

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549**

**FORM 8-K**

**CURRENT REPORT  
Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): June 7, 2022**

**PMV Pharmaceuticals, Inc.**

(Exact name of Registrant as Specified in Its Charter)

**Delaware**  
(State or Other Jurisdiction  
of Incorporation)

**001-39539**  
(Commission  
File Number)

**46-3218129**  
(IRS Employer  
Identification No.)

**8 Clarke Drive, Suite 3,  
Cranbury, NJ**  
(Address of Principal Executive Offices)

**08512**  
(Zip Code)

**Registrant's Telephone Number, Including Area Code: (609) 642-6670**

**Not Applicable**  
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.00001 par value per share	PMVP	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 7.01 Regulation FD Disclosure.**

On June 7, 2022, on behalf of PMV Pharmaceuticals, Inc. (the "Company"), Ecaterina Ileana Dumbrava, M.D., Assistant Professor of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center delivered a scientific presentation at the 2022 American Society of Clinical Oncology ("ASCO") Annual Meeting announcing the initial results from the Company's ongoing Phase 1/2 PYNNAACLE study of PC14586 in patients with advanced solid tumors harboring a p53 Y220C mutation. The initial results demonstrated anti-tumor activity across multiple tumor types with an acceptable safety profile. On June 7, 2022, the Company also issued a press release and held an investors conference call via webcast regarding its initial results from the ongoing Phase 1/2 PYNNAACLE study of PC14586.

A copy of the press release and the ASCO investors presentation (the "ASCO Investors Presentation") are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K.

The information in this Item 7.01 of this Form 8-K, including the attached Exhibits 99.1 and 99.2 to this report, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing, whether made before or after the date hereof, regardless of any general incorporation language in such a filing.

The press release attached as Exhibit 99.1 and the ASCO Investors Presentation attached as Exhibit 99.2 to this Current Report on Form 8-K includes "safe harbor" language pursuant to the Private Securities Litigation Reform Act of 1995, as amended, indicating that certain statements contained therein are "forward-looking" rather than historical.

**Item 9.01 Financial Statements and Exhibits.****(d) Exhibits:**

<u>Exhibit Number</u>	<u>Description</u>
99.1	<a href="#">Press Release issued by PMV Pharmaceuticals, Inc., dated June 7, 2022.</a>
99.2	<a href="#">ASCO Investors Presentation.</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

PMV Pharmaceuticals, Inc.

Date: June 8, 2022

By: \_\_\_\_\_  
/s/ Winston Kung  
**Winston Kung**  
**Chief Operating Officer, and**  
**Chief Financial Officer**  
**(Principal Financial Officer)**

**PMV Pharmaceuticals Initial PC14586 Phase 1 Data Presented at ASCO Demonstrated Anti-Tumor Activity Across Multiple Solid Tumor Types With a p53 Y220C Mutation**

- Overall response rate (ORR) of 32% (8/25) achieved in higher dose cohorts per RECIST v1.1
- Partial responses observed across six distinct tumor types
- Data featured as an oral presentation at ASCO; Company to host investor event via webcast today at 6:30 pm CDT to review data presented

CRANBURY, N.J., June 7, 2022 (GLOBE NEWSWIRE) — PMV Pharmaceuticals, Inc. (Nasdaq: PMVP; “PMV Pharma”), a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53, today announced that preliminary results from the ongoing Phase 1/2 PYNACLE study of PC14586 in patients with advanced solid tumors harboring a p53 Y220C mutation demonstrated anti-tumor efficacy across multiple tumor types with an acceptable safety profile. PC14586 is a first-in-class precision oncology small molecule investigational therapy that selectively targets the p53 Y220C mutation in solid tumors.

The data were featured in an oral presentation at the 2022 American Society of Clinical Oncology (ASCO) annual meeting. The presentation entitled, “First-in-human study of PC14586, a small molecule structural corrector of Y220C mutant p53, in patients with advanced solid tumors harboring a TP53 Y220C mutation,” was delivered by Ecaterina Ileana Dumbrava, M.D., Assistant Professor of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center.

Dr. Dumbrava commented, “p53 is a target that until now was widely believed to be undruggable. The favorable safety and tolerability of PC14586, along with the clinical activity across six distinct tumor types, supports the potential of PC14586 to become a new treatment modality that can address the unmet need of patients with advanced solid tumors harboring a TP53 Y220C mutation.”

#### **Safety**

- The most common treatment-emergent adverse events (>15%) included nausea, vomiting, AST increase, ALT increase, anemia, blood creatinine increase, and fatigue.
- The maximum tolerated dose (MTD) was reached at 1500 mg twice daily.
- Enrollment at doses below the MTD is ongoing to support the determination of a recommended Phase 2 dose.

#### **Efficacy**

- ORR assessed by investigators according to RECIST v1.1 was 32% (8/25) in patients receiving an initial total daily dose of 1150 mg and above. Of the 8 responding patients, 6 have confirmed partial responses and 2 have unconfirmed partial responses, pending confirmation.
- ORR was 24% (8/33) across all dose cohorts.
- Responses were observed across six distinct tumor types including breast, endometrial, prostate, pancreatic, ovarian, and small cell lung cancer.
- Best Response of stable disease or partial response was observed in 19/25 patients at doses  $\geq$ 1150 mg (76%).

“These encouraging Phase 1 safety and preliminary efficacy data provide proof of concept for PC14586 as monotherapy to selectively reactivate p53 across multiple tumor types,” said Leila Alland, M.D., Chief Medical Officer of PMV Pharma. “We look forward to completing the Phase 1 portion of the PYNACLE study in the second half of this year and initiating the potentially pivotal Phase 2 portion of the study early in 2023.”

**Investor Event**

Management will host an investor event via webcast on June 7, 2022, at 6:30 pm CDT to discuss the PC14586 Phase 1 data. The event will feature a presentation by Dr. Dumbrava who will review the data presented at ASCO.

To listen to the webcast and view the accompanying slide presentation, please refer to the [Events and Presentations](#) section of the PMV Pharma website.

**About the PYNNAACLE Study**

PYNNAACLE is an open-label, multicenter Phase 1/2 clinical study assessing safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of PC14586 in patients with advanced solid tumors harboring a p53 Y220C mutation. A total of 41 patients were enrolled as of May 10, 2022; 36 patients with measurable disease at baseline including 33 patients determined to be eligible for response evaluation. During the Phase 1 dose-escalation portion of the study, multiple dose levels of PC14586 were evaluated (150 mg QD, 300 mg QD, 600 mg QD, 1150 mg QD, 1500 mg QD, 2000 mg QD, 2500 mg QD, and 1500 mg BID). Preliminary efficacy was assessed by RECIST v1.1. A recommended Phase 2 dose will be selected at the end of Phase 1. For more information on the Phase 1/2 PYNNAACLE study (PMV-586-101), refer to [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT study identifier NCT04585750).

**About PC14586**

PC14586 is a first-in-class, small molecule p53 reactivator designed to selectively bind to the crevice present in the p53 Y220C mutant protein, hence, restoring the wild-type, or normal, p53 protein structure and tumor-suppressing function. PC14586 is being developed for the treatment of patients with locally advanced or metastatic solid tumors that have a p53 Y220C mutation. Fast Track designation has been granted by the Food and Drug Administration (FDA) for evaluating PC14586 for the treatment of patients with locally advanced or metastatic solid tumors that have a p53 Y220C mutation.

**About PMV Pharma**

PMV Pharma is a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53. p53 mutations are found in approximately half of all cancers. The field of p53 biology was established by our co-founder Dr. Arnold Levine when he discovered the p53 protein in 1979. Bringing together leaders in the field to utilize over four decades of p53 biology, PMV Pharma combines unique biological understanding with pharmaceutical development focus. PMV Pharma is headquartered in Cranbury, New Jersey. For more information, please visit [www.pmvpharma.com](http://www.pmvpharma.com).

**Forward-Looking Statements**

Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding the Company’s future plans or expectations for PC14586, including expectations regarding success of its current clinical trial for PC14586 and any future commercialization plans for the product candidate; and the future plans or expectations for the Company’s discovery platform for its other early-stage and clinical candidates. Any forward-looking statements in this statement are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of the Company’s product candidate development activities and planned clinical trials, the Company’s ability to execute on its strategy and operate as an early

clinical stage company, the potential for clinical trials of PC14586 or any future clinical trials of other product candidates to differ from preclinical, preliminary or expected results, the Company's ability to fund operations, and the impact that the current COVID-19 pandemic may have on the Company's clinical trials, supply chain, and operations, as well as those risks and uncertainties set forth in the section entitled "Risk Factors" in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on March 1, 2022, the Company's Quarterly Report on Form 10-Q filed with the SEC on May 10, 2022 and its other filings filed with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

**Contacts**

Investor Contact:

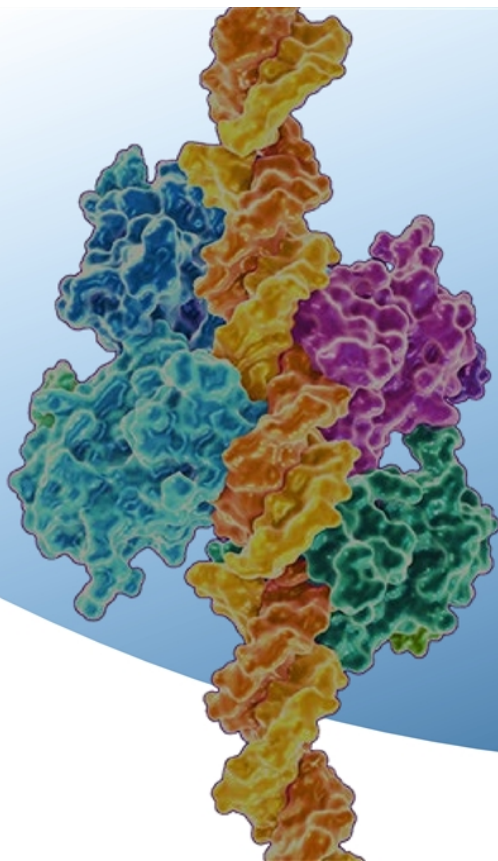
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Greig Communications  
kathy@greigcommunications.com

# ASCO PC14586 INVESTOR EVENT

June 7, 2022



# 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 and our pipeline programs, plans regarding regulatory filings, our expectations regarding the relative benefits of our product candidates versus competitive therapies, and our expectations regarding the therapeutic and commercial potential of our product candidates. 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



## 01 Introduction

David Mack, PhD, President & Chief Executive Officer



## 02 ASCO 2022 & Clinical Experience

Ecaterina Dumbrava, MD  
Assistant Professor, Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center



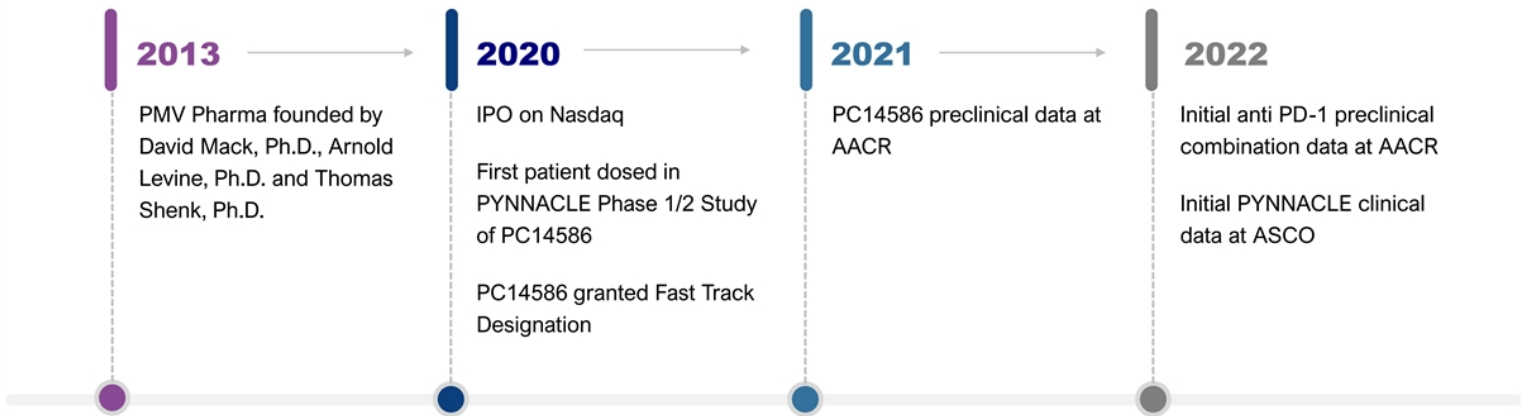
## 03 Looking Ahead

Leila Alland, MD, Chief Medical Officer



## 04 Q&A Session

## PMV founded on the expertise in p53 biology



# Novel Approach in Precision Oncology

Harnessing the Power of p53

## Mission

PMV is **pioneering** the discovery and development of small molecule, tumor-agnostic therapies targeting p53

Our **unique expertise** and **drug discovery** capabilities enable the identification and development of highly **selective small molecules** that reactivate and restore p53 function

## Clinical Stage Programs

**Lead program** PC14586 under evaluation in the Phase 1/2 PYNNACLE trial across all solid tumors with the p53 Y220C mutation

Compelling preclinical **synergy** observed with PC14586 and **anti PD-1** inhibitors support the planned clinical evaluation of the combination

## Discovery Stage Programs

**WIP1** program targeting wild-type p53 tumors in lead optimization

Continued progress on **hotspot p53** programs

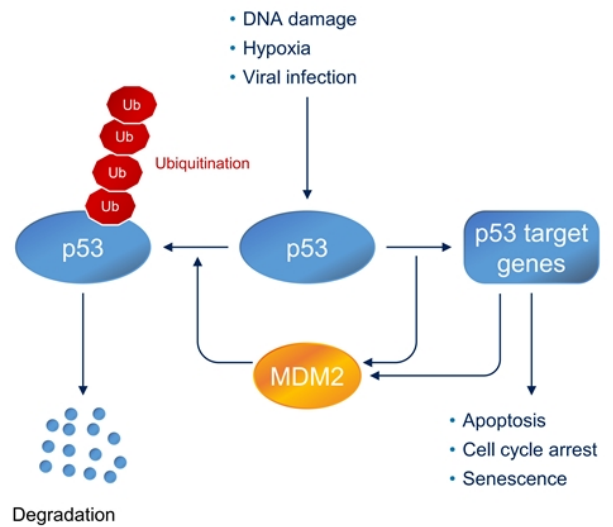
# First-in-Human Study of PC14586, a Small Molecule Structural Corrector of Y220C Mutant p53, in Patients With Advanced Solid Tumors Harboring a *TP53* Y220C Mutation

Ecaterina E. Dumbrava,<sup>1</sup> Melissa L. Johnson,<sup>2</sup> Anthony W. Tolcher,<sup>3</sup> Geoffrey I. Shapiro,<sup>4</sup> John A. Thompson,<sup>5</sup> Anthony B. El-Khoueiry,<sup>6</sup> Andrae L. Vandross,<sup>7</sup> Shivaani Kummer,<sup>8</sup> Aparna R. Parikh,<sup>9</sup> Pamela N. Munster,<sup>10</sup> Erika Daly,<sup>11</sup> Laura DeLeon,<sup>12</sup> Megan Khaddar,<sup>12</sup> Kimberley LeDuke,<sup>12</sup> Kimberly Robell,<sup>12</sup> Lisa Sheehan,<sup>12</sup> Meagen St Louis,<sup>12</sup> Amy Wiebesiek,<sup>12</sup> Leila Alland,<sup>12</sup> Alison M. Schram<sup>13</sup>

<sup>1</sup>The University of Texas MD Anderson Cancer Center, Houston, TX; <sup>2</sup>Sarah Cannon Research Institute, Nashville, TN; <sup>3</sup>NEXT Oncology, San Antonio, TX; <sup>4</sup>Dana Farber Cancer Institute, Boston, MA; <sup>5</sup>Seattle Cancer Care Alliance, Seattle, WA; <sup>6</sup>USC Norris Cancer Center, Los Angeles, CA; <sup>7</sup>NEXT Oncology, Austin, TX; <sup>8</sup>OHSU Knight Cancer Institute, Portland, OR; <sup>9</sup>Massachusetts General Hospital, Boston, MA; <sup>10</sup>University of California, San Francisco, San Francisco, CA; <sup>11</sup>Cytel, Inc., Waltham, MA; <sup>12</sup>PMV Pharmaceuticals, Inc., Cranbury, NJ; <sup>13</sup>Memorial Sloan Kettering Cancer Center, New York, NY.

# p53 Has a Pivotal Role in the Body's Defense Against Cancer

- *TP53* is a tumor suppressor gene<sup>1-2</sup>
- The p53 protein binds to DNA and has key roles in cell cycle arrest, DNA repair, and apoptosis<sup>1-3</sup>
  - Activated following cellular stress and DNA damage
  - Supports DNA repair before cellular replication
  - Induces apoptosis
- Protein levels are tightly controlled by MDM2<sup>4</sup>
- *TP53* mutation resulting in p53 inactivation is a key step in oncogenesis<sup>3</sup>



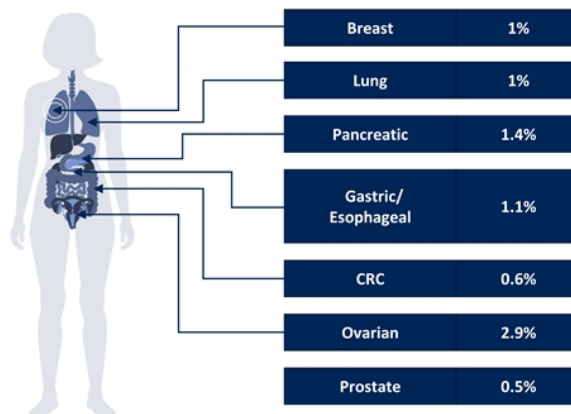
DNA, deoxyribonucleic acid; MDM2, mouse double minute 2 homolog.

1. Chillemi G, et al. *Cold Spring Harb Perspect Med.* 2017;7:a028308. 2. Kasthuber ER, et al. *Cell.* 2017;170:1062–1078. 3. Levine AJ. *Nat Rev Cancer.* 2020;20:471–480. 4. Levine AJ. *J Mol Cell Biol.* 2019;11:524–530.

# TP53 Y220C Hotspot Mutation is Detected across Solid Tumor Types

- TP53 mutations are the most common genomic events across all human cancers<sup>1</sup>
- 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 cancer<sup>1-2</sup>
- p53 Y220C is a key hot-spot TP53 missense mutation that destabilizes p53<sup>1,3</sup>
- p53 Y220C is present in ~1% of all solid tumors<sup>4</sup>

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® Database<sup>4</sup> 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.

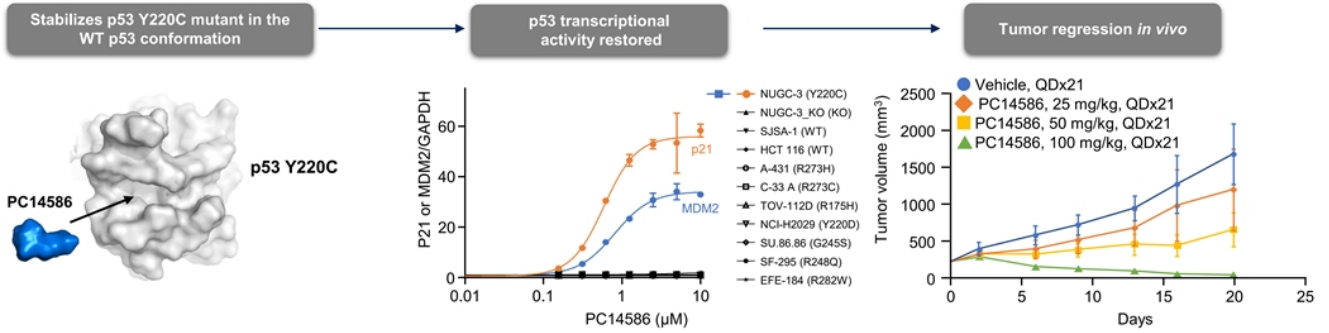
2. Roszkowska KA, et al. *Int J Mol Sci.* 2020;21:1334.

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

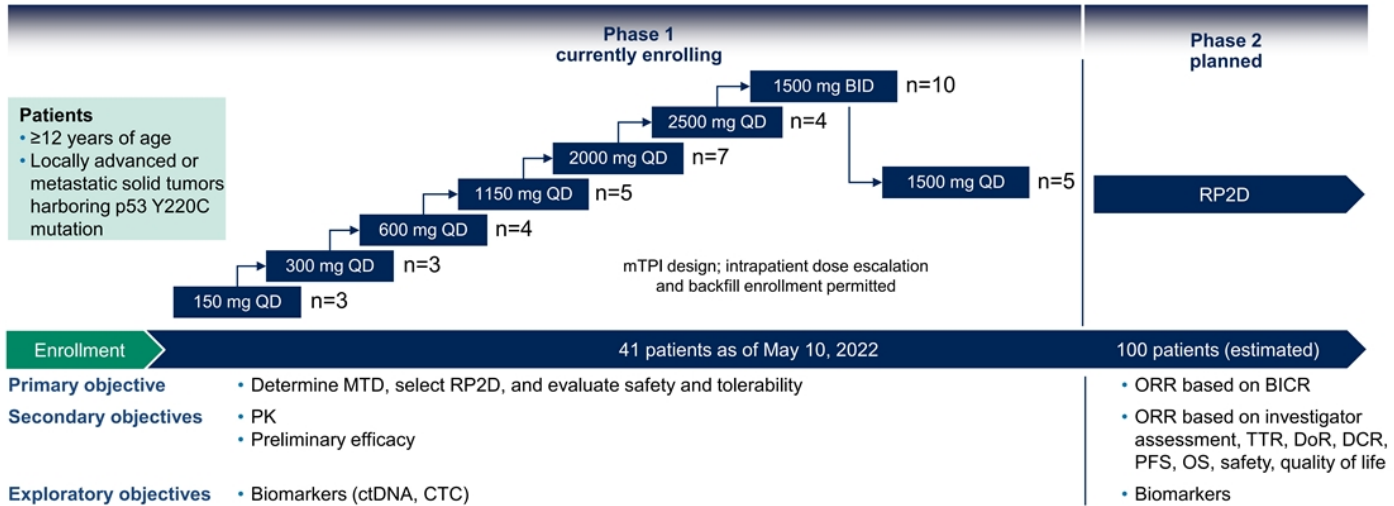
- Orally available small molecule designed to selectively bind to the crevice contained in the p53 Y220C mutant protein<sup>1</sup>
- Stabilizes the p53 Y220C mutant protein in the wild-type p53 conformation, thereby restoring transcription and tumor-suppressor function<sup>1</sup>



MDM2, mouse double minute 2 homolog; KO, knockout; WT, wild-type.  
1. Dumble M, et al. *Cancer Res.* 2021;81(13\_Suppl):Abstract LB006.

# A Seamless Phase 1/2 Clinical Trial (PYNACLE trial)

Patients With Advanced Solid Tumors Harboring p53 Y220C Mutation



BICR, blinded independent central review; BID, twice daily; CTC, circulating tumor cells; ctDNA, circulating tumor DNA; DCR, disease control rate; DoR, duration of response; MTD, maximum tolerated dose; mTPI, modified toxicity probability interval design; ORR, objective response rate by RECIST (Response Evaluation Criteria in Solid Tumors) 1.1; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; QD, once daily; RP2D, recommended Phase 2 dose; TTR, time-to-response.  
**NCT study identifier: NCT04585750.**

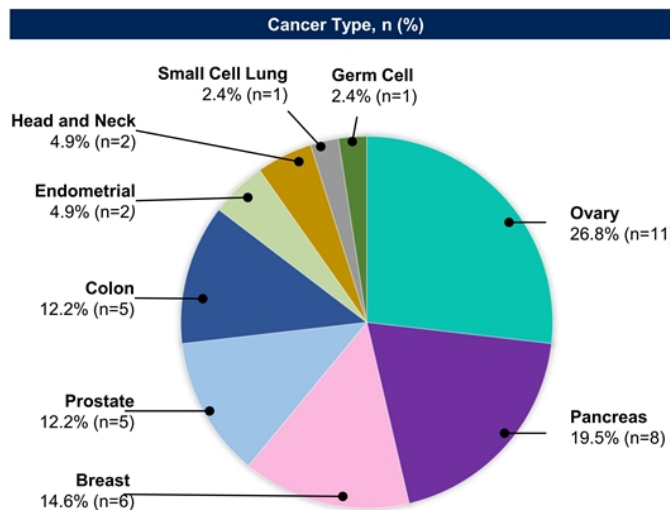


BICR, blinded independent central review; BID, twice daily; CTC, circulating tumor cells; ctDNA, circulating tumor DNA; DCR, disease control rate; DoR, duration of response; MTD, maximum tolerated dose; mTPI, modified toxicity probability interval design; ORR, objective response rate by RECIST (Response Evaluation Criteria in Solid Tumors) 1.1; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; QD, once daily; RP2D, recommended Phase 2 dose; TTR, time-to-response.



# Patient Demographics and Disease Characteristics

	n=41
<b>Age, years</b>	
Median (min-max)	62 (32-84)
<b>Sex, n (%)</b>	
Female	25 (61)
Male	16 (39)
<b>Race, n (%)</b>	
White	31 (76)
Asian	3 (7)
Black or African American	3 (7)
Other	1 (2)
Not Reported/Unknown	3 (7)
<b>ECOG status, n (%)</b>	
0	18 (44)
1	23 (56)
<b>Prior systemic therapies, n (%)*</b>	
1-2	17 (42.5)
≥3	23 (57.5)
Median (min-max)	3 (1-9)
<b>Germline TP53 Y220C, n (%)</b>	
Negative	38 (93)
Positive	2 (5)
Pending	1 (2)



\*One patient with unknown prior systemic therapies.

Data cut-off May 10, 2022

# Treatment-Emergent Treatment-Related Adverse Events

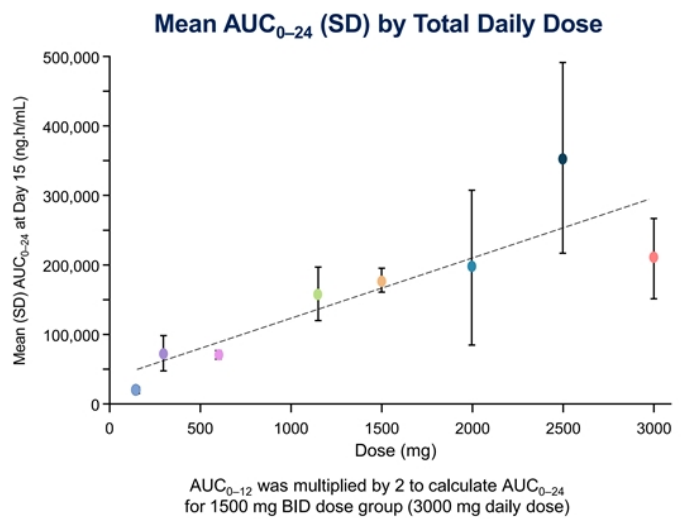
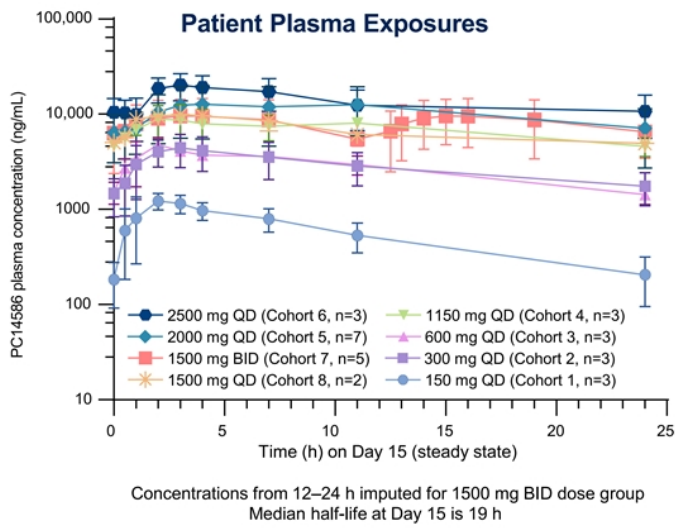
All Patients (n=41)

All Treatment-Emergent Treatment-Related AEs (Occurring in ≥3 Patients)		Max CTCAE			
Preferred Term	Any Grade	1	2	3	4
<b>Any treatment-related AE, n (%)</b>	<b>33 (80.5)</b>	<b>12 (29.3)</b>	<b>11 (26.8)</b>	<b>9* (22.0)</b>	<b>1* (2.4)</b>
Nausea	18 (43.9)	11 (26.8)	7 (17.1)		
Vomiting	11 (26.8)	6 (14.6)	5 (12.2)		
AST increased	9 (22.0)	7 (17.1)	1 (2.4)	1 (2.4)	
ALT increased	8 (19.5)	2 (4.9)	4 (9.8)	2 (4.9)	
Anemia	7 (17.1)	1 (2.4)	4 (9.8)	2 (4.9)	
Blood creatinine increased	7 (17.1)	3 (7.3)	4 (9.8)		
Fatigue	7 (17.1)	6 (14.6)	1 (2.4)		
Diarrhea	5 (12.2)	5 (12.2)			
Decreased appetite	3 (7.3)	2 (4.9)	1 (2.4)		
Headache	3 (7.3)	3 (7.3)			
Neutrophil count decreased	3 (7.3)	2 (4.9)		1 (2.4)	
Platelet count decreased	3 (7.3)	1 (2.4)	1 (2.4)	1 (2.4)	

- Most frequent treatment-related AEs (>15%) included nausea, vomiting, AST/ALT increase, anemia, blood creatinine increase, and fatigue
- Dose-limiting toxicities reported in 2 patients at 1500 mg BID
  - Grade 3 AST/ALT increase
  - Grade 3 acute kidney injury
- Maximum tolerated dose reached at 1500 mg BID
- RP2D not yet defined

\*Grade 3 and 4 treatment-related AEs not shown in the table (each in one patient) are Grade 3 acute kidney injury, hypokalemia, and pneumonitis, and Grade 4 immune thrombocytopenia. Data cut-off May 10, 2022  
 AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; RP2D, recommended Phase 2 dose.

# Dose-Proportional Increases in AUC at Steady State



Data are preliminary with 29 out of 41 patients having Day 15 samples at time of data cut-off. Dose-proportional increases in  $C_{max}$  were also observed (not shown).  
AUC, area under the curve; BID, twice daily;  $C_{max}$ , maximum serum concentration; QD, once daily; SD, standard deviation.

# Objective Response Rate Per RECIST 1.1

Based on Investigator Assessment

	Dose Cohorts		All
	150 mg QD–600 mg QD	1150 mg QD–1500 mg BID	
Enrolled, n	10	31	41
Patients with measurable disease at baseline, n	8	28	36
Eligible for response evaluation*, n	8	25	33
<b>ORR‡, n (%)</b>	<b>0 (0)</b>	<b>8 (32.0)</b>	<b>8 (24.2)</b>
PR	0	6	6
uPR	0	2	2
SD§	4	11	15
PD	4	3	7
Not evaluable*	0	3	3

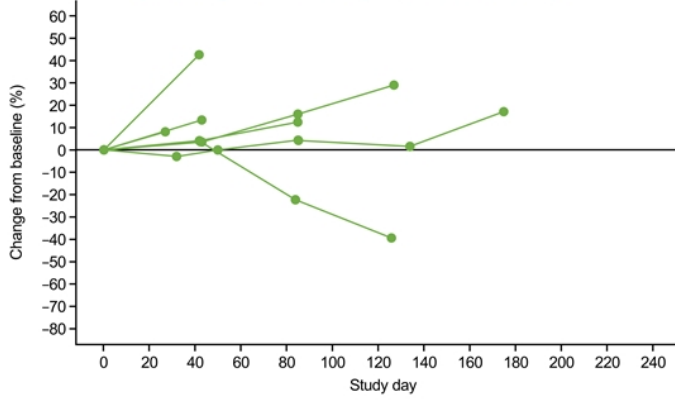
\*Patients without a post-baseline assessment are either excluded from "eligible for response evaluation" if ongoing, or considered "not evaluable" if discontinued;  
‡ORR = PR + uPR; §Includes three initially unconfirmed PR that progressed on the next tumor assessment.

BID, twice daily; ORR, objective response rate; PD, progressive disease; PR, partial response; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; uPR, unconfirmed PR pending confirmation.

Data cut-off May 10, 2022

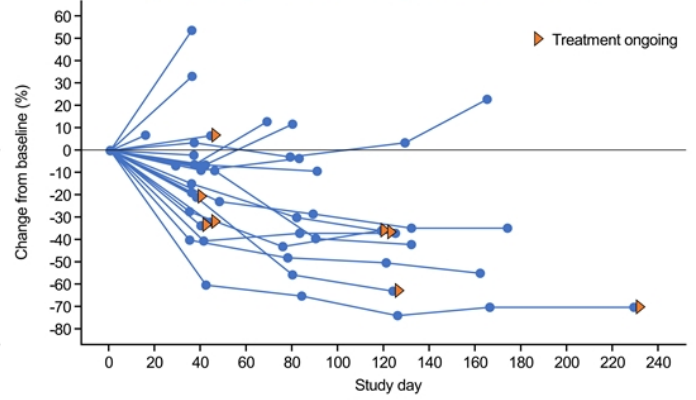
# Target Lesion Reduction in Low vs High Dose Cohorts

**% Change From Baseline in Tumor Target Lesion  
(150 mg QD–600 mg QD dose Level)**



**Dose Cohorts 1 through 3  
(150 mg QD to 600 mg QD)**

**% Change From Baseline in Tumor Target Lesion  
(1150 mg QD–1500 mg BID dose level)**

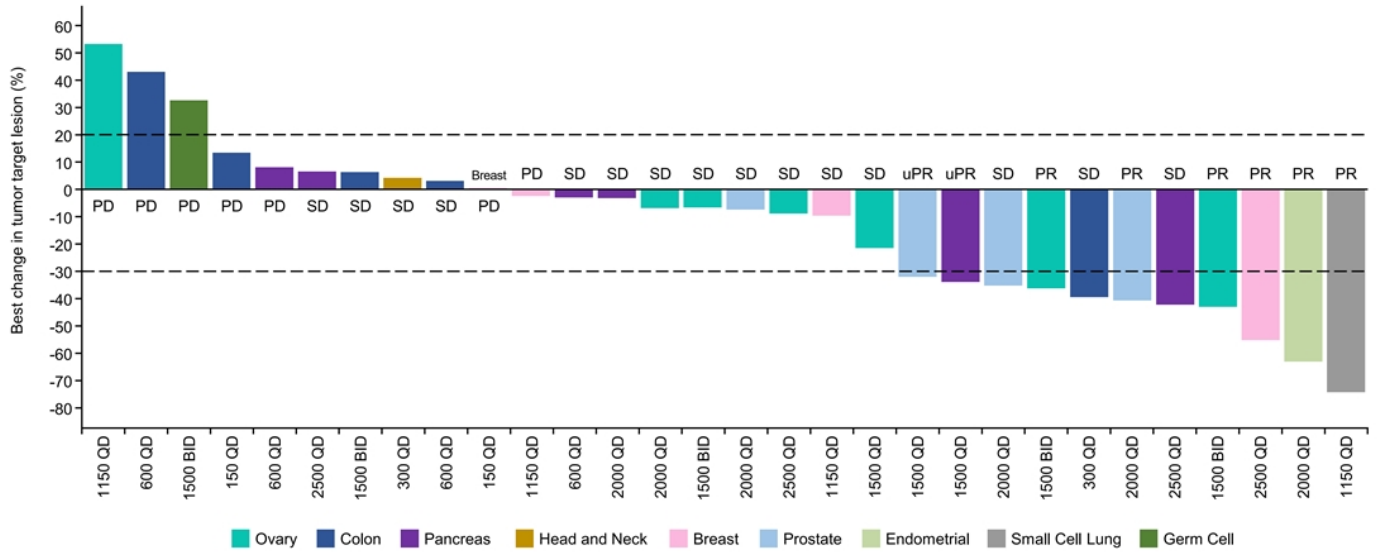


**Dose Cohorts 4 through 8  
(1150 mg QD to 1500 mg BID)**

Patients censored at the time of progression.  
 BID, twice daily; QD, once daily.

Data cut-off May 10, 2022

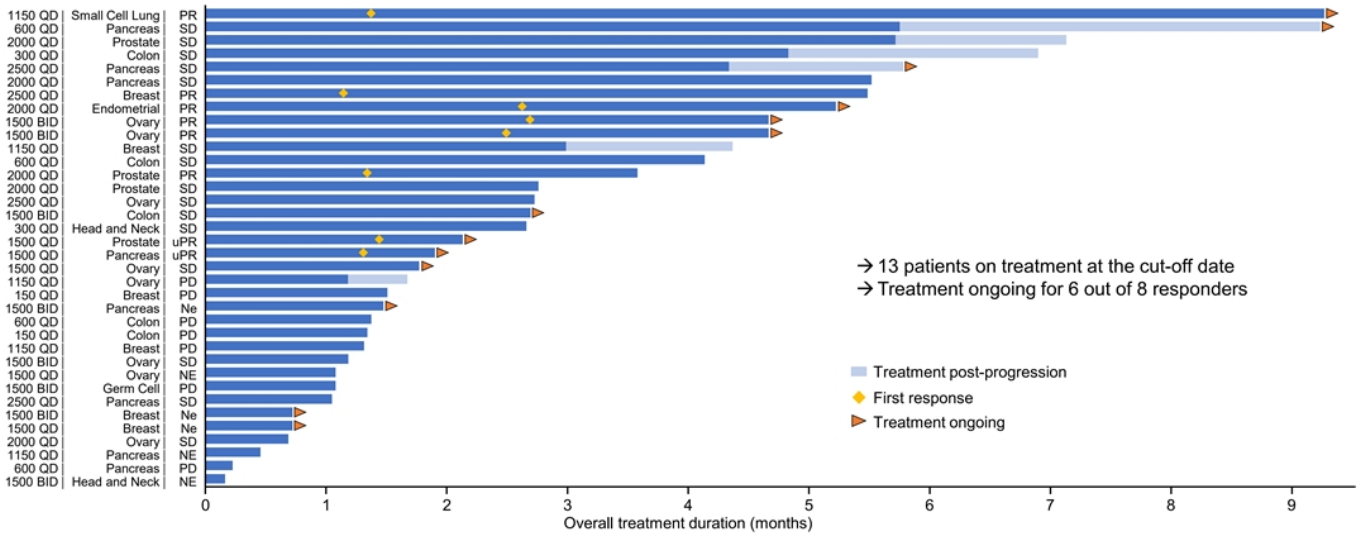
# Target Lesion Reduction Across Tumor Types



Includes patients with measurable disease and one post-baseline assessment. All doses are in mg. BID, twice daily; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; uPR, unconfirmed PR pending confirmation.

Data cut-off May 10, 2022

# Duration of PC14586 Therapy

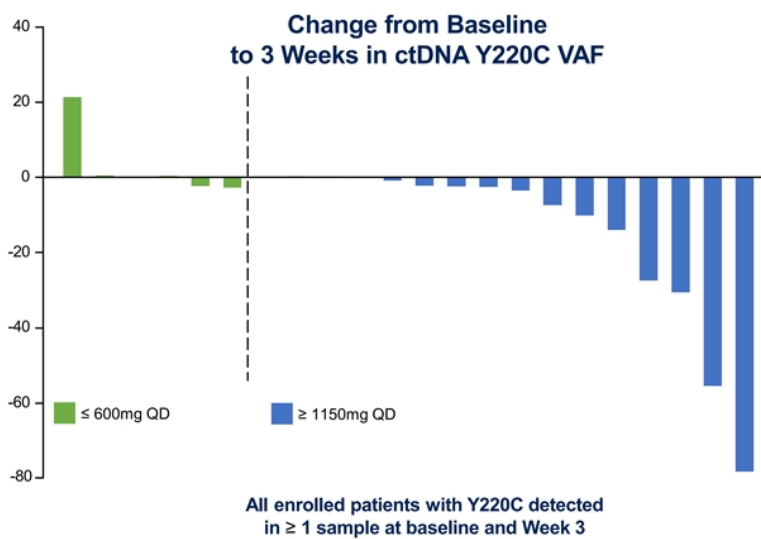
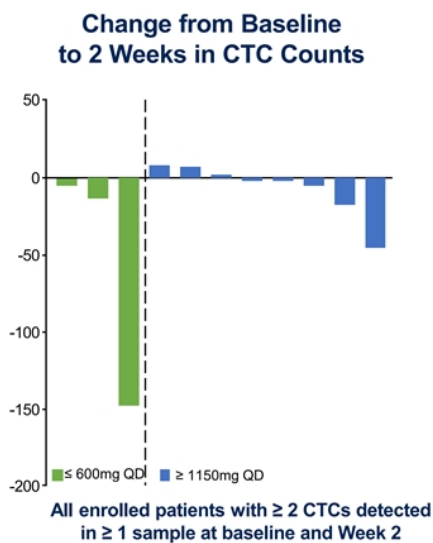


Data cut-off May 10, 2022

Includes all patients with measurable disease at baseline (n=36). All doses are in mg.

BID, twice daily; NE: not evaluable; Ne, not eligible for response assessment; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; uPR, unconfirmed PR pending confirmation.

# CTC & ctDNA Decreases May Be Early Biomarkers Anti-Tumor Activity



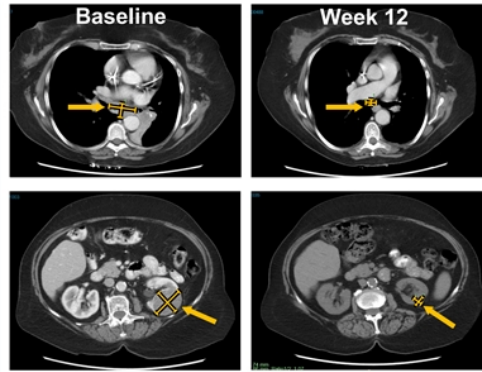
CTC, circulating tumor cells; ctDNA, circulating DNA, VAF: Variant Allelic Frequency

Data cut-off May 10, 2022

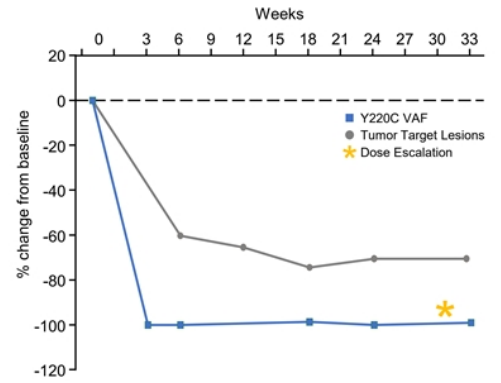


# SCLC Patient With Rapid and Sustained Partial Response

- 71-year-old woman with ES-SCLC
- Progressed after 2 prior lines of therapy with worsening dyspnea and complete occlusion of the left bronchus with atelectasis
  - Etoposide, carboplatin and atezolizumab (10 months)
  - Topotecan (4 months)
- Prior radiotherapy of brain metastasis
- *TP53 Y220C* detected by NGS
- PC14586 1150mg QD was started
  - PR after 6 weeks with relief of respiratory symptoms
  - Increased to 2000mg QD at week 30
- Well tolerated with transient treatment related Grade 3 neutropenia
- Treatment ongoing for 9+ months



60% reduction in target lesions at Week 6 and at 70% at Week 12



Correlation between radiographic tumor shrinkage and Y220C ctDNA decrease

AE, adverse event; ctDNA, circulating tumor DNA; ES, extensive stage; NGS, next-generation sequencing; PR, partial response; QD, once daily; SCLC, small cell lung carcinoma; VAF, variant allelic frequency. Images courtesy of Dr Melissa Johnson, Sarah Cannon Research Institute.

# Metastatic Castration-Resistant Prostate Cancer Patient with Sustained PSA Response

Disease control for 8+ months and ongoing

57-year-old man  
with high grade  
prostate  
adenocarcinoma  
(Gleason Score 9)  
with bone  
metastases at  
diagnosis  
(nonmeasurable  
per RECIST v1.1)



- Prior treatments
  - Hormonal therapy X 2 years then switched to enzalutamide X 7 months
  - Multiple courses of Radiotherapy to the thoracic and sacral bone metastases
  - Abiraterone
  - Radiotherapy of the prostate
  - Cabazitaxel
- Presence of *TP53 Y220C* detected
- PC14586 initiated at 2000 mg QD
  - Rapid reduction in PSA, with >50% decrease by 8 weeks and ongoing
  - PC14586 reduced to 1000 mg QD at week 25 due to Grade 2 creatinine increase
  - Disease control ongoing for 33 weeks and treatment continues

## Conclusions

- PC14586 has an acceptable safety profile, with MTD reached
- PC14586 exposure is generally dose proportional over a wide dose range and supports once daily dosing
- Preliminary efficacy in patients across solid tumor types harboring TP53 Y220C mutation was demonstrated
- Enrollment at dose(s) below the MTD to support RP2D determination is ongoing

# Acknowledgments

## We would like to thank:

All the patients, their families and caregivers who have participated, and continue to participate in this clinical trial

Investigators and research staff

MedPace, Resolution Biosciences, Foundation Medicine, and Rarecyte

## US clinical trial sites

Dana Farber Cancer Institute, Boston, MA

OHSU Knight Cancer Institute, Portland, OR

NEXT Oncology, Austin, TX

NEXT Oncology, San Antonio, TX

Massachusetts General Hospital, Boston, MA

MD Anderson Cancer Center, Houston, TX

Memorial Sloan Kettering Cancer Center, New York, NY

Sarah Cannon Research Institute, Nashville, TN

Seattle Cancer Care Alliance, Seattle, WA

UC San Francisco, San Francisco, CA

USC Norris Cancer Center, Los Angeles, CA

Hoag Cancer Institute, Newport Beach, CA

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# LOOKING AHEAD



# Opportunity to target mutant p53 Y220C across multiple tumor types

Overall Annual US incidence<sup>1,2</sup>

## 17,000 patients



TP53 Y220C mutations occur in multiple tumor types including most common tumor types

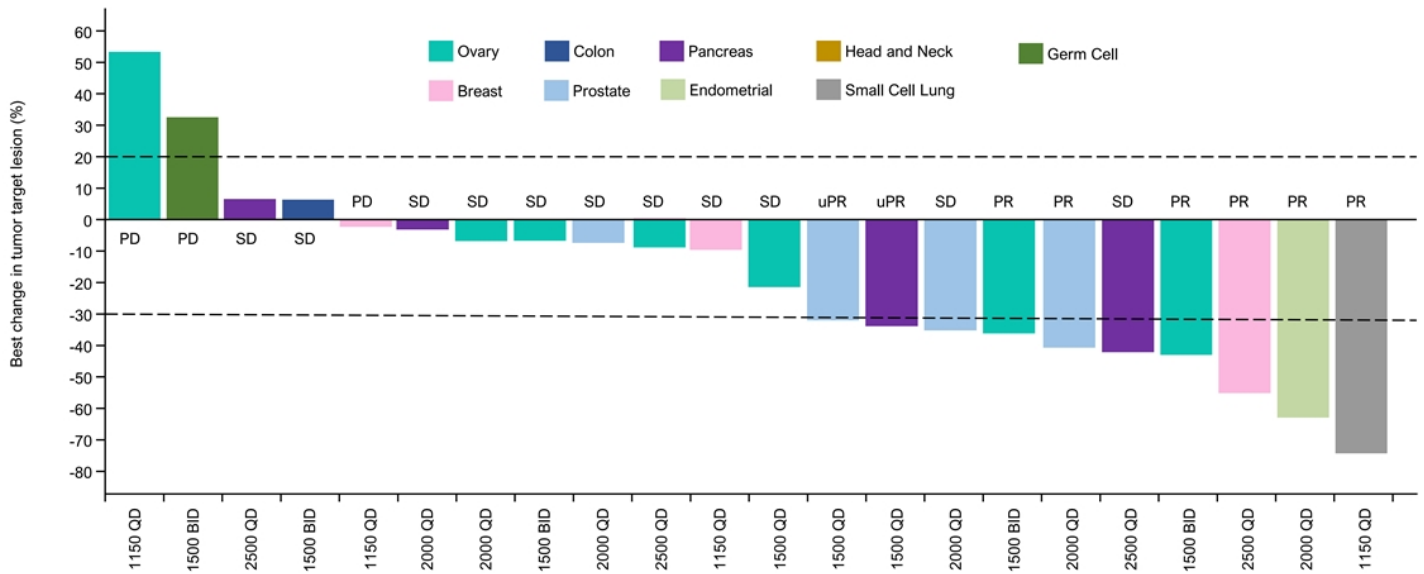


### Y220C Mutation Frequency<sup>2</sup>

~1%	All Solid Tumors
2.9%	Ovarian
1.4%	Pancreatic
1.1%	Gastric/Esophageal
1%	Breast
1%	Lung
0.6%	CRC
0.5%	Prostate

# Target Lesion Reductions Across Different Tumor Types

at Doses  $\geq 1150\text{mg}$



Includes patients with measurable disease and one post-baseline assessment. All doses are in mg. BID, twice daily; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; uPR, unconfirmed PR pending confirmation.

# Responses Across 6 Tumor Types Supports a Pan Tumor Approach

32% ORR at Doses  $\geq$  1150mg

Tumor Type	Response evaluable <sup>1</sup> , n	SD, n (%)	ORR <sup>2</sup> , n (%)
Ovarian	8	4 (50)	2 (25)
Prostate	4	2 (50)	2 (50)
Pancreatic	5	3 (60)	1 (20)
Breast	3	1 (33)	1 (33)
Endometrial	1		1 (100)
Small cell lung	1		1 (100)
Colorectal	1	1 (100)	
Germ Cell	1		
Head & Neck	1		
<b>All</b>	<b>25</b>	<b>11 (44)</b>	<b>8 (32)</b>

Best Response of SD or PR observed in **19/25 patients (76%)**








<sup>1</sup> Includes 3 patients eligible for response assessment and without a post baseline assessment, <sup>2</sup> ORR per tumor type per RECIST 1.1 based on Investigator assessment, 6 patients have confirmed partial responses; 1 pancreatic and 1 prostate patient have response confirmation pending



# PC14586 Preliminary Efficacy Appears Favorable Relative to SOC

Relevant 2L+ SOC Outcomes in Key Tumor Types

Tumor Type	Line of Tx	ORR (%)
 Breast	3L	3.9-11.2%
 NSCLC / SCLC	2L	3.3-15.5% / 7%
 CRC	3L+	0.4-1%
 Pancreatic	2L	8.5-10.8%
 Ovarian (platinum-resistant)	2L	12.7%

## SOC RESPONSE RATES

in late line patients in tumor types of interest are generally <15%

## SOC DATA

reflect a general population and not a specific p53 Y220C population.

## PHASE 1 PYNNACLE TRIAL PATIENTS

have generally exhausted all available treatment options (*median of 3 prior systemic regimens*)

For illustrative purposes only, no head to head trials exist



SOC = standard of care

Cortes et al. 2020, Herbst et al. 2016, Shepherd et al. 2000, Garon et al. 2014, Garassino et al. 2013, O'Brien et al. 2006, Grothey et al. 2013, Mayer et al. 2015, de Jesus et al 2020, Chae et al 2020, Gaillard et al 2021

## PC14586: Next Steps



### RP2D optimization

In line with Project Optimus FDA initiative

Determine optimal dose in support of RP2D



### Phase 2 clinical footprint expansion

New US trial sites late 2022

Sites in Europe, Asia-Pacific planned to start in 1H2023

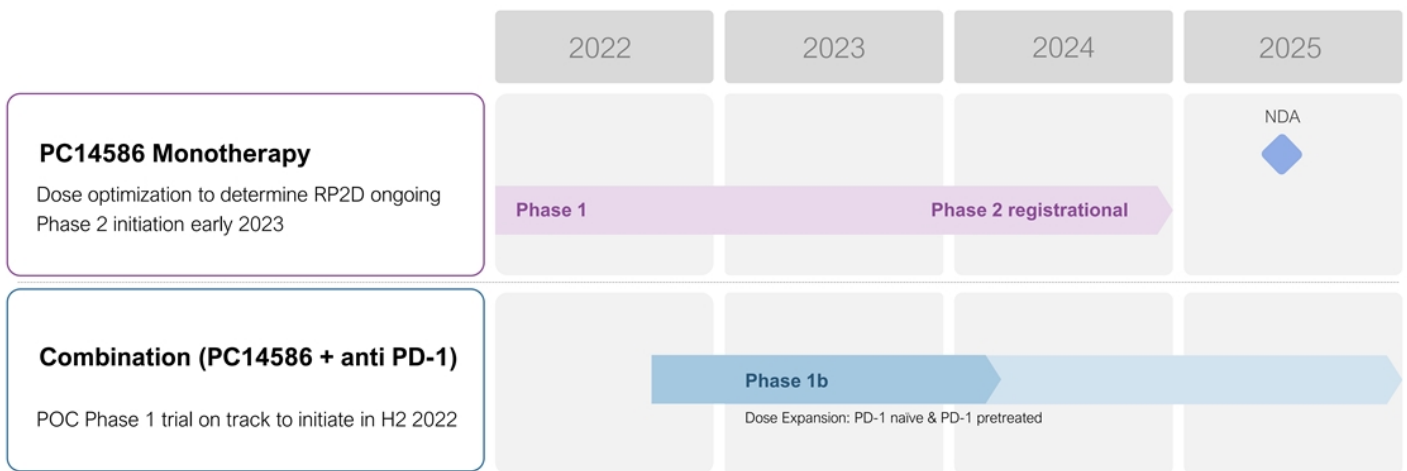


### Building the value proposition

Real World Evidence generation to contextualize PC14586 data

Addressing payors' needs proactively to support accessibility

# PC14586: Continued Development Progress



## PC14586

A first-in-class molecule for what has long been considered an “undruggable” target



**Proof of concept achieved with first demonstration of p53 reactivation and functional restoration in patients with p53 Y220C mutant tumors**



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



**Meaningful single-agent clinical activity observed across multiple tumor types supporting continued pan-tumor development**

## Key Upcoming Milestones

Program	Update	Timing
PC14586 Monotherapy	Updated Phase 1 data	Q4 2022/Q1 2023
	Initiation of Phase 2 study	Early 2023
PC14586 + PD1 Combination Study	Initiation of Combination trial	2H 2022

# Q&A SESSION

