



Repare Therapeutics Presents Initial Clinical Data from the Phase 1/2 TRESR and ATTACC Trials Evaluating Camonsertib in Combination with Three PARP Inhibitors at the 2023 AACR Annual Meeting

April 18, 2023

Camonsertib PARPi combinations demonstrated 48% CBR in patients with unmet medical needs, across tumor types, and regardless of PARPi partner or platinum resistance, with a favorable safety and tolerability profile

Combination results showed most benefit in late-line ovarian cancer demonstrating 32% overall response, 58% CBR and mPFS of approximately 7 months

Early ctDNA molecular responses in 66% of evaluable patients confirms antitumor activity of low dose intermittent PARPi + ATRi therapy

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Apr. 18, 2023--

Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today presented initial data from its ongoing Phase 1/2 TRESR clinical trial evaluating camonsertib (RP-3500/RG6526, partnered with Roche), a potent and selective oral small molecule inhibitor of ATR (Ataxia-Telangiectasia and Rad3-related protein kinase), in combination with a poly (ADP-ribose) polymerase inhibitor (PARPi), talazoparib, and initial data from its ongoing Phase 1b/2 ATTACC clinical trial, evaluating camonsertib in combination with two additional PARPis, niraparib or olaparib, in patients with advanced solid tumors.

The data involving novel combinations of low doses of camonsertib and three different PARPis are featured today at the 2023 AACR Annual Meeting in a clinical plenary session titled, "Safety and efficacy of three PARP inhibitors (PARPi) combined with the ataxia telangiectasia- and Rad3-related kinase inhibitor (ATRi) camonsertib in patients (pts) with solid tumors harboring DNA damage response (DDR) alterations" (abstract presentation number CT018). This study population comprised patients with a broad range of historically difficult to treat tumors, including patients with platinum-resistant tumors, patients who had either recurred or progressed during or after treatment with PARPis, and patients who had developed known BRCA-reversion mutations.

"We see promise in the camonsertib-PARPi combinations when administered concomitantly, at low doses across tumor types, especially in recurrent ovarian cancer given that nearly all had recurred after prior PARPi treatment. We are particularly encouraged by the depth of response and duration of treatment," said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. "Dose optimization to refine the combinatorial dose in additional tumor-specific expansions beyond ovarian within our ATTACC study is ongoing as part of our collaboration with Roche."

"We previously established a promising safety and early efficacy profile of camonsertib as a monotherapy and this year's data at AACR further support camonsertib as a partner for combinational regimens and provides a clear rationale for further development of this compound," said Lloyd M. Segal, President and Chief Executive Officer of Repare. "Notably, the circulating tumor DNA (ctDNA) data showed a strong correlation with the degree of tumor shrinkage and duration of disease control, and provide a mechanistic explanation for the observed durable clinical benefit in heavily pretreated patients, beyond the natural history of the disease. We look forward to refining our dose optimization efforts and efficacy assessment in tumor specific expansions. This data remains consistent with what we were anticipating at the time of entering our partnership with Roche and we are excited to continue this important clinical development together."

Key Initial Findings from the TRESR Phase 1/2 and ATTACC 1b/2 PARPi Combination Studies:

TRESR (NCT04497116) is a first-in-human, multi-center, open-label Phase 1/2 dose-escalation and expansion study, designed to establish the recommended Phase 2 dose and schedule, evaluate safety and pharmacokinetics and identify preliminary anti-tumor activity associated with camonsertib, given alone and in combination with talazoparib or in combination with gemcitabine.

ATTACC (NCT04972110) is a first-in-human, multi-center, open-label Phase 1b/2 dose-escalation and expansion study, designed to evaluate safety and pharmacokinetics and identify preliminary anti-tumor activity associated with camonsertib in combination with niraparib or olaparib.

The clinical plenary session described initial combination Phase 1/2 results from 107 patients, of which 90 patients were evaluable for efficacy treated at least 13 weeks prior to the data cutoff of February 27, 2023.

Key highlights from the data presented at the 2023 AACR Annual Meeting include:

- Camonsertib combination resulted in durable clinical benefit across tumor types and different genomic alterations, regardless of choice of PARPi and presence of platinum resistance. Overall clinical benefit rate (CBR) for all patients was 48%. Patients with platinum-resistant tumors had an overall response rate (ORR) of 12% and CBR of 49%, and benefited similarly to non-platinum-resistant tumors (ORR 13%, CBR 46%).
- Compelling results were observed particularly in patients with advanced ovarian cancer (n = 19). In these patients, overall response was 32%, CBR was 58% and median progression-free survival (mPFS) was approximately 7 months with treatment >16 weeks and ongoing in 9 patients.
- Early ctDNA molecular responses in 66% (31/47) of evaluable patients confirms antitumor activity of low dose, intermittent PARPi + ATRi therapy. The molecular response rate (MRR) was significantly higher in patients with clinical benefit (83%) compared to those without (48%; p=0.015), confirming treatment effect. Molecular responses were observed in patients with prior PARPi exposure (57%) and platinum resistance (64%).

- Camonsertib combinations appear to be well tolerated. Dose limiting toxicity (DLTs) in 68 patients treated with the proposed combination doses were related to myelotoxicity only (Grade 3+ anemia 3%, thrombocytopenia 6%, neutropenia 7%, and febrile neutropenia 3%). No prophylactic growth factors were required when administering the PARPis at evaluated doses.

Additional relevant presentations at AACR:

Title: Characterization of CCNE1 amplifications and associated genomic features in ovarian and uterine cancers

Session: Biomarkers of Therapeutic Benefit 5, Tuesday April 18, 2023, 1:30 PM - 5:00 PM

Abstract Number: 5469

Title: Tumor heterogeneity of CCNE1 copy number assessed by fluorescence *in situ* hybridization (FISH) in ovarian and uterine cancers and correlation with cyclin E protein expression

Session: Biomarkers of Therapeutic Benefit 2, Monday April 17, 2023, 9:00 AM - 12:30 PM

Abstract Number: 2132

Title: Targeting PKMYT1 kinase is an effective treatment strategy in triple negative breast cancers with low molecular weight cyclin E (LMW-E) expression

Session: Biomarkers of Therapeutic Benefit 1, Sunday April 16, 2023, 1:30 PM - 5:00 PM

Abstract Number: 950

Title: Investigating Wee1 and Myt1 combined inhibition as a potential cancer therapeutic strategy

Session: Combination Therapies for Cancer, Tuesday April 18, 2023, 1:30 PM - 5:00 PM

Abstract Number: 5511

About Repare Therapeutics' SNIPRx® Platform

Repare's SNIPRx® platform is a genome-wide CRISPR-based screening approach that utilizes proprietary isogenic cell lines to identify novel and known synthetic lethal gene pairs and the corresponding patients who are most likely to benefit from the Company's therapies based on the genetic profile of their tumors. Repare's platform enables the development of precision therapeutics in patients whose tumors contain one or more genomic alterations identified by SNIPRx® screening, in order to selectively target those tumors in patients most likely to achieve clinical benefit from resulting product candidates.

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 RP-6306, a PKMYT1 inhibitor currently in Phase 1 clinical development; camonsertib (also known as RP-3500 or RG6526), a potential leading ATR inhibitor currently in Phase 1/2 clinical development and partnered with Roche; a preclinical Polθ inhibitor program; as well as several additional, undisclosed preclinical programs. For more information, please visit [reparerx.com](https://www.reparerx.com).

SNIPRx® is a registered trademark of Repare Therapeutics Inc.

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 safety, efficacy and clinical progress of the Company's clinical trials of camonsertib and the Company's continued development of camonsertib in partnership with Roche. 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 impacts of macroeconomic conditions, including the COVID-19 pandemic, the conflict in Ukraine, rising 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, 2022 filed with the Securities and Exchange Commission ("SEC") and the Québec Autorité des Marchés Financiers ("AMF") on February 28, 2023, and its other documents subsequently filed with or furnished to the SEC and AMF. 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](https://www.reparerx.com) and follow Repare on Twitter at @RepareRx and on LinkedIn at <https://www.linkedin.com/company/repare-therapeutics/>.

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