Repare Therapeutics Announces Publication of Preclinical Data in Nature Demonstrating the Potential of PKMYT1 Inhibitor RP-6306 in Tumors With CCNE1 Amplification

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Data show PKMYT1 inhibition is a promising therapeutic target in CCNE1-amplified cancers

RP-6306, a first-in-class, oral PKMYT1 inhibitor, is currently being evaluated in Phase 1 clinical trials

CAMBRIDGE, Mass. & MONTREAL--(BUSINESS WIRE)--Apr. 20, 2022-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today announced that preclinical data demonstrating inhibition of CCNE1-amplified tumor growth *in vivo* by selective inhibition of PKMYT1 using RP-6306, a first-in-class small molecule candidate targeting PKMYT1, were published in *Nature*. SNIPRx®, Repare’s proprietary, genome-wide, CRISPR-based screening approach, was used to uncover CCNE1 amplification as synthetic lethal to PKMYT1 inhibition.

The article, entitled “CCNE1 amplification is synthetic lethal with PKMYT1 kinase inhibition” is available at www.nature.com.

“RP-6306 is a first-in-class and highly selective PKMYT1 inhibitor, and these preclinical data show its ability to target CCNE1-amplfied tumors and profoundly inhibit tumor growth,” said Michael Zinda, PhD, EVP and Chief Scientific Officer of Repare. “We are excited as this is another example of the power of genetic interaction screens to uncover new oncology drug targets, in this case in a cellular model of CCNE1 amplification. This led to the identification of a previously uncharacterized vulnerability to PKMYT1 inhibition that spurred the development of RP-6306 by Repare Therapeutics."

“We are thrilled that this work demonstrates both the power of our CRISPR-based SNIPRx platform to uncover novel synthetic lethal targets and Repare’s capacity to prosecute these targets resulting in first-in-class small molecule therapeutics,” said Maria Koehler, MD, PhD, EVP and Chief Medical Officer of Repare. “It is uncommon that a new and validated target is published in a top tier journal concurrent with a launched clinical trial for a candidate drug on that target, and this speaks volumes about the innovative capacity of Repare and its collaborators.”

Phase 1 clinical trials are currently evaluating RP-6306 as a monotherapy as well as in combination with gemcitabine for the treatment of molecularly selected advanced solid tumors. The Company recently initiated an additional Phase 1 MINOTAUR clinical trial of RP-6306 in combination with FOLFIRI also for the treatment of molecularly selected advanced solid tumors.

This work is the result of a long-standing collaboration between Repare Therapeutics and the laboratory of Daniel Durocher, PhD, a Senior Investigator at the Lunenfeld-Tanenbaum Research Institute, part of Sinai Health, in Toronto, Canada Dr. Durocher is also a Professor in the Department of Molecular Genetics at the University of Toronto. Work on CCNE1 in the Durocher laboratory was led by David Gallo, PhD, now a Senior Scientist at Repare and was financially supported by Repare Therapeutics and the Canadian Institutes of Health Research (CIHR).

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 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, statements regarding the clinical development of the Company’s pipeline and its research and development programs, and the ability of RP-6306 to target CCNE1-amplfied tumors and inhibit tumor growth. 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.

References and links to websites have been provided for convenience, and the information contained on any such website is not a part of, or incorporated by reference into, this press release. Repare is not responsible for the contents of any third-party website.

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