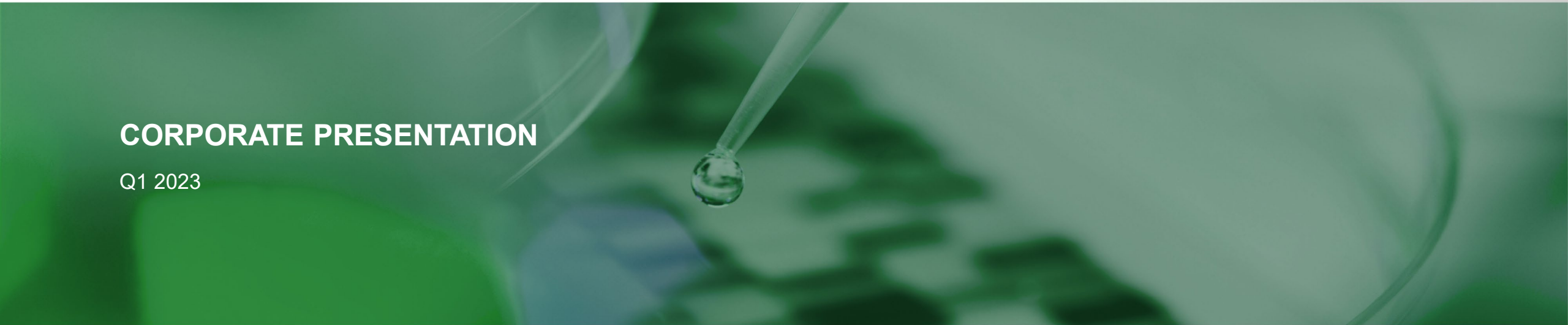
Repare Therapeutics

Insight that enriches. Precision that empowers.



CORPORATE PRESENTATION

Q1 2023

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 RP-6306 and camonsertib; 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 ongoing 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-K filed with the SEC on February 28, 2023, 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.

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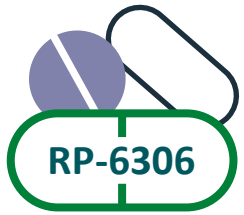
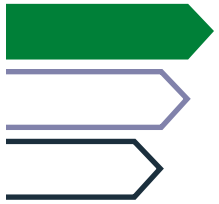
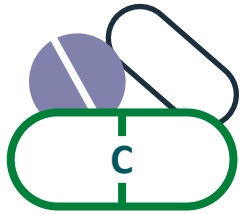
Leading precision oncology company focused on synthetic lethality



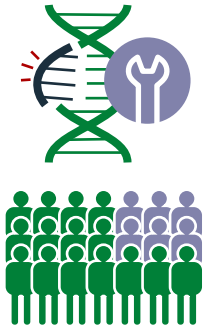
RP-6306, a first-in-class, oral PKMYT1 inhibitor, drives genomic instability in CCNE1-amplified tumors with Ph 1 monotherapy and multiple combination trials ongoing



Robust pipeline of SL-based therapeutic opportunities, including Polθ and a pipeline of advanced preclinical opportunities



Camonsertib (RP-3500 / RG6526), a potential best-in-class ATR inhibitor with durable responses and clinical benefit in Ph 1/2 and strategic validation through Roche partnership



Proprietary **genome-wide CRISPR-enabled SNIPRx platform,** focused on **genomic instability** and **DNA damage repair**, enabling novel target identification and differentiated patient selection insights

Balance Sheet of $344M funds Repare through multiple value-creating milestones into 2026

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Proven experience in drug discovery and development

Leadership Team

Lloyd M. Segal
President & CEO

McKinsey & Company · CAPRION · PCP

Steve Forte, CPA
Chief Financial Officer

clementia · APTALIS

Michael Zinda, PhD
Chief Scientific Officer

AstraZeneca · Lilly

Maria Koehler, MD, PhD
Chief Medical Officer

gsk · Pfizer · AstraZeneca

Cameron Black, PhD
Head of Discovery

MERCK · aneqpharma

Philip Herman
Head of Commercial & New Product Dev

-mAbs Therapeutics, Inc. · santhera · Pfizer · Dyax

Kim A. Seth, PhD
Chief Business Officer

Pfizer · Goldman Sachs

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

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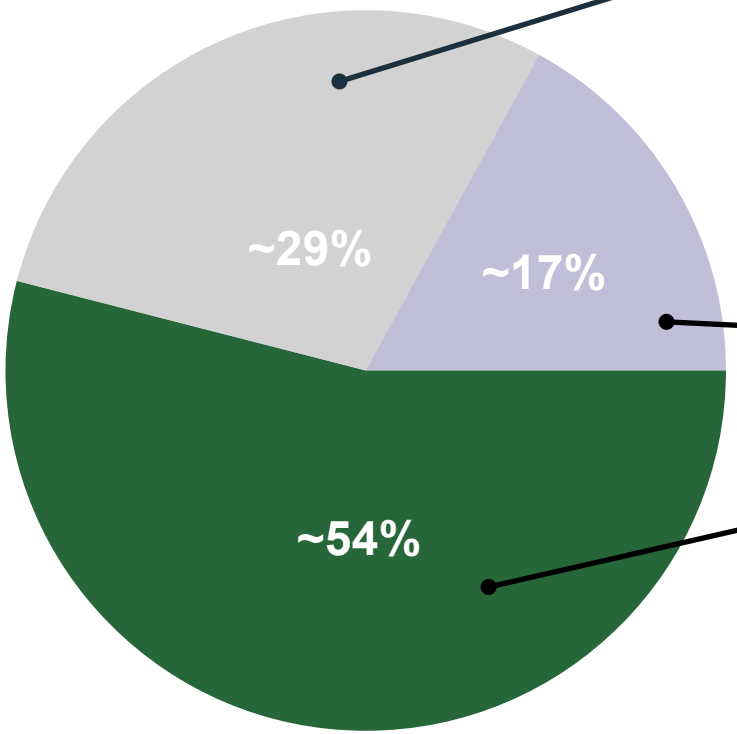
Focused on precision oncology for untapped cancer lesions

Focused on 71% untapped target space
(% of tumors)



Focus of precision oncology for 20 years:
Gain of function (targetable; e.g., EGFR)

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Gain of function
(un-targetable; e.g., CCNE1)

Loss of function
(no known driver; e.g., BRCA1)

The NEW ENGLAND JOURNAL of MEDICINE
N ENGL J MED 380;25 NEJM.ORG JUNE 20, 2019

"…known cancer targets represent a small minority of strong cancer dependencies … synthetic lethal targets are particularly attractive as new targets…"

Repare has identified several novel and proprietary targets to date

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Robust pipeline of SL-based precision oncology therapeutics

SL Pair

		Lesion Network	Drug Target	Discovery	IND-Enabling	Phase 1/2	Pivotal	Anticipated Milestones	Rights
Clinical	Camonsertib (RP-3500 / RG6526)	ATM + 16 STEP² lesions	ATR	Ph1/2 TRESR: Monotherapy Ph1/2 TRESR: PARP (talazoparib) Combo Ph1/2 ATTACC: PARP (olaparib/niraparib) Combo Ph1/2 TRESR: Gemcitabine Combo				▪ **H1'23** initial PARP combination data ▪ **Summer/Fall '23** initial gemcitabine combination data	Roche REPARE THERAPEUTICS
Clinical	PKMYT1 inhibitor RP-6306	CCNE1, FBXW7, PPP2R1A	PKMYT1	Ph2 CCTG BASKET IST Ph1 MYTHIC: Mono + Camonsertib Combo Ph1 MAGNETIC: Gemcitabine Combo Ph1 MINOTAUR: FOLFIRI Combo				▪ **2023** Ph2 Basket IST start ▪ **H1'23** Ph1 carboplatin combination study start ▪ **H1'23** initial Ph1 monotx data ▪ **Q4'23** initial Ph1 combination data	REPARE THERAPEUTICS
Preclinical	Undisclosed	Undisclosed	Undisclosed					▪ **H1'23** IND-enabling studies ▪ **Late '23/Early '24** Clinic	REPARE THERAPEUTICS
Preclinical	Polθ inhibitor	BRCA1/2 + others	Polθ					▪ **2024** Clinical entry	REPARE THERAPEUTICS ono
Discovery	SNIPRx® platform	Additional SL targets in advanced stages of development							REPARE THERAPEUTICS
Discovery	SNIPRx® platform	Discovery and validation of new SL precision oncology targets							Bristol Myers Squibb REPARE THERAPEUTICS

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SNIPRx® platform

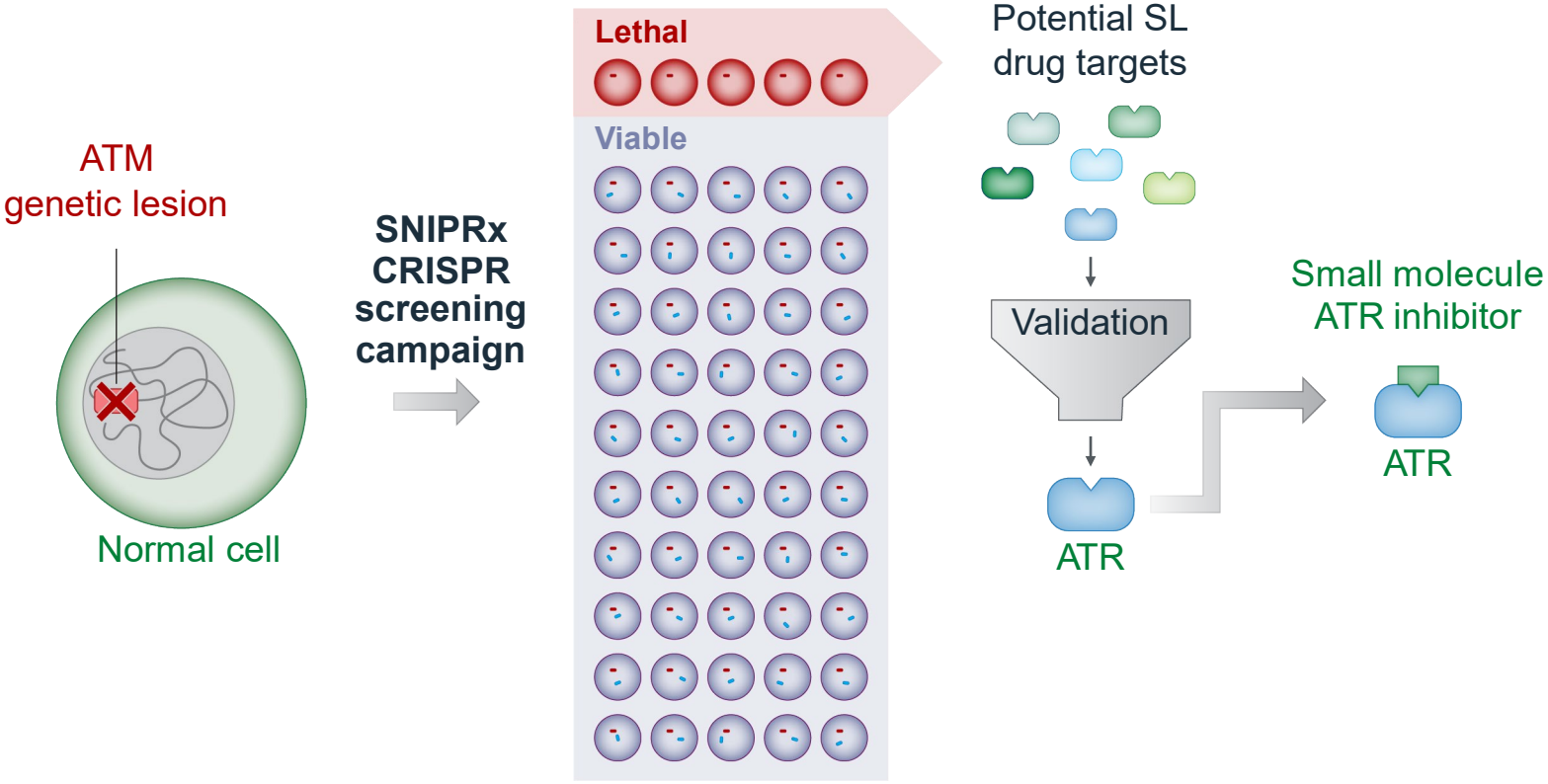
SNIPRx® platform for synthetic lethal ("SL") drug discovery

1 Select tumor lesion of interest

2 Execute SNIPRx® screen campaign

3 Prioritize, select and validate druggable targets

4 Develop potent and selective inhibitors



- Starts with the patient's unique genetic lesion
- Proprietary genome-wide, CRISPR-Cas9 enabled platform and isogenic cell lines
  - Optimizes sensitivity, reproducibility
  - Decreases false negatives
- Finds targets and patient selection markers that others miss
- Novel SL targets identified from every campaign completed to-date

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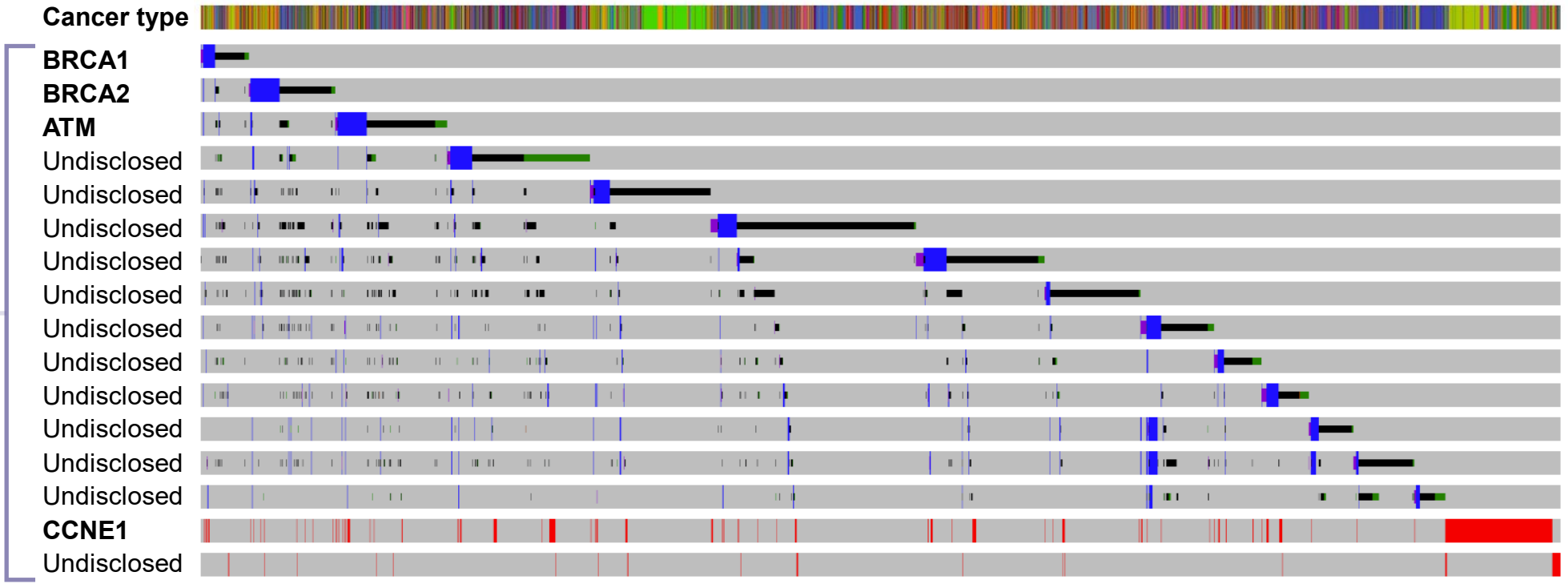
SNIPRx® campaigns mine targeted genomic instability lesions

Lesion campaigns completed to-date



We have mined an initial 16 largely mutually exclusive tumor lesions representing ~30% of all tumors

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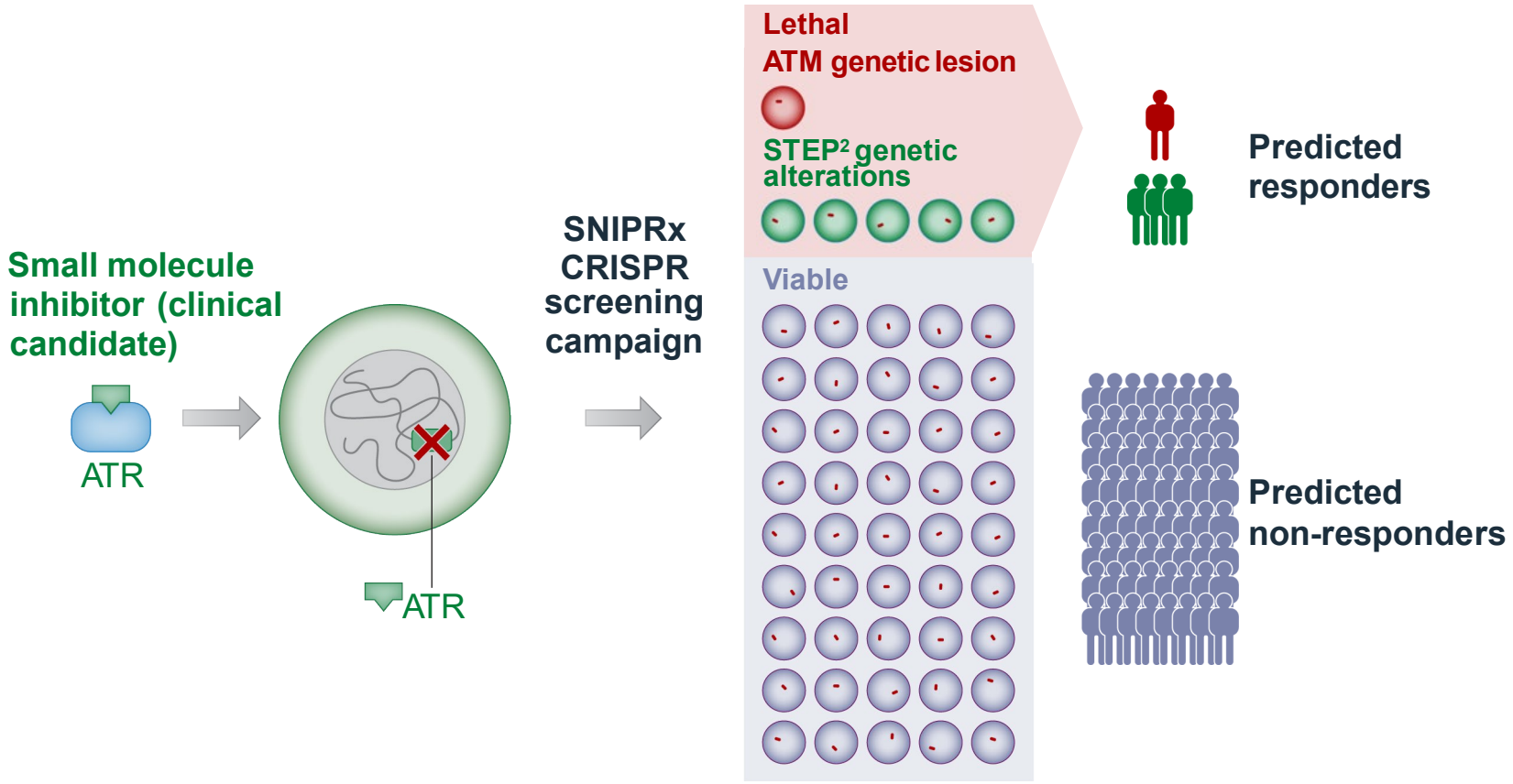
STEP^2 screens expand patient population tailored to each program

4 Develop potent and selective inhibitors

5 Perform SNIPRx® Targeted Expansion of Patient Populations (STEP^2) screens

6 Conduct clinical trials in an enriched patient population



STEP^2 screens: SNIPRx Targeted Expansion of Patient Populations

- Expands patient populations beyond those identified by original SL pair
- STEP^2 insights enable precision medicine-driven clinical trials

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Bristol Myers Squibb – SNIPRx® target discovery collaboration

Multi-target discovery collaboration with Bristol Myers Squibb to leverage Repare's proprietary SNIPRx® synthetic lethal discovery platform to identify multiple oncology drug candidates

~$65M upfront
Including $50M non-dilutive cash and $15M equity investment

~$3 billion
Potential total milestone payments in addition to royalties (~$300M/program)

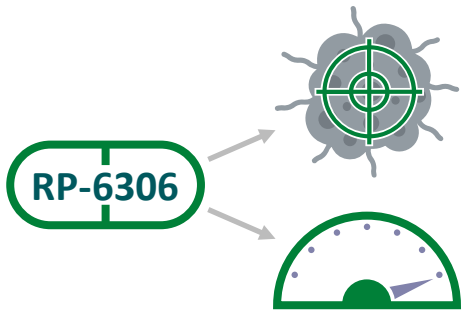
Target focused
Includes both small molecule SL targets and "undruggable" targets outside our focus

Discovery only
Repare retains all rights to its remaining pipeline

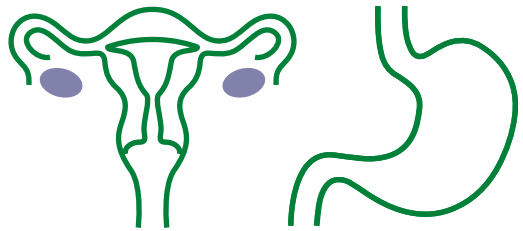
PKMYT1 inhibitor RP-6306

RP-6306: first-in-class, oral, small molecule, PKMYT1 inhibitor

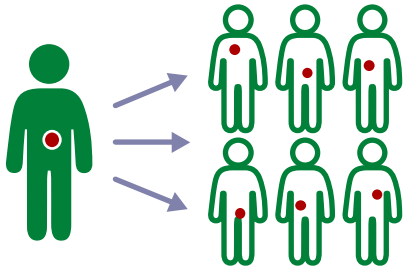
RP-6306 exploits vulnerabilities caused by increases in CCNE-1, not previously considered a druggable target



Preclinical data differentiates as potent and highly selective, with anti-tumor activity especially in combination



Many affected tumor types, including gynecological and gastrointestinal malignancies



Synthetic lethal combinations with CCNE1 amplified, FBXW7 loss, PPP2R1A, and other STEP[2] genes aid in patient selection

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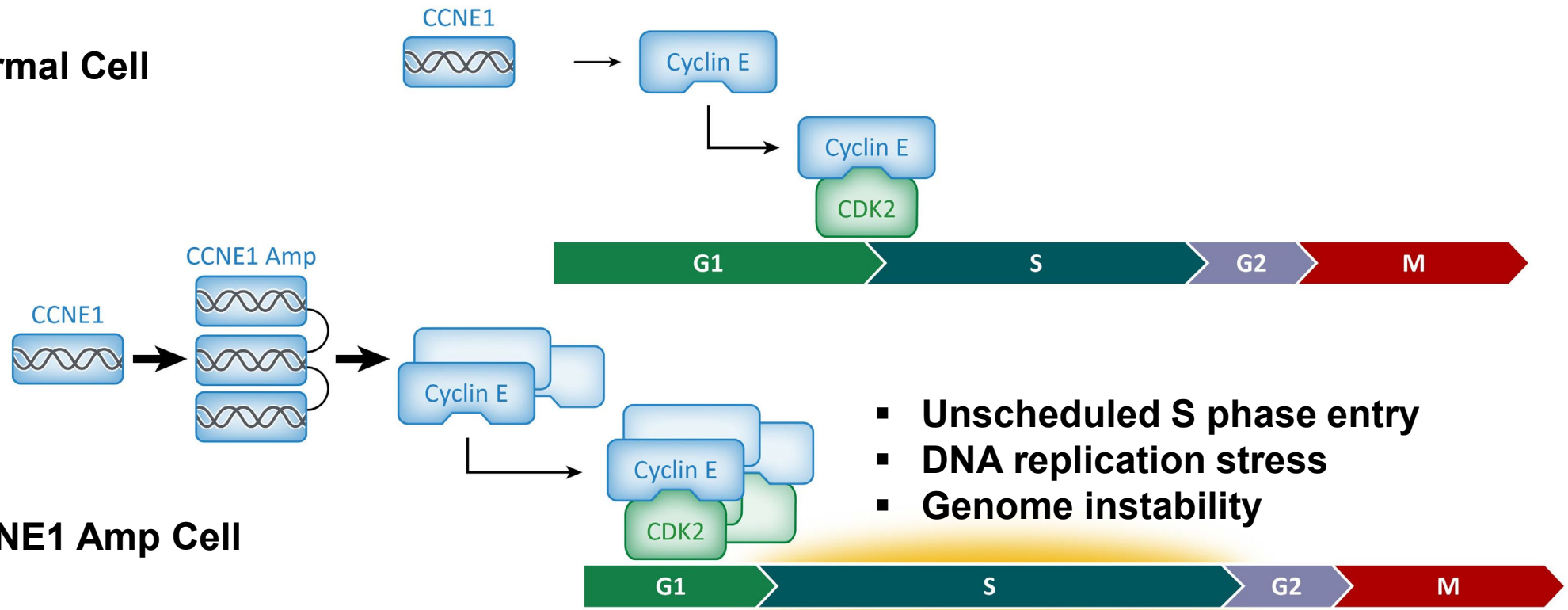
CCNE1 amplification drives genome instability



- Unscheduled S phase entry
- DNA replication stress
- Genome instability

CCNE1-overexpression drives premature entry into S-phase and overloads the DNA replication machinery, resulting in genome instability

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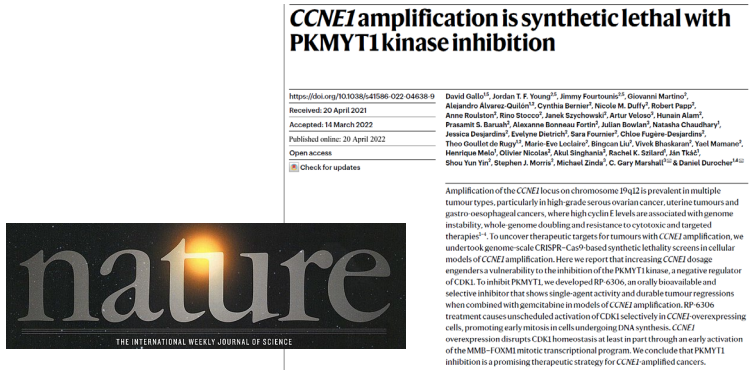
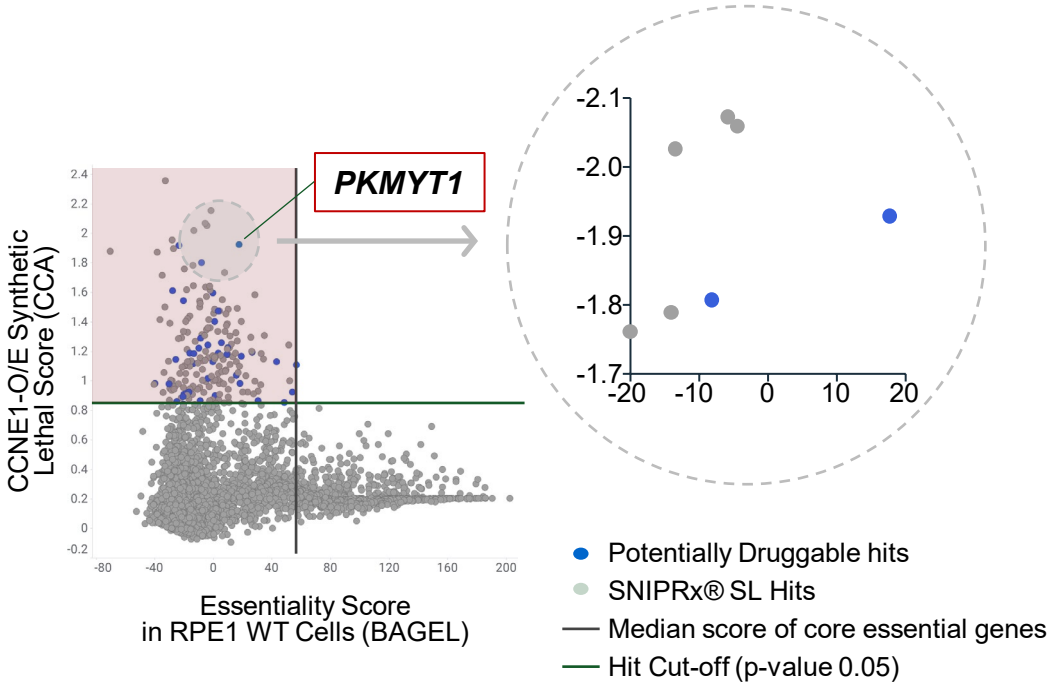
PKMYT1: strong hit in a CCNE1-overexpression ("O/E") SL screen

PKMYT1 (also known as Myt1):

- Membrane-associated serine/threonine protein kinase
- Member of WEE1 protein kinase family
- Negatively regulates the G2/M transition of the cell cycle by inactivating CDK1
- Not previously linked to CCNE1 amplification





- Genome-wide CRISPR screen
- PKMYT1 was the highest scoring druggable hit
- PKMYT1 was also a high scoring hit in the DepMap

Nature. 604 (7907), pp. 749-756 (Apr 2022). https://doi.org/10.1038/s41586-022-04638-9

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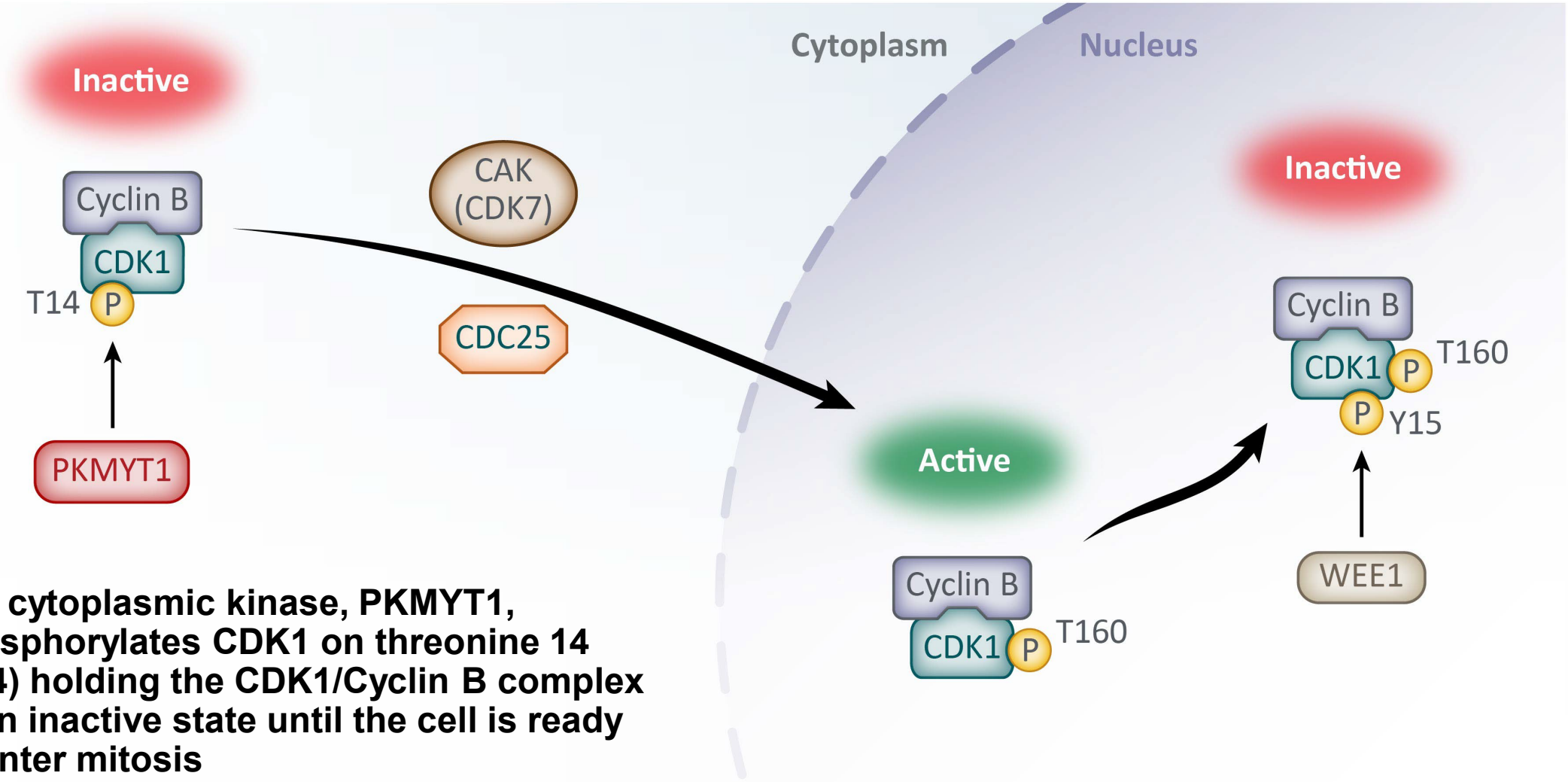
PKMYT1 selectively regulates cyclin B-CDK1 complexes

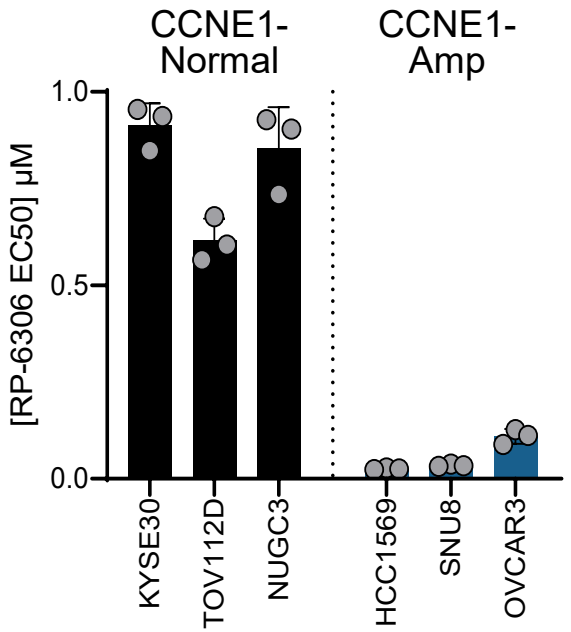


- **The cytoplasmic kinase, PKMYT1, phosphorylates CDK1 on threonine 14 (T14) holding the CDK1/Cyclin B complex in an inactive state until the cell is ready to enter mitosis**

REPARE THERAPEUTICS

RP-6306: potent and selective first-in-class PKMYT1 inhibitor

	Parameter	RP-6306
Potency	Enzyme potency (IC_{50}, nM)	3
	HCC1569 CDK1 T14 phosphorylation (IC_{50}, nM)	20
	HCC1569 cell viability (EC_{50}, nM)	19
	PKMYT1 selectivity over WEE1 (cell-based)	>100-fold
ADME Properties	CYP inh (3A4, 2D6, 2C9, 1A2, 2C19)	all >30 µM
	Hepatocytes: rat, dog, human Cl_{int} (µL/min/10^6cells)	28, <6, <6
	Human plasma protein binding	79%
	Rat PK (%F, $t_{1/2}$)	44%, 2.6h
	Dog PK (%F, $t_{1/2}$)	74%, 5.5h



Tumor cell lines with CCNE1-Amp are **hypersensitive** to PKMYT1 inhibition compared to cells with normal CCNE1 levels

RP-6306 profile:

- Highly potent and selective inhibitor
- PanLabs Lead Profiling screen on 68 assays showed no significant activity at 10 µM
- No activity (>100 µM) in patch clamp assays for hERG, hNaV1.5, and hCaV1.2 ion channels
- Favorable pre-clinical PK profile
- Low potential for clinical drug-drug interactions

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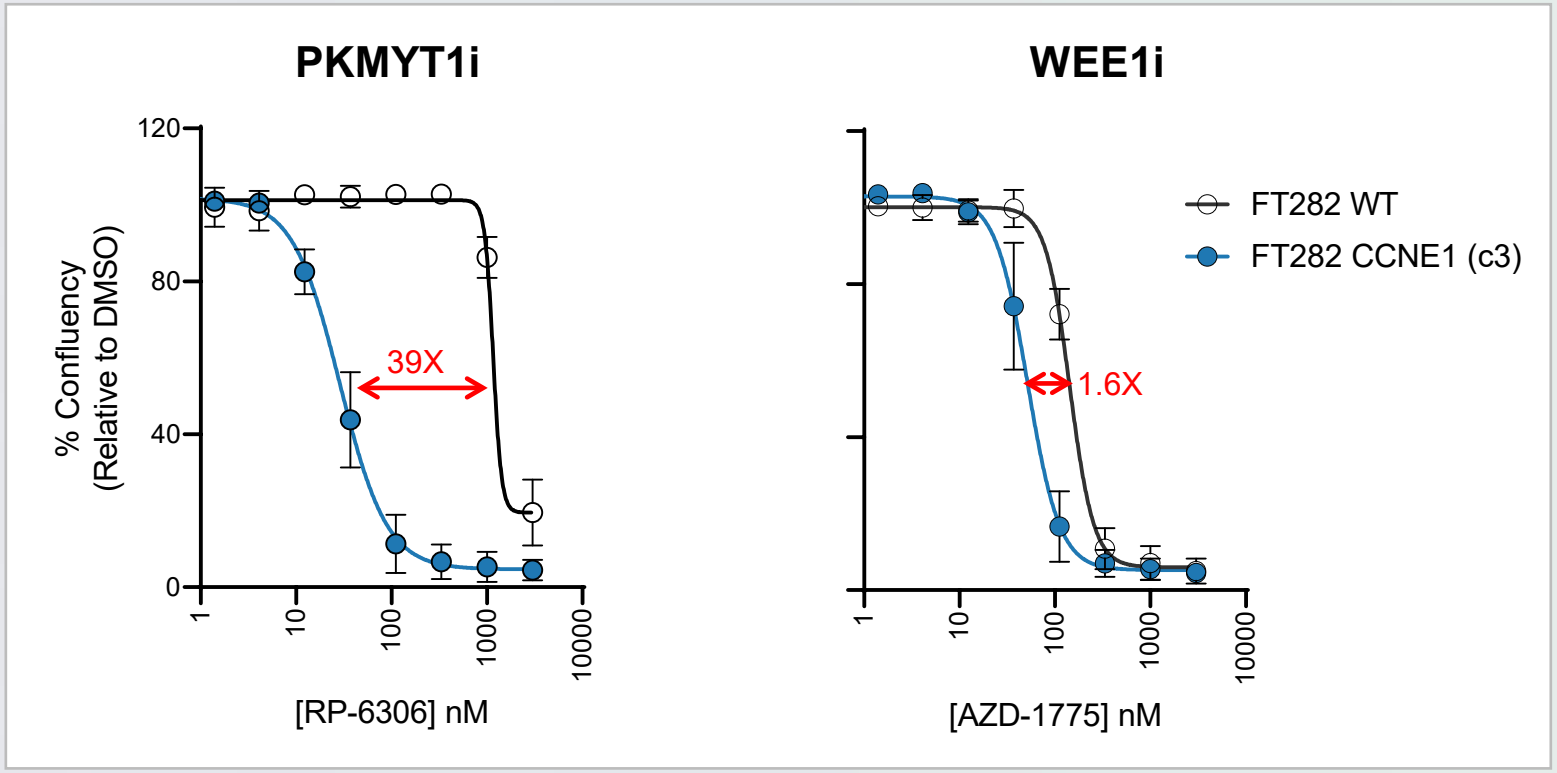
RP-6306 selectivity on CCNE1-O/E cells vs. WEE1 inhibition



- **PKMYT1 inhibition results in a 39-fold increase in sensitivity in CCNE1-O/E FT282 cells vs. wild type**
- **WEE1 inhibits both wild type and CCNE1-O/E cells**

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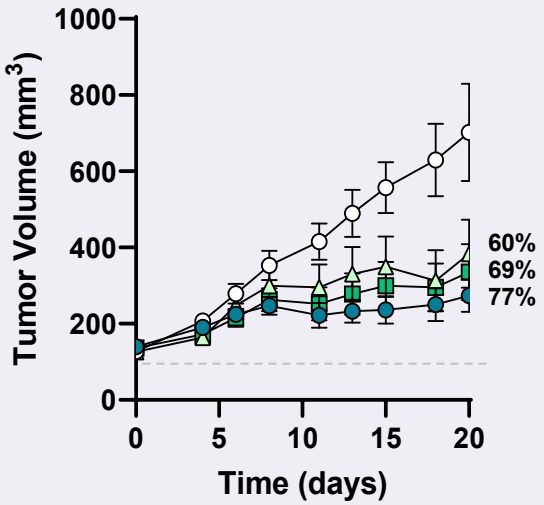
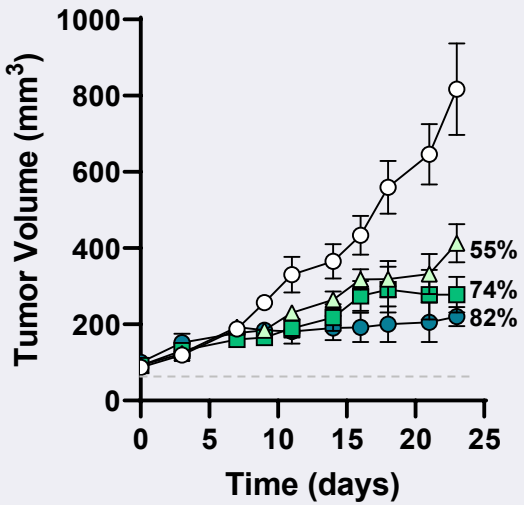
RP-6306 inhibits growth of multiple CCNE1-amplified xenograft tumors

HCC1569 Breast



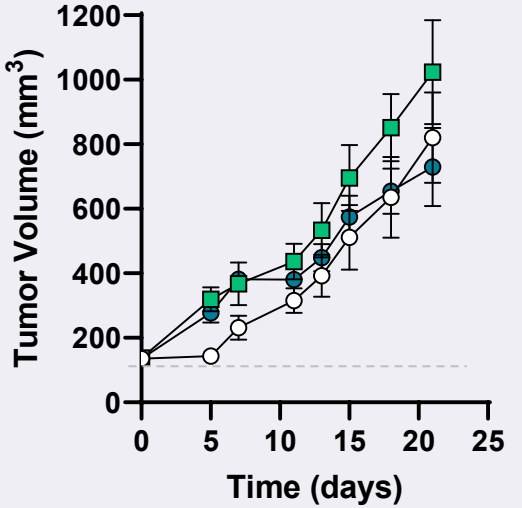
CCNE1 CN = 34

OVCAR3 Ovarian



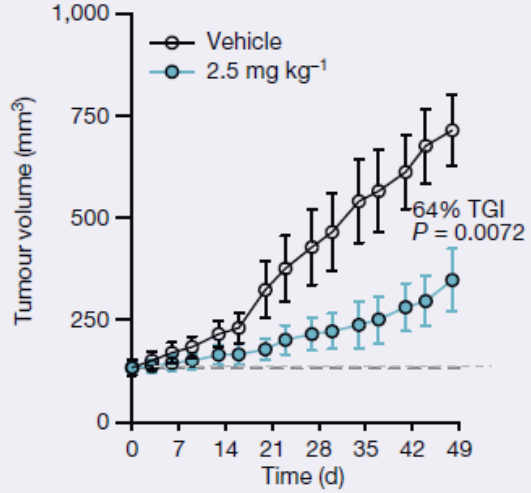
CCNE1 CN = 14

SUM149PT TN Breast

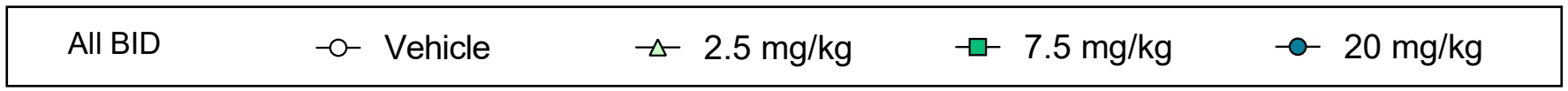


CCNE1 CN = 2 (WT)

PA1443 Pancreatic PDX



CCNE1 CN = 17



RP-6306 anti-tumor activity seen or demonstrated at doses well below MTD

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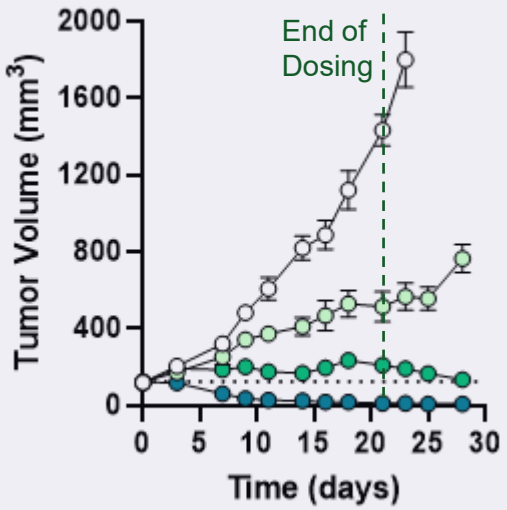
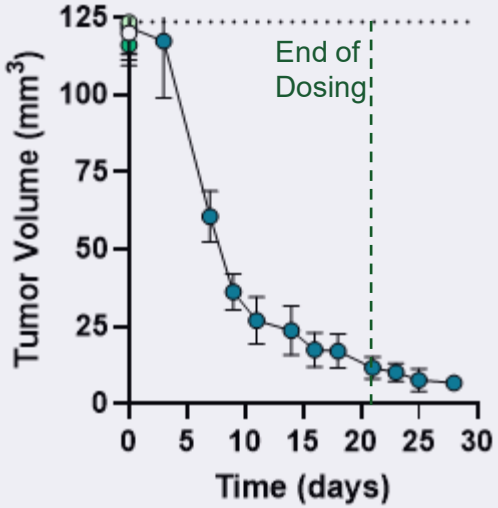
RP-6306 + gemcitabine synergize to drive regression with tolerability

Activity (OVCAR3)

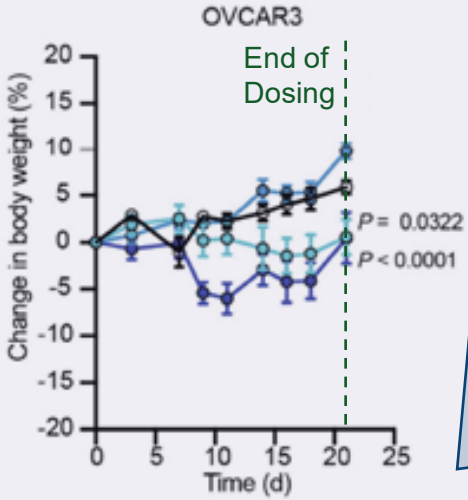


Activity (Robust regression)

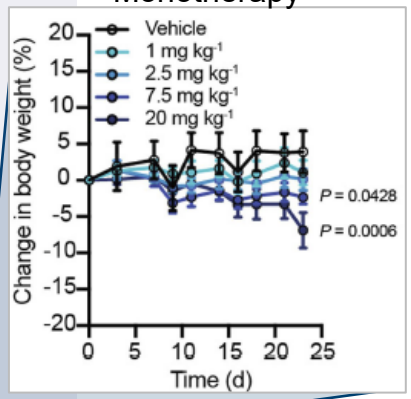


Vehicle
RP-6306 10mg/kg
Gem 20mg/kg
RP-6306 10mg/kg + Gem 20mg/kg

Tolerability



Monotherapy



Vehicle
Gemcitabine (20 mg kg⁻¹)
RP-6306 (10 mg kg⁻¹)
RP-6306 (10 mg kg⁻¹) Gemcitabine (20 mg kg⁻¹)

- **Xenograft tumors continue to regress after dosing cessation with several mice having no measurable tumor detected**
- **Measured three times a week, mice at each dose level experienced <7% (monotherapy) and maximum of 10% (gemcitabine combo) body weight loss**

Gemcitabine dosed once a week and RP-6306 dosed twice daily; CCNE1 CN = 14

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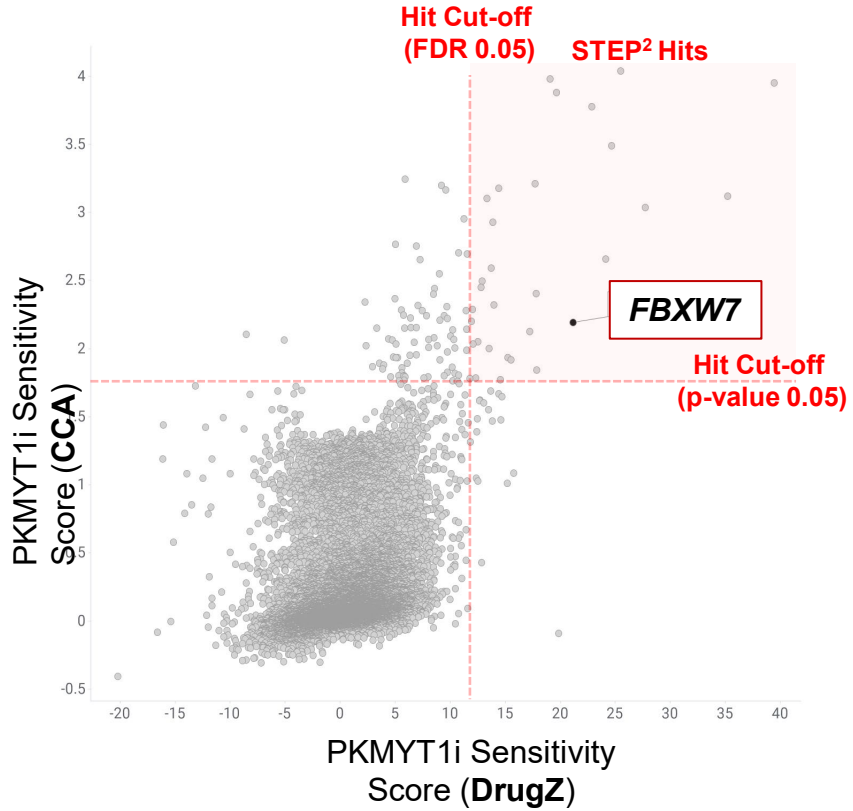
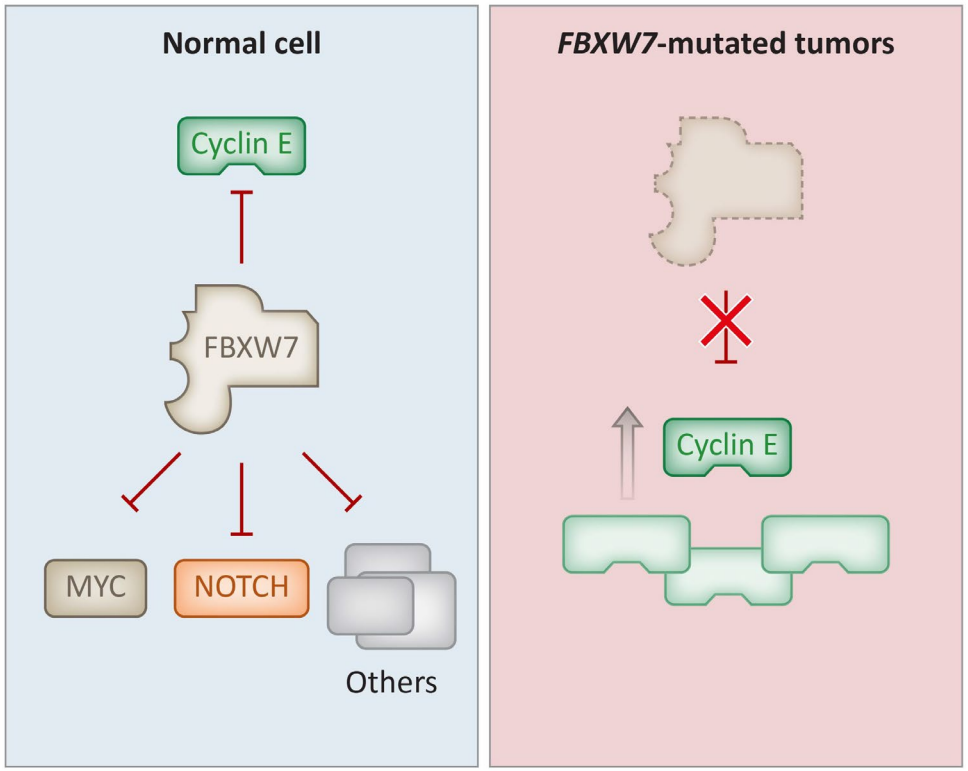
STEP² screen identified FBXW7 as sensitive to PKMYT1 inhibition

FBXW7

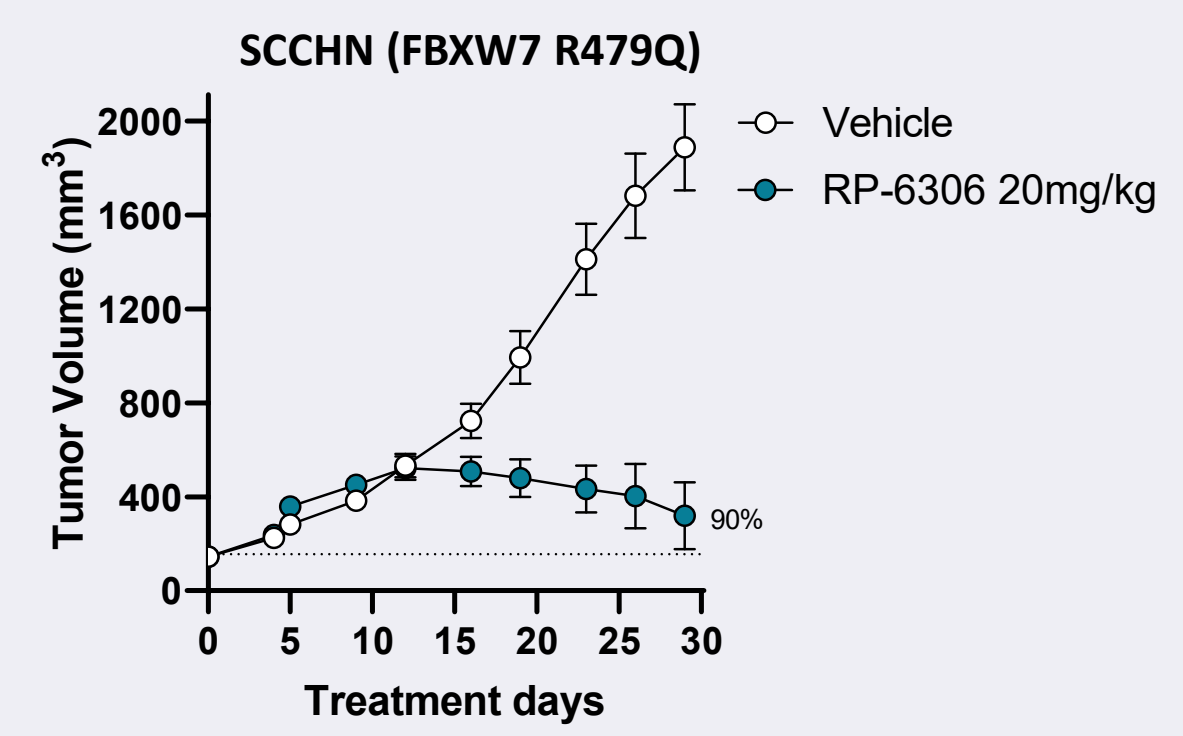
- **E3 ubiquitin ligase that targets proteins, such as CCNE, for proteasomal degradation**
- **Frequently mutated in tumors**
- **Inactivating mutations can increase CCNE levels**

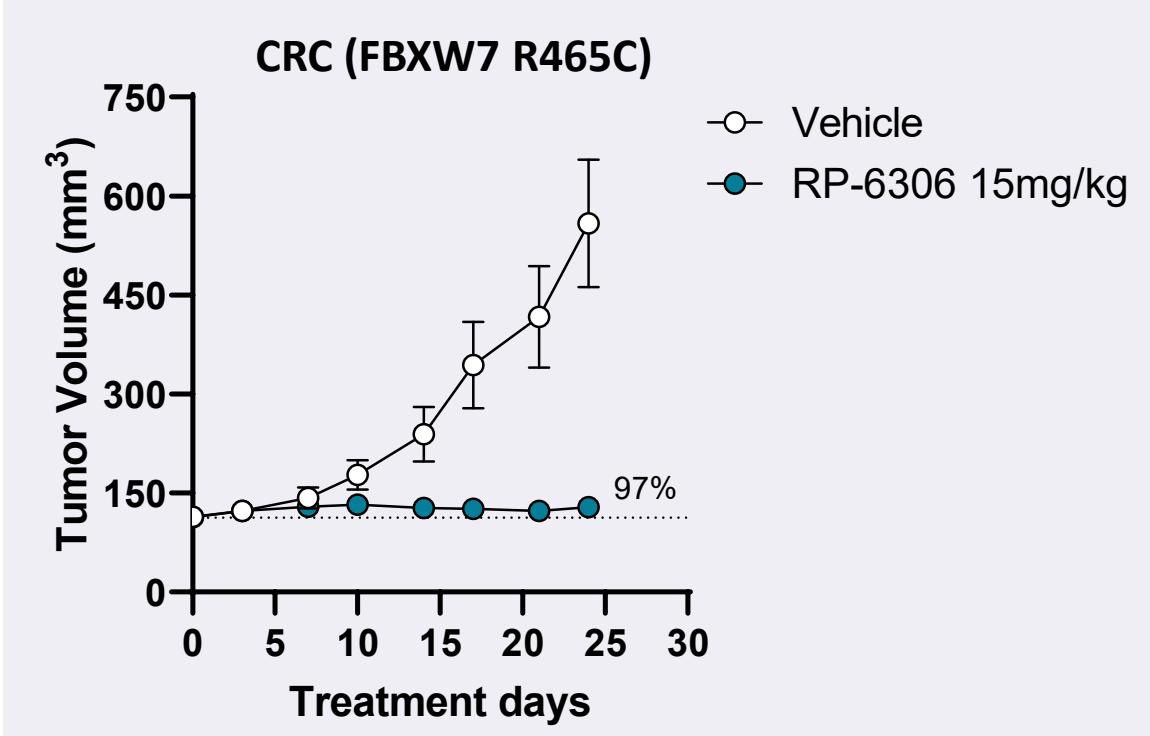




REPARE THERAPEUTICS

RP-6306 inhibits growth of FBXW7 mutant PDX models



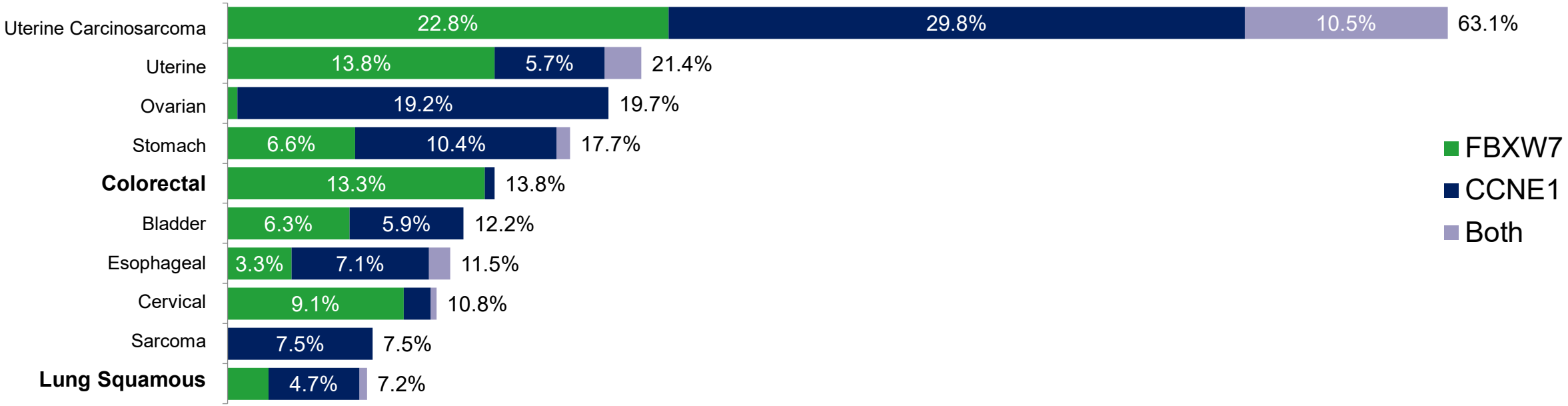


- **RP-6306 is active across tumor models with clinically relevant hotspot mutations**
- **Pre-clinical data supports expanding patient populations for RP-6306**

REPARE THERAPEUTICS

Potential addressable patient populations with RP-6306

Top 10 tumor types with highest prevalence of CCNE1 amplification and FBXW7 mutations deficiency



- **CCNE1 amplification or FBXW7 loss occurs in multiple cancers with significant unmet medical need**
- **These lesions are largely mutually exclusive and represent distinct patient populations**

Source: TCGA

REPARE THERAPEUTICS

RP-6306 clinical program profile and objectives

Targeting tumors with STEP^2 genomic alterations, including CCNE1 amplification, FBXW7 loss, PPP2R1A

Trial summary & development objectives:

Eligibility:
Any solid tumor with STEP^2 gene alterations per local NGS or FISH with subsequent retrospective central confirmation

Early Program Objectives:
1. Safety, tolerability, dose and schedule Phase 1
2. Efficacy in tumors with STEP2 gene alterations: several Proof of Concept (POC) studies
3. Multiple RP-6306 based combination POC trials

Global program: North America and Europe

Designed to deliver "go" decisions for broader development

Enrollment started Q2 2021

Initial monotherapy data H1 2023

RP-6306 profile/plan

- Orally available ATP-competitive inhibitor
- Maximized potency and specificity
- Genomically defined, tumor-specific and tumor agnostic indications
- Early combination testing

REPARE THERAPEUTICS

RP-6306 initial global clinical trial program

Phase 1 — April 2021 Start

Dose escalation → Dose & schedule

Monotherapy: RP-6306

Combinations: RP-6306 +

- MAGNETIC: Gemcitabine – Dec 21
- MINOTAUR: FOLFIRI – Aug 22
- MYTHIC: Camonsertib – May 22
- IST: Carboplatin – expected H1 2023

Key inclusion criteria

- Recurrent solid tumors
- CCNE1 amplification, FBXW7 loss and/or PPP2R1a

Initial data expected: H1'23 Monotherapy Q4'23 Combination

Determine RP2D dose / schedule

Progress to POC trials in:

- Selected tumors with amplified CCNE1
- Selected tumors with FBXW7 Loss
- Tumors with high rate of STEP^2 genes
- STEP^2 genes altered tumors: basket trial

Phase 2 Basket IST — 2023 Start

Combinations: RP-6306 + standard agents

- + Gemcitabine
- + FOLFIRI Protocol
- + Trastuzumab (Standard Q3 Weekly)

→ Response rate, safety, recommended dose

Sub-study: Combo RP-6306 with Gemcitabine in patients with CD4/6i-resistant ER+/HER2- metastatic breast cancer

Key inclusion criteria

- Advanced/metastatic/recurrent or unresectable cancer
- Histologically confirmed cancer + specified biomarkers

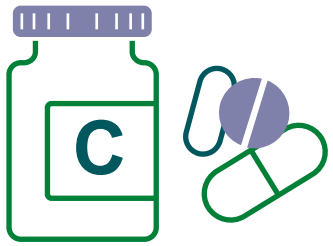
Est. Primary Completion: Dec 2024

Note: Phase 2 study is an investigator-sponsored basket trial planned with the Canadian Cancer Trials Group (ClinicalTrials.gov Identifier: NCT05605509).

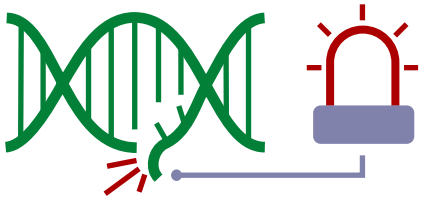
REPARE THERAPEUTICS

Camonsertib (RP-3500 / RG6526) ATR inhibitor

Overview of camonsertib: a potential best-in-class ATR inhibitor



Oral ATR inhibitor and Repare's first clinical therapeutic candidate (now partnered with Roche)



ATR is a critical DNA Damage Response ("DDR") protein with a central role in regulation of replication stress

Began monotherapy trial in July 2020; progressed three combination trials with compelling rationale

AACR
American Association for Cancer Research®

Clinical validation of ATR/ATM SL relationship disclosed by Repare at AACR-NCI-EORTC (Oct 2021) and AACR (Apr 2022)

Differentiation driven by:

- Potential best-in-class profile (safety and efficacy)
- Enhanced chemical properties (potency and selectivity)
- Proprietary patient selection insights to expand addressable patient populations

REPARE THERAPEUTICS

Overview of camonsertib clinical trial program

Trial results to date support expanded clinical development now partnered with Roche

TRESR Module 1 | Jul 2020 Start

Monotherapy: Camonsertib

dose escalation → dose and schedule refinement

Enrollment Complete Oct 2021

- N=120 enrolled
- RP2D and schedule identified

TRESR Module 2 | Feb 2022 Start

Expansion phase (monotherapy)

Signal seeking POC 3 arms

- **ATM loss of function**
  - Selected ATM LoF patients
- **STEP² gene alteration(s)**
  - Focused tumor population enriched for two STEP² genes
- **Other STEP² gene alterations**
  - Focused on Step² genes not-or-under-represented in Module 1

TRESR Module 3 | May 2021 Start | Data H1'23

Combination: Camonsertib + Talazoparib

dose escalation; safety/activity confirmation

Safety & preliminary efficacy of camonsertib + PARPi
Completed

ATTACC | Aug 2021 Start | Data H1'23

Combination: Camonsertib + Olaparib | + Niraparib

dose escalation; safety/activity confirmation

Safety & preliminary efficacy of camonsertib + PARPi
Ongoing

TRESR Module 4 | Dec 2021 Start | Interim Data Summer/Fall 23

Combination: Camonsertib + Gemcitabine

dose escalation; safety/activity confirmation

Safety & preliminary efficacy of camonsertib + gemcitabine
Ongoing

REPARE THERAPEUTICS

Camonsertib: potential best-in-class ATR inhibitor

Ph1/2 monotherapy trial demonstrated proof of concept in ovarian cancer

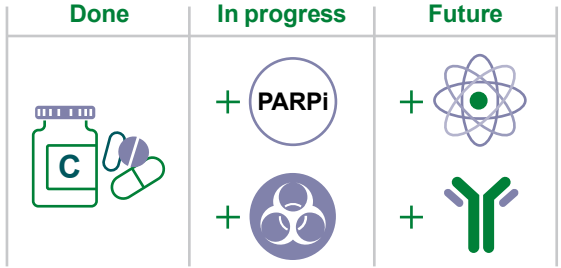
25% Overall response (5/20*): 1 CR, 3 PRs by RECIST, 1 CA125 Response

35w Median PFS

75% Clinical benefit rate (CBR)

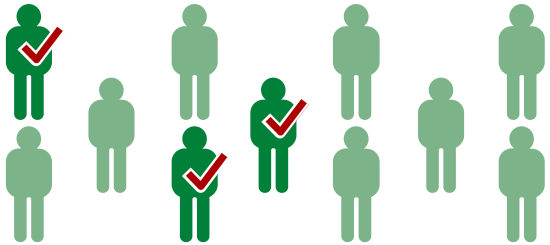
90% (18/20) of patients had prior PARPi

85% (17/20) of patients were platinum refractory/resistant*



Compelling rationale for ATRi combination therapy with PARPi, radiotherapy and PD-1/L1

Potential for best-in-class safety, potency and selectivity



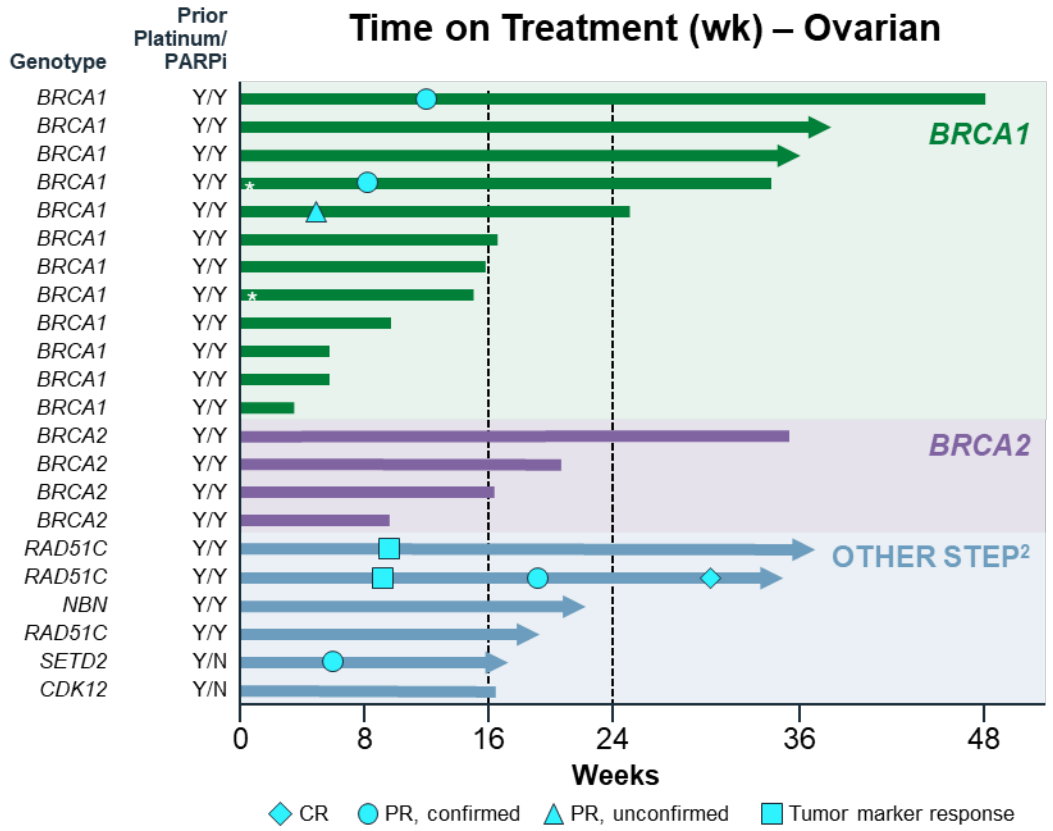
Proprietary patient selection insights to expand addressable patient populations

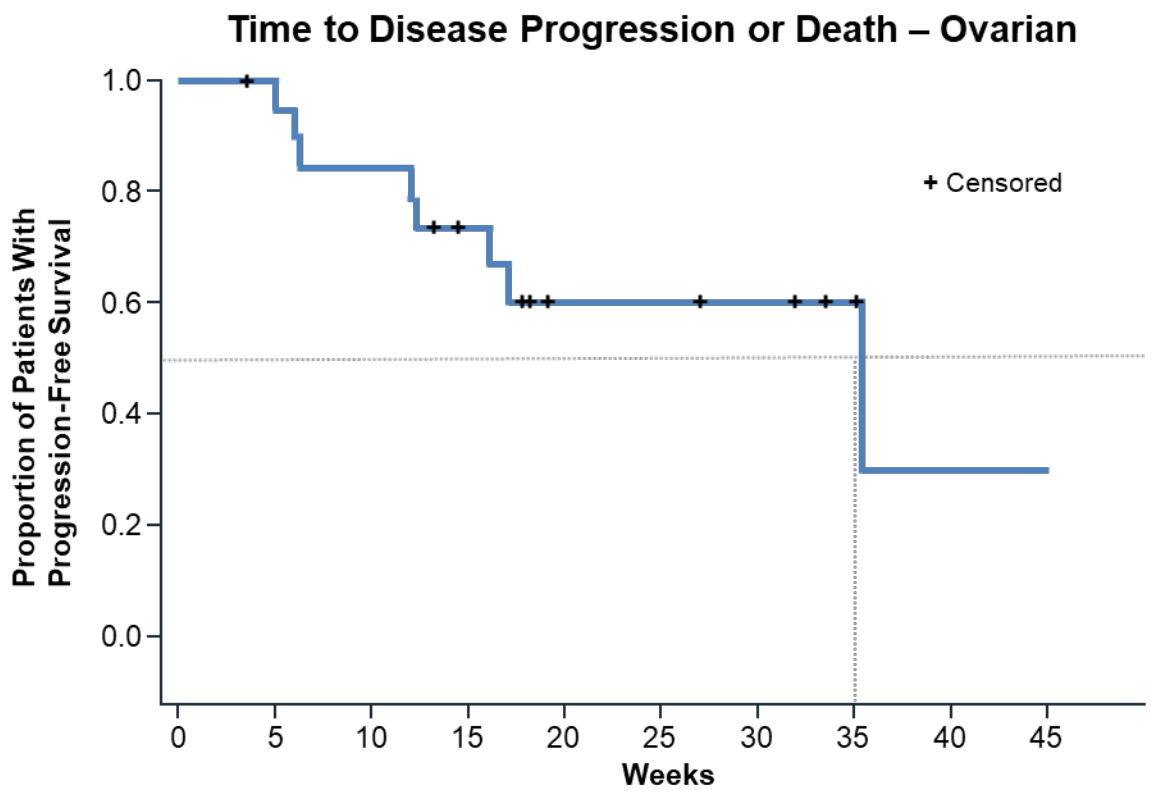
*Platinum refractory/resistant: progression on platinum or a platinum-free interval of <6 mo. CBR: OR or ≥16w on therapy without progression

REPARE THERAPEUTICS

Clinically relevant benefit in advanced ovarian cancer

Ovarian cancer patients were heavily pretreated with platinum and PARPi therapies





*2 additional pts are included in the swim plot that started Tx on PARPi combination for ≤3w and switched to monoTx; duration of Tx calculated from start of monoTx.
**Platinum refractory/resistant: progression on platinum or a platinum-free interval of <6 mo. CBR: OR or ≥16w on therapy without progression

REPARE THERAPEUTICS

Clinically relevant benefit in patients with *BRCA1/2* mutated tumors

14%

Overall response in BRCA1/2 (RECIST, 5/37)

Responders included patients with ovarian (2), breast, head and neck squamous cell carcinoma, and melanoma (1 each)

43%

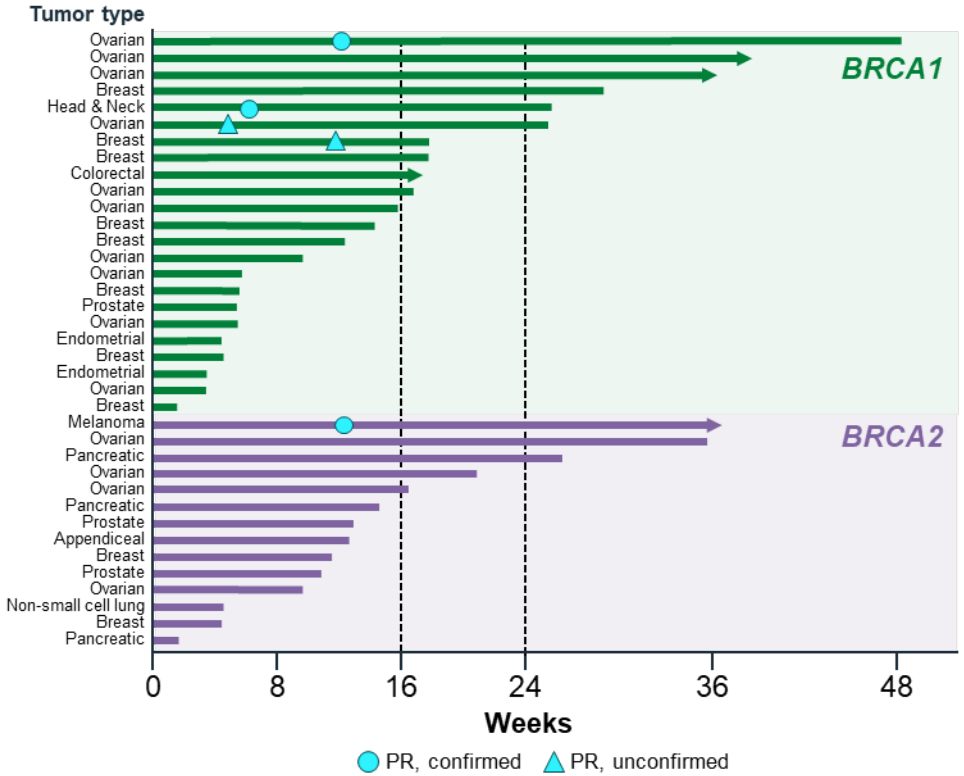
CBR for BRCA1/2 tumors

48%

CBR for post-PARPi BRCA1/2 tumors

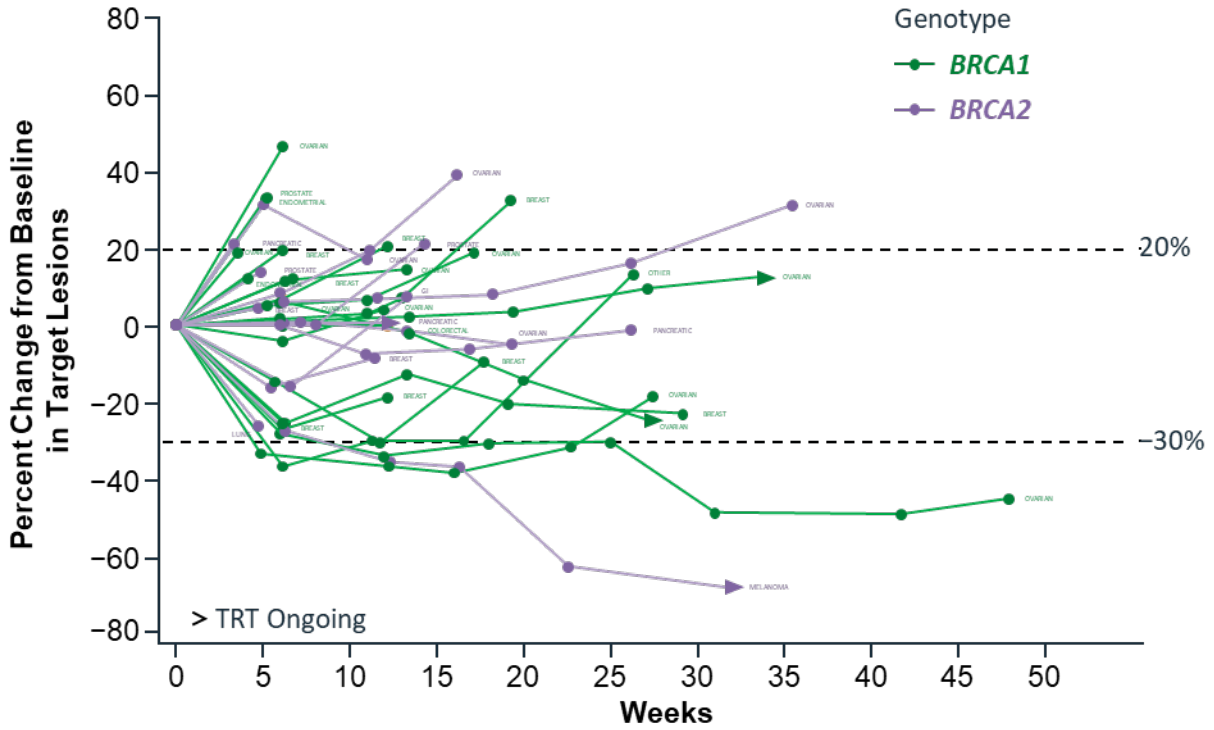
Time on Treatment (wk) – *BRCA1/BRCA2*

Module 1 subjects with >100mg/day dose levels



Percent change from baseline in target lesions (*BRCA1/BRCA2*)

Module 1 subjects with >100mg/day dose levels



CBR (OR or ≥16w on therapy without progression) was 48% for BRCA1 population, and 36% for BRCA2

REPARE THERAPEUTICS

Durable clinical benefit in patients with *ATM LOF* tumors

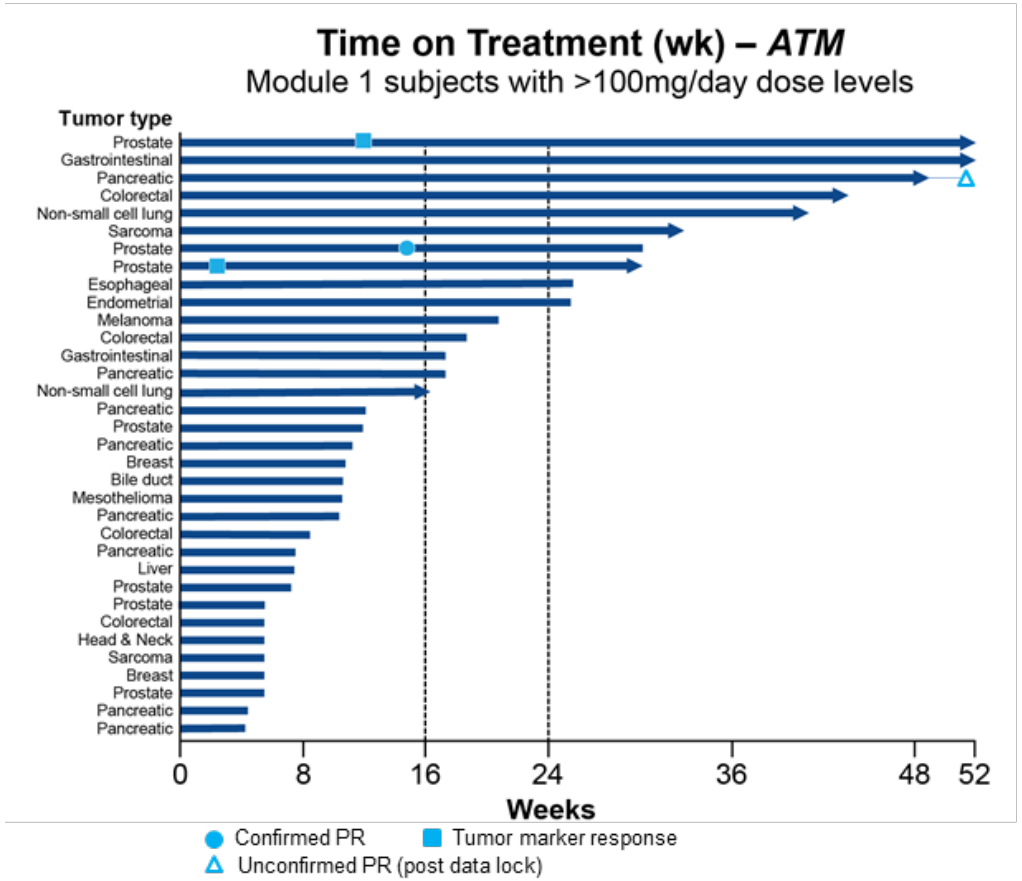
12%
Overall response (4/34)

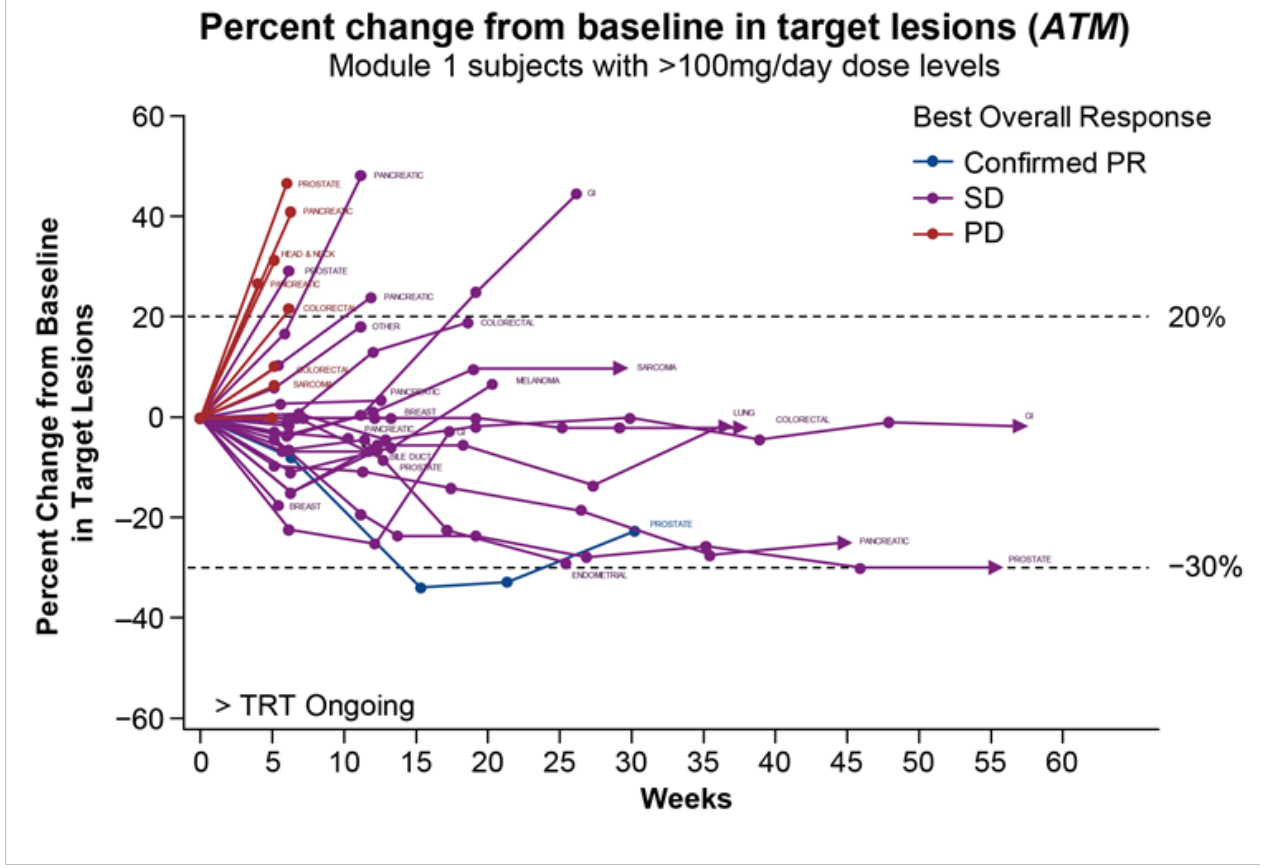
3 responders: prostate cancer (1 RECIST, 2 PSA), and 1 pancreatic cancer (RECIST)

29%
Received camonsertib for at least 6 mos (10/34)

44%
CBR for ATM population

17 wks
Median PFS





CBR (OR or ≥16w on therapy without progression)

REPARE THERAPEUTICS

Anti-tumor activity is largest in tumors with biallelic loss of function

Biallelic gene loss of function (LOF) is an emerging biomarker for synthetic lethal therapies

(Not reported by routine clinical NGS assays)

47% ***vs.*** **15%**

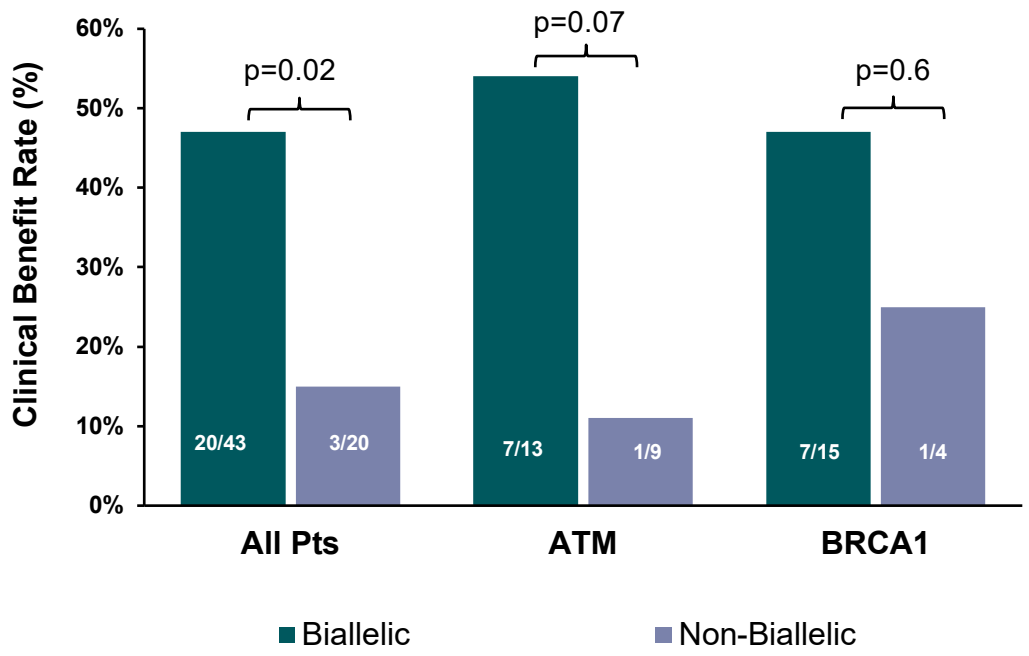
CBR significantly higher in biallelic tumors (p=0.02)

Longer PFS for biallelic (17 weeks) vs non-biallelic (11 weeks) for all subjects (not shown)

Central NGS assay, SNiPDx, (*AACR 2022 poster #2801*) determines biallelic LOF, germline status and CHIP alterations in TRESR

Further analysis in additional patients ongoing; Confirmation in prospective studies required

Clinical benefit rate (%) in biallelic vs. non-biallelic tumors



Nature. 604 (7907), pp. 749-756 (Apr 2022). https://doi.org/10.1038/s41586-022-04638-9

REPARE THERAPEUTICS

Treatment-related adverse events (TRAE)

Expected, manageable anemia; potentially best in class safety profile at well studied doses

	5d on/2d off (N=25)			3 d on/4 d off (N=95)		
Preferred Term	**Grade 3 N (%)**	**Grade 4 N (%)**	**All Grade N (%)**	Grade 3 N (%)	Grade 4 N (%)	All Grade N (%)
Any TRAE	14 (56.0)	1 (4.0)	22 (88.0)	28 (29.5)	4 (4.2)	81 (85.3)
Anemia	13 (52.0)	0	20 (80.0)	**23 (24.2)**	**0**	**58 (61.1)**
Fatigue	1 (4.0)	0	7 (28.0)	2 (2.1)	0	26 (27.4)
Neutrophil count decreased	3 (12.0)	0	6 (24.0)	10 (10.5)	3 (3.2)*	25 (26.3)
Nausea	0	0	3 (12.0)	0	0	22 (23.2)
Platelet count decreased	2 (8.0)	1 (4.0)	7 (28.0)	5 (5.3)	1 (1.1)**	17 (17.9)
Decreased appetite	0	0	4 (16.0)	0	0	14 (14.7)
Diarrhea	0	0	0	0	0	13 (13.7)
Vomiting	0	0	3 (12.0)	0	0	9 (9.5)
White blood cell count decreased	0	0	1 (4.0)	4 (4.2)	0	11 (11.6)
Dyspnea	0	0	5 (20.0)	0	0	6 (6.3)

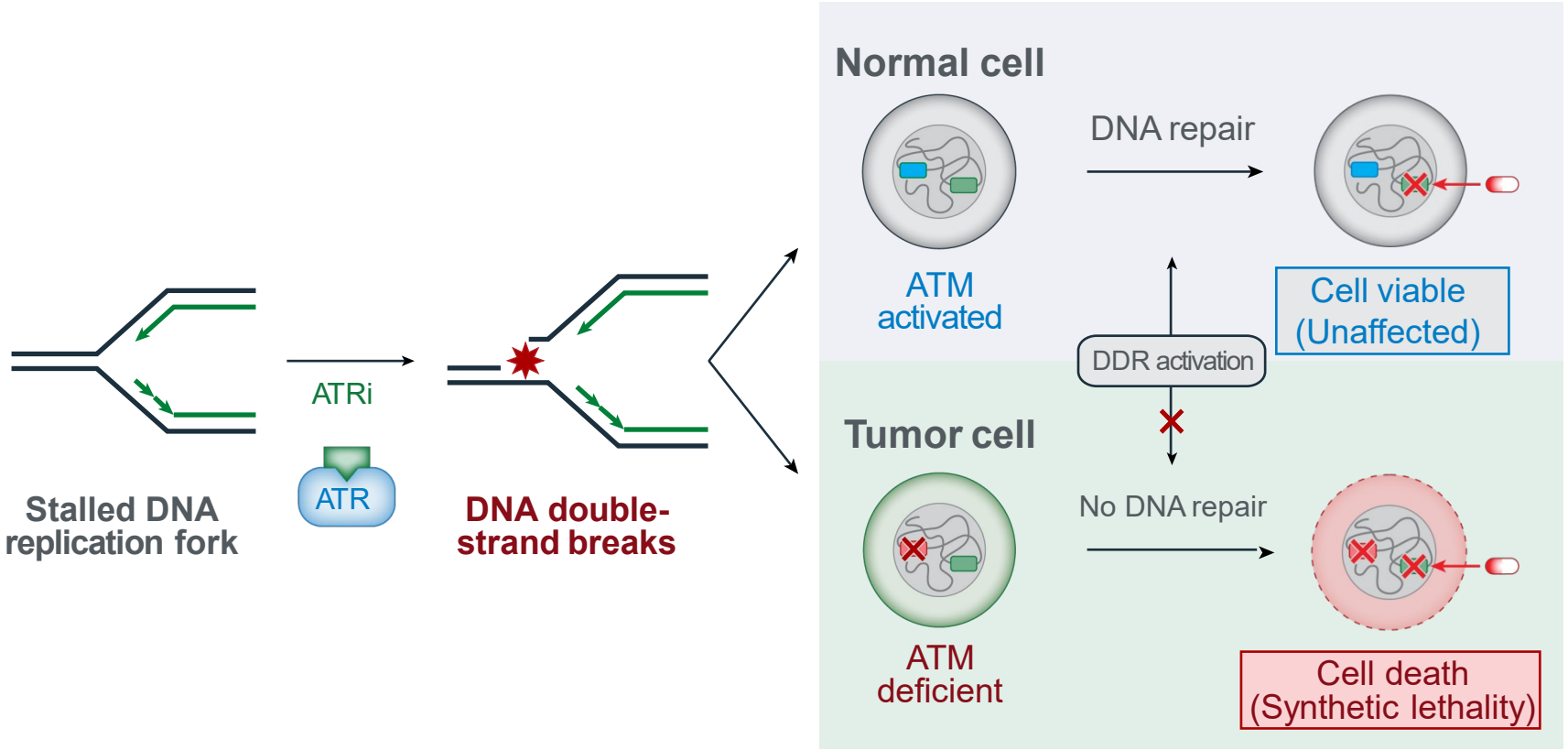
*Detailed safety analysis at 3/4 schedule at various dose levels reported at AACR-NCI-EORTC, December 2021 (Yap et al., oral presentation, #4950) and ESMO-TAT, March 2022 (Fontana et al, oral presentation #202). No incidences of Gr4 anemia reported. * 2/3 with documented "outlier" high exposure. ** at 200mg non-tolerated dose level. No Grade 5 TRAE reported.*

REPARE THERAPEUTICS

Mechanism of ATM-ATR synthetic lethality

Inhibition of ATR

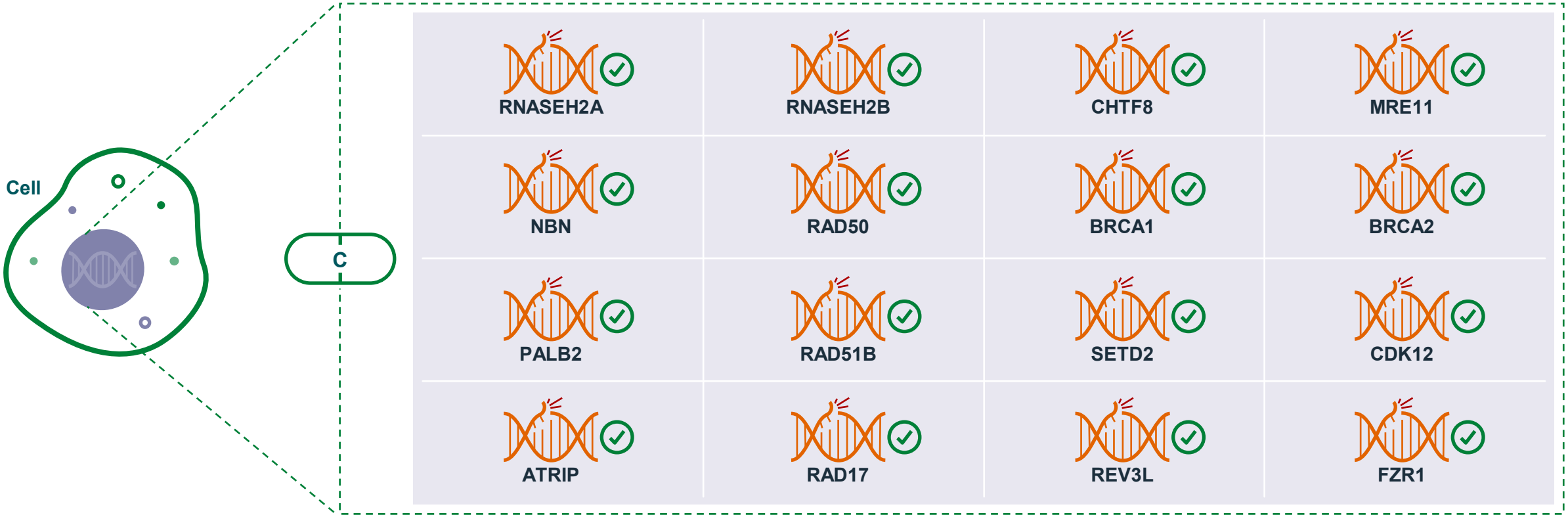
- Induces cell death in ATM-deficient cancer cells
- Compromises the stabilization of DNA replication forks
- Is associated with increases in DNA double-strand breaks



REPARE THERAPEUTICS

Repare discovered a network of alterations that are SL pairs with ATRi

We are evaluating 16 STEP^2-identified genomic alterations in addition to ATM deficiency, including several novel genes not previously reported as sensitive to ATRi

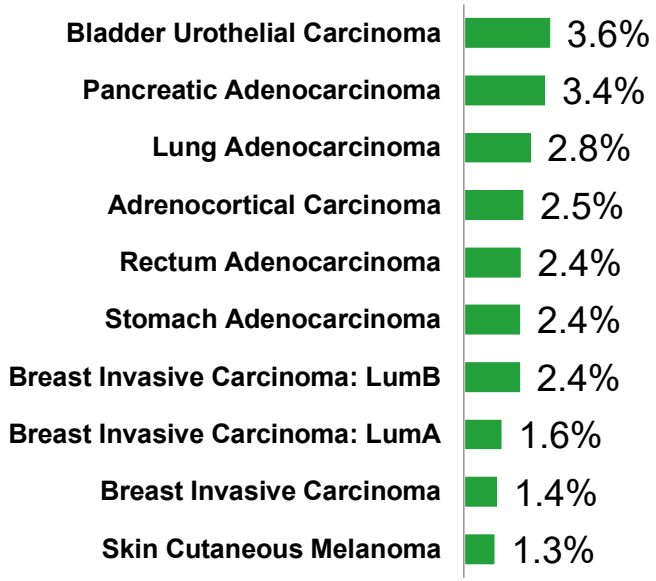


REPARE THERAPEUTICS

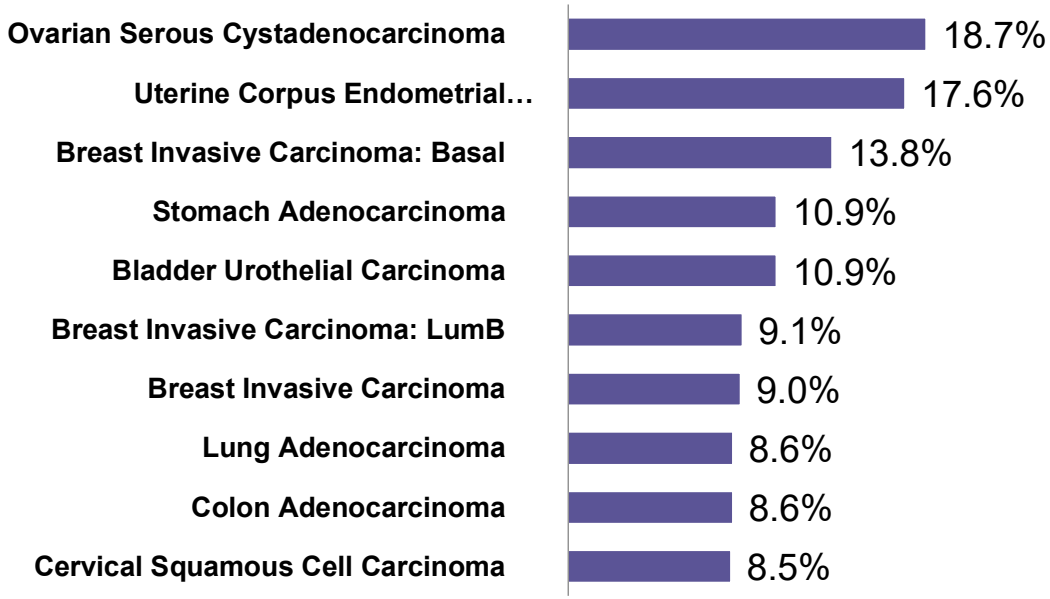
Camonsertib patient opportunity with STEP² selection tools

C → ATM

Top 10 tumor types* with highest prevalence of ATM deficiency



Top 10 tumor types* with highest prevalence of ATM deficiency or STEP² genomic alterations



Represents expanded, clinically relevant populations with unmet medical needs

Average prevalence of ~2% (ATM) to ~10% (STEP² genes) across multiple tumors

C → Other mutations

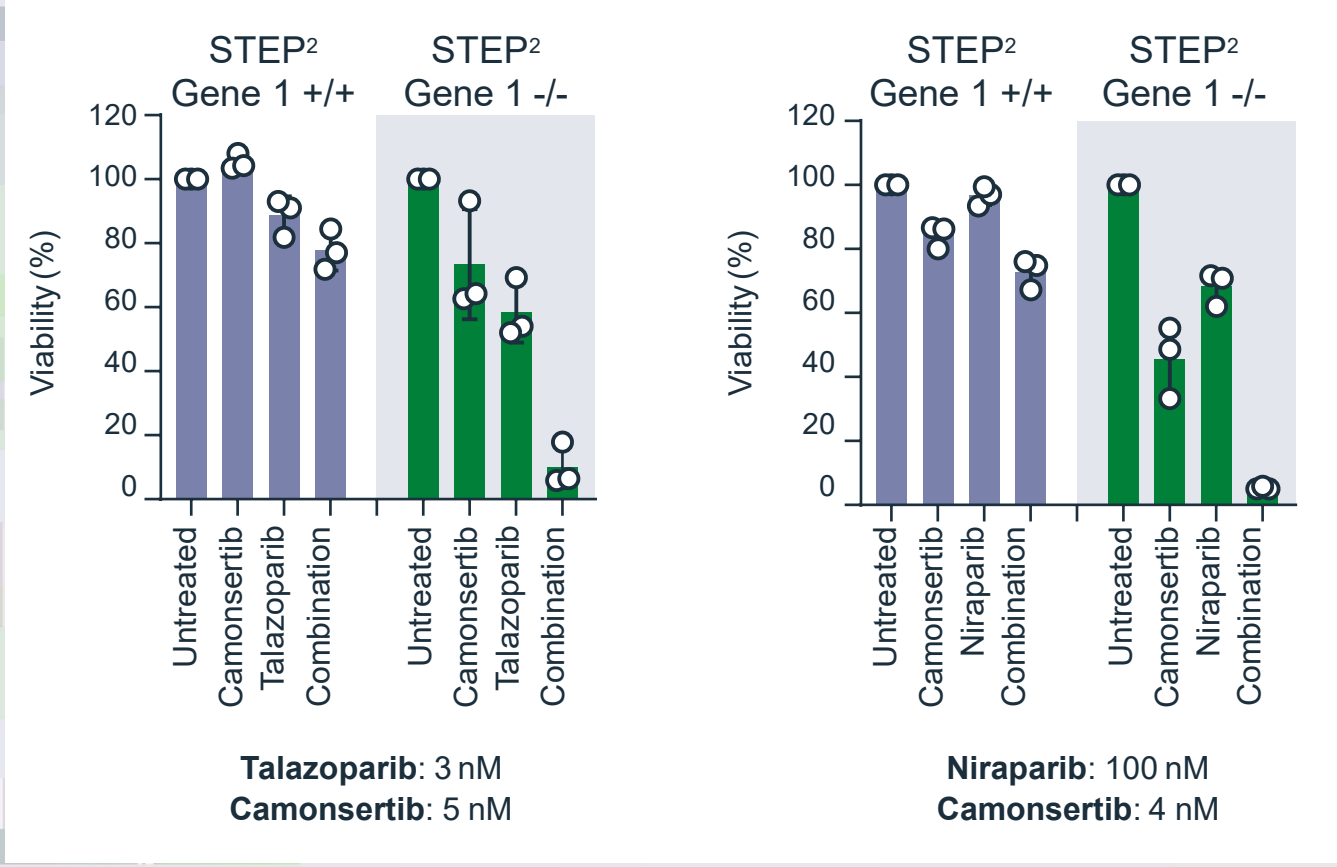
Beyond ATM, 16 of 19 additional, mutually exclusive genomic alterations identified as SL with camonsertib are eligible for recruitment into the ongoing trial

*Source: *TCGA; Not weighted for tumor prevalence*

REPARE THERAPEUTICS

STEP² approach identifies genes to predict combination response

Significant synergy demonstrated by combination of camonsertib and PARP inhibitors



+/+: Wild Type
-/-: Genomically Altered

- Identified tumors with STEP² genes sensitive to the combination of camonsertib and PARP inhibitors
- The activity observed at low doses of camonsertib and PARPi could lead to efficient anti-tumor activity and potentially address know PARPi toxicities
- Significant new approach to select patients for response to combinations

REPARE THERAPEUTICS

Camonsertib monotherapy data suggests potentially best-in-class ATRi

Potentially best-in-class safety profile confirmed with larger cohort and longer observation time

- Long-term tolerability further show; anemia non-cumulative, no new adverse safety findings
- Potency/selectivity/PK differentiation increasingly clear

Large trial size (N=120) allowed for comprehensive assessment of dose and schedule

- Multiple dose/schedules rigorously tested to maximize patient benefit and evaluate tumors/molecular alterations to convincingly see a path to further development (*AACR 2022*)

POC in ovarian cancer clearly demonstrated – engagement with regulator(s) in near-term

- 25% OR, 75% CBR and PFS 8+mo in PARPi and platinum pretreated patients with ovarian cancer
- Several long/deep ovarian cancer tumor responses (BRCA1, SETD2, RAD51c)

Early data supports further exploration of POC for ATM and STEP^2 alterations

- Current data suggests need for further efficacy exploration – meaningful CBR noted in early data
- Tools identified to potentially better select ATM LOF and improve clinical outcomes
- Additional validation of STEP^2 platform opportunities beyond ATM and BRCA1 LOF

REPARE THERAPEUTICS

Camonsertib collaboration with Roche announced June 2022

Long-term, global camonsertib collaboration with U.S. co-development, profit/cost share and co-promotion option

REPARE THERAPEUTICS

- Potential best-in-class ATRi
- Compelling clinical data across tumors & backgrounds
- Potential for multiple combinations
- Leader in synthetic lethality

+

Roche

- Unique expertise in precision oncology
- Global reach and footprint
- Track record of success
- Shared, ambitious vision for the asset

Camonsertib

REPARE THERAPEUTICS

Key terms of the collaboration with Roche

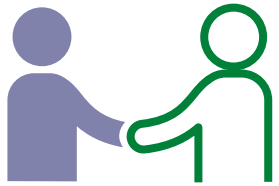
REPARE THERAPEUTICS + Roche

Upfront

$135M

Includes $125M upfront +
$10M additional payments

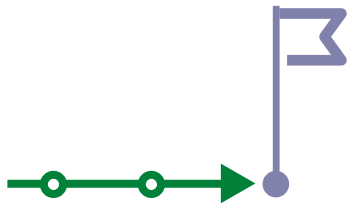
U.S. Development, Profit/Cost & Co-promotion option



Partnership

50/50 US co-development
& profit share & US co-promotion
milestone payments

Milestones



$55M

Near-term

$1.2B

Total

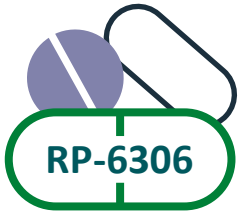
Royalties

**High single-digit
to high-teens**

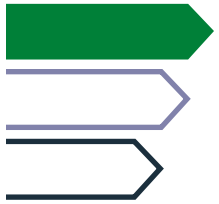
- **Collaboration adds resources and extends funding into 2026 assuming robust development plans**
- **Repare to complete ongoing TRESR and ATTACC clinical studies**

REPARE THERAPEUTICS

Leading precision oncology company focused on synthetic lethality

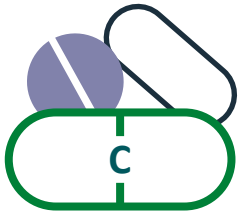


RP-6306, a first-in-class, oral PKMYT1 inhibitor, drives genomic instability in CCNE1-amplified tumors with Ph 1 monotherapy and multiple combination trials ongoing

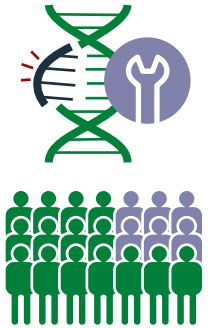


Robust pipeline of SL-based therapeutic opportunities, including Polθ and a pipeline of advanced preclinical opportunities

Balance Sheet of $344M funds Repare through multiple value-creating milestones into 2026



Camonsertib (RP-3500 / RG6526), a potential best-in-class ATR inhibitor with durable responses and clinical benefit in Ph 1/2 and strategic validation through Roche partnership



Proprietary **genome-wide CRISPR-enabled SNIPRx platform,** focused on **genomic instability** and **DNA damage repair**, enabling novel target identification and differentiated patient selection insights

REPARE THERAPEUTICS

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RepareRx.com