Repare Therapeutics Announces New Data Underscoring Need for Additional Treatment Solutions for Patients with Metastatic Gynecologic Cancers

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Data presented at AACR's Ovarian Cancer Research Symposium confirm that ovarian and endometrial cancers with CCNE1 amplifications, FBXW7 or PP2R1A mutations carry poor prognosis

Significant survival disparities were identified in patients harboring lunresertib- and camonsertib-sensitizing biomarkers, including CCNE1 *amplifications or mutations in* FBXW7 *or* PPP2R1A

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Sep. 23, 2024-- Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company, presented new data on Friday highlighting the impact of alterations in *FBXW7, PPP2R1A* and *CCNE1* in patients with metastatic ovarian and endometrial cancers based on an analysis in approximately 2,000 patients from Cancer Genome Atlas Research Network and Memorial Sloan Kettering's Metastatic Events and Tropisms.

The poster presentation was shared at the American Association of Cancer Research's (AACR) 15 th Annual Ovarian Cancer Research Symposium in Seattle, underscores inherent chemotherapy resistance and the lack of treatment options for metastatic gynecologic cancer patients with these biomarkers.

"Patients with recurrent ovarian and endometrial cancers are already at a disadvantage when it comes to treatment options," said Maria Koehler, MD, PhD, Executive Vice President and Chief Medical Officer of Repare. "These new data highlight the urgent need for innovative therapeutic approaches to address the specifically poor prognosis associated with *FBXW7, PPP2R1A* and *CCNE1* alterations treated with standard of care-based chemotherapy. We look forward to reporting data from our MYTHIC dose expansion trial evaluating lunresertib in combination with camonsertib in patients with ovarian and endometrial cancers with these biomarkers in the fourth quarter of 2024."

Repare Therapeutics' Phase 1 MYTHIC clinical trial (NCT04855656) is studying the combination of lunresertib, a first-in-class oral small molecule PKMYT1 inhibitor, and camonsertib, a potential best-in-class oral small molecule ATR inhibitor, in patients harboring lunresertib-sensitizing biomarkers (Lunre BM), including *CCNE1* amplifications or mutations in *FBXW7* or *PPP2R1A*. While *CCNE1* amplifications occur in approximately 30% of platinum-resistant ovarian cancers,[1-2] and are well established as a poor prognostic indicator in ovarian cancer,[3-6] little is known about other Lunre BM in ovarian and endometrial cancers.

Ovarian Cancer:

The presence of Lunre BM (alterations in *CCNE1*, *PPP2R1A*, or *FBXW7*) in ovarian cancer patients (n=1,029) is linked to a substantially lower survival rate compared to those without these biomarkers, underscoring their prognostic significance:

- Median overall survival (mOS) for patients with these biomarkers (Lunre BM+) is 26 months (95% CI, 18-38), compared to 36 months (95% CI, 30-43) for patients without these biomarkers (Lunre BM-; HR = 1.46 [95% CI, 1.14-1.87], p=0.003), a 28% decrease in mOS

Endometrial Cancer:

Endometrial cancer patients (n=895) with biomarkers *CCNE1*, *PPP2R1A*, and *FBXW7* demonstrate poorer survival outcomes, which are influenced by their association with high-risk histologies and genetic alterations:

- Median overall survival (mOS) for patients with these biomarkers (Lunre BM+) is 30 months (95% CI, 24-38), compared to 41 months (95% CI, 31-60) for patients without these biomarkers (Lunre BM-; HR = 1.29 [95% CI, 1.03-1.60], p=0.024), a 27% decrease in mOS
- The presence of these biomarkers also correlates with high-risk histologies (uterine carcinosarcoma and uterine serous carcinoma) and p53 mutant genotypes, well known for adverse prognosis

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 preclinical Polθ ATPase inhibitor program; 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 impact of alterations in FBXW7, PPP2R1A and CCNE1 in patients with metastatic ovarian and endometrial cancers; the design, objectives, initiation, timing, progress and results of current and future clinical trials of the Company’s product candidates, including the timing of data from the expansion of its Phase 1 MYTHIC trial evaluating lunresertib alone and in combination with camonsertib; the potential of lunresertib in combination with camonsertib in patients harboring lunresertib-sensitizing biomarkers and the tolerability, efficacy and clinical progress of the Company’s product candidates. 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, 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; 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 June 30, 2024 filed with the Securities and Exchange Commission (“SEC”) and the Québec Autorité des Marchés Financiers ("AMF") on August 6, 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/.

1. Cancer Genome Atlas Research Network. *Nature.* 2011;474(7353):609–615

2. Smith P, et al. *Nat Commun.* 2023;14(1):4387

3. Chan AM, et al. *J Pathol Clin Res*. 2020;6(4):252–262

4. Kang E-Y, et al. *Cancer*. 2023;129(5):697–713

5. Nakayama N, et al. *Cancer.* 2010;116(11):2621–2634

6. Stronach EA, et al. *Mol Cancer Res*. 2018;16(7):1103–1111.

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