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

December 12, 2024

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 Polθ 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 plan 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/.

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