD, MS, FACOG
Director, Gynecologic Oncology
Co-chair of the Cancer Research Center
Mount Sinai Medical Center

Steve Forte
EVP, Chief Financial Officer

Maria Koehler, M.D., Ph.D.
EVP, Chief Medical Officer
Repare Therapeutics

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Thank you.

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