Repare Therapeutics and Debiopharm Partner to Explore the Synthetic Lethal Combination of PKMYT1 and WEE1 Inhibition in Cancer

January 4, 2024

Collaborative clinical study will investigate a novel combination of lunresertib, Repare's first-in-class PKMYT1 inhibitor, and Debio 0123, Debiopharm's potent, brain-penetrant inhibitor of WEE1

MONTREAL & LAUSANNE, Switzerland--(BUSINESS WIRE)--Jan. 4, 2024-- Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today announced that it has entered into a clinical study and collaboration agreement with 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. This clinical collaboration aims to explore the synergy between lunresertib, a first-in-class, selective and potent oral, small molecule inhibitor of PKMYT1 with demonstrated anticancer activity, and Debio 0123, a potential best-in-class, brain-penetrant and highly selective WEE1 inhibitor.

Under the clinical study and collaboration agreement, the combination of lunresertib and Debio 0123 will be evaluated in a new arm of Repare's ongoing global MYTHIC study (NCT04855656) under Repare's sponsorship. The Phase 1/1b clinical trial is anticipated to initiate in the first half of 2024. Repare and Debiopharm will collaborate on the design of the trial arm for the development of the combination and will share all costs equally. Repare and Debiopharm will each supply their respective drugs, and each retain all commercial rights to their respective compounds, including as monotherapy or as combination therapies.

"Combining with Debiopharm's highly selective WEE1 inhibitor is the ideal strategy to further extend our leadership in PKMYT1 inhibitor development," said Lloyd M. Segal, CEO of Repare. "The compelling mechanistic rationale and preclinical data Repare and Debiopharm have each generated for this combination give us confidence in its potential to deliver transformative benefit to patients with high unmet medical need."

At the AACR-NCI-EORTC conference held in Boston in October 2023, Repare presented data showing that the combination of lunresertib and Debio 0123 is highly synergistic, and drives rapid and deep tumor regressions (Gallo et al., Poster #A023). Unpublished data independently generated by Debiopharm confirmed the dramatic synergy of the Debio 0123/lunresertib combination in vivo, further supporting the rationale for this clinical collaboration. In addition, several recent preclinical studies published by Repare and its collaborators have demonstrated proof-of-concept for the combination of WEE1 and PKMYT1 inhibition in relevant cancer cell lines and animal models of cancer (Sokhi et al. "Investigating Wee1 and Myt1 combined inhibition as a potential cancer therapeutic strategy", AACR 2023, Poster #5511; Benada et al., 2023).

"We are delighted to enter into this clinical collaboration with Repare, the leader in PKMYT1 inhibition, to reinforce our commitment to the DDR space with our potential best-in-class WEE1 inhibitor. We believe this synthetic lethality approach will bring an innovative precision medicine therapy to patients," said Bertrand Ducrey, CEO of Debiopharm. "This is the first time that Debiopharm has initiated a collaboration to combine two investigational compounds, demonstrating our excitement by the potential of this therapeutic approach in hard-to-treat cancers."

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, EU and Canada. Repare has presented positive initial Phase 1 data from its ongoing Phase 1 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 and partnered with Roche, expanded clinical studies for which are ongoing.

About Debio 0123

Debio 0123 is a 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, allowing cells to repair their DNA before resuming their cell cycle. WEE1 inhibition, particularly in combination with DNA damaging agents, induces an overload of DNA breaks. In conjunction with abrogation of other checkpoints such as G1, the compound pushes the cells through cell cycle without DNA repair, promoting mitotic catastrophe and inducing apoptosis of cancer cells. Currently in research for solid tumors in monotherapy and combination, Debio 0123 is being developed to respond to 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 or RG6526), a potential leading ATR inhibitor currently in Phase 1/2 clinical development and partnered with Roche; RP-1664, a preclinical PLK4 inhibitor program; RP-3467, a preclinical Polθ 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. 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, 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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