PERSPECTIVE THERAPEUTICS

Investor Call

October 11, 2024

NYSE: CATX

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SMR 2024 Abstract P-091

First-in-Human Peptide Receptor Radionuclide Therapy (PRRT) of [$^{203/212}$Pb]VMT01 for Patients with Previously Treated Unresectable or Metastatic Melanoma(NCT05655312)

Morris ZS[1], Menda Y[2], Block MS[3], Wahl R[4], Osman MM[5], Arays R[6], Olszanski AJ[7], Mehr SA[8], Puhlmann M[9], Hanna A[9], Johnson FL[9], and Cho SY[1]

[1]University of Wisconsin, [2]University of Iowa, [3]Mayo Clinic, [4]Washington University, [5]St. Louis University, [6]University of Kentucky, [7]Fox Chase Cancer Center, [8]Nebraska Cancer Specialists, [9]Perspective Therapeutics, Inc.

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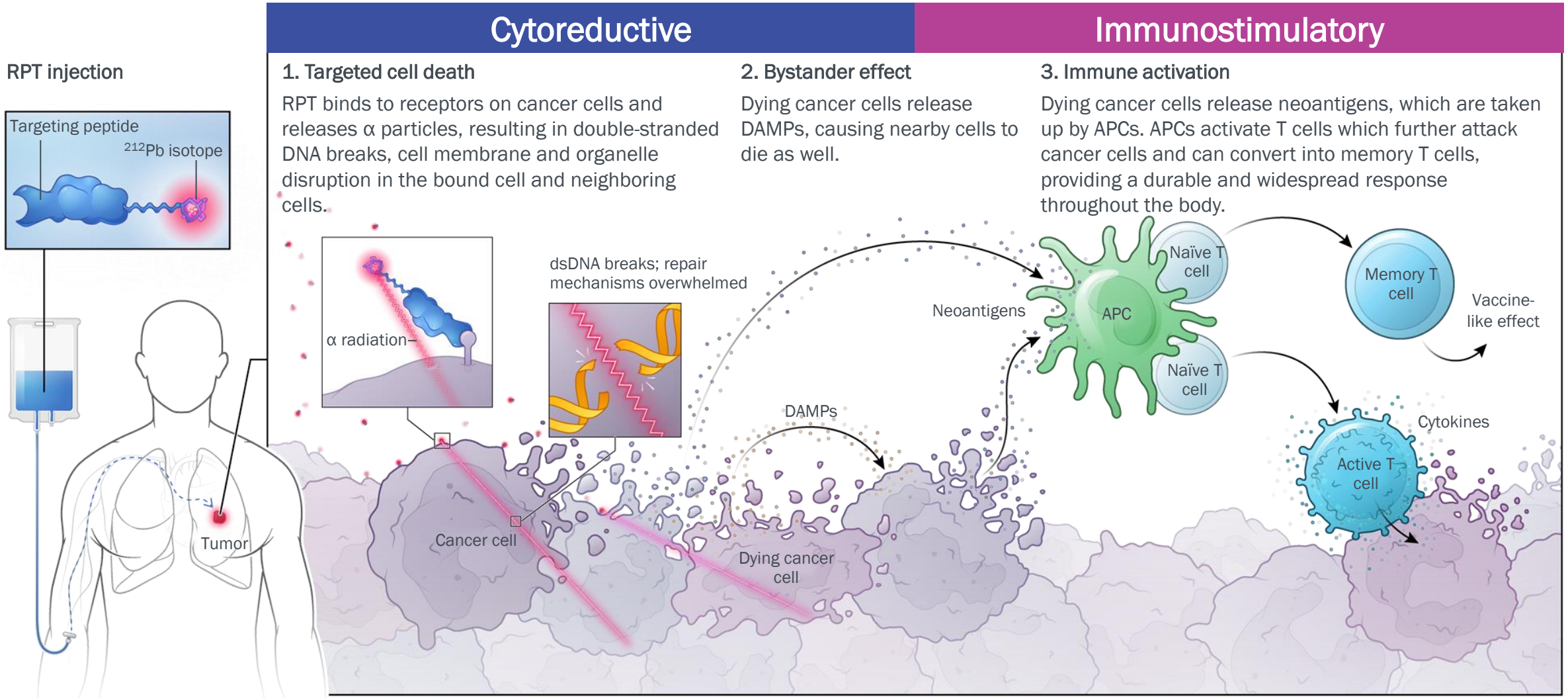
Proposed Mechanism of Action for [^{212}Pb]VMT01



Abbreviations: APC, antigen-presenting cell; DAMPs, damage-associated molecular patterns; dsDNA, double-stranded DNA; RPT, radiopharmaceutical therapy.
Adapted from Pouget JP, Chan TA, Galluzzi L, Constanzo J. Radiopharmaceuticals as combinatorial partners for immune checkpoint inhibitors. Trends Cancer. 2023 Nov;9(11):968-981. doi: 10.1016/j.trecan.2023.07.014. Epub 2023 Aug 21. PMID: 37612188; PMCID: PMC11311210.

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Melanoma may represent a paradigm shift in Radiopharmaceutical Therapy (RPT)

Preclinical data supports a dual mechanism of action (MOA) for [^{212}Pb]VMT01 activity in melanoma

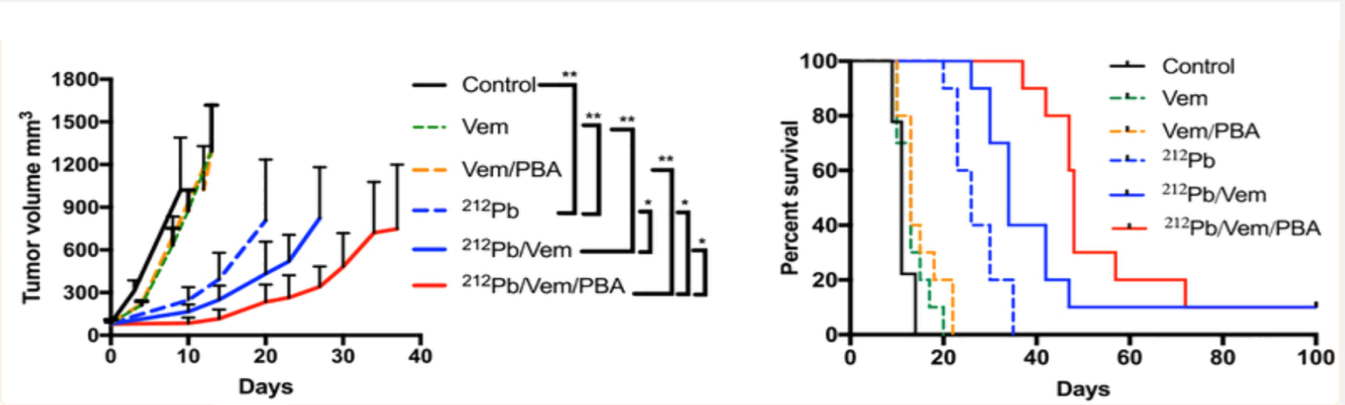
The complex radiobiology of targeted alpha-particle therapy can be separated into two principal MOAs

A Cytotoxic Effects

Upregulation of MC1R expression with BRAF and HDAC inhibitors increases targeted radiation delivery to tumors and enhances efficacy of ^{212}Pb α -particle therapy for melanoma in immunodeficient murine xenograft models.[1]

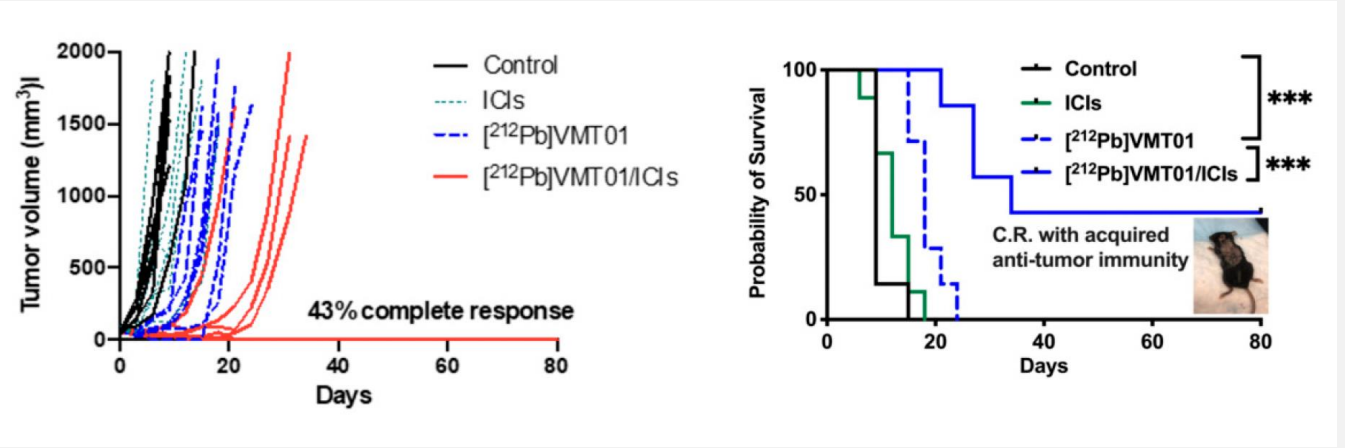
BRAF*i* Vem – vemurafenib

HDAC*i* PBA – 4-phenylbutyrate



B Immuno-stimulatory Effects

Combination of ICIs and [^{212}Pb]VMT01 induces significant tumor inhibition and lasting anti-tumor immunity in immune competent, ICI resistant, murine melanoma models (C57 B6 with B16: F10 mouse melanoma)[2]



1. Li M, et.al. Enhancing the Efficacy of Melanocortin 1 Receptor-Targeted Radiotherapy by Pharmacologically Upregulating the Receptor in Metastatic Melanoma. Mol Pharm. 2019 Sep 3; 16(9): 3904–3915
2. Li Met. al. Targeted Alpha-Particle Radiotherapy and Immune Checkpoint Inhibitors Induce Cooperative Inhibition on Tumor Growth of Malignant Melanoma. Cancers 2021, 13, 3676

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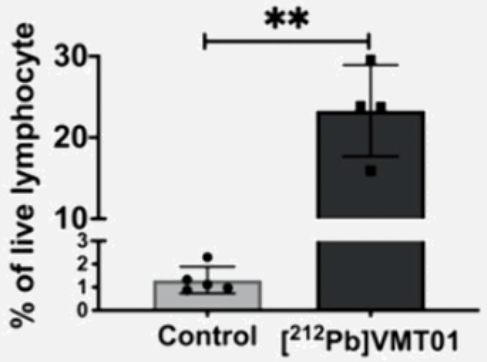
[^{212}Pb]VMT01 treatment increases tumor infiltrating lymphocytes

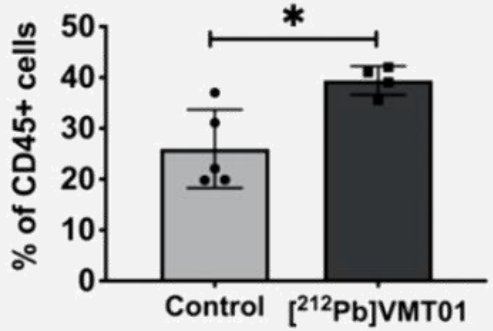
Lymphocyte subsets in immunocompetent murine melanoma models following treatment

- [^{212}Pb]VMT01 enhances tumor infiltrating lymphocytes in B16-F10 melanoma compared to untreated controls.
- C57BL6 mice bearing B16-F10 tumors were treated with 1.4 MBq [^{212}Pb]VMT01. Tumor infiltrating lymphocytes (TILs) were analyzed 7 days post treatment by flow cytometry using CD45 for leukocytes, CD3 for T cells, CD19 for B cells, CD4 for helper T cells, CD8 for cytotoxic T cells.[3]

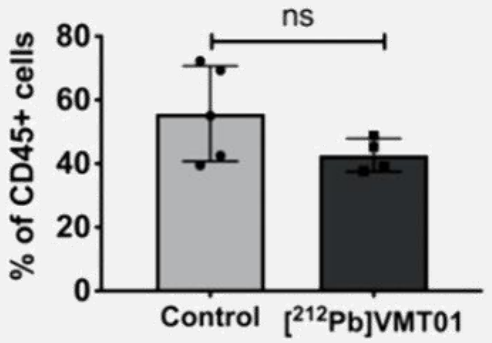
CD45+



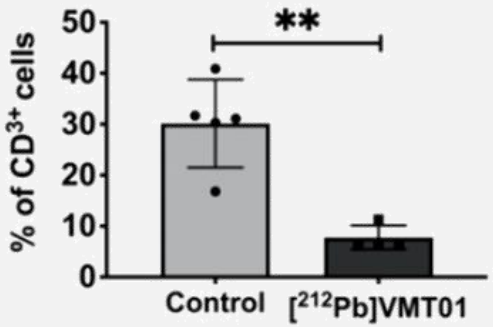
CD3+



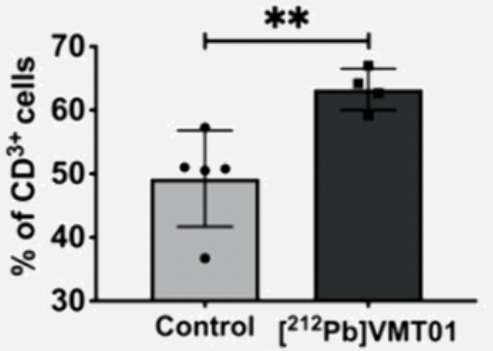
CD19+



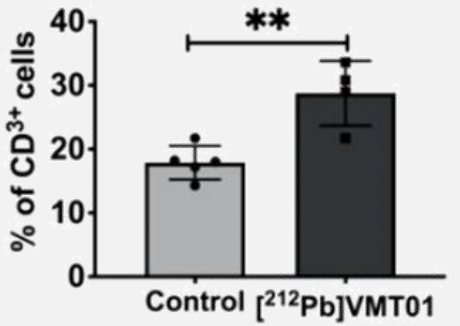
CD4-/CD8-



CD4+



CD8+



1. Li Met. al. Targeted Alpha-Particle Radiotherapy and Immune Checkpoint Inhibitors Induce Cooperative Inhibition on Tumor Growth of Malignant Melanoma. Cancers 2021, 13, 3676

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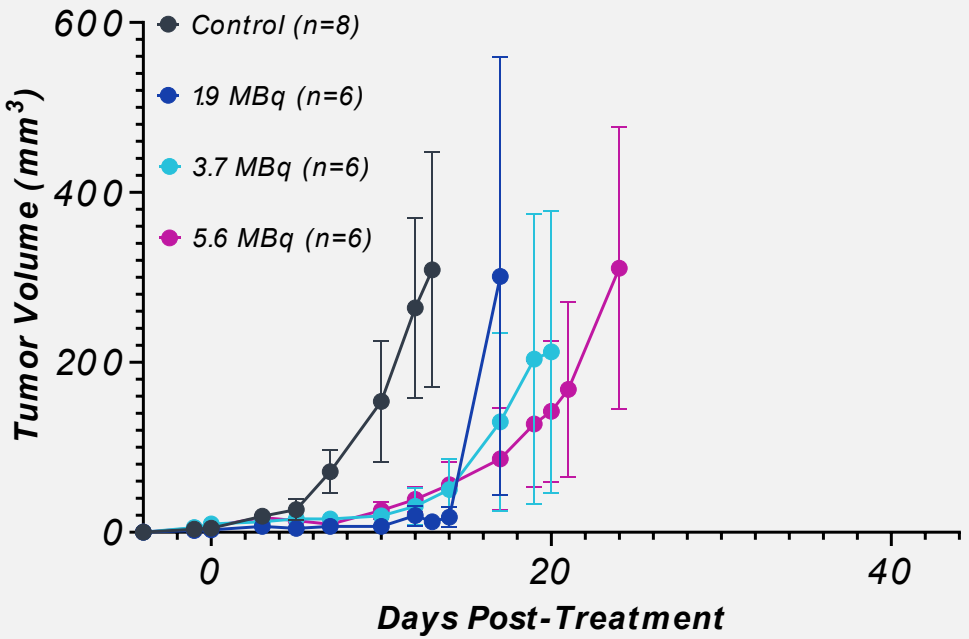
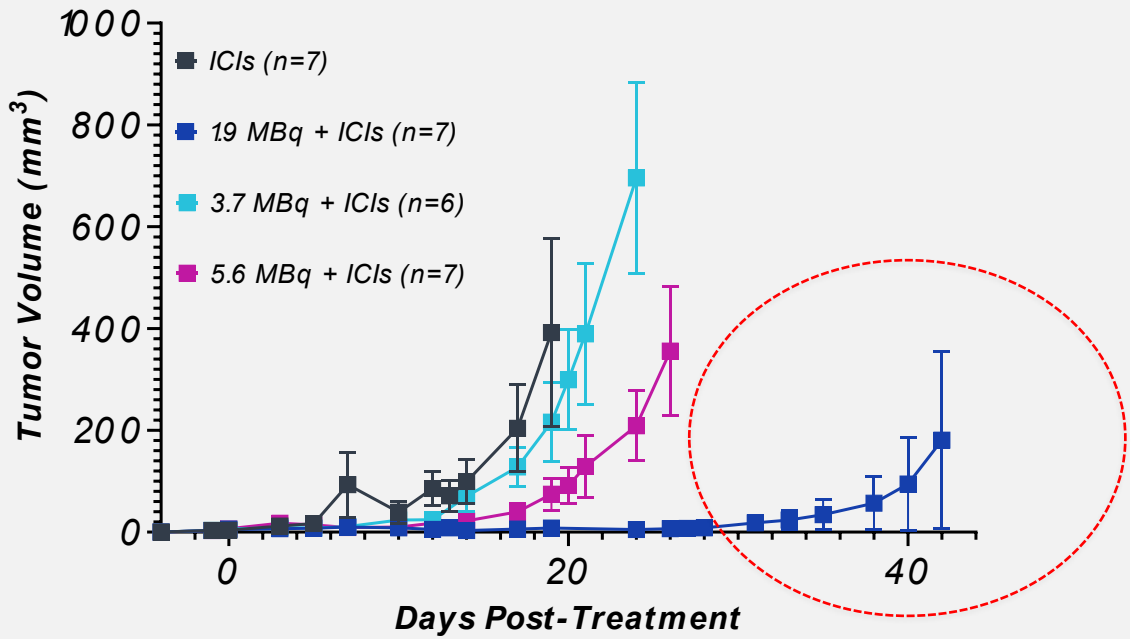
Low-dose targeted alpha therapy induces strong anti-tumor effectiveness in combination with immune checkpoint inhibitors

Monotherapy [^{212}Pb]VMT01



Combination Therapy [^{212}Pb]VMT01 + ICIs



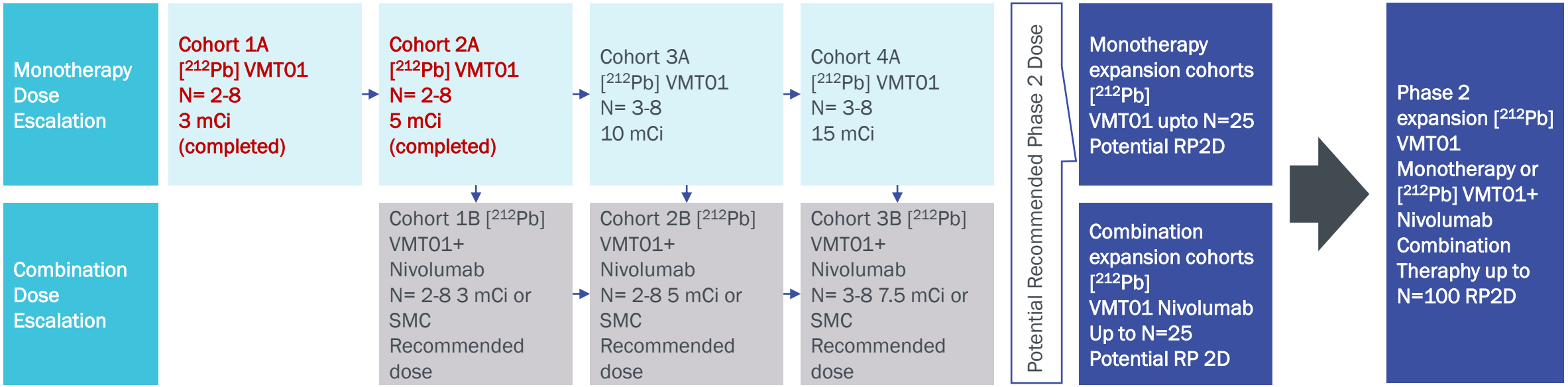
In C57Bl6 albino mice inoculated with B16.F10 allograft tumors, treatment with [^{212}Pb]VMT01 monotherapy shows increasing efficacy with higher doses (left). When combined with immune checkpoint inhibition lower doses of [^{212}Pb]VMT01 show increased efficacy (right). Doses roughly translate to 10 Gy, 20 Gy, and 30 Gy delivered to the tumor, respectively.[1]

1. Rodman et al., International Symposium on Radiopharmaceutical Sciences iSRS 2023, 22-26 May 2023, Honolulu, Hawaii.

Study Design

- Patients were being selected for MC1R expression by [^{203}Pb]VMT01 SPECT/CT
- The first two cohorts incorporated voluntary, multiple-time points dosimetry using [^{203}Pb]VMT01 SPECT/CT scans
- Up to 3 treatment cycles of [^{212}Pb]VMT01, 8 weeks apart

Primary Objectives	To determine the MTDs,MFDs, and RP2Ds in Combination with PD-1 inhibitor (nivolumab)	**MC1R Dosimetry**	MC1R[^{203}Pb] VMT01 SPECT/CT
MC1R Imaging patients Selection	MC1R[^{203}Pb] VMT01 SPECT/CT MC1R[^{68}Ga] VMT02 PET/CT	**Design Methodology**	mTPI-2



NIVO will be administered every 4 weeks up to 24 months

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Patient Characteristics (N=10)		
Age		
N	10	
Mean (SD)	67.2	
Median	67	
Range	49, 81	
Sex, N (%)		
Female	4 (40)	
Male	6 (60)	
Race, N (%)		
White	10 (100)	
Fitzpatrick Skin Phototype, N (%)		
TYPE I	2 (20)	
TYPE II	1 (10)	
TYPE III	2 (20)	
TYPE IV	5 (50)	
Time from diagnosis to C1D1 (yrs)		
N	10	
Mean (SD)	5.1	
Median	4.5	
Min, Max	1.3, 10.4	
ECOG Performance Status, N (%)		
0	6 (60)	
1	4 (40)	
Best Response to last systemic therapy, N (%)		
PD	4 (40)	
SD	6 (60)	
	Prior Lines Systemic Therapy (median)	**Prior Lines IO Therapy (median)**
Cohort 1 (3mCi) (N = 3)	5	3
Cohort 2 (5 mCi) (N = 7)	5	3

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Treatment-emergent Adverse Events (TEAEs) by Preferred Term and Grade (Frequency >1 and / or Grade >1)

	[212]-VMT01 3 mCi (n=3)			[212]-VMT01 5 mCi (n=7)			Total (n=10)		
Grade	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Total Number of TEAEs Reported for All patients	31	6	-	12	12	4	43	18	4
AEs by Preferred Term and Grade Reported per Patient *[no patients with AE (% of pts treated per cohort)]*									
Grade 1 and Frequency > 1									
Anaemia	3 (100)	-	-	-	1 (14)	-	3 (30)	1 (10)	-
Lymphocyte count decreased	2 (67)	1 (33)	-	1 (14)	1 (14)	1 (14)	3 (30)	2 (20)	1 (10)
Nausea	2 (67)	-	-	1 (14)	1 (14)	-	3 (30)	1 (10)	-
Hyponatraemia	2 (67)	-	-	-	-	-	2 (20)	-	-
Thrombocytopenia/platelet count decreased	2 (67)	-	-	-	-	-	2 (20)	-	-
Abdominal pain	-	-	-	-	1 (14)	-	-	1 (10)	-
Back pain	-	-	-	-	1 (14)	-	-	1 (10)	-
Grade ≥2									
Cough worsening, not coded	-	-	-	-	1 (14)	-	-	1 (10)	-
COVID-19	-	2 (67)	-	-	-	-	-	2 (20)	-
Dysphagia	-	-	-	-	1 (14)	-	-	1 (10)	-
Dyspnoea (incl 'Dyspnea worsening, not coded')	-	1 (33)	-	-	1 (14)	-	-	2 (20)	-
Fatigue (incl 'Fatigue worsening, not coded')	-	-	-	-	2 (28.6)	1 (14)	-	2 (20)	1 (10)
Haemoptysis	-	-	-	-	-	1 (14)	-	-	1 (10)
Hepatic vein thrombosis	-	-	-	-	1 (14)	-	-	1 (10)	-
Pneumonitis, not coded	-	-	-	-	1 (14)	1 (14)	-	1 (10)	1 (10)
Sinusitis	-	1 (33)	-	-	-	-	-	1 (10)	-
Urinary tract infection	-	1 (33)	-	-	-	-	-	1 (10)	-

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[^{203}Pb]-VMT01 theranostic dosimetry for [^{212}Pb]-VMT01

ROI	Dose Coefficients (Gy/mCi) and Cumulative Dose to Date (Gy)						Mean Coefficient, & Est'd Cumulative Dose	
	01-116		02-117		03-114			
	Coefficient (Gy/mCi)	Cumulative 2 x 5 mCi (Gy)	Coefficient (Gy/mCi)	Cumulative 1 x 5 mCi (GY)	Coefficient (Gy/mCi)	Cumulative 2 x 5 mCi (Gy)	Coefficient Mean ± SD (GY/mCi)	Cumulative 3 x 3 mCi (GY)
Liver	0.22	2.21	0.12	0.62	0.15	1.52	0.17 ± 0.05	1.49
Kidneys	2.96	29.6	3.07	15.4	2.56	25.6	2.87 ± 0.27	25.8
Spleen	0.23	2.27	0.34	1.72	0.29	2.85	0.29 ± 0.06	2.57
Marrow	0.11	1.08	0.08	0.41	0.08	0.82	0.09 ± 0.02	0.81
Tumors	0.25	2.53	0.14, 0.15	0.70 - 0.77	0.17, 0.26, 0.28	1.72 - 2.83	0.21 ± 0.06	1.26 - 2.55

Note: MC1R is expressed in normal renal parenchyma.[9] Tumor dosimetry does not account for partial volume effects
Translational research suggests that MC1R is expressed in normal renal parenchyma. Tumor dosimetry does not account for partial volume effects

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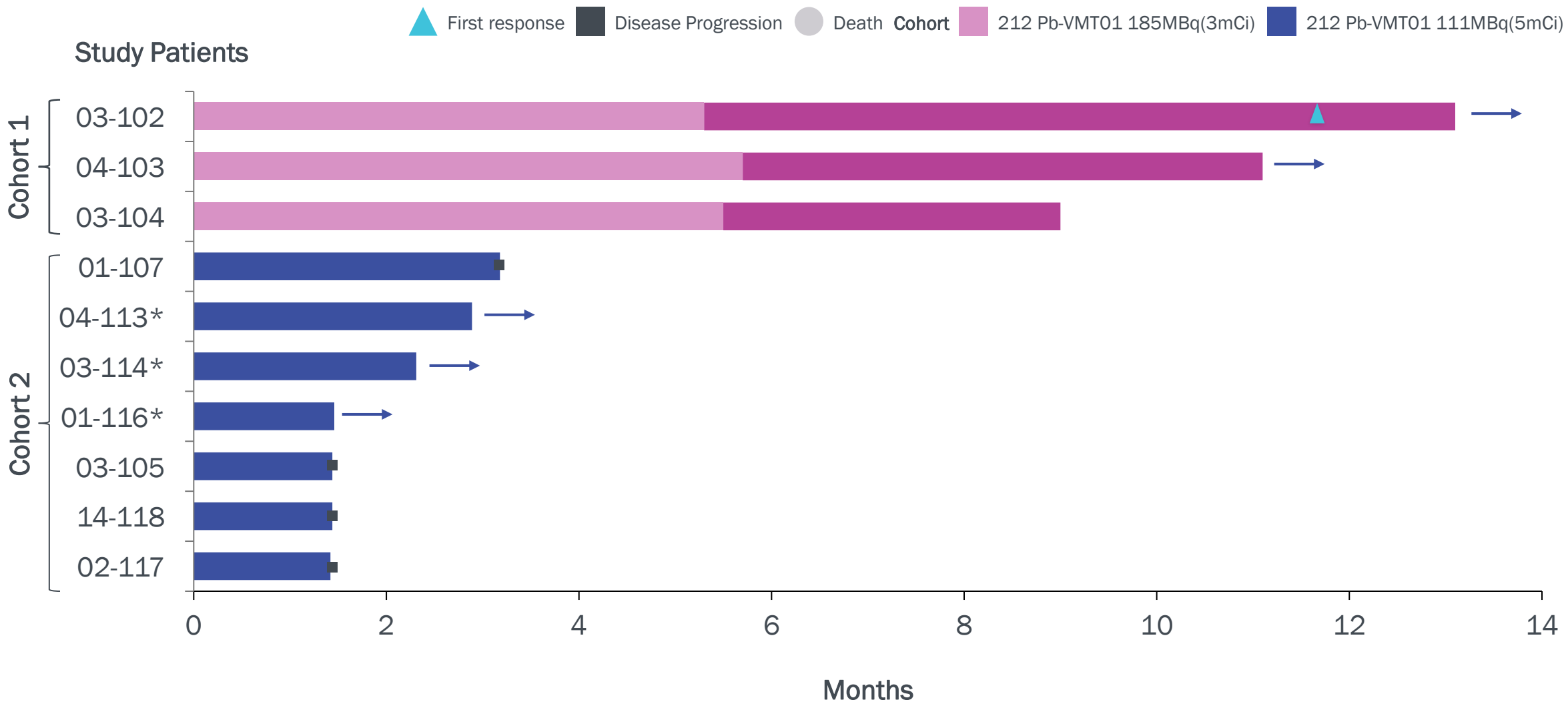
VMT01 Efficacy: Swim Lane Plot



Notes: Data cutoff (DCO) 04-SEP-2024. Patients 113, 114 and 116 had PD after DCO.

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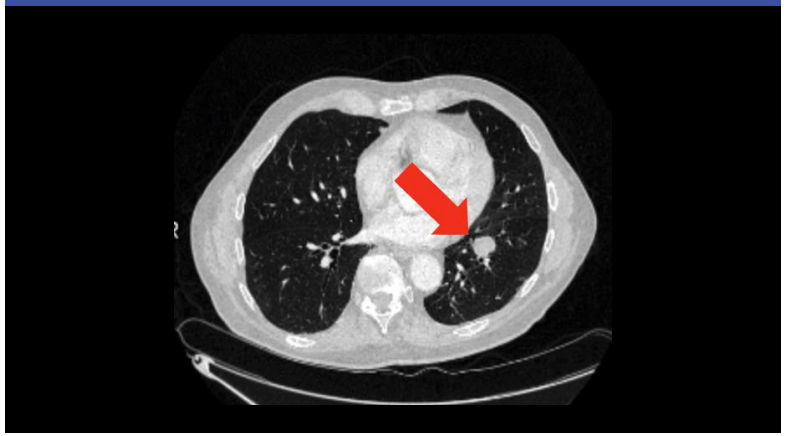
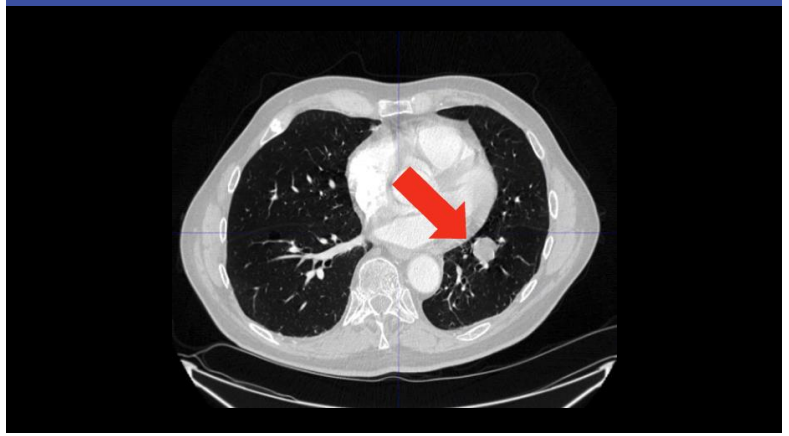
Patient with uPR after [^{212}Pb]VMT01

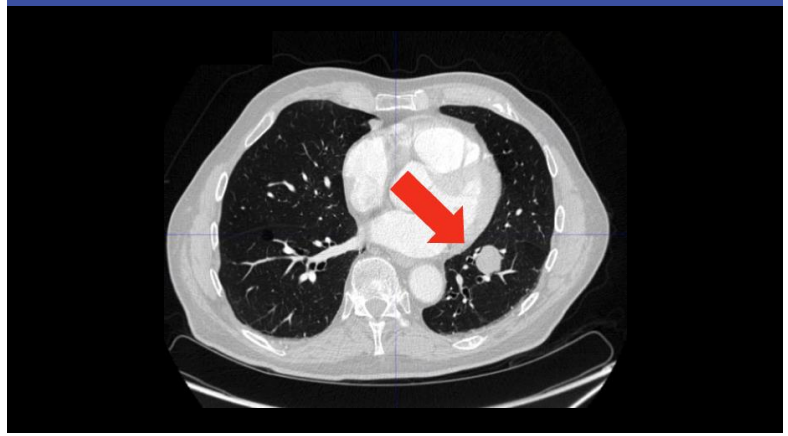
07/6/2023 Baseline



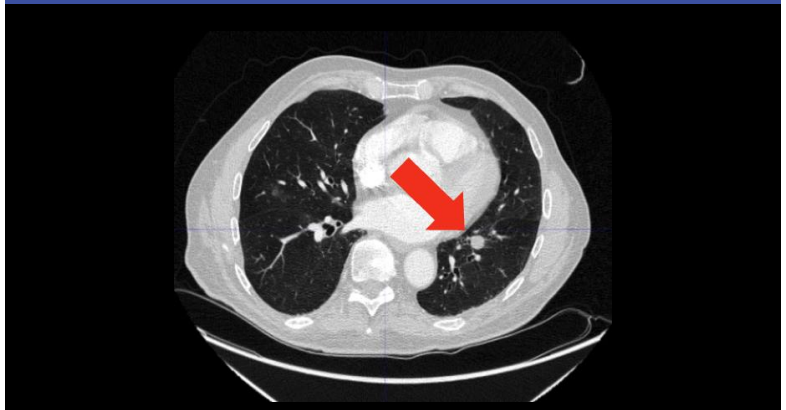
09/13/2023> C1



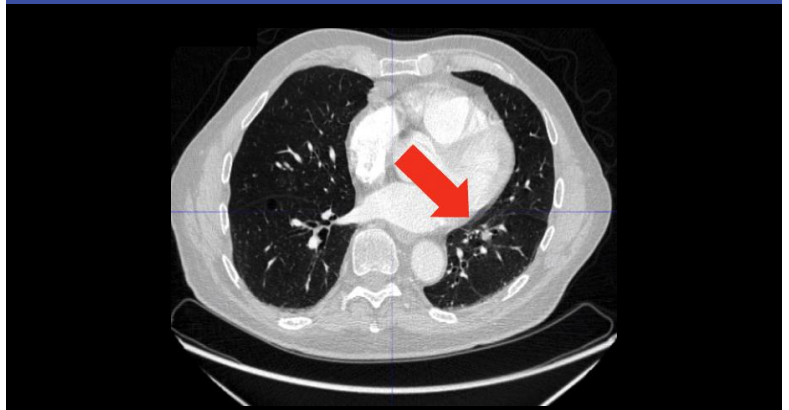
01/02/2024> C3



03/28/2024: FU Week 34



08/08/2024: FU Week 52



Pulmonary Metastasis with almost complete resolution occurred after three cycles in the post-treatment observation phase

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Efficacy Summary

- In Cohort 1, all subjects completed the planned treatment cycles; two subjects showed prolonged SD of 9 months and 11 months, respectively, from start of treatment
- One subject in Cohort 1 developed an objective response (PR – unconfirmed to date) after completion of all three VMT01 administrations and is still on trial after 13 months from start of treatment
- In Cohort 2, all subjects progressed after either the first cycle (3 subjects) or the second cycle (4 subjects)
- Preclinical experiments demonstrated higher immunostimulatory efficacy in combination with immune checkpoint inhibitors at lower doses whereas direct cytotoxic tumor effects were observed at higher activity doses[3]; here we see a delayed anti-tumor response at a lower dose with monotherapy
- We hypothesize that low-dose monotherapy in Cohort 1 leads to immunostimulatory activation within the tumor microenvironment (TME) resulting in prolonged disease control. This suggests the potential for the cooperation of [^{212}Pb]VMT01 with ICI in patients
- **Unexpectedly, we may have defined between Cohort 1 and Cohort 2 dose levels with VMT01 which may delineate the immunostimulatory and immunosuppressive effects on the TME in melanoma**

Conclusion

- At 3 mCi and 5 mCi activity levels, [^{212}Pb]VMT01 was safe and no DLTs were observed
- Dosimetry demonstrates high kidney estimates limiting monotherapy escalation
- SMC recommendation included dose reduction to 1.5 mCi for both monotherapy and the upcoming combination cohort with nivolumab
- **An objective response and prolonged PFS was observed at the 3 mCi activity level**
- The observed efficacy in Cohort 1 may be a result of the immunostimulatory effect of low dose ^{212}Pb-targeted alpha particle radiation on the TME, as observed in preclinical studies
- An amendment to test lower dose levels for monotherapy is planned
- **The combination cohort with nivolumab is active and now open for enrollment**

Q & A