Repare Therapeutics Announces Dosing of First Patient in Phase 1/2 Clinical Trial of RP-3500

July 29, 2020

- RP-3500 is a potent and selective oral small molecule inhibitor of ATR being developed for the treatment of solid tumors with selected genomic alterations -

- Multi-center trial will evaluate RP-3500 as a monotherapy and in combination with Pfizer's PARP inhibitor, talazoparib (Talzenna®) -

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Jul. 29, 2020--

Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading precision oncology company enabled by its proprietary synthetic lethality approach to the discovery and development of novel therapeutics, today announced the first patient has been dosed in the Phase 1/2 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 genome instability-related genomic alterations including those in ATM gene (ataxia teleangectasia mutated kinase). The multi-center trial will enroll patients with advanced solid tumors of any histology that harbor gene alterations that suggest sensitivity to ATR inhibition as discovered by Repare's proprietary SNIPRx® platform. Dosing follows acceptance by the U.S. Food and Drug Administration (FDA) of the Company's investigational new drug (IND) application earlier this month.

"The TRESR (Treatment Enabled by SNIPRx) study of RP-3500 as a monotherapy or in combination with talazoparib is a promising targeted approach for a range of difficult-to-treat cancers in patients with tumors harboring genetic alterations we have identified and we believe could predict response," said Lloyd M. Segal, President and Chief Executive Officer of Repare. "The RP-3500 development plan reflects our strategy to develop differentiated oncology treatments in highly targeted tumors."

The Phase 1/2 clinical trial is a multi-center, open-label, dose-escalation and expansion trial that is expected to enroll approximately 230 patients with advanced solid tumors of any histology that harbor gene alterations determined pre-clinically to suggest sensitivity to RP-3500 alone or in combination with the PARP inhibitor, talazoparib. The primary outcome measure in the Phase 1 part of the study will be an assessment of safety and tolerability and determination of a dose for the Phase 2 portion of the trial. The Phase 2 monotherapy portion of the trial is expected to further evaluate the efficacy of RP-3500 in biomarker-selected tumors. Additional objectives include assessments of anti-tumor activity, pharmacokinetics (PK), pharmacodynamics (PD) and confirmation of the predictive biomarkers. The first patient dosing took place at The University of Texas MD Anderson Cancer Center ("MDACC") under the direction of the principal investigator Timothy Yap, M.D., Ph.D., Associate Professor in the Department of Investigational Cancer Therapeutics at MDACC. Additional centers in the United States, Canada, and Europe are anticipated to be opened in the near-term for patient recruitment.

RP-3500 has shown substantial anti-tumor activity in multiple preclinical models of solid tumors at doses below the maximum tolerated dose. In preclinical studies, sustained responses were associated with the presence of specific molecular alterations that will be tested in clinical studies. RP-3500 has also shown pre-clinical anti-tumor activity in combination with several PARP inhibitors in the presence of specifically identified genetic alterations. Repare selected talazoparib to test in combination with RP-3500 in collaboration with Pfizer. Talazoparib is being provided by Pfizer to Repare for the purposes of the clinical trial.

About Repare's 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 patients most likely to achieve clinical benefit from resulting product candidates.

About Repare Therapeutics, Inc.

Repare Therapeutics is a leading 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 response. The Company's pipeline includes its lead product candidate RP-3500, a potential leading ATR inhibitor, as well as CCNE1-SL inhibitor and Polθ inhibitor programs. For more information, please visit 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. All statements other than statements of historical facts are "forward-looking statements," including those relating to future events. In some cases, you can identify forward-looking statements by terminology such as "may," "might," "will," "should," "expect," "plan," "anticipate," "project," "believe," "estimate," "predict," "potential," "intend" or "continue," the negative of terms like these or other comparable terminology, and other words or terms of similar meaning. 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. Forward-looking statements contained in this press release include, but are not limited to, statements regarding the clinical development and therapeutic potential of RP-3500 and the Company's Phase 1/2 clinical trial of RP-3500 including the design of the trial, patient enrollment, clinical site activation and locations. 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 final prospectus dated June 18, 2020 and filed with the Securities and Exchange Commission pursuant to Rule 424(b) promulgated under the U.S. Securities Act of 1933, as amended. Except as required by law, the Company assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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