Precision oncology

Corporate Presentation
January 2022

REPARE THERAPEUTICS

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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 and the evolving situation regarding the Omicron variant of COVID-19 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 Quarterly Report on Form 10-Q filed with the SEC on November 10, 2021, 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.

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REPARE THERAPEUTICS

Leading clinical-stage precision oncology company focused on synthetic lethality

RP-3500, a potential best-in-class ATR inhibitor and **RP-6306, a first-in-class PKMYT1 inhibitor** both currently in clinical Phi 1 or Ph1/2 monotherapy and combination trials with multiple data readouts expected in 2022

Robust pipeline of SL-based therapeutics with our Polθ inhibitor program expected to initiate IND-enabling studies in H1 22 and a pipeline of pre-clinical opportunities we are pursuing

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

Unaudited cash, restricted cash and marketable securities of $341.7 million as of December 31, 2021, funding Repare through 2023 and multiple clinical catalysts

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Experienced team proven in drug discovery and development

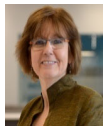
Management team

Lloyd M. Segal
President & Chief executive officer

McKinsey & Company · CAPRION · PCP

Michael Zinda, PhD
Chief scientific officer

AstraZeneca · Lilly



Maria Koehler, MD, PhD
Chief medical officer

gsk · Pfizer · AstraZeneca

Laurence Akiyoshi, Ed.D.
EVP, Organizational & Leadership Development

CROWDSTRIKE · CISCO

Steve Forte, CPA
Chief financial officer

clementia · APTALIS

Kim A. Seth, PhD
Head, business & corporate development

Pfizer · Goldman Sachs

Cameron Black, Ph.D.
Head, discovery

MERCK · aneqpharma

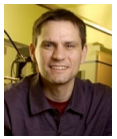
Philip Herman
EVP, Commercial & New Product Development

-mAbs Therapeutics, Inc. · santhera THEIR FUTURE - OUR FOCUS · Pfizer · Dyax

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
- NYU Langone Medical Center & associate professor, Skirball Institute



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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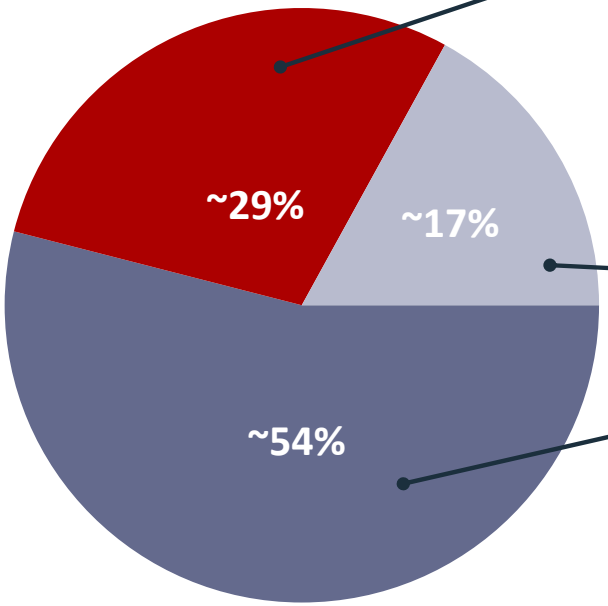
Focused on precision oncology for untapped cancer lesions

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…"

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SNIPRx platform

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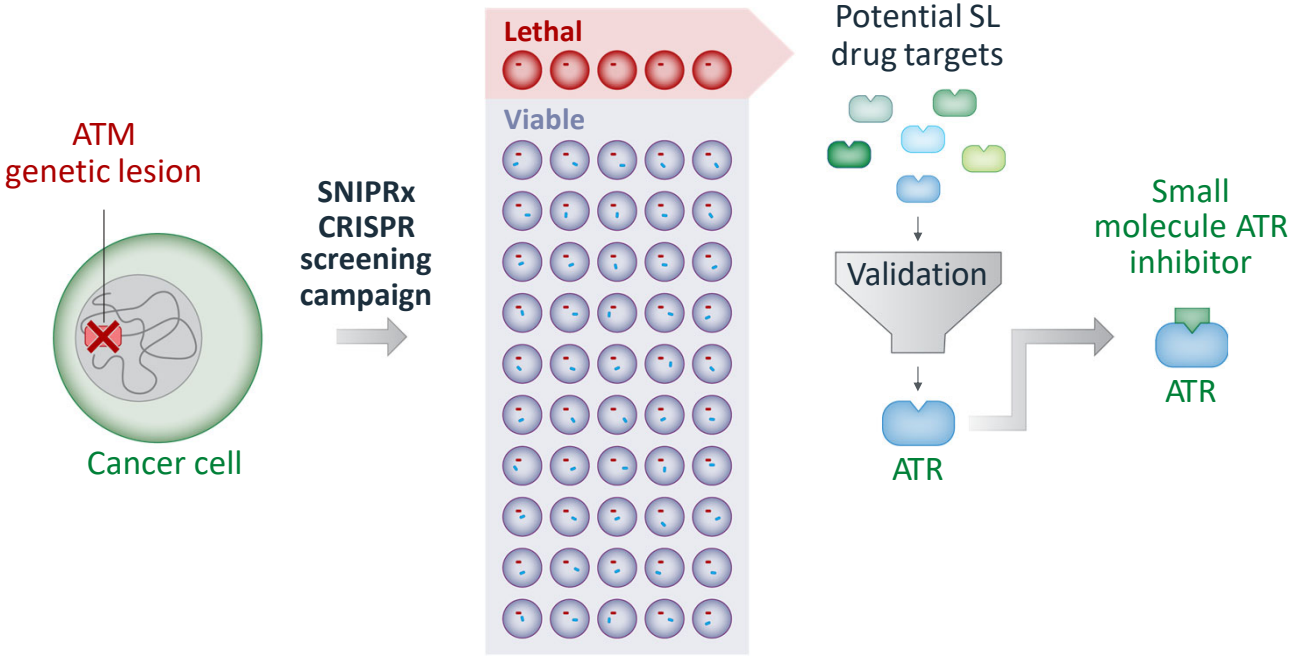
SNIPRx for synthetic lethal ("SL") drug discovery

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-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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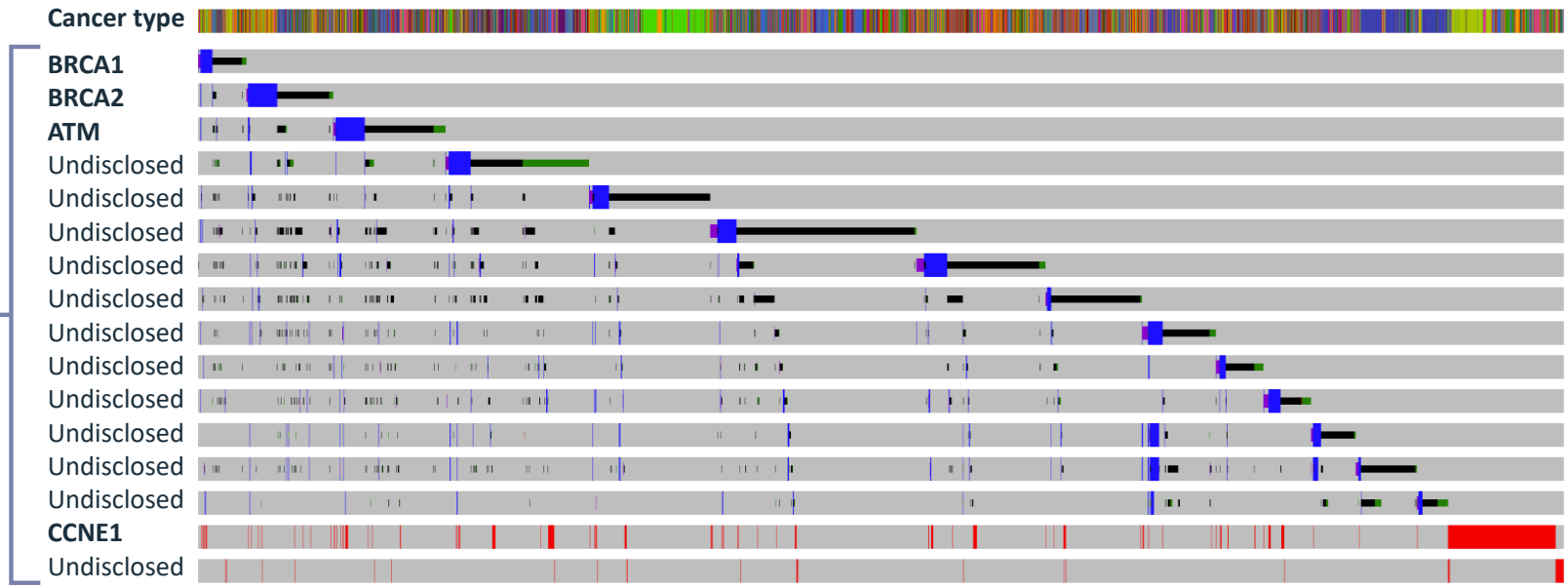
SNIPRx campaigns mine targeted genomic instability lesions

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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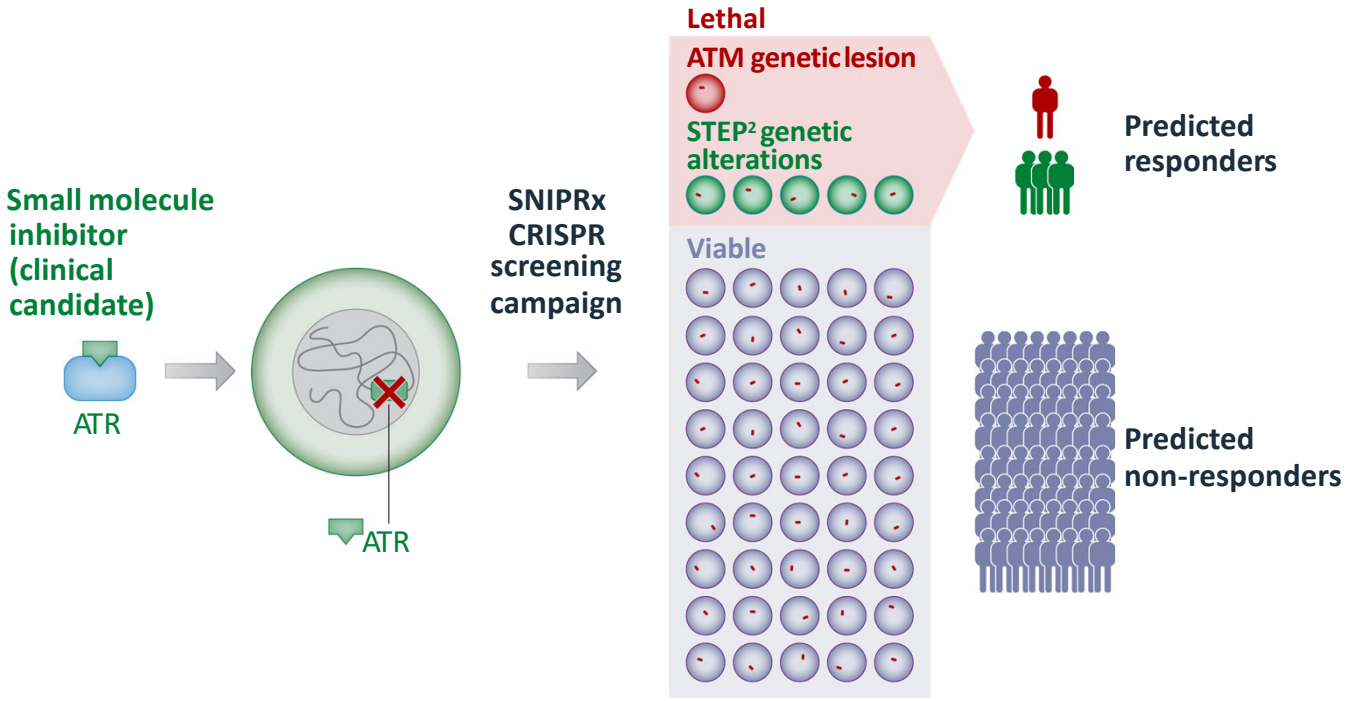
STEP^2: Repare's patient selection advantage enabled by SNIPRx discovery

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 clinical and pre-clinical pipeline

Robust pipeline of SL-based precision oncology therapeutics

SL Pair

		Tumor lesion	Drug target	Discovery	IND-Enabling	Phase 1/2	Registration-directed	Anticipated milestones	Rights
Clinical	ATR inhibitor RP-3500	ATM + 16 STEP[2] lesions	ATR	TRESR: Monotherapy TRESR: PARP (Talazoparib) Combo ATTACC: PARP (Olaparib/Talazoparib) Combo TRESR: Gemcitabine Combo				▪ Q1 22 start TRESR Phase 2 monotherapy and Phase 1 pediatric trials ▪ Q2 22 comprehensive TRESR monotherapy data ▪ H2 22 PARP combination initial data (targeting Q3)	REPARE THERAPEUTICS
	PKMYT1 inhibitor RP-6306	CCNE1, FBXW7 + others	PKMYT1	MYTHIC: Monotherapy MAGNETIC: Gemcitabine Combo				H2 22 early Phase 1 readout	REPARE THERAPEUTICS
Preclinical	Polθ inhibitor	BRCA1/2 + others	Polθ					IND-enabling studies in H1 22	REPARE THERAPEUTICS ono
Discovery	SNIPRx® platform	8 additional SL targets							REPARE THERAPEUTICS
		Discovery and validation of new SL precision oncology targets							REPARE THERAPEUTICS Bristol Myers Squibb

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ATR inhibitor RP-3500

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RP-3500: Potential best-in-class ATR inhibitor

Oral ATR inhibitor to treat cancers with DNA Damage Response ("DDR") defects and high replication stress

ATR is a critical DDR protein with a central role in regulation of replication stress

Clinical validation of ATR/ATM SL relationship demonstrated at ASCO 2019

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

RP-3500 differentiation driven by:

- **Enhanced chemical properties (potency and selectivity)**
- **Proprietary patient selection insights to expand addressable patient populations**

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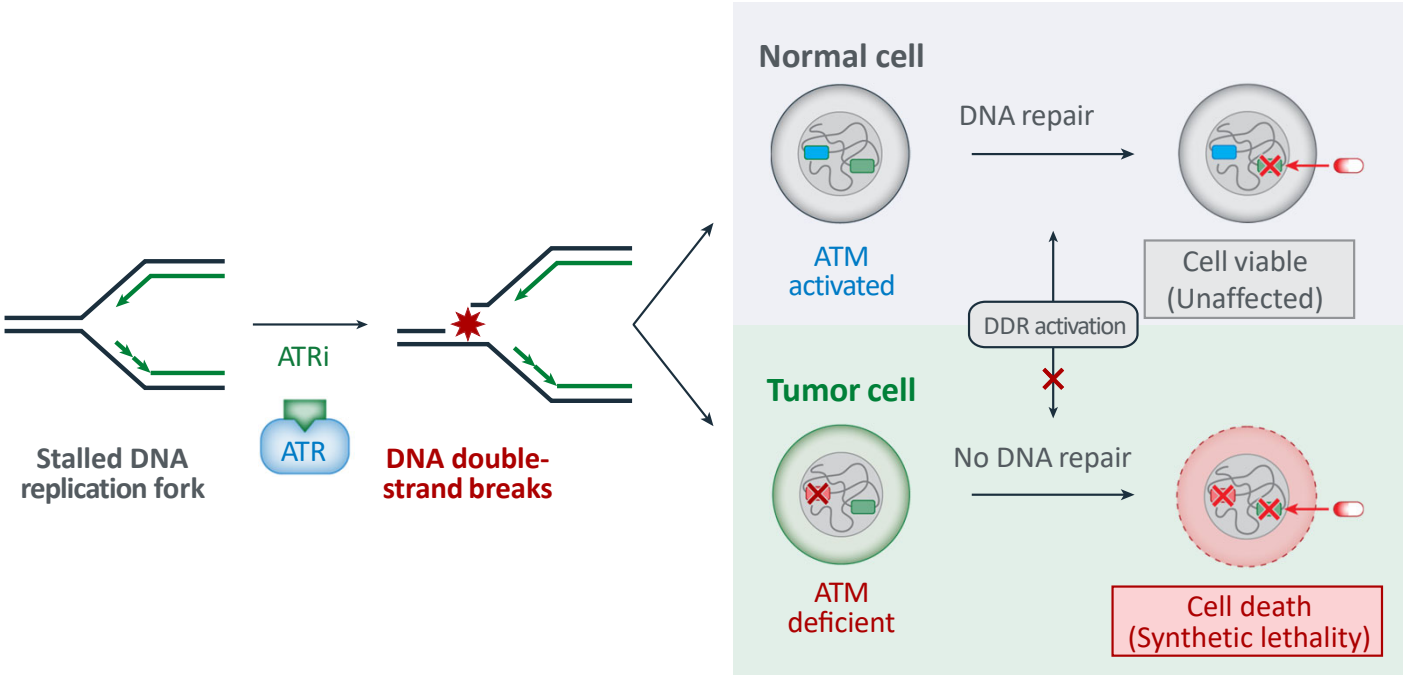
Mechanism of ATM-ATR synthetic lethality



- **Inhibition of ATR:**
  - **Compromises the stabilization of DNA replication forks**
  - **Is associated with increases in DNA double-strand breaks**
- **SL screens have identified that ATR is SL with ATM**

ATR inhibitors induce cell death in ATM-deficient cancer cells

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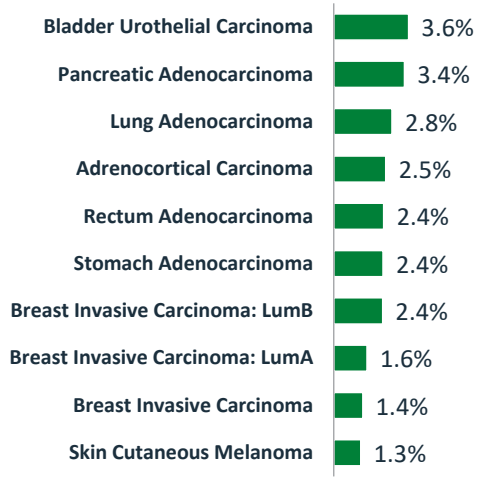
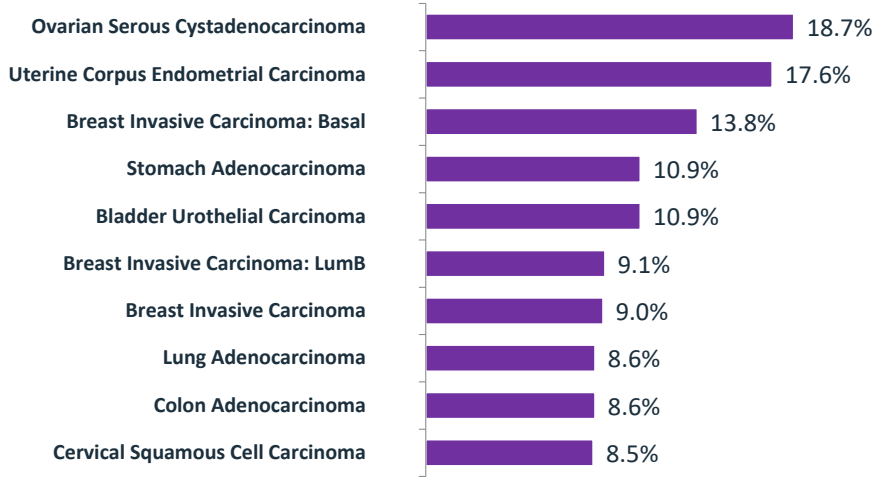
Expanding RP-3500 patient opportunity with STEP^2 selection tools*

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



- Beyond ATM, **16 of 19 additional, mutually exclusive genomic alterations identified as SL with RP-3500 are eligible for recruitment into the ongoing trial**
- Represents **expanded, clinically relevant populations with unmet medical needs**
- **Average prevalence of ~2% (ATM) to ~10% (STEP^2 genes)** across multiple tumors

* TCGA; Not weighted for tumor prevalence

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First-in-human Phase 1/2 TRESR trial design

Phase 1/2 TRESR (Treatment Enabled by SNIPRx) study

NCT04497116 (accruing)

Inclusion Criteria

- Patients ≥18yo with solid tumors resistant, refractory, and/or intolerant to standard therapy
- Tumors with *centrally reviewed** deleterious STEP[2] alterations
- ECOG PS 0 or 1
- Hgb ≥9.5g/dL, Platelets ≥140K/uL, ANC ≥1.7K/uL

Module 1: single agent RP-3500

Primary endpoints:

- Safety and tolerability
- Recommended Phase 2 dose (RP2D), schedule

Other endpoints

- Pharmacokinetics
- Pharmacodynamics in paired tumor biopsies
- Preliminary antitumor activity
- Kinetics of circulating tumor DNA (ctDNA)

Presented **early data** from this ongoing study at the October 2021 AACR-NCI-EORTC meeting:

- TRESR initiated July 2020
- Data cut-off date: August 15, 2021
- 101 patients included in this early dataset

*Central review performed by Precision Oncology Decision Support (PODS) Group at MDACC

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TRESR - Dose and schedule selection: patient characteristics*

All patients	N = 101
Male	42
Female	59
Median age, years (range)	63 (33-77)
≥65 yrs	46
ECOG status	
0	48
1	53
Lines of prior therapy	
1-3	51
4 or more	45
Pending	5
Prior Platinum	62
Prior PARP inhibitor	28
Prior PD-1/L1 inhibitor	20

Tumor types	
Ovarian	19
Prostate	18
Breast	13
Pancreas	8
Sarcoma	8
Other**	35
Most common genotypes	
ATM	37
BRCA1	21
BRCA2	13
CDK12	7
Other STEP^2**	23

* As of August 15th, 2021

**other tumor types:
- CRC
- Bile Duct
- GI
- Endometrial
- Lung
- Ampullary
- Appendix
- HNSCC
- Melanoma
- Mesothelioma
- Skin

***STEP^2 genotypes:
- CHEK2
- NBN
- PALB2
- RAD51C/B
- RNASEH2
- SETD2

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Systematic tolerability assessment to establish recommended dose and schedule

Comprehensive assessment for RP-3500 MTD/RP2D

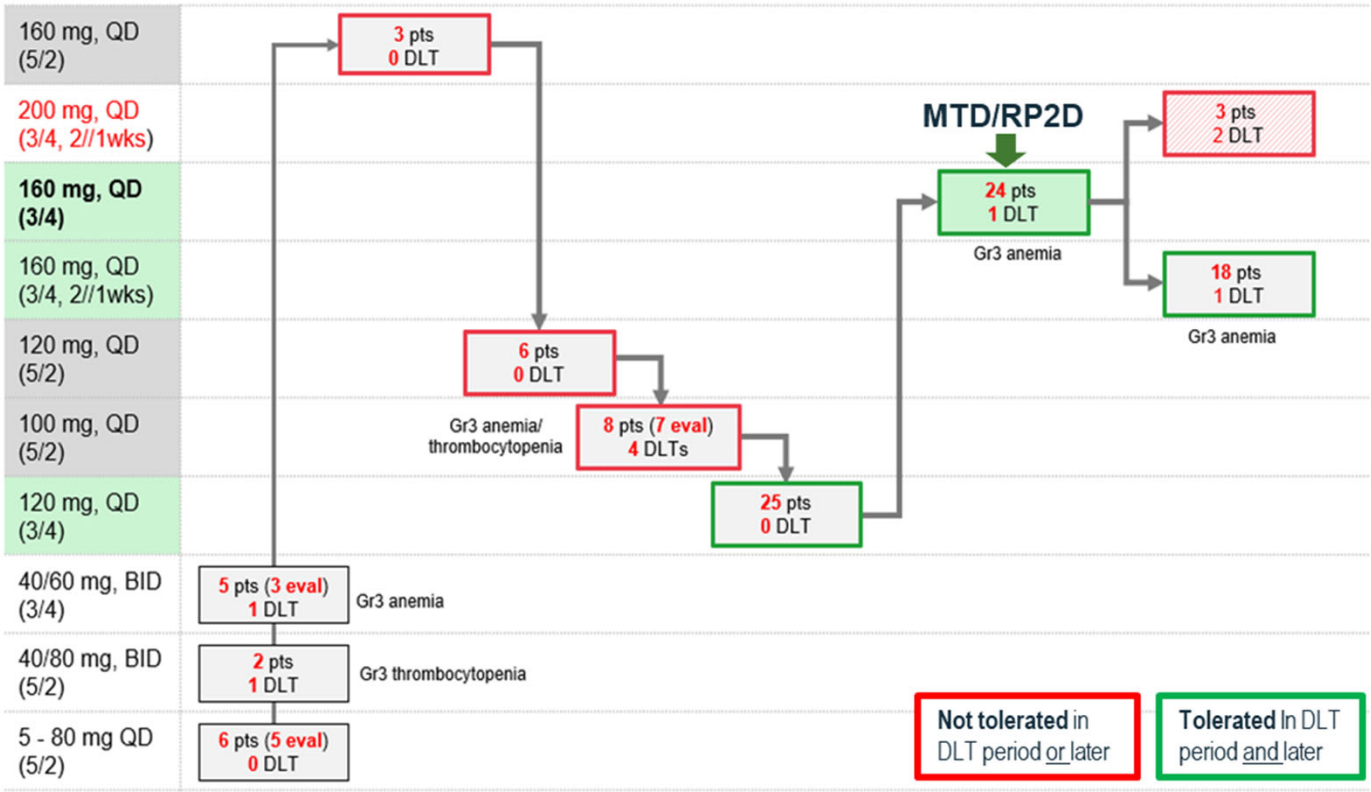
Single agent RP-3500 tested at multiple doses and schedules

- Adaptive BOIN design and sufficient cohort sizes to ensure confidence in MTD/RP2D decision
- Once daily (QD) and twice daily (BID)
- 5d on/2d off and 3d on/4d off; continuously and 2w on/1w off

DLTs: anemia, thrombocytopenia

MTD/RP2D of RP-3500:

160mg QD, 3d on/4d off



Treatment well tolerated at chosen schedule: RP-3500 emergent adverse events

All grades, occurring in ≥10% of patients*

	5/2 Schedule (N=25)			**3/4 Schedule (N=76)**			All Patients (N=101)		
Preferred term	All Grade n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grade n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grade n (%)	Grade 3 n (%)	Grade 4 n (%)
Any TEAE	25 (100)	15 (60)	2 (8)	58 (76.3)	**19 (25.0)**	**1 (1.3)**	83 (82.2)	34 (33.7)	3 (3.0)**
Anemia	**19 (76)**	**11 (44)**	**0**	**40 (52.2)**	**11 (14.5)**	**0**	**59 (58.4)**	**22 (21.8)**	**0**
Fatigue	9 (36)	1 (4)	0	19 (25.0)	2 (2.6)	0	28 (27.7)	**3 (3.0)**	0
Decreased appetite	6 (24)	0	0	17 (22.4)	0	0	23 (22.8)	0	0
Nausea	6 (24)	0	0	16 (21.1)	1 (1.3)	0	22 (21.8)	**1 (1.0)**	0
Neutrophil count decreased	5 (20)	2 (8)	0	14 (18.4)	4 (5.3)	0	19 (18.8)	6 (5.9)	0
Platelet count decreased	7 (28)	2 (8)	1 (4)	12 (15.8)	3 (3.9)	1 (1.3)	19 (18.8)	5 (5.0)	2 (2.0)**
Diarrhea	3 (12)	0	0	14 (18.4)	0	0	17 (16.8)	**0**	0
Abdominal pain	3 (12)	0	0	8 (10.5)	1 (1.3)	0	11 (10.9)	**1 (1.0)**	0

MTD/RP2D established at 160mg QD, 3d on/4d off

*As of August 15th, 2021

**DLT

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Schedule established: 3 days on/4 days off

Manageable impact of on-target anemia

- **Anemia most common cause of dose interruptions, modifications**
- **At preferred 3/4 schedule, dose interruptions, reductions and transfusions were infrequent**
- **No discontinuations related to RP-3500 emergent adverse events**

	5/2 Schedule ≥100 mg/day* (N=18)	**3/4 Schedule ≥100 mg/day* (N=75)**
# Cycles, mean (SD) [Range]	3.9 (2.62) [0, 10]	1.9 (1.72) [0, 8]
Subjects Exposed to RP-3500 n (%)		
≥1 cycle	17 (94.4%)	57 (76.0%)
≥2 cycles	14 (77.8%)	37 (48.7%)
Interruptions n (%)		
1	8 (44.0%)	16 (21.3%)
2	**2 (11.1%)**	**3 (4.0%)**
≥3	**5 (27.8%)**	**2 (2.7%)**
Dose Reductions, n (%)		
1	6 (33.3%)	10 (13.3%)
2	**3 (16.7%)**	**1 (1.3%)**
Transfusions, n (%)		
Cycle 1	4 (22.2%)	6 (8.0%)
Cycles 1-2	9 (50.0%)	9 (12.0%)
Cycles 1-3	**12 (66.7%)**	**10 (13.2%)**

*Data presented include only patients treated at therapeutic doses to allow more accurate representation of safety at the recommended dose range

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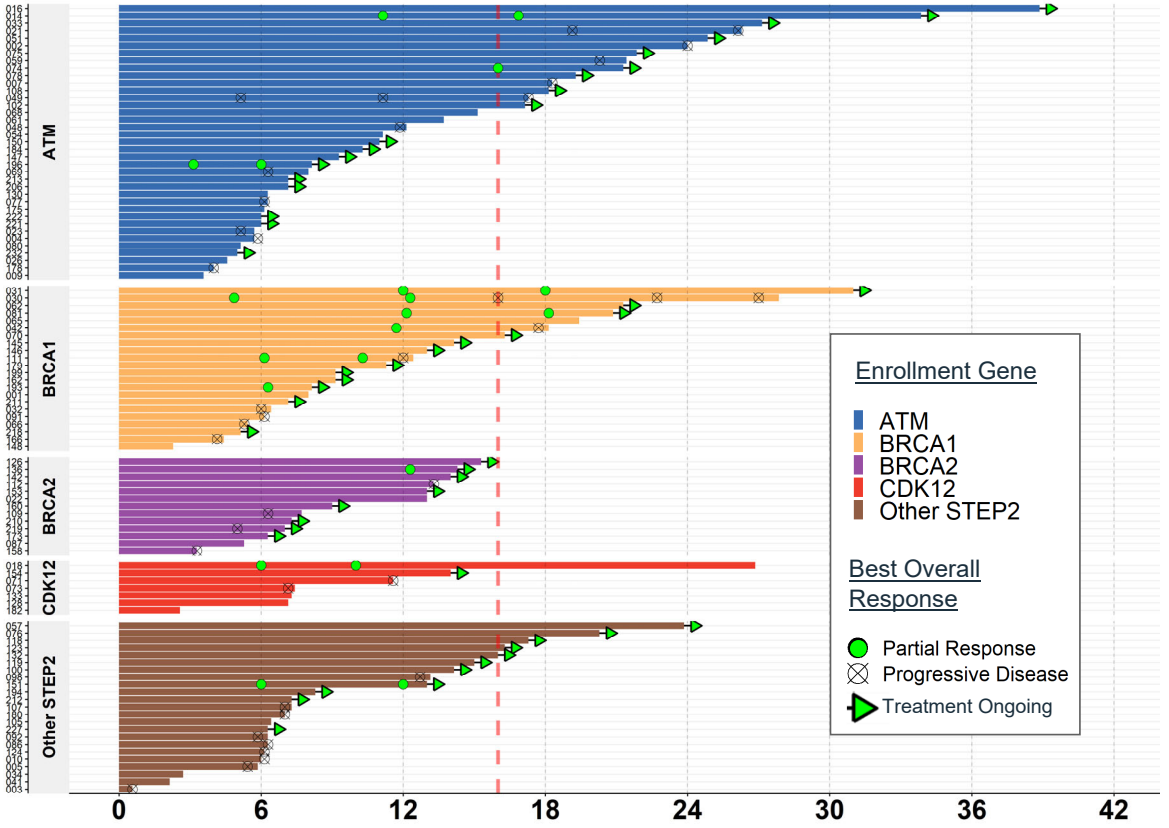
Early analysis of treatment duration

Therapy ongoing in approximately half of enrolled patients*

- **Early analysis of therapy duration shows clinical activity across tumor types and STEP[2] alterations**
- **Responses** included:**
  - CRPC (ATM, CDK12)
  - Ovarian, post-PARPi (4 BRCA1, 1 RAD51C)
  - ER+ breast (BRCA1)
  - HNSCC (BRCA1)
  - Melanoma (BRCA2)
- **Copy number analysis of enrolled gene alterations is ongoing**



*As of August 15, 2021

**Response Evaluation Criteria in Solid Tumors (RECIST); Prostate Cancer Working Group 3 (PCWG3); Gynecological Cancer InterGroup (GCIG)

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Early response observed with RP-3500 ≥100 mg/day (updated from ANE talk)

Broad spectrum of response observed

Meaningful clinical benefit in 34 (49%) of 69 evaluable patients

Across STEP[2] gene alterations

Across schedules & after PARPi failure

- **12 responses**: 8 RECISTv1.1 cPR/uPR, 2 pts by PCWG3 and 2 pts by GCIG (ATM, CDK12, BRCA1, BRCA2, RAD51B, RAD51C)
- **14 pts ongoing SD** ≥ 16 weeks
- **8 pts <16w on study**: early significant decreases in tumor markers and tumor shrinkage (<30%)

Late responses observed:
initial RECISTv1.1 PRs seen at week 16

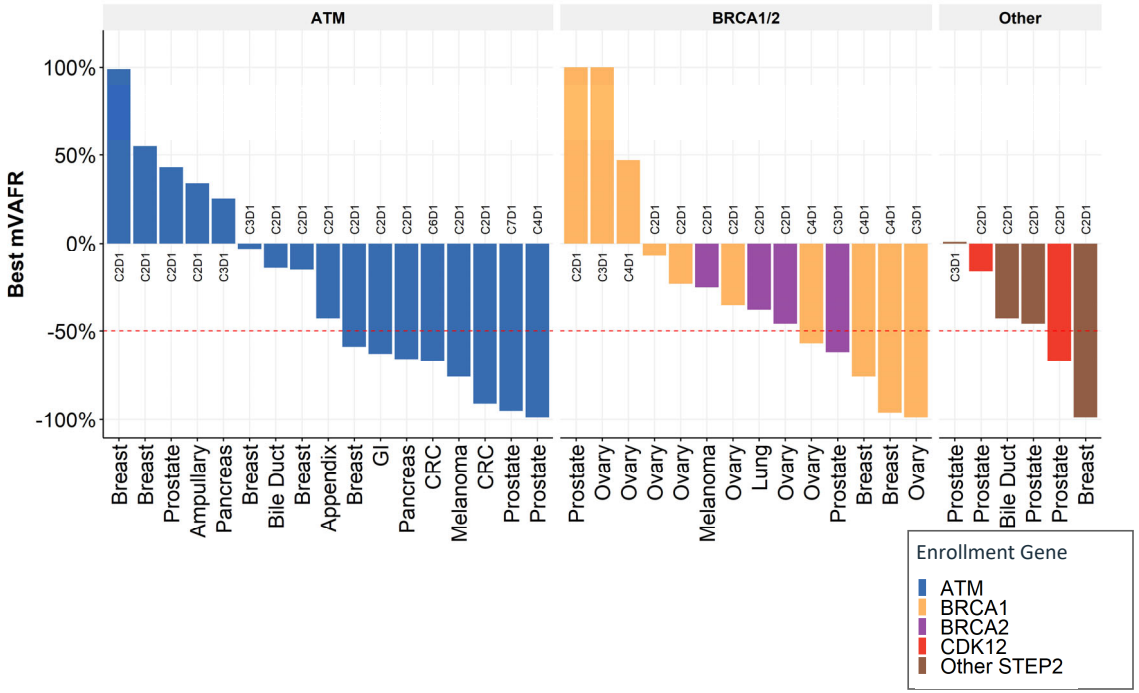
	5/2 Schedule **≥100 mg/day** (N=18)	3/4 Schedule **≥100 mg/day** (N=76)	All patients **≥100 mg/day** (N=94)
Evaluable pts (≥1 post baseline scan)	17	52	69
Best response	**4**	**8**	**12**
RECISTv1.1	3 cPR*	4 cPR; 1 uPR[#]	7 cPR; 1uPR
PCWG3 PSA	1	1	2
GCIG CA125	-	2	2
SD (≥16w)%	6	8	14
SD (≥6w)[&]	6	23	29
PD	6	21	27
Data pending	1	0	1
Discontinued w/o scan	1	3	4
On treatment w/o scan	0	21	21

*1 pt with cPR required radiotherapy to brain lesions early in trial. No brain scan at study entry.
[#]1 pt began on PARPi+RP3500 for 2 weeks, before transitioning to RP-3500 monotherapy, now week 56
[&] includes the SD>16w patients
% includes pt 8 Mo on therapy (SD last scan **-26% on Sept 23rd**) On-Tx and another with SD **(-28.7% at last scan on 07Sep)**

Deep molecular responses in TRESR

Circulating tumor DNA (ctDNA) measured serially in 37 patients

- ctDNA, fragmented tumor DNA detected in blood, reflects the entire tumor genome and as “liquid biopsies” is used to monitor antitumor activity during treatment
- Published data suggest that early molecular responses in ctDNA may be correlated with patient benefit during treatment with anticancer drugs
- ctDNA best mean variant allele frequency (mVAF*) measures change in tumor burden
- RP-3500 data show early and significant decrease (>50%) in mVAFR** in tumors with multiple genotypes



*mVAF calculated as % decrease from baseline

**mVAFR is the mean variant allele frequency ratio (relative to baseline). mVAFR capped at +100%

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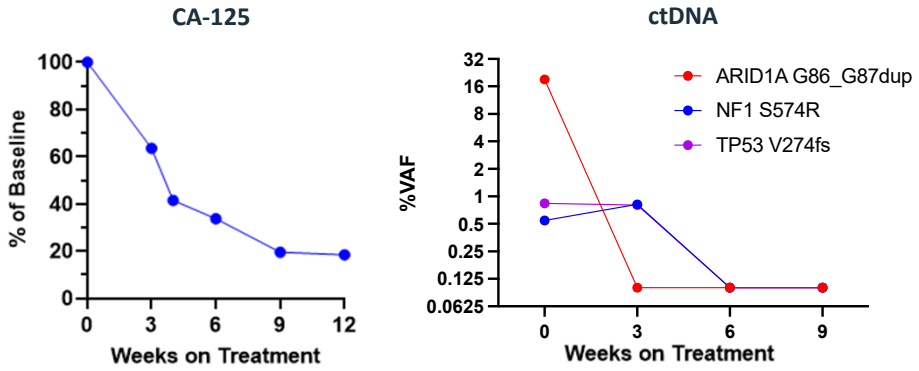
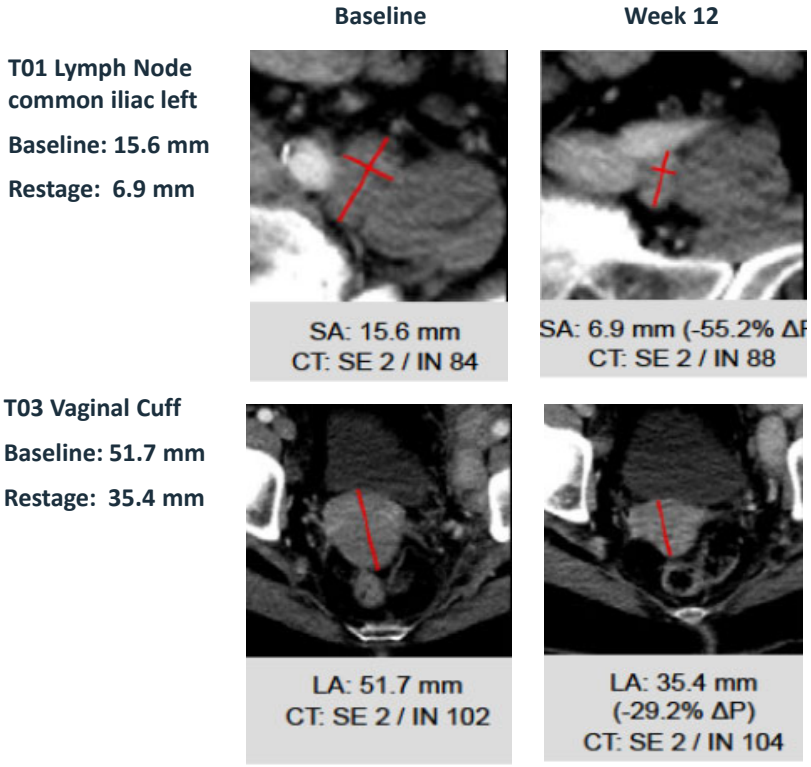
Ovarian cancer with gBRCA1 mutation*

Ongoing RECIST cPR*

Ongoing GCIG CA125 response



59 y/o female with 4 prior therapeutic regimens for metastatic ovarian cancer: Prior platinum, previous failure of PARP inhibitor (best response PD) and docetaxel + avastin (best response PD)



*RECISTv1.1 PR was confirmed after August 15, 2021 data cut-off date

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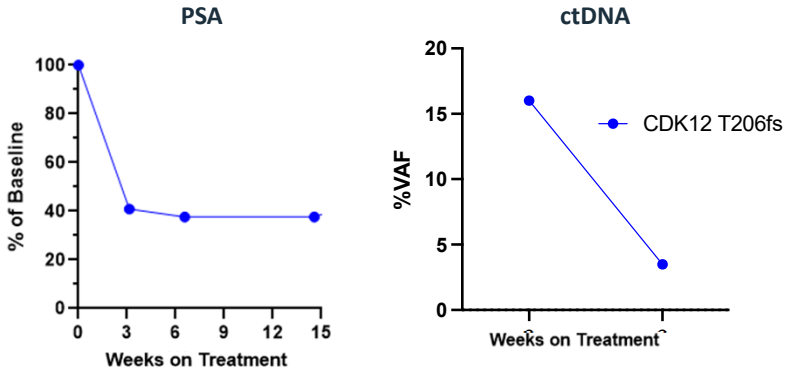
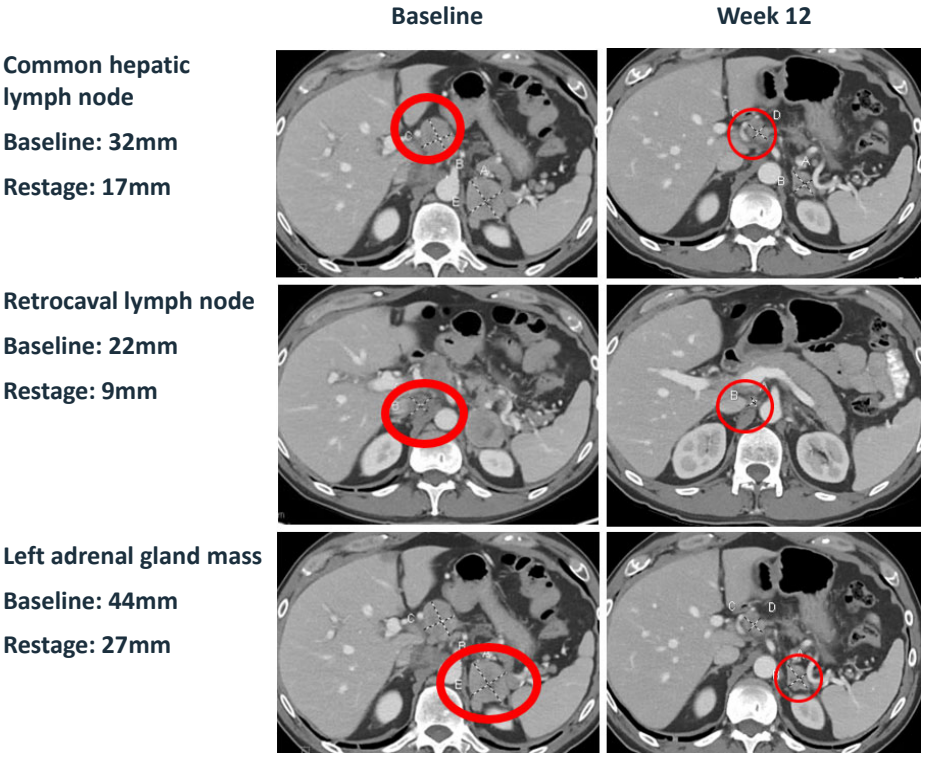
CRPC with CDK12 mutation*

Ongoing RECIST cPR

Ongoing PCWG3 PSA response



57 y/o male with CRPC received 6 prior regimens, incl. best response of PD on docetaxel, platinum/etoposide and Ipi/Nivo



* As of August 15, 2021

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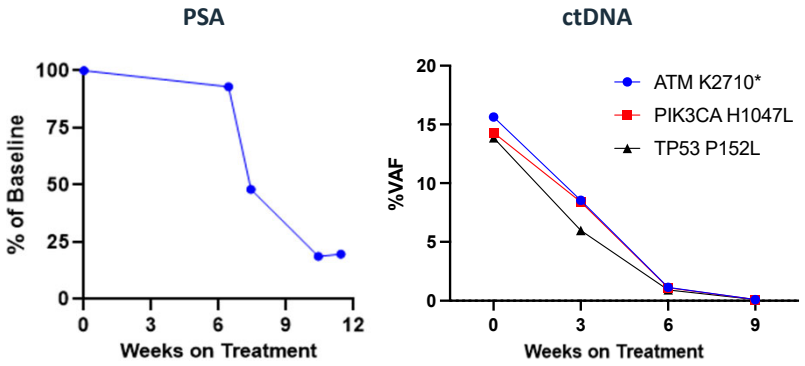
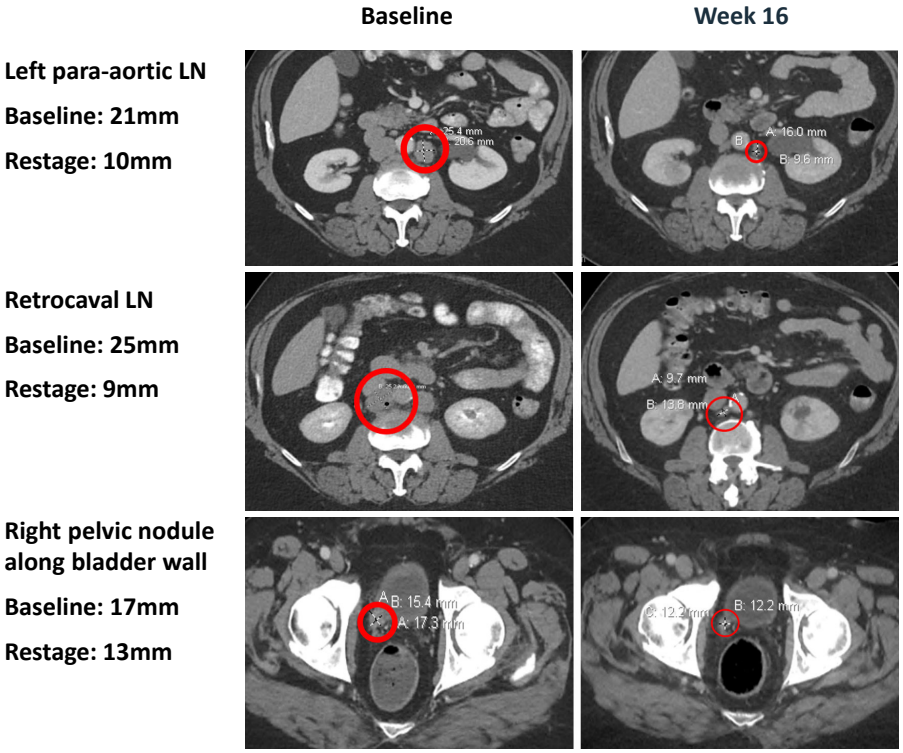
CRPC with ATM mutation*

Ongoing PCWG3 PSA response

Ongoing RECISTv1.1 uPR, confirmation of response awaited



68 y/o male with CRPC, multiple bone metastases and lymph node disease, with disease progression on 2 prior regimens



* As of August 15, 2021

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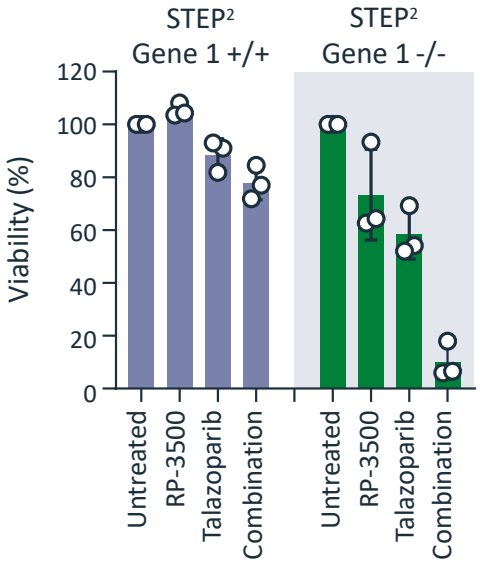
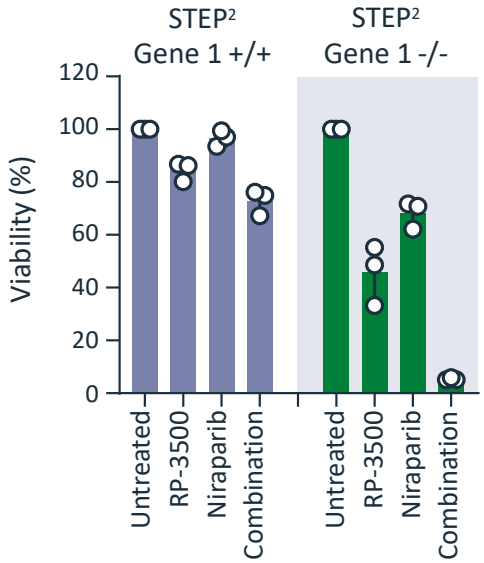
STEP² approach identifies genes to predict combination response

Significant synergy demonstrated by combination of RP-3500 and PARP inhibitors



Talazoparib: 3 nM
RP-3500: 5 nM



Niraparib: 100 nM
RP-3500: 4 nM

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

- **Identified tumors with STEP² genes sensitive to the combination of RP-3500 and PARP inhibitors**
- **The activity observed at low doses of RP-3500 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

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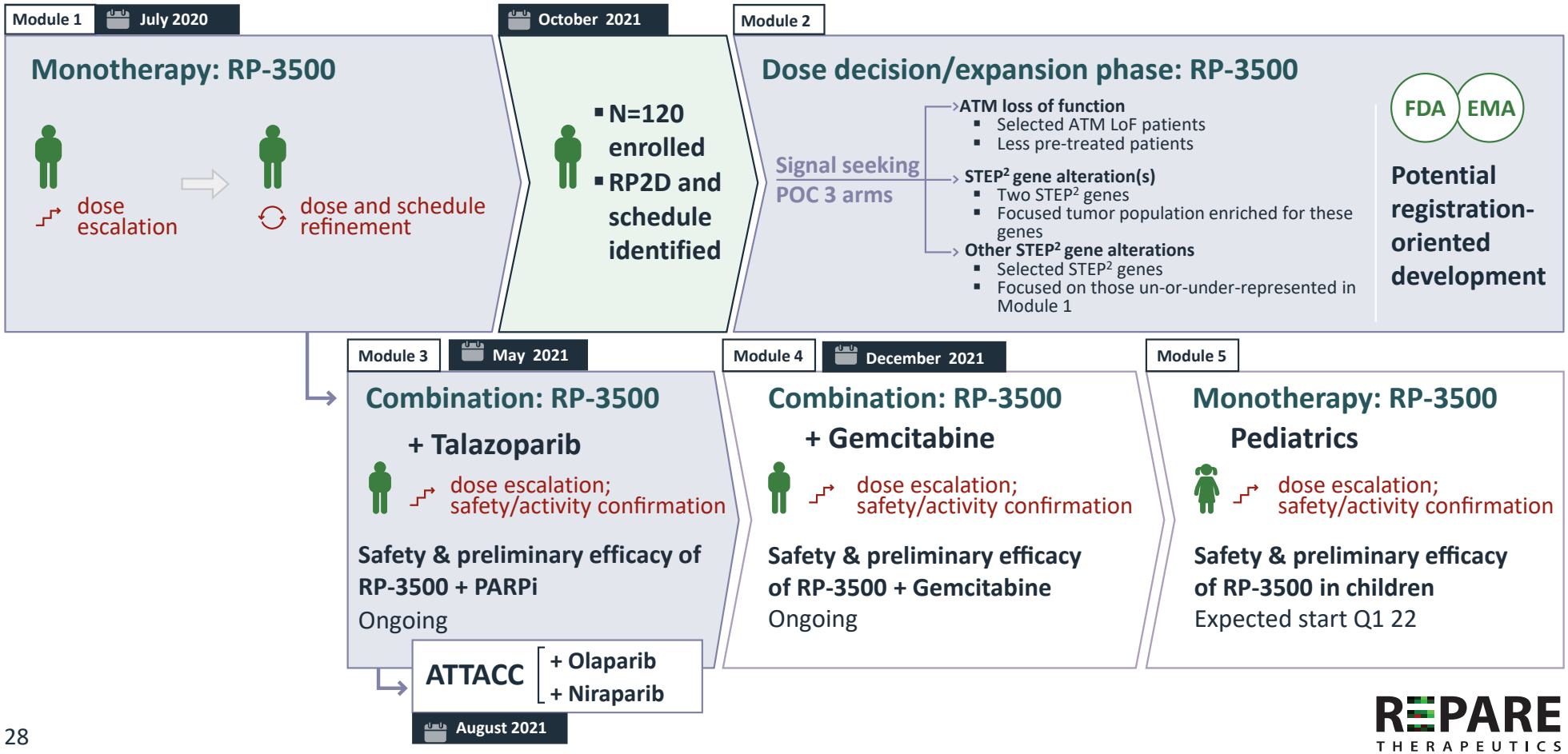
RP-3500 updated clinical trial program: additional modules

Trial results to date support expanded clinical development



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Summary early results from our ongoing TRESR monotherapy trial

- **RP-3500 is in development as a potent, potentially best-in-class, highly selective ATRi**
- **The TRESR study is the largest biomarker-selected trial testing ATRi as single agent (appr. 120 pts)***
- **RP-3500 was well tolerated:** mainly G1-2 anemia (14.5% Grade 3 at 3 days on 4 days off schedule, early data)
- **Meaningful clinical benefit in 34 (49%) of 69 pts with cancers harboring selected genomic alterations**
- **RP-3500 RP2D established for further monotherapy evaluation:** weekly 160mg QD 3d on/4d off
- **Favorable & differentiated safety profile observed at RP2D**
- **Biomarker data confirm multi-tumor proof-of-mechanism across several molecular backgrounds**
- **Early TRESR data provide clinical POC and validate Repare Therapeutics' SNIPRx/STEP^2 platform**

Favorable & differentiated safety profile and promising early results provide a clear direction for further development of RP-3500

* Study ongoing

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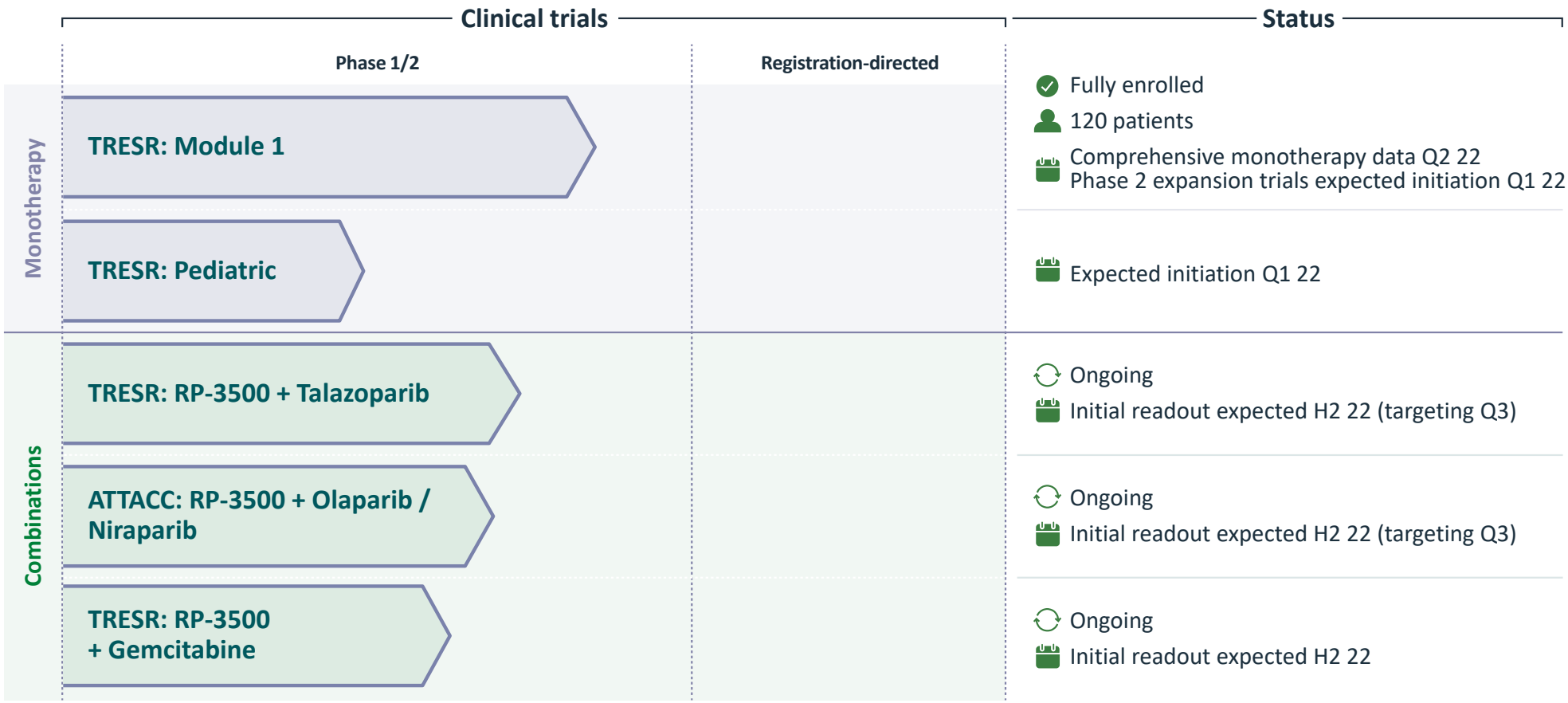
RP-3500: Executive Summary



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PKMYT1 inhibitor RP-6306

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RP-6306: First-in-class small molecule program

Oral PKMYT1 inhibitor, serving unmet need in tumors with CCNE1 amplification and other lesions

First in class drug PKMYT1 inhibitor, synthetic lethal in CCNE1 amplified, FBXW7 loss and tumors with other specific alterations

Amplification of CCNE1 drives genome instability; found in many tumor types, including gynecological and gastrointestinal malignancies

Compelling preclinical anti-tumor activity confirms SL relationship of PKMYT1 and CCNE amplification and FBXW7 alterations

RP-6306 key differentiators include:

- Potent and highly selective
- Proprietary patient selection: CCNE1 amp, FBXW7 loss, other STEP[2] genes
- Combinability with several drug classes

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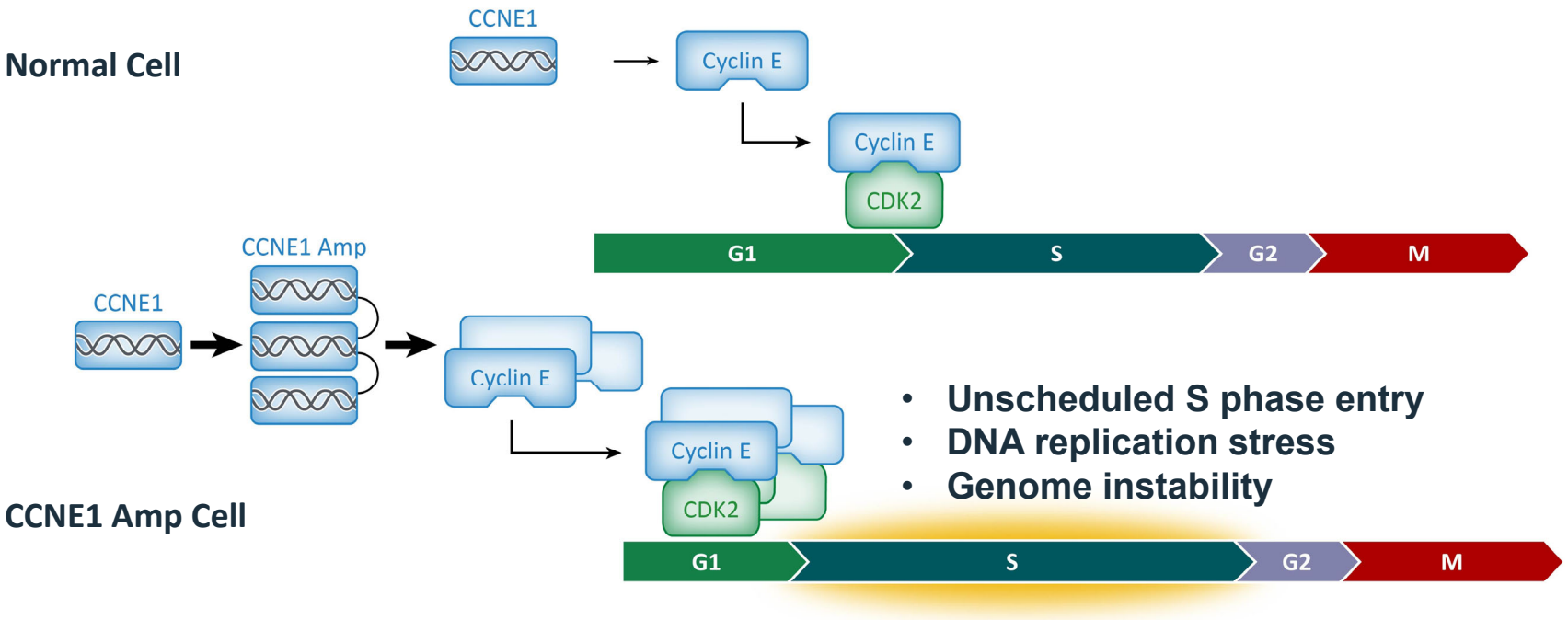
CCNE1 amplification drives genome instability



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

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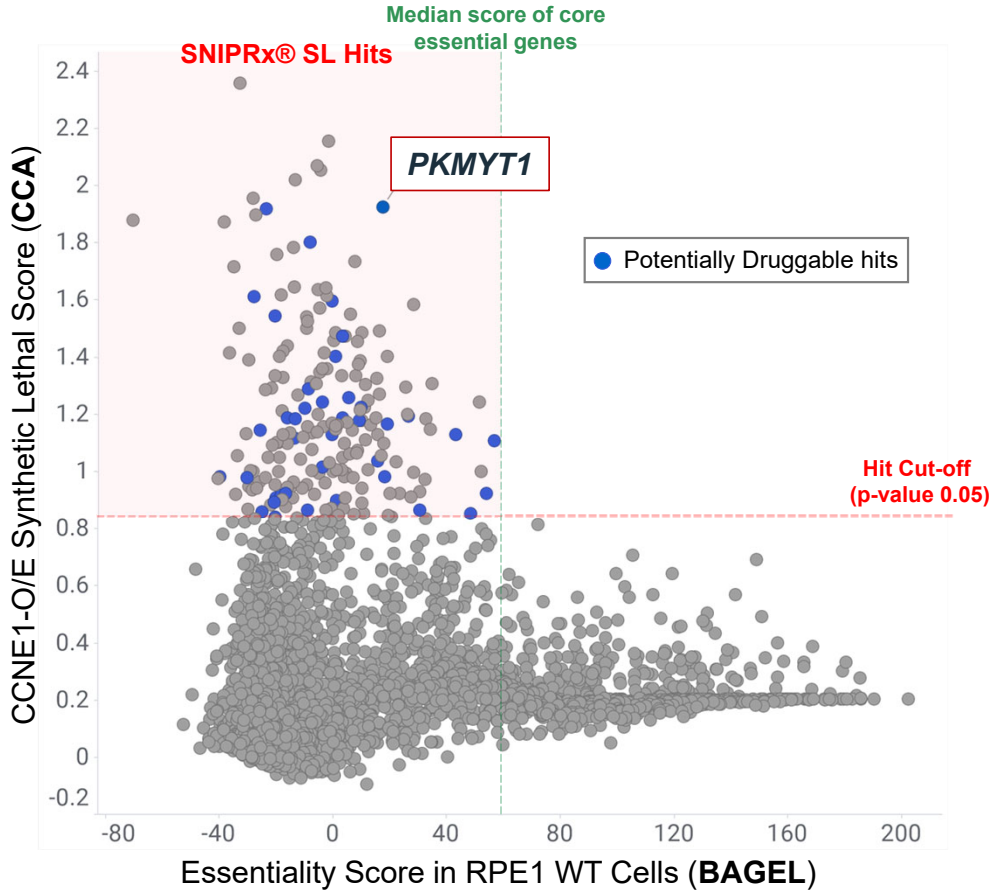
PKMYT1: Strong hit in a CCNE1-overexpression ("O/E") SL screen



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

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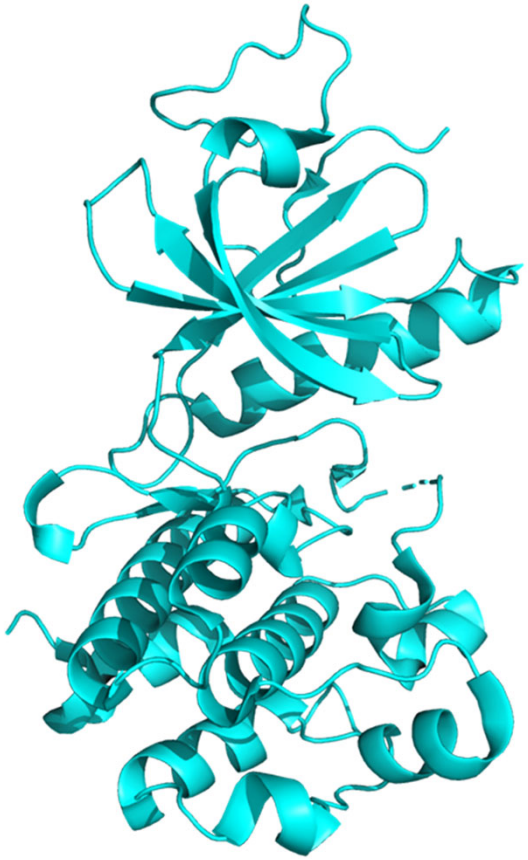
What is PKMYT1?



PKMYT1 (also known as Myt1):

- **Membrane-associated serine/threonine protein kinase**
- **Member of WEE1 protein kinase family**
- **Selectively phosphorylates cyclin-dependent kinase 1 (CDK1) – no other known substrates**
- **Negatively regulates the G2/M transition of the cell cycle by inactivating CDK1**
- **Not previously linked to CCNE1 amplification**

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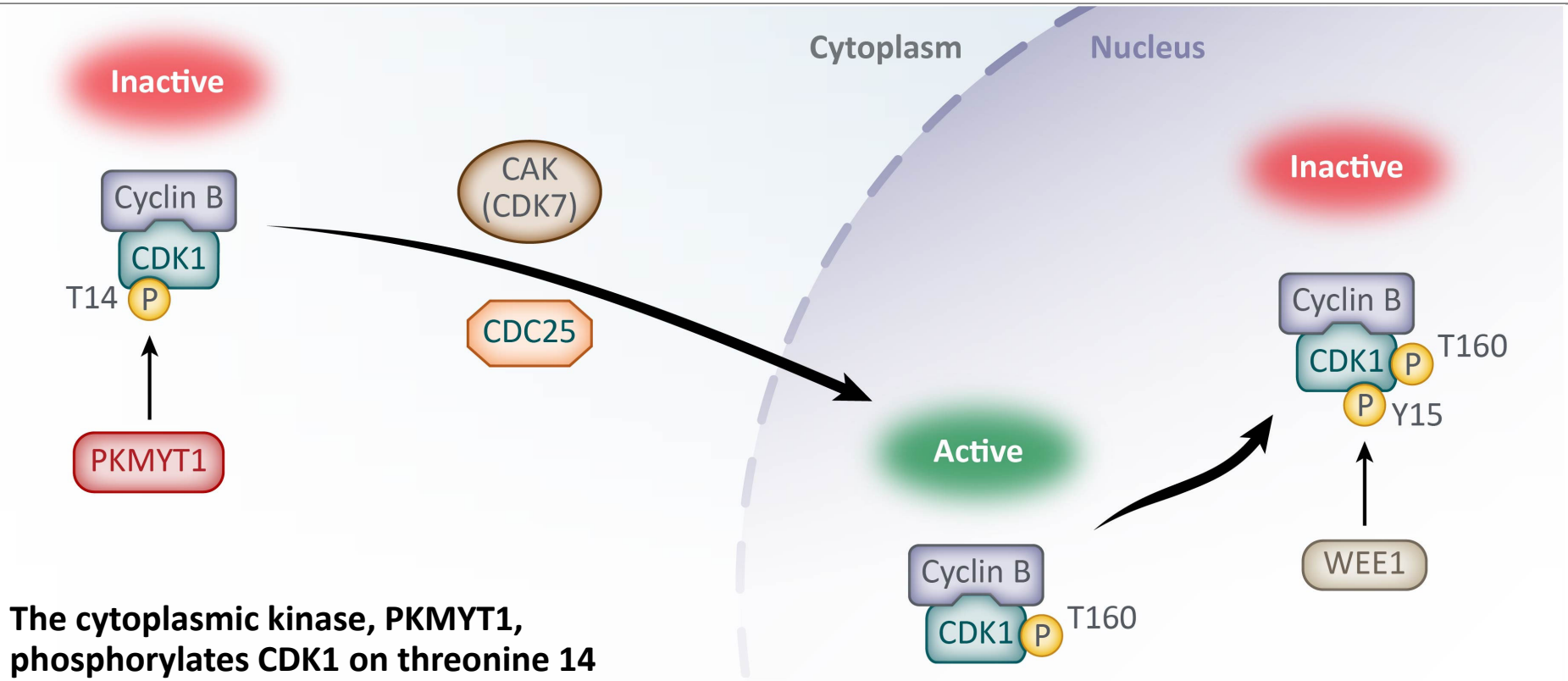
RP-6306: Potent and selective first-in-class PKMYT1 inhibitor

	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

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

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

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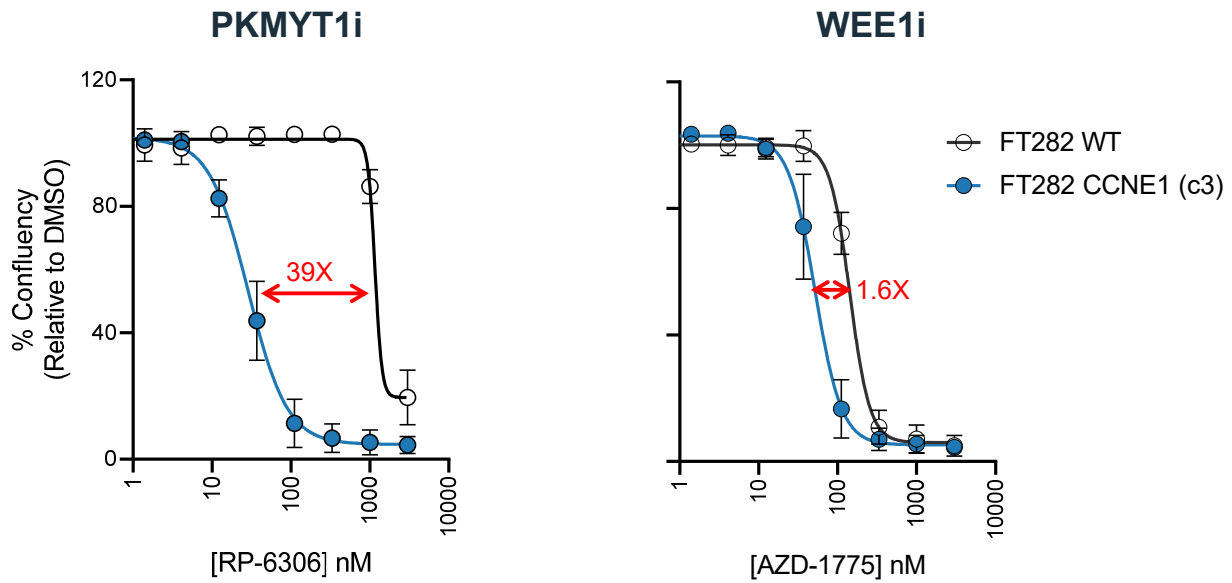
RP-6306 Delivers a selective effect on CCNE1-O/E cells vs. WEE1 inhibition



- **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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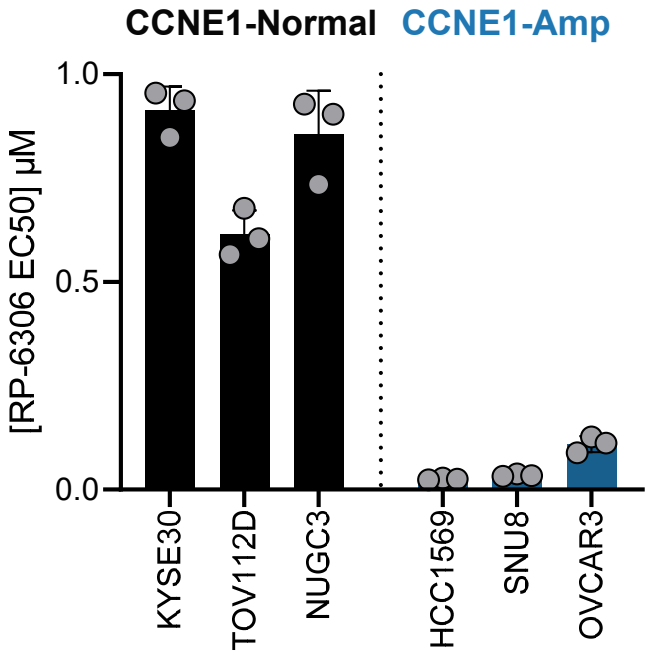
RP-6306 selectively targets CCNE1-amplified tumor cell lines



Tumor cell lines with CCNE1-Amp are hyper-sensitive to PKMYT1 inhibition compared to cells with normal CCNE1 levels

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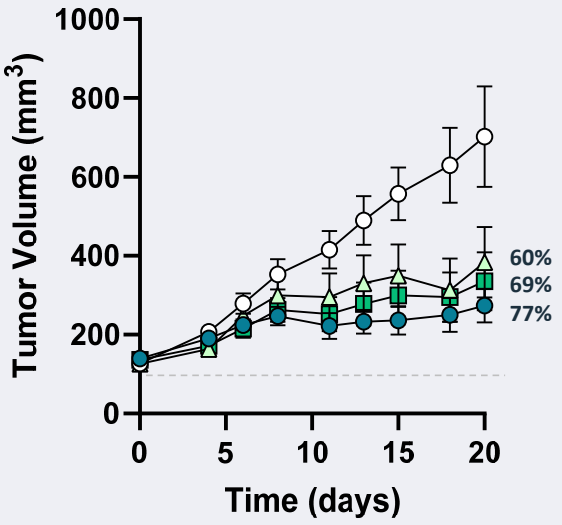
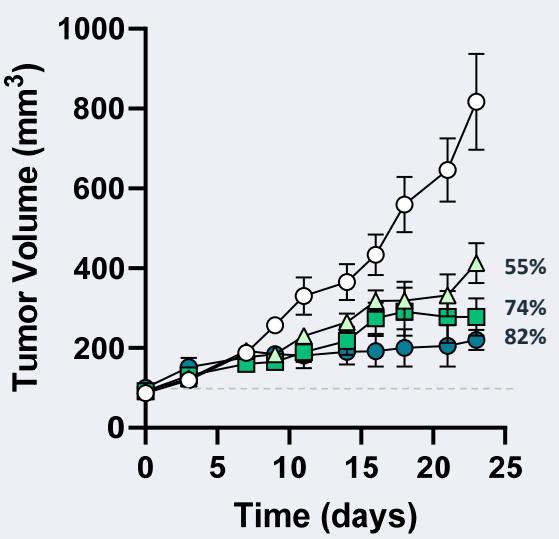
RP-6306 inhibits the growth of multiple CCNE1-amplified xenograft tumors

HCC1569 Breast



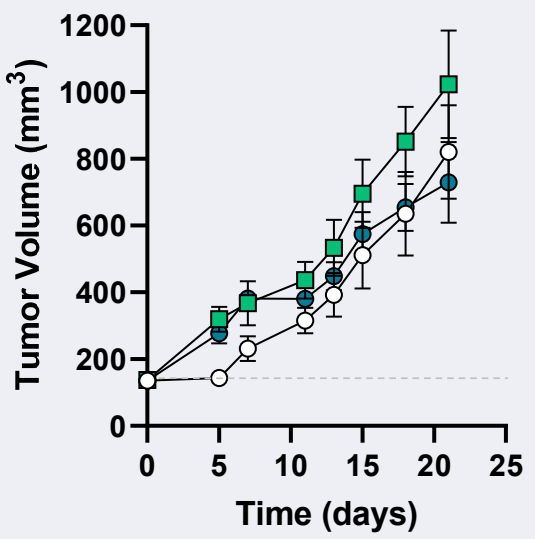
CCNE1 CN = 34

OVCAR3 Ovarian

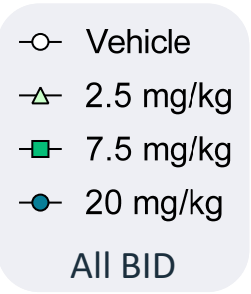


CCNE1 CN = 14

SUM149PT TN Breast



CCNE1 CN = 2 (WT)



RP-6306 demonstrates activity in CCNE1-amplified tumors and is active at doses well below MTD

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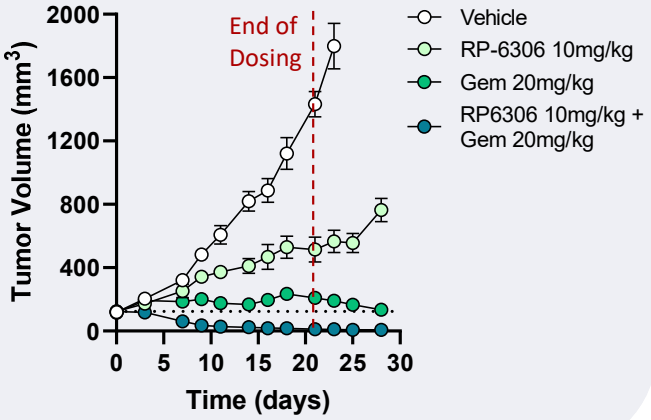
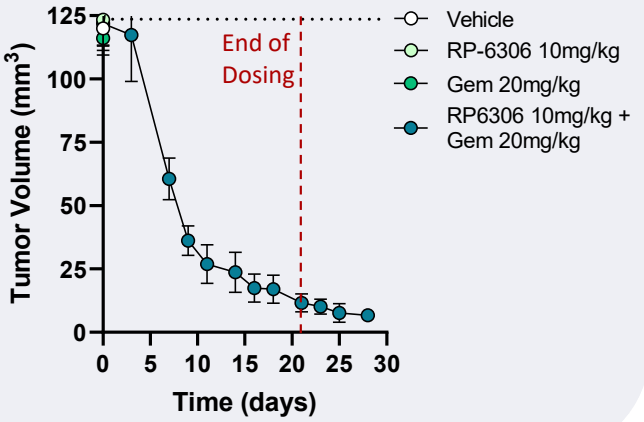
RP-6306 + Gemcitabine drives regression and no serious toxicity

Activity
(OVCAR3; CCNE1 CN = 14)



Activity
(Robust regression)



Gemcitabine dosed once a week and RP-6306 dosed twice daily

Xenograft tumors continue to regress after cessation of dosing with several mice having no measurable tumor detected

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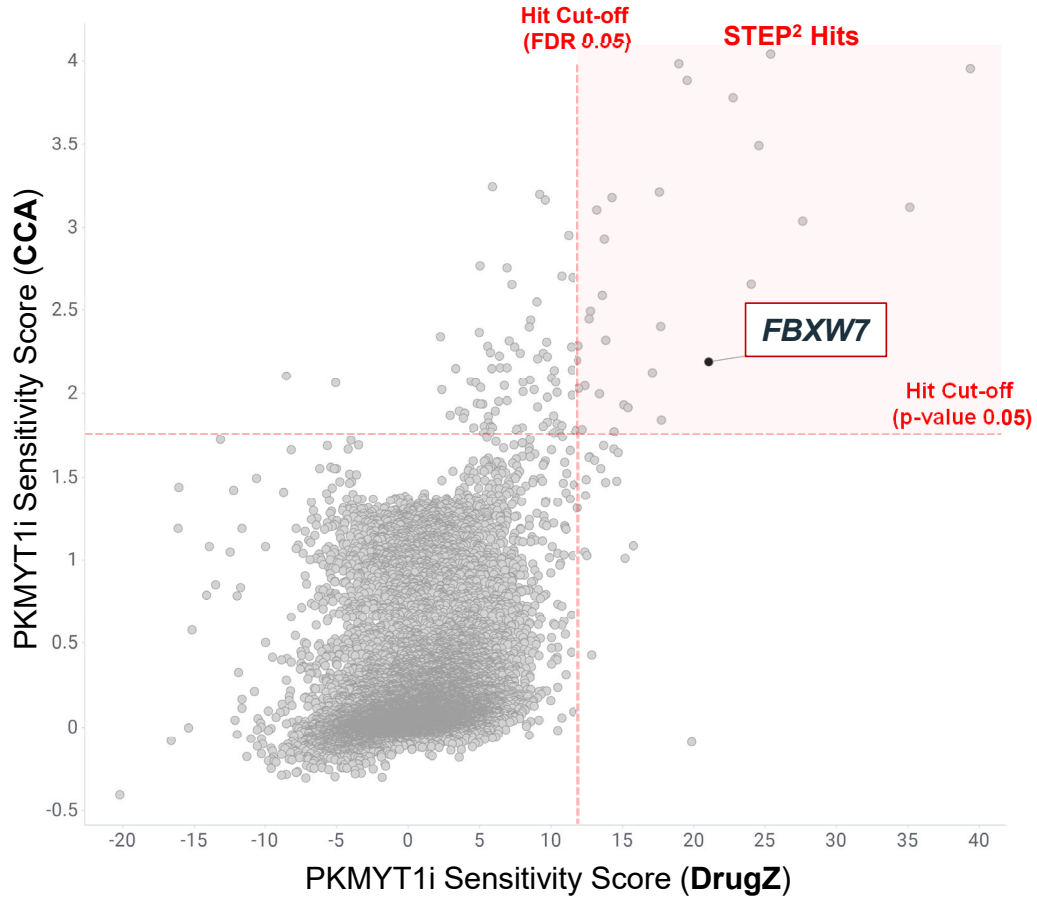
RP-6306 STEP^2 screen identifies FBXW7 tumor population



RP-6306 STEP^2 genome-wide chemical genetic screen identifies novel patient populations, including FBXW7 alterations

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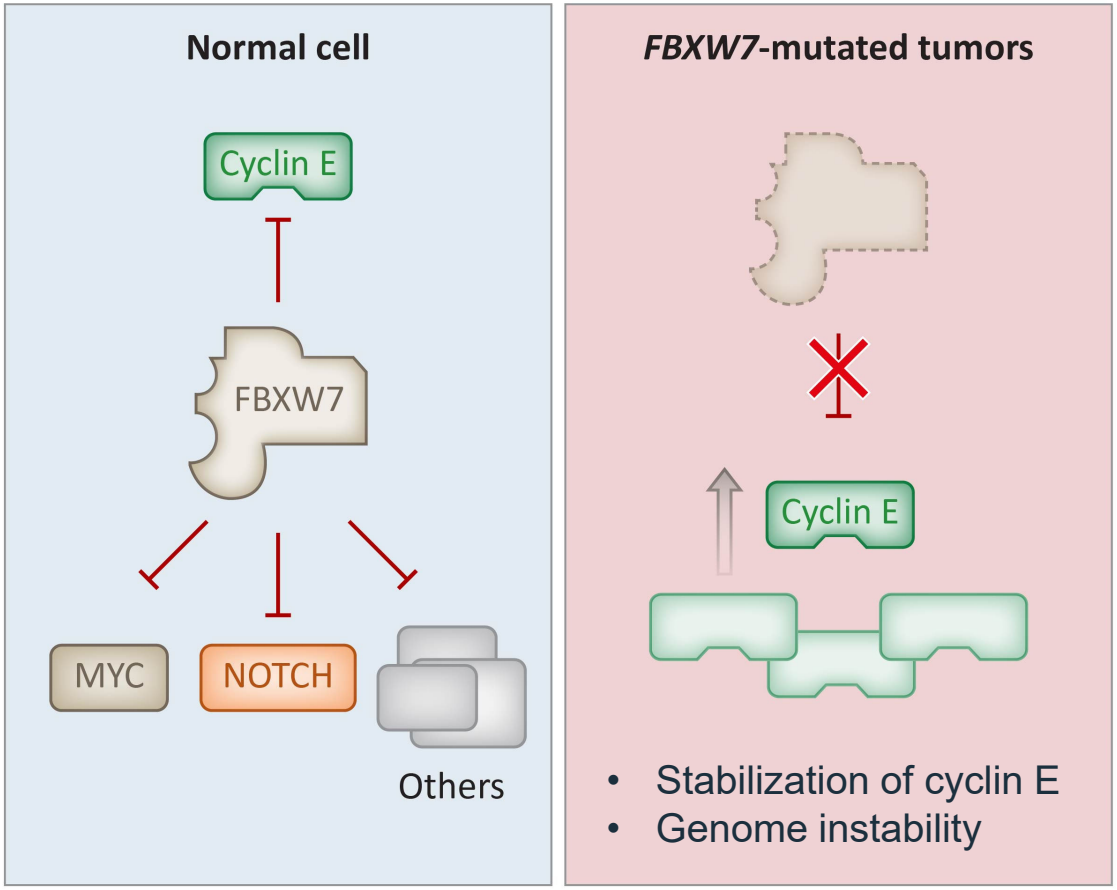
The rationale for targeting FBXW7-mutated tumors with RP-6306



FBXW7:

- **E3 ubiquitin ligase that targets proteins, such as CCNE, for proteasomal degradation**
- **Frequently mutated in tumors**
- **Inactivating mutations can increase CCNE levels**
- **STEP[2] screens show that FBXW7 mutations cause sensitivity to PKMYT1 inhibition**

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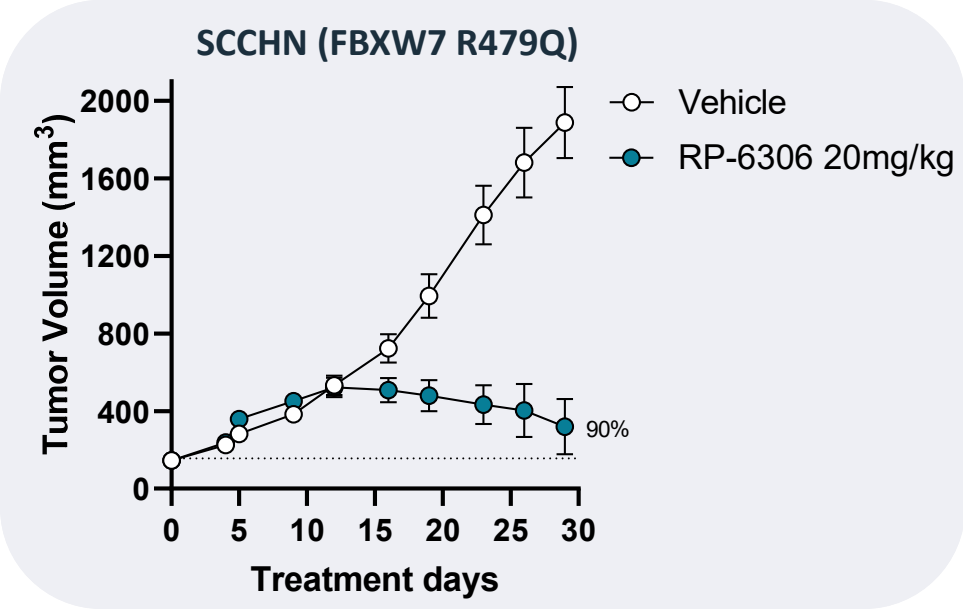
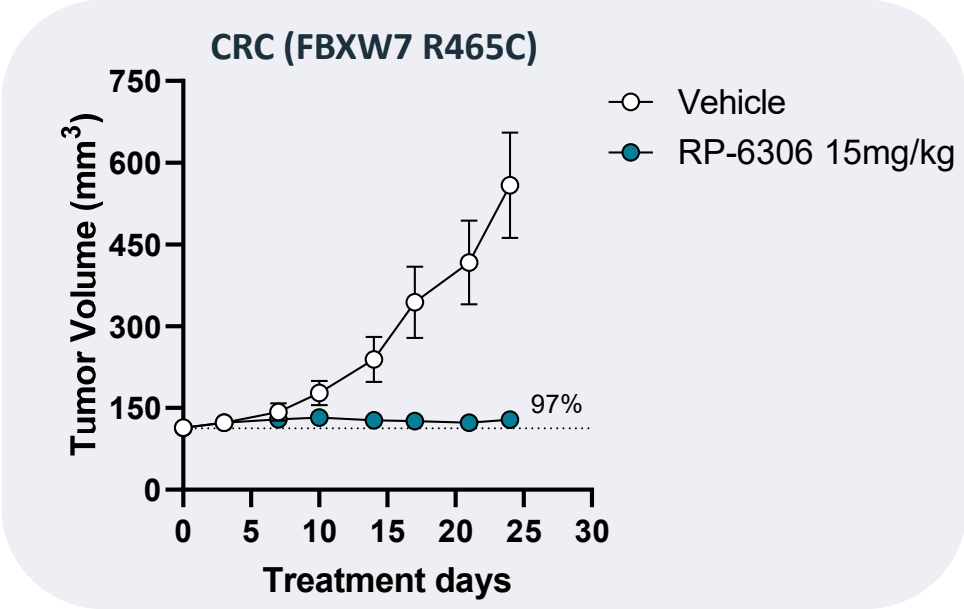
RP-6306 inhibits growth of FBXW7 mutant PDX models





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

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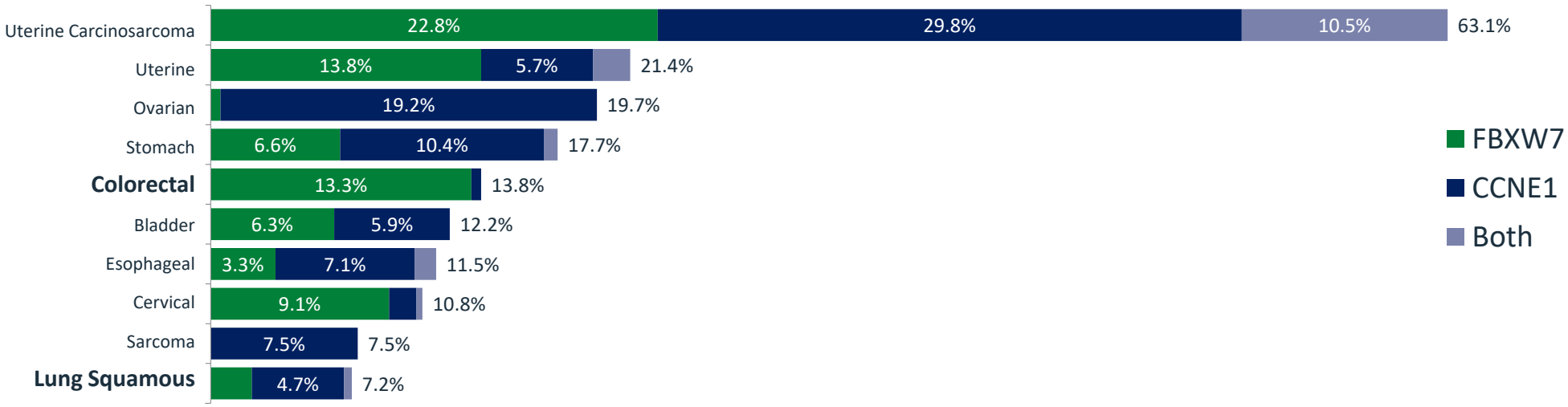
Potential addressable patient populations with RP-6306

Top 10 tumor types with highest prevalence of CCNE1 amplification and FBXW7 mutations deficiency (Source: TCGA)



FBXW7 and CCNE1 amplification occur in multiple cancers with significant unmet medical need
These lesions are largely mutually exclusive and represent distinct patient populations

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RP-6306 clinical program

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

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 STEP^2 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

Preliminary data H2 2022

RP-6306 profile/plan

- Designed to be an orally available ATP- competitive inhibitor
- Maximized potency and specificity
- Genomically defined, tumor-specific and tumor agnostic indications
- Early combination testing

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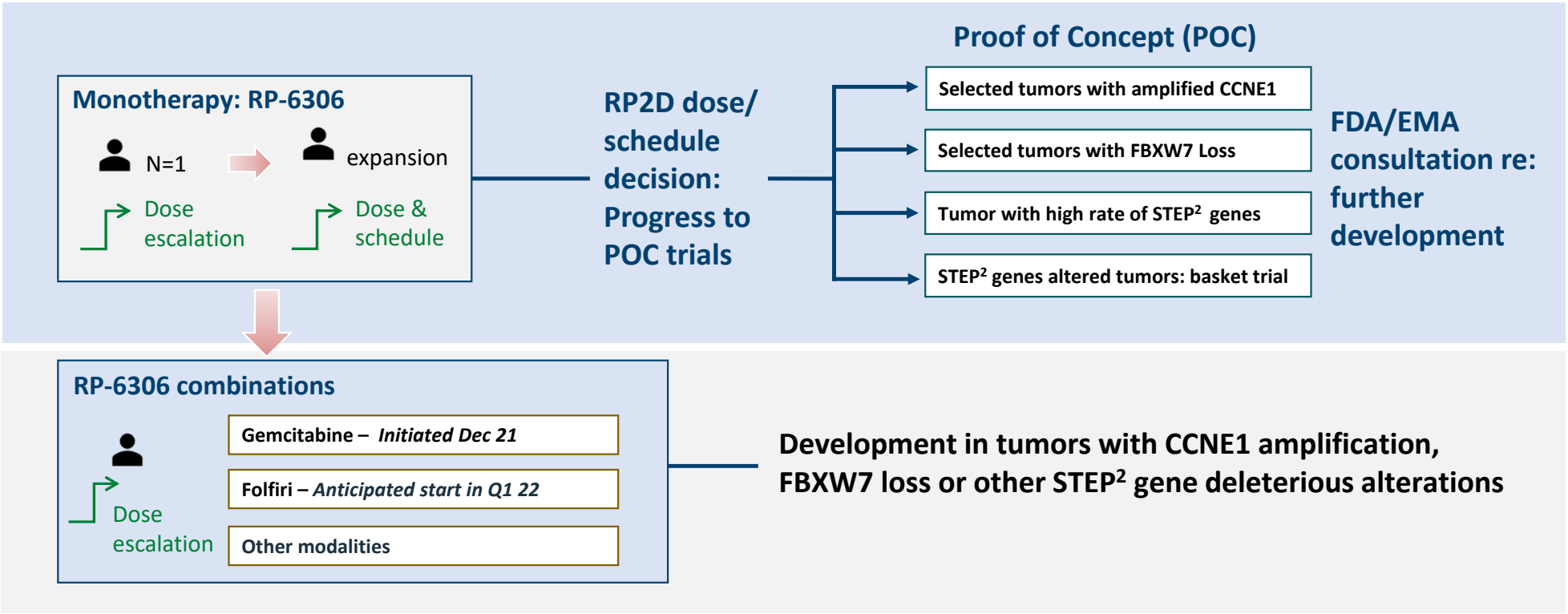
RP-6306 initial global clinical trial program

Key inclusion criteria

- Recurrent solid tumors
- CCNE1 amplification, FBXW7 loss and/or other undisclosed RP-6306 STEP^2 alterations



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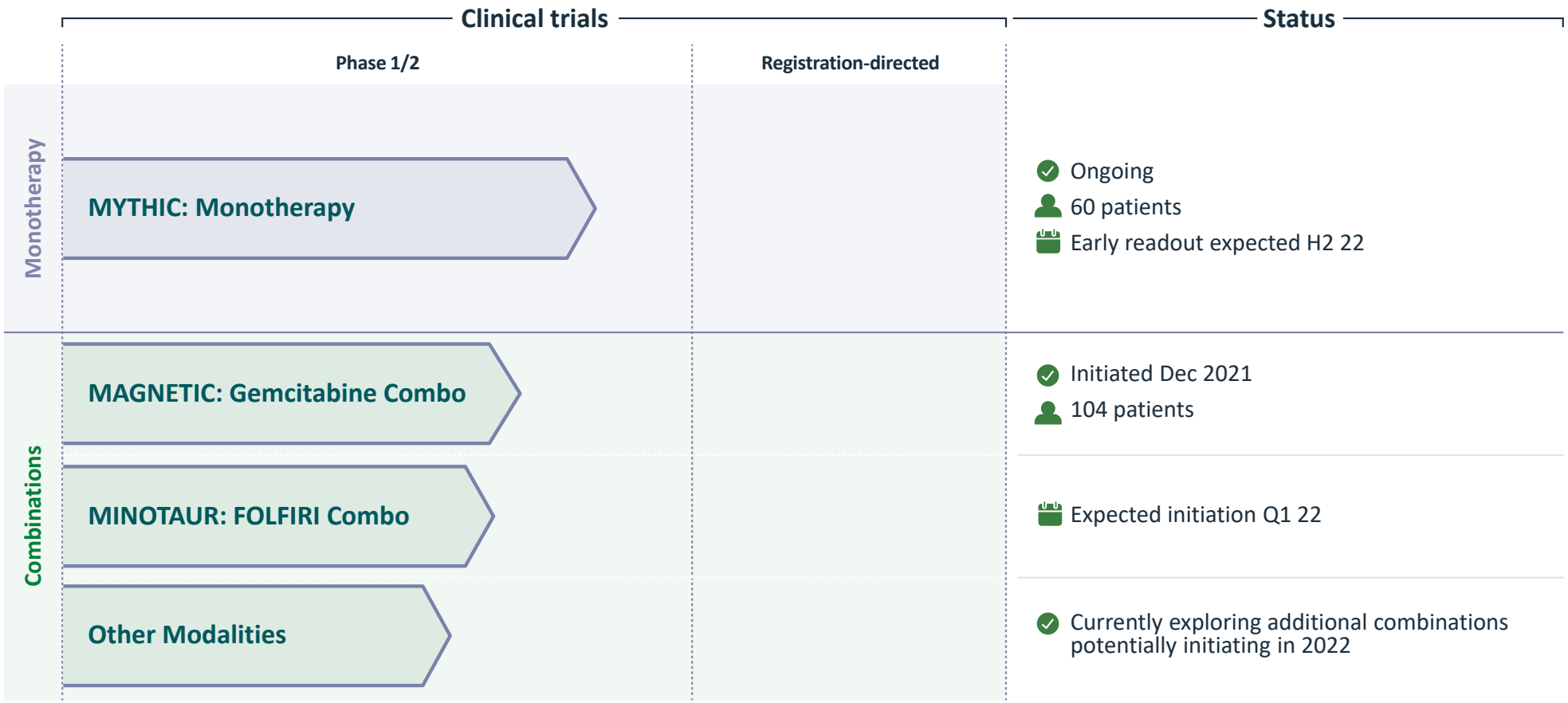
RP-6306: Executive Summary



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Highlights and milestones

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Financial highlights

$341.7M

Cash, restricted cash and marketable securities

Balance sheet
31-Dec-2021
(Unaudited)

Funded through 2023

Expected runway with cash on hand
(inclusive of November 2021 follow-on proceeds)

41.7M

Pro-forma basic and fully diluted shares outstanding

Shares outstanding
30-Sep-2021
(Includes 4.6M shares issued from November 2021 follow-on)

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Key anticipated 2022 milestones

RP-3500: ATR Inhibitor

H1

Q1 Initiate Phase 2 monotherapy TRESR trial

Q1 Initiate Pediatric Phase 1 Module of TRESR trial

Q2 Comprehensive results of TRESR Phase 1 Module 1

H2

Q3 Initial clinical data for RP-3500 in combination with PARP (from TRESR and ATTACC)

H2 Recommended Phase 2 dose for RP-3500 in combination with gemcitabine

RP-6306: PKMYT1 Inhibitor

H1

Q1 Initiate Phase 1 RP-6306 combination FOLFIRI trial

H2

H2 Initial MYTHIC Phase 1 monotherapy readout

Polθ Inhibitor

H1

H1 Initiate IND-enabling studies

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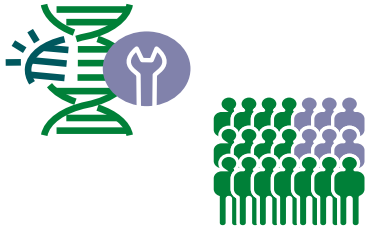
Repare: Summary of key differentiators

Clinical programs

- RP-3500, potential best-in-class ATR inhibitor
- RP-6306, first-in-class PKMYT1 inhibitor
- Both in Ph 1 or Ph 1/2 clinical trials with multiple 2022 readouts

Pipeline

- Portfolio of assets with 2 clinical SL compounds in ’21
- Multi-target discovery collaboration with Bristol Myers Squibb



Platform

- SNIPRx platform reveals novel insights
- 16+ tumor lesion campaigns complete
- STEP^2 screens enable expanded patient selection tailored to program

Balance sheet

- Funded for multiple key value-creating milestones in 2022 and 2023

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