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PYNNACLE PHASE 2 TRIAL ASSESSING SELECTIVE P53 REACTIVATOR REZATAPOPT: FOCUS ON *TP53* Y220C- POSITIVE GYNECOLOGIC CANCERS

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Disclosure

	No, nothing to disclose
X	Yes, please specify:

Company Name	Consulting/ Advisory Board	Funded Research to Institution	Other (please specify)
AstraZeneca		X	
ArQule		X	
BeiGene/Springworks		X	
Black Diamond Therapeutics		X	
Boehringer Ingelheim	X	X	
Day One Biopharmaceuticals	X		
Debiopharm		X	
Elevar Therapeutics		X	
Elevation Oncology		X	
Endeavor Biomedicines	X		
Guardant	X		
Kura		X	
Lilly		X	
Mersana	X		
Merus	X	X	X (advisory role)
Northern Biologics		X	
Partner Therapeutics	X	X	
Pfizer		X	X (advisory role)
Pheon Therapeutics		X	
PMV Pharma	X	X	X (advisory role)
Relay Therapeutics	X	X	X (advisory role)
Repare Therapeutics	X	X	X (advisory role)
Revolution Medicine		X	
Schrodinger			X (advisory role)
Surface Oncology		X	
Transcode Therapeutics	X		

This clinical trial is sponsored by PMV Pharmaceuticals, Inc. Rezatapopt is an investigational treatment that has not been approved by the US Food and Drug Administration, European Medicines Agency, or any other regulatory agency for the treatment of cancer.

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PYNNACLE: an ongoing global, pivotal, phase 2 multi-cohort clinical trial evaluating rezatapopt, a selective p53 reactivator, in patients with advanced *TP53* Y220C-positive solid tumors^{1,2}



PYNNACLE Pivotal Phase 2 Study Design

Patient population

- Adults aged ≥18 years^a
- Adolescents aged 12–17 years^b
- Locally advanced or metastatic solid tumors, excluding primary CNS tumors
- Documented *TP53* Y220C and *KRAS* wildtype only (no *KRAS* SNV mutations)^c
- Prior standard therapy or ineligible for appropriate SOC therapy

**Basket
N≈200**

**Patient cohorts
defined by tumor
type**

**Rezatapopt
2000 mg QD
with food**

Cohort 1: Ovarian cancer



Cohort 2: Lung cancer



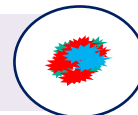
Cohort 3: Breast cancer



Cohort 4: Endometrial cancer



Cohort 5: All other solid tumors



Endpoints

Primary: ORR per BICR

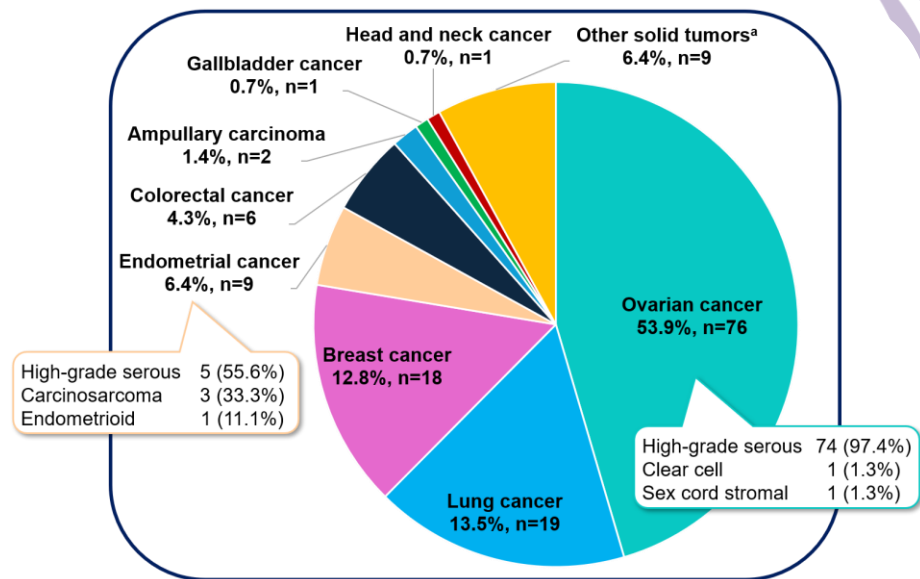
- Ovarian cancer cohort
- Across all cohorts

Key Secondary:

- ORR per investigator
- TTR
- DOR
- DCR
- PFS per BICR and investigator
- OS
- Safety

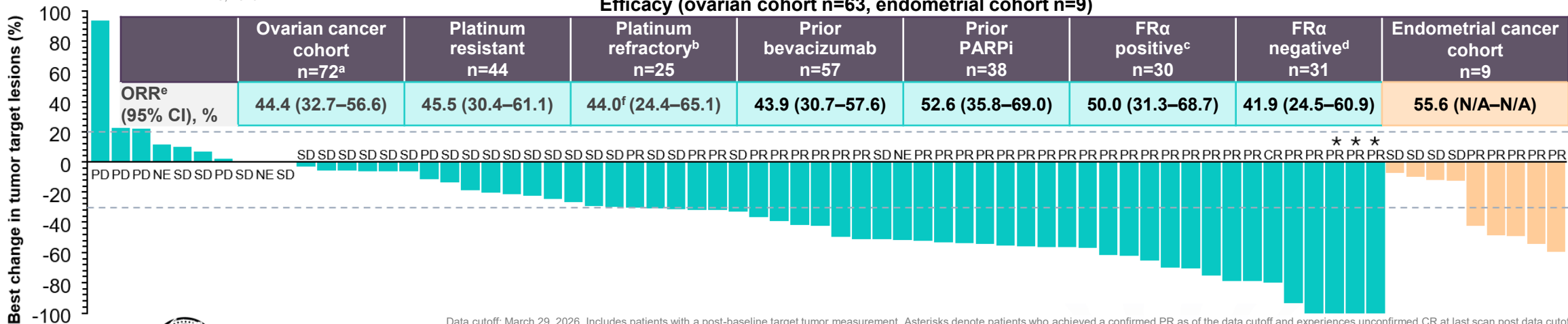
Rezatapopt shows single-agent efficacy in heavily pretreated patients with *TP53* Y220C-positive advanced gynecological cancers

	Ovarian Cancer cohort, n=76	Endometrial Cancer cohort, n=9
Age, median (min–max), years	66 (46–91)	70 (62–74)
ECOG performance status, n (%)		
0/1	36 (47)/40 (53)	5 (56)/4 (44)
Prior lines of systemic therapy		
Median (min–max)	4 (1–10)	2 (0–7)
Prior bevacizumab, n (%)	61 (80)	N/A
Platinum status, n (%)		
Sensitive/resistant /refractory	3 (4)/46 (61)/27 (36)	N/A
Primary platinum refractory	10 (13)	
FRα status, n (%)	n=63	
Positive/negative	30 (48)/33 (52)	N/A
BRCA 1/2 mutation, n (%)	7 (9)	
Somatic/germline	3 (4)/4 (5)	N/A
HRD status, n (%)	n=67	
Positive/negative	27 (40)/40 (60)	N/A
MMR status, n (%)		n=7
pMMR/dMMR	N/A	0/7 (100)
Microsatellite status,	n=53	n=8
MSI/MSS	0/53 (100)	0/8 (100)



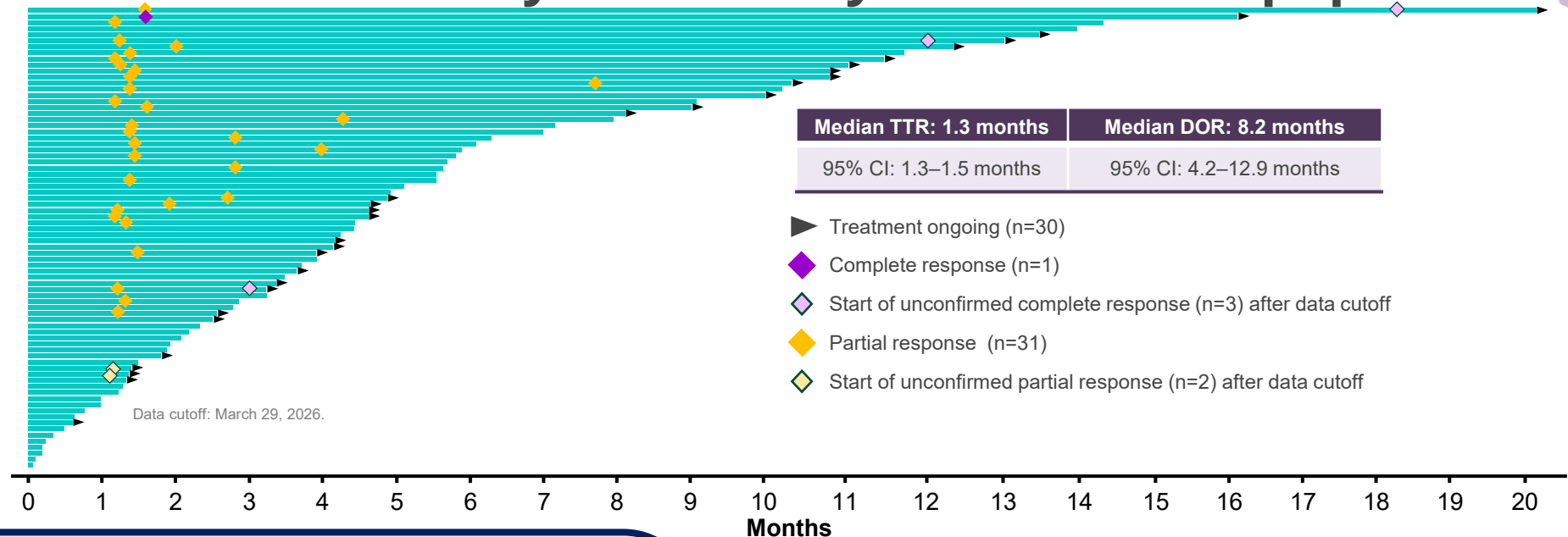
Data cutoff: March 29, 2026.

Efficacy (ovarian cohort n=63, endometrial cohort n=9)



Data cutoff: March 29, 2026. Includes patients with a post-baseline target tumor measurement. Asterisks denote patients who achieved a confirmed PR as of the data cutoff and experiences unconfirmed CR at last scan post data cutoff. ^a Patients with the opportunity to reach first post-baseline scan. Patients discontinuing before the first post-baseline scan are included in the efficacy-evaluable population. ^b Platinum refractory: relapse during platinum therapy or within 1 month of the last dose of a platinum agent. ^c FRa positive: FRa expression ≥75% viable tumor cells. ^d FRa negative: FRa expression <75% viable tumor cells. ^e ORR is calculated from confirmed CR and confirmed PR. Two patients have experienced unconfirmed PRs post data cutoff at their first scans (34/74 [45.9%]). The first patient is platinum refractory, received prior bevacizumab, received prior PARPI, and has unknown FRa status. The second patient is platinum refractory, received prior bevacizumab, received prior PARPI, and is FRa negative ^f. In the primary platinum-refractory population (n=10), 3 patients experienced a confirmed PR as of March 29, 2026. *BRCA*, breast cancer gene; CR, complete response; dMMR, DNA mismatch repair deficiency; ECOG, Eastern Cooperative Oncology Group; FRa, folate receptor alpha; HRD, homologous recombination deficiency; MSI, microsatellite instability; MSS, microsatellite stability; N/A, not available; NE, non-evaluable; ORR, overall response rate; PD, progressive disease; pMMR, proficient DNA mismatch repair; PR, partial response.

Rezatapopt displays rapid/durable responses in the ovarian cohort (n=76) and favorable safety/tolerability in the overall population (n=141)



- TRAEs were mostly Grade 1 or 2
- Most frequent TRAEs: nausea, fatigue, and blood creatinine increased
- Laboratory abnormalities were manageable/monitorable, and most cases were transient and reversible
- A similar safety profile was observed in patients with ovarian and endometrial cancers
- 7/141 patients (5.0%) discontinued treatment due to TRAEs, including 4 patients with ovarian cancer and 1 patient with endometrial cancer

Total safety population patients (n=141), n (%)		Maximum CTCAE grade ^a				
Preferred term	Any grade	1	2	3	4	
Nausea	59 (41.8)	41 (29.1)	18 (12.8)	–	–	
Fatigue	36 (25.5)	15 (10.6)	20 (14.2)	1 (0.7)	–	
Blood creatinine increased	31 (22.0)	10 (7.1)	19 (13.5)	2 (1.4)	–	
ALT increased	26 (18.4)	11 (7.8)	5 (3.5)	8 (5.7)	2 (1.4)	
Anemia	26 (18.4)	7 (5.0)	11 (7.8)	8 (5.7)	–	
AST increased	26 (18.4)	12 (8.5)	5 (3.5)	8 (5.7)	1 (0.7)	
Vomiting	24 (17.0)	16 (11.3)	8 (5.7)	–	–	
Decreased appetite	18 (12.8)	12 (8.5)	6 (4.3)	–	–	
Diarrhea	16 (11.3)	14 (9.9)	1 (0.7)	1 (0.7)	–	
Pruritus	15 (10.6)	10 (7.1)	5 (3.5)	–	–	
Asthenia	13 (9.2)	6 (4.3)	7 (5.0)	–	–	
Constipation	10 (7.1)	9 (6.4)	1 (0.7)	–	–	
Platelet count decreased	10 (7.1)	4 (2.8)	2 (1.4)	2 (1.4)	2 (1.4)	
Headache	8 (5.7)	5 (3.5)	2 (1.4)	1 (0.7)	–	
Rash maculopapular	8 (5.7)	1 (0.7)	3 (2.1)	4 (2.8)	–	

Conclusions

- In this interim analysis of the PYNNAACLE Phase 2 clinical trial, single-agent rezatapopt showed clinically meaningful efficacy and a manageable safety profile in heavily pretreated patients with *TP53* Y220C-positive advanced ovarian and endometrial cancers
 - Overall response rates were 44.4% (ovarian; n=72) and 55.6% (endometrial; n=9)
 - Median duration of response in the ovarian cohort was 8.2 months (95% CI: 4.2–12.9 months)
 - Low discontinuation rate due to a TRAE among all patients (5.0%), including 4 in the ovarian cohort and 1 in the endometrial cohort
- Rezatapopt offers a promising orally-administered, chemotherapy-free, targeted monotherapy for patients with gynecologic cancers harboring a *TP53* Y220C mutation

The PYNNAACLE Phase 2 clinical trial is ongoing
in patients with *TP53* Y220C-positive tumors



For a full list of trial sites and investigators, please
scan the QR code or visit pynnaclestudy.com