Preliminary Phase 1 Data From Ongoing First-in-Human Phase 1/2 TRESR Study of RP-3500

Virtual Investor Update
October 8, 2021

REPARE THERAPEUTICS

Today's agenda

Brief introduction	Lloyd M. Segal & Maria Koehler, MD, PhD	President & CEO, Repare Therapeutics EVP & CMO, Repare Therapeutics
Summary of AACR-NCI-EOTRC data and select case studies	Timothy Yap, MBBS, PhD, FRCP	Medical Director, Institute for Applied Cancer Science, Associate Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, MD Anderson Cancer Center
RP-3500 next steps	Maria Koehler, MD, PhD Timothy Yap, MBBS, PhD, FRCP	EVP & CMO, Repare Therapeutics MD Anderson Cancer Center
Concluding remarks	Lloyd M. Segal & Maria Koehler, MD, PhD	President & CEO, Repare Therapeutics EVP & CMO, Repare Therapeutics
Q&A		

REPARE THERAPEUTICS

REPARE participants

Lloyd M. Segal
President & CEO

Maria Koehler, MD, PhD
Chief Medical Officer

Joining for Q&A

Mike Zinda, PhD
Chief Scientific Officer

Steve Forte
Chief Financial Officer

REPARE THERAPEUTICS

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; 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 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 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 August 12, 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.

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.

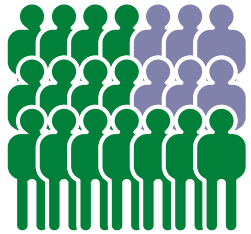
REPARE THERAPEUTICS

Leading clinical-stage precision oncology company focused on synthetic lethality

Lead clinical-stage candidate RP-3500, a potential best-in-class ATR inhibitor; currently in Phase 1/2 monotherapy and combination therapy

Robust pipeline of SL-based therapeutics; including RP-6306, our PKMYT1 inhibitor currently in Phase 1, and our Polθ inhibitor

Proprietary **genome-wide CRISPR-enabled SNIPRx platform**, focused on genomic instability and DNA damage repair



Powerful SL-based approach and proprietary platform provides **differentiated patient selection insights**

Cash, restricted cash and marketable securities of $301 million as of June 30, 2021

REPARE THERAPEUTICS

Expert participant: Timothy Yap, MBBS, PhD, FRCP

Medical Oncologist and Physician-Scientist at the University of Texas, MD Anderson Cancer Center

- Associate Professor, Department for Investigational Cancer Therapeutics
- Medical Director of the Institute for Applied Cancer Science
- Associate Director of Translational Research in the Institute for Personalized Cancer Therapy
- Primary research focuses on the first-in-human and combinatorial development of molecularly targeted agents and immunotherapies, and their acceleration through clinical studies using novel predictive and pharmacodynamic biomarkers
- Main interests include the targeting of the DNA damage response with novel therapeutics, such as ATR and PARP inhibitors, as well as the development of novel immuno-therapeutics
- BSc degree in Immunology and Infectious Diseases and MD from Imperial College London, UK

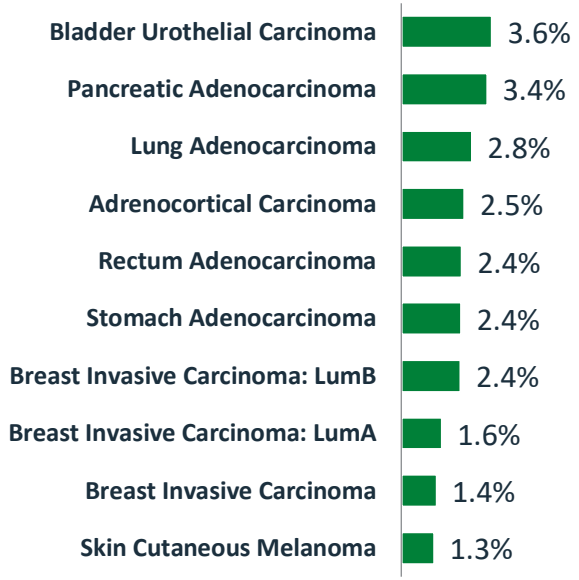
Robust pipeline of SL-based precision oncology therapeutics

		SL Pair: Tumor lesion	SL Pair: Drug target	Discovery	IND-Enabling	Phase 1/2	Registration-directed	Anticipated milestones	Rights
Clinical	ATR inhibitor RP-3500	ATM + 16 STEP[2] lesions	ATR					▪ Q2 22 TRESR final MonoRx data ▪ Q3 22 PARP combo early data	REPARE THERAPEUTICS
Clinical	PKMYT1 inhibitor RP-6306	CCNE1, FBXW7 + others	PKMYT1					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	SNIPRx® platform	Discovery and validation of new SL precision oncology targets							REPARE THERAPEUTICS; Bristol Myers Squibb

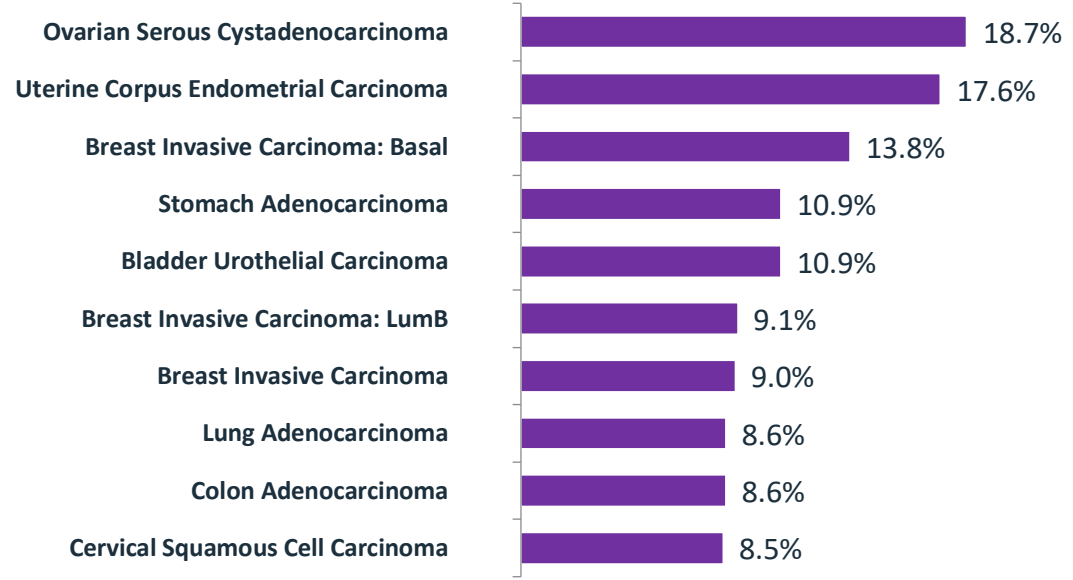
REPARE THERAPEUTICS

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



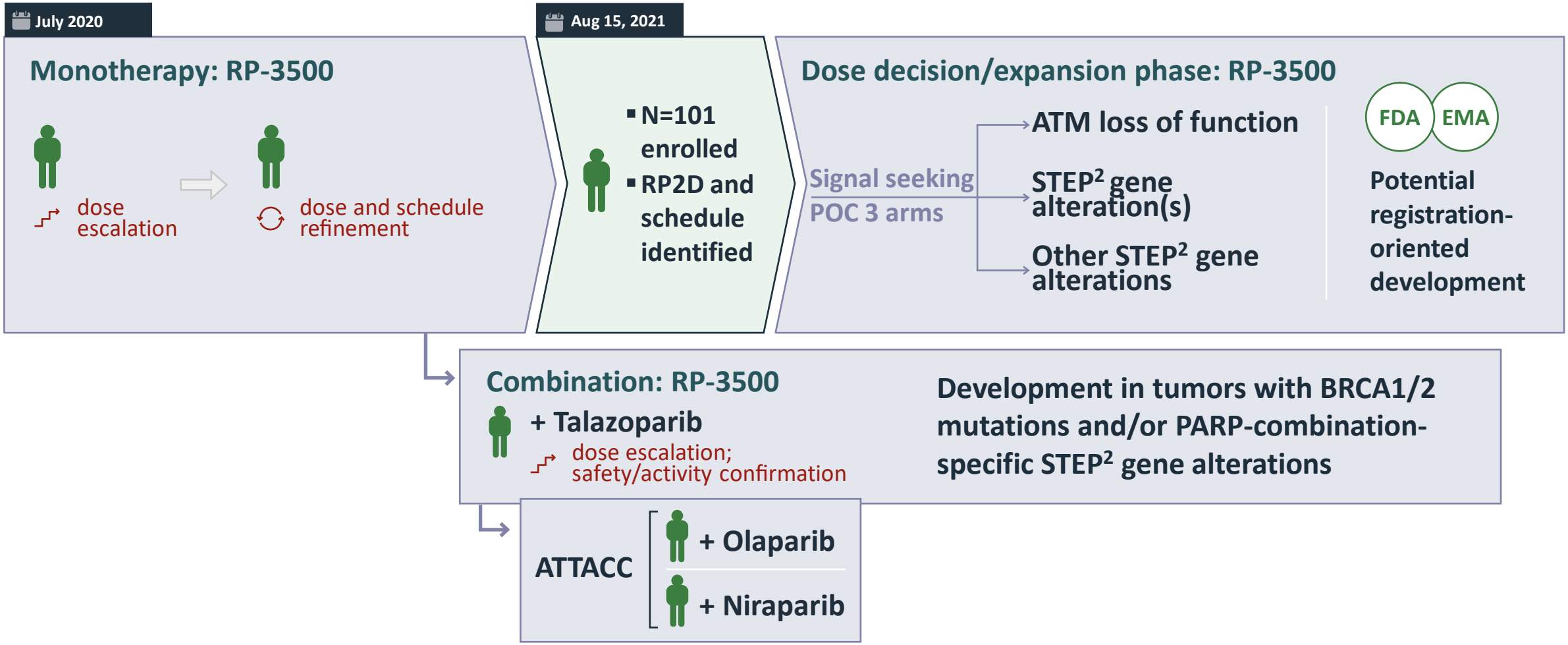
- Beyond ATM, **16 of 19 additional, mutually exclusive genomic alterations identified as SL with RP-3500 are eligible for recruitment into the ongoing trial**
- Represents **expanded, clinically relevant populations with unmet medical needs**
- **Average prevalence of ~2% (ATM) to ~10% (STEP^2 genes)**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

* TCGA; Not weighted for tumor prevalence

REPARE THERAPEUTICS

RP-3500 clinical progress to-date

Global multicenter study designed for patients with recurrent tumors with ATM loss or loss of any of the additional 16 STEP^2 genes



REPARE THERAPEUTICS

Summary of AACR-NCI-EORTC data and select case studies

REPARE THERAPEUTICS

First-in-Human biomarker-driven Phase I TRESR trial of ATR inhibitor RP-3500 in patients with advanced solid tumors harboring synthetic lethal genomic alterations

Timothy A. Yap[1], Elizabeth Lee[2], David Spigel[3], Elisa Fontana[4], Martin Hojgaard[5], Stephanie Lheureux[6], Niharika Mettu[7], Louise Carter[8], Ruth Plummer[9], Victoria Rimkunas[10], Ian M. Silverman[10], Adrian J. Fretland[10], Danielle Ulanet[10], Peter Manley[10], Ezra Rosen[11]

[1]University of Texas MD Anderson Cancer Center, Houston, TX; [2]Dana-Farber Cancer Institute, Boston, MA; [3]Sarah Cannon Research Institute, Nashville, TN; [4]Sarah Cannon Research Institute, London, UK; [5]Copenhagen University Hospital, Herlev, Denmark; [6]Princess Margaret Cancer Centre, Toronto, Canada; [7]Duke University Medical Center, Durham, NC; [8]The Christie NHS Foundation Trust, Manchester, UK; [9]Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [10]Repare Therapeutics, Cambridge, MA; [11]Memorial Sloan Kettering Cancer Center, New York, NY

REPARE THERAPEUTICS

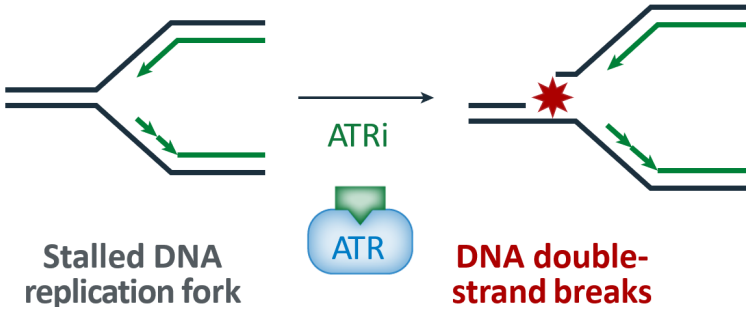
Speaker Disclosures: Timothy Yap, MD

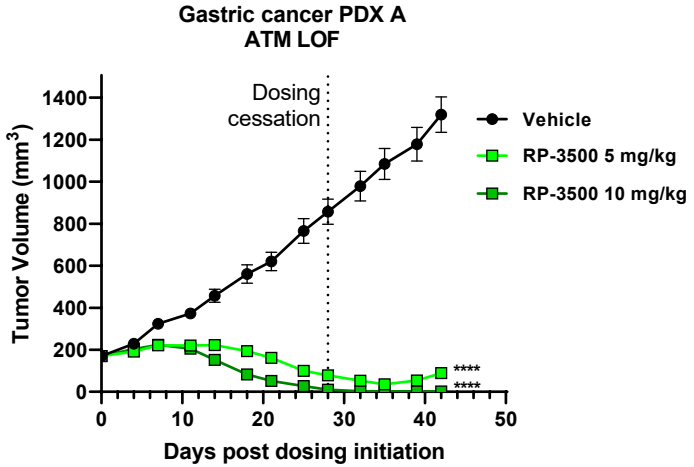
I have the following financial relationships to disclose:

- **Employee of:** University of Texas MD Anderson Cancer Center, where I am Medical Director of the Institute for Applied Cancer Science, which has a commercial interest in DDR and other inhibitors.
- **Grant/Research support (to Institution) from:** Repare, AstraZeneca, Artios, Bayer, Beigene, BioNTech, BMS, Clovis, Constellation, Cyteir , Eli Lilly, EMD Serono, Forbius, F-Star, Artios, GlaxoSmithKline, Genentech, Haihe, ImmuneSensor, Ionis, Ipsen, Jounce, Karyopharm, KSQ, Kyowa, Merck, Novartis, Pfizer, Ribon Therapeutics, Regeneron, Rubius, Sanofi, Scholar Rock, Seattle Genetics, Tesaro and Vivace.
- **Consultant for:** Repare, AstraZeneca, Almac, Aduro, Artios, Athena, Atrin, Axiom, Bayer, Bristol Myers Squibb, Calithera, Clovis, Cybrexa, EMD Serono, F-Star, GLG, Guidepoint, Ignyta, I-Mab, ImmuneSensor, Jansen, Merck, Pfizer, Roche, Schrodinger, Seattle Genetics, Varian, Zai Labs and ZielBio
- **Stockholder in:** Seagen
- **I will discuss the following off label use and/or investigational use in my presentation:** RP-3500

REPARE THERAPEUTICS

RP-3500: a potential best-in-class, highly selective inhibitor of ATR kinase





ATR inhibition is synthetically lethal with genomic alterations affecting DNA damage response

- ATR is a key mediator of cellular DNA damage response (DDR) and is activated in response to DNA replication stress
- A genome-wide CRISPR-based screening platform identified multiple synthetic lethal genomic alterations that predict for sensitivity to RP-3500 (STEP^2* genes)
  - ATM, ATRIP, BRCA1/2, CHEK2, CDK12, CHTF8, FZR1, MRE11, NBN, PALB2, RAD17, RAD50, RAD51B/C/D, REV3L, RNASEH2A/B, SETD2

*STEP^2 = SNIPRX** targeted expansion of patient populations
**SNIPRx = SyNthetic lethal Interactions for Precision Rx

RP-3500 is a potent and highly selective inhibitor of ATR

- Low nanomolar potency in biochemical (1.0 nM) and cell-based assays (0.33 nM)
- >2,000-fold selectivity over ATM, DNA-PK and PI3Ka
- Single agent activity in tumor models of different histologies and DDR defects

Roulston et al., ENA 2021, #PO54

REPARE THERAPEUTICS

First-in-human Phase 1/2 TRESR study 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)

Presentation of **early data** from this ongoing study:

- TRESR initiated in 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

REPARE THERAPEUTICS

Phase 1/2 TRESR: 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	31
BRCA2	13
CDK12	7
Other STEP2**	23

*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
- FZR1

REPARE THERAPEUTICS

RP-3500 MTD/RP2D established at 160mg QD, 3d on/4d off schedule

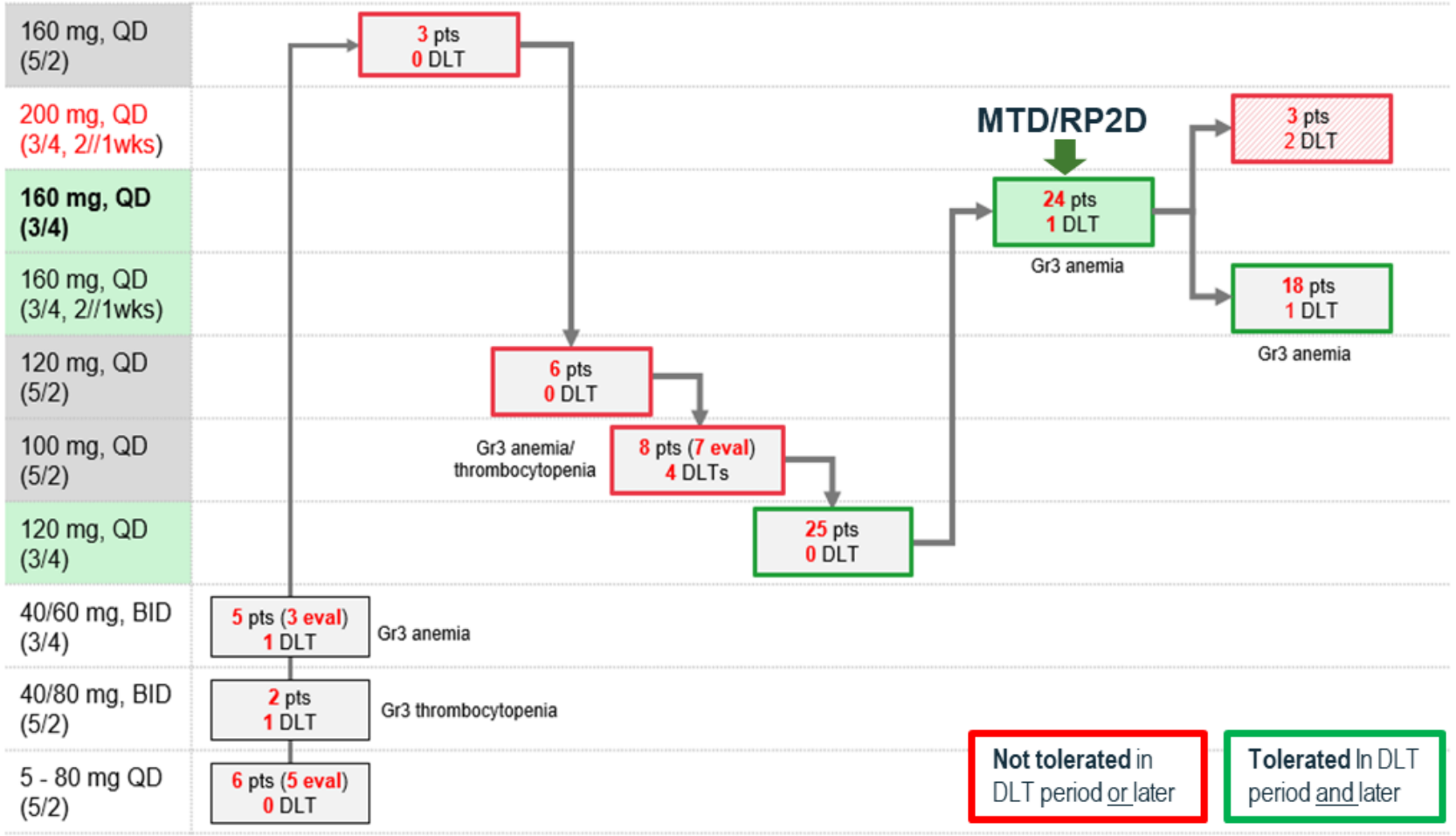
Comprehensive assessment for RP-3500 MTD/RP2D

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



REPARE THERAPEUTICS

RP-3500 treatment 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

*DLT

REPARE THERAPEUTICS

3 days on/4 days off schedule preferred

Manageable impact of on-target anemia

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

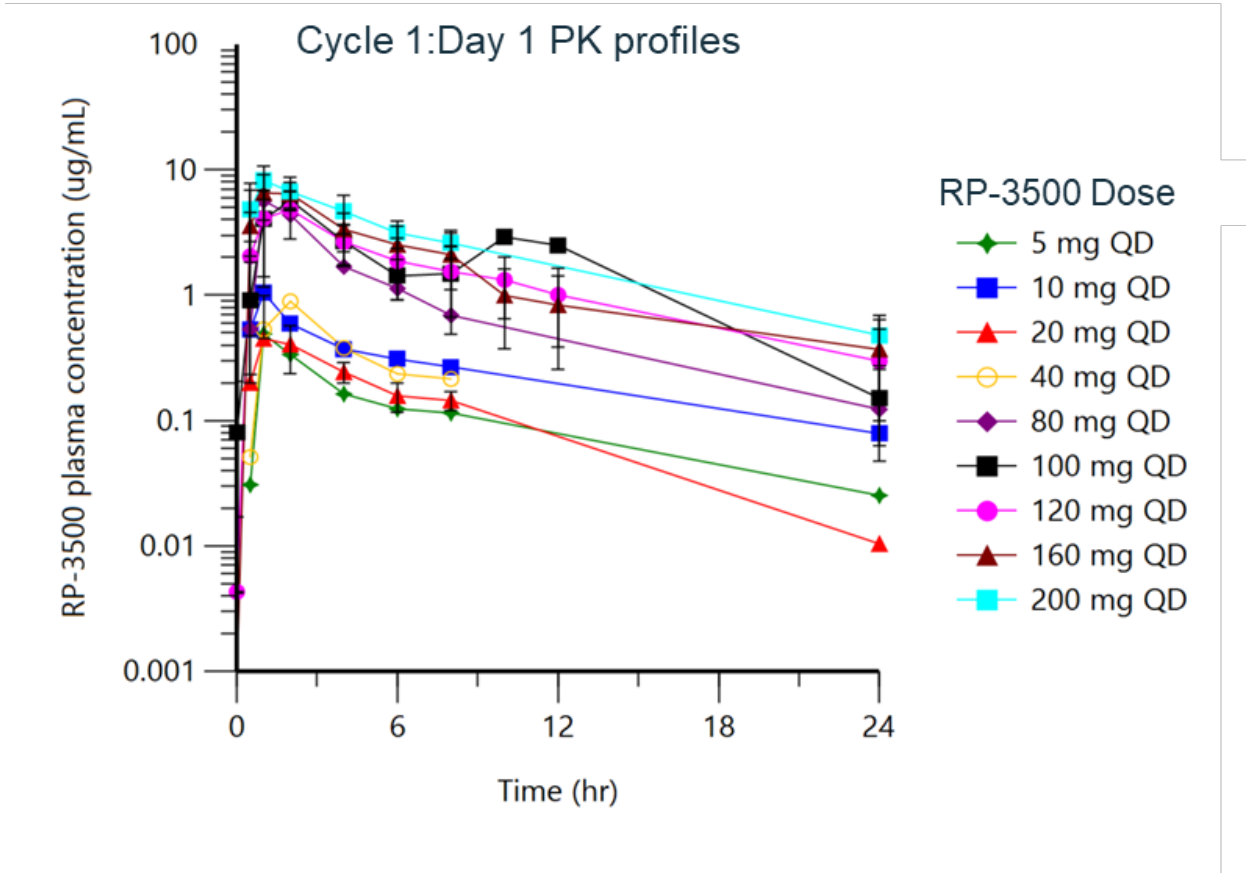
	5/2 Schedule ≥100 mg/day* (N=18)	**3/4 Schedule ≥100 mg/day* (N=75)**
# Cycles, mean (SD) [Range]	3.9 (2.62) [0, 10]	1.9 (1.72) [0, 8]
Subjects Exposed to RP-3500 n (%)		
≥1 cycle	17 (94.4%)	57 (76.0%)
≥2 cycles	14 (77.8%)	37 (48.7%)
Interruptions n (%)		
1	8 (44.0%)	16 (21.3%)
2	**2 (11.1%)**	**3 (4.0%)**
≥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

REPARE THERAPEUTICS

Pharmacokinetic profile RP-3500 exposures meet efficacy targets at ≥100mg

- **Half-life is ~ 6 hrs**
- **Linear Cmax and AUC, consistent across all doses**
- **Doses ≥100 mg QD achieve predicted efficacious RP-3500 exposures**
  - Once daily (QD) regimen selected over twice daily (BID) based on minimal differences in target coverage between these 2 regimens
  - Based on the results of the RP-3500 food effect study, RP-3500 can be given with and without food

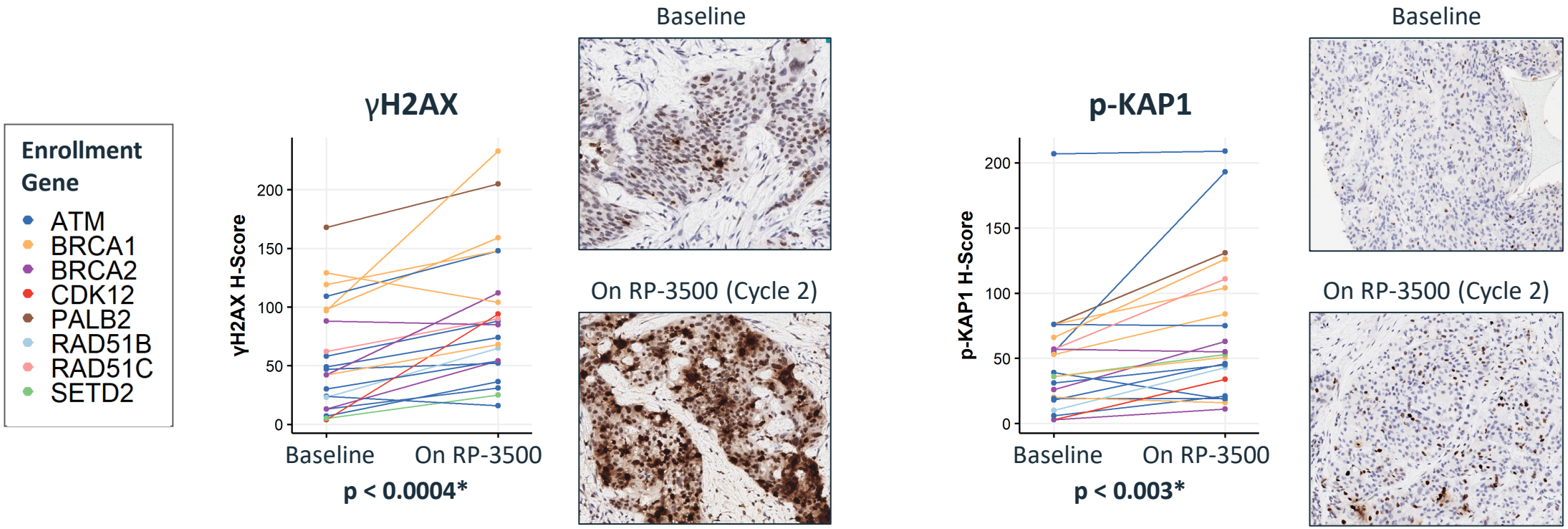


REPARE THERAPEUTICS

RP-3500 Pharmacodynamics

Robust pathway modulation in paired tumor biopsies

Consistent and statistically significant on-treatment increases
in DNA damage-induced γH2AX and p-KAP1 across tumor genotypes (N=21)



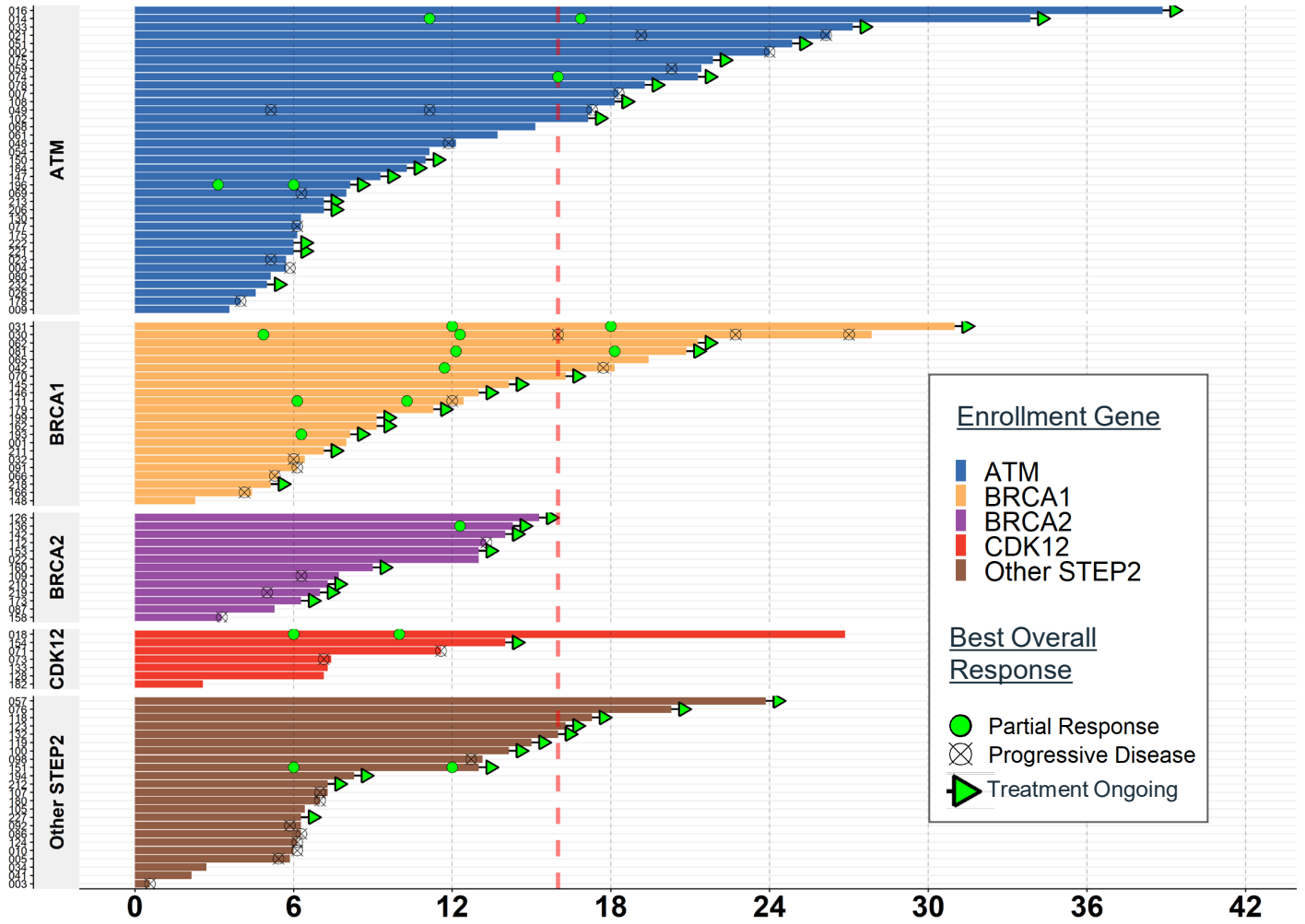
*Wilcoxon test

REPARE THERAPEUTICS

Early analysis of treatment duration

Therapy ongoing in 54* (54%) of 101 patients

- **Early analysis of therapy duration shows clinical activity across tumor types and STEP2 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)

REPARE THERAPEUTICS

Early efficacy observed with RP-3500 ≥100 mg/day

Broad spectrum of efficacy observed

- **Meaningful clinical benefit in 34 (49%) of 69 evaluable patients**
- **Across STEP2 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 and FZR1)
  - **14 patients** ongoing SD ≥ 16 weeks
  - **8 patients** <16w on study: early significant decreases in tumor markers and tumor shrinkage (<30%)
- **Late responses also observed: initial RECISTv1.1 partial response (PR) 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	2 cPR*; 1uPR **	2 cPR; 3 uPR#	4 cPR; 4uPR
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

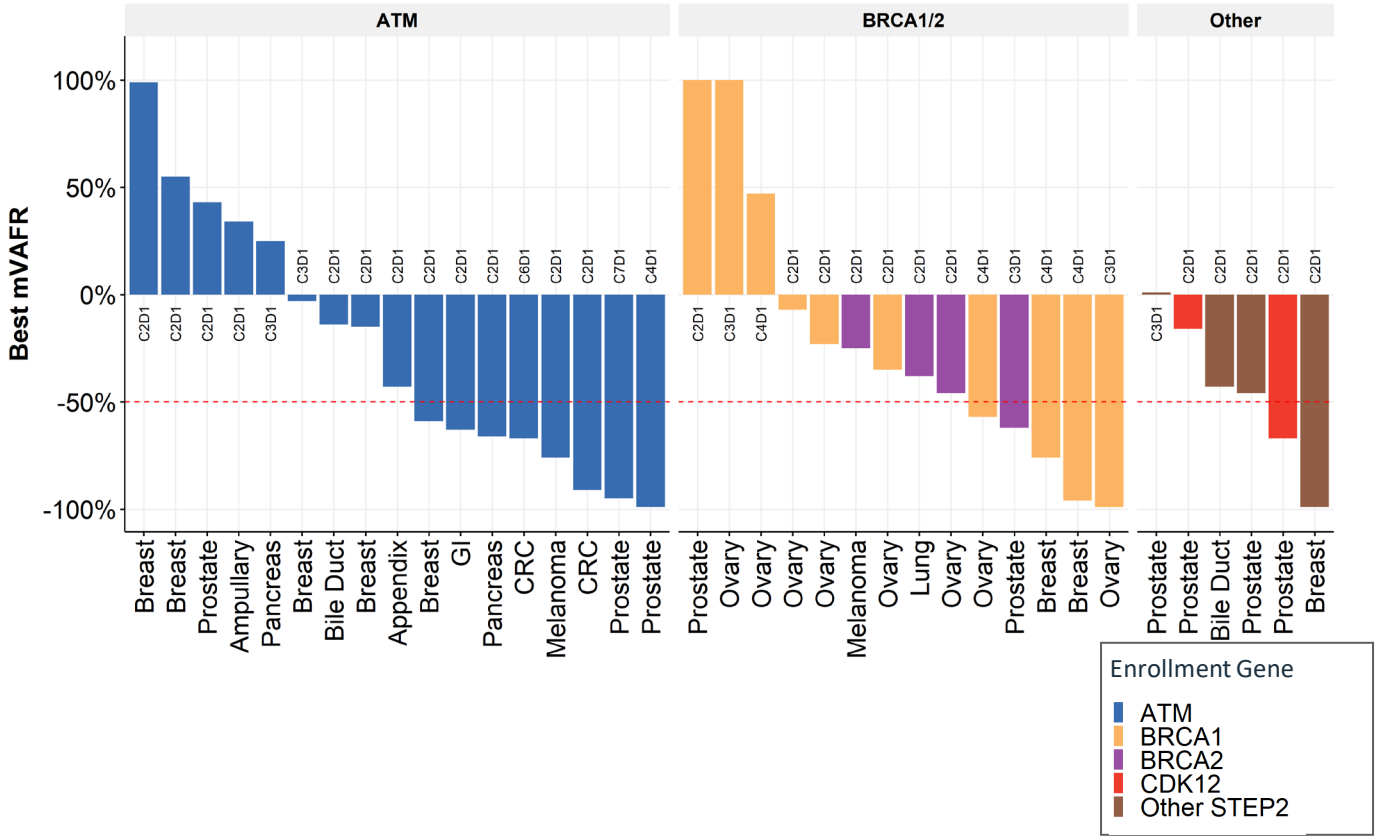
*1 patient with cPR required radiotherapy to brain lesions early in trial. No brain scan at study entry.
**Patient started on 5/2 schedule and changed to 3/4, later achieved uPR response on 3/4
#1 patient began on PARPi+RP3500 for 2 weeks, before transitioning to RP-3500 monotherapy.
& includes the SD>16w patients

REPARE THERAPEUTICS

Deep molecular responses in TRESR

Circulating tumor DNA (ctDNA) measured serially in 37 pts

- ctDNA, fragmented tumor DNA in circulating blood, may reflect the entire tumor genome as “liquid biopsies” at various time points to monitor tumor 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



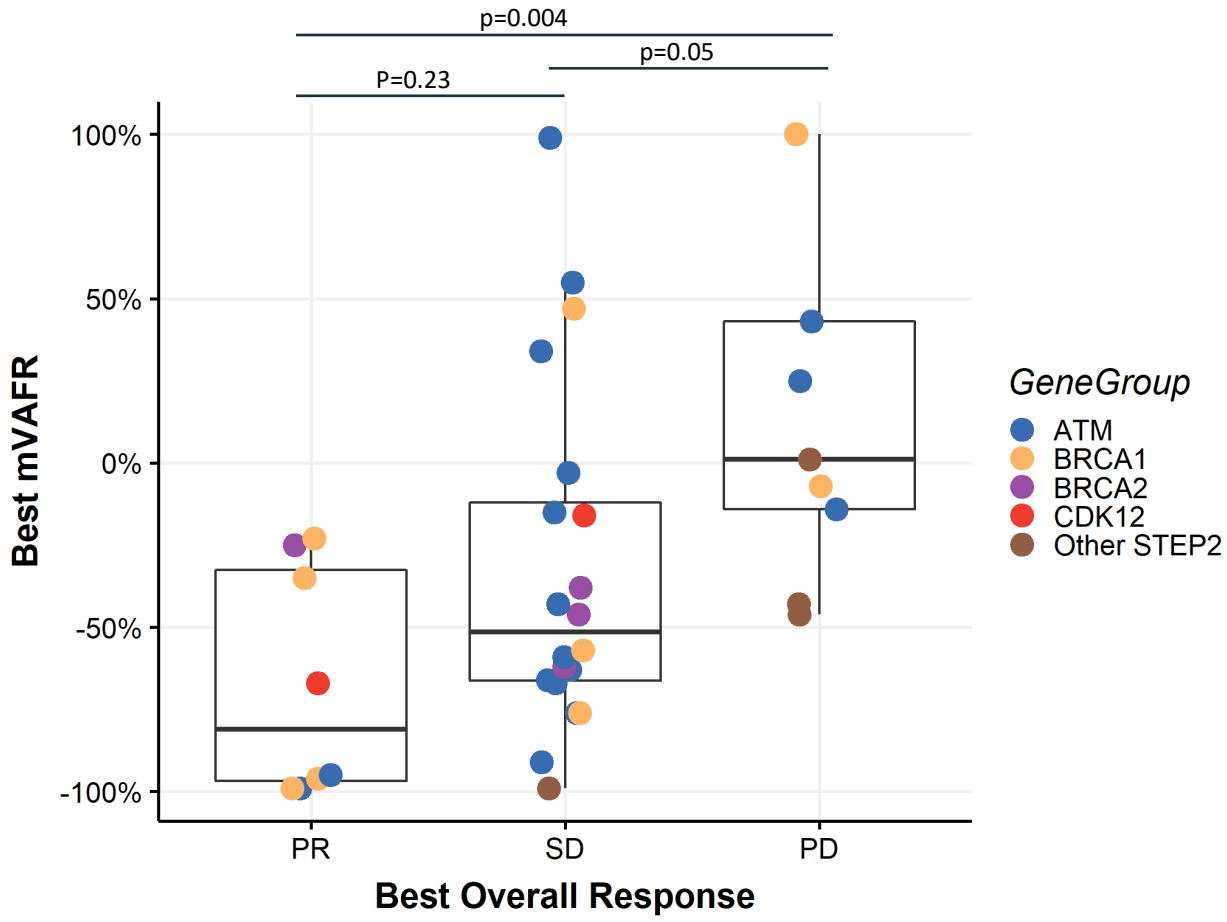
*mVAF calculated as % decrease from baseline

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

REPARE THERAPEUTICS

Preliminary analysis suggests ctDNA response may predict clinical benefit

- **RP-3500 patients with PRs showed early and frequently significant (>50%) reductions in mVAFR in ctDNA**
- **Analyses are ongoing to correlate ctDNA responses with clinical efficacy in order to evaluate the predictive power of serial ctDNA measurements**



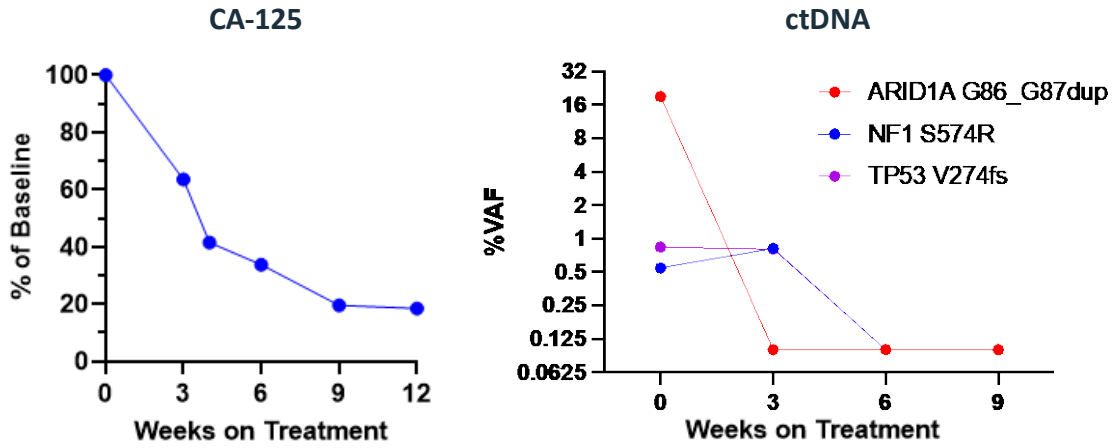
- ctDNA cohort = 37/101 enrolled patients
- mVAFR = mean variant allele frequency ratio as an indirect measure of tumor burden

REPARE THERAPEUTICS

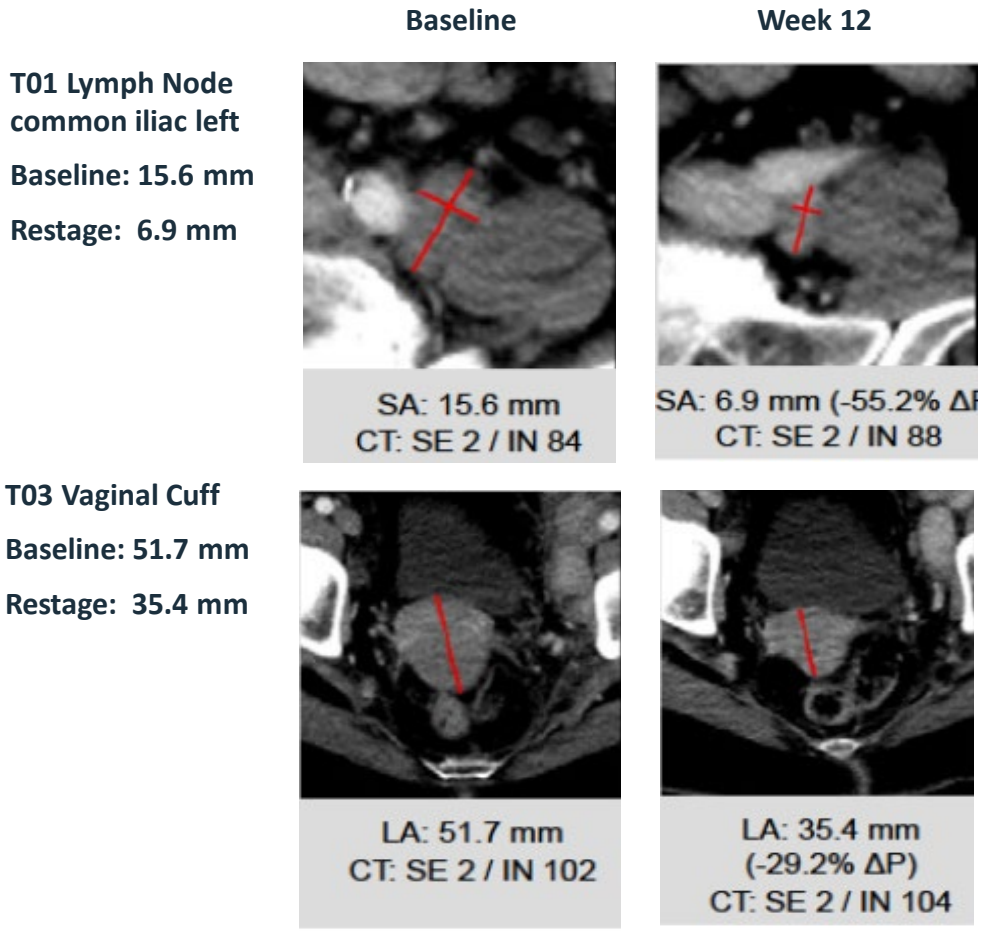
Ovarian cancer with gBRCA1 mutation

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)



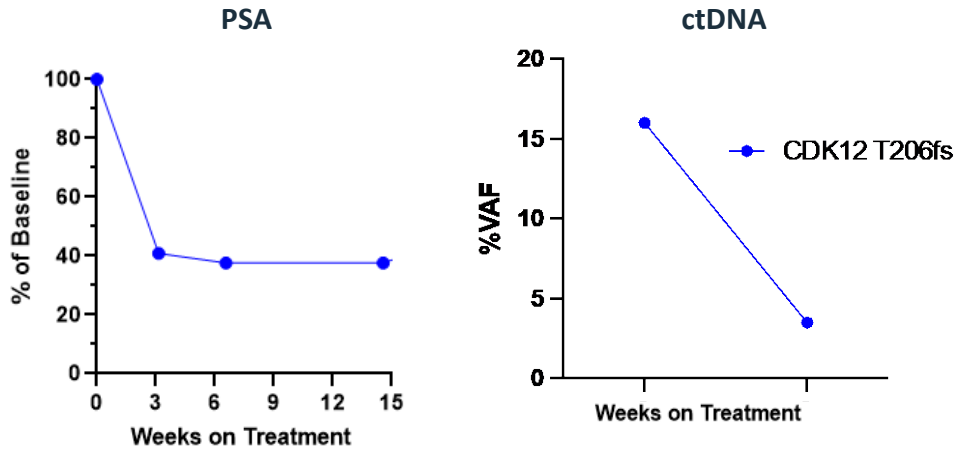
*RECISTv1.1 PR was confirmed after 15th Aug data cut

REPARE THERAPEUTICS

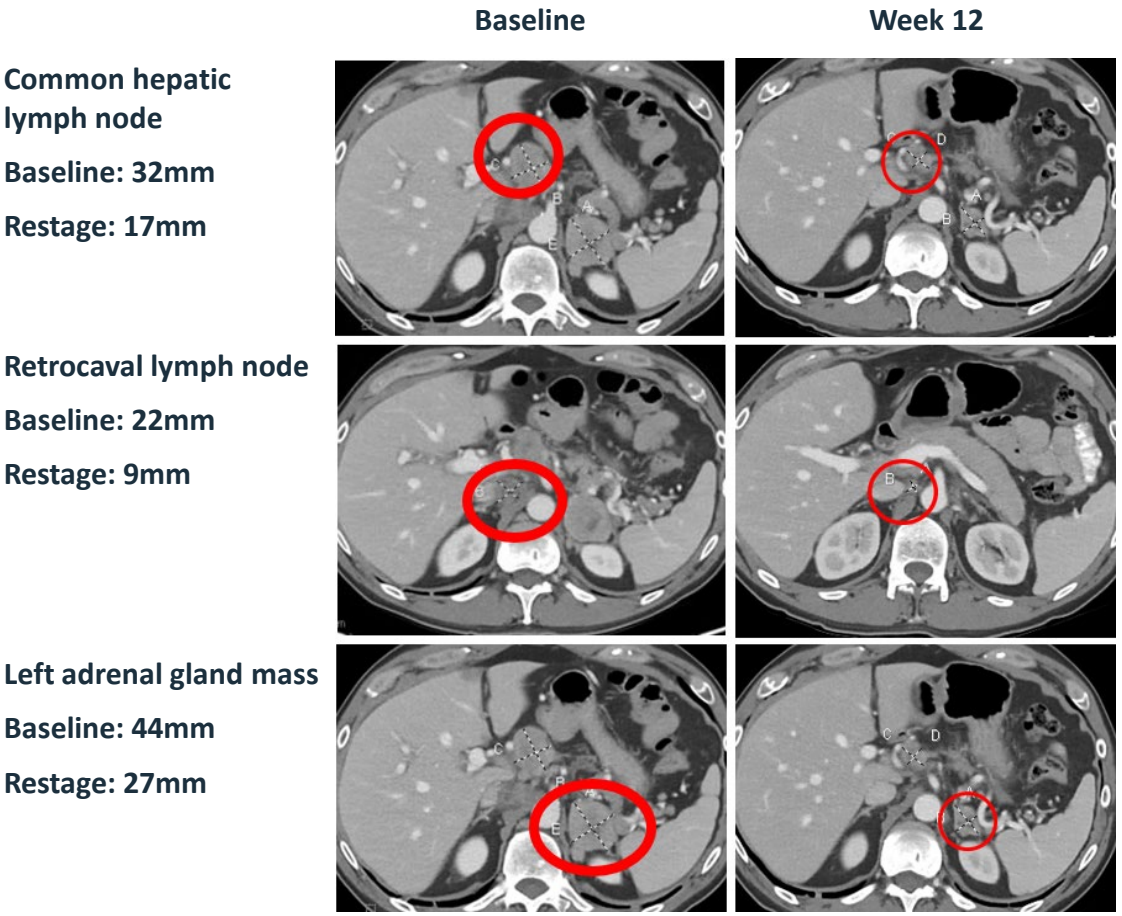
CRPC with CDK12 mutation

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



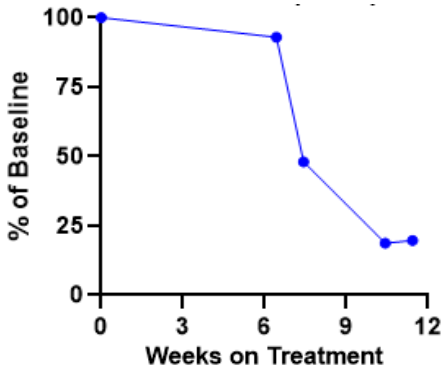
REPARE THERAPEUTICS

CRPC with ATM mutation

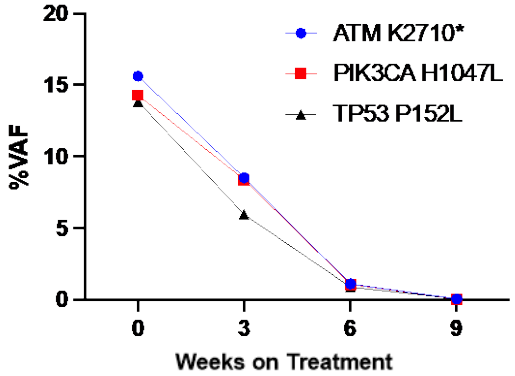
Ongoing PCWG3 PSA response

Ongoing RECISTv1.1 uPR, confirmation of response awaited

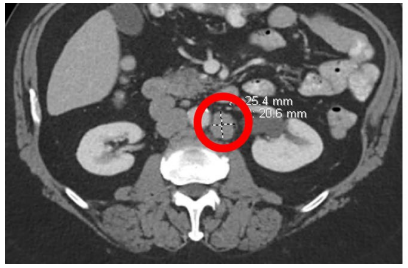
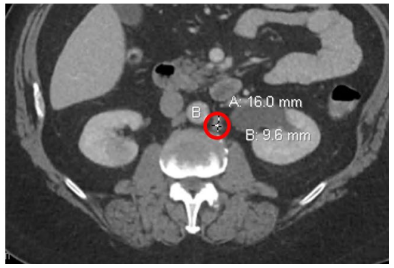
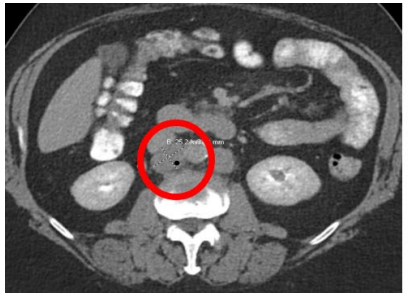
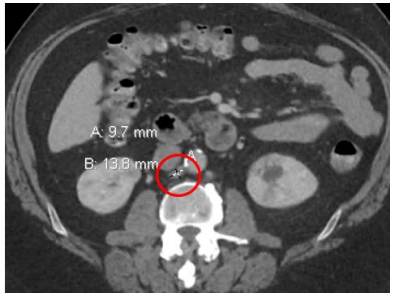
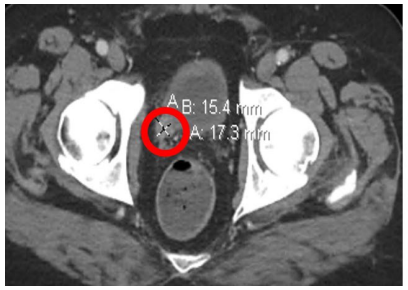
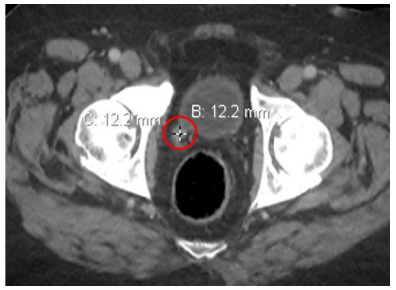
PSA



ctDNA



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

	Baseline	Week 16
Left para-aortic LN **Baseline: 21mm** **Restage: 10mm**		
Retrocaval LN **Baseline: 25mm** **Restage: 9mm**		
Right pelvic nodule along bladder wall **Baseline: 17mm** **Restage: 13mm**		

REPARE THERAPEUTICS

Summary – Early Phase 1/2 TRESR trial data

RP-3500 is safe and well tolerated, with mainly G1-2 anemia (only 21.8% G3 overall and 14.5% in chosen schedule)

- Likely off-target toxicities, e.g., fatigue or GI events, are infrequent (only up to 3% G3)

RP-3500 RP2D for further monotherapy evaluation is 160mg QD 3d on/4d off

Biomarker data confirm proof-of-mechanism across different tumors with multiple molecular backgrounds

Preliminary antitumor activity observed in patients with cancers harboring selected genomic alterations at doses ≥100mg

- **Meaningful clinical benefit in 34 (49%) of 69 patients**
  - **12 patients** with objective tumor responses:
    - 8 RECIST V1.1: cPR/uPR (7 confirmed, 1 unconfirmed)
    - 2 PCWG3 PSA responses
    - 2 GCIG CA125 responses
  - **14 patients** with ongoing RECIST v1.1 SD for at least 16 weeks
  - **8 patients** <16 weeks on study: SD with early significant decreases in tumor markers and <30% tumor shrinkage

Conclusions

RP-3500 is in development as a potent, potentially best-in-class, highly selective ATR inhibitor

The TRESR Phase 1/2 study is the largest biomarker-selected trial testing a single agent ATR inhibitor (N=101) and continues to enroll

Early TRESR data provide clinical POC and validate Repare Therapeutics' SNIPRx platform for molecular selection of tumors for ATR inhibitor therapy

Favorable and differentiated safety profile, along with promising and distinct early efficacy, offer a clear direction for further development of RP-3500

Next steps include:

- TRESR Phase 2 expansion cohorts to open imminently
- Combination studies are ongoing or will open shortly

REPARE THERAPEUTICS

Acknowledgements

The patients and their families who make this trial possible

Participating TRESR Sites for their work and contribution

Billy Hoadley; Christian Brown; Sandra Montez	University of Texas MD Anderson Cancer Center
Emily Gibson; Mary Liebers	Dana Farber Cancer Institute
Danielle McCreary	Sarah Cannon Research Institute/Tennessee Oncology
Alissa Casas, Arousiak Kazarian	Memorial Sloan Kettering Cancer Center
Paula Lee	Duke Cancer Institute
Jocelyn Hubbard	Massachusetts General Hospital
Rachael DiGiulio; Brenton Travers	Rhode Island Hospital/Lifespan
Rachel Wildman	Princess Margaret Cancer Center
Terry Wood; Sinead O'Reilly	The Christie NHS Foundation Trust
Helen Blair	Newcastle Hospital NHS Foundation Trust
Victoria Hall; Victoria Borja Bernal	Sarah Cannon Research Institute UK
Cecilia Sonander Westphal; Emma-Sofie Sønderskov Darre	Righospitalet, Denmark

Precision Oncology Decision Support (PODS) Group at the University of Texas MD Anderson Cancer Center

The Repare Clinical Study Team

Livia Gjylameti, Danielle Ulanet, Parham Nejad, Peter Manley, Marisa Wainszelbaum, Biljana Bazdar-Vinovrski, Stephanie Guerrera, Joseph O'Connell, Victoria Rimkunas, Ian Silverman, Adrian Fretland and Maria Koehler

Treximo (part of the ProPharma Group)

This Study is funded by Repare Therapeutics

REPARE THERAPEUTICS

RP-3500 next steps

REPARE THERAPEUTICS

Update on TRESR (as of Oct 6th)

Update on TRESR Module 1

Enrollment to the main component of TRESR Module 1 (RP2D determination) is closed

Recruitment to Module 1 is now closed (goal 120 pts)

Unchanged safety/tolerability profile as of Oct 6th

Update of 4 patients with uPR reported as of AACR-NCI-EORTC 2021 meeting: 3 cPR, 1 uPR

Final results of Module 1 expected to be reported in 2Q 2022 with expected 3-4 months follow up of all M1 patients

Additional Modules in TRESR anticipated to open imminently

REPARE THERAPEUTICS

Additional details on clinical responders

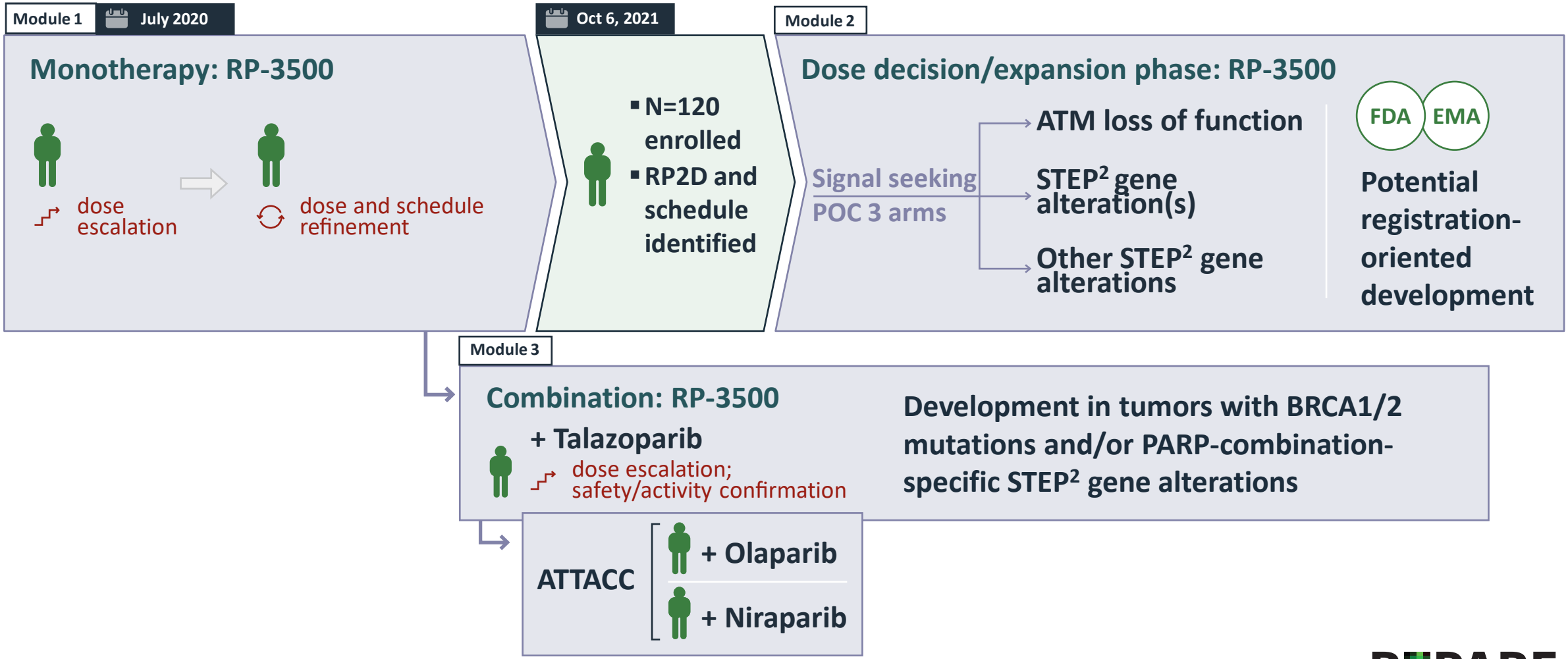
Tumor type	Genotype	Enrolled Dose Level	Schedule Modifications	Best Response (Aug 15)	Update on uPRs (Oct 6)
Prostate	**CDK12**	120 QD (5/2)	PR at 6w. Switched to 3/4 after 11w	cPR	
Ovarian	**BRCA1**	160 QD (3/4)		cPR	
Ovarian	**BRCA1**	160 QD (5/2)	Switched to 3/4 after 6w	cPR	
Breast	**BRCA1**	160 QD (3/4)		**uPR**	**Unconfirmed**
Prostate	**ATM**	120 QD (5/2)	Switched to 3/4 after 7w	**uPR**	**Confirmed**
Ovarian	**BRCA1**	120 QD (3/4)*	Switched to monotherapy after 2w	cPR	
Melanoma	**BRCA2**	120 QD (3/4)		**uPR**	**Confirmed**
SCC	**BRCA1**	160 QD (3/4)		**uPR**	**Confirmed**
Prostate	**ATM**	120 QD (5/2)	Switched to 3/4 after 17w	cPSA**	
Prostate Nonmeasurable disease	**ATM**	160 QD (3/4)		cPSA	
Ovarian	**BRCA1**	120 QD (3/4)		cCA-125	
Ovarian	**RAD51C**	160 QD (3/4)		cCA-125***	

* Initial 32 weeks on talazoparib combination, 23 w on therapy
** Approx. 8 Mo on therapy (SD last scan **-26% on Sept 23rd**)
*** On-Tx 15weeks: SD **(-28.7% at last scan on 07Sep**)

REPARE THERAPEUTICS

RP-3500 clinical program as of Oct 6th

Global multicenter study designed for patients with any recurrent tumor with ATM loss or loss of any of the additional 16 STEP^2 genes



REPARE THERAPEUTICS

RP-3500 TRESR study – Updates to upcoming Module 2

Global multi-center study:

- Phase 2 study with 3 distinct arms designed to deliver PoC
- Expected 4Q 2021 start
- Results will inform discussion with the FDA/EMA on next steps

ATM loss of function

- Selected ATM LoF patients
- Less heavily pre-treated patients than in Module 1

STEP^2 gene alteration(s)

- Two STEP^2 genes
- Focused tumor population enriched for these genes

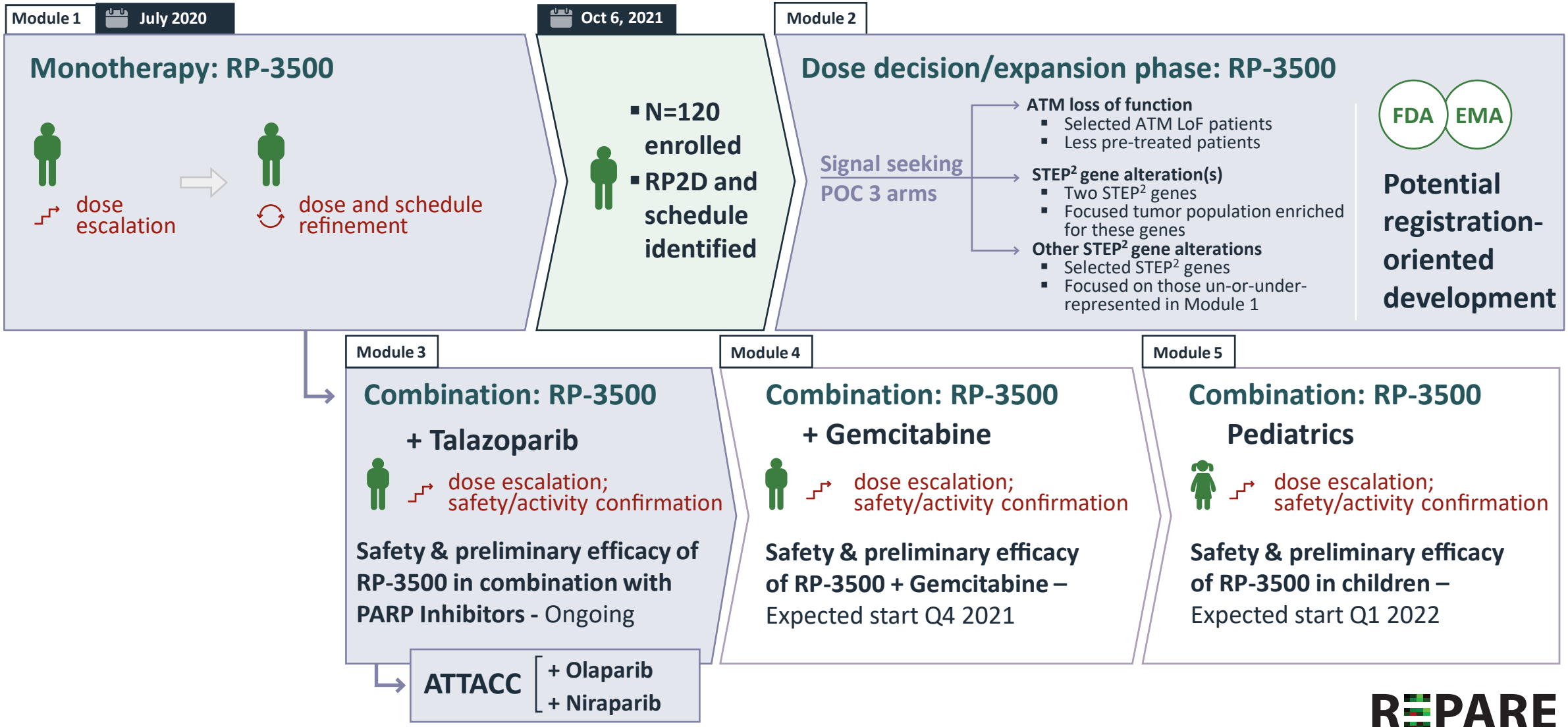
Other STEP^2 gene alteration(s)

- Selected STEP^2 genes
- Focused on those un/under-represented in Module 1

REPARE THERAPEUTICS

RP-3500 updated clinical trial program: additional modules

Trial results to date support expanded clinical development



REPARE THERAPEUTICS

RP-3500 key clinical summary

Early TRESR data provide clinical POC and validate Repare Therapeutics' SNIPRx platform

Favorable and differentiated safety profile and distinct early activity, offer a clear direction for further development

RP-3500 RP2D for further monotherapy evaluation is 160mg QD 3d on/4d off

Biomarker data confirm proof-of-mechanism across different tumors with multiple molecular backgrounds

Preliminary results observed in tumors with selected genomic alterations continue to mature

Final efficacy and safety analysis from Module 1 expected in 2Q 22

Meaningful clinical benefit in 34 (49%) of 69 patients as of 15th August**:**

- **12 patients** with objective tumor responses:
  - 8 RECIST V1.1 cPR/uPR- 1 unconfirmed PR
  - 2 PCWG3 PSA responses
  - 2 GCIG CA125 responses
- **14 patients** with ongoing RECIST v1.1 SD for at least 16 weeks
- **8 patients** <16w on study: SD with early significant decreases in tumor markers and <30% tumor shrinkage

REPARE THERAPEUTICS

Recent progress and upcoming anticipated milestones

2021				2022		
Q1	Q2	Q3	Q4	Q1	Q2	Q3
RP-3500: combined with talazoparib: M3 TRESR 1st patient ✓	RP-6306: 1st patient ✓	RP-3500: combined with olaparib or niriparib: ATTACC 1st patient ✓	RP-3500: TRESR single agent M1 early readouts ✓	RP-3500: TRESR pediatrics 1st patient	RP-3500: TRESR M1 final data	RP-3500: combined with PARPi early readouts
			RP-3500: TRESR gemcitabine 1st patient		RP-6306 early clinical readouts	
					Polθ: Initiate IND Enabling Studies	

REPARE THERAPEUTICS

Q&A Session

REPARE THERAPEUTICS