

KOL Webinar for Phase 1/2
PYNNAACLE study of PC14586
from the 2023 AACR-NCI-
EORTC International Conference

October 12, 2023

Disclaimer

Forward-Looking Statements

This presentation contains forward looking statements. Such statements include, but are not limited to, statements regarding our research, preclinical and clinical development activities, plans and projected timelines for PC14586, including the timing of disclosures regarding clinical data updates of its current clinical trial for PC14586, expected therapeutic benefits of PC14586 including potential efficacy and tolerability, and our pipeline programs, plans regarding regulatory filings and approvals, including initiation of the potentially pivotal Phase 2 portion of the study, ongoing safety and response rate of participants in our clinical trials, as well as the overall success of its the current and future clinical trials for PC14586, and the adequacy of the data to support its regulatory approval, and our expectations regarding the therapeutic and commercial potential of our product candidates, as well as our cash runway forecast. The words “believe,” “may,” “should,” “will,” “estimate,” “promise,” “plan”, “continue,” “anticipate,” “intend,” “expect,” “potential” and similar expressions (including the negative thereof), are intended to identify forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: our preclinical studies and clinical trials may not be successful; the U.S. Food and Drug Administration (FDA) may not agree with our interpretation of the data from clinical trials of our product candidates; we may decide, or the FDA may require us, to conduct additional clinical trials or to modify our ongoing clinical trials; we may experience delays in the commencement, enrollment, completion or analysis of clinical testing for our product candidates, or significant issues regarding the adequacy of our clinical trial designs or the execution of our clinical trials may arise, which could result in increased costs and delays, or limit our ability to obtain regulatory approval; the commencement, enrollment and completion of clinical trials and the reporting of data; the COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity; our product candidates may not receive regulatory approval or be successfully commercialized; unexpected adverse side effects or inadequate therapeutic efficacy of our product candidates could delay or prevent regulatory approval or commercialization; and we may not be able to obtain additional financing. Additional risks and uncertainties may emerge from time to time, and it is not possible for PMV Pharma’s management to predict all risk factors and uncertainties.

All forward-looking statements contained in this presentation speak only as of the date on which they were made. Other risks and uncertainties affecting us are described more fully in our filings with the Securities and Exchange Commission. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Agenda

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AACR-NCI-EORTC
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Aparna Parikh, MD

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Phase 2

Deepika Jalota, PharmD

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Q&A Session

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Panel



David Mack, PhD
President and Chief
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Aparna Parikh, MD
Director Global Cancer
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Chief Development
Officer



Leila Alland, MD
Chief Medical Officer

PMV Pharma is Harnessing the Power of p53 to Treat Cancer

PMV's lead candidate is PC14586, a first-in-class p53 Y220C reactivator
The p53 Y220C mutation, a previously undruggable target, is found in 1% of solid tumors

PC14586 has achieved clinical proof of concept with favorable safety and preliminary efficacy observed across multiple tumor types

FDA End of Phase 1 meeting confirmed the RP2D, and a path for a single arm, tumor agnostic Phase 2 study to be initiated in early 2024 and plan to file an NDA in 2026

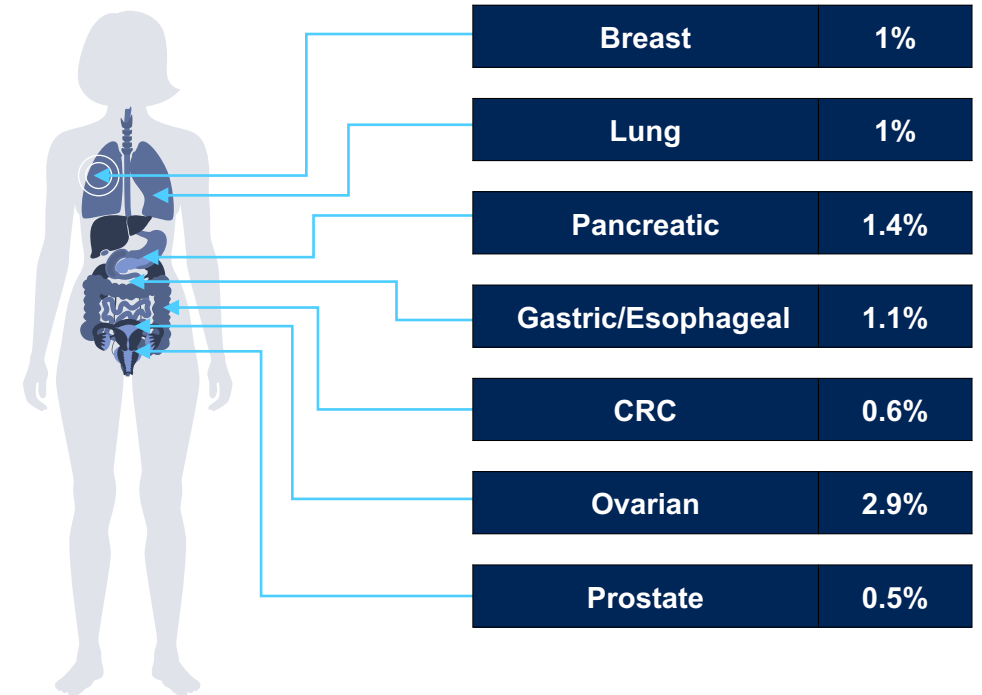
Favorable safety profile opens the opportunity to combine PC14586 with multiple standard of care regimens, including anti-PD1

Strong balance sheet ~\$219MM as of June 30, 2023 with a cash runway into year end 2025

TP53 Y220C Hotspot Mutation is Detected across Solid Tumor Types

- TP53 mutations are the most common genomic events across all human cancers¹
- Most TP53 mutations occur in the central DNA-binding domain and ten of them are referred to as 'hot-spot' mutations, accounting for ~30% of the TP53 mutations observed in human cancer¹⁻²
- p53 Y220C is a key hot-spot TP53 missense mutation that destabilizes p53^{1,3}
- p53 Y220C is present in ~1% of all solid tumors⁴

Frequency of TP53 Y220C Across Common Solid Tumors
Foundation Medicine Tissue and Heme assay test results
collected between 1/1/12 and 12/31/2020



The prevalence of TP53 Y220C across different diseases was analyzed by using the FoundationInsights® web-based software platform to query a pan-solid tumor cohort of ~367,651 US-based, consented-for-research patients in the FoundationCore® Database⁴ that received FMI's Commercial Tissue or Heme assays between 1/1/12 and 12/31/2020

CRC, colorectal cancer; DNA, deoxyribonucleic acid.

1. Baugh EH, et al. *Cell Death Differ.* 2018;25:154–160.

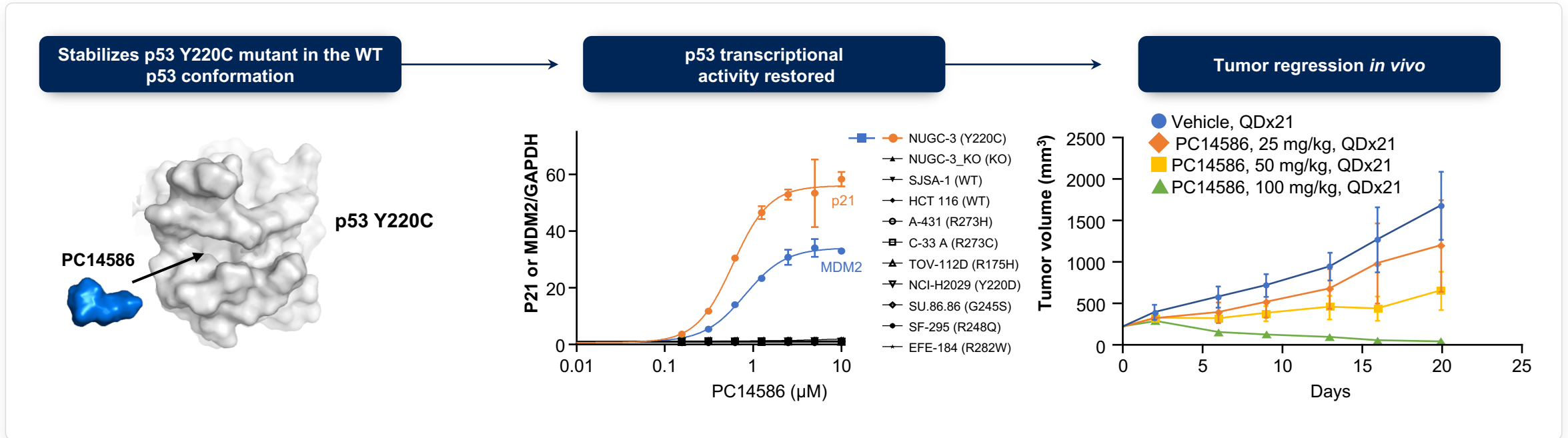
2. Roszkowska KA, et al. *Int J Mol Sci.* 2020;21:1334.

3. Bouaoun L, et al. *Hum Mutat.* 2016;37:865–876.

4. Westphalen CB, et al. *NPJ Precis Oncol.* 2021;20;5(1):69.

PC14586 is a p53 Y220C-Selective First-in-Class p53 Reactivator

- Orally available small molecule designed to selectively bind to the pocket contained in the p53 Y220C mutant protein¹
- Stabilizes the p53 Y220C mutant protein in the wild-type p53 conformation, thereby restoring transcription and tumor-suppressor function¹
- Inhibits proliferation across all Y220C-expressing cell lines; increased sensitivity to PC14586 correlates with the absence of RAS pathway mutation



PYNNACLE

BY 220C7E

Updated Phase 1 results from the PYNNACLE Phase 1/2 study of PC14586, a selective p53 reactivator, in patients with advanced solid tumors harboring a *TP53* Y220C mutation

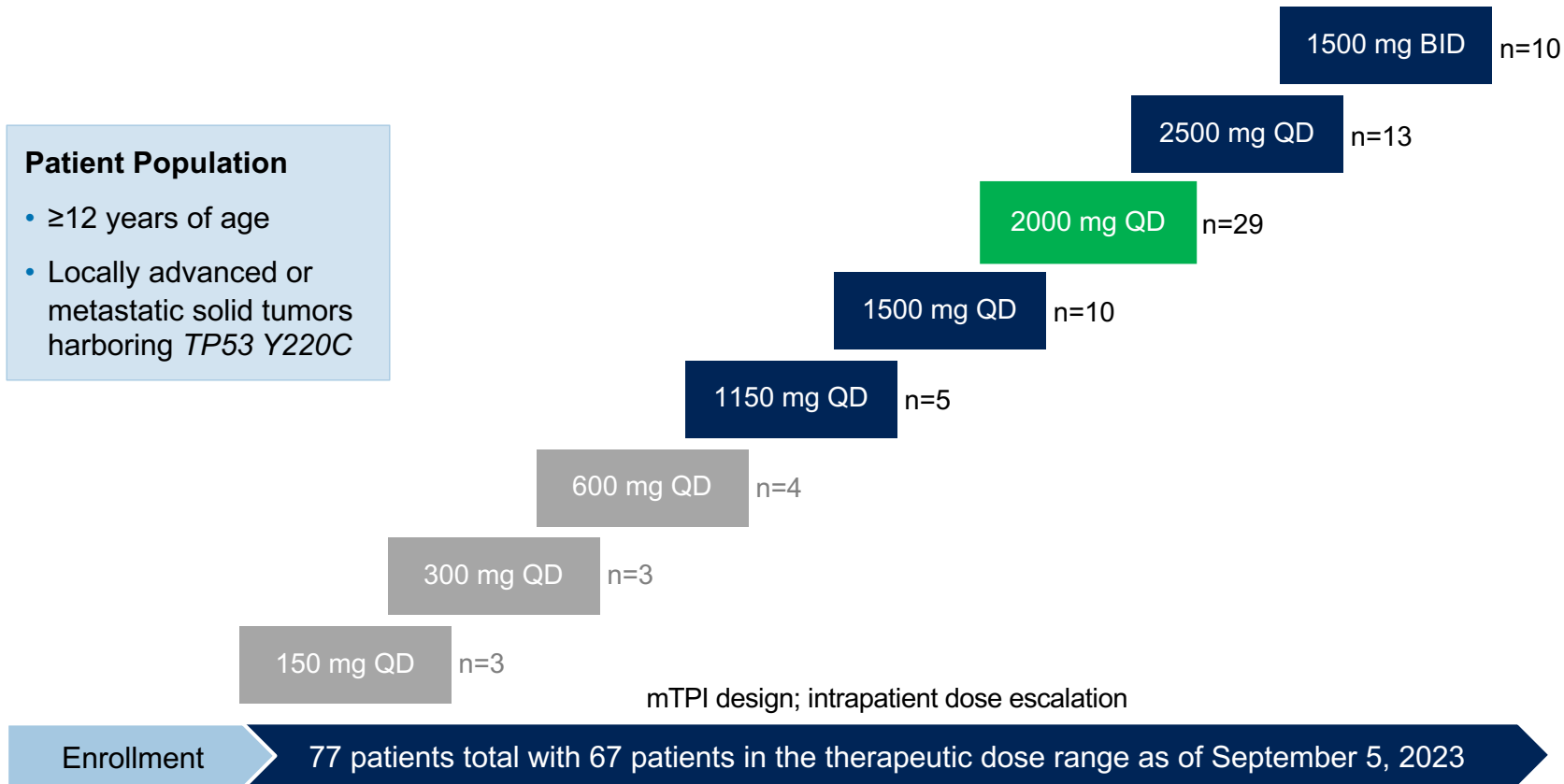


Aparna Parikh, M.D., M.S.

Director of the Global Cancer Care Program at
Mass General Hospital Cancer Center

PYNNACLE Phase 1/2 Trial – Phase 1 Study Design

Patients With Advanced Solid Tumors Harboring TP53 Y220C Mutation



Patient Population

- ≥12 years of age
- Locally advanced or metastatic solid tumors harboring TP53 Y220C

Primary objective	<ul style="list-style-type: none"> • Determine MTD, select RP2D, and evaluate safety and tolerability
Secondary objectives	<ul style="list-style-type: none"> • PK • Preliminary efficacy
Exploratory objectives	<ul style="list-style-type: none"> • Biomarkers/PD

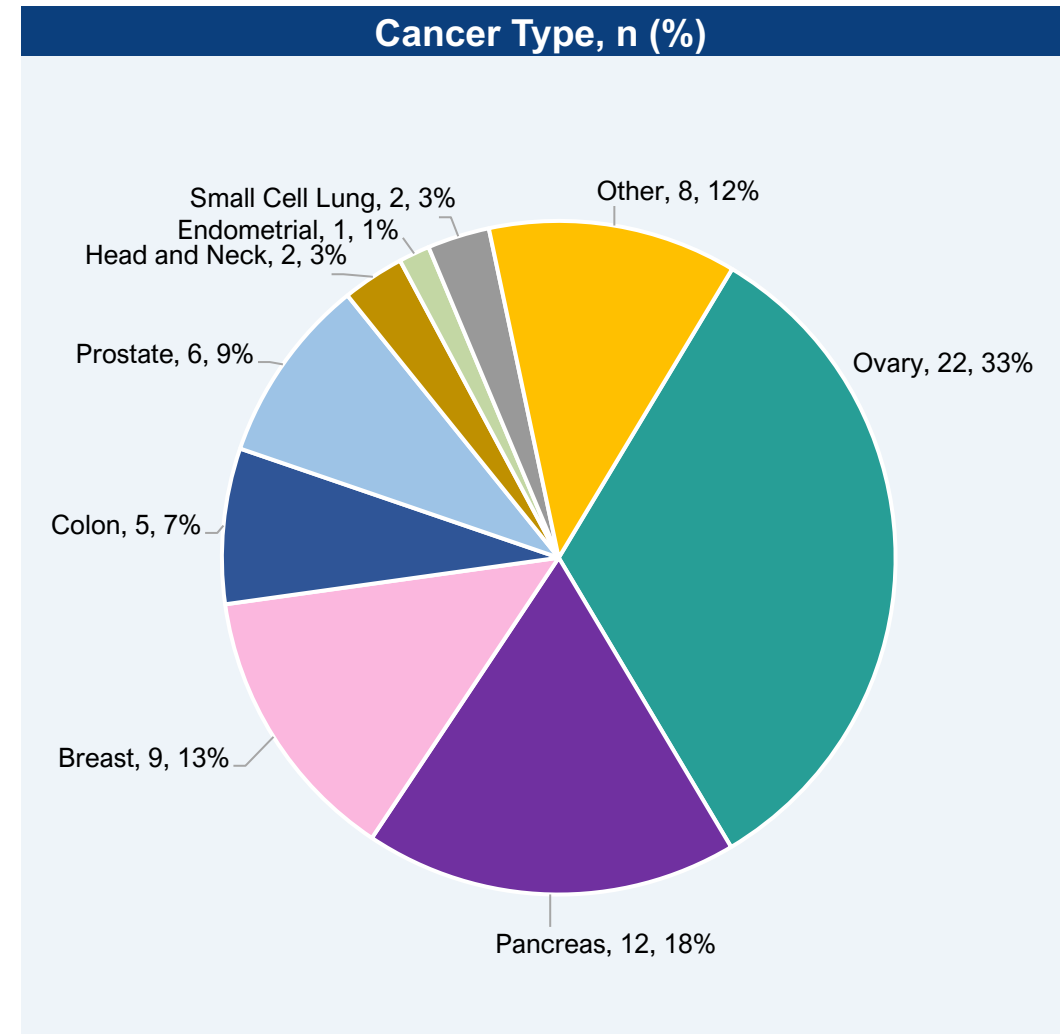
BID, twice daily; MTD, maximum tolerated dose; mTPI, modified toxicity probability interval design; QD, once daily
NCT study identifier: NCT04585750

Patient Demographics and Disease Characteristics

Efficacious dose range (1150 mg QD to 1500 mg BID)

		n=67
Age, years		
Median (min–max)		63 (32–84)
Sex, n (%)		
Female		41 (61)
Male		26 (39)
Race, n (%)		
White		51 (76)
Asian		5 (7)
Black or African American		6 (9)
Other		1 (1)
Not Reported/Unknown		4 (6)
ECOG status, n (%)		
0		22 (33)
1		45 (67)
Prior systemic therapies, n (%)		
1		6 (9)
2		19 (28)
≥3		37 (55)
Not reported		5 (6)
Median (min–max)		3 (1–9)
Germline TP53 Y220C, n (%)		
Negative		66 (99)
Positive		1 (1)
KRAS status, n (%)		
Wild type		50 (75)
KRAS Single Nucleotide Variant (SNV)		17* (25)

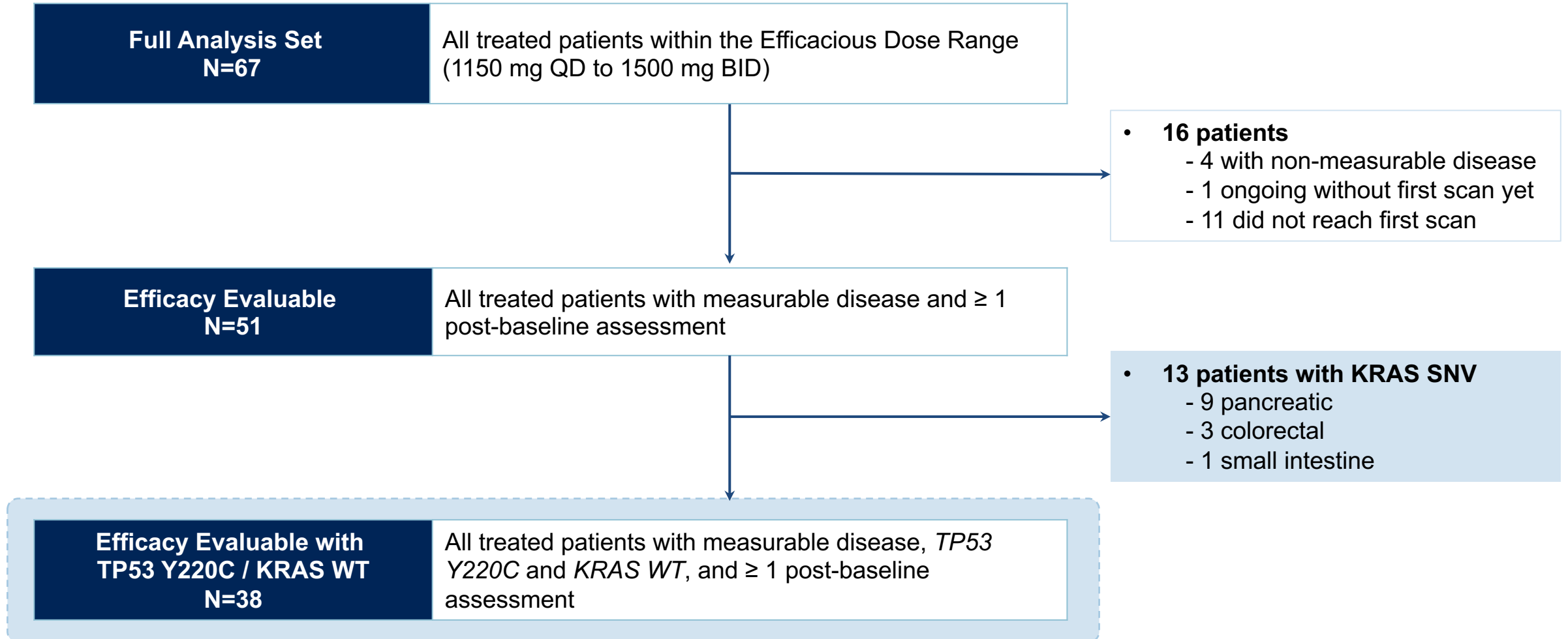
* 12 pancreas, 3 colon, 1 small intestine, 1 cholangiocarcinoma



“Other” include sarcoma, cholangiocarcinoma, esophageal cancer, gastro-esophageal cancer, germ cell tumor, pleomorphic rhabdomyosarcoma, small intestine cancer, and urothelial cancer

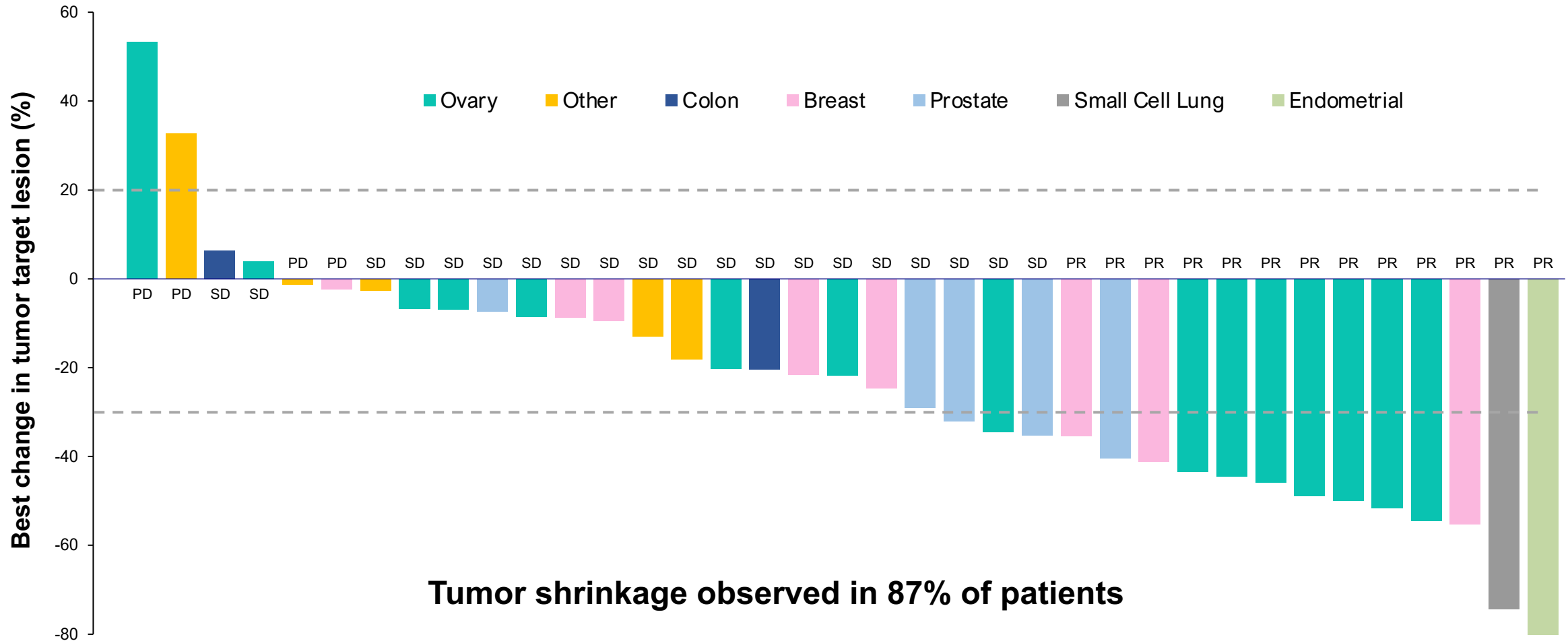
PMV-586-101 Phase 1: Efficacy Evaluable Population

Efficacious Dose Range (1150 mg QD to 1500 mg BID)



Target Lesion Reduction Across Tumor Types

Efficacious dose range TP53 Y220C / KRAS WT (1150 mg QD to 1500 mg BID)



Tumor shrinkage observed in 87% of patients

Includes patients with measurable disease at baseline and ≥ 1 post-baseline assessment. One SCLC patient without tumor measurement at 1st scan is not represented
Other tumor types include sarcoma, esophageal cancer, germ cell tumor, pleomorphic rhabdomyosarcoma, and urothelial cancer

Confirmed Responses at RP2D And Across Efficacious Dose Range In Multiple Tumor Types

TP53 Y220C / KRAS WT Patients

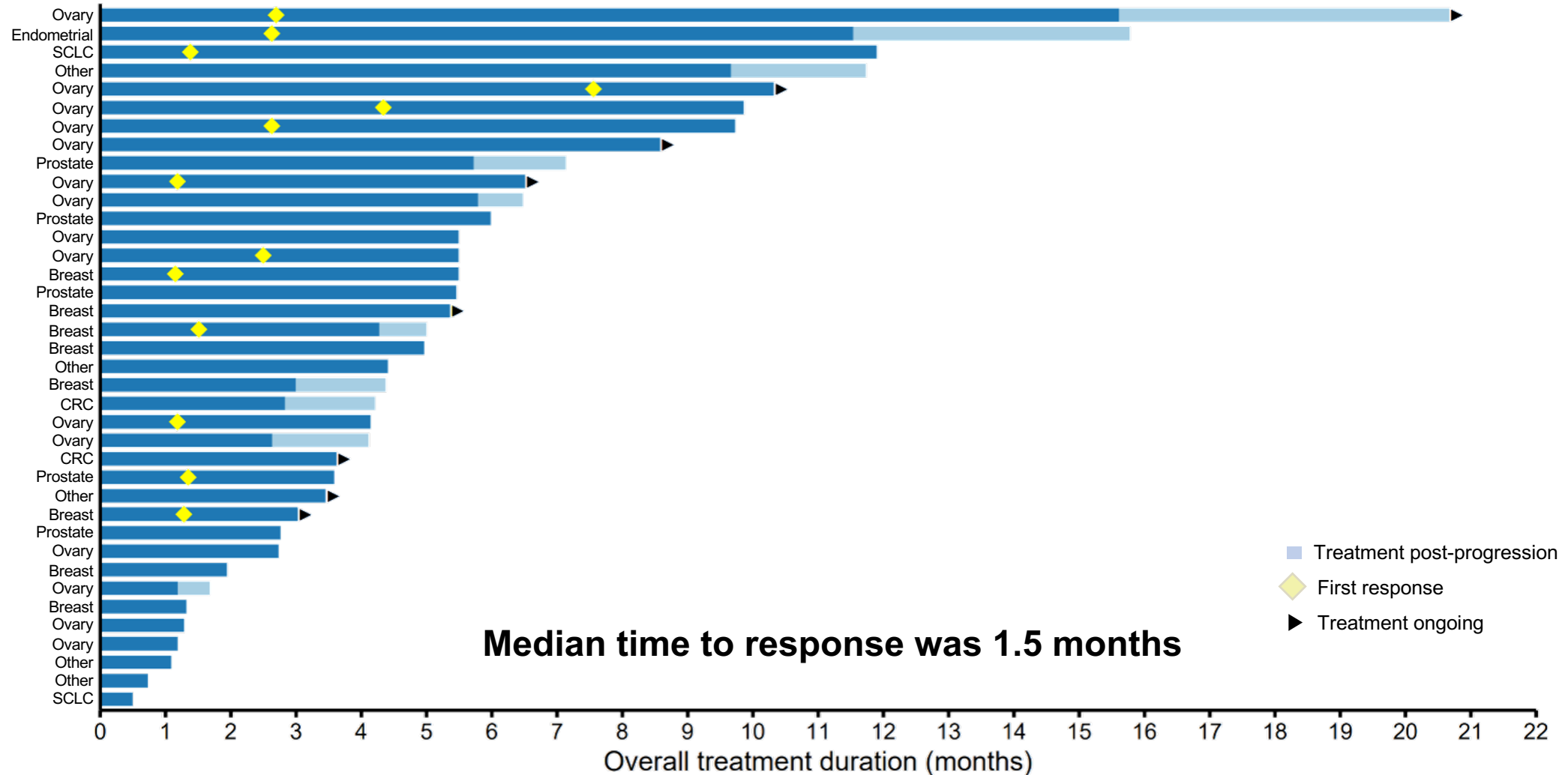
	RP2D 2000 mg QD N=16	Efficacious Dose Range 1150 mg QD – 1500 mg BID N=38
	ORR n (%)	ORR n (%)
Overall	6 (38%)	13 (34%)
Partial Response (PR)	6	13
Stable Disease (SD)	8	20
Progressive Disease (PD)	2	5

Tumor type	RP2D 2000 mg QD N=16	Efficacious Dose Range 1150 mg QD – 1500 mg BID N=38
	ORR n (%)	ORR n (%)
Ovary	2/5 (40)	7/15 (47)
Breast	2/3 (67)	3/8 (38)
Small cell lung	0/1 (0)	1/2 (50)
Endometrial	1/1 (100)	1/1 (100)
Other solid tumors	1/6 (17)	1/12 (8)

38% confirmed ORR at the RP2D
7 months median Duration of Response

Time to Response & Duration of Treatment

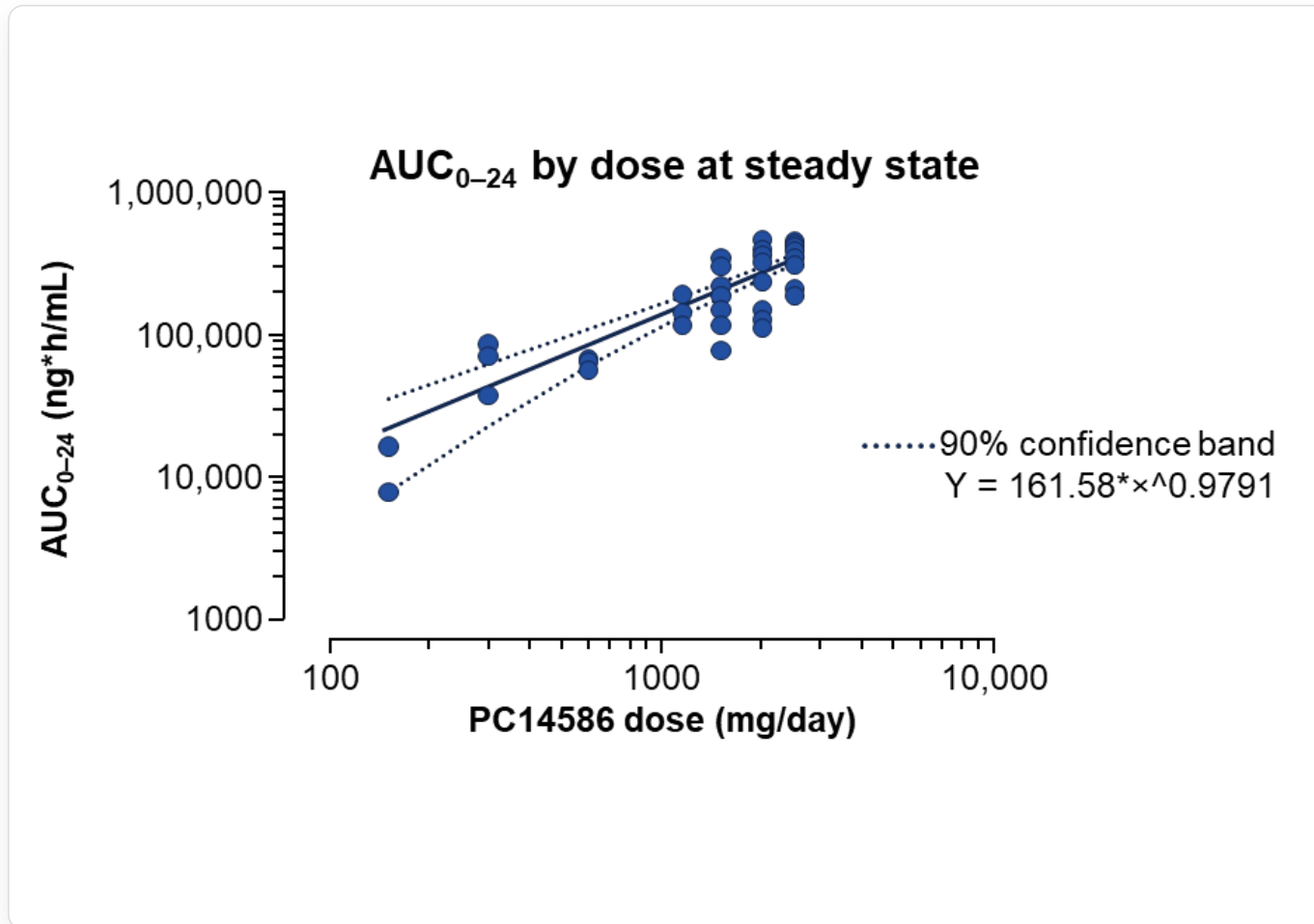
Efficacious Dose Range – TP53 Y220C/KRAS WT



Includes all patients with measurable disease at baseline, KRAS WT and ≥ 1 post-baseline assessment (n=38)

Data cut-off Sep 5, 2023

PC14586 Displays Linear and Dose Proportional PK



Median PC14586 T_{1/2} of 19 hours at steady state across all patients allowing for QD dosing

PC14586 Demonstrated a Favorable Safety Profile

Efficacious dose range (1150 mg QD to 1500 mg BID)

All TRAEs (≥ 5% of Patients) Preferred Term, n (%)	Max CTCAE				
	Overall n=67	1	2	3	4
Any TRAE	60 (89.6)	16 (23.9)	27 (40.3)	16* (23.9)	1**(1.5)
Nausea	34 (50.7)	22 (32.8)	11 (16.4)	1 (1.5)	
Vomiting	29 (43.3)	16 (23.9)	12 (17.9)	1 (1.5)	
Blood creatinine increased	18 (26.9)	10 (14.9)	8 (11.9)		
Diarrhea	13 (19.4)	12 (17.9)		1 (1.5)	
Fatigue	13 (19.4)	8 (11.9)	5 (7.5)		
ALT increased	12 (17.9)	4 (6.0)	5 (7.5)	3 (4.5)	
AST increased	11 (16.4)	7 (10.4)	2 (3.0)	2 (3.0)	
Anemia	10 (14.9)	1 (1.5)	6 (9.0)	3 (4.5)	
Decreased appetite	7 (10.4)	2 (3.0)	4 (6.0)	1 (1.5)	
Proteinuria	6 (9.0)	1 (1.5)	5 (7.5)		
Rash maculo-papular	6 (9.0)	1 (1.5)	3 (4.5)	2 (3.0)	
Headache	5 (7.5)	4 (6.0)	1 (1.5)		
Lipase increased	5 (7.5)	4 (6.0)		1 (1.5)	
Platelet count decreased	4 (6.0)	1 (1.5)	1 (1.5)	2 (3.0)	
Amylase increased	4 (6.0)	3 (4.5)	1 (1.5)		
Dehydration	4 (6.0)		4 (6.0)		

TRAEs were mostly grade 1/2

Most frequent TRAEs were nausea and vomiting which improved when PC14586 was given with food

Low rate (3%) of drug discontinuation due to a TRAE

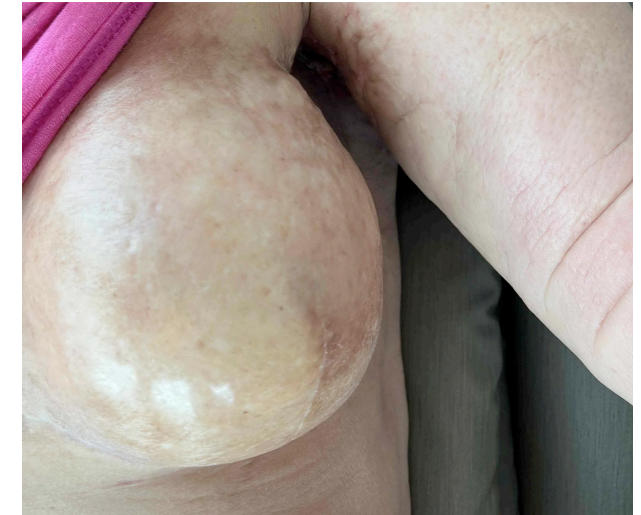
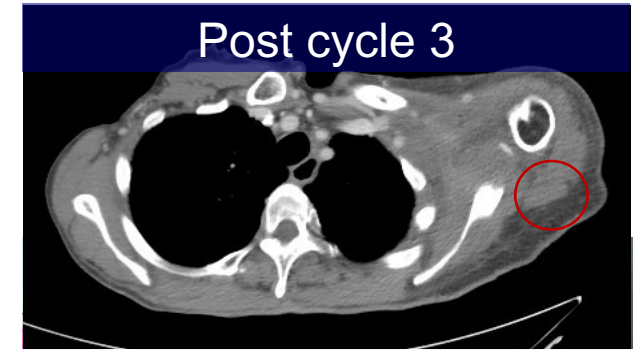
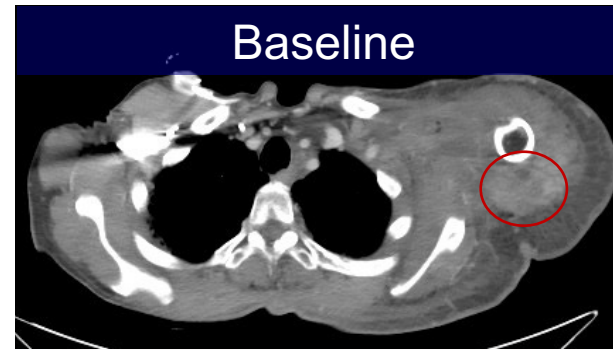
*Includes 5 additional grade 3 treatment-related adverse events: neutrophil count decreased, acute kidney injury, pancreatitis, pneumonitis, and rash erythematous

** Includes 1 patient with grade 4 immune thrombocytopenia. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; QD, once daily.

Patient with Triple Negative Breast Cancer with Rapid Onset of response

51-year-old woman with metastatic TNBC

- Prior treatment course:
 - Neoadjuvant therapy (carbo + pac + pembro followed by cp + dox + pembro)
 - Bilateral mastectomy followed by pembro maintenance, radiotherapy, and breast reconstruction
 - Pegylated liposomal doxorubicin for disease recurrence
- Progressive disease in axilla with extensive skin lesions on adjacent breast and arm, limiting mobility
- *TP53 Y220C* detected by NGS
- PC14586 2000 mg QD was started
 - Rapid, visible reduction in arm swelling and improved mobility of arm and fingers within the 1st week
 - PR at 6 weeks (41% reduction in axilla lesion) confirmed at 12 weeks and ongoing



Images courtesy of Dr. Shivaani Kummar, OHSU

carbo, carboplatin; pac, paclitaxel; pembro, pembrolizumide; cp, cyclophosphamide; dox, doxorubicin; NGS, next-generation sequencing; PR, partial response; QD, once daily; TNBC, triple negative breast cancer.

Conclusion

- PC14586 demonstrated single agent clinical efficacy in heavily pre-treated patients across multiple *TP53* Y220C and *KRAS* WT tumor types.
- A favorable safety profile was observed, with improvement in gastrointestinal adverse events when PC14586 is taken with food.
- Based on the overall data, 2000 mg QD was selected as the RP2D.
- The PYNNAACLE registrational Phase 2 trial will assess PC14586 as monotherapy at the RP2D of 2000 mg QD in patients with *TP53* Y220C mutation and *KRAS* WT advanced solid tumors.

Looking Ahead & Phase 2

Defined Registration Paths in Ovarian and Tumor Agnostic Patient Populations

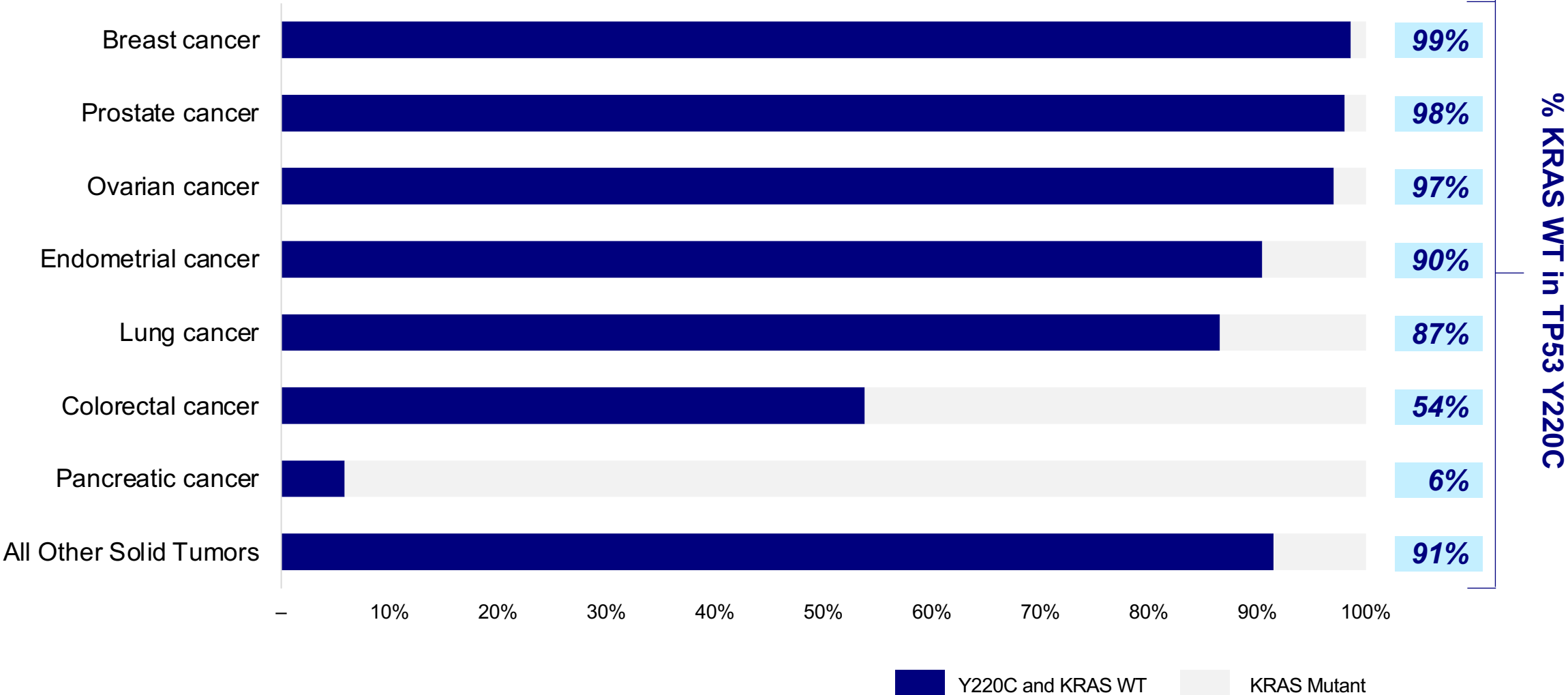
FDA alignment on RP2D, patient population and pivotal single arm Phase 2 study design obtained at EOP1 Meeting

Patient Population	Basket N = 114 PC14586 at 2000mg QD	Cohorts	
• Aged \geq 12 years		Cohort 1: Ovarian cancer	n = 42
• Locally advanced or metastatic solid tumors, excluding primary CNS tumors		Cohort 2: Lung cancer	n ~18
• Documented <i>TP53 Y220C</i> and <i>KRAS WT</i> only		Cohort 3: Breast cancer	n ~18
• Prior standard therapy or ineligible for appropriate standard of care therapy		Cohort 4: Endometrial cancer	n ~18
		Cohort 5: All other solid tumors	n ~18

Opportunity to accelerate development of specific tumor types while also pursuing a tumor-agnostic strategy






Most TP53 Y220C Patients are KRAS WT

Overall, approximately 90% TP53 Y220C patients are KRAS WT



PC14586 May Benefit 14,000+ patients/yr with solid tumors in the US

Favorable Preliminary Efficacy Relative to Standard of Care (SOC) in 2L+

Tumor Type	TP53 Y220C Frequency (%) ¹	Patients (US) TP53 Y220C / KRAS WT ^{1,2}
 All Solid Tumors	~1	14,000+
 Ovarian	2.9	1,200
 Breast	1	2,800
 Lung	1	1,800
 Endometrial	1.1	700

SOC ORR (%) all-comer, 2L+ ³⁻⁸
<15
12 (platinum-resistant)
12 (3L+, all subtypes)
<15 (NSCLC 3L) 7 (SCLC 2L)
<15 (3L)

TP53 MUTATED TUMORS
Have correlated with **poor clinical survival** and outcomes across multiple tumor types⁹⁻¹²

HIGH UNMET NEED
Phase 2 will enable the generation of additional patient data **across multiple tumor types** to support a **tumor agnostic approach**

¹ Foundation Insights, Schram *et al.* AACR-NCI-EORTC Conference 2023 ² Incidence based on Cancer Facts & Figures, 2021; Ovarian Cancer: DRG Epidemiology Report 2021 ³ Pujade-Lauraine, E. *et al.* 2014 ⁴ Cortes, J. *et al.* 2011 ⁵ Herbst, R.S. *et al.* 2016 ⁶ Fehrenbacher, L. *et al.* 2018 ⁷ O'Brien, M. *et al.* 2006 ⁸ Makker, V. *et al.* 2022 ⁹ Donehower *et al.* 2019 ¹⁰ Sadighi *et al.* 2017 ¹¹ Li *et al.* 2019 ¹² Tuna *et al.* 2019

PC14586 – Advancing to a Phase 2 Single Arm Pivotal Study



Single-agent clinical activity observed across multiple tumor types supporting continued tumor agnostic development



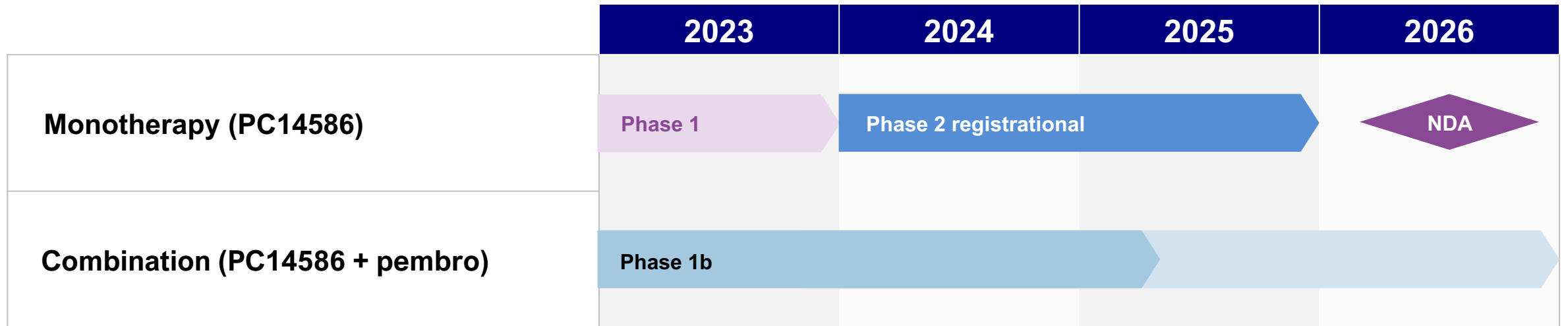
Acceptable safety profile with Grade 1 / 2 adverse events most frequently observed



Successful FDA EOP1 meeting completed in Q3 2023

Confirmed RP2D with a single-arm Phase 2 design to support a potential accelerated approval

PC14586: On a Path to NDA Submission in 2026



Key Upcoming Milestones

Program	Update	Timing
PC14586 Monotherapy	Initiate Phase 2 trial	2024
	Initial Phase 2 data	2025
	Planned NDA submission	2026
PC14586 + PD1 Combination Study	Initial Phase 1b data	2024
Cash Balance	As of June 30, 2023	\$219mm

Q&A Session