Repare Therapeutics Presents Preliminary Phase 1 Monotherapy Clinical Data from the Ongoing First-in-Human Phase 1/2 TRESR Study of RP-3500 in Solid Tumors at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

October 8, 2021

Initial TRESR data provide clinical proof of concept and validate Repare Therapeutics' SNIPRx platform for molecular selection of tumors for therapy with RP-3500

Favorable and differentiated safety profile, along with promising and distinct early activity, offer clear direction for future development of RP-3500

Company-sponsored Virtual Webcast Event Today at 5:00 p.m. ET

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Oct. 8, 2021-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today announced the presentation of preliminary Phase 1 monotherapy clinical data from its 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 teleangectasia mutated kinase), at the AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics.

The data are featured today at the AACR-NCI-EORTC conference in an oral presentation titled, “First-in-Human biomarker-driven Phase I TRESR trial of ATR inhibitor RP-3500 in patients with advanced solid tumors harboring synthetic lethal genomic alterations” (Abstract number 4950). Preliminary data show that monotherapy RP-3500 is safe and well tolerated, with compelling early efficacy signals across multiple genotypes and tumor types in heavily pretreated patients.

The Company will subsequently host a virtual webcast event today, October 8th at 5:00 p.m. Eastern Time to discuss the latest results from the TRESR trial.

“Our initial data for 101 patients treated with RP-3500 in the ongoing TRESR study resulted in a firm recommendation for Phase 2 dose and schedule, suggest a favorable and differentiated safety profile and provide compelling early evidence of broad clinical efficacy across genotypes predicted by our SNIPRX platform,” said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. “The evolving nature of the data from this ongoing study and specifically the stable tolerability profile and maturing efficacy data offer a clear direction for further development of RP-3500. Additionally, we are excited to see that even at this early point in our clinical program, the pharmacokinetic and pharmacodynamic biomarker data already confirm proof-of-mechanism for RP-3500 in tumors with diverse molecular backgrounds.”

“The TRESR study is the largest ever biomarker-selected trial testing single agent ATR inhibitor. We are very pleased that these data suggest RP-3500 may have a best-in-class profile as a potent and highly selective ATR inhibitor and represent compelling validation for the ability of our SNIPRx platform and our STEP^2 process to improve efficacy through molecular selection of tumors,” said Lloyd M. Segal, President and Chief Executive Officer of Repare. “We look forward to the imminent expansion of the TRESR study in a range of genotypes and, continuing and broadening our combination therapy studies, including with a range of PARP inhibitors and gemcitabine.”

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 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.

Data presented in the abstract reflect the monotherapy cohort at data cutoff of June 4, 2021 and include 62 patients, while data presented at the conference reflect a data cutoff of August 15, 2021 and include 101 patients. Highlights from the data presented at the AACR-NCI-EORTC conference include:

- RP-3500 appears safe and well tolerated. The most common treatment emergent adverse events (TEAE) in any of the 101 patients treated, expectedly, was grade 1-2 anemia, with only 21.8% of all patients experiencing Grade 3 anemia (no Grade 4), and only 14.5% of those patients treated on the recommended weekly schedule of 3 days on/4 days off.
- There were no discontinuations related to RP-3500 emergent adverse events and dose interruptions, reductions or red blood cell transfusions were infrequent on the recommended 3 days on/4 days off regimen.
- Recommended Phase 2 dose (RP2D) and schedule for further monotherapy RP-3500 evaluation is 160mg, taken weekly for 3 days on and 4 days off. This schedule assures repeated weekly exposure to RP-3500 at an efficacious dose.
- Antitumor activity was observed in patients with tumors harboring SNIPRX predicted genomic alternations at doses >100mg (ATM, CDK12, BRCA1, BRCA2, RAD51B, RAD51C, FZR1), across multiple tumor types and included patients after PARP inhibitor failure.
- Meaningful clinical benefit was observed in 49% of 69 patients with available scans. Those include 12 patients with tumor responses per established international efficacy criteria, 14 patients with ongoing stable disease for at least 16 weeks and 8 patients with stable disease who only had two radiological evaluations, but had demonstrated significant decreases in tumor markers and tumor shrinkage of less than 30%.
- Promising deep molecular responses in circulating tumor DNA (ctDNA) for tumors with STEP^2 genomic alterations were

observed in the initial set of patients available for serial ctDNA analysis

Company Virtual Webcast Event:

The Company will host a virtual investor webcast with accompanying slides for analysts and investors today at 5:00 p.m. Eastern Time to further discuss the RP-3500 data presented at the AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics. 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, Texas. At this event, the Company will provide an update on the status of the unconfirmed partial responses presented at the AACR-NCI-EORTC conference since the August 15, 2021 data cutoff.

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 eight other 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 lead product candidate, RP-3500 including details of the ongoing Phase 1/2 clinical trials of RP-3500 and the Company's plans for presentation of data relating to the clinical development program. 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 Quarterly Report for the period ended June 30, 2021 filed with the Securities and Exchange Commission ("SEC") on August 12, 2021 and any subsequent filings with the SEC. 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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