UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 12, 2024

Repare Therapeutics Inc.
(Exact Name of Registrant as Specified in Its Charter)

Québec	001-39335	Not applicable
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

7171 Frederick-Banting, Building 2 Suite 270 St-Laurent, Québec, Canada	H4S 1Z9
(Address of Principal Executive Offices)	(Zip Code)

Registrant's Telephone Number, Including Area Code: (857) 412-7018

Not Applicable
(Former Name or Former Address, if Changed Since Last Report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common shares, no par value	RPTX	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On December 12, 2024, Repare Therapeutics Inc. (the "Company") issued a press release announcing the presentation of positive data from its MYTHIC Phase 1 gynecologic expansion clinical trial evaluating the combination of lunresertib and camonsertib ("Lunre+Camo") at the recommended Phase 2 dose ("RP2D") in patients with endometrial cancer and platinum-resistant ovarian cancer ("PROC") harboring lunre-sensitizing biomarkers. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

As described in the accompanying press release, the Company will host a conference call and live audio webcast today, December 12, 2024 at 4:30 p.m., Eastern Time, to discuss the presentation of data described above.

The live audio webcast may be accessed through the "Events & Presentations" page in the "Investors and Media" section of the Company's website at ir.reparerx.com. Alternatively, participants may dial (646) 357-8785 (U.S. and Canada) or (800) 836-8184 (international). A copy of the presentation to be used by the Company during the conference call is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

The Company's website and any information contained on the Company's website are not incorporated into this Current Report on Form 8-K.

Item 8.01 Other Events.

On December 12, 2024, the Company reported positive initial data from its MYTHIC Phase 1 gynecologic expansion clinical trial evaluating Lunre+Camo at the optimized RP2D in patients with endometrial cancer and PROC harboring lunre-sensitizing biomarkers.

The MYTHIC clinical trial is a first-in-human, global, open-label Phase 1 dose-escalation clinical trial to evaluate safety, pharmacokinetics, pharmacodynamics, and preliminary anti-tumor activity of Lunre+Camo in patients with advanced solid tumors. As of the data cut-off date of November 14, 2024, 51 evaluable patients were enrolled in the gynecologic cancer expansion cohort of the MYTHIC trial. The key points from the most recent data cut are summarized below.

Across all solid tumor types treated at the optimized RP2D (n=67), Lunre+Camo therapy demonstrated a favorable and differentiated tolerability profile when compared to current and emerging therapies. The most common adverse event was anemia (26.9%).

Key Findings from Endometrial Cancer Patient Cohort:

- 27 evaluable patients with endometrial cancer were evaluated in the trial. The patients in the cohort had a median age of 67 years. All patients in the cohort exhibited high-risk profiles:
  - 100% of patients have undergone prior platinum therapy
  - 77.8% of patients received immune checkpoint inhibitors
  - 59% of patients received the combination as a fourth line of therapy or beyond
  - 18.5% of patients had carcinosarcoma
  - 85% of tumors had p53 mutations
  - No tumors with microsatellite instability (MSI)-high status were enrolled indicating proficient mismatch repair (pMMR) status
  - Within the Lunre BM+ subset: 56% of tumors had PPP2R1A mutations; 22% carried FBXW7 mutations; 15% had CCNE1 amplification; and 7% of tumors had multiple mutations

- Key efficacy outcomes in evaluable patients with endometrial cancer (N=27):
  - ORR was 25.9% (confirmed ORR in 5 out of 7 patients)
  - Clinical benefit was observed in 48.1% of patients, with responses frequently occurring after 12 weeks or more
  - At the 24-week landmark analysis, nearly half of patients experienced durable clinical benefit (24-week PFS [PFS24w] = 43% [95% CI, 21-63%])

Key Findings from Platinum-Resistant Ovarian Cancer Patient Cohort:

- 24 evaluable patients with PROC were evaluated in the trial. The patients in the cohort had a median age of 63 years. All patients in the cohort exhibited high-risk profiles:
  - 100% of patients were platinum-resistant or platinum ineligible
  - 45.8% of patients had received prior PARP inhibitors
  - 70.8% of patients had received prior bevacizumab
  - 54% of patients received the combination as a fourth line of therapy or beyond
  - 100% of tumors had p53 mutations
  - Within the Lunre BM+ subset: 87.5% of tumors had CCNE1 amplification; 4.2% of tumors had FBXW7 mutations; 4.2% of tumors had PPP2R1A mutations; and 4.2% of tumors had multiple mutations
- Key efficacy outcomes in evaluable patients with PROC (N=24):
  - ORR was 37.5% (confirmed ORR in 4 out of 9 patients)
  - Clinical benefit was observed in 77.3% of patients, with responses frequently occurring after 12 weeks or more
  - PFS at the 24-week landmark analysis was (PFS 24w=45% [90% CI, 22-66%]).

The Company has consulted with both the U.S. Food and Drug Administration ("FDA") and the European Medicines Agency, who have provided guidance into the Company's registrational development plans for Lunre+Camo in gynecologic tumors, including assessment of the contribution of components, dose and schedule and preliminary alignment on the proposed registrational development approach. The Company plans to provide the final Phase 3 registrational trial protocols for regulatory clearance imminently, and intends to start the first Phase 3 Lunre+Camo trial in endometrial cancer in the second half of 2025. Additionally, the Company expects to initiate a small contribution of components trial in up to 40 patients with endometrial cancer in the first quarter of 2025.

Cautionary Regarding Forward-Looking Statements

Certain statements in this Current Report on Form 8-K contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 and securities laws in Canada. All statements in this Current Report on Form 8-K other than statements of historical facts are "forward-looking statements. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding: statements regarding the Company's future plans for clinical development of Lunre+Camo, including the Company's plans to begin a Phase 3 registrational trial in the second half of 2025 and a contribution of components trial in patients with endometrial cancer in the first quarter of 2025; the tolerability, efficacy and clinical progress of Lunre+Camo; the potential of Lunre+Camo as a new treatment option and standard of care for patients with endometrial and platinum-resistant ovarian cancers, if approved; camonsertib's potential as a best-in-class small molecule inhibitor of ATR; and the Company's interactions with the FDA and the European Medicines Agency regarding registrational development plans for Lunre+Camo. These forward-looking statements are based on the Company's expectations and assumptions as of the date of this Current Report on Form 8-K. Each of these forward-looking statements involves risks and uncertainties that could cause the Company's clinical development programs, future results or performance to differ materially from those expressed or implied by the forward-looking statements. Many factors may cause differences between current expectations and actual results, including: success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate; the impacts of macroeconomic conditions, including the conflict in Ukraine and the conflict in the Middle East, heightened inflation and uncertain credit and financial markets on the Company's business, clinical trials and financial position; unexpected safety or efficacy data observed during preclinical studies or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; changes in expected or existing competition; changes in the regulatory environment; the uncertainties and timing of

the regulatory approval process; and unexpected litigation or other disputes. Other factors that may cause the Company's actual results to differ from those expressed or implied in the forward-looking statements in this press release are identified in the section titled "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 filed with the Securities and Exchange Commission ("SEC") and the Québec Autorité des Marchés Financiers ("AMF") on February 28, 2024, and its other documents subsequently filed with or furnished to the SEC and AMF including the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed with the SEC on November 7, 2024. The Company expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Press Release dated December 12, 2024
99.2	Conference Call Presentation dated December 12, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REPARE THERAPEUTICS INC.

Date: December 12, 2024

By: /s/ Lloyd M. Segal
Lloyd M. Segal
President and Chief Executive Officer

Repare Therapeutics Announces Positive Results of the Lunresertib and Camonsertib Combination from the MYTHIC Phase 1 Gynecologic Expansion Clinical Trial

Heavily-pretreated patients on lunresertib and camonsertib combination achieved 25.9% overall response rate (ORR) in endometrial cancer and 37.5% in platinum-resistant ovarian cancer

Nearly half of patients with gynecologic cancers maintained progression-free survival at 24 weeks, comparing favorably to current standard of care

Company plans to initiate a registrational Phase 3 trial of lunresertib in combination with camonsertib in endometrial cancer in 2H 2025

Repare to host conference call and webcast today at 4:30 p.m. ET to discuss these results

CAMBRIDGE, Mass. & MONTREAL—(BUSINESS WIRE)—Dec. 12, 2024—Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today reported positive data from its MYTHIC Phase 1 gynecologic expansion clinical trial evaluating the combination of lunresertib and camonsertib (Lunre+Camo) at the recommended Phase 2 dose (RP2D) in patients with endometrial cancer and platinum-resistant ovarian cancer (PROC) harboring lunre-sensitizing biomarkers.

Lunresertib is a first-in-class precision oncology small molecule PKMYT1 inhibitor which targets cell cycle regulation in Lunre BM+ tumors (CCNE1 amplifications or FBXW7 or PPP2R1A deleterious alterations). Camonsertib is a potential best-in-class oral small molecule inhibitor of ATR, a critical component of the DNA damage response pathway.

"We are encouraged by the strong response and the clear benefit we observed in patients with endometrial and platinum-resistant ovarian cancers in the MYTHIC clinical trial," said Lloyd M. Segal, President and Chief Executive Officer of Repare. "These patients need new treatment options and our results support the potential for Lunre+Camo to make a real, positive difference if approved, particularly as a chemotherapy alternative. We have positive feedback from regulatory agencies in both the US and Europe and we look forward to getting started on a registrational Phase 3 trial of Lunre+Camo in endometrial cancer in the second half of 2025."

The MYTHIC clinical trial (NCT04855656) is a first-in-human, global, open-label Phase 1 dose-escalation clinical trial to evaluate safety, pharmacokinetics, pharmacodynamics, and preliminary anti-tumor activity of Lunre+Camo in patients with advanced solid tumors. As of the data cut-off date of November 14, 2024, 51 evaluable patients were enrolled in the gynecologic cancer expansion cohort of the MYTHIC trial.

Across all tumor types treated at the optimized RP2D (n=67), Lunre+Camo therapy demonstrated a favorable and differentiated tolerability profile when compared to current and emerging therapies. The most common adverse event was anemia (26.9%, Grade 3).

Key Cohort Clinical Findings

Endometrial Cancer Patients:

The 27 evaluable patients with endometrial cancer had a median age of 67 years. All patients exhibited high-risk profiles:

- 100% of patients have undergone prior platinum therapy
- 77.8% of patients received immune checkpoint inhibitors
- 59% of patients received the combination as a fourth line of therapy or beyond
- 18.5% of patients had carcinosarcoma
- 85% of tumors had p53 mutations
- No tumors with microsatellite instability (MSI)-high status were enrolled indicating proficient mismatch repair (pMMR) status
- Within the Lunre BM+ subset: 56% of tumors had PPP2R1A mutations; 22% carried FBXW7 mutations; 15% had CCNE1 amplification; and 7% of tumors had multiple mutations

Key efficacy outcomes in evaluable patients with endometrial cancer (N=27):

- ORR was 25.9% (confirmed ORR in 5 out of 7 patients)
- Clinical benefit was observed in 48.1% of patients, with responses frequently occurring after 12 weeks or more
- At the 24-week landmark analysis, nearly half of patients experienced durable clinical benefit (24-week PFS [PFS24w] = 43% [95% CI, 21-63%])

Platinum-Resistant Ovarian Cancer Patients:

The 24 evaluable patients with PROC had a median age of 63 years. All patients exhibited high-risk profiles:

- 100% of patients were platinum-resistant or platinum ineligible
- 45.8% of patients had received prior PARP inhibitors
- 70.8% of patients had received prior bevacizumab
- 54% of patients received the combination as a fourth line of therapy or beyond
- 100% of tumors had p53 mutations
- Within the Lunre BM+ subset: 87.5% of tumors had CCNE1 amplification; 4.2% had FBXW7 mutations; 4.2% had PPP2R1A mutations; and 4.2% of tumors had multiple mutations

Key efficacy outcomes in evaluable patients with PROC (N=24):

- ORR was 37.5% (confirmed ORR in 4 out of 9 patients)
- Clinical benefit was observed in 79% of patients
- PFS at the 24-week landmark analysis was (PFS24w = 45% [95% CI, 22-66%]).

“Those patients with recurrent gynecologic cancers have limited treatment options as tumors often become resistant to standard of care therapy,” said Brian Slomovitz, MD, MS, FACOG, Director, Gynecologic Oncology, Co-chair of the Cancer Research Center, Mount Sinai Medical Center. “They urgently need new treatment options. Repare’s differentiated, biomarker-driven approach addresses this population and may offer a solution. These data support the potential of Lunre+Camo as a new treatment option to fill this unmet need for patients with endometrial and platinum-resistant ovarian cancers.”

Repare has consulted with both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency, who have provided guidance into the Company’s registrational development plans for Lunre+Camo in gynecologic tumors, including assessment of the contribution of components, dose and schedule and preliminary alignment on the proposed registrational development approach. Repare plans to provide the final Phase 3 trial protocols for regulatory clearance imminently and intends to start the first Phase 3 Lunre+Camo trial in endometrial cancer in the second half of 2025. Additionally, the Company expects to initiate a small contribution of components trial in up to 40 patients with endometrial cancer in the first quarter of 2025.

“The results of the MYTHIC clinical trial increase our confidence in the potential to bring Lunre+Camo to patients living with this aggressive subset of recurrent endometrial cancer,” said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. “We are deeply grateful to the patients and investigators who participated in this trial, and we look forward to building on these promising data through the registrational clinical trials using Lunre+Camo as a potential new standard of care for those patients, if approved.”

Conference Call and Webcast:

Repare will host a conference call and webcast today, December 12, at 4:30 p.m. ET to discuss the results. Repare’s executive management team will be joined by Brian Slomovitz, MD, MS, FACOG, Director, Gynecologic Oncology, Co-chair of the Cancer Research Center, Mount Sinai Medical Center.

To access the call, please dial (646) 357-8785 (U.S. and Canada) or (800) 836-8184 (international) at least 10 minutes prior to the start time and ask to be joined to the Repare Therapeutics call. A live webcast and presentation materials will be available in the Investor section of the Company’s website at https://ir.reparerx.com/events-and-presentations/events. A webcast replay will also be archived for at least 30 days.

About Repare Therapeutics Inc.

Repare Therapeutics is a leading clinical-stage precision oncology company enabled by its proprietary synthetic lethality approach to the discovery and development of novel therapeutics. The Company utilizes its genome-wide, CRISPR-enabled SNIPRx® platform to systematically discover and develop highly targeted cancer therapies focused on genomic instability, including

DNA damage repair. The Company's pipeline includes lunresertib (also known as RP-6306), a PKMYT1 inhibitor currently in Phase 1/2 clinical development; camonsertib (also known as RP-3500), a potential leading ATR inhibitor currently in Phase 1/2 clinical development; RP-1664, a Phase 1 PLK4 inhibitor; RP-3467, a Phase 1 Polq ATPase inhibitor; as well as additional, undisclosed preclinical programs. For more information, please visit reparerx.com and follow @Reparerx on X (formerly Twitter) and LinkedIn.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 and securities laws in Canada. All statements in this press release other than statements of historical facts are "forward-looking statements. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding the Company's future plans for clinical development of camonsertib in combination with lunresertib (Lunre+Camo), including the Company's plans to initiate a registrational Phase 3 trial of Lunre+Camo in endometrial cancer in the second half of 2025 and a contribution of components trial in the first quarter of 2025; the tolerability, efficacy and clinical progress of Lunre+Camo; the potential of Lunre+Camo as a new treatment option and standard of care for patients with endometrial and platinum-resistant ovarian cancers, if approved; camonsertib's potential as a best-in-class small molecule inhibitor of ATR; and the Company's interactions with the FDA and the European Medicines Agency regarding registrational development plans for Lunre+Camo. These forward-looking statements are based on the Company's expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties that could cause the Company's clinical development programs, future results or performance to differ materially from those expressed or implied by the forward-looking statements. Many factors may cause differences between current expectations and actual results, including: the potential that success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate; the impacts of macroeconomic conditions, including the conflict in Ukraine and the conflict in the Middle East, fluctuations in inflation and uncertain credit and financial markets, on the Company's business, clinical trials and financial position; unexpected safety or efficacy data observed during preclinical studies or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; the Company's ability to realize the benefits of its collaboration and license agreements; changes in expected or existing competition; changes in the regulatory environment; the uncertainties and timing of the regulatory approval process; and unexpected litigation or other disputes. Other factors that may

cause the Company's actual results to differ from those expressed or implied in the forward-looking statements in this press release are identified in the section titled "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed with the Securities and Exchange Commission ("SEC") and the Québec Autorité des Marchés Financiers ("AMF") on November 7, 2024. The Company expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law. For more information, please visit reparerx.com and follow Repare on X (formerly Twitter) at @RepareRx and on LinkedIn at https://www.linkedin.com/company/repare-therapeutics/.

Investor Relations & Media Contact:

Robin Garner
Vice President and Head of Investor Relations
Repare Therapeutics Inc.
investor@reparerx.com

Exhibit 99.2


REPARE
THERAPEUTICS
MYTHIC Lunre+Camo
Clinical Data Update
December 12, 2024

Safe Harbor Statement

Statements contained in this presentation regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "anticipates," "believes," "expects," "intends," “plans,” “potential,” "projects," “would” and "future" or similar expressions are intended to identify forward-looking statements. Each of these forward-looking statements involves substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by such forward-looking statements. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including specifically our Phase 1/2 MYTHIC trial evaluating lunresertib in combination with camonsertib in patients with endometrial cancer and platinum-resistant ovarian cancer and our plans to begin a Phase 3 registration trial in 2025; the expected timing of program updates and data disclosures; the timing of NDA submissions and other regulatory developments; the timing and likelihood of seeking regulatory approval for our product candidates; and the competitive landscape and market potential for our product candidates, including the commercial opportunity of lunresertib combinations for the treatment of endometrial cancer and additional tumor types.

These forward-looking statements reflect our current beliefs and expectations. Many factors may cause differences between current expectations and actual results, including the impacts of macroeconomic conditions, including the conflict in Ukraine and the conflict in the Middle East, unexpected safety or efficacy data observed during preclinical or clinical studies, clinical site activation rates or clinical trial enrollment rates that are lower than expected, changes in expected or existing competition, changes in the regulatory environment, and unexpected litigation or other disputes. These and other risks are described more fully in our filings with the Securities and Exchange Commission (“SEC”), including the “Risk Factors” section of our Annual Report on Form 10-Q filed with the SEC on November 7, 2024, and other documents we subsequently filed with or furnished to the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Except as required by law, we assume no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Solely for convenience, the trademarks and trade names in this presentation may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.

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

REPARE THERAPEUTICS

REPARE THERAPEUTICS

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 → Today's Focus; Chemotherapy Combinations (FOLFIRI/Gemcitabine); Debio 0123 WEE1i Combination				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.

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.

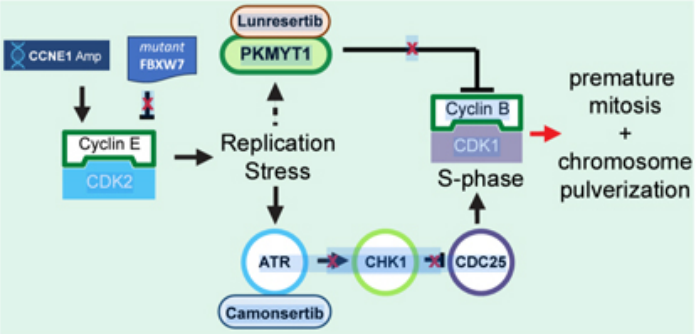
Some key terms and abbreviations in today's discussion

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

REPARE THERAPEUTICS

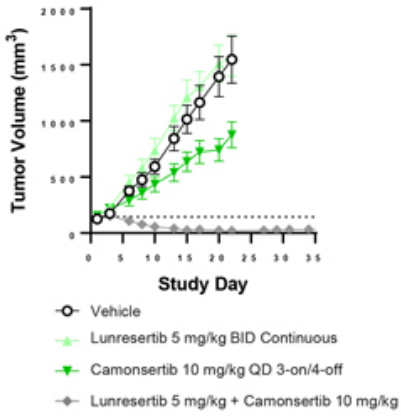
Our mechanistic rationale for lunre+camo

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



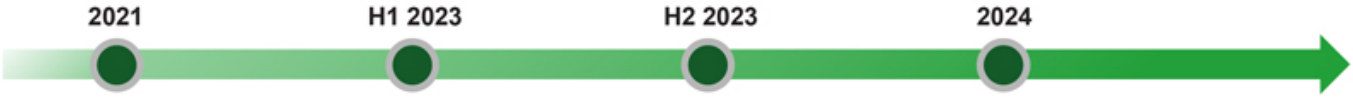
References: 1 ANE poster B057: Gallo et al. Preclinical development of PKMYT1 and ATR inhibitor combinations. ATR, ataxia telangiectasia and Rad-3 related; CDC25, cell division cycle-25; CDK, cyclin-dependent kinase; CHK1, checkpoint kinase 1; PKMYT1, protein kinase, membrane associated tyrosine/threonine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

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



REPARE THERAPEUTICS

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**

REPARE THERAPEUTICS

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

REPARE THERAPEUTICS

REPARE THERAPEUTICS

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

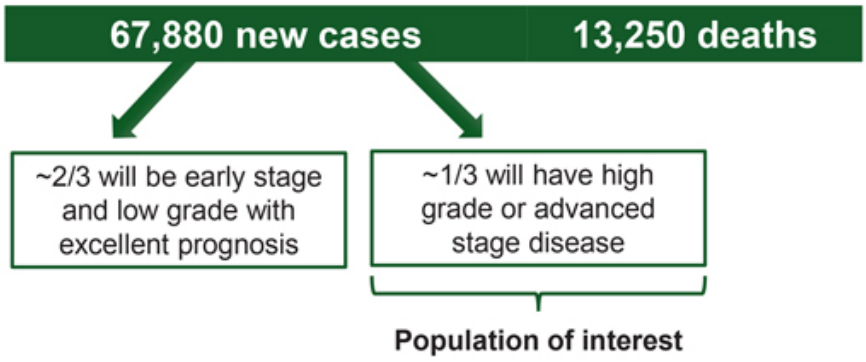
Professor, Obstetrics and Gynecology
Florida International University

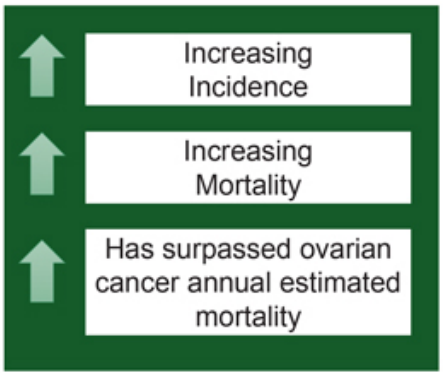
Member, Board of Directors GOG Foundation
Uterine Cancer Clinical Trial Lead, GOG Partners

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

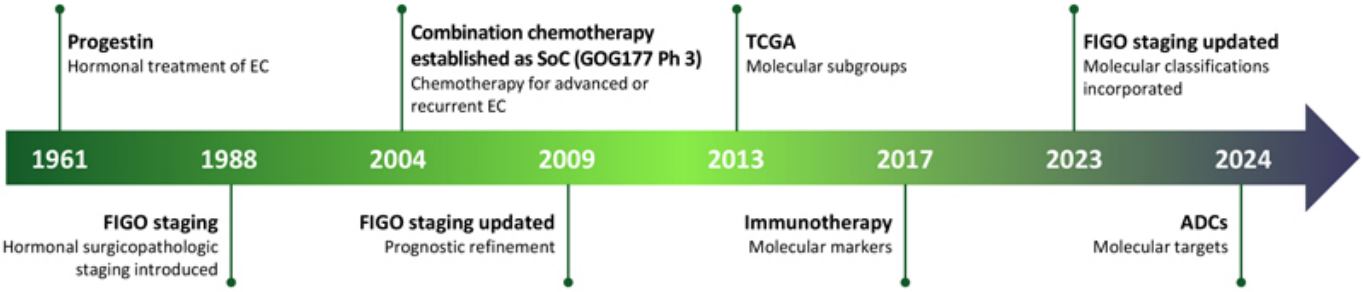




References: Siegel et al. Cancer Statistics 2024
Cancer Facts & Figures 2023. American Cancer Society. Available at https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf. Accessed January 31, 2023.

REPARE THERAPEUTICS

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.

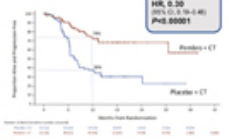
References: Yang S, et al. *Discov Med*. 2011;12:205-212; Haltia U-M, et al. *J Gynecol Oncol*. 2014;25:30-35; Fleming GF, et al. *J Clin Oncol*. 2004;22:2159-2166; The Cancer Genome Atlas Research Network, et al. *Nature*. 2013;497:67-73; Concin N, et al. *Int J Gynecol Cancer*. 2021;31:12-39; Berek 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.

REPARE THERAPEUTICS

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

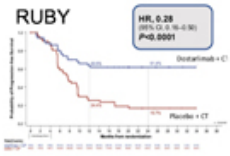
dMMR

GY018



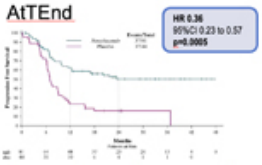
	No with events%	Median
Pembro + CT	23.2	NR (30.6-NR)
Placebo + CT	52.2	7.6 (6.4-9.9)

RUBY



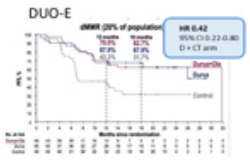
	No with events%	Median
Dorsta + CT	35.8	NR (11.8-NR)
Placebo + CT	72.3	7.7 (5.6-9.7)

AtTEnd



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

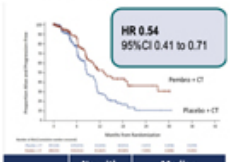
DUO-E



	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)

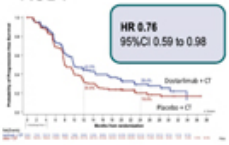
pMMR

GY018



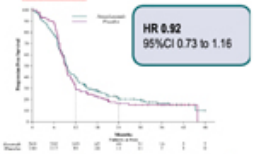
	No with events%	Median
Pembro + CT	30.6	13.1 (10.5-18.8)
Placebo + CT	45.5	8.7 (8.4-10.7)
Maturity	38.1%	

RUBY



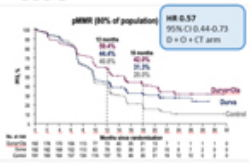
	No with events%	Median
Dorsta + CT	60.4	9.9 (9.0-13.3)
Placebo + CT	70.7	7.9 (7.6-9.8)
Maturity	65.4%	

AtTEnd



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

DUO-E



	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 benefi in dMMR (<30%) tumors

Less benefit in pMMR (>70+%) tumors

MYTHIC tumors a pMMR

Approval for "all comers"

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

REPARE THERAPEUTICS

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?

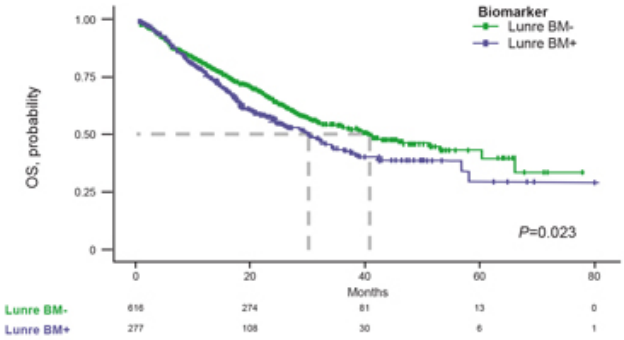
1. Treatment **solution after patients received ICI** and chemotherapy – especially pMMR
   - Lunre+camo data in pMMR to follow
   - ADCs are effective – **is there an alternative to chemo-based ADC? Where do ADCs fit?**
2. What is the optimal treatment for the specific patient I am seeing – **biomarker-based 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

Tumors with Lunre BM+ have significantly worse outcomes

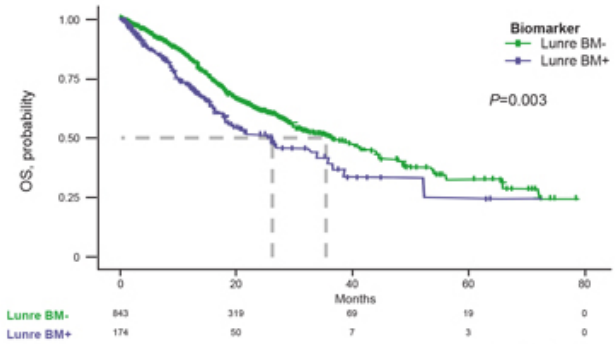
Probability of survival for a subset of 30% of patients with Lunre BM+ *(CCNE1, PPP2R1A, FBXW7)*

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]



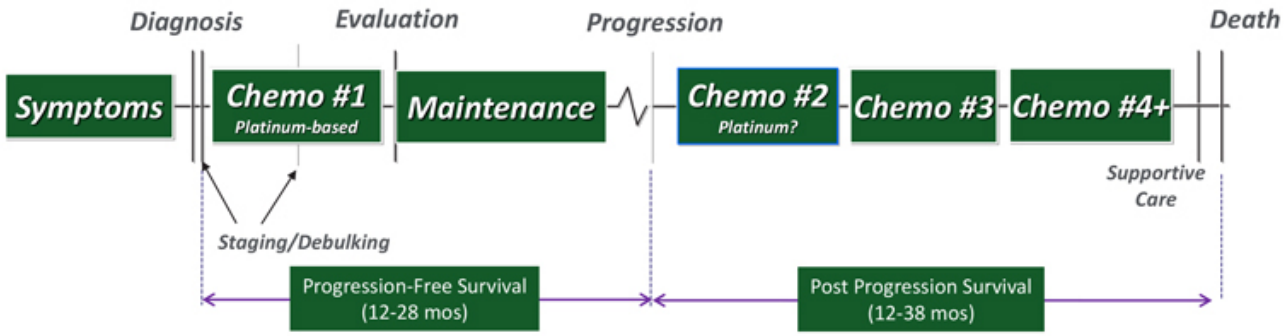
Biomarker	Patients, n	mOS (95% CI), months
Lunre BM–	843	36 (30-43)
Lunre BM+	174	26 (18-38)

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.

REPARE THERAPEUTICS

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

REPARE THERAPEUTICS

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.

REPARE THERAPEUTICS

MYTHIC Study Data

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

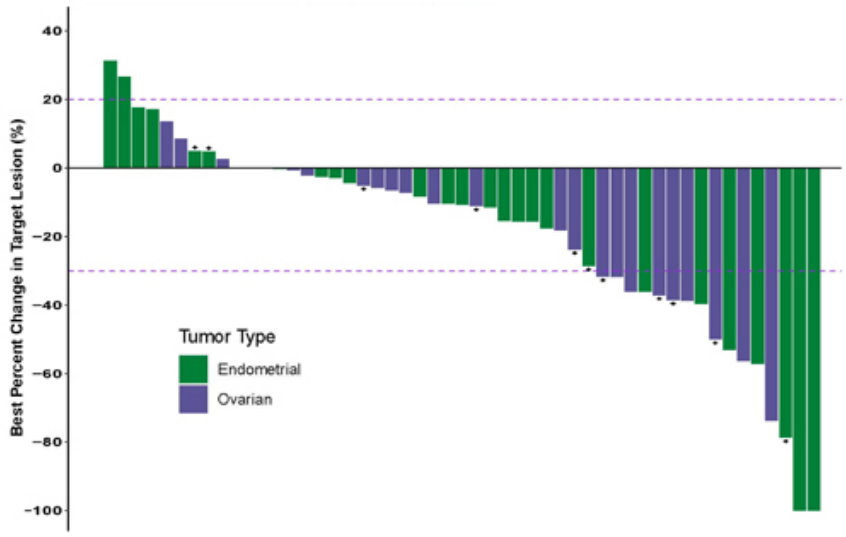
Paul Basciano, M.D.
VP, Clinical Development
& Medical Affairs
Repare Therapeutics

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

Significant overall efficacy observed with lunre+camo in gyn tumors

Tumor shrinkage with lunre+camo in recurrent gynecologic cancers



Note: +, denotes treatment ongoing

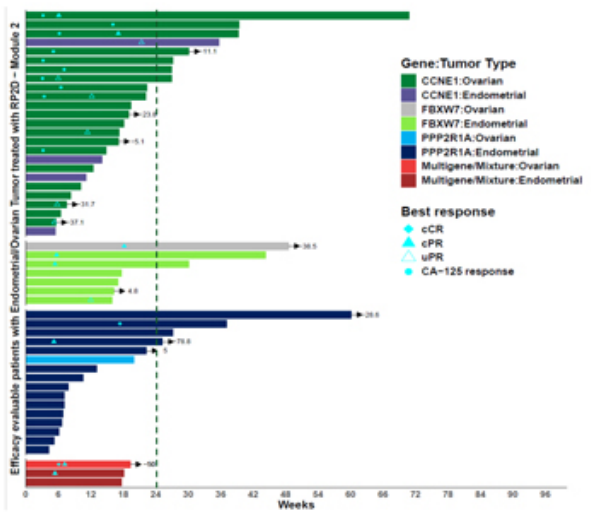
In efficacy-evaluable patients with or PROC at RP2D:

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

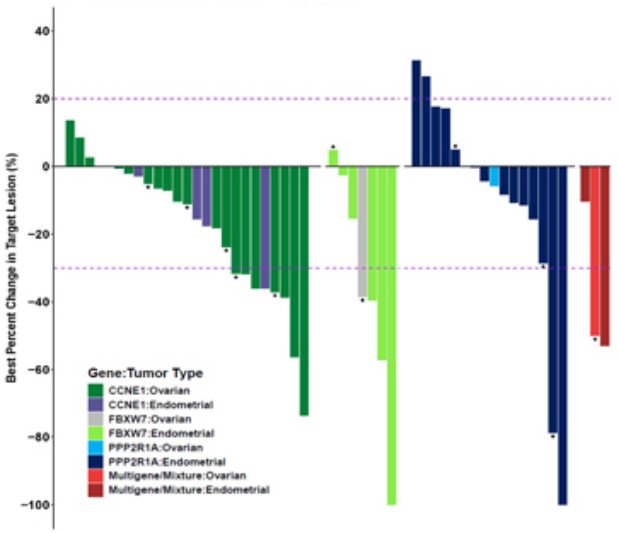
REPARE THERAPEUTICS

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

REPARE THERAPEUTICS

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 anem addressed with dose optimization based on hemoglobin level**
- **No thrombocytopenia or alopecia of any grad**
- **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).

REPARE THERAPEUTICS

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

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

Endometrial cancer
N=27

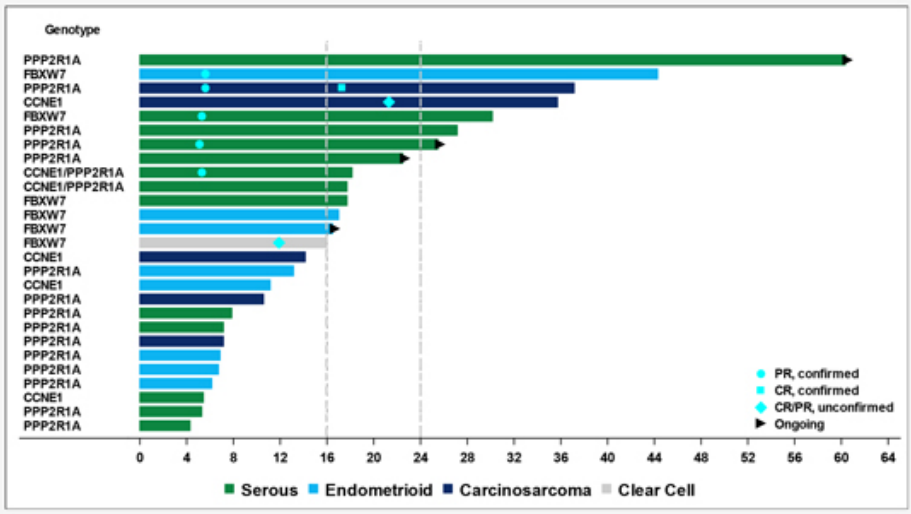
Heavily pre-treated patients:

- **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%

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

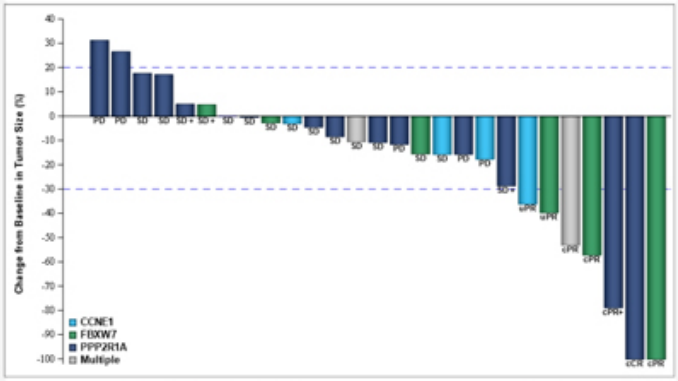
Abbreviations: **KM**, Kaplan Meier estimate. **CBR**, clinical benefit rate defined as having CR, PR, or at least 16 weeks treatment without PD.

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

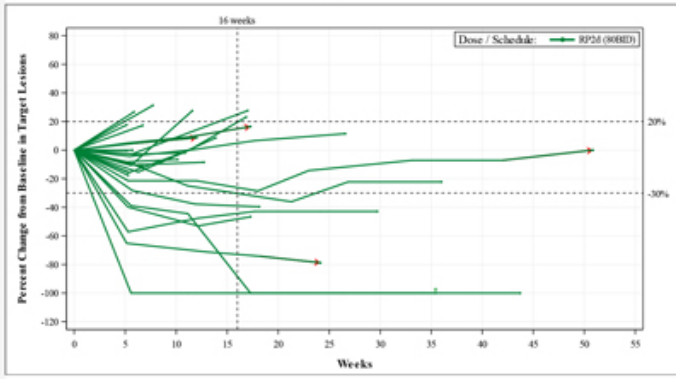
EC: Deep and durable responses across all lunre BM+ subsets

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

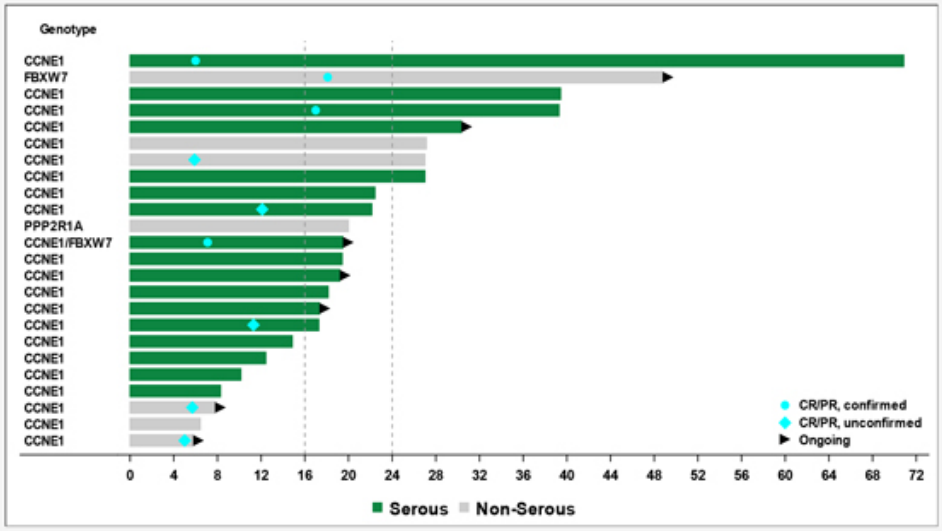
Heavily pre-treated patients:

- **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

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 respons 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 wit first scan pending**

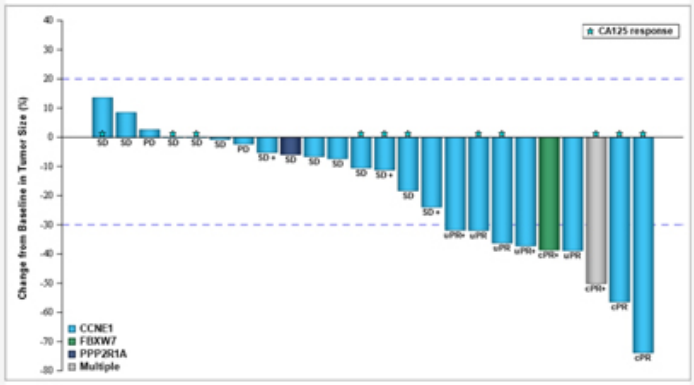
CBR, %	79%
PFS (%) at 24-weeks (90% CI)	45% (22-66%)
TRT ongoing w/o PD, n (%)	29%

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

REPARE THERAPEUTICS

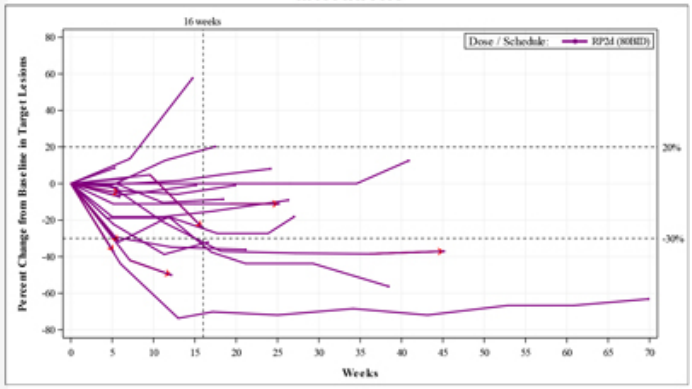
PROC: Strong efficacy in lunre BM+ tumors

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

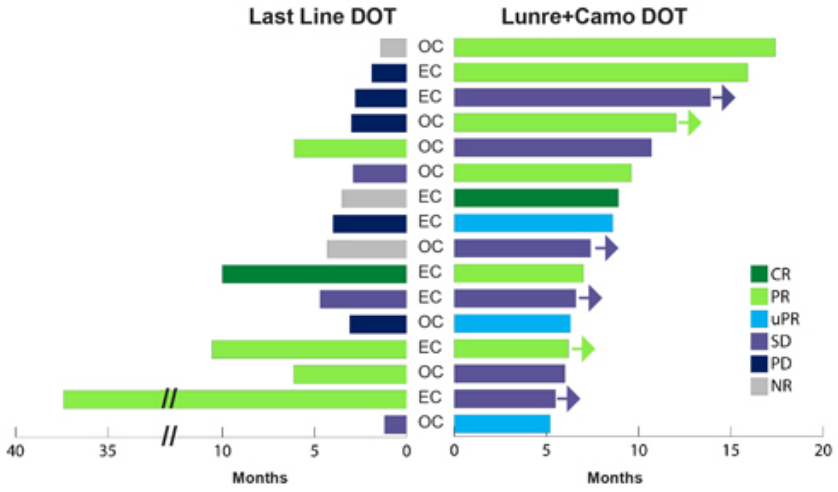
Lunre+camo combination demonstrated:

- 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%)

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 o lunre+camo had generally short treatmer 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 hi risk, high unmet need Lunre BM+ tumors**

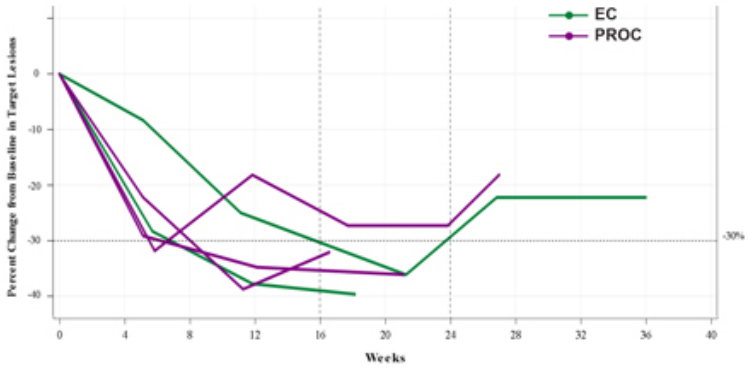
Reference: 1. https://pubmed.ncbi.nlm.nih.gov/27234642/; https://medelis.com/abstracts/the-lost-opportunity-in-phase-i-oncology-clinical-trials/.

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** culminatin in benefit in patients with late PRs
- This **later response and benefit pattern** is expected to:
  - **Enable our planned and regulator-supported Ph randomized trial primary endpoint** (PFS)
  - **Meet requirements for accelerated approval** in th 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**

Pivotal development for EC supported by data and regulators

Path forward

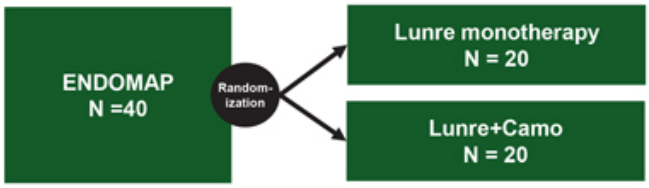
Focus on EC Pivotal trial start in 2025

- 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)**

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)

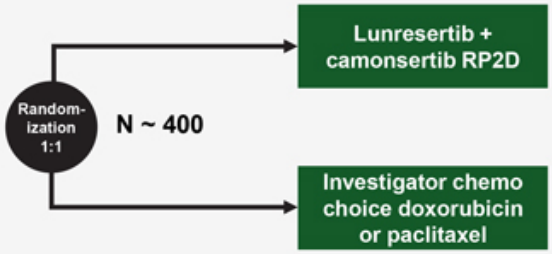
REPARE THERAPEUTICS

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

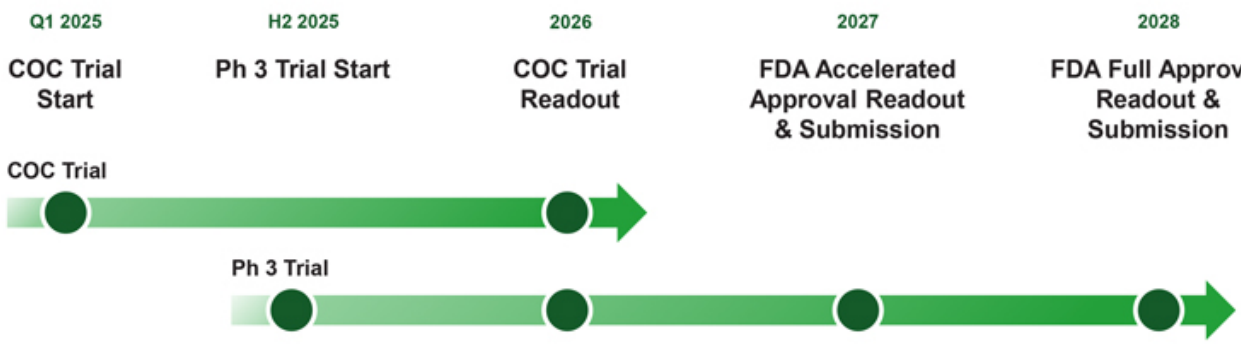
Targeted label: *Lunre+camo indicated for adult patients with CCNE1, FBXW7, PPP2R1A altered,* serous, endometroid or carcinosarcoma endometrial cancer, who have disease progression following prior systemic treatment regimens with ICI and at least one chemotherapy/ADC in any setting. Patients selected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

Note: BICR, Blinded Independent Central Review

Registrational path forward for endometrial cancer

EC as lead indication: Targeting 2028 NDA submission

Anticipated milestones starting with Q1 2025 initiation of COC trial



REPARE THERAPEUTICS

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

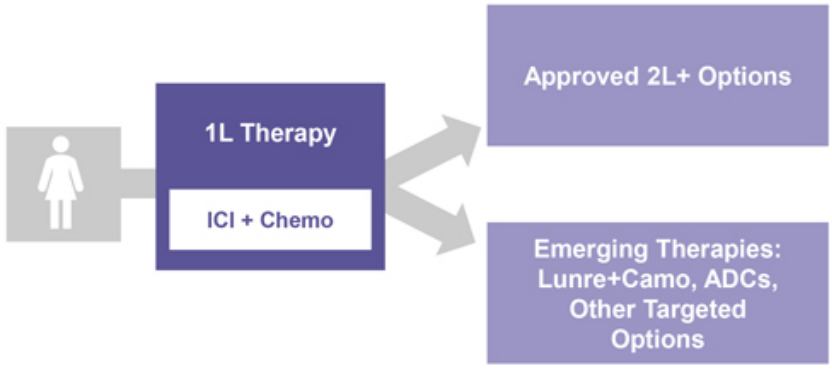
"One doctor says, 'we have a chemo you haven't tried; we guarantee it'll make you sick, but we don't guarantee you'll recover.' And another doctor says that chemo has not been shown to help with your specific cancer…There is no reason to torture myself on a 'maybe.'"

-Patient

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

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**



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

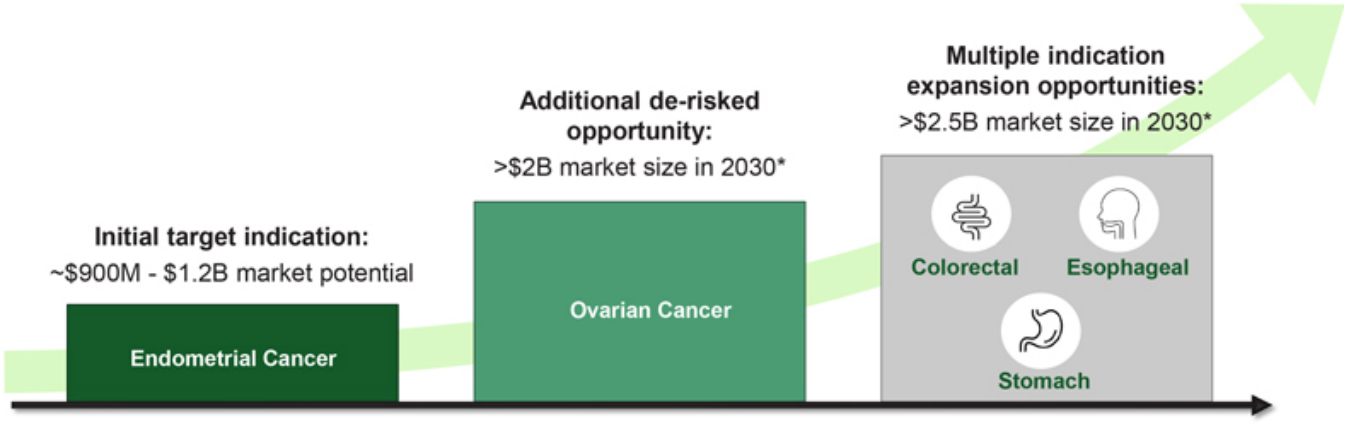
Lunre+camo indicated for adult patients with CCNE1, FBXw7, PPP2R1a altered, serous, endometroid or carcinosarcoma endometrial cancer, who have disease progression following prior systemic treatment regimens with ICI and at least one chemotherapy/ADC in any setting. Patients selected based on an FDA-approved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

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


REPARE
THERAPEUTICS
Thank you.
RepareRx.com
©2024 Repare Therapeutics