Repare Therapeutics & Debiopharm Announce First Patient Dosed in Phase 1/1b MYTHIC Trial Evaluating the Synthetic Lethal Combination of PKMYT1 and WEE1 Inhibition

April 30, 2024

MONTREAL & LAUSANNE, Switzerland--(BUSINESS WIRE)--Apr. 30, 2024-- Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, and Debiopharm (www.debiopharm.com), a privately-owned, Swiss-based biopharmaceutical company aiming to establish tomorrow’s standards of care to cure cancer and infectious diseases, today announced that the first patient has been dosed in Module 4 of the ongoing Phase 1/1b MYTHIC (NCT04855656) clinical trial investigating lunresertib in combination with Debio 0123. In this trial, Debiopharm and Repare seek to assess the safety, pharmacokinetics, pharmacodynamics and preliminary clinical activity of this PKMYT1 and WEE1 inhibitor combination.

In early January, Repare and Debiopharm announced a collaboration to evaluate the clinical combination of lunresertib, a first-in-class, selective and potent oral small molecule inhibitor of PKMYT1, and Debio 0123, an oral, brain-penetrant, highly selective WEE1 kinase inhibitor. This collaboration is based on preclinical *in vivo* data and other data showing rapid, remarkable tumor regressions and high predicted clinical tolerability and represents the first clinical-stage approach to inhibiting both PKMYT1 and WEE1.

“We are excited to have treated our first patient with lunresertib and Debio 0123,” said Maria Koehler, MD, PhD, Executive Vice President and Chief Medical Officer of Repare. “Each of these compounds is well understood and clinically characterized. This combination provides us a unique opportunity to optimize dosing between two selective compounds and overcome limitations inherent to dual-inhibitor approaches. We expect this clinical collaboration will allow us to optimize the excellent synergy we saw preclinically to maximize patient benefit and tolerability.”

"Lunresertib and Debio 0123 have the potential to be a transformative combination therapy for cancer patients with high unmet medical need,” said Angela Zubel, Chief Development Officer of Debiopharm. “Treating the first patient in this new Module of the MYTHIC clinical trial is an important milestone for our collaboration, as it allows us to execute clinical development swiftly. We look forward to working closely with Repare to further characterize these innovative precision medicine therapies.”

About Lunresertib

Lunresertib (RP-6306) is a first-in-class, selective and potent oral small molecule inhibitor of PKMYT1, a cancer target Repare discovered and identified as synthetic lethal with CCNE1 amplification, FBXW7 and PPP2R1A alterations in solid tumors. Lunresertib is currently the sole PKMYT1 inhibitor known to be in clinical trials and is being evaluated alone and in combinations across several studies in the US, UK/EU4, and Canada. Repare has presented positive initial Phase 1 data from its ongoing Phase 1/1b MYTHIC trial (NCT04855656) demonstrating proof of concept for lunresertib alone and in combination. In addition to being well tolerated and having a compelling safety profile, Repare presented anti-tumor activity for lunresertib in combination with camonsertib, an ATR inhibitor developed by Repare, expanded clinical studies for which are ongoing.

About Debio 0123

Debio 0123 is an oral, brain-penetrant, highly selective WEE1 kinase inhibitor. WEE1 is a key regulator of the G2/M and S phase checkpoints, activated in response to DNA damage and replication stress, allowing cells to repair their DNA before resuming their cell cycle. WEE1 inhibition, particularly in combination with DNA damaging agents, induces an accumulation of DNA damage and pushes the cells through cell cycle without DNA repair, promoting mitotic catastrophe and induction of apoptosis in cancer cells. Debio 0123 is currently being investigated in clinical trials in patients with solid tumors as a monotherapy and in combination. Debio 0123 is being developed to address high unmet needs of patients living with the burden of difficult-to-treat cancers.

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 program; RP-3467, a preclinical Polθ ATPase inhibitor program; as well as additional, undisclosed preclinical programs. For more information, please visit reparerx.com.

SNIPRx® is a registered trademark of Repare Therapeutics Inc.

Debiopharm's Commitment to Patients

Debiopharm aims to develop innovative therapies that target high unmet medical needs in oncology and bacterial infections. Bridging the gap between disruptive discovery products and real-world patient reach, we identify high-potential compounds and technologies for in-licensing, clinically demonstrate their safety and efficacy, and then hand stewardship to large pharmaceutical commercialization partners to maximize patient access globally.

For more information, please visit www.debiopharm.com

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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 Company’s clinical collaboration with Debiopharm including the benefits and results that may be achieved through the collaboration; the potential therapeutic benefits of lunresertib in combination with Debio 0123; and the anticipated timing, patient enrollment, outcomes or associated costs of the Phase 1/1b clinical trial of lunresertib in combination with Debio 0123, including timing of preliminary data from Module 4 of the MYTHIC trial. 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 macroeconomic conditions, including the COVID-19 pandemic, the conflict in Ukraine, the Hamas-Israel conflict, 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; the risk that Repare may not realize the potential benefits of this collaboration with Debiopharm; the discovery, development and potential commercialization of potential product candidates using Repare’s SNIPRx ® platform technology , including the development of lunresertib under the clinical study and collaboration agreement; 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, 2023 filed with the Securities and Exchange Commission (“SEC”) and the Québec Autorité des Marchés Financiers ("AMF") on February 28, 2024. 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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