Repare Therapeutics to Highlight Program Progress for RP-6306 at Today's Virtual Investor Day Event

April 8, 2021

-Company highlights pre-clinical anti-tumor activity of RP-6306, a first-in-class, selective, oral inhibitor of PKMYT1, which is synthetic lethal with CCNE1 amplification and other genomic mutations-

- Initiation of Phase 1 clinical trial enrollment for RP-6306 anticipated to begin during this quarter-

-Conference call and webcast on Thursday, April 8 at 10:30 a.m. ET will feature academic experts Carol Aghajanian, M.D. and Timothy Yap, MBBS, Ph.D., FRCP-

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Apr. 8, 2021-- Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company enabled by its proprietary synthetic lethality approach to the discovery and development of novel therapeutics, will host a virtual Investor Day webcast today from 10:30 a.m. – 12:00 p.m. ET, highlighting the progress of its proprietary RP-6306 program for tumors with genetic alterations characterized by CCNE1 amplification. The Company expects to initiate a Phase 1 clinical trial of RP-6306 in the second quarter of 2021.

"At today's event, we will be reviewing the compelling pre-clinical anti-tumor activity of RP-6306, our first- in-class, selective, oral inhibitor of PKMYT1 to treat CCNE1-amplified, FBXW7-altered and other undisclosed PKMYT1 inhibitor-sensitive cancers. Our *in vivo* and other pre-clinical data indicate that RP-6306 can selectively inhibit tumors with these specific alterations when used as a monotherapy and in combination with other agents. We plan to initiate a Phase 1 clinical trial during this quarter, which is a quarter ahead of previously announced guidance," said Lloyd M. Segal, President and Chief Executive Officer of Repare. "We look forward to advancing our RP-6306 program into the clinic."

"There is a high unmet medical need for better treatments for patients with homologous recombinant-proficient cancers. The incidence of such cancers is rising and represents a growing therapeutic challenge," said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. "Targeting DNA damage repair using synthetic lethal strategies is a massive opportunity to build on the success of PARP inhibitors. The field is rapidly expanding beyond PARP inhibitors and has been accelerated by the discovery of novel targets enabled by cancer genome sequencing and CRISPR technologies."

Highlights from the Virtual Investor Day

Pre-Clinical Data Findings
Using its proprietary, CRISPR-based SNIPRx discovery platform, Repare has identified PKMYT1 as a strong hit in a CCNE1-overexpression synthetic lethal screen. PKMYT1 is a kinase that phosphorylates CDK1, thereby holding the cyclin B-CDK1 complex in an inactive state until the cell is ready to enter mitosis. The Company's product candidate RP-6306 is being developed as a highly potent and selective PKMYT1 inhibitor that preferentially kills tumor cells overexpressing CCNE1 and has shown to inhibit the growth of a broad range of CCNE1-amplified tumors in xenograft/PDX preclinical models, both as a single agent and in combination therapy settings. RP-6306 has been observed to have a favorable pre-clinical PK profile as well as low potential for drug-drug interactions. Application of Repare's STEP ^{2} genome-wide chemical screen has identified other gene alterations beyond CCNE1 amplification that are uniquely targetable by RP-6306, including tumors that have loss of FBXW7 function, a cell-cycle regulator that has been implicated as a key genetic driver in a broad range of cancers, and represent further areas of unmet medical need.

RP-6306 Phase 1 Clinical Trial Design
Repare plans to initiate enrollment of a Phase 1 clinical trial of RP-6306 during this quarter. Study objectives include assessment of safety, tolerability, dose and schedule (including the recommended Phase 2 dose). Subject to completion and review of the Phase 1 clinical trial, the Company expects to advance RP-6306, both as monotherapy and in combination with chemotherapies and other agents, into proof-of-concept studies in 2022 targeting a variety of patient populations, including those with tumors with CCNE1 amplification, FBXW7 loss or other undisclosed alterations identified through its proprietary STEP^2 screen. Prospective enrichment of study patient populations will be guided by its ongoing efforts to develop patient selection biomarkers covering both target engagement and functional (DNA damage) readouts.

Virtual Investor Day Agenda

10:30 a.m. – 10:35 a.m. ET
Introduction
Lloyd Segal, President and Chief Executive Officer, Repare Therapeutics

10:35 a.m. – 10:50 a.m. ET
Targeting DNA Damage Repair in the Clinic
Timothy Yap, MBBS, Ph.D., FRCP
Medical Director, Institute for Applied Cancer Science, and Associate Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine at MD Anderson Cancer Center

10:50 a.m. – 11:05 a.m. ET
Genomic Classifications of Endometrial & Ovarian Cancers is Standard of Care
Unmet Need: Therapies Targeting CCNE1 & FBXW7
Carol Aghajanian, M.D.
Chief of Gynecologic Medical Oncology Service and Professor of Medicine, Weill Cornell Medical College, Memorial Sloan Kettering Cancer Center

11:05 a.m. – 11:35 a.m. ET

Target Discovery & Biology of RP-6306 & STEP Characterization Table
Michael Zinda, Ph.D., Executive Vice President, Chief Scientific Officer, Repare Therapeutics

11:35 a.m. – 11:45 a.m. ET
Translational & Clinical Plan for RP-6306
Maria Koehler, M.D., Ph.D., Executive Vice President, Chief Medical Officer, Repare Therapeutics

11:45 a.m. – 12:00 p.m. ET
Conclusion & Q&A Session

Conference Call and Webcast

To access the event virtual event, please dial (833) 638-9655 (U.S. and Canada) or (602) 585-9856 (international) at least 10 minutes prior to the start time and refer to conference ID 1093819. 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 available on the corporate website at the conclusion of the call.

About RP-6306

RP-6306, the result of Repare's proprietary drug discovery program, is a first-in-class, selective, oral inhibitor of PKMYT1 to treat CCNE1-amplified, FBXW7-altered and other PKMYT1 inhibitor-sensitive cancers that typically do not respond well to platinum or PARP inhibitor treatment. Through Repare's SNIPRx screen campaign for targets that are SL with CCNE1 amplification, the Company identified and validated this novel SL gene that has the characteristics of a therapeutic target. Subsequently, the Company developed novel and selective inhibitors against PKMYT1, which repeatedly demonstrated compelling anti-tumor activity, and announced the advancement of a clinical candidate for this first-in-class program. Repare anticipates initiating a Phase 1 clinical trial of RP-6306 during the quarter ending June 30, 2021. This trial is expected to enroll patients suffering from recurrent tumors characterized by CCNE1 amplification or other genomic alterations predicted to be sensitive to RP-6306. The primary objective of the trial is to assess preliminary safety in patients and to establish the RP2D and schedule for RP-6306 for further studies as a monotherapy . Dependent on Phase 1 result, an additional trial is planned to evaluate the combination of RP-6306 with approved anti-cancer agents, including chemotherapy.

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 best-in-class ATR inhibitor currently in Phase 1/2 clinical development, as well as RP-6306, a first-in-class, selective, oral inhibitor of PKMYT1 to treat CCNE1-amplified, FBXW7-altered and other PKMYT1 inhibitor-sensitive cancers, and a Polθ inhibitor program. For more information, please visit 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 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, the clinical development of RP-6306 including the initiation, timing, design and results of the Phase 1 clinical trial of RP-6306; the efficacy of RP-6306 as a monotherapy or in combination with other therapies; and the Company's ability to identify and develop additional product candidates using its SNIPRx 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 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, 2020 filed with the Securities and Exchange Commission ("SEC") on March 4, 2021. 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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