Repare Therapeutics Presents Updated Clinical Data from the Ongoing Phase 1/2 TRESR Study of RP-3500 Monotherapy in Solid Tumors at the 2022 AACR Annual Meeting

April 11, 2022

RP-3500 shows robust activity in ovarian cancer demonstrating 75% CBR, with 25% ORR and mPFS of 35 weeks

Updated monotherapy results show 43% CBR in solid tumors across genotypes, and potential best-in-class safety and tolerability

Encouraging data in tumors harboring STEP^2 genes, including BRCA1/2 mutations, where RP-3500 monotherapy led to 43% CBR and mPFS of 15 weeks

Company to host conference call today at 6:30 p.m. ET

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Apr. 11, 2022-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today presented updated data from its ongoing Phase 1/2 TRESR (Treatment Enabled by SNIPRx) clinical trial of RP-3500, a potent and selective oral small molecule inhibitor of ATR (Ataxia-Telangiectasia and Rad3-related protein kinase) for the treatment of solid tumors with specific synthetic-lethal genomic alterations including those in the ATM gene (Ataxia-Telangiectasia mutated kinase) at the 2022 AACR Annual Meeting.

“We see promising monotherapy data across tumor types, particularly in advanced ovarian cancer where 90% of patients had failed previous treatment with PARP inhibitors and platin based therapy. We are especially pleased with the 25% overall response observed, the clinical benefit rate of 75% and a median PFS of 35 weeks in this heavily pre-treated patient population with a growing unmet need,” said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. “These findings, together with anticipated initial data of RP-3500 in combination with PARP inhibitors or gemcitabine expected in the second half of this year, will help us refine our development strategy for this potential best-in-class drug.”

The data were featured today at the AACR Annual Meeting in an oral presentation titled, “Genomic and pathologic determinants of response to RP-3500, an ataxia telangiectasia and Rad3-related inhibitor, in patients with DNA damage repair loss-of-function mutant tumors in the Phase 1/2 TRESR trial” (abstract number CT030).

“The data presented today continue to demonstrate RP-3500’s promising clinical benefit given as monotherapy in patients with solid tumors with multiple genotypes, as predicted by our SNIPRx platform, as well as a potential industry-leading safety and tolerability profile for ATR inhibitors,” said Lloyd M. Segal, President and Chief Executive Officer of Repare. “Our comprehensive new dataset shows ATM loss of function as a compelling opportunity to offer durable clinical benefit to patients with genetically defined tumors. Additional results beyond ATM, such as the early efficacy seen in other genotypes involving BRCA1/2, SETD2 and RAD51C alterations, represent substantial validation of our STEP^2 platform to identify other synthetic lethalities as we expand TRESR and develop our pipeline of synthetic lethal candidates.”

The Company will subsequently host a conference call today, April 11th at 6:30 p.m. Eastern Time to discuss the latest results from the TRESR trial.

Key Initial Findings from the TRESR Phase 1/2 Study:

TRESR 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 (RP2D) and schedule, evaluate safety and pharmacokinetics and identify preliminary anti-tumor activity associated with RP-3500, given alone and in combination with talazoparib. The study also examined biomarker responses and their relationship with response to RP-3500 treatment.

The oral presentation described monotherapy Phase 1 (Module 1) results from 120 patients, of which 99 patients were evaluable for efficacy, including 95 patients at RP2D of 160mg and schedule taken weekly for 3 days on/4 days off, and reflecting a data cutoff of 14th February, 2022. Key highlights from the data presented at the 2022 AACR Annual Meeting include:

- RP-3500 monotherapy continues to appear safe and well tolerated. Expectedly, Grade 1-2 anemia was the most common treatment-related adverse event and well controlled in patients. Only 24.2% of all patients in the 3 days on 4 days off schedule experienced Grade 3 anemia, and none Grade 4 anemia.
- RP-3500 monotherapy resulted in durable clinical benefit across tumor types and genomic alterations. Overall clinical benefit rate (CBR) for all patients was 43%, and 47% in patients after PARP inhibitor (PARPi) failure.
- Promising results were observed particularly in patients with advanced ovarian cancer (n = 20). 90% of evaluated patients had prior PARPi failure, and 85% of evaluated patients were platinum resistant. In these patients, overall response (OR) was 25%, including one complete response (CR), three partial responses (PR) as determined by RECIST 1.1 criteria, and one durable and ongoing CA125 response. CBR was 75% and median progression-free survival (mPFS) was 35 weeks.
- Clinical benefit was also observed in patients with tumors harboring BRCA1 and BRCA2 genomic alterations, as predicted by SNIPRx. In patients with BRCA1/2 mutated tumors (n = 37), ORR was 14% and included two patients with ovarian cancer, and one each with breast cancer, head and neck squamous cell carcinoma, and melanoma. CBR was 43% with a mPFS of 15 weeks in the BRCA1/2 population; in patients specifically with BRCA1 mutations, the CBR was 48%.
- In patients with ATM loss-of-function (LOF) tumors (n = 34), ORR was 9% including one RECIST 1.1 confirmed/unconfirmed response, and two prostate specific antigen (cPSA) responses. CBR in patients with ATM LOF was 44%, with mPFS of 17 weeks.

- New sequencing data demonstrated biallelic gene LOF, an emerging biomarker for synthetic lethal therapies, can potentially be leveraged to further enrich for patients most likely to benefit from RP-3500. CBR in patients with biallelic LOF was significantly higher (47%) compared to the CBR in patients with non-biallelic tumors (15%).

A second poster presentation titled, “Detection of biallelic loss of DNA repair genes in formalin-fixed, paraffin embedded (FFPE) tumor samples using a novel tumor-only sequencing panel with error correction” (abstract number 2801) will be presented on Tuesday, April 12, 2022. Results demonstrated the role of SNiPDx, a central next-generation sequencing assay, in determining biallelic LOF, germline status and clonal hematopoiesis of indeterminate potential (CHIP) alterations, in patients enrolling in the TRESR study.

Company Conference Call:

The Company will host a conference call with accompanying slides for analysts and investors today at 6:30 p.m. Eastern Time to further discuss the RP-3500 data presented at the 2022 AACR Annual Meeting. Repare’s executive management team will be joined by Timothy Yap, MBBS, PhD, FRCP, Principal Investigator and Medical Director, Institute for Applied Cancer Science, Associate Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX.

To access the call, please dial (877) 870-4263 (U.S. and Canada) or (412) 317-0790 (international) at least 10 minutes prior to the start time and ask to be joined to the Repare Therapeutics call. A live video webcast will be available in the Investor section of the Company’s website at https://ir.reparerx.com/news-and-events/events. A webcast replay will also be archived for at least 30 days.

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 its lead product candidate RP-3500, a potential leading ATR inhibitor currently in Phase 1/2 clinical development, its second clinical candidate, RP-6306, a PKMYT1 inhibitor currently in Phase 1 clinical development, a Polθ inhibitor program, as well as several early-stage, pre-clinical programs. For more information, please visit reparerx.com.

SNIPRx® is a registered trademark of Repare Therapeutics Inc.

Forward-Looking Statement

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. 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 clinical development of the Company’s pipeline and its research and development programs, including the anticipated timing, anticipated patient enrollment, trial outcomes or associated costs of its Phase 1/2 TRESR clinical trial of RP-3500. 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 the COVID-19 pandemic 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, 2021 filed with the Securities and Exchange Commission (“SEC”) and the Québec Autorité des Marchés Financiers ("AMF") on March 1, 2022, 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.

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