Repare Therapeutics Doses First Patient in Phase 1 Clinical Trial of RP-1664

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RP-1664 is a Potential First-in-Class, Selective, PLK4 Inhibitor

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Feb. 15, 2024-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today announced the first patient has been dosed in the Company’s Phase 1 LIONS (P **L**K4 Inh**i**bit**o**r i**n** Advanced **S**olid Tumors) clinical trial evaluating RP-1664, a potential first-in-class, highly selective, oral polo-like kinase 4 (PLK4) inhibitor, for the monotherapy treatment of adult and adolescent patients enriched for TRIM37-high solid tumors.

“RP-1664 exhibited deep tumor growth inhibition and regressions in multiple TRIM37-high solid tumor and neuroblastoma xenograft models, both internally and in collaboration with Children’s Hospital of Philadelphia. After evaluating safety in the LIONS clinical trial, we expect to move rapidly into a Phase 1/2 clinical trial in high risk, recurrent pediatric neuroblastoma, in which patients have a high prevalence of TRIM37-altered tumors and limited treatment options,” said Maria Koehler, MD, PhD, Executive Vice President and Chief Medical Officer of Repare. “RP-1664 is Repare’s third internally-developed clinical therapeutic candidate, a testament to the productivity of our platform.”

The LIONS clinical trial (NCT06232408) is a first-in-human, multicenter, open-label Phase 1 study to investigate safety, pharmacokinetics, pharmacodynamics and the preliminary efficacy of RP-1664. The clinical trial is expected to enroll approximately 80 patients with molecularly selected advanced solid tumors, including those with gain or amplification of TRIM37, among other genetic alterations. The primary endpoints are to determine the safety, tolerability, dose and schedule of RP-1664 and assess any early antitumor activity.

About RP-1664

RP-1664 is a potential first-in-class, highly selective, oral PLK4 inhibitor designed to harness the synthetic lethal relationship with TRIM37 amplification or overexpression in solid tumors. Tumors rely on PLK4 for centriole biogenesis in S-phase of the cell cycle when TRIM37, an E3 ligase that reduces pericentriolar material, is high. Preclinical studies demonstrate that RP-1664 selectively inhibits PLK4 and drives potent synthetic lethality in TRIM37-high tumor models, both in vitro and in vivo. Elevated TRIM37 is a feature found across a range of solid tumors and in approximately 80% of all high-grade neuroblastomas. RP-1664 is the only selective PLK4 inhibitor known to be in the clinic.

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 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.

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 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, enrollment, timing, progress and results of current and future preclinical studies and clinical trials of the Company’s product candidates, including its Phase 1 LIONS trial of RP-1664 and potential future Phase 1/2 study in high risk, recurrent pediatric neuroblastoma; the tolerability, efficacy and clinical progress of camonsertib, lunresertib, RP-1664 and RP-3467; the potential of RP-1664 as a first-in-class oral PLK4 inhibitor; 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: 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 COVID-19 pandemic, 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; 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, 2022 filed with the Securities and Exchange Commission ("SEC") and the Québec Autorité des Marchés Financiers ("AMF") on February 28, 2023, and its other documents subsequently filed with or furnished to the SEC and AMF including the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed with the SEC on November 9, 2023. 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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Repare:
Robin Garner
Vice President and Head of Investor Relations
Repare Therapeutics Inc.
investor@reparerx.com

Investors:
Matthew DeYoung
Argot Partners
repare@argotpartners.com

Media:
David Rosen
Argot Partners
david.rosen@argotpartners.com
212-600-1902

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