Repare Therapeutics Announces Updated Positive Safety and Tolerability Results from the Phase 1 MYTHIC Clinical Trial

October 23, 2024

Data presented at EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Oct. 23, 2024-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today presented updated data highlighting the benefits of its individualized schedule for the management of anemia in the Phase 1 MYTHIC clinical trial treating patients with the combination of lunresertib, a first-in-class PKMYT1 inhibitor, and camonsertib, a potential best-in-class oral small molecule ATR inhibitor (lunre+camo).

Lunre+camo in the MYTHIC clinical trial (NCT04855656) previously demonstrated promising clinical activity in molecularly selected patients across multiple tumor types. In this analysis, Repare followed patients for approximately nine months at the recommended Phase 2 dose (RP2D) to assess the effectiveness of an individualized schedule. The analysis demonstrated a successful approach to mitigating mechanism-based anemia while maintaining clinical benefit. Further, Repare observed no thrombocytopenia of any grade nor serious neutropenia in these patients.

Dr. Martin Højgaard of Rigshospitalet, Denmark presented this data in a poster titled, “Individualized schedule improves rates and severity of anemia in patients treated with lunresertib, a PKMYT1 inhibitor, and camonsertib, an ATR inhibitor, in the Phase I MYTHIC study (NCT04855656)” at the 36th EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics, being held October 23-25, 2024 in Barcelona, Spain.

“This individualized schedule in heavily pretreated patients with advanced cancers from our MYTHIC clinical trial met its goal of maintaining antitumor activity while reducing rates of grade 3 anemia,” said Maria Koehler, MD, PhD, Executive Vice President and Chief Medical Officer of Repare. “We believe that these data demonstrate a favorable and differentiated tolerability profile versus both current and emerging therapies. We look forward to sharing efficacy data from the gynecological cancer expansion cohort of the MYTHIC clinical trial in December 2024.”

Key Clinical Trial Findings:

- The individualized schedule mitigated mechanism-based anemia based on entry hemoglobin observed in a minority of patients
- Overall clinical benefit was maintained after schedule change with generally maintained radiographic regressions and molecular responses:
  - Despite the change in schedule, deepening of target lesion regression was noted in some patients
  - After 9 weeks on therapy, there was no observed impact on Progression Free Survival (PFS) in patients who started on or switched to the schedule of 2 weeks on / 1 week off of treatment
- Dose optimization meaningfully reduced Grade 3 anemia (22.6% vs. 51.4%, previously) in all patients:
  - Baseline marrow function was the key reason for Grade 3 anemia as opposed to exposure to therapy
  - Baseline hemoglobin, prior therapies, and treatment intensity (weekly vs. 2 weeks on / 1 week off) predicted Grade 3 anemia frequency with lunre+camo
  - Anemia reduction was greatest in patients with baseline hemoglobin less than 11g/dL (Grade 3 anemia at week 12: 34% vs. 68%, previously; overall risk reduction: 58%)
  - Red blood cell transfusions (13% vs. 43%, previously), dose interruptions (13% vs. 23%) and dose reductions (6% vs. 17%) were also reduced with the new schedule
  - Other Grade 3 events were already uncommon (<5% incidence) and remained consistently low, regardless of schedule

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 design, objectives, timing, progress and results of the Phase 1 MYTHIC clinical trial of camonsertib in combination with lunresertib; and the tolerability, efficacy and clinical progress of the Company’s product candidates, including camonsertib and lunresertib. 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, 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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