Repare Therapeutics Announces Positive Initial Data at ESMO GI from Phase 1 MINOTAUR Trial Evaluating Lunresertib in Combination with FOLFIRI

June 26, 2024

Overall response of 18.2% in heavily pretreated patients across gastrointestinal tumors with target alterations regardless of prior irinotecan exposure

Prolonged clinical benefit in patients with CRC, with 40% of irinotecan-naïve patients receiving treatment for greater than nine months

Preliminary RP2D established as 60mg BID lunresertib continuous plus standard FOLFIRI

Safety profile of combination consistent with FOLFIRI alone

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Jun. 26, 2024-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today reported positive initial data from the ongoing Phase 1 MINOTAUR clinical trial evaluating lunresertib (RP-6306) in combination with FOLFIRI in patients with advanced solid tumors. The data are being presented in a mini oral presentation by Elisa Fontana, M.D., Ph.D., Medical Director, Sarah Cannon Research Institute UK at the European Society of Medical Oncology (ESMO) Gastrointestinal (GI) Cancers Congress 2024, being held June 26-29 in Munich, Germany.

“The initial results from the ongoing MINOTAUR trial demonstrate promising efficacy and tolerability data of lunresertib plus FOLFIRI in genomically defined tumors that represent 20% of all gastrointestinal cancers,” said Dr. Elisa Fontana. “These early data suggest that lunresertib plus FOLFIRI combination therapy may effectively treat patients with *CCNE1* amplification and deleterious *FBXW7* mutations, who often suffer from poor prognosis and lack approved treatment options. We are excited by the prolonged benefit that some patients continue to experience on therapy, especially in colorectal cancer, and the favorable tolerability of this lunresertib combination therapy across tumor types, unlike other agents combined with irinotecan.”

Lunresertib is a first-in-class precision oncology small molecule PKMYT1 inhibitor that targets *CCNE1* amplification, *FBXW7* and *PPP2R1A* alterations in solid tumors. Lunresertib is being evaluated in combination with other therapies across several Phase 1 and Phase 2 clinical trials, as well as in multiple investigator-sponsored trials.

Key Initial Findings from the Phase 1 MINOTAUR Clinical Trial:

MINOTAUR (NCT05147350) is a Phase 1, multi-center, open-label, dose-scalation study to evaluate safety, pharmacokinetics, pharmacodynamics and preliminary anti-tumor activity of lunresertib in combination with FOLFIRI in advanced solid tumors. Primary objectives of the study were safety and tolerability, and determination of the recommended Phase 2 dose (RP2D) and schedule. Secondary objectives were pharmacokinetics, preliminary evidence of anti-tumor activity, pharmacodynamics, and circulating tumor DNA (ctDNA) monitoring. As of May 2, 2024, the cutoff date for the data presented at the ESMO GI Congress, 38 patients were enrolled in the clinical trial.

- Preliminary RP2D established as 60mg BID lunresertib continuous plus standard FOLFIRI
- Promising efficacy in heavily pretreated population with tumors that harbor *CCNE1* amplification and *FBXW7* mutation alterations
    - Overall response (OR) across tumor types was 18.2% (n=33), including four confirmed and two unconfirmed partial responses (PR), regardless of prior irinotecan exposure
    - Prolonged clinical benefit rate (CBR) across tumor types, primarily digestive system tumors, was 51.5%, including 46.7% of patients with recurrent colorectal cancer (CRC)
    - Patients with CRC (n=15) had prolonged duration of therapy, with 40% (2/5) of irinotecan-naïve patients and 20% (2/10) of irinotecan-experienced patients on treatment for over nine months, compared to clinical benchmarks of 20% and 5-10%, respectively
    - ctDNA molecular response rate was 61% among evaluable patients (14/23)
- Lunresertib combination therapy was well tolerated without excess toxicity above expected rates for lunresertib or standard FOLFIRI alone
    - No safety-related treatment discontinuations at preliminary RP2D
    - Neutropenia and leukopenia were the most common Grade 3/4 treatment-related adverse events (TRAE), consistent with that reported for FOLFIRI alone and reversible with FOLFIRI interruption
    - Rate of low-grade, reversible rash was consistent with lunresertib monotherapy experience

“The encouraging tolerability and early antitumor efficacy data and the potential duration of treatment advantage of the combination of lunresertib plus FOLFIRI in this heavily pretreated patient population warrant further development in a randomized Phase 2 study,” said Maria Koehler, MD, PhD, Executive Vice President and Chief Medical Officer of Repare. “Lunresertib in combination with FOLFIRI has the potential to provide a new therapeutic option targeting tumors harboring *CCNE1* amplification and *FBXW7* mutation alterations in gastrointestinal tumors, which are known to be associated with poor prognosis and where there are currently no approved treatment options.”

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.

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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, initiation, timing, progress and results of current and future clinical trials of the Company's product candidates, including its Phase 1 MINOTAUR trial of lunresertib; the potential of lunresertib in combination with FOLFIRI to treat patients with advanced solid tumors; the tolerability, efficacy and clinical progress of lunresertib; and the benefits and ability to discover further targets and clinical candidates from the Company's discovery platform. 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 between Israel and Hamas, 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 collaborations 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 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 its Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 filed with the SEC on May 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 Twitter at @RepareRx and on LinkedIn at https://www.linkedin.com/company/repare-therapeutics/.

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