UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 7, 2023

Repare Therapeutics Inc.
(Exact Name of Registrant as Specified in Its Charter)

Québec	**001-39335**	**Not applicable**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

7210 Frederick-Banting, Suite 100 **St-Laurent, Québec, Canada** **(Address of Principal Executive Offices)**	**H4S 2A1** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (857) 412-7018

Not Applicable
(Former Name or Former Address, if Changed Since Last Report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common shares, no par value	RPTX	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On June 7, 2023, Repare Therapeutics Inc. (the "Company") issued a press release reporting initial proof of concept monotherapy data from its Phase 1 MYTHIC clinical trial evaluating lunresertib (RP-6306), a first-in-class, oral PKMYT1 inhibitor in molecularly selected advanced solid tumors. A copy of the press release is furnished as Exhibit 99.1 to this Current Report and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibit.

(d) Exhibits

Exhibit No.	Description
99.1	Press release dated June 7, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REPARE THERAPEUTICS INC.

By: /s/ Lloyd M. Segal
Lloyd M. Segal
President and Chief Executive Officer

Dated: June 7, 2023

Exhibit 99.1

Repare Therapeutics Reports Proof of Concept for Lunresertib (RP-6306) in Clinic, Initial Monotherapy Data from Phase 1 MYTHIC Clinical Trial and Early Insights from Ongoing Combination Trials

Findings from the ongoing Phase 1 MYTHIC study demonstrated a favorable and distinctive tolerability profile for monotherapy lunresertib

Monotherapy antitumor activity observed, including confirmed partial response and several patients with long stable disease

Identified both intermittent and continuous schedules to enable combination studies

Encouraging early responses across gemcitabine, camonsertib and FOLFIRI clinical combinations

Repare to host a virtual webcast event to discuss initial results from MYTHIC study and provide updates on the lunresertib program including early combination trial insights today at 4:30 p.m. ET

CAMBRIDGE, Mass. & MONTREAL (BUSINESS WIRE)—June 7, 2023— Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today reported initial proof of concept monotherapy data from its Phase 1 MYTHIC clinical trial evaluating lunresertib (RP-6306), a first-in-class, oral PKMYT1 inhibitor in molecularly selected advanced solid tumors.

"These initial proof of concept results for lunresertib monotherapy show a favorable and distinct tolerability profile and preliminary antitumor activity that support our development plans for this program." said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. "The data demonstrate that lunresertib effectively inhibits PKMYT1 and offers a synthetic lethal combination with *CCNE1* amplification or inactivating mutations in *FBXW7* and *PPP2R1a*. These genetic alterations have previously been considered undruggable and represent a significant unmet medical need. These findings, along with the continued advancement of the lunresertib program across multiple ongoing combination clinical trials, validate our proprietary STEP^2 platform and precision medicine approach."

"While early, these promising proof-of-concept data continue to support our belief in the potential transformative role that lunresertib could play, either alone or in combination with other therapies, in patients with molecularly selected advanced solid tumors," said Lloyd M. Segal, President and Chief Executive Officer of Repare. "We look forward to reporting initial combination data of lunresertib with camonsertib, as well as lunresertib with gemcitabine, in the fourth quarter of this year, while also advancing multiple other trials to further our understanding of our first-in-class PKMYT1 inhibitor program."

Key Initial Findings from the Phase 1 MYTHIC Clinical Trial:

MYTHIC (NCT04855656) Module 1 is a first-in-human, global, open-label Phase 1 dose-escalation study to evaluate safety, pharmacokinetics, pharmacodynamics and preliminary anti-tumor activity of a novel and potent small molecule PKMYT1 inhibitor, lunresertib. MYTHIC Module 2 will investigate lunresertib in combination with camonsertib (RP-3500/RG6526), a potent and selective oral inhibitor of ATR developed by Repare and now partnered with Roche (excluding the lunresertib combination), in molecularly selected advanced solid tumors. As of the data cutoff date of April 28, 2023, 63 patients were enrolled in lunresertib monotherapy Module 1 of the MYTHIC study, which is ongoing and accruing patients.

- Tolerability profile of lunresertib monotherapy appears favorable and differentiated from other clinical cell cycle inhibitors, which have been characterized with myelotoxicity and diarrhea. No grade 4 toxicity was observed with lunresertib, where grade 3 treatment emergent adverse events of interest included rash (7.9%), anemia (6.3%) and nausea or vomiting (1.6%) The only dose limiting toxicity was reversible rash, alleviated with dose modifications and simple supportive measures.
- Two recommended dose/schedules were identified – 240mg daily continuously and 80-100mg BID intermittent weekly – to offer maximum flexibility in combination studies.
- Pharmacodynamic analysis confirmed lunresertib treatment results in PKMYT1 target inhibition at active doses and increases DNA damage.
- Preliminary anti-tumor activity was observed, including moderate tumor shrinkages and a confirmed partial response per RECIST 1.1 criteria. Several patients demonstrated long stable disease and remain on treatment for greater than 11 months and ongoing.
- Early clinical combination insights demonstrated greater anti-tumor activity in patients treated with the combination of lunresertib and camonsertib than lunresertib alone, based on higher molecular response rates and RECIST 1.1 responses. Examples of confirmed partial responses are provided for the three tested sensitivity genotypes in endometrial adenocarcinoma, cholangiocarcinoma and colorectal cancer, with more details planned for the Q4 scientific presentation.
- Encouraging early responses observed across gemcitabine, camonsertib, and FOLFIRI clinical combinations in multiple tumor types and genotypes.
- Favorable and distinct tolerability profile and preliminary antitumor activity demonstrated thus far support potential development plans that may include further trials of lunresertib in various combination and maintenance approaches.

Repare is also currently evaluating lunresertib in combination with gemcitabine in the Phase 1 MAGNETIC study and in combination with FOLFIRI in the Phase 1 MINOTAUR study. Repare is working with Princess Margaret Cancer Center to initiate clinical testing, as part of an investigator-sponsored trial (IST), of a fourth lunresertib combination with carboplatin and paclitaxel for the treatment of recurrent TP53 mutated ovarian and uterine cancer, with first patient dosing expected this year. The Company is also collaborating with the Canadian Cancer Trials Group in an ongoing basket Phase 2 IST that is enrolling patients with selected, advanced cancers receiving lunresertib as combination (NCT05605509), and in a second active study that will evaluate lunresertib in combination with gemcitabine in patients with CDK4/6 inhibitor treated ER+/HER2- metastatic breast cancer (NCT05601440). These studies aim to expand the treatment opportunities for lunresertib to earlier stages of cancer treatment or additional tumor types.

Company Virtual Webcast Event:

The Company will host a virtual investor webcast with accompanying slides for analysts and investors today at 4:30 p.m. Eastern Time to further discuss the lunresertib program, including initial proof-of-concept monotherapy data from MYTHIC and an update on ongoing combination clinical trials.

To access the call, please dial (877) 870-4263 (U.S. and Canada) or (412) 317-0790 (international) at least 10 minutes prior to the start time and ask to be joined to the Repare Therapeutics call. 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 archived for at least 30 days.

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 (RP-6306), a PKMYT1 inhibitor currently in Phase 1 clinical development; camonsertib (RP-3500/RG6526), a potential leading ATR inhibitor currently in Phase 1/2 clinical development and partnered with Roche; a preclinical Polq inhibitor program; as well as several additional, undisclosed preclinical programs, including RP-1664. 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 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 safety, efficacy and clinical progress of the Company's clinical programs, including lunresertib (RP-6306) and camonsertib; the clinical and preclinical development of the Company's pipeline and its research and development programs, including the anticipated timing, anticipated patient enrollment, trial outcomes or associated costs of its clinical trials of lunresertib and camonsertib; and the status of clinical trials (including, without limitation, expectations regarding the data that is being presented, the expected timing of data releases and development, as well as completion of clinical trials) and development timelines for the Company's product

candidates. 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, rising 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. 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/.

Repare Contact:

Robin Garner
Executive Director 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