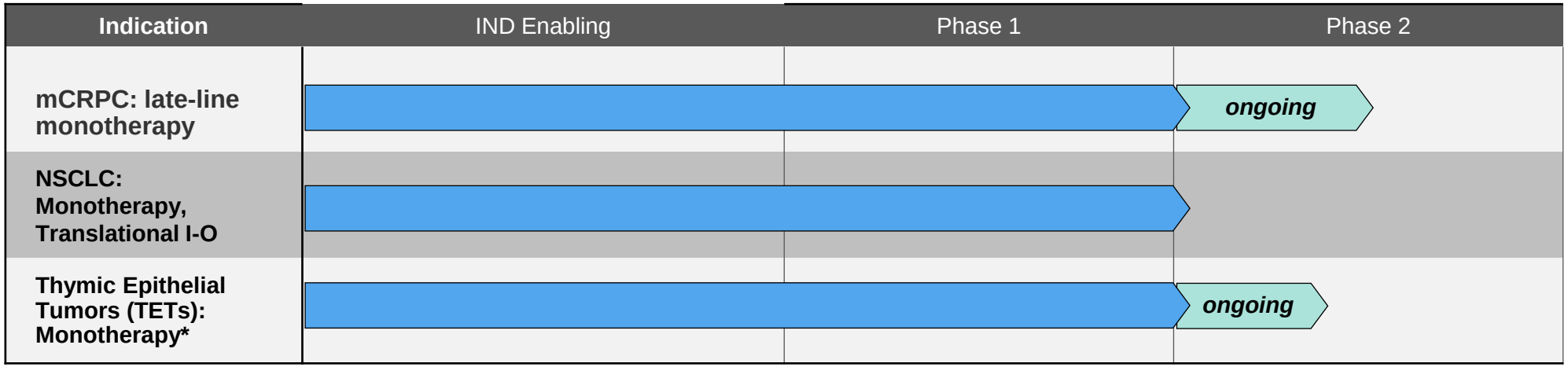

promontory™
THERAPEUTICS
Clinical Development

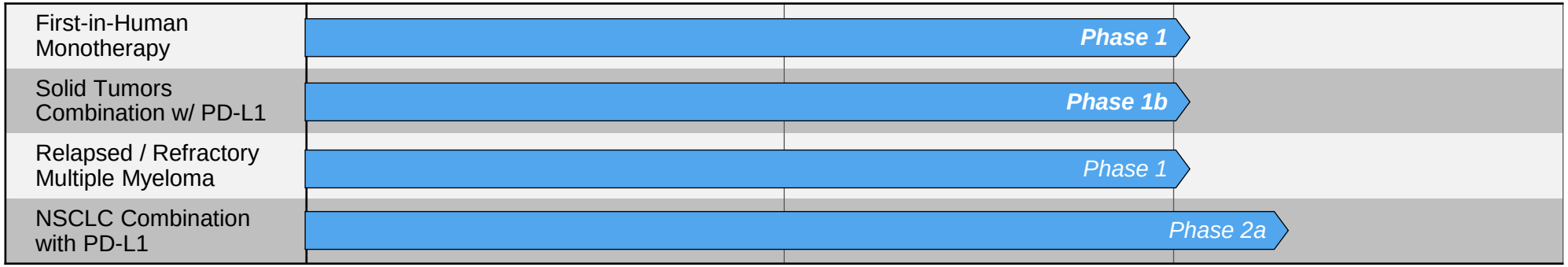
Robust Clinical Development Pipeline for PT-112

Solid Tumors



* NCI will be treating patients at their own cost. Promontory contributes material.

Other Programs / Completed Studies



Completed **Ongoing**

Monotherapy Peer-Reviewed Phase 1 Study in Solid Tumors *Resulted in Prioritizing Three Indications for Phase 2*

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Phase 1 First-in-Human Study Demonstrated Safety and Single Agent Activity

- PT-112 was safe and well-tolerated among heavily pre-treated “all-comers”:
  - No Grade 4-5 events
  - No DLT trend / MTD not reached
  - Recommended Phase 2 dose (RP2D) established based on activity
- Durable RECIST responses within all-comers population (NSCLC, SCLC, Thymoma)
- Pronounced signal of activity in heavily pre-treated mCRPC patients
- Findings led to three Phase 2 studies in solid tumors

Phase I study of PT-112, a novel pyrophosphate-platinum immunogenic cell death inducer, in advanced solid tumours

eClinicalMedicine
Part of THE LANCET *Discovery Science*

Daniel D. Karp,[a] D. Ross Camidge,[b] Jeffery R. Infante,[c] Tyler D. Ames,[d] Matthew R. Price,[d] José Jimeno,[d] and Alan H. Bryce[e]*

Summary

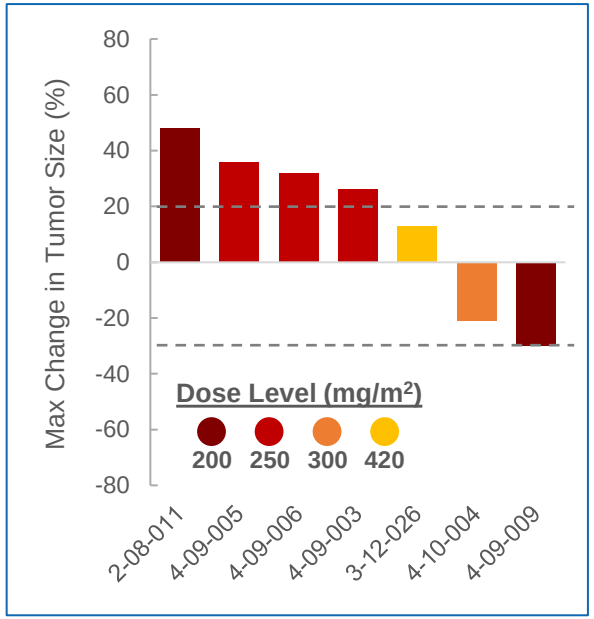
Background PT-112, the first pyrophosphate-platinum conjugate, causes immunogenic cell death in experimental models, leading to recruitment of tumour-infiltrating lymphocytes. PT-112 also associates with bone (osteotropism), likely driven by its pyrophosphate moiety. This is the first-in-human study of PT-112 monotherapy, exploring its safety and efficacy in a patient population where standard of care therapies were exhausted and novel treatment options are needed.

eClinicalMedicine
2022;00: 101430
Published online xxx
https://doi.org/10.1016/j.eclinm.2022.101430

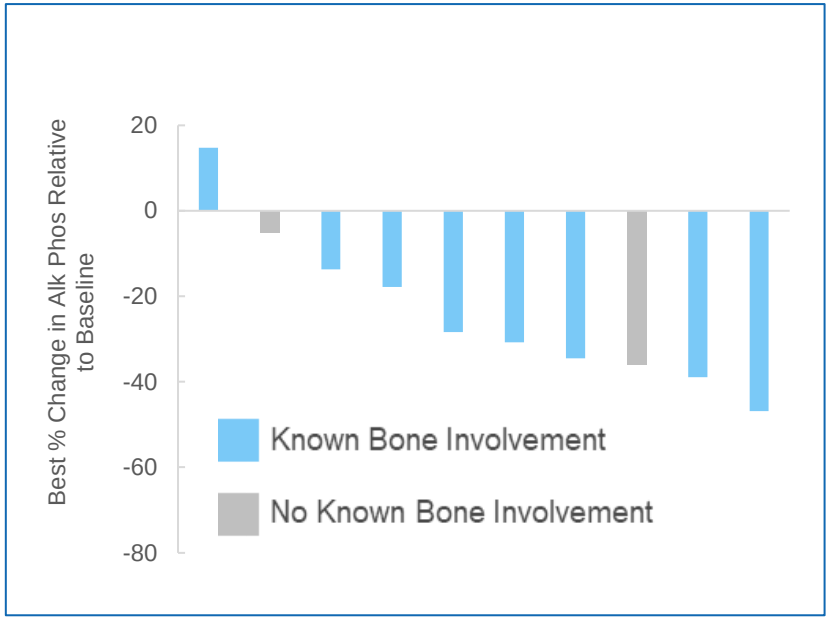
Metastatic Castration-Resistant Prostate Cancer (mCRPC)

Phase 1 Monotherapy Activity in mCRPC:
Radiographic, serologic and clinical benefit in heavily pre-treated (7th line) patients

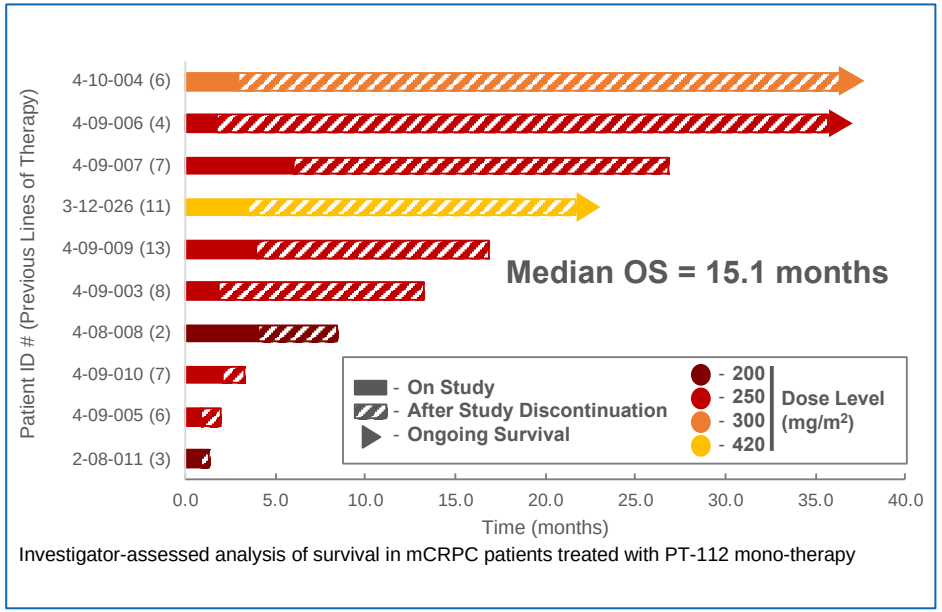
Tumor Volume Reductions



Reductions in Alkaline Phosphatase



Early Survival Data



Investigator-assessed analysis of survival in mCRPC patients treated with PT-112 mono-therapy

ASCO Genitourinary Cancers Symposium

Source: eClinical Medicine, The Lancet, "Phase I study of PT-112, a novel pyrophosphate-platinum immunogenic cell death inducer, in advanced solid tumours," Karp D., et al, 2022; Bryce, Alan Haruo, et al. "A Phase 1b Study of Novel Immunogenic Cell Death Inducer PT-112 plus PD-L1 Inhibitor Avelumab in Metastatic Castrate-Resistant Prostate Cancer (mCRPC) Patients." Journal of Clinical Oncology, vol. 39, no. 15_suppl, 2021, https://doi.org/10.1200/jco.2021.39.15_suppl.e17025.

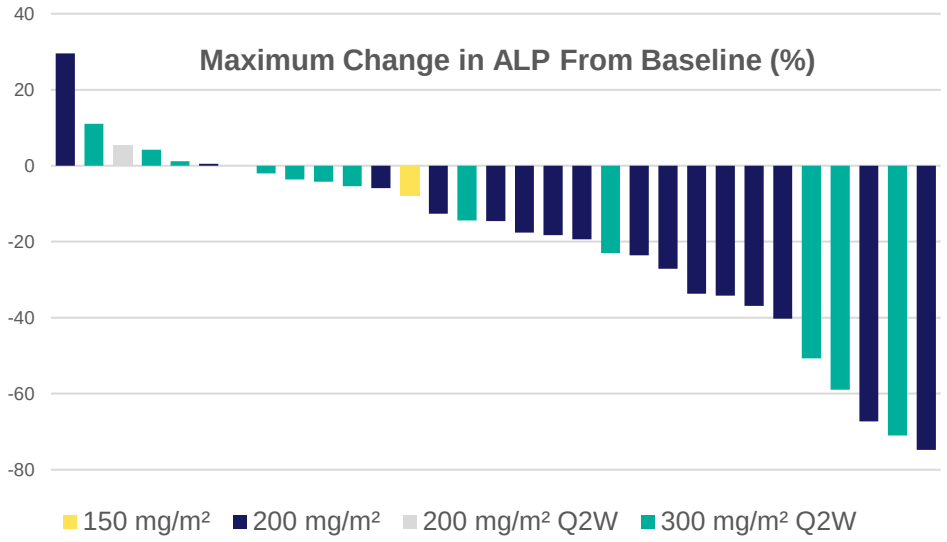
Phase 1b PD-L1 Combination: mCRPC Sub-population (n=32)
PT-112 shown to be active and safe in I-O combination

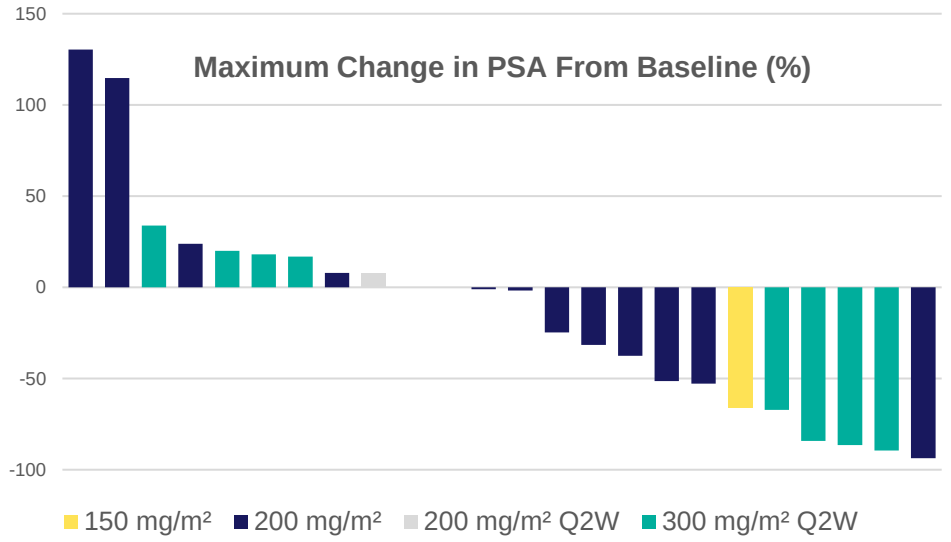
Radiographic Evidence of Efficacy

- Late-line population with avg. 7 prior lines of Tx
- 3 of 10 patients with RECIST-measurable disease had tumor reductions, of which 1 patient had a confirmed RECIST PR

Serologic Evidence of Efficacy

- Consistent reduction in Alkaline Phosphatase (ALP), correlated in other studies with improved survival
- 25% of evaluable patients with PSA reduction > 50%

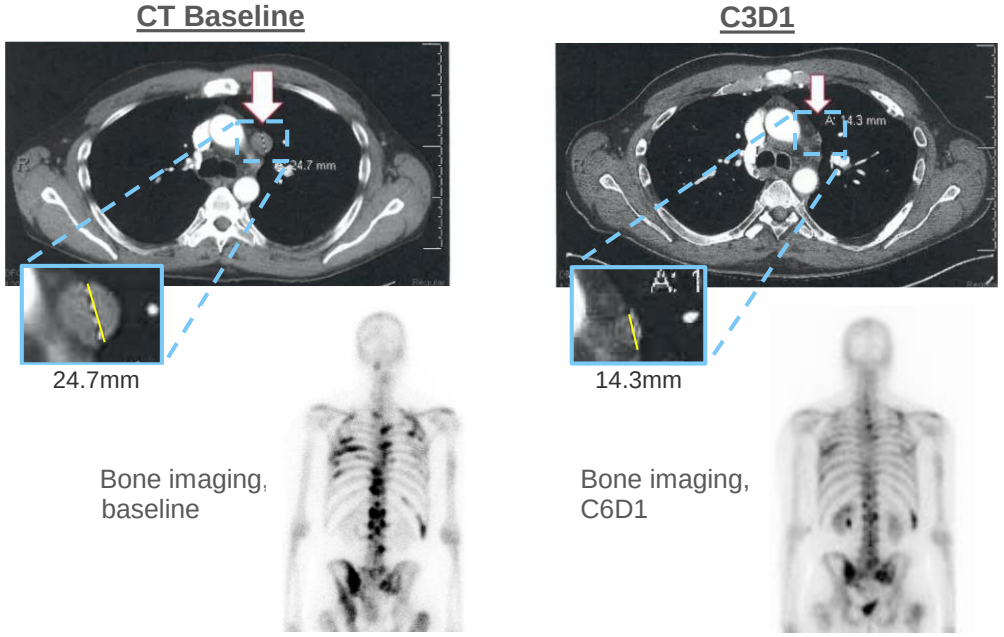




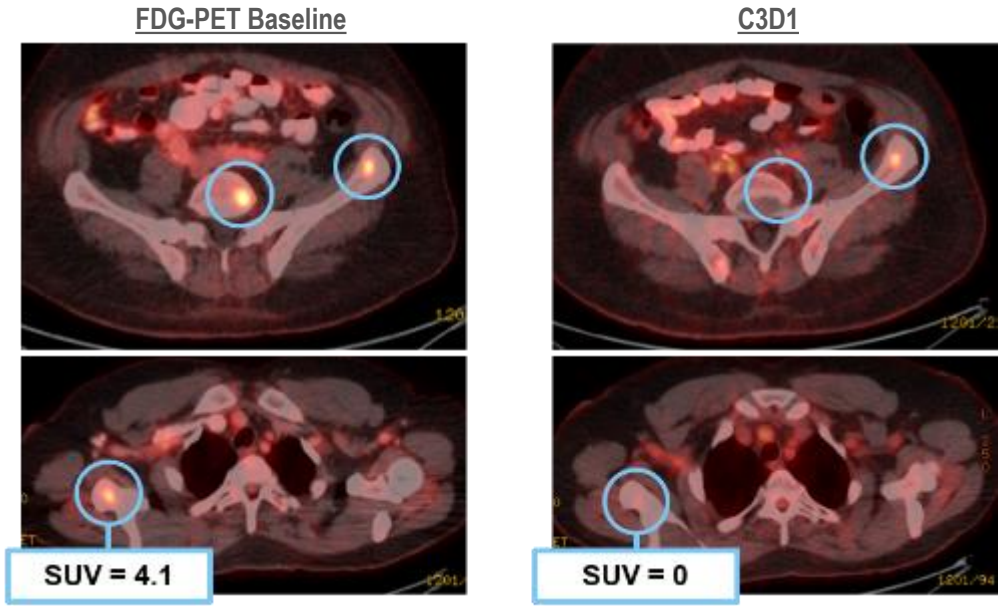
Sources: Karp, D.D., et al. "1026mo Phase IB Dose Escalation Study of Novel Immunogenic Cell Death (ICD) Inducer PT-112 plus PD-L1 Inhibitor Avelumab in Solid Tumours." Annals of Oncology, vol. 31, 1 Sept. 2020, https://doi.org/10.1016/j.annonc.2020.08.1146. Bryce, Alan Haruo, et al. "A Phase 1b Study of Novel Immunogenic Cell Death Inducer PT-112 plus PD-L1 Inhibitor Avelumab in Metastatic Castrate-Resistant Prostate Cancer (mCRPC) Patients." Journal of Clinical Oncology, vol. 39, no. 15_suppl, 2021, https://doi.org/10.1200/jco.2021.39.15_suppl.e17025.

Phase 1b PD-L1 Combination: Prostate Cancer Case Studies
Durable Response and Benefit Observed at Low Doses

Durable RECIST PR, serologic responses and bone met resolution *Heavily pre-treated mCRPC, visceral mets, severe bone pain, and MSS w/ PTEN loss*



FDG-PET response, serologic response / bone met resolution *Heavily pre-treated mCRPC, I-O naïve, severe bone pain, and MSS*



Case study 1: patient characteristics	
Number of Prior Therapies	8, including prior ipilimumab
PT-112 Dose Level	200 mg/m^2
RECIST Response	Confirmed PR
PSA Reduction	94%
Alk Phos Reduction	75%
PFS	8.4 months

Case study 2: patient characteristics	
Number of Prior Therapies	7
PT-112 Dose Level	150 mg/m^2
FDG-PET Response	Bone met resolution
PSA Reduction	66%
Alk Phos Reduction	8%
PFS	11.4 months

Sources: Karp, D.D., et al. “1026mo Phase IB Dose Escalation Study of Novel Immunogenic Cell Death (ICD) Inducer PT-112 plus PD-L1 Inhibitor Avelumab in Solid Tumours.” Annals of Oncology, vol. 31, 1 Sept. 2020, https://doi.org/10.1016/j.annonc.2020.08.1146. Bryce, Alan Haruo, et al. “A Phase 1b Study of Novel Immunogenic Cell Death Inducer PT-112 plus PD-L1 Inhibitor Avelumab in Metastatic Castrate-Resistant Prostate Cancer (mCRPC) Patients.” Journal of Clinical Oncology, vol. 39, no. 15_suppl, 2021, https://doi.org/10.1200/jco.2021.39.15_suppl.e17025.

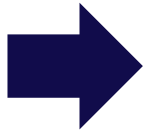
Ongoing Phase 2 Monotherapy Study in Prostate Cancer: *Delivers POC and Satisfies FDA Project Optimus*

STUDY DESIGN

Total N = 115 patients

- mCRPC w/ progression after ≥3 intended life-prolonging therapies
- Patients w/ "bone-only" disease allowed

(NCT 02266745)



- 360 mg/m^2 q2wk N=20
- 250 mg/m^2 q2wk N=45
- 360mg/m^2 cycle 1, 250mg/m^2 monthly N=45

STUDY RATIONALE

- Design fulfills FDA "Optimus" recommendations for enabling pivotal study
- Delivers robust PoC on safety, activity and immune effects
- Prostate Cancer Working Group 3 criteria employed for evaluation: disease control rate (DCR) at 4 months, by disease manifestation
- Cutting-edge correlative research: immune and disease profiling / PD monitoring tools
- Program will be pivotal-ready at conclusion

EXTENSIVE CORRELATIVE RESEARCH

T CELL PROFILING

Delivering human data related to PT-112's ICD mechanism

Documenting patient immune responses to monotherapy using TCR sequencing via Adaptive Biotechnologies

CIRCULATING TUMOR CELL (CTC) PROFILING

CTC reductions correlate with improvements in overall survival

Enumerating and profiling CTC responses to monotherapy using the Epic Sciences next-gen platform

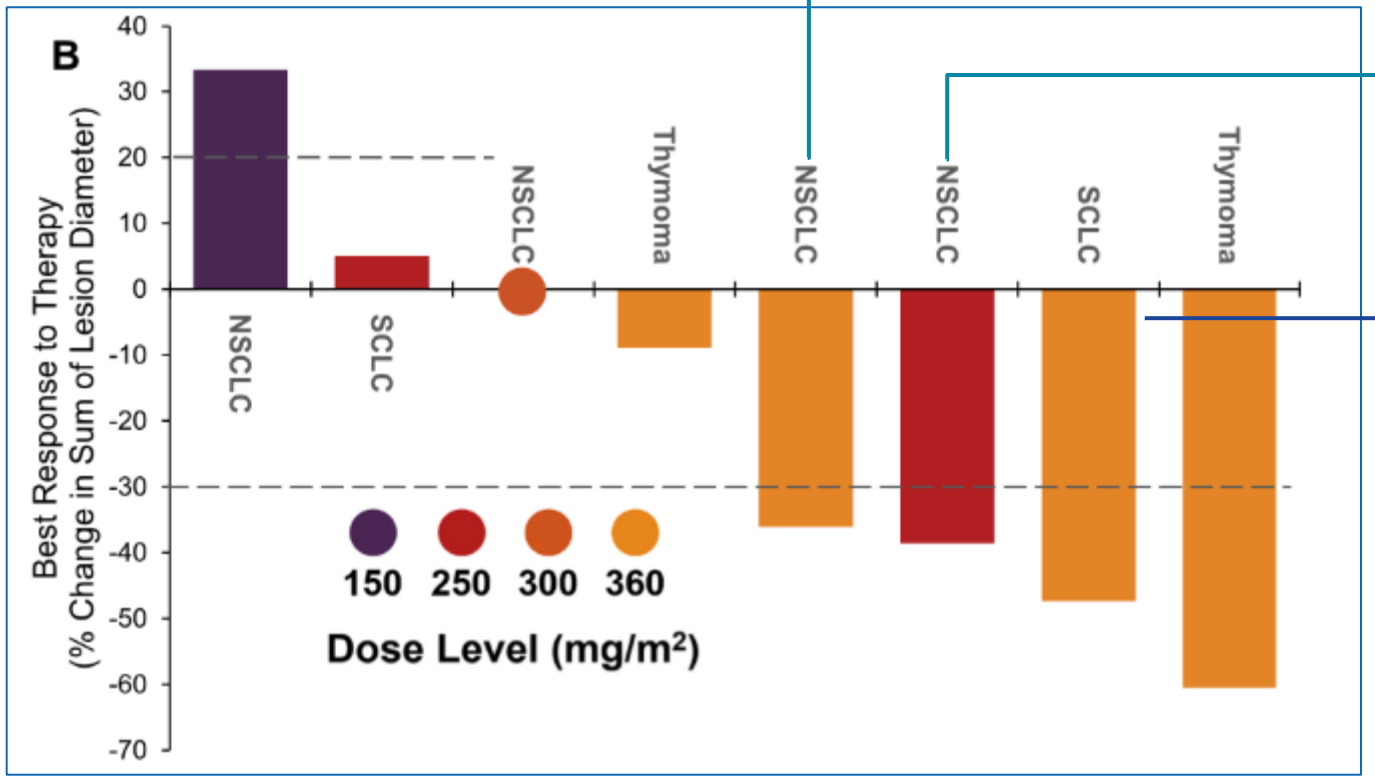
Phase 2 in mCRPC:
Expansion to EU under ANSM study approval, via sites in France (GETUG)

Start-up

16 – IGR, Paris
29 – Institut Paoli Calmettes, Marseille
30 – Hospital Jean Minjoz, Besancon
31 – Institut Bergonie, Bordeaux
32 – Centre Eugene Marquis (CEM), Rennes
33 – Centre Jean Perrin (CJP), Clermont-Ferrand
34 – Centre Francois Baclesse (CFB), Caen
35 – Centre Antoine Lacassagne (CAL), Nice
36 – ADHP – Georges Pompidou, Paris
37 – Hospital Begin, Saint Mande (Paris metro area)

Non-Small Cell Lung Cancer (NSCLC)

Monotherapy Activity in Thoracic Cancers:
Durability Observed in All Confirmed Responses



Unconfirmed PR

Prior Nivo: Best response SD
RECIST PR
Complete FDG-PET response in bone, liver, lung
PFS 6.8 months

Prior Ipi-Nivo: PD with new lesions
RECIST PR → late-onset CR
Target lesion disappeared post-Tx
PFS now over 4 years with no further therapy

Single-agent activity

Durable confirmed responses and high rate of disease control achieved in heavily pre-treated thoracic cancers (NCT 02266745)

Durability of Responses

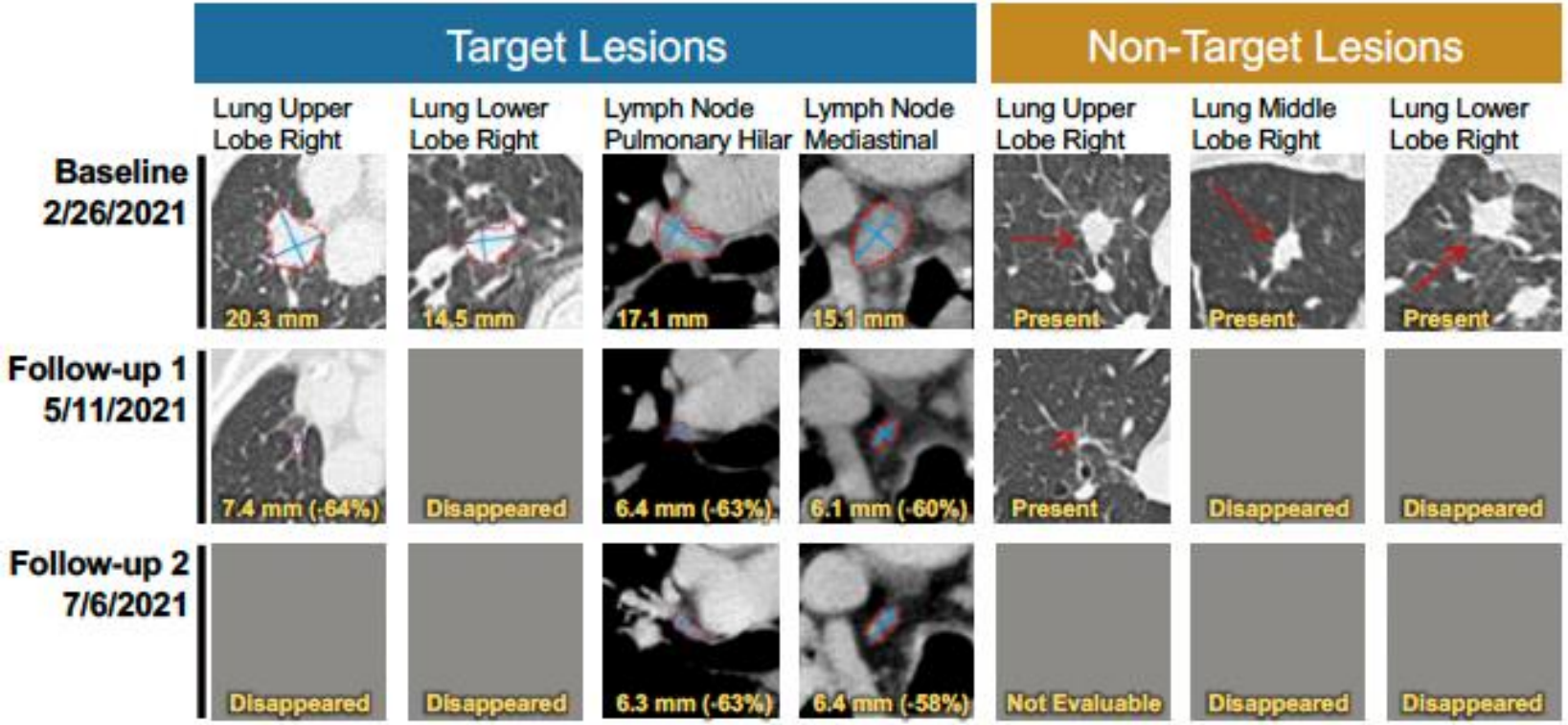
Responses crossed I-O failed and I-O naïve patients

PFS of responding patients was between 6 and 38+ months, indicative of immune nature of response

Source: eClinical Medicine, The Lancet, "Phase I study of PT-112, a novel pyrophosphate-platinum immunogenic cell death inducer, in advanced solid tumours," Karp D., et al, 2022

Phase 2a PD-L1 Combination: NSCLC Case Study
Complete Remission, Clinical and Immune Response

Tumor assessment according to iRECIST



Baseline Immune and Genomic Profiling

Microsatellite Stability	PD-L1 TPS	TMB	CD8 Pattern	Mutations
MSS	5%	Low (4 mutations/Mb)	Minimally Infiltrating	APC, RB1, TP53

Source: https://doi.org/10.1016/j.iotech.2022.100237

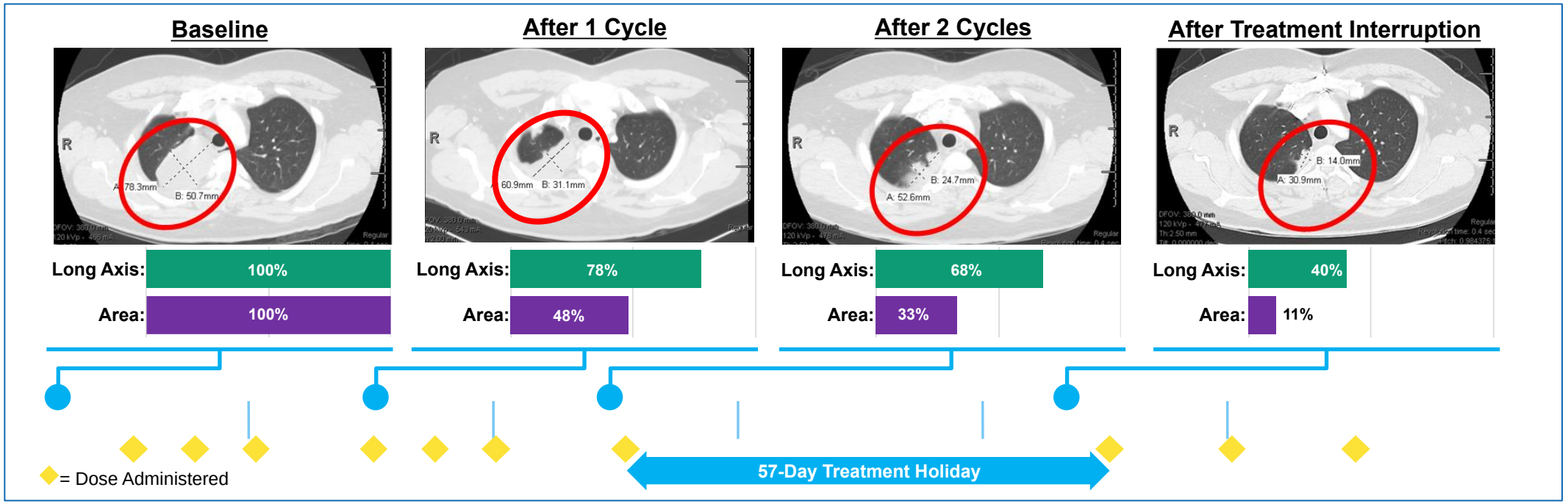
Deep Response in patient with primary resistance to 1L treatment

- Squamous NSCLC patient with prior ipilimumab-nivolumab-carboplatin-gemcitabine combination, with best response of PD
- Complete response in target and non-target lesions along with relief of pulmonary symptoms
- No further systemic therapy required for two years
- Baseline profiling (Microsatellite status, PD-L1 TPS and TMB) at baseline did not indicate a likely response to checkpoint therapy
- Increase in T cell fraction on treatment (see prior slide)

Thymic Epithelial Tumors (TETs)

Phase 1 Monotherapy Activity in Thymoma:
Signature of Immune Involvement in Durable Response

Example of Phase 1 Responses: Durable PR in Advanced Thymoma Patient



Adaptive Immune Response

Durable response cited above continued to deepen during extended Tx holiday

PT-112 Orphan Drug Designation

Rare disease with no FDA approved agent

Durable Responses

PR with PFS of 17 months was followed by a re-challenge of the patient, with a *second durable PR*

Promontory formal CRADA with NIH

Phase 2 recruiting currently at NCI (NCT 05104736)

NIH NATIONAL CANCER INSTITUTE

Source: eClinical Medicine, The Lancet, "Phase I study of PT-112, a novel pyrophosphate-platinum immunogenic cell death inducer, in advanced solid tumours," Karp D., et al, 2022

NCI Phase 2 of PT-112 Monotherapy, Thymic Epithelial Tumors (TETs): ASCO 2023 Abstract

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PT-112 safety, activity and immune activation documented by the National Cancer Institute in early Phase 2 data

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Organizations

Thoracic and GI Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, Center for Immuno-Oncology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, Thoracic and GI Malignancies Branch, Center for Cancer Research and Lung and Upper Aerodigestive Cancer Research Group, Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, Bethesda, MD, Pharmacy Department, National Institutes of Health Clinical Center, Bethesda, MD, Promontory Therapeutics Inc., New York, NY, Biostatistics and Data Management Section, National Cancer Institute, National Institutes of Health, Bethesda, MD, Thoracic and GI Malignancies Branch and Center for Immuno-Oncology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD

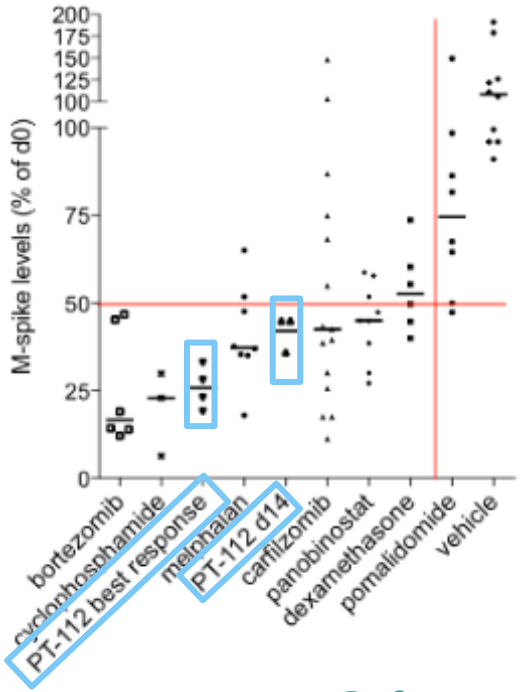
Conclusions:

PT-112 is safe and clinically active in pts with recurrent TETs. In contrast to ICIs, no new irAEs were observed. Immune analyses show evidence of early treatment-related immune activation and support the rationale underlying this novel treatment approach for TETs. Enrollment is ongoing with an accrual ceiling of 53. These initial results support further evaluation of PT-112 in TETs as monotherapy and in combination with other immunomodulatory interventions. Clinical trial information: NCT05104736.

2023 ASCO® ANNUAL MEETING

Multiple Myeloma

PT-112 Monotherapy in Multiple Myeloma:
Additional Opportunity Supported by Safety and Efficacy Data



Top-tier pre-clinical data

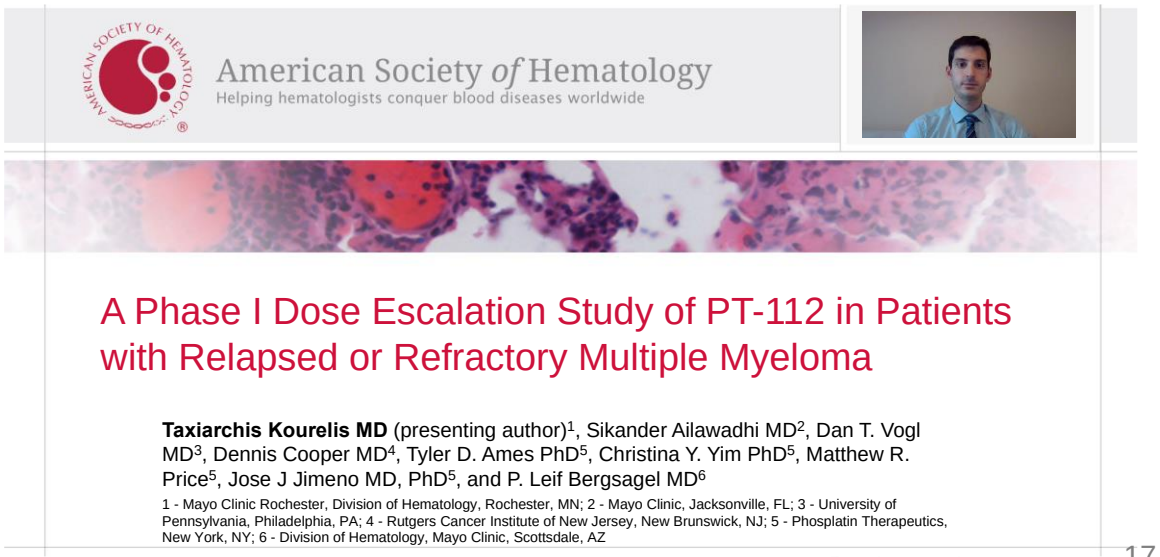
- PT-112 assessed in the genetically engineered, highly-predictive, immune-competent, orthotopic Vk*Myc model of multiple myeloma
- PT-112 is one of the most active agents ever tested
- M-protein reduction continued following PT-112 treatment discontinuation, consistent with immune effects

Source: Ames, et al., Blood 2017 130:1797

Safety and single-agent activity, Phase 1

Phase 1 results presented at ASH demonstrated:

- PT-112 safety profile consistent with solid tumor data, and well tolerated
- Single-agent responses to therapy observed, including in a BCMA-CAR-T non-responding patient
- Manuscript submitted
- FDA Orphan Drug Designation



Source: Kourelis, et al., Blood 2020: 136, Suppl. 1