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): May 07, 2024

Repare Therapeutics Inc.

(Exact name of Registrant as Specified in Its Charter)

Quebec	**001-39335**	**Not applicable**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
7171 Frederick-Banting, Building 2 Suite 270 St-Laurent, Quebec, Canada **(Address of Principal Executive Offices)**		**H4S 1Z9** **(Zip Code)**

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

(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(s)**	**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 2.02 Results of Operations and Financial Condition.

On May 7, 2024, Repare Therapeutics Inc. (the "Company") issued a press release announcing its recent business highlights and financial results for the three months ended March 31, 2024. A copy of the press release is furnished hereto as Exhibit 99.1 and is incorporated herein by reference.

Additionally, on May 7, 2024, the Company posted an updated corporate presentation to its website. The corporate presentation is available under the “Events & Presentations” tab in the “Investors & Media” section of the Company’s website, located at www.reparerx.com. The Company intends to use this presentation in meetings with analysts, investors and others from time to time. A copy of the presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, is being furnished and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) or otherwise subject to the liabilities of that section. The information contained herein and in the accompanying exhibits is not incorporated by reference in any filing of the Company 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 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Press Release dated May 7, 2024
99.2	Company Presentation dated May 2024
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: May 7, 2024

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

REPARE THERAPEUTICS

Repare Therapeutics Provides Business and Clinical Update and Reports First Quarter 2024 Financial Results

Phase 1 MYTHIC clinical trial of lunresertib in combination with camonsertib demonstrated a significant reduction in Grade 3 anemia and continued trends of patient response and benefit; FDA agrees with RP2D

First patient dosed in Phase 1 MYTHIC clinical trial of lunresertib in combination with the WEE1 inhibitor, Debio 0123; first clinical trial inhibiting both PKMYT1 and WEE1

Initiating Phase 2 TRESR expansion in ~20 patients evaluating monotherapy camonsertib in NSCLC; initial data expected in 2025

First patient dosed in Phase 1 LIONS monotherapy trial for PLK4 inhibitor RP-1664

Announced the appointment of Steven H. Stein, M.D. to Repare's Board of Directors, effective in June 2024

$237.0 million in cash and cash equivalents and marketable securities to advance clinical programs and portfolio to mid-2026

CAMBRIDGE, Mass. & MONTREAL (BUSINESS WIRE)—May 7, 2024— Repare Therapeutics Inc. ("Repare" or the "Company") (Nasdaq: RPTX), a leading clinical-stage precision oncology company, today reported financial results for the first quarter ended March 31, 2024.

"This was a quarter of clinical progress as we await key, near-term data on a rich set of distinctive clinical approaches for our four wholly-owned compounds in 2024," said Lloyd M. Segal, President and Chief Executive Officer of Repare. "We have agreement with the FDA regarding our recommended Phase 2 dose (RP2D) for our lunresertib plus camonsertib combination, with significantly improved tolerability at the RP2D with our updated dosing schedule. We are seeing continuing trends of patient response and benefit, and we are on track to report the updated dataset in the fourth quarter of 2024. Our objective is to determine the best opportunity for a registrational trial, to start in 2025. Additionally, we are initiating a small clinical trial to rapidly confirm a camonsertib monotherapy signal in non-small cell lung cancer (NSCLC) and expect that readout to be available in 2025. Our clinical portfolio also includes the LIONS trial of our RP-1664 PLK4 inhibitor, the PKMYT1 and WEE1 inhibitor combination in MYTHIC, and the upcoming clinical start of our Polθ inhibitor program, RP-3467, in the second half of 2024."

First Quarter 2024 and Recent Portfolio Highlights:

- **Lunresertib (RP-6306)**
  - On track for a potential registrational trial decision in gynecologic expansion cohorts in the fourth quarter of 2024 based on the Phase 1 expansion in MYTHIC trial evaluating lunresertib in combination with camonsertib in patients harboring CCNE1 amplification or FBXW7 or PPP2R1A deleterious alterations. Grade 3 anemia has been significantly reduced to 25% as of the March 2024 cut-off date in patients treated at the RP2D and updated dosing schedule, from 45% as previously presented at the September 2023 data cut-off date. The U.S. Food and Drug Administration (FDA) has agreed with

the RP2D of lunresertib 80mg BID and camonsertib 80mg QD. Efficacy and tolerability assessment at RP2D is ongoing, and the Company expects to present data from the dose expansion cohorts in patients with ovarian and endometrial cancer in the fourth quarter of 2024.

- First patient was dosed in April 2024 in the Phase 1 MYTHIC clinical trial evaluating lunresertib in combination with Debio 0123, a highly selective, brain-penetrant, clinical WEE1 inhibitor, in advanced solid tumors harboring CCNE1 amplification or FBXW7 or PPP2R1a deleterious alterations. The primary endpoints are safety, tolerability and RP2D, as well as preliminary efficacy of the combination. Repare is expected to report initial data from this trial in 2025.
- Initial data from the Phase 1 MINOTAUR trial evaluating lunresertib in combination with FOLFIRI for the treatment of advanced solid tumors demonstrated no significant incremental toxicities in the combination of lunresertib and FOLFIRI over FOLFIRI alone. In addition, Repare has observed favorable tolerability in colorectal and other gastrointestinal tumors, unlike some other agents combined with irinotecan. This data will be presented at the European Society of Medical Oncology (ESMO) Gastrointestinal (GI) Cancers Congress 2024, taking place in Munich, Germany on June 26-29.

- **Camonsertib (RP-3500)**
  - Regained global development and commercialization rights for camonsertib from Roche, effective May 7, 2024. Since inception of the Roche camonsertib collaboration, Repare has earned a cumulative total of $182.6 million from Roche, including the upfront and milestone payments, in addition to certain additional reimbursements from Roche.
  - Initiating Phase 2 TRESR expansion in approximately 20 patients with ATM-mutated (ATMm) NSCLC, supported by early, promising camonsertib monotherapy signal in patients with ATMm NSCLC from the ongoing Phase 1/2 TRESR trial. Repare is expected to report initial data in 2025.

- **RP-1664**
  - First patient dosed in the multicenter, open-label Phase 1 dose escalation trial (LIONS) of its polo-like kinase 4 (PLK4) inhibitor, RP-1664, in adult and adolescent patients with TRIM37-high and other biomarkers in February 2024.

- **RP-3467**
  - Initiation of a Phase 1 dose finding trial of RP-3467, a potential best-in-class Polθ ATPase inhibitor, is expected in the second half of 2024.

- **Other Highlights**
  - In March 2024, Bristol-Myers Squibb exercised its one remaining option to in-license an undruggable target for a combined total of five druggable targets and one undruggable target over the course of the collaboration.
  - In April 2024, Repare announced the appointment of Steven H. Stein, M.D., Chief Medical Officer of Incyte Corporation, to Repare's Board of Directors, effective as of June 17, 2024, the date of the Company's upcoming annual meeting of shareholders (the "Annual Meeting"). The Company also announced that Todd Foley has decided not to stand for re-election as a director of the Company following the end of his current term as a Class I director on the date of the Annual Meeting, after serving more than seven years on the Board.

Summary of Expected Milestones:

- **H1 2024**
  - Initial Phase 1 MINOTAUR (lunresertib + FOLFIRI combination) data to be reported at ESMO GI in June 2024
- **H2 2024**
  - Camonsertib monotherapy expansion to NSCLC in TRESR
  - Initiation of Phase 1 clinical trial of RP-3467
  - Additional data from dose expansion cohorts for the MYTHIC lunresertib + camonsertib combination in ovarian and endometrial cancers by end of Q4 2024
- **2025**
  - Lunresertib + Debio 0123 combination data
  - Camonsertib monotherapy data in NSCLC
  - Initiate first pivotal trial in an indication for lunresertib + camonsertib

First Quarter 2024 Financial Results:

- **Cash, cash equivalents and marketable securities:** Cash, cash equivalents and marketable securities as of March 31, 2024 were $237.0 million, as compared to $223.6 million as of December 31, 2023. The Company believes that its cash, cash equivalents, and marketable securities are sufficient to fund its current operational plans at least into mid-2026.
- **Revenue from collaboration agreements:** Revenue from collaboration agreements was $52.4 million and $5.7 million for the three months ended March 31, 2024 and 2023, respectively. The increase in revenue for the three-month period was primarily due to the $40.0 million Roche milestone achievement in the first quarter of 2024.
- **Research and development expenses, net of tax credits (Net R&D):** Net R&D expenses were $33.0 million and $31.8 million for the three months ended March 31, 2024 and 2023, respectively. The increase in Net R&D for the three-month period was primarily due to higher direct external costs related to the progress of Repare's lunresertib clinical program, offset by lower direct external costs of its camonsertib clinical program.
- **General and administrative (G&A) expenses:** G&A expenses were $8.6 million and $8.5 million for the three months ended March 31, 2024 and 2023, respectively.
- **Net income (loss):** Net income was $13.2 million, or $0.30 per diluted share, for the three months ended March 31, 2024, and net loss was $34.9 million, or $0.83 per diluted share, for the three months ended March 31, 2023.

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; RP-3467, a preclinical Polθ ATPase inhibitor program; as well as additional, undisclosed preclinical programs. For more information, please visit www.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 design, objectives, initiation, timing, progress and results of current and future preclinical studies and clinical trials of the Company’s product candidates, including the expansion of its Phase 1 MYTHIC trial evaluating lunresertib alone and in combination with camonsertib, its Phase 1 MINOTAUR trial evaluating lunresertib in combination with FOLFIRI, the Module of the Company’s Phase 1/1b MYTHIC trial of, its Phase 1/1b trial of Debio 0123 and lunresertib in partnership with Debiopharm, the expansion of its Phase 2 TRESR trial of camonsertib in patients with ATMm, its Phase 1 LIONS trial of RP-1664, its Phase 1 trial of RP-3467; its planned expansion of development of lunresertib plus camonsertib combination; a potential registrational trial in 2025; the tolerability, efficacy and clinical progress of camonsertib, lunresertib, RP-1664 and RP-3467; the potential of RP-3467 as a best-in-class Polθ ATPase inhibitor; the potential synergies of Debio 0123 in combination with lunresertib, lunresertib in combination with camonsertib and lunresertib in combination with FOLFIRI; the Company’s anticipated cash runway; and the benefits and ability to discover further targets and clinical candidates from the Company’s discovery platform. 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 potential that 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 conflict in Ukraine and the conflict in the Middle East, 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 Company’s ability to realize the benefits of its collaboration and license agreements; 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 filed with the Securities and Exchange Commission (“SEC”) and the Québec Autorité des Marchés Financiers ("AMF") on May 7, 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/.

Repare Therapeutics Inc.
Consolidated Balance Sheets
(Unaudited)
(Amounts in thousands of U.S. dollars, except share data)

	As of March 31, 2024	As of December 31, 2023
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 103,217	$ 111,268
Marketable securities	133,784	112,359
Income tax receivable	10,829	10,813
Other current receivables	3,377	4,499
Prepaid expenses	3,463	4,749
Total current assets	254,670	243,688
Property and equipment, net	3,714	4,215
Operating lease right-of-use assets	2,763	3,326
Income tax receivable	1,630	2,276
Other assets	307	396
TOTAL ASSETS	$ 263,084	$ 253,901
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 6,825	$ 2,400
Accrued expenses and other current liabilities	20,454	24,057
Operating lease liability, current portion	2,218	2,400
Deferred revenue, current portion	1,073	10,222
Total current liabilities	30,570	39,079
Operating lease liability, net of current portion	561	1,010
Deferred revenue, net of current portion	—	1,730
TOTAL LIABILITIES	31,131	41,819
SHAREHOLDERS' EQUITY		
Preferred shares, no par value per share; unlimited shares authorized as of March 31, 2024 and December 31, 2023, respectively; 0 shares issued and outstanding as of March 31, 2024, and December 31, 2023, respectively	—	—
Common shares, no par value per share; unlimited shares authorized as of March 31, 2024 and December 31, 2023; 42,445,406 and 42,176,041 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	486,375	483,350
Additional paid-in capital	65,638	61,813
Accumulated other comprehensive (loss) income	(113)	28
Accumulated deficit	(319,947)	(333,109)
Total shareholders' equity	231,953	212,082
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 263,084	$ 253,901

Repare Therapeutics Inc.
Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(Amounts in thousands of U.S. dollars, except share and per share data)

	Three Months Ended March 31,	
	2024	2023
Revenue:		
Collaboration agreements	$ 52,404	$ 5,678
Operating expenses:		
Research and development, net of tax credits	32,970	31,830
General and administrative	8,618	8,529
Total operating expenses	41,588	40,359
Income (loss) from operations	10,816	(34,681)
Other income (expense), net		
Realized and unrealized gain (loss) on foreign exchange	31	(56)
Interest income	2,968	3,427
Other expense	(24)	(15)
Total other income, net	2,975	3,356
Income (loss) before income taxes	13,791	(31,325)
Income tax expense	(629)	(3,616)
Net income (loss)	$ 13,162	$ (34,941)
Other comprehensive (loss) income:		
Unrealized (loss) gain on available-for-sale marketable securities	$ (141)	$ 193
Total other comprehensive (loss) income	(141)	193
Comprehensive income (loss)	$ 13,021	$ (34,748)
Net income (loss) per share attributable to common shareholders:		
Basic	$ 0.31	$ (0.83)
Diluted	$ 0.30	$ (0.83)
Weighted-average common shares outstanding:		
Basic	42,234,001	42,040,674
Diluted	44,024,198	42,040,674

Investor Relations & Media Contact:

Robin Garner
Vice President and Head of Investor Relations
Repare Therapeutics Inc.
investor@reparerx.com

Source: Repare Therapeutics Inc.


REPARE
THERAPEUTICS
Insight that enriches.
Precision that empowers.
Corporate Presentation
May 2024

Disclaimer

Statements contained in this presentation regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "anticipates," "believes," "expects," "intends," “plans,” “potential,” "projects,” “would” and "future" or similar expressions are intended to identify forward-looking statements. Each of these forward-looking statements involves substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by such forward-looking statements. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including specifically our clinical trials of lunresertib, camonsertib, RP-1664, and preclinical studies of RP-3467; the expected timing of program updates and data disclosures; the timing of filing INDs and other regulatory documents; the timing and likelihood of seeking regulatory approval for our product candidates; the competitive landscape for our product candidates; our ability to identify and develop additional product candidates using our SNIPRx platform; and our estimates regarding expenses, future revenue, capital requirements, cash runway and needs for additional financing.

These forward-looking statements reflect our current beliefs and expectations. Many factors may cause differences between current expectations and actual results, including the duration and impact of the COVID-19 pandemic on our business and market volatility, unexpected safety or efficacy data observed during preclinical or clinical studies, clinical site activation rates or clinical trial enrollment rates that are lower than expected, changes in expected or existing competition, changes in the regulatory environment, and unexpected litigation or other disputes. These and other risks are described more fully in our filings with the Securities and Exchange Commission (“SEC”), including the “Risk Factors” section of our Annual Report on Form 10-Q filed with the SEC on May 7, 2024, and other documents we subsequently filed with or furnished to the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Except as required by law, we assume no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Solely for convenience, the trademarks and trade names in this presentation may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.

Developing Next-Generation Precision Oncology Medicines

Differentiated, proprietary clinical pipeline

- Lunresertib: First-in-class oral PKMYT1 inhibitor (Phase 1/2)
- Camonsertib: ATR inhibitor (Phase 1/2)
- RP-1664: First-in-class selective PLK4 inhibitor (Phase 1)

Proprietary CRISPR-enabled SNIPRx platform

- Focused on genomic instability and DNA damage repair
- Clinical trials enriched for patients with tumors carrying a network of synthetic lethal alterations (STEP[2])

Multiple clinical catalysts expected in 2024

- Key readouts from ongoing trials
- New clinical entries (PLK4 and Polθ ATPase inhibitors)

Strong balance sheet

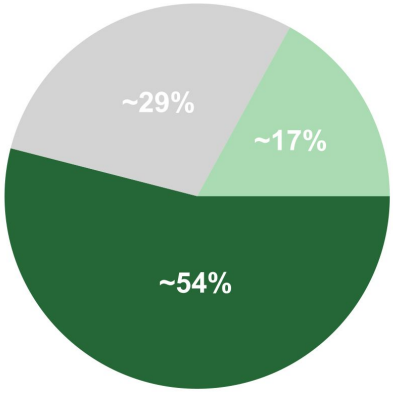
- Cash and investments of ~$237M[1] fund operations to mid-2026
- Multiple clinical catalysts in that timeframe

[1] *As of March 31, 2024.*

REPARE THERAPEUTICS

Targeting the untargetable through synthetic lethality

Precision oncology last 20 years:
Targetable gain of function (e.g., EGFR)



REPARE THERAPEUTICS

Focused on 71% untapped target space, conventionally untargetable

- **Gain of function (e.g., CCNE1, 17%)**
- **Loss of function (no known driver; e.g., BRCA1, 54%)**

Specifically targeting and disrupting genes essential for cancer cell survival

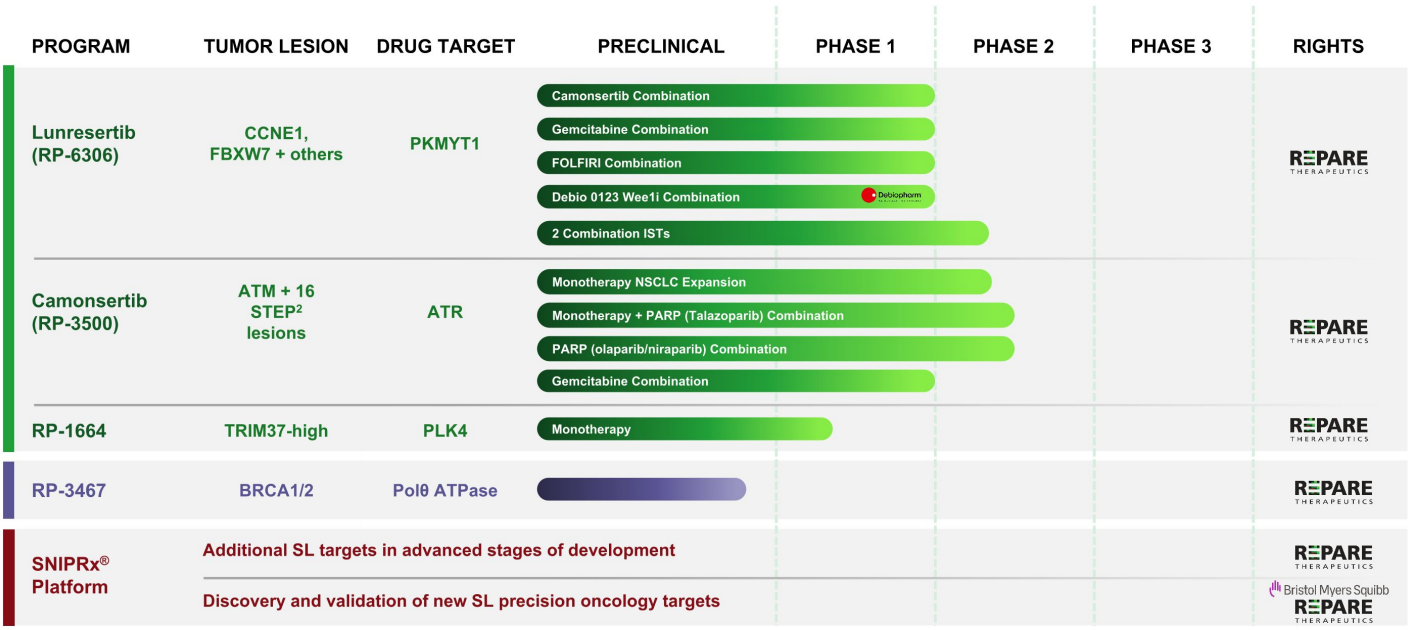
SNIPRx identifies and targets necessary genes to induce synthetic lethality

- Highly targeted & tumor-type agnostic approach
- Exploiting cancer cell genomic instability, including DNA damage repair

Platform validated with established and expanding clinical-stage pipeline

REPARE THERAPEUTICS

Expanding pipeline of precision oncology therapeutics



REPARE THERAPEUTICS

Proven experience in drug discovery and development

Leadership Team

Lloyd M. Segal
President & CEO
McKinsey & Company · PCP · CAPRION

Steve Forte, CPA
Chief Financial Officer
clementia · APTALIS

Michael Zinda, PhD
Chief Scientific Officer
AstraZeneca · Lilly

Maria Koehler MD, PhD
Chief Medical Officer
gsk · AstraZeneca · Pfizer

Cameron Black, PhD
Head of Discovery
MERCK · kaneqpharma

Philip Herman
Chief Commercial, Portfolio Development Officer
-mAbs Therapeutics, Inc. · Pfizer · santhera · Dyax

Kim A. Seth, PhD
Chief Business Officer
Pfizer · Goldman Sachs

Daniel Bélanger
Head of Human Resources
ADARE PHARMA SOLUTIONS · APTALIS

Scientific Founders

Daniel Durocher, PhD
- Developed CRISPR SL platform
- Deep DNA repair knowledge
- Lunenfeld-Tanenbaum Research Institute (LTRI) & professor at University of Toronto

Agnel Sfeir, PhD
- DDR and cancer pathway investigator
- Pioneer in Polθ, genome instability
- Professor, MSKCC

Frank Sicheri, PhD
- Globally recognized structural biologist, expert in eukaryotic cell signaling, drug mechanism of action
- LTRI & professor at University of Toronto

REPARE THERAPEUTICS

Lunresertib (RP-6306)

REPARE THERAPEUTICS

Lunresertib:
First-in-class, oral, small molecule, PKMYT1 inhibitor

Large, genomically defined potential addressable patient population of ~90k

- 50% RECIST response in camonsertib combination in gynecological tumors

Anti-tumor activity observed

- Across multiple tumor types and genotypes
- POC in patients established
- FDA agreed with RP2D; safe and well tolerated

Repare discovered synthetic lethality of PKMYT1 inhibition

- Initially identified CCNE1 amplification
- STEP[2] screen identified additional genes – FBXW7 and PPP2R1A
  - First and currently the only PKMYT1 inhibitor in clinical trials

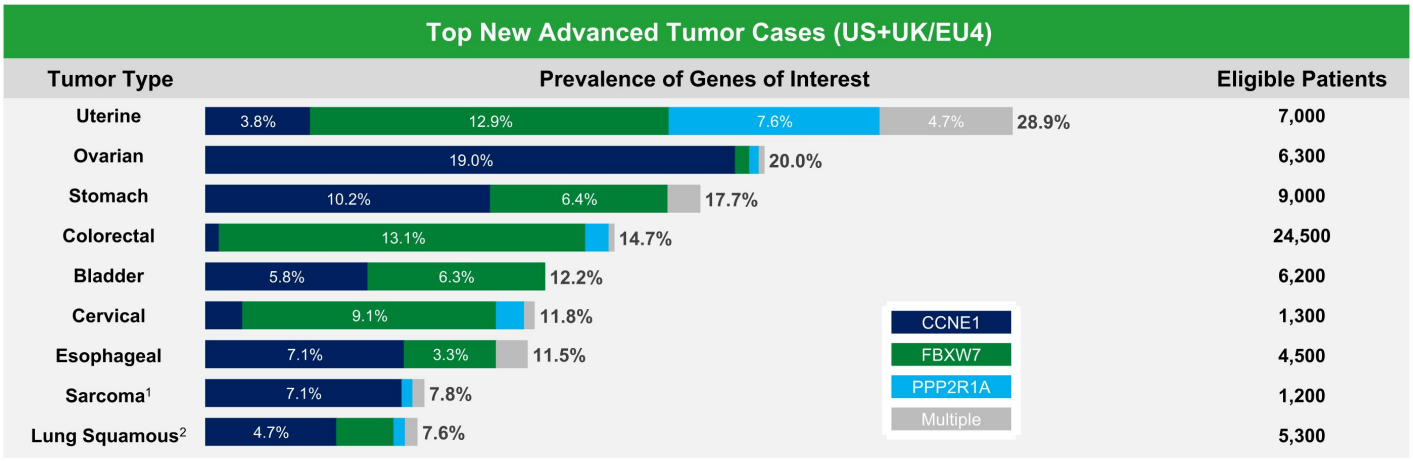
Supported preclinical synergy hypothesis and patient selection approach from proprietary SNIPRx platform

POC, proof of concept; RP2D, recommended Phase 2 dose.

REPARE THERAPEUTICS

Large, genomically defined potential patient population

~90K addressable patients including ~65K among top tumors with genetic alterations largely mutually exclusive



** Based on estimated number of pts US+UK/EU4 treated in 1st line, advanced setting for diagnosed and new recurrent patients (CancerMPact®, Treatment Architecture, United States, 2021; accessed 5/19/23) and lesion prevalence (TCGA). [1] Soft Tissue Sarcoma only; [2] Squamous subtype of Non-Small Cell Lung Cancer only*

REPARE THERAPEUTICS

Evolving broad trial program: sponsored and collaborative

Key inclusion criteria:

Recurrent solid tumors

CCNE1

amplification or

PPP2R1A

FBXW7

inactivating mutations

Lunresertib Combination Therapy

- **MAGNETIC: + Gemcitabine**
- **MYTHIC: + Camonsertib; + Debio 0123 (Wee1 inhibitor)**
- **MINOTAUR: + FOLFIRI**
- **Multiple Investigator Sponsored Trials (CCTG[1], Carbo/paclitaxel[2])**

Determine RP2D dose / schedule

Progress to late-stage trials

Future Opportunities

Selected tumors with amplified CCNE1	Ovarian, Lung, Esophageal / Gastric
Selected tumors with FBXW7 loss	CRC, Other GI, Pan Tumor
Tumors with high rate of sensitivity genes	Endometrial, Bladder
Basket trial	Breast, Sarcoma, Bile Duct

[1] *Canadian Clinical Trial Group (CCTG) collaborations include NCT05605509 and NCT05601440.*
[2] *Standard of care ("SOC") for 1st line ovarian cancer is carbo/paclitaxel (6 cycles) + PARPi maintenance therapy or carbo/paclitaxel with bevacizumab + bev maintenance therapy; this IST supports future potential 1st line combination studies as triplet therapy in patients with CCNE1 amplified tumors.*

REPARE THERAPEUTICS

Lunresertib:

MYTHIC Preliminary Phase 1 Trial Results
(M1: Monotherapy)
(M2: Camonsertib Combination Therapy)

CAMONSERTIB COMBINATION THERAPY

Safe, well tolerated and promising anti-tumor activity observed across tumors and all lunresertib-sensitizing genomic alterations (N=59)

23.6% OR; 41.8% CBR in efficacy-evaluable patients (N=55)

33.3% OR; 50.0% CBR at preliminary RP2D range, across all tumors (N=18)

38.5% OR; 57.7% CBR in patients with heavily pre-treated gynecologic cancers (N=26); **50% RECIST response** at preliminary RP2D (N=10)

Dose/schedule optimization complete; RP2D of lunresertib 80mg twice daily and camonsertib 80mg once daily

MONOTHERAPY

Safe, well tolerated and anti-tumor activity observed (N=67)

Recommended Phase 2 dose: 80 mg twice daily in intermittent schedule

OR, overall response; CBR, clinical benefit rate.

REPARE THERAPEUTICS

Key updates since ENA 2023; registrational decision on track

Registrational decision on track in gyn expansions in Q4 2024

Continuing trends of patient response and benefit

Grade 3 anemia reduced from 45% to 25% at RP2D with **updated dosing**

- 2 weeks on / 1 week off for patients with low Hg, otherwise weekly

FDA agreed with RP2D

Efficacy assessment is ongoing, continues to be **promising and on track** to be shared by end of Q4 2024

Data is expected to include **~20-30 patients per histology (ovarian and endometrial) at RP2D**

REPARE THERAPEUTICS

Lun + cam responses across tumor types and genotypes

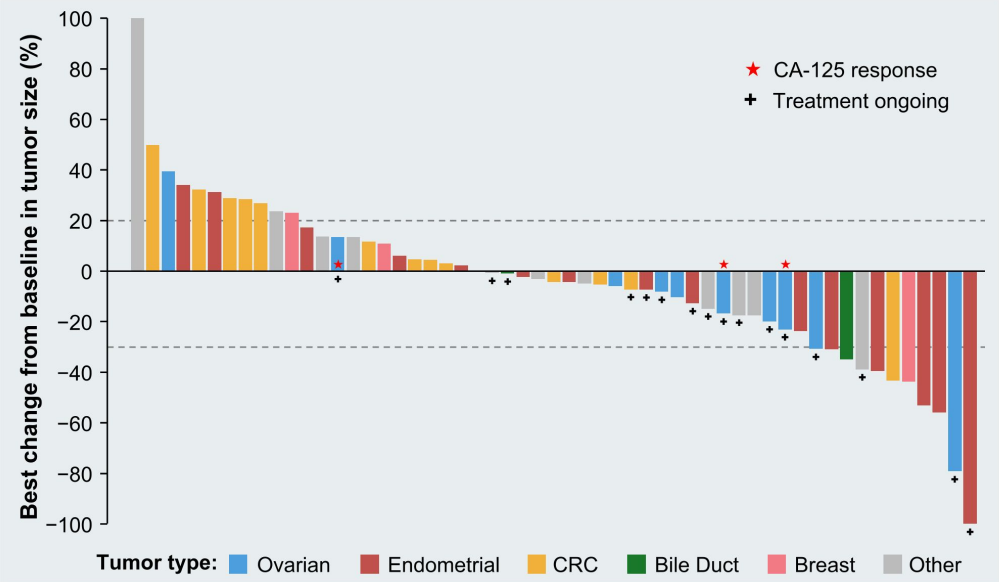
RECIST and tumor marker responses occurred early despite heavily pre-treated, relapsed/refractory patient population

Tumor type	Genotype	Response	Best % change in TL from BL	Therapy (weeks)	Lines of prior Tx/ prior platinum
Endometrial	*PPP2R1A/FBXW7*	cPR	-55.9	30.4	3/Y
	PPP2R1A/CCNE1	cPR	-53.0	18.1	2/Y
	FBXW7	cPR*	-100.0	11.1+	3/Y
	FBXW7	uPR	-39.6	16.0	3/Y
	FBXW7	uPR*	-44.7	11.4+	3/Y
Ovarian	*CCNE1*	cPR*	-70.2	21.4+	2/Y
	CCNE1†	cPR*	-30.8	12.6+	3/Y
	CCNE1	CA-125	-16.9	29.0+	9/Y
	CCNE1	CA-125	-23.1	37.0+	2/Y
	CCNE1	CA-125	13.6	12.9+	5/Y
Cervical	*PPP2R1A*	cPR*	-44.4	11.0+	1/Y
Colorectal	*FBXW7*	cPR	-43.3	27.6	3/Y
Bile duct	*CCNE1*	cPR	-35.0	28.1	2/Y
Breast	*FBXW7*‡	uPR	-43.8	18.1	2/N

** One response evaluable patient became uPR and four patients had responses confirmed after the Sept. 5, 2023 cutoff, data as of Oct. 6, 2023Relevant patient tumor co-mutations †BRCA1 rearrangement and ‡BRCA2 biallelic loss. +Treatment ongoing. BL, baseline; cPR, confirmed partial response; RECIST, Response Evaluation Criteria in Solid Tumors; TL, target lesion; Tx, treatment; uPR, unconfirmed partial response.*

REPARE THERAPEUTICS

Frequent and deep tumor reductions observed with lun + cam



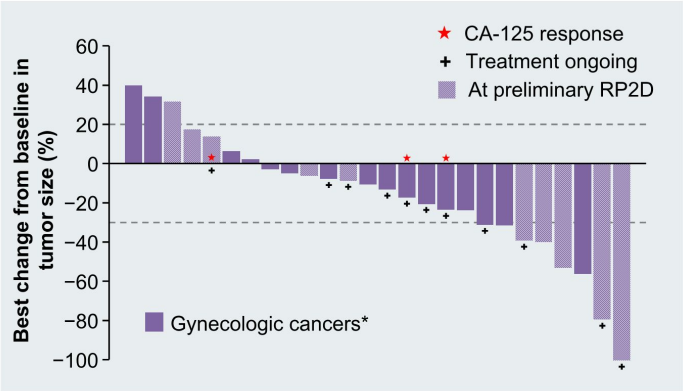
- **In evaluable patients*, across all tumors/doses:**
  - OR: 23.6% (n=55)
  - CBR: 41.8% (n=55)
  - MRR: 50.0% (n=24)
- **At preliminary RP2D, across all tumors:**
  - OR: 33.3% (n=18)
  - CBR: 50.0% (n=18)

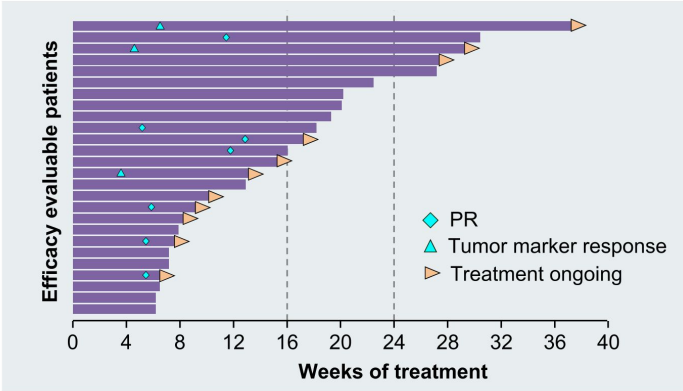
**Efficacy evaluable patients only (≥1 post-baseline tumor assessment). Other tumor types include cervical (n=1), esophageal (n=1), GI (n=1), liver (n=1), lung (n=3), melanoma (n=1), osteosarcoma (n=1), pancreatic (n=2), and upper GI (n=1). CBR: overall response or time on treatment ≥ 16 wk w/o progression; CRC, colorectal cancer; RECIST, Response Evaluation Criteria in Solid Tumors (RECIST) Gynecologic Cancer InterGroup (GCIG); MRR, molecular response rate; OR, overall response based on RECIST or GCIG CA-125 response; RP2D, recommended phase 2 dose; lun, lunresertib.*

REPARE THERAPEUTICS

Combination treatment effective in gynecologic tumors

Meaningful tumor reductions, durable clinical benefit observed in heavily pre-treated patients to date





Across all doses (n=26):

- Overall response: 38.5%; RECIST Response: 26.9%
- CBR: 57.7%; MRR: 8/10 (80%)

At preliminary RP2D (n=10):

- Overall response: 60%; RECIST Response: 50%
- CBR: 70%

- Patients had 1-9 prior therapies (median=3); treatment ongoing in 11 patients; enrollment in expansion cohorts at RP2D continues

** Gynecologic cancers: ovarian, endometrial, and cervical cancers. Data represent the efficacy evaluable population (≥1 post-baseline tumor assessment). CBR, clinical benefit rate;OR, overall response based on RECIST or GCIG CA-125 response; MRR, molecular response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors ; Gynecological Cancer InterGroup (GCIG); RP2D, recommended phase 2 dose.*

REPARE THERAPEUTICS

Significant improvement in anemia observed with updated dosing

RP2D: lunresertib 80mg BID + camonsertib 80mg QD 3d/4d

Selected hematologic TRAEs, n (%)	RP2D (ENA Cutoff)[a] N=20			RP2D (Cohort Post ENA) N=44		
	All Grades	Gr3	Gr4	All Grades	Gr3	Gr4
Anemia	13 (65.0)	9 (45.0)	0	29 (65.9)	11 (25.0)	0
Leukopenia	3 (15.0)	0	0	9 (20.5)	3 (6.8)	0
Neutropenia	3 (15.0)	2 (10.0)	0	7 (15.9)	5 (11.4)	0
Thrombocytopenia	0	0	0	0	0	0

Updated dosing strategy reduced Grade 3 anemia by ~half
Hematologic safety profile similar to commercial SL agents
No thrombocytopenia observed

[a] *ENA data cutoff of September 2023. TRAEs, treatment-related adverse events.*

Continued favorable safety profile observed to date

TRAEs in ≥10% of patients, n (%)	Lun+Cam RP2D N=65[a] All Grades	Gr3	Gr4
Nausea/Vomiting	34 (52.3)	0	0
Rash[a]	26 (40.0)	1 (1.5)	0
Fatigue	18 (27.7)	1 (1.5)	0
Stomatitis	18 (27.7)	4 (6.2)	0
Decreased appetite	13 (20.0)	0	0
Diarrhea	10 (15.4)	0	0
Headache	7 (10.8)	0	0
Constipation	5 (7.7)	0	0

- **Patient demographics remain comparable:**
  - Entry Hg
  - Gender and age
  - Prior lines and therapies
  - ECOG
  - Histologies and DOT
- **Differences in anemia rates likely a result of the updated dosing strategy**

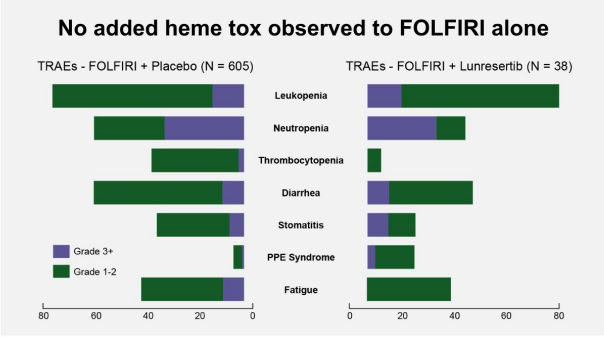
FDA agreement on RP2D
No FDA comments raised about safety profile observed in lun + cam combination

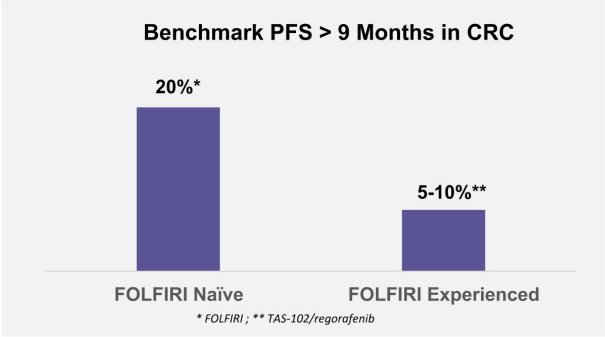
[a] *Data as of March 2024; all patients treated at exposures consistent with RP2D at any time of the trial. DOT, duration of treatment.*

Lun + FOLFIRI combination promising

MINOTAUR demonstrating overall favorable tolerability and early signal in CRC and other GI tumors

- Favorable tolerability: lunresertib given continuously daily (QD), demonstrating promising tolerability profile vs. other FOLFIRI combinations
- No new toxicities observed; no treatment withdrawals at RP2D
- Focus on potential for duration of treatment advantage in both FOLFIRI-naïve and experienced patients



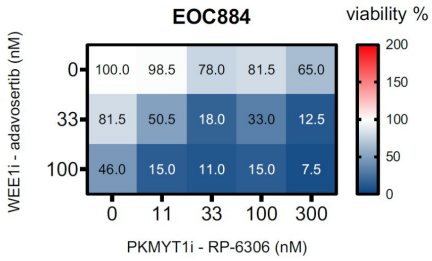


Full data to be shared at ESMO GI in June 2024

Source: Clarivate-Decision Resources Group,

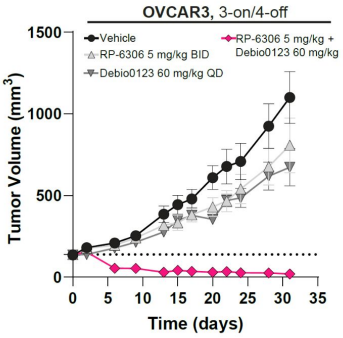
First clinical trial inhibiting both PKMYT1 and WEE1

Strong preclinical evidence of PKMYT1 + WEE1 inhibitor combination potential; Ph1/1b now enrolling



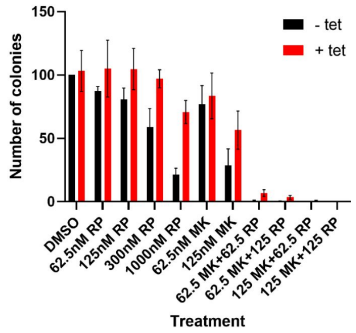
Combination synergistically eradicates ovarian cancer cells and organoid models at a low doses…

Benada et al., NAR Cancer, 2023.



…drives tumor regressions on intermittent schedule at doses below monotherapy EC_{50} …

Gallo et al., ANE 2023, Poster #A023.

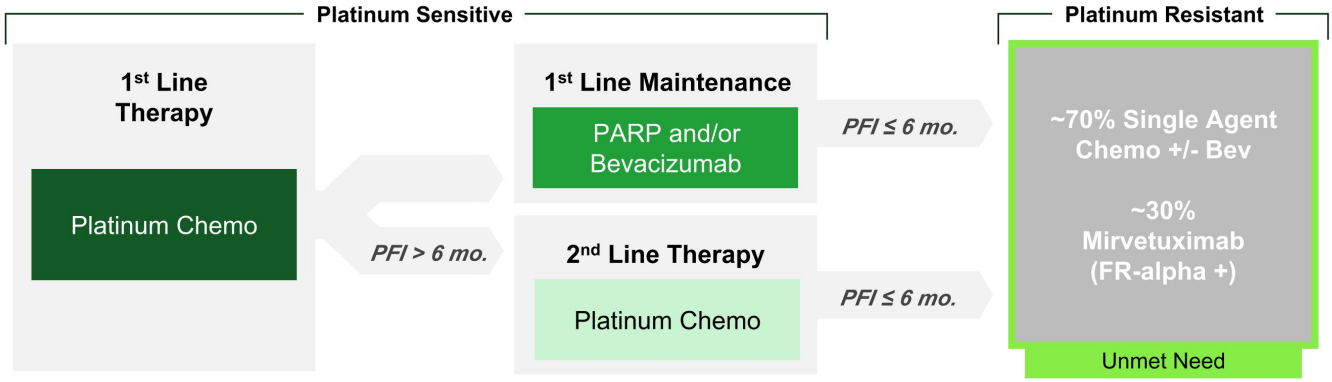


… and overcomes resistance to MK-1775 (adavosertib) mediated by tet-induced Myt1 upregulation

Sokhi et al., AACR 2023, Poster #5511.

Platinum-resistant ovarian cancer (PROC) market opportunity

Unmet need remains significant for platinum resistant patients



Chemo + Bevacizumab[1]	Single Agent Chemo[1,2]	Mirvetuximab[2]
28% ORR	13 - 16% ORR	42% ORR
6.8 mo. PFS	**3.4 - 4.0 mo. PFS**	**5.6 mo. PFS**
16.6 mo. OS	12.8 - 13.3 mo. OS	16.5 mo. OS

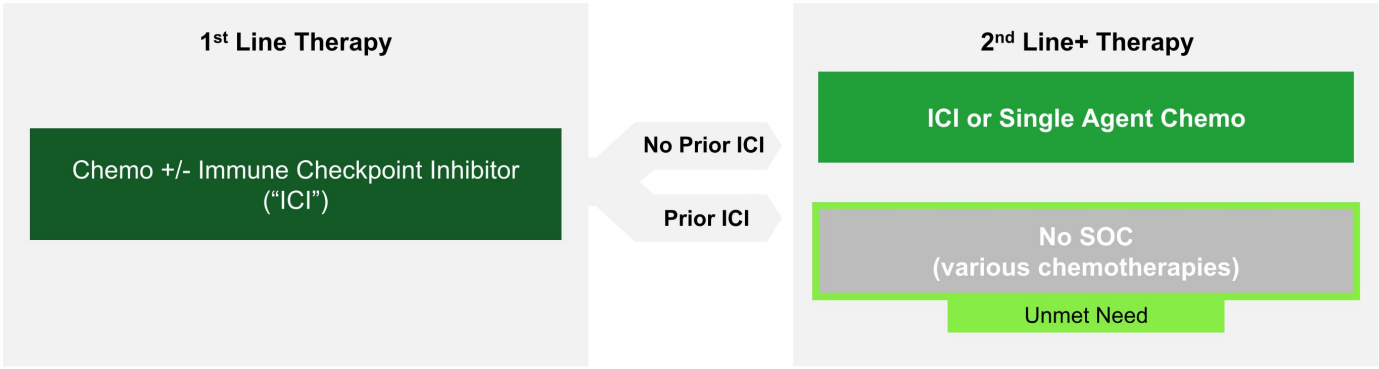
~2,900 2L+ Patients
with CCNE1[3]

1 Chemo+Bevacizumab vs Chemo (AURELIA); Source: Bevacizumab FDA Label
2 Mirvetuximab vs Chemo (MIRASOL); Source: Mirvetuximab FDA Label, ASCO 2023. Mirvetuximab is approved for ~1/3 of PROC patients who are folate receptor positive
3 Eligible Patients in US and EU4/UK Based On Company Estimates from TCGA and GENIE, 2L+ (2L - 5L)
PFI, progression-free interval.

REPARE THERAPEUTICS

Endometrial cancer market opportunity

Evolving 1L SOC towards Chemo + ICI creating large unmet need in future 2L+ setting



Single Agent Chemo[1,2]

15 - 16% ORR

3.8 - 4.0 mo. PFS

12.0 - 12.3 mo. OS

~3,600 2L+ Patients

with CCNE1, FBXW7, or PPP2R1A[3]

1 Lenvatinib/Pembrolizumab vs Single Agent Chemo (KEYNOTE-775); Source: Lenvatinib FDA Label
2 Ixabepilone vs Paclitaxel or Doxorubicin; McMeekin S. Gynecologic Oncology 2015 https://doi.org/10.1016/j.ygyno.2015.04.026
3 Eligible Patients in US and EU4/UK Based On Company Estimates from TCGA and GENIE, 2L+ (2L - 5L)

REPARE THERAPEUTICS

Metastatic CRC is a large market opportunity for MINOTAUR

Unmet need in 2L+ oxaliplatin-treated mCRC patients

1st Line Therapy

Oxaliplatin-based Chemotherapy +/- VEGF

2nd Line+ Therapy

Irinotecan-based Chemotherapy +/- VEGF
KRAS Inhibitors (KRAS G12C)
Encorafenib + Cetuximab (BRAF V600)

Unmet Need

FOLFIRI+ VEGF[1,2,4]

13 - 20% ORR
5.7 - 9.2 mo. PFS
13.3 - 21.4 mo. OS

FOLFIRI[1,2,3]

11 - 15% ORR
4.5 - 5.6 mo. PFS
11.7 - 13.8 mo. OS

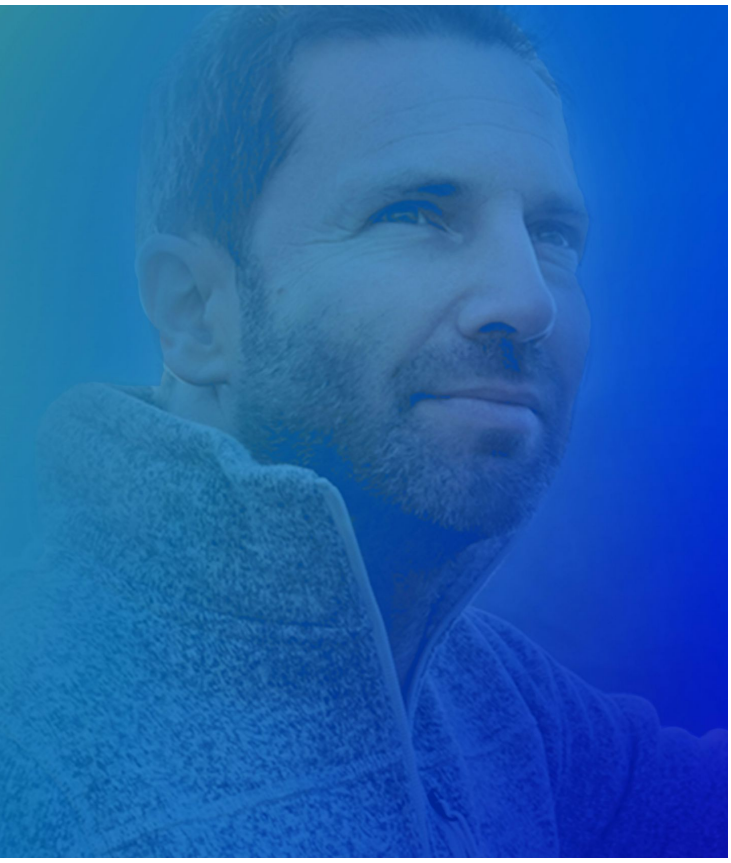
~11,300 2L+ Patients
with FBXW7[5] (~13% of CRC)

G7 Colorectal Cancer market:
>$8B today (>$10B by 2032)

1 FOLFIRI+Aflibercept vs FOLFIRI (VELOUR); Source: Aflibercept FDA Label
2 FOLFIRI+Ramucirumab vs FOLFIRI (RAISE); Source: Ramucirumab FDA Label, Lancet 2015
3 Napabucasin+FOLFIRI vs FOLFIRI+Bevacizumab (CanStem303C); Source: Shah M. Clinical Colorectal Cancer 2022
4 Panitumumab+FOLFIRI vs FOLFIRI+Bevacizumab (SPIRITT); Source: Hecht JR. Clinical Colorectal Cancer 2015
5 Eligible Patients in US and EU4/UK Based On Company Estimates from TCGA and GENIE, 2L+ (2L - 5L)

REPARE THERAPEUTICS

Camonsertib (RP-3500)



REPARE THERAPEUTICS

Camonsertib:
Potential best-in-class ATR inhibitor

Demonstrated synthetic lethal interaction of ATR and a network of genes identified by SNIPRx and STEP^2 process

Proof of concept established in Phase 1/2 monotherapy trial

Durable antitumor activity in combination with PARPi; meaningful clinical benefit observed in ovarian cancer

Global development and commercialization rights **wholly-owned** by Repare

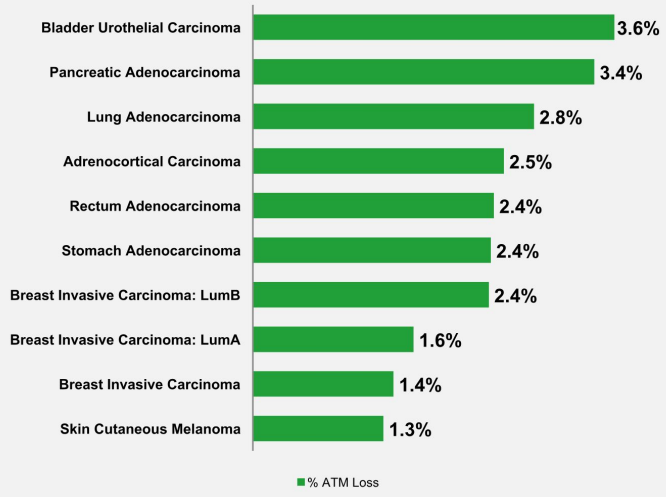
- Rapid monotherapy signal confirmation in **NSCLC**

NSCLC, non-small cell lung cancer.

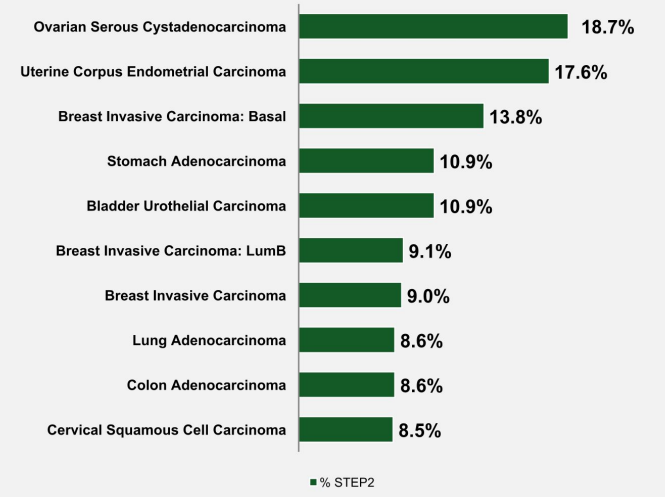
REPARE THERAPEUTICS

Potential across significant additional patient populations

Top 10 Tumor Types* with Highest Prevalence of ATM Deficiency



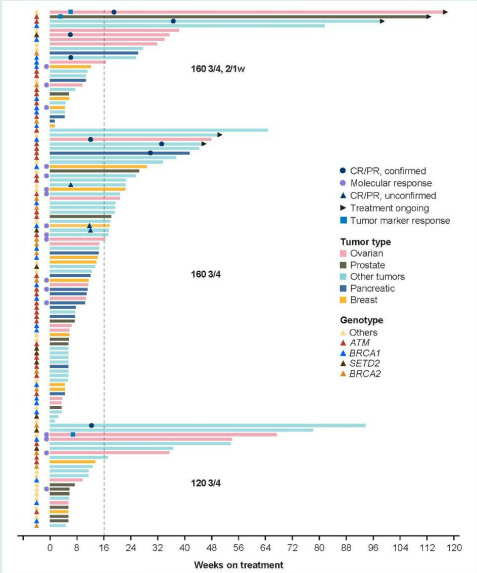
Top 10 Tumor Types* with Highest Prevalence of ATM Deficiency or STEP^2 Genomic Alterations



** TCGA; Not weighted for tumor prevalence*

Updated camonsertib monotherapy data in ATM*m* tumors

- **Updated data continues to support ATR-ATM synthetic lethality thesis across various tumor types and genotypes**
- **114 total efficacy evaluable patients treated at 3 efficacious dose levels**
- **36 patients enrolled with ATM alterations**
  - 4 with responses and treatment durations 41-112+ weeks
  - 9/36 (25%) total with Tx duration >6 months

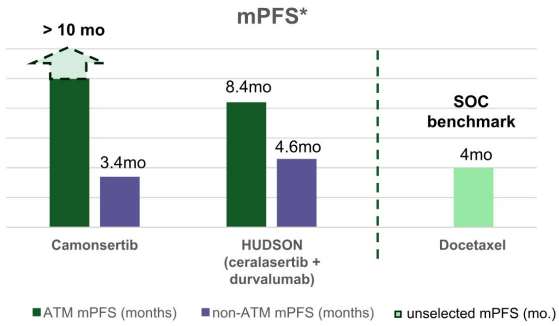


REPARE THERAPEUTICS

Camonsertib: rapid monotherapy signal confirmation in NSCLC

- **>12 months durability observed in >20% of patients with ATMm tumors treated with camonsertib monotherapy**
- **ATMm NSCLC (~4% of NSCLC) an attractive opportunity**
  - Camonsertib monotherapy signal potentially offers rapid and cost-efficient path to PoC with ~15-20 more patients within TRESR
  - 11 NSCLC patients (4 with ATMm) highlight improved mPFS in ATMm NSCLC vs non-ATMm
  - AstraZeneca HUDSON Ph2 data subset (ATR + PD-L1 post IO) further supports ATMm hypothesis in NSCLC
  - ATMm tumors do not have better outcomes in NSCLC
- **TRESR open to enrollment; data expected in 2025, with potential for expansion**
- **IO collaborations beyond monotherapy an obvious, substantial opportunity**

Promising Camonsertib mPFS in NSCLC

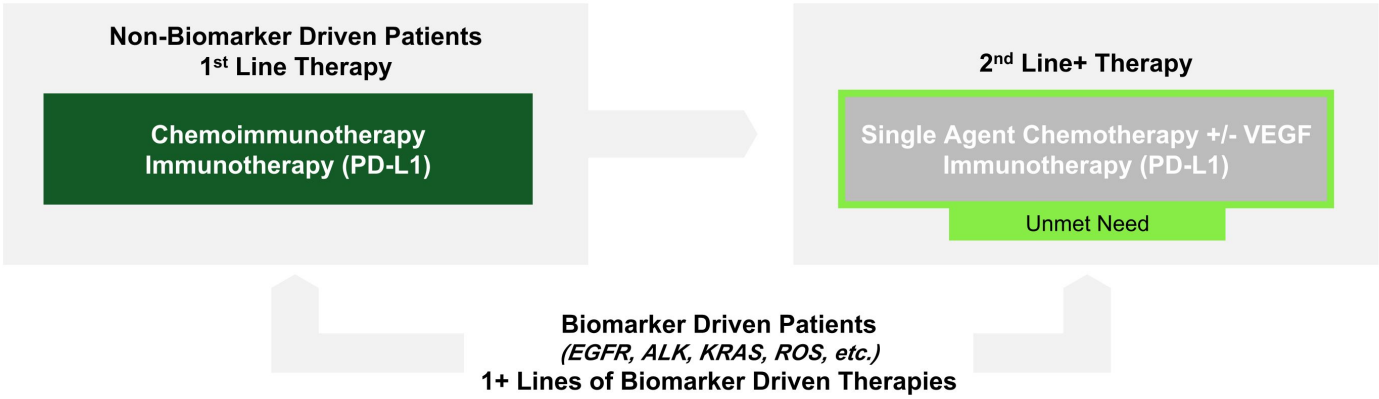


** mPFS of 4.6 months reported for both primary resistance and acquired resistance cohorts in the biomarker non-matched group, as reported in Besse, B. et alBiomarker-directed targeted therapy plus durvalumab in advanced non-small-cell lung cancer: a phase 2 umbrella trial. Nature Medicine. 13 February 2024 (HUDSON trial).*

REPARE THERAPEUTICS

Camonsertib NSCLC market opportunity

Significant unmet need for non-biomarker driven NSCLC patients



Ramucirumab + Chemo[2]
23% ORR
4.5 mo. PFS
10.5 mo. OS

Single Agent Chemo[1,2]
13 - 14% ORR
3.0 - 4.0 mo. PFS
9.1 - 9.6 mo. OS

~5,300 2L+ Patients
with ATM[3]

1 Atezolizumab vs Chemo (OAK); Source: Atezolizumab FDA Label
2 Ramucirumab+Chemo vs Chemo (REVEL); Source: Ramucirumab FDA Label
3 Eligible Patients in US and EU4/UK Based On Company Estimates from TCGA and GENIE, 2L+ (2L - 5L)

REPARE THERAPEUTICS

RP-1664

REPARE THERAPEUTICS

RP-1664

First-in-class,
oral PLK4 inhibitor

Highly potent, selective and bioavailable PLK4 inhibitor synthetically lethal with TRIM37 gain of function

Strong, dose-dependent anti-tumor activity observed as monotherapy across preclinical models

Actively enrolling in **solid tumors** and **neuroblastoma**

~63K addressable patient population with limited treatment options; potential across multiple tumor types

REPARE THERAPEUTICS

High prevalence in patient populations with limited treatment options

~63K patients with TRIM37 amplification or overexpression, with ~53K among top tumors

Top TRIM37 Altered Tumors (New Advanced Cases, US+UK/EU4)

Tumor type	Prevalence of TRIM37 alterations	Eligible patients*
Neuroblastoma[1]	81.0%	<1,000
Breast: HER2+	29.6%	5,900
Breast: HR+/HER2-	17.9%	11,800
Breast: TNBC	12.8%	2,200
Lung Non-Squamous[2]	8.6%	19,300
Bladder	8.1%	4,100
Liver	7.4%	2,200
Lung Squamous[3]	6.7%	4,700
Soft Tissue Sarcoma	6.1%	<1,000
Esophageal	5.1%	2,000

*Based on estimated number of pts available for 1st line treatment in the advanced setting (CancerMPact®, Patient Metrics, 2022;accessed 8/18/23) and lesion prevalence (TCGA; GENIE-Neuroblastoma Only). [1] Represents only gene amplification for high risk Neuroblastoma; [2] Non-Squamous subtype of Non-Small Cell Lung Cancer only; [3] Squamous subtype of Non-Small Cell Lung Cancer only

REPARE THERAPEUTICS

Compelling synthetic lethal rationale for targeting PLK4

Biomarker-driven patient selection hypothesis for development of oral PLK4i for TRIM37-high tumors

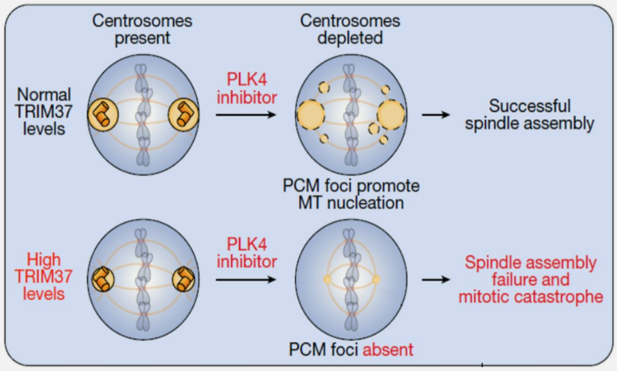
Centrosomes use centrioles and pericentriolar material (PCM) for mitotic spindle formation

Polo-Like Kinase 4 (PLK4) required for centriole creation in S-phase

TRIM37 (an E3 Ligase) reduces PCM stability; excess TRIM37 depletes PCM, increasing cell reliance on centrioles for spindle assembly

Thus, PLK4 inhibition is harmful in cells with high TRIM37 and low PCM

Validated in two 2020 *Nature* publications



Chapman/Holland Nature volume 585, pages 447–452 (2020)

Source: Holland AJ Nature 2020; Oegema K Nature 2020.

Potential first-in-class oral PLK4 inhibitor

	Key Parameter	RP-1664
In vitro	PLK4 Enzyme IC_{50}	1 nM
	PLK4 cell binding IC_{50}	3 nM
	Cell proliferation in MCF7 / T47D (TRIM37 amp) EC_{50}	51 / 17 nM
	Cell-base selectivity vs AurA, AurB	>2000-fold
	Kinome screen at 90x PLK4 IC_{50}	8/280 kinases >50% inh
ADME	Human Hepatocyte Clearance (µL/min/10^6 cells)	2.2
	Rat PK (%F, $t_{1/2}$)	28%, 4h
	Monkey PK (%F, $t_{1/2}$)	96%, 9h

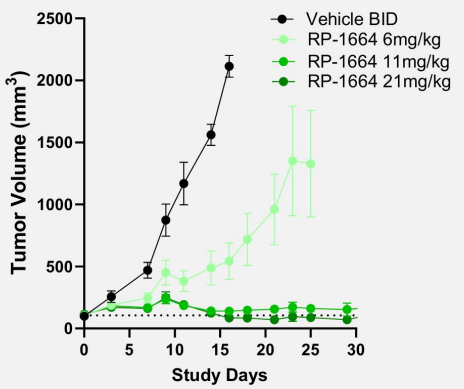
- **Highly potent, selective and orally bioavailable PLK4 inhibitor**
  - **~10x more potent than competitor molecules[1] with vastly improved selectivity vs AurB**
- **Clean in PanLabs safety pharmacology screen**

[1] CFI-400945 and EXEL-7871. *Source: internal data and Exelixis corporate presentation*

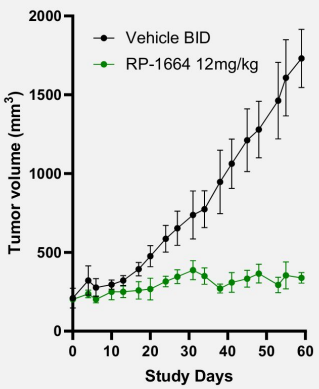
Robust monotherapy efficacy across solid tumor PDX/CDX models

Monotherapy drives tumor stasis to regression in TRIM37-high models

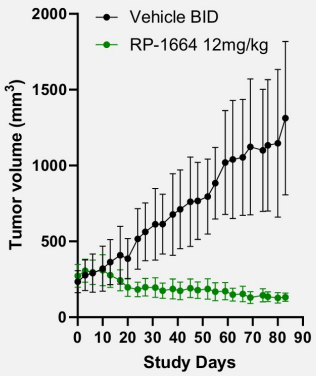
Breast (Triple Negative) CDX



Breast (ER positive) PDX



NSCLC PDX

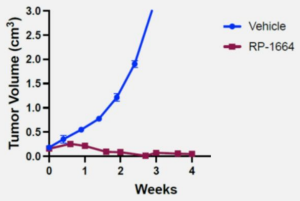


REPARE THERAPEUTICS

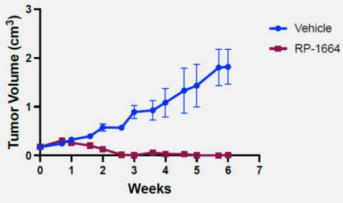
Highly efficacious as monotherapy in neuroblastoma models

Neuroblastoma PDX and CDX models (all TRIM37-high) conducted at Children's Hospital of Philadelphia demonstrate deep and prolonged monotherapy regressions in 5 of 6 evaluable models

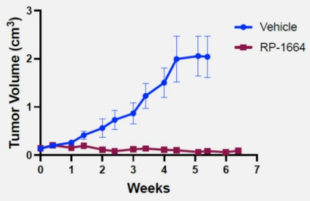
COG-N-424X



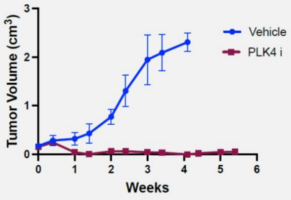
COG-N-421



NBSD



Felix



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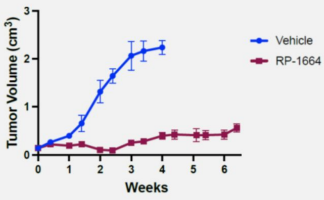
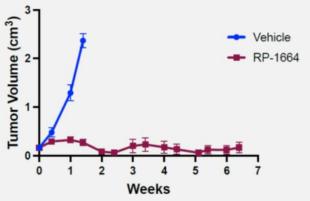


Ebc1

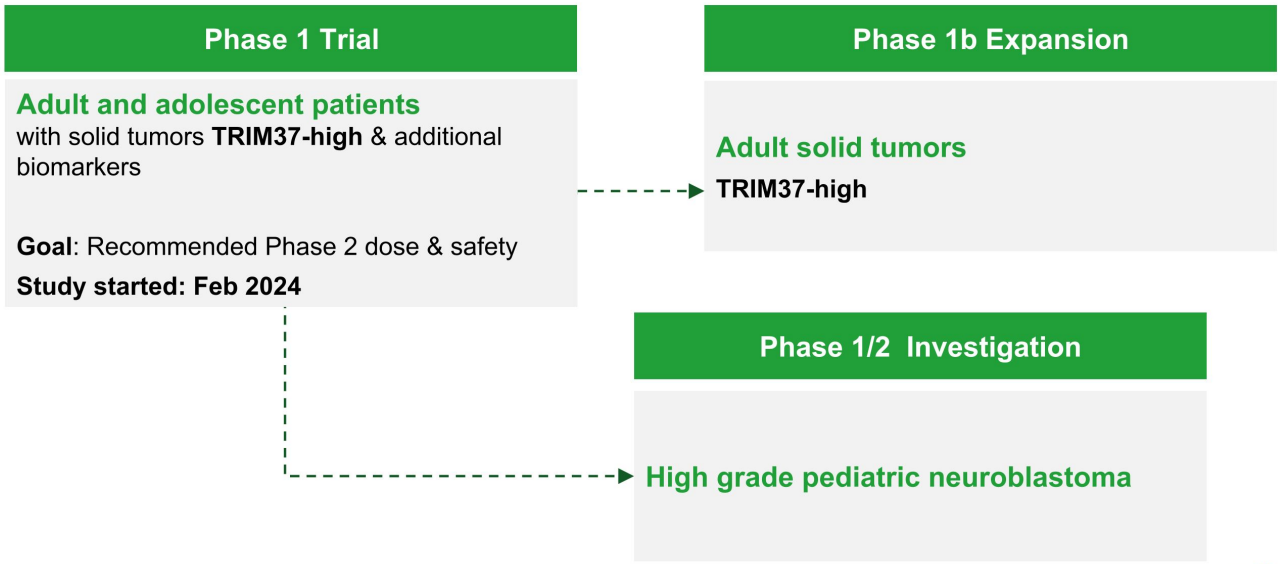


*J Maris and Y Mosse, CHOP

REPARE THERAPEUTICS

RP-1664 Phase 1/2 monotherapy clinical development plan

Efficient RP-1664 Phase 1 plan enables early start for pediatric dose finding study in neuroblastoma and clear view on adult solid tumor opportunity



RP-3467

REPARE THERAPEUTICS

RP-3467

Potential best-in-class Polθ ATPase inhibitor

FPI in 2H 2024

Highly potent, selective Polθ ATPase inhibitor; inhibits DNA repair and is **synthetic lethal** with **BRCA loss**

Demonstrates compelling potential for **combination efficacy** without added toxicity

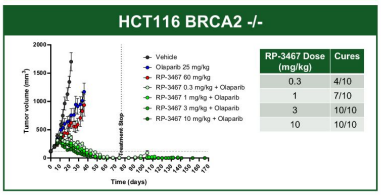
RP-3467 capable of **complete regressions** and synergies in **PARPi resistance** preclinical models

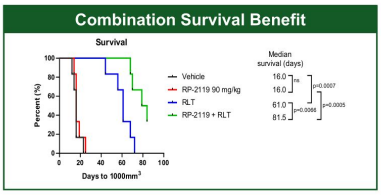
Global market segments comprise $16 billion in PARP inhibitors, RLT, and chemotherapy

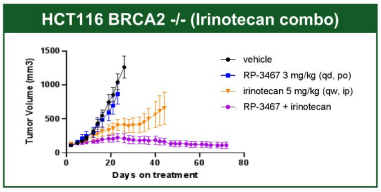
REPARE THERAPEUTICS

RP-3467 clinical plan: multiple potential Phase 1/2 trials

Phase 1 Trial	Phase 1/2 Trials	Preclinical Results	Global Market Segment
Initiation expected in H2 2024 **Goal: PK, safety and RP2D**	**PARPi combination – PARP1/2 or PARP1** Deep/durable complete responses preclinically, with no additional toxicity	HCT116 BRCA2 -/-	~$3 Billion
	RLT combination Survival benefit preclinically in unselected tumor backgrounds, with no additional toxicity	Combination Survival Benefit	~$8 Billion
	Chemotherapy / ADC Payloads Well tolerated preclinically in combination with carboplatin and irinotecan, including topoisomerase ADC payloads	HCT116 BRCA2 -/- (Irinotecan combo)	~$5 Billion





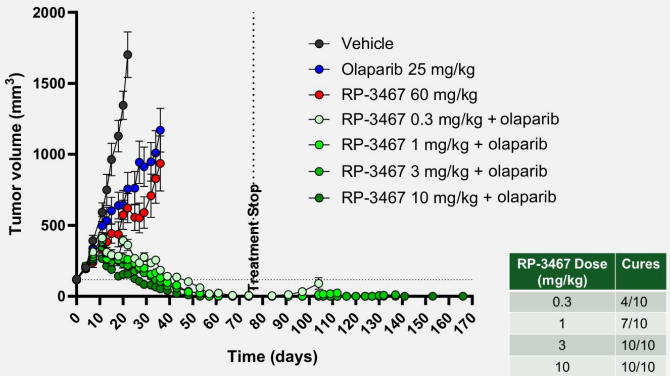


REPARE THERAPEUTICS

Profound, durable synergy observed with PARP inhibition

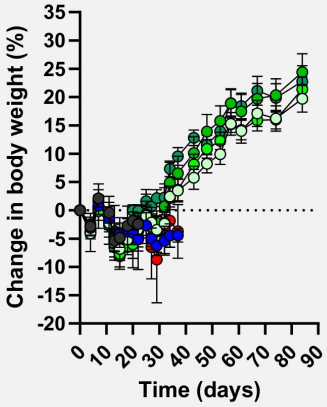
Deep/durable complete regressions observed across a wide dose range and well tolerated

HCT116 BRCA2 -/-



RP-3467 Dose (mg/kg)	Cures
0.3	4/10
1	7/10
3	10/10
10	10/10

Body Weight



REPARE THERAPEUTICS

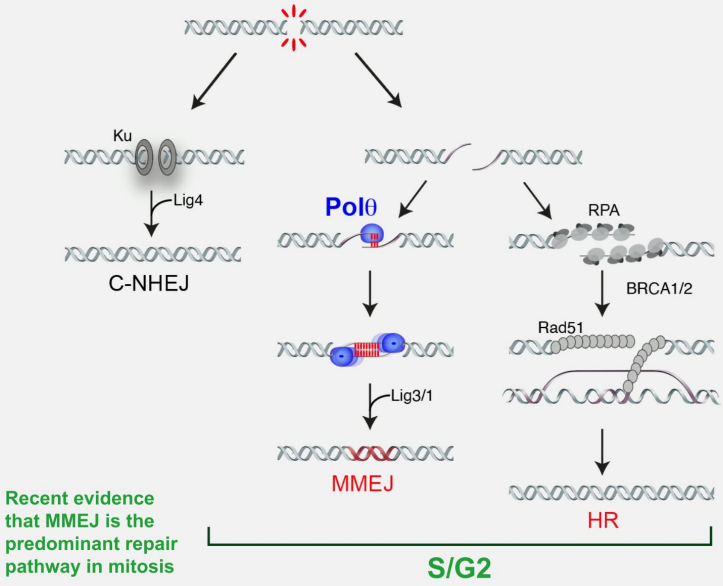
Polθ: uniquely promising therapeutic target

Polθ is a unique multifunctional DNA polymerase with ATP-dependent **DNA helicase activity**

Required for microhomology-mediated end joining (MMEJ), a **key mechanism** of double-strand DNA break repair

Uniquely active to repair double-strand DNA breaks during mitosis

Minimally expressed in normal tissue and knockout animals have **no significant phenotype**



Recent evidence that MMEJ is the predominant repair pathway in mitosis

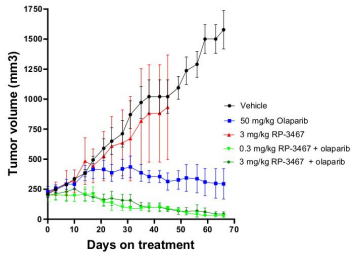
REPARE THERAPEUTICS

Target profile: potent, tolerable, capable of complete regressions

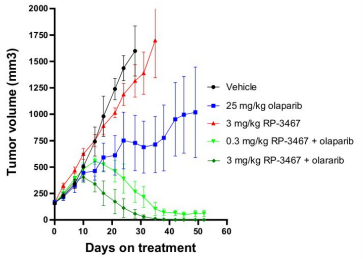
	Parameter	RP-3467
Potency	Polθ ATPase Enzyme IC_{50}	<0.25 nM
	CETSA cellular target engagement IC_{50}	5 nM
	Cell proliferation DLD1 / HCT116 (BRCA2mt) EC_{50}	4 / 7 nM
Selectiv.	Off-target ATPase (HELQ, WRN, BLM) IC_{50}	> 10 µM
	Off-target Polθ polymerase domain IC_{50}	> 100 µM
ADME	Human Hepatocyte Clearance (µL/min/10^6 cells)	2.1
	Rat PK (%F, $t_{1/2}$)	123%, 6h
	Monkey PK (%F, $t_{1/2}$)	60%, 3h

Complete regressions in PDX models at low doses

HBCx-22 (BRCA2null)



HBCx-10 (BRCA2null)



- **Highly potent, selective and orally bioavailable Polθ ATPase inhibitor; clean PanLabs safety pharmacology screen**
- **RP-3467 demonstrated complete regressions in BRCA1/2 null PDX models, also synergy in a PARPi resistance model**

REPARE THERAPEUTICS

Addressing unmet need in critical patient populations

~26K among patients with PARP-naïve and PARP-treated tumors

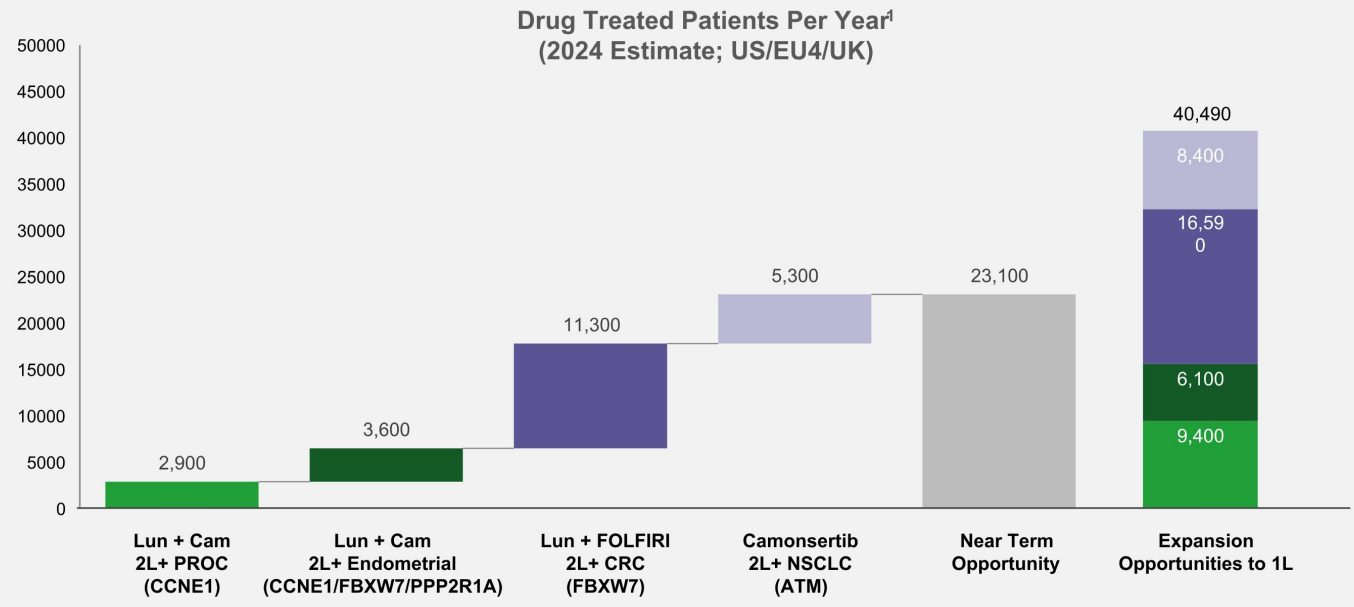
PARP-naïve and PARP-treated (Treated Patients US+UK/EU4)*

Tumor type	Prevalence of gene of interest	PARP-naïve opportunity (1L)	PARP-resistant opportunity (2L)
Ovarian	10.7% / 5.6% / 6.4% — 22.7%	7,700	3,500
Castrate-Resistant Prostate	5.9% — 8.2%	5,100	2,400
HER2- Breast**	3.7%	2,900	1,600
Pancreatic**	2.6%	1,700	500

** Based on estimated number of drug treated pts in the advanced setting likely to be naïve to PARP inhibitor treatment or previously treated with a PARP inhibitor (CancerMPact®, Patient Metrics, 2022; accessed 9/25/23) and lesion prevalence (TCGA; Riaz, N. et al. Pan-cancer analysis of bi-allelic alterations in homologous recombination DNA repair genes. Nat Commun 8, 857 (2017)). Other HRD gene mutations include: BRIP1, ATM, RAD51B, RAD51C, RAD51D, PALB2, BARD1, CDK12, CHEK1, CHEK2, FANCL, RAD54L. ** Includes germline BRCA1/2 only*

REPARE THERAPEUTICS

Multiple potential market opportunities for near term milestones



1 Eligible Patients Based On Company Estimates from TCGA and GENIE; Source: Drug Treated patients from CernerEnviza/CancerMpact

REPARE THERAPEUTICS

Recent and expected milestones

1H 2024	2H 2024	2025
✓ **RP-1664 (PLK4i)** clinical trial initiation	**Camonsertib monotherapy** expansion to NSCLC in TRESR	**Lunresertib + Debio 0123** combination data
✓ **Lunresertib + Debio 0123** combination Ph1/1b clinical trial initiation	**RP-3467** Ph1 clinical trial initiation	**Camonsertib monotherapy data** in NSCLC
✓ Regained **camonsertib** rights	**Lunresertib + camonsertib** expansion cohort data in ovarian and endometrial in Q4	Initiate first **pivotal trial** for **lun+cam** in 2025
Initial **lunresertib + FOLFIRI** combination Ph1 data at ESMO GI in June		

REPARE THERAPEUTICS

Developing Next-Generation Precision Oncology Medicines

Differentiated, proprietary clinical pipeline

- Lunresertib: First-in-class oral PKMYT1 inhibitor (Phase 1/2)
- Camonsertib: ATR inhibitor (Phase 1/2)
- RP-1664: First-in-class selective PLK4 inhibitor (Phase 1)

Proprietary CRISPR-enabled SNIPRx platform

- Focused on genomic instability and DNA damage repair
- Clinical trials enriched for patients with tumors carrying a network of synthetic lethal alterations (STEP[2])

Multiple clinical catalysts expected in 2024

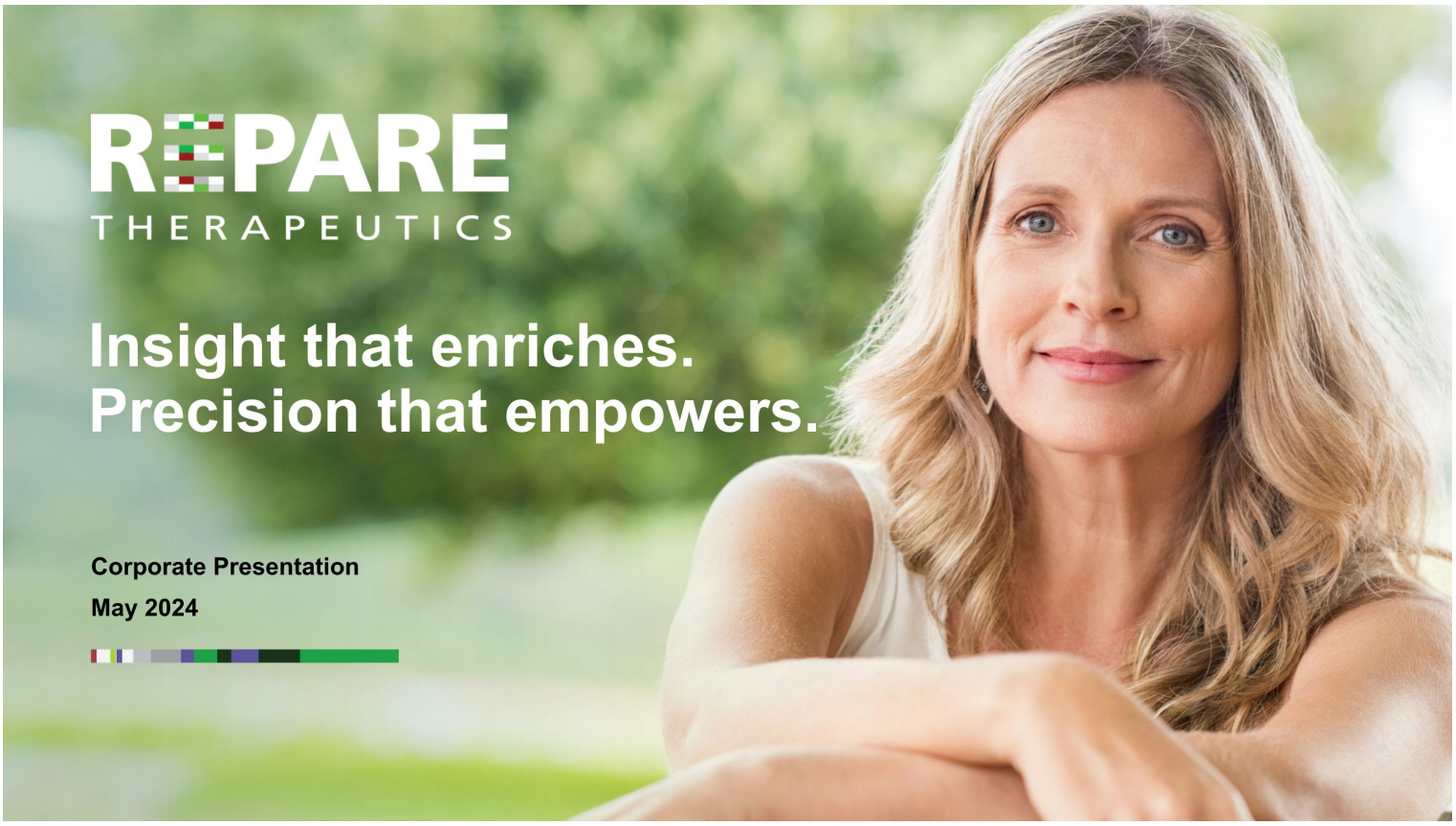
- Key readouts from ongoing trials
- New clinical entries (PLK4 and Polθ ATPase inhibitors)

Strong balance sheet

- Cash and investments of ~$237M[1] fund operations to mid-2026
- Multiple clinical catalysts in that timeframe

[1] *As of March 31, 2024.*

REPARE THERAPEUTICS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May 2024