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): October 13, 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.)**

7171 Frederick-Banting, Building 2 **St-Laurent, Québec, Canada** **(Address of Principal Executive Offices)**	**H4S 1Z9** **(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 7.01 Regulation FD Disclosure.

On October 13, 2023, Repare Therapeutics Inc. (the "Company") issued a press release announcing the presentation of positive initial data from Modules 1 and 2 of its ongoing Phase 1 MYTHIC clinical trial evaluating lunresertib alone and in combination with camonsertib, an ATR inhibitor, at the 2023 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, being held October 11-15, 2023 in Boston, Massachusetts. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. A copy of the presentation at the 2023 AACR-NCI-EORTC will posted on the "Investor" section of the Company's website at https://ir.reparerx.com/news-and-events/events.

As previously announced and as described in the accompanying press release, the Company will host a conference call and live audio webcast today, October 13, 2023 at 5:30 p.m., Eastern Time, to discuss the results presented at the 2023 AACR-NCI-EORTC conference, including a discussion of additional information on its product candidate lunresertib (RP-6306) in combination with camonsertib since the September 5, 2023 data cut-off date. The live audio webcast may be accessed through the "Events & Presentations" page in the "Investors and Media" section of the Company's website at ir.reparerx.com. Alternatively, participants may dial (877) 870-4263 (U.S. and Canada) or (412) 317-0790 (international).

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

The Company's website and any information contained on the Company's website are not incorporated into this Current Report on Form 8-K.

Item 8.01 Other Events.

On October 13, 2023, the Company reported positive initial data from Modules 1 and 2 of the Company's ongoing Phase 1 MYTHIC clinical trial evaluating lunresertib alone and in combination with camonsertib. The data are being presented today by Dr. Timothy A. Yap, The University of Texas MD Anderson Cancer Center, in a plenary session titled, "New Drugs on the Horizon" at the 2023 AACR-NCI-EORTC scheduled to begin at 9:40 a.m., Eastern Time. The data includes a more mature data set of more patients treated at clinically relevant doses than the data included in the abstract posted by American Association for Cancer Research on October 4, 2023.

The MYTHIC trial is a first-in-human, global, open-label Phase 1 dose-escalation clinical trial to evaluate safety, pharmacokinetics, pharmacodynamics and preliminary anti-tumor activity of lunresertib alone as a monotherapy (Module 1) or in combination with camonsertib (Module 2) in patients with advanced solid tumors harboring *CCNE1* amplification or *FBXW7* or *PPP2R1A* deleterious alterations.

The newly reported data includes assessment as of the September 5, 2023 data cut-off date for 67 patients enrolled in Module 1 and 59 patients enrolled in Module 2. The key points from the data cut are summarized below.

- In Module 2, it was observed that the protocol-defined overall response (RECIST or GCIG CA-125 responses) of the combination therapy was 33.3% in the 18 patients evaluated at the preliminary recommended Phase 2 dose level. The clinical benefit rate ("CBR") was defined as overall response or stable disease of at least 16 weeks without tumor progression and was 50.0% in the same patient subset.
- It was observed that overall response in all 55 response-evaluable patients was 23.6% across all dose levels being evaluated and CBR was 41.8%.
- In the 10 patients with gynecologic tumors treated at the preliminary recommended Phase 2 dose level, the RECIST response was 50%, overall response was 60%, and CBR was 70%. Patients in this cohort had a median of 3 and up to 9 prior lines of therapy prior to treatment with lunresertib in combination with camonsertib.

- The RECIST responses in the ongoing trial also included 8 confirmed responses and 3 unconfirmed partial responses. Additionally, three patients with ovarian tumors had cancer antigen 125 (CA-125) responses.
- RECIST responses and clinical benefit of treatment of the combination with lunresertib in combination with camonsertib was seen across all three lunresertib-sensitizing alterations: *CCNE1* amplification, *FBXW7* or *PPP2R1A* deleterious alterations. Molecular response rate ("MRR") was observed to be significantly higher in the combination therapy module of the trial (Module 2), as compared to the monotherapy module of the trial (Module 1) (p=0.003), providing further evidence of enhanced anti-tumor activity, MRR in the combination therapy module was observed to be 50% (n=24), as compared to 10% (n=30) observed in the lunresertib monotherapy module.
- In Module 2, encouraging and highly manageable safety and tolerability data was observed for 59 patients enrolled in the combination therapy module. The most common treatment-related adverse event ("TRAE") observed was anemia, with Grade 3 occurring in 42% of patients enrolled in Module 2. Further, anemia usually improved for patients with a one-week treatment interruption and standard supportive care, and, notably, anemia did not lead to any therapy discontinuations of treatment at the preliminary recommended Phase 2 dose level. There were no Grade 4 or Grade 5 TRAEs reported at the preliminary recommended Phase 2 dose level.
    - Data indicates that anemia management may be individualized and alleviated with patient monitoring. This approach is now being tested in the MYTHIC trial.
    - 35% of patients in the MYTHIC trial in Module 2 did not develop anemia at the preliminary recommended Phase 2 dose level. Generally, those patients who developed Grade 3 anemia had the lowest hemoglobin values at entry into the trial, were intensely pretreated prior to trial enrollment with greater than four prior therapies and were of advanced age.

Clinical proof of concept was established in the MYTHIC trial for both lunresertib alone as a monotherapy and in combination with camonsertib. Further, the Company believes that the MYTHIC trial is the first clinical proof-of-concept for a synthetic lethal strategy with a PKMYT1 inhibitor combined with an ATR inhibitor in patients with molecularly-selected cancers.

Patient enrollment in the MYTHIC trial is ongoing, with the goal of optimizing the schedule for the combination module and to further investigate the promising antitumor signals seen to date in a larger number of patients with selected tumors and genomic alterations. The Company expects to complete multiple expansions of the MYTHIC trial and report additional data from the MYTHIC trial in the second half of 2024, with later-stage trials expected to initiate shortly thereafter.

Cautionary Regarding Forward-Looking Statements

Certain statements in this Current Report on Form 8-K 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 Current Report on Form 8-K 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 timing, safety, efficacy, clinical progress and results of the monotherapy of lunresertib and the combination therapy of lunresertib and camonsertib, and proposed further development of the combination therapy of lunresertib and camonsertib. These forward-looking statements are based on the Company's expectations and assumptions as of the date of this Current Report on Form 8-K. 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: success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate; 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 including the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2023 filed with the SEC on August 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.

Item 9.01 Financial Statements and Exhibit.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated October 13, 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.

Date: October 13, 2023

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

Repare Therapeutics Announces Positive Initial Data from Phase 1 MYTHIC Clinical Trial Evaluating Lunresertib Alone and in Combination with Camonsertib

Lunresertib + camonsertib combination demonstrated clear signals of anti-tumor activity across multiple tumor types and all selected genotypes

Overall response of 33.3% across all tumor types and 50% RECIST response in patients with heavily pre-treated gynecologic tumors, including endometrial, ovarian and cervical, at the preliminary recommended phase 2 dose

Encouraging safety and tolerability profile observed as monotherapy and in combination with camonsertib

Repare to host conference call and webcast today at 5:30 p.m.ET to discuss these results

CAMBRIDGE, Mass. & MONTREAL (BUSINESS WIRE)—October 13, 2023— Repare Therapeutics Inc. (“Repare” or the “Company”) (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today reported positive initial data from Modules 1 and 2 of its ongoing Phase 1 MYTHIC clinical trial evaluating lunresertib alone and in combination with camonsertib, an ATR inhibitor. The data are being presented in a plenary session titled, “New Drugs on the Horizon” at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, being held October 11-15, 2023 in Boston, Mass.

Lunresertib (RP-6306) is a first-in-class precision oncology small molecule PKMYT1 inhibitor that targets CCNE1 amplification, FBXW7 and PPP2R1A alterations in solid tumors. Lunresertib is being evaluated alone and in combination with camonsertib (RP-3500 / RG6526), a potent and selective oral inhibitor of ATR developed by Repare and now partnered with Roche for development *excluding* the lunresertib + camonsertib combination.

“We’re excited by these first clinical proof-of concept results and believe that they further validate the pipeline power of our SNIPRx discovery platform and demonstrate the potential of lunresertib as the only clinical-stage PKMYT1 inhibitor,” said Lloyd M. Segal, President and Chief Executive Officer of Repare. “We saw early efficacy signals across multiple tumor types and in each genotype selected, most notably in gynecological tumors where the lunresertib + camonsertib combination provides a potential new treatment option for these patients. Today is an important step forward in Repare’s mission to deliver next-generation precision oncology medicines to patients with genomically-defined tumor alterations predicted by our platform to respond to our candidate drugs.”

“The data presented today, although early, are highly promising as lunresertib in combination with camonsertib results in clear clinical activity across several tumor types and genotypes along with a favorable safety and tolerability profile,” said Dr. Timothy A. Yap, MBBS, PhD, FRCP, Professor in the Department of Investigational Cancer Therapies (Phase 1 Program) and Vice President, Head of Clinical Development in the Therapeutics Discovery Division at The University of Texas MD Anderson Cancer Center and Principal

Investigator on the MYTHIC trial. “These early data suggest treatment with lunresertib in combination with camonsertib could result in efficacy outcomes for patients in the gynecological cancer setting, an area where we’re still seeing unmet patient needs despite current therapies.”

Key Initial Findings from the Phase 1 MYTHIC Clinical Trial:

MYTHIC (NCT: NCT04855656), a first-in-human, global, open-label Phase 1 dose-escalation clinical trial to evaluate safety, pharmacokinetics, pharmacodynamics and preliminary anti-tumor activity of lunresertib as a monotherapy (Module 1) or in combination with camonsertib (Module 2) in patients with advanced solid tumors harboring *CCNE1* amplification or *FBXW7* or *PPP2R1A* deleterious alterations achieved clinical proof of concept. As of September 5, 2023, the cutoff date for the data presented at the AACR-NCI-EORTC conference, 67 patients were enrolled in Module 1 and 59 patients in Module 2.

- Protocol-defined overall response (OR) (RECIST or GCIG CA-125 responses) at the combination preliminary recommended phase 2 dose (RP2D) was 33.3% (N=18); CBR at the combination preliminary RP2D (overall response or stable disease of at least 16 weeks without tumor progression) was 50.0%. In all evaluable patients, across all doses (N-55), OR was 23.6% and CBR was 41.8%.
- In patients with gynecologic tumors at the combination preliminary RP2D (N=10), the RECIST response was 50%, OR 60%, and CBR 70%. Patients in this cohort had a median of 3 and up to 9 prior lines of therapy.
- RECIST responses in this ongoing combination trial included 8 confirmed and 3 unconfirmed partial responses (PR). Additionally, 3 patients with ovarian tumors had cancer antigen 125 (CA-125) responses.
- RECIST responses and clinical benefit with combination therapy was seen across all 3 lunresertib-sensitizing alterations: *CCNE1* amplification or *FBXW7* or *PPP2R1A* deleterious alterations. Molecular response rate (MRR) was significantly higher in combination compared to monotherapy (p=0.003), providing further evidence of enhanced anti-tumor activity: observed MRR in combination therapy was 50% (n=24), compared to 10% (n=30) with lunresertib monotherapy.
- Encouraging and highly manageable safety and tolerability was observed for the combination therapy (n=59). The most common treatment-related adverse event (TRAE) was anemia, with grade 3 occurring in 42% of patients:
    - Anemia usually improved with a one-week treatment interruption and standard supportive care and did not lead to any therapy discontinuations at preliminary RP2D.
    - There were no Grade 4 or Grade 5 TRAEs reported at preliminary RP2D.
    - Data clearly indicates that anemia management can be individualized and alleviated with simple patient monitoring. This approach is now being tested in the MYTHIC trial.
    - 35% of patients did not develop anemia at preliminary RP2D. Generally, those with grade 3 anemia had the lowest hemoglobin values at entry, were intensely pretreated with >4 prior therapies and were of advanced age.
- Achieved the first clinical proof-of-concept for a synthetic lethal strategy with a PKMYT1 inhibitor combined with an ATR inhibitor in patients with molecularly-selected cancers.

- Patient enrollment in MYTHIC continues both to optimize the schedule for the combination and to further investigate the promising antitumor signals seen to date in a larger number of patients with selected tumors and genomic alterations.

“The encouraging Phase 1 safety and tolerability profile and early antitumor efficacy data provide proof of concept for lunresertib and clear direction for further development of the chemotherapy-free combination of lunresertib + camonsertib to selectively target the lunresertib-relevant alterations across multiple tumor types, including line of sight on later stage randomized or otherwise definitive studies as the data continue to mature,” said Maria Koehler, MD, PhD, Chief Medical Officer of Repare. “This novel, orally delivered combination may provide new therapeutic options in areas of high unmet need, and we look forward to completing the multiple expansions of the Phase 1 MYTHIC study and reporting results in 2024 with later-stage trials expected to initiate shortly thereafter.”

Company Virtual Webcast Event:

Repare will host a conference call and webcast today, October 13, 2023, at 5:30 p.m. Eastern Time to discuss the results presented at the AACR-NCI-EORTC conference, including updated data since the September 5, 2023 data cutoff. Repare’s executive management team will be joined by Dr. Timothy A. Yap, MBBS, PhD, FRCP, Principal Investigator, Professor in the Department of Investigational Cancer Therapies (Phase 1 Program) and Vice President, Head of Clinical Development in the Therapeutics Discovery Division at the University of Texas MD Anderson Cancer Center in Houston, Texas.

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 webcast will be available in the Investor section of the Company’s website at https://ir.reparerx.com/events-and-presentations/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 (also known as RP-6306), a PKMYT1 inhibitor currently in Phase 1 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-3467, a preclinical Polq inhibitor program; as well as several additional, undisclosed preclinical programs, including RP-1664. For more information, please visit reparerx.com and follow @Reparerx on X (formerly Twitter) and LinkedIn.

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 and camonsertib; and proposed further development of the combination therapy of lunresertib and camonsertib. 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: success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate; 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 including the Company’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2023 filed with the SEC on August 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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