

First-In-Human Phase 1 Study of ATNM-400, a Novel HER3-Targeting, Actinium-225 Antibody Radioconjugate, in Metastatic Castration-Resistant Prostate Cancer (mCRPC)

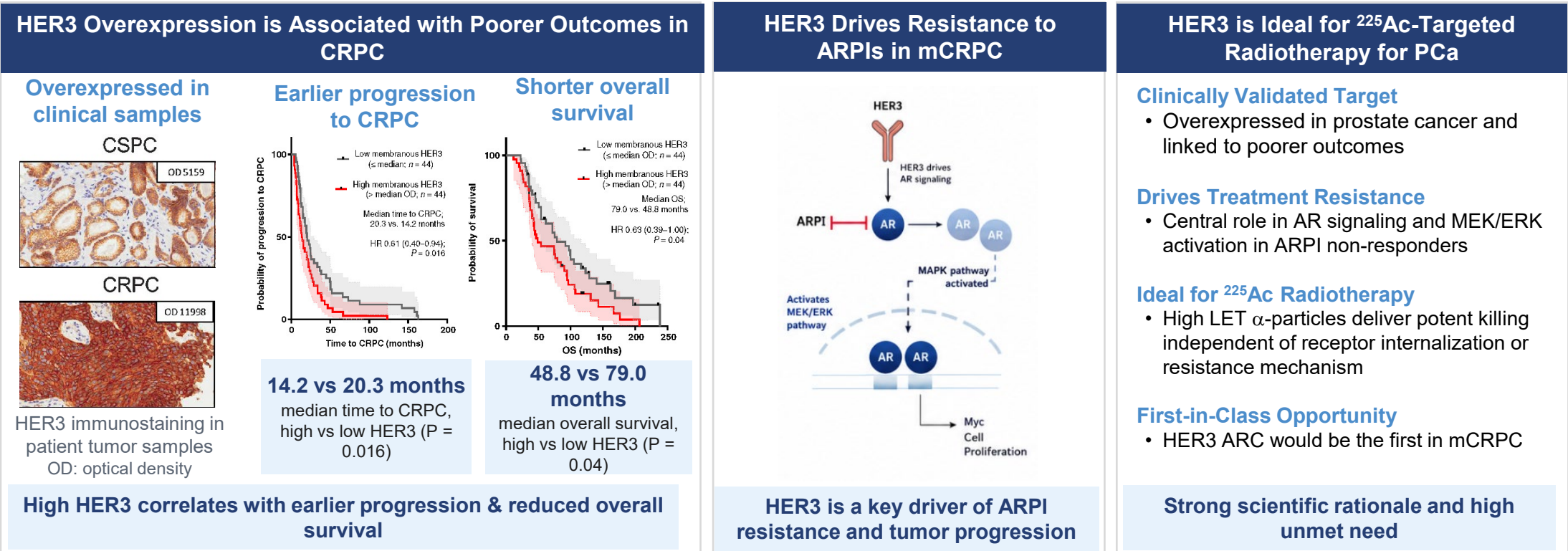
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EANM Disclosure of Interest Statement

- 1) All clinical nuclear medicine images and data in the submitted abstract were obtained under EARL PET/CT | PET/MR accreditation.
- 2) JK and SH are employees of Actinium Pharmaceuticals, Inc.
- 3) No other co-authors receive support from a pharmaceutical, device, or biotechnology company.
- 4) No co-authors hold property rights or patents for (radio)pharmaceuticals or medical devices or have interests in medical consulting firms.
- 5) No co-authors have written articles for (radio)pharmaceutical, medical device, biotechnology, or consulting companies in the past five years.



HER3 is a High-Value Target for Actinium-225 Radiotherapy in Prostate Cancer



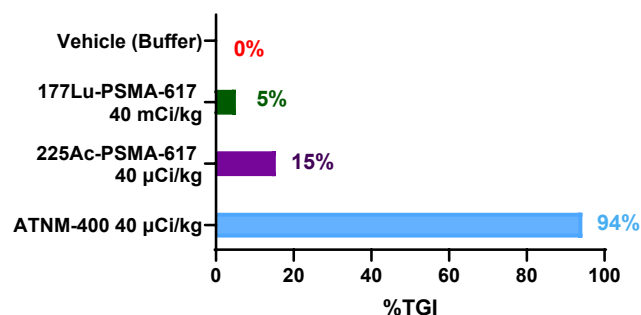
Targeting HER3 with ATNM-400 combines potent alpha-radiation with dual benefit: direct tumor cell killing and reversal of ARPI resistance in mCRPC



ATNM-400 is Efficacious Across Varying Levels of PSMA & HER3 Expression

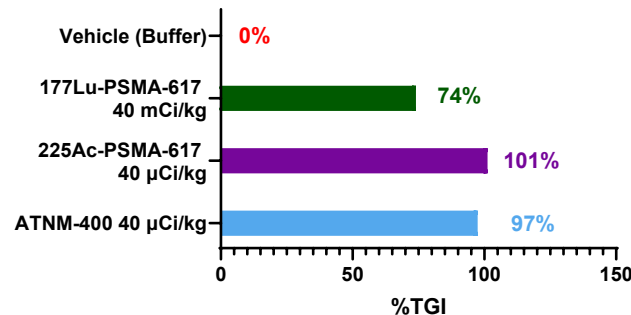
In vivo efficacy in 22Rv1 prostate cancer cells
(Low PSMA, Moderate HER3)

Mean tumor growth inhibition (%TGI) at day 20



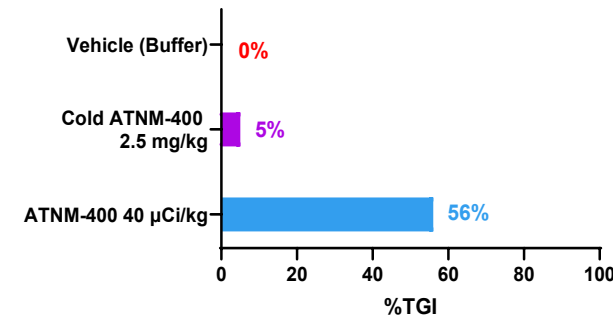
In vivo efficacy in C4-2 prostate cancer cells
(High PSMA, High HER3)

Mean tumor growth inhibition (%TGI) day 25



In vivo efficacy in DU145 prostate cancer cell
(Negative PSMA, Low HER3)

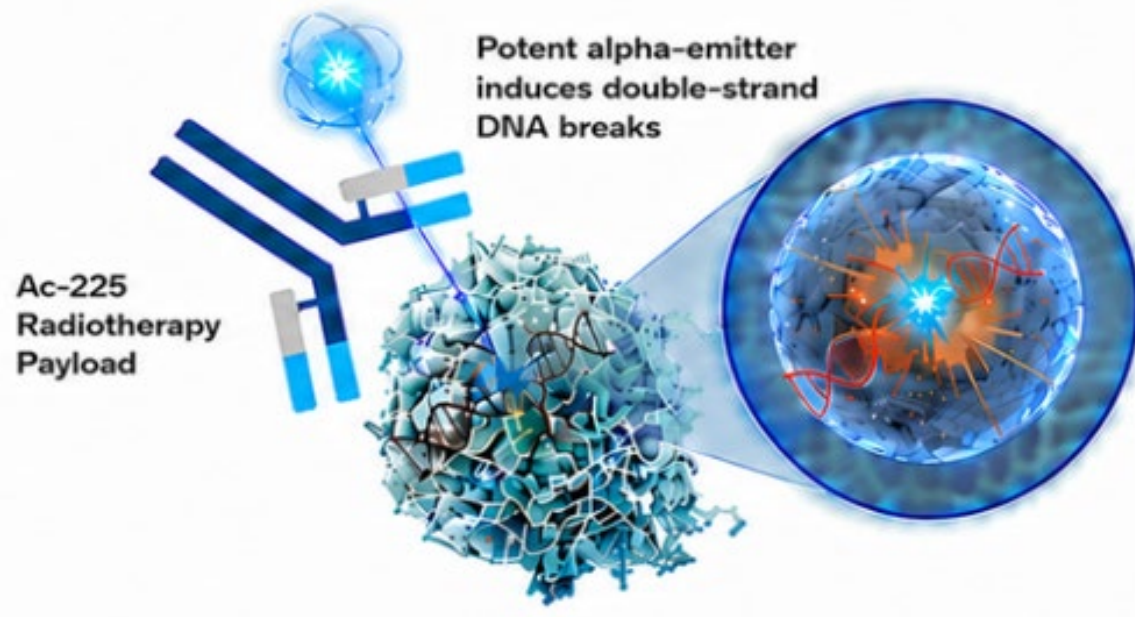
Mean tumor growth inhibition (%TGI) day 30



- ATNM-400 ($[^{225}\text{Ac}]$ Ac-barecetamab-DOTA) is efficacious in PSMA high, low and negative prostate cancer models as well as in ATNM-400 HER3-high, moderate and low prostate cancer models



ATNM-400: A HER3-Targeting Radiotherapy in Prostate Cancer



Theranostic Approach

- Theranostic approach with Zr-89 for imaging and Ac-225 for therapy being utilized in the Phase 1 dose escalation study in mCRPC
 - [^{89}Zr]Zr-barecetamab-DFO
 - [^{225}Ac]Ac-barecetamab-DOTA
- HER3-positive lesions (SUV ≥ 1.5 times that of pelvic muscle) on day 4 [^{89}Zr]Zr-barecetamab-DFO PET (imaging on days 0, 1, 4 and 7)



Study Design

Key Inclusion & Exclusion Criteria

- Confirmed progressive mCRPC
- Received at least one ARPI
- Received at least one taxane regimen (unless deemed unsuitable or patient declined chemotherapy)
- [¹⁷⁷Lu]Lu-PSMA permitted
- ECOG PS 0-1
- Adequate organ function
- No prior radiotherapeutic agents or ADCs targeting HER3

Imaging Assessment & Dosimetry

- Theranostic-based patient selection [⁸⁹Zr]Zr-barecetamab-DFO Day 4 HER3 positive

Dose Escalation

N=22-40

- ATNM-400 IV q6w, up to 4 cycles
- 4 dose levels: 1.0, 1.5, 2.25, 3.0 µCi/kg (37, 55.5, 83, 111 kBq/kg)

Dose Expansion

N=18

- ATNM-400 IV q6w, up to 4 cycles
- Dose level: RP2D

• Objectives — 3+3 Dose Escalation

- Primary: TEAEs & DLTs
- Secondary: Dosimetry & PK

• Objectives — Dose Expansion

- Primary: RP2D, Safety & Tolerability
- Secondary: Antitumor activity — PSA50 · ORR · rPFS · OS



Patient Summary

- Imaging dose (2 ± 0.2 mCi); Treatment dose (1.0 μ Ci/kg, 0.037 MBq/kg)

Pt Number	Age (yr)	Prior Treatments	HER3 +*	ATNM-400 (C1D1)	ATNM-400 (C2D1)	ATNM-400 (C3D1)	ATNM-400 (C4D1)
1	88	ARPI Cabazitaxel + Carboplatin	√	√	√	√	
2	79	ARPI Docetaxel [¹⁷⁷ Lu]Lu-PSMA Cabazitaxel	√	√	√	√	
3	87	ARPI	√	√	√		

*Based on Day 4 [⁸⁹Zr]Zr-barecetamab-DFO PET scan

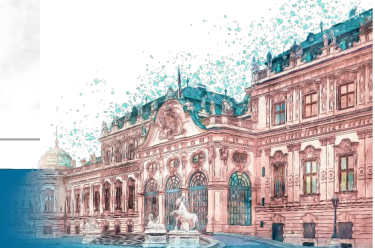
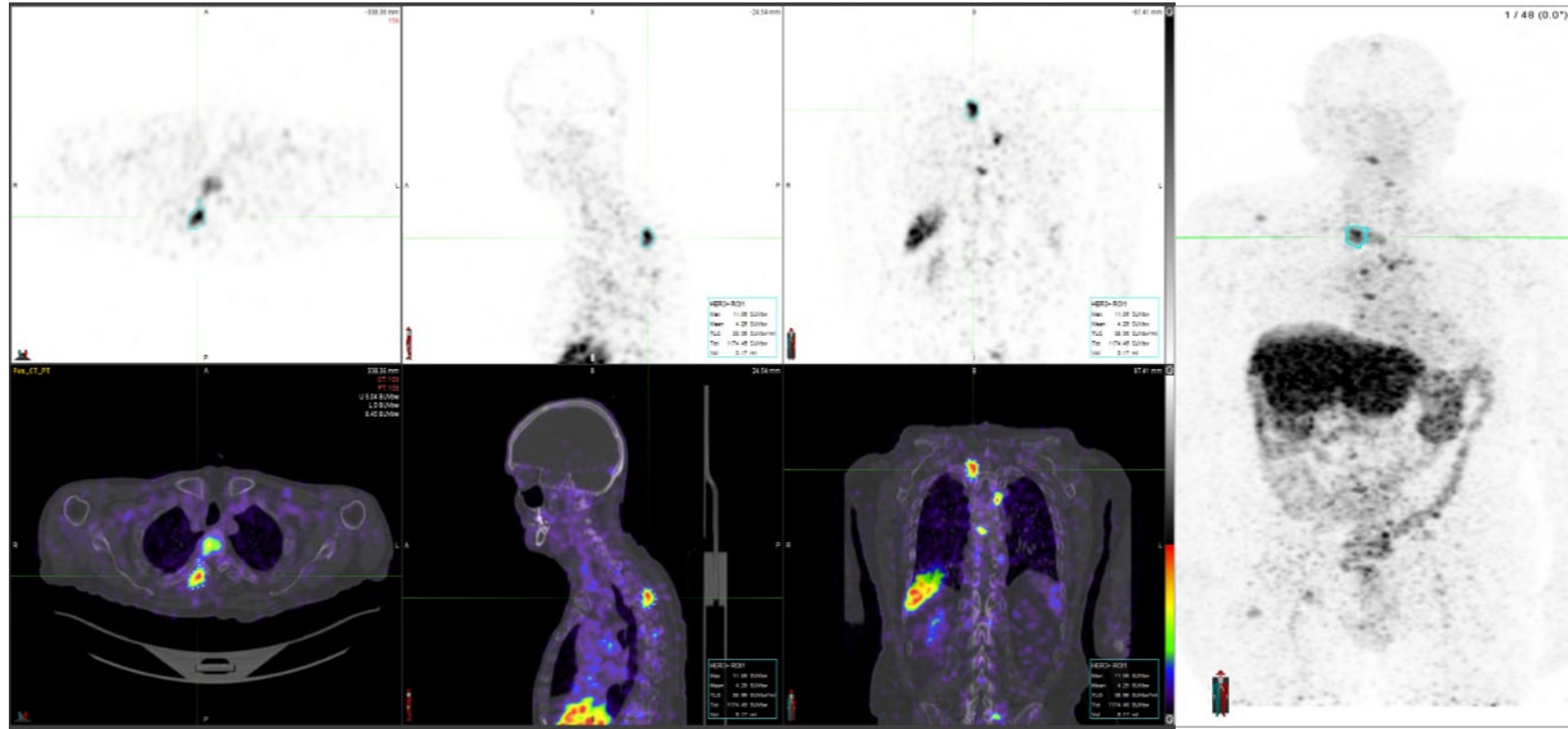


Safety

- No xerostomia
- No DLTs observed
- No Gr3/4 hematologic AEs observed during DLT window and beyond
- No ALT/AST elevation
- No Cr elevation
- Gr 2 nausea (1 pt) managed with metoclopramide
- No injection site or infusion-related reaction

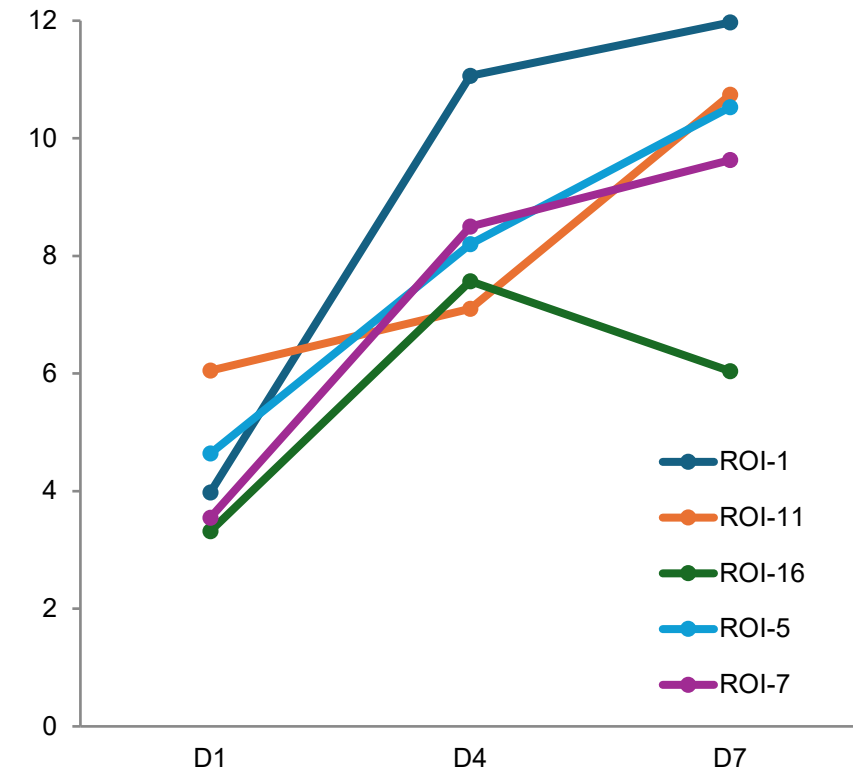


Biodistribution Day 4 post [⁸⁹Zr]Zr-barecetamab-DFO administration



[⁸⁹Zr]Zr-barecetamab-DFO Lesion Uptake

Lesion	D1	D4	D7
	SUV max	SUV max	SUV max
ROI-1	3.98	11.06	11.97
ROI-5	4.64	8.2	10.53
ROI-7	3.55	8.5	9.63
ROI-11	6.05	7.10	10.74
ROI-16	3.32	7.57	6.04



Conclusion

- HER3 is a compelling target for alpha therapy in mCRPC
- Dose escalation of ATNM-400 has cleared dose level 1 (1 $\mu\text{Ci/kg}$) with no DLTs
- No xerostomia and no Gr3/4 hematologic toxicity were observed
- ^{89}Zr -barecetamab-DFO imaging supports patient selection
- PET shows encouraging tumor uptake and retention through Day 7
- ATNM-400 dose escalation has advanced to dose level 2 (1.5 $\mu\text{Ci/kg}$) and is ongoing



Acknowledgements

- The Investigators and Actinium Pharmaceuticals would like to thank all the care teams and staff at the clinical sites for their hard work
- Most importantly, our deepest thanks to the patients, their families and caregivers who participated in this study

Site	Location	Status
Genesis Care Murdoch	Perth, Western Australia	Enrolling
ICON Cancer Centre – Hollywood	Perth, Western Australia	Enrolling
Melbourne Theranostic Innovation Centre (MTIC)	North Melbourne, Victoria	Enrolling
Macquarie University Hospital	North Ryde, New South Wales	Enrolling
Genesis Care St. Andrews	Adelaide, South Australia	Enrolling
Genesis Care Malvern	Malvern, Australia	Site-Start Up

● SITE DETAILS

