Actinium Pharmaceuticals, Inc.

Building a Transformative Ac-225 Portfolio for Next-Generation Precision Oncology

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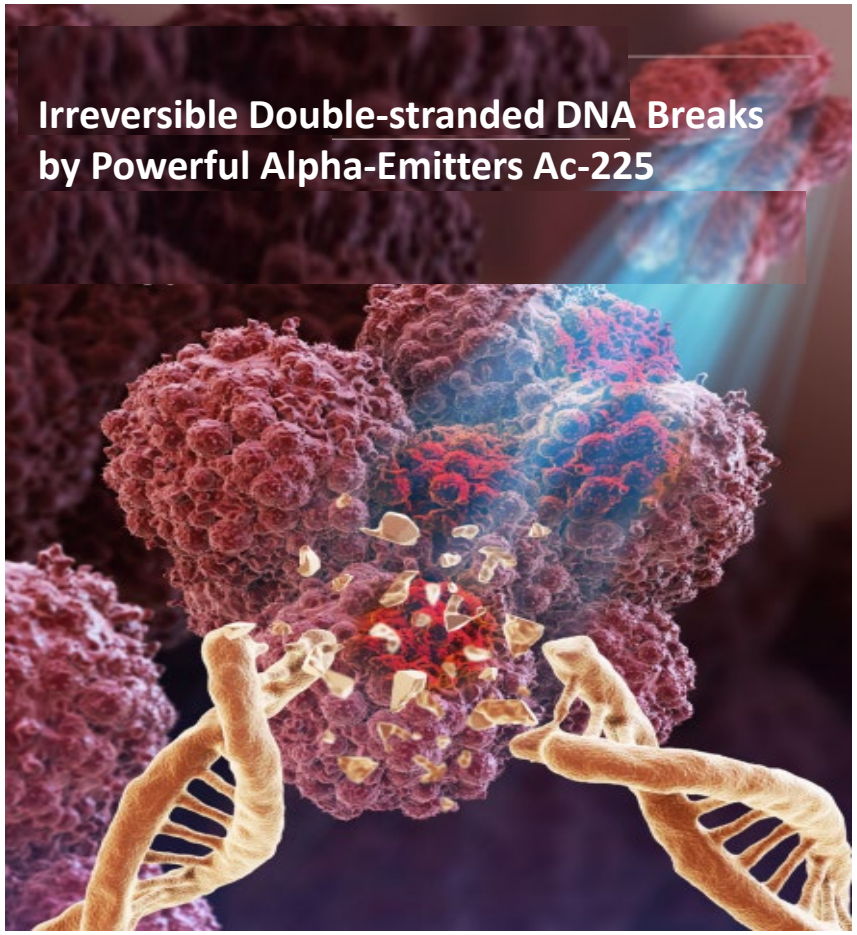
Today's Presentation

- Introduction to Actinium Pharmaceuticals
- Bridging preclinical to clinical: translational studies to optimize efficacy and patient selection
    1. Actimab-A for mutation agnostic AML
    2. ATNM-400 for therapy resistant Prostate Cancer
- Addressing high unmet need: Leveraging the powerful alpha-emitter Actinium-225 to overcome tumor resistance mechanisms



Source: Modified from *Nature* cover – Sep 2022 Vol 3 No. 9

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Introduction to Actinium

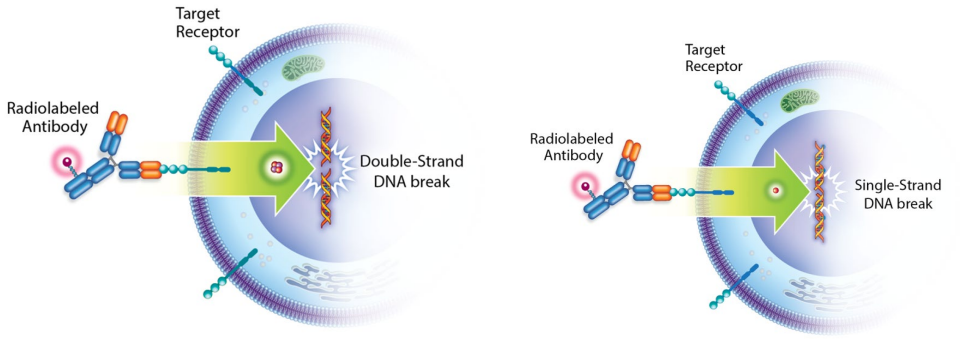
Developing first-in-class targeted radiotherapies for indications with high unmet needs to improve patient access and outcomes

Innovation Focused R&D Yields Differentiated, High-Value Programs

Robust Experience Across Multiple Validated Cancer Targets & Isotopes

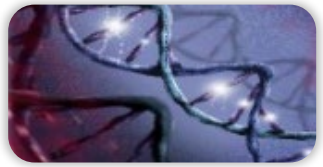
CD33	CD45	CD38	ICI	Undisclosed
AML, MDS and MM	Leukemia, Lymphoma and immune cells	MM and leukemia cells	Solid tumors and blood cancers	Solid tumor theranostics

Iodine-131	Actinium-225	Lutetium-177
Range: 2.3 mm	*Range: .048 mm*	*Range: 1.8 mm*
Energy: 0.6 MeV	*Energy: 24 MeV*	*Energy: 0.50 MeV*

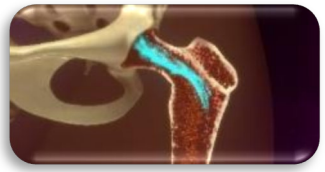


Broad Areas of Focus Leveraging Significant Clinical Development Experience

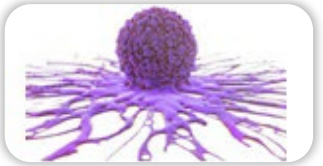
Hematology



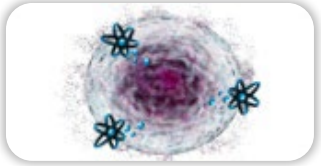
Targeted Conditioning



Solid Tumors



Next-Generation Radiotherapies



Strong, IP Portfolio of 230+ Patents including Ac-225 cyclotron-based manufacturing technology

ICI: Immune checkpoint Inhibitors
Actinium-225 linear energy transfer includes daughter emissions

Robust Pipeline for Hematology, Solid Tumors and Conditioning

	Program	Indication	Stage of Development
			Preclinical *Phase 1* *Phase 2* *Phase 3*
AML and Hematology	Actimab-A + CLAG-M	Fit R/R AML	*Seeking Collaborator for Ph 2/3*
	Actimab-A Triplet Combo	Frontline AML	
	Actimab-A Combinations *(FLT3, IDH 1/2, Menin)*	R/R AML	
Solid Tumors	Actimab-A with PD-1 inhibitors	MDSC Depletion in Solid Tumors	
	ATNM-400 (Undisclosed Target)	Prostate Cancer	
	Undisclosed Targets / Theranostics	Solid Tumor	
Conditioning	Iomab-ACT Prior to Commercial CAR-T	Hematological Malignancies	
	Iomab-ACT Prior to BMT / GeneTx	Sickle Cell Disease	
	Iomab-B BMT Targeted Conditioning	Active R/R AML	*Seeking U.S. Partner for Ph 2/3*

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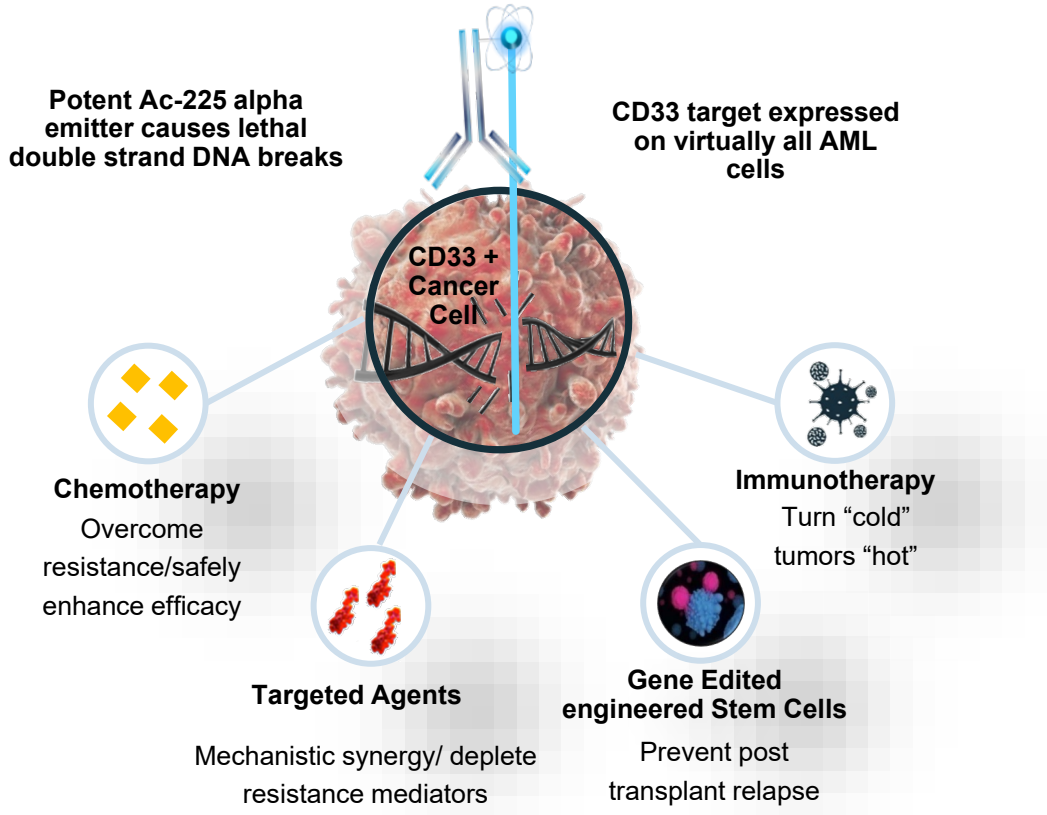
Heme: Actimab-A for AML

Clinical Therapeutics Program Investigating Combination Approaches

Actimab-A Program: Bolstered by Strong Clinical Data in AML

Backbone therapy potential with mutation agnostic mechanism of action and synergistic potential



Clinical experience supports late-stage trials and broad development plan in partnership with NCI CRADA

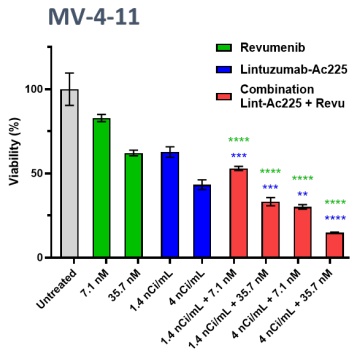
- Actimab-A links the Ac-225 alpha emitter targets validated CD33 antigen in a highly precise manner
- Clinical experience in ~150 AML patients across 6 clinical trials is also most developed Ac-225 program
  - Actimab-A clearly demonstrated high potency and minimal non-hematologic toxicities >grade 3 outside of myelosuppression in Phase 1/2 POC trial
- Actimab-A + CLAG-M combination clinical trial results provide strong validation of promise of this approach
- Potential in solid tumor indications by depleting MDSCs to enhance impact of immune checkpoint inhibitors
- Multiple opportunities to use Actimab-A in combination with chemotherapy, targeted agents and immunotherapy
- **Evidence of mutation agnostic mechanism of Actimab-A provides strong rationale for SoC combos in mutant AML**

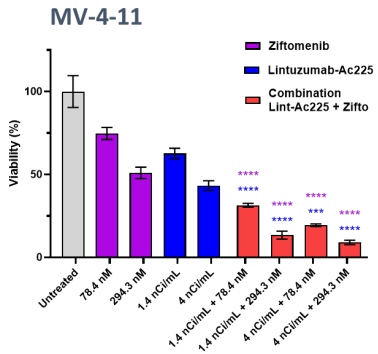
Enhanced Cytotoxicity: Actimab-A and SoC Combinations in Mutant AML

Potent Cytotoxicity with Menin Inhibitors that Target AML Mutations

KMT2A mutation

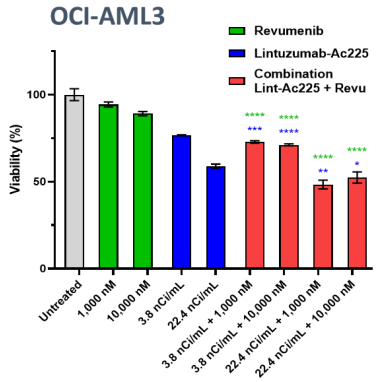
Menin Inhibitors Combination

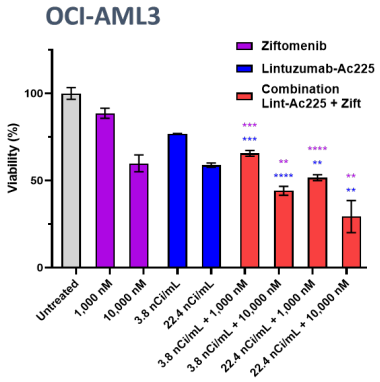




NPM1 mutation

Menin Inhibitors Combination

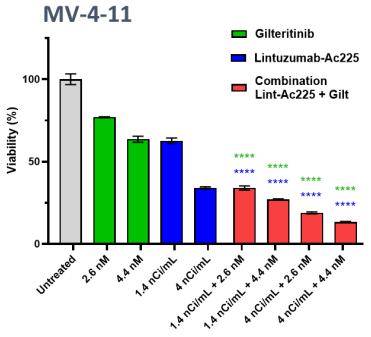


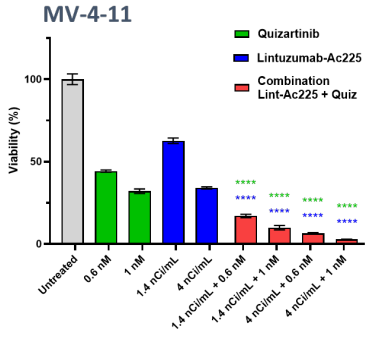


Potent Cytotoxicity with FLT3 Inhibitors or 5-Azacytidine that Target AML Mutations

FLT3 mutation

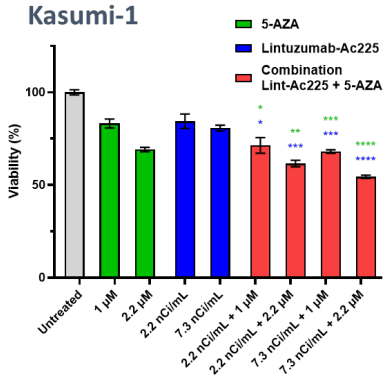
FLT3 Inhibitor Combination

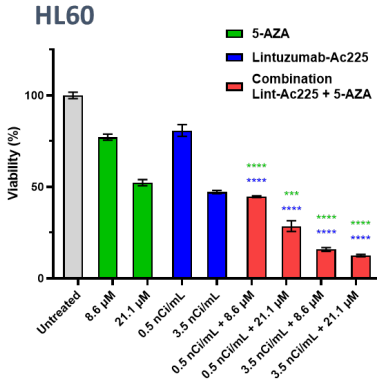




TP53 mutation

5-Azacitidine Combination





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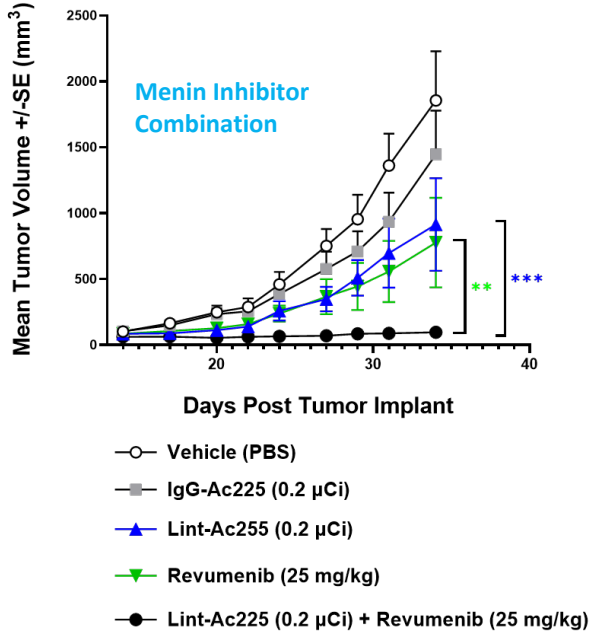
Lintuzumab-225Ac = Actimab-A

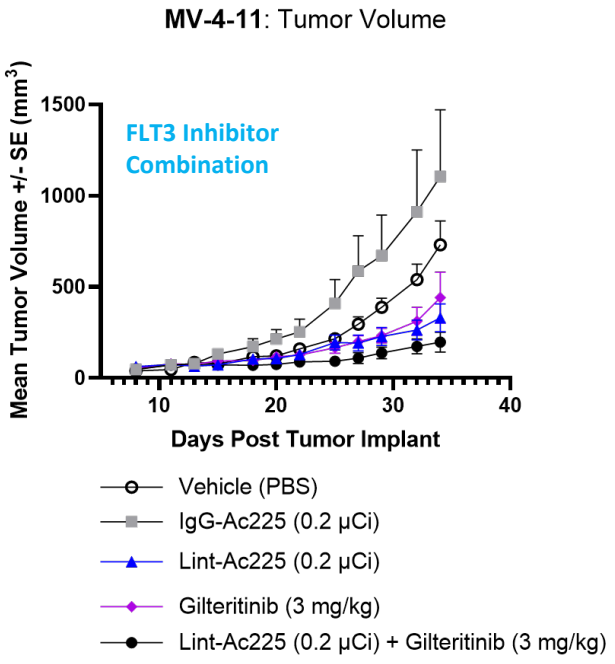
Combination of Actimab-A with Menin or FLT3 Inhibitors Potentiates In Vivo AML Cell Death

Anti-AML Efficacy was Significantly Potentiated by SoC Combination in Mice bearing AML Mutant Xenografts

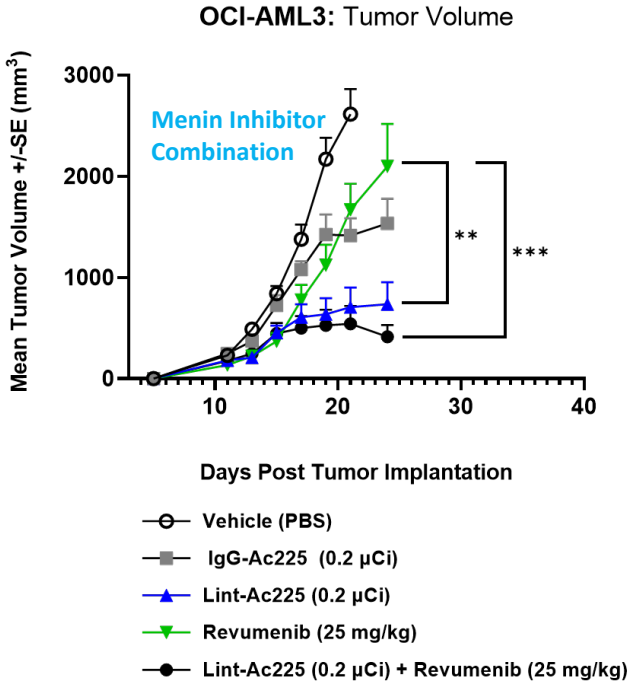
KMT2A mutation



FLT3 mutation



NPM1 mutation

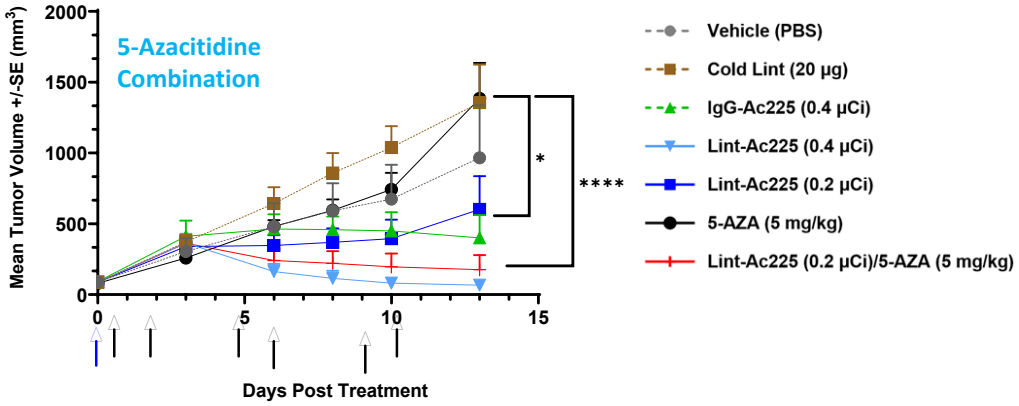


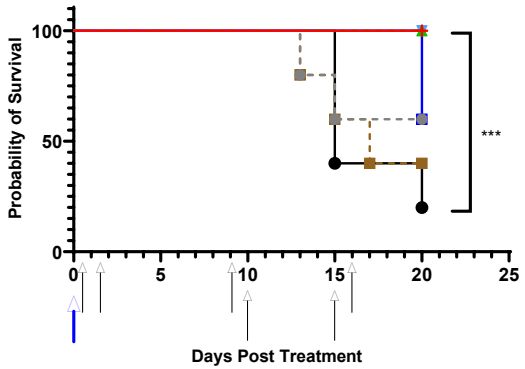
Combination of Actimab-A with Azacitidine Potentiates In Vivo AML Cell Death

Actimab-A is Efficacious as Monotherapy and in Combination with 5-Aza in s.c. model

TP53 mutation

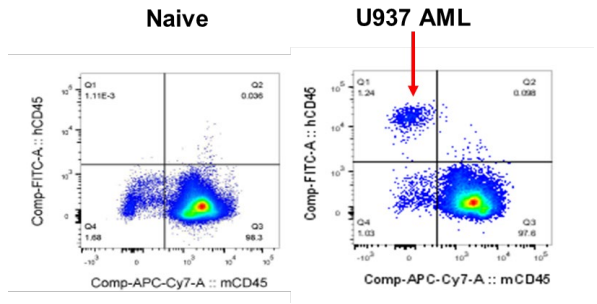
HL60: Tumor Volume



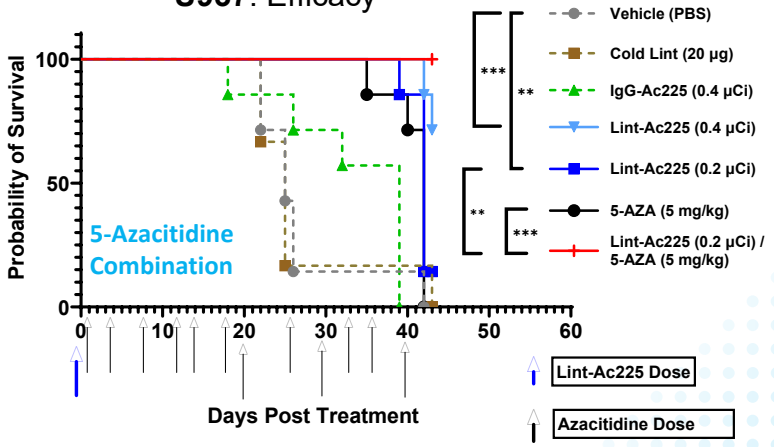


Actimab-A is Efficacious as Mono and in Combo with 5-Aza in disseminated model

TP53 mutation

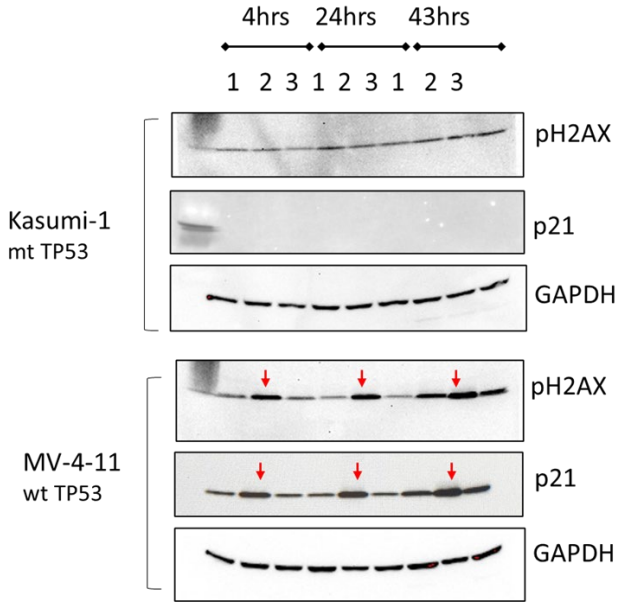


U937: Efficacy



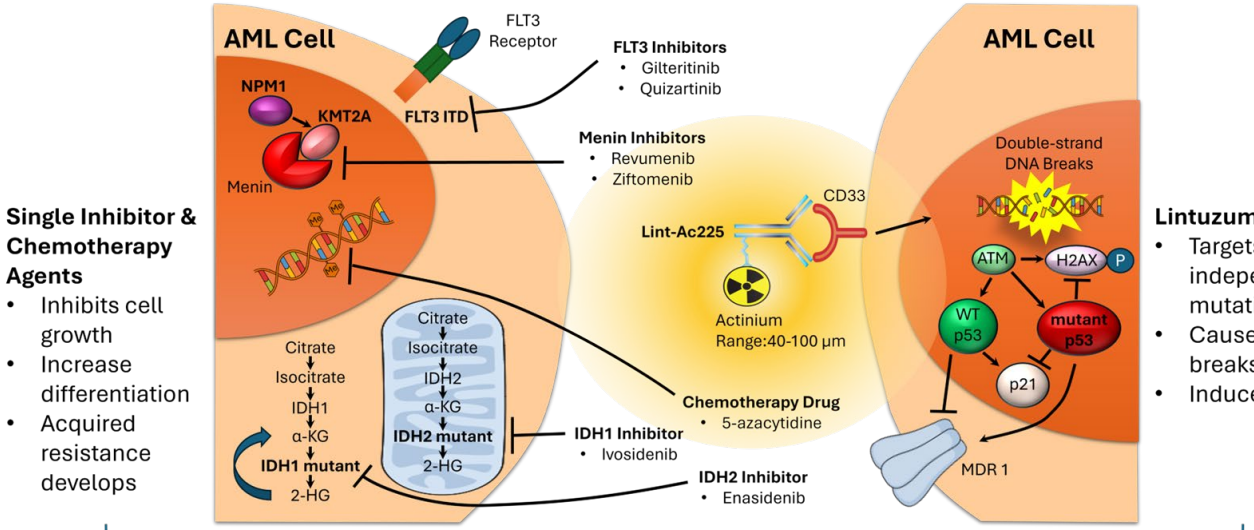
Actimab-A Mechanism of Action: DNA Stress and Damage Signaling

Actimab-A Induces pH2AX and p21 in WT TP53 but not mutant TP53 AML Cells



1= Non-treated
2= Lintuzumab Ac225 (10nCi/mL)
3= Lintuzumab

Actimab-A MOA and Effects of Combining with Various Inhibitors to Address AML Mutations



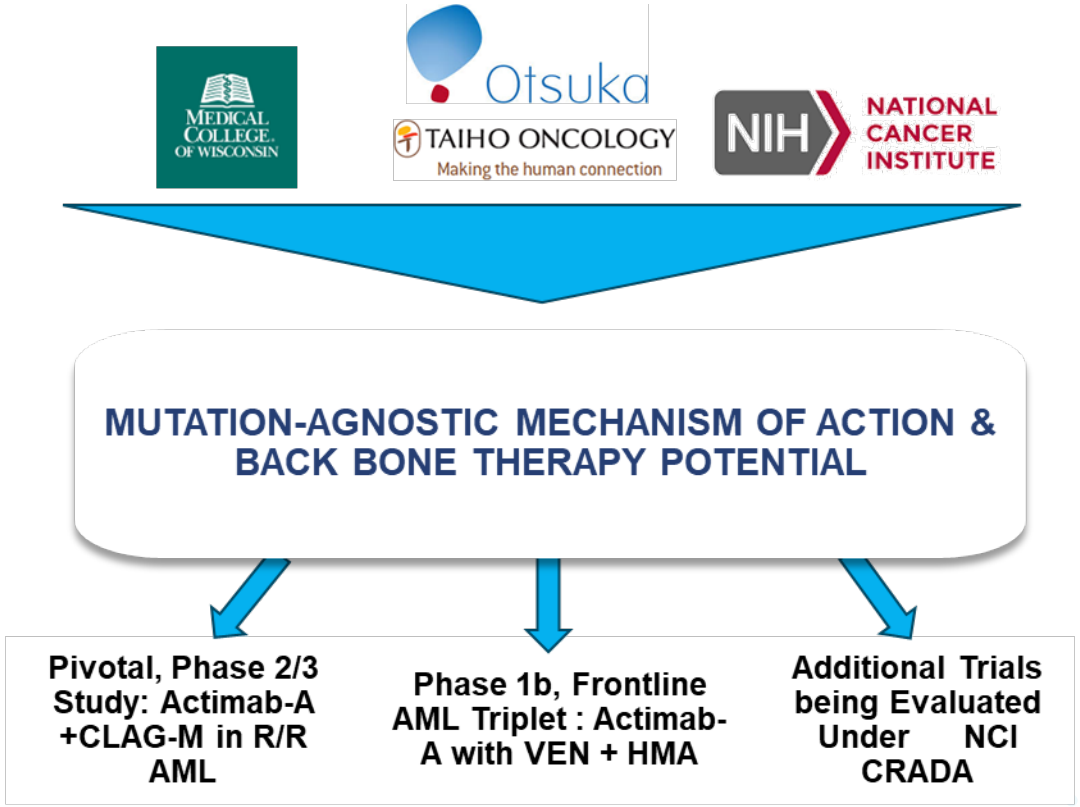
Single Inhibitor & Chemotherapy Agents
- Inhibits cell growth
- Increase differentiation
- Acquired resistance develops

Lintuzumab-Ac225
- Targets CD33+ cells independent of mutations
- Cause dsDNA breaks
- Induce cell death

Combination provides enhanced potency targeting AML cells

Actimab-A Summary

- **Broad Anti-Leukemic Activity:** Effective across AML cell lines, regardless of high-risk mutations (FLT3, NPM1, TP53, KMT2A rearrangements)
- **Enhanced Efficacy:** Improves disease control and durability of response in high-risk AML when used with standard-of-care therapies
- **Clinical Promise:** Supports development of Actimab-A as a backbone therapy for relapsed/refractory AML



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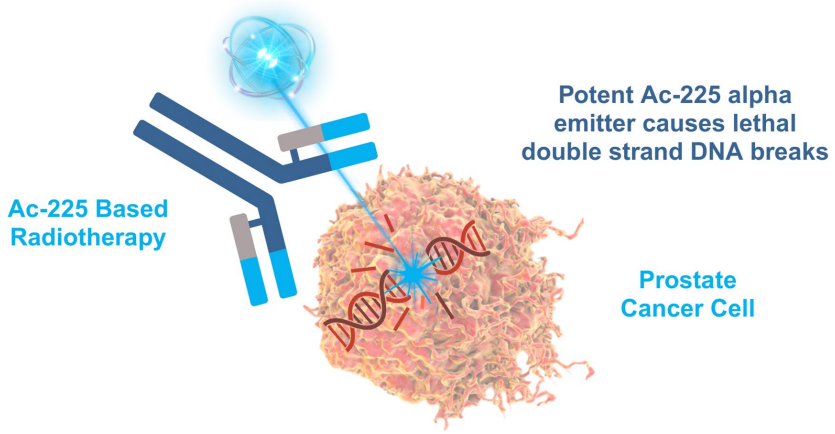
Solid Tumors: ATNM-400 for Prostate Cancer

ATNM-400 – First-in-class, non-PSMA Ac-225 targeted radiotherapy for prostate cancer

ATNM-400: Next-Generation, Non-PSMA Prostate Cancer Radiotherapy

Novel, First-in-Class Ac-225 Based Radiotherapy



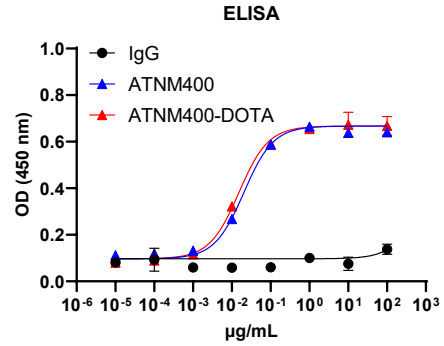
High Unmet Medical Need in Prostate Cancer for Patients Progressing after Pluvicto Treatment

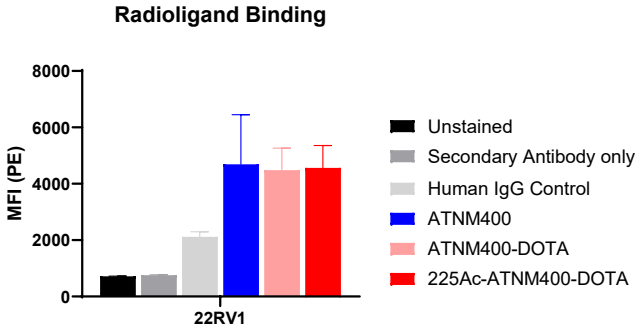
- Over 300,000 patients will be diagnosed with prostate cancer in the U.S. in 2025 and approximately 1.5 million patients globally[1]
- Pluvicto (177Lutetium-PSMA-617) is approved for mCRPC but many patients fail (biochemical or clinical non-responders)[2]
- ATNM-400 is a novel Actinium-225 antibody radioconjugate for advanced prostate cancer
- ATNM-400 targets a non-PSMA protein overexpressed in CRPC
  - Functionally drives cell survival and resistance pathways
  - Expression linked to rapid disease progression, shorter time to castration resistance, and poor survival in CRPC patients
  - Target is elevated in CRPC patients resistant to enzalutamide, highlighting a role in ARPI therapy resistance

1) American Cancer Society
2) Gafita et al (2024) J Nuc Med https://doi.org/10.2967/jnumed.124.267723

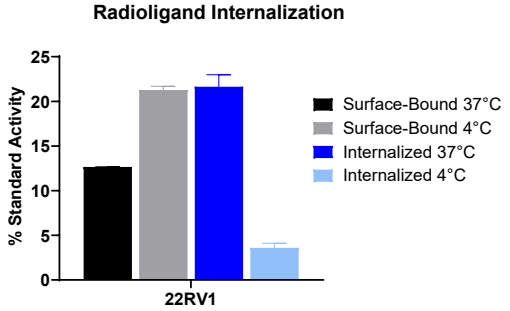
ATNM-400 Binds, Internalizes and Causes Cytotoxicity in Human Prostate Cancer Cells

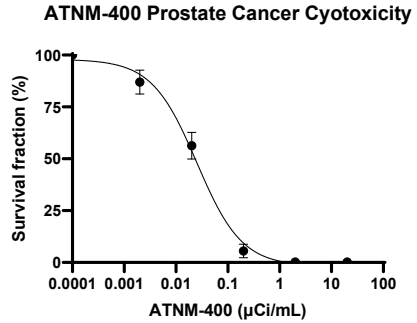
ATNM-400 Binds Recombinant Target Protein and Target-Positive PCa Cells





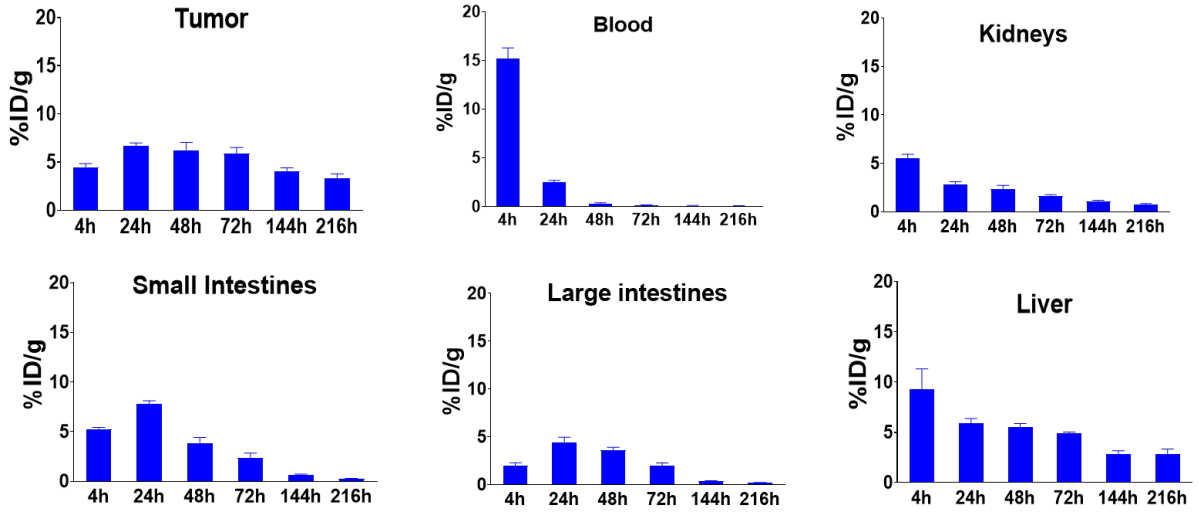
ATNM-400 Internalizes and Causes Dose-Dependent Cytotoxicity in PCa Cells



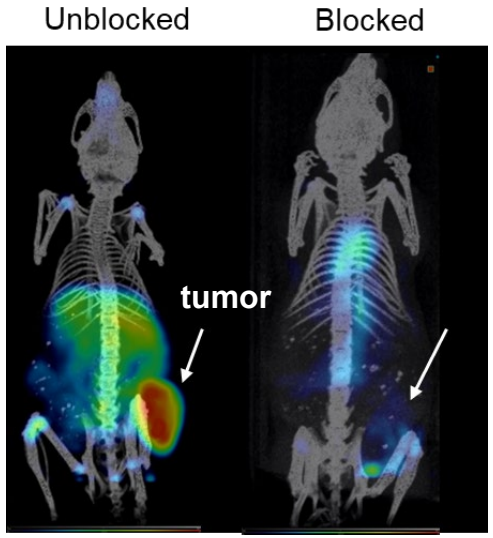


ATNM-400 Exhibits Tumor Uptake and Clearance from Normal Organs

Sustained Tumor Uptake and Rapid Clearance from Normal Organs in Prostate Cancer In Vivo Model



PET Imaging: Specifically Accumulates in Prostate Cancer Tumor-bearing Animals

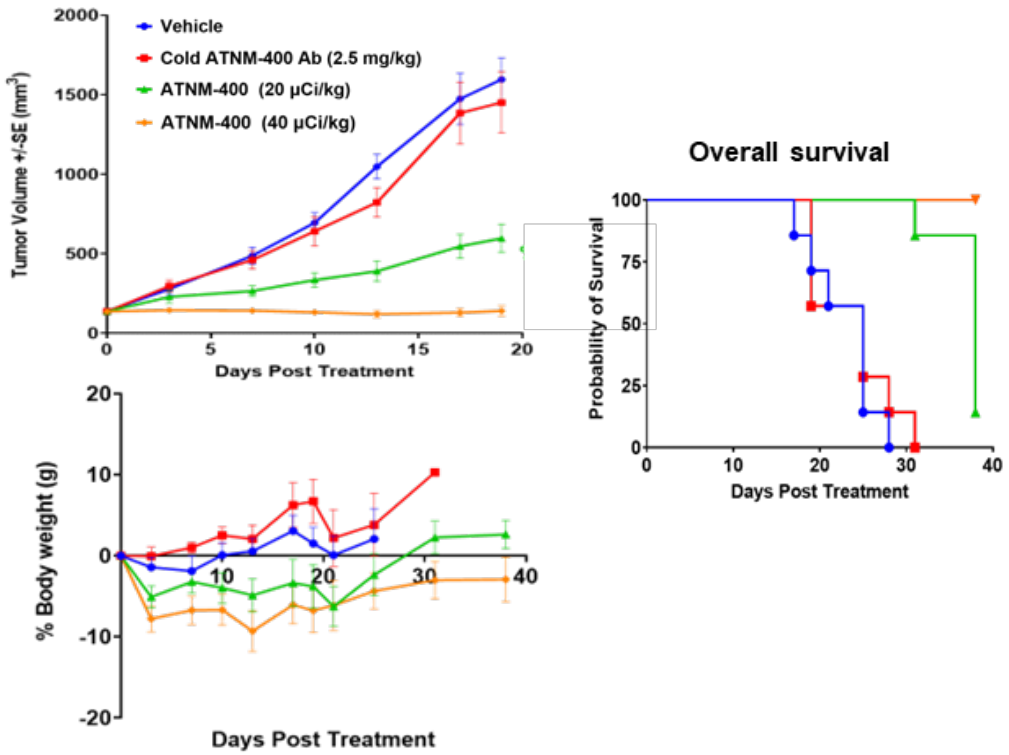


[89Zr]-mAb

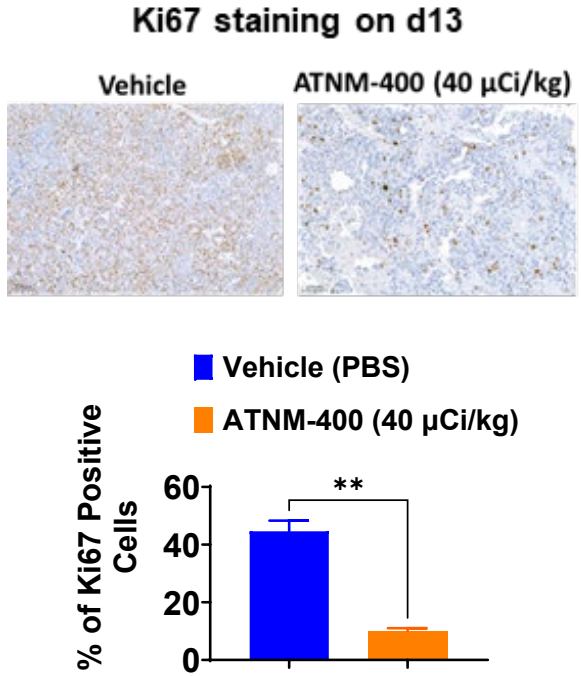
[89Zr]-mAb + Cold mAb

ATNM-400 Has Potent Efficacy in Preclinical Model of Prostate Cancer

ATNM-400 causes Dose-Dependent Efficacy and Improved Overall Survival in PCa In Vivo Model

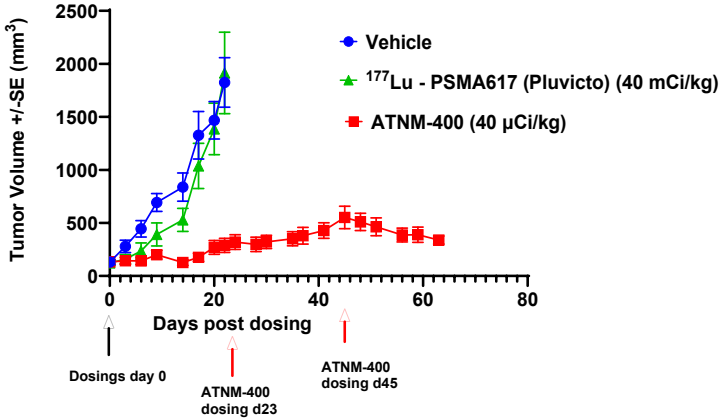


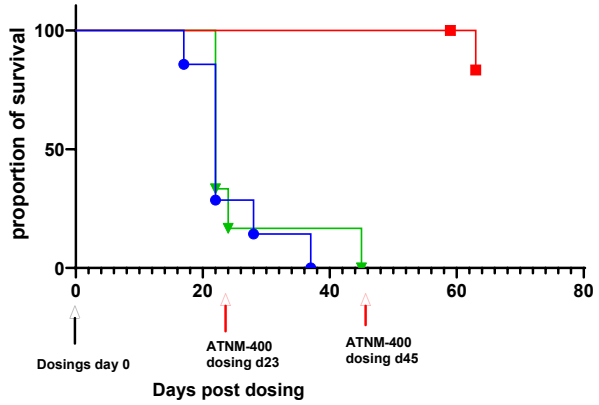
ATNM-400 Significantly Inhibits Tumor Cell Proliferation in PCa In Vivo Model



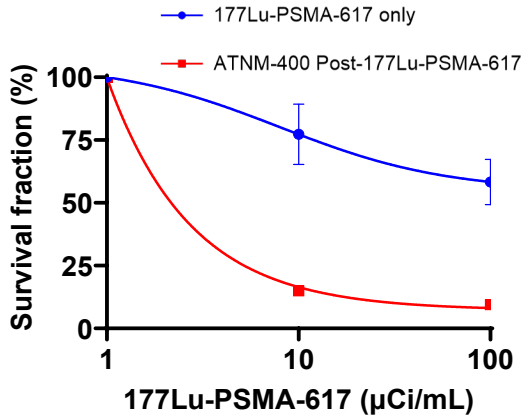
ATNM-400 is Highly Efficacious and Durable after Pluvicto Resistance in Prostate Cancer Models

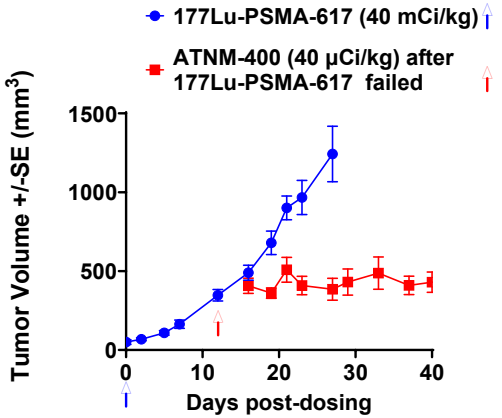
ATNM-400 Shows Significantly Higher and Durable Efficacy than Pluvicto in PCa

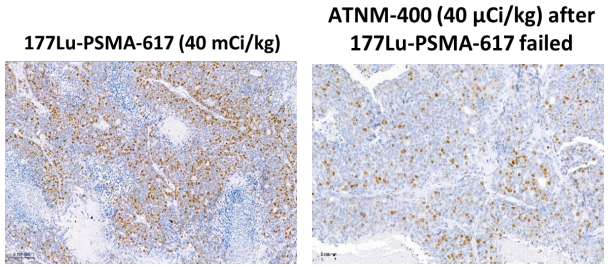


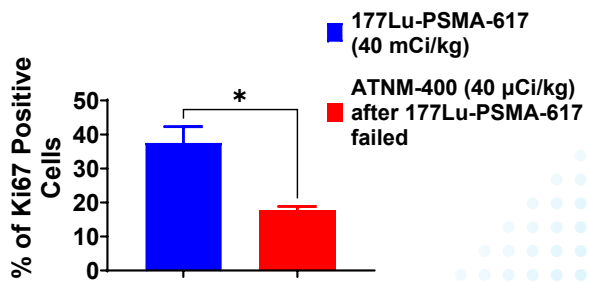


ATNM-400 Demonstrates Potent Efficacy and Sustained Tumor Growth Inhibition After Pluvicto Stops Working



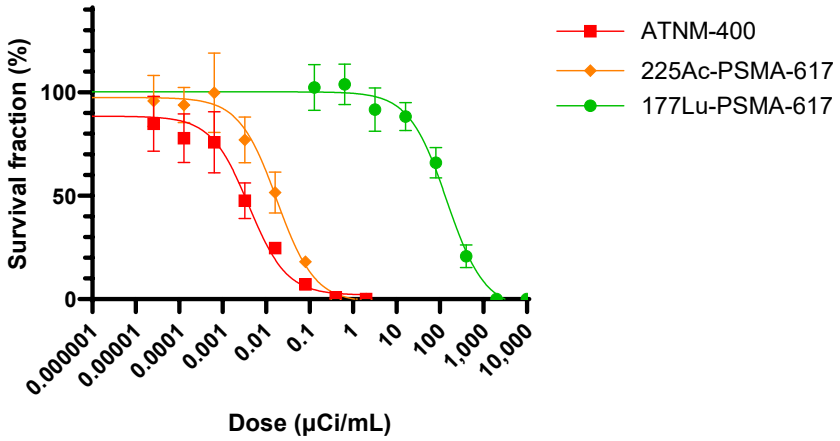






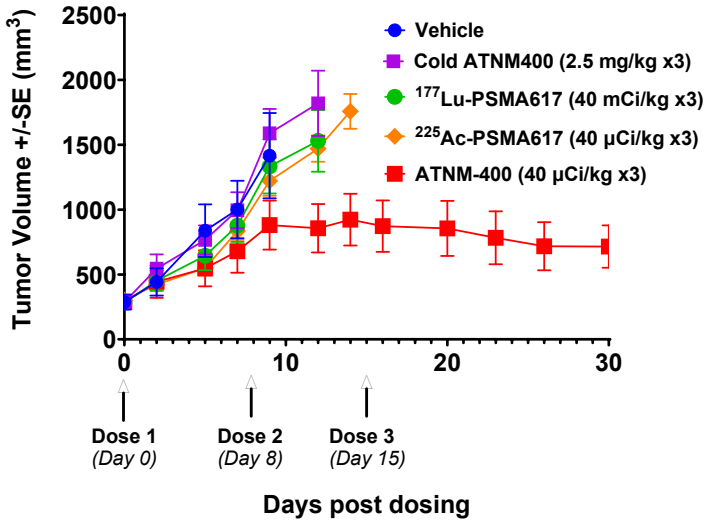
ATNM-400 is More Efficacious than 177Lu-PSMA-617 or 225Ac-PSMA-617

In Vitro: ATNM-400 is More Cytotoxic than 225Ac-PSMA-617 or 177Lu-PSMA-617 in PCa



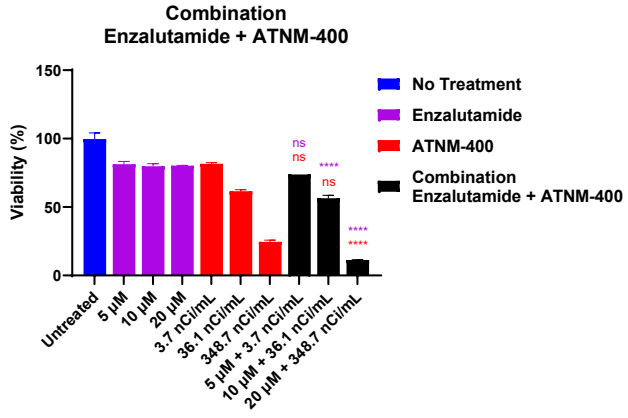
	IC50	P value
177Lu-PSMA-617	142.1 µCi/mL	
225Ac-PSMA-617	17.56 nCi/mL	<0.0001
ATNM-400	3.978 nCi/mL	

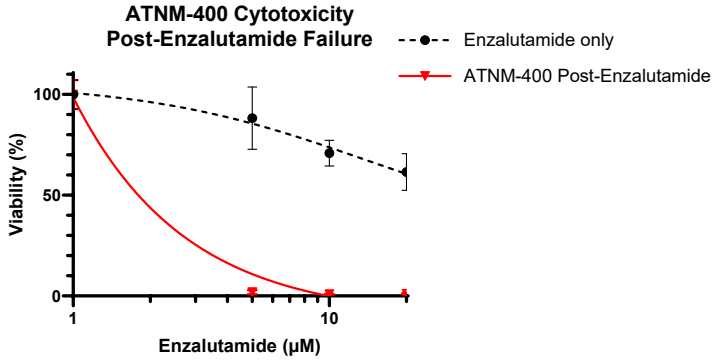
In Vivo: ATNM-400 is More Efficacious than 225Ac-PSMA-617 or 177Lu-PSMA-617 in PCa



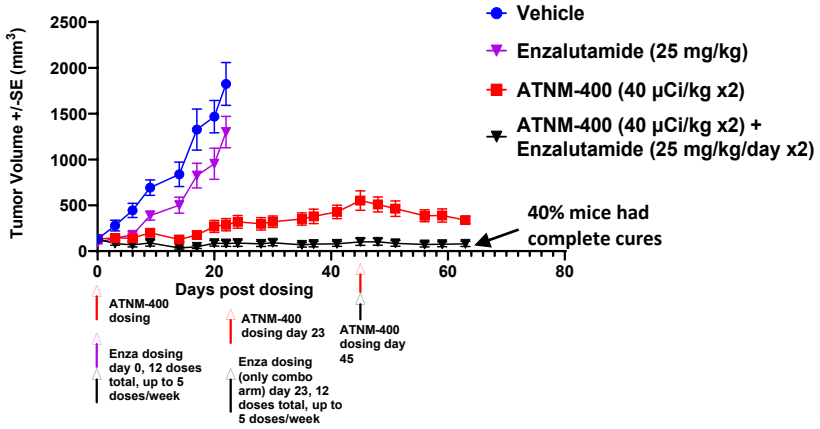
ATNM-400 Exhibits Superior and Durable Efficacy versus Enzalutamide

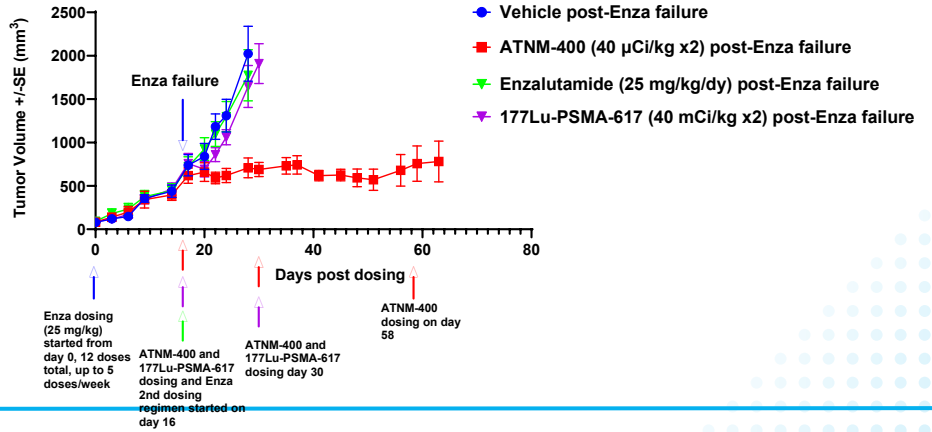
In Vitro: ATNM-400 is Cytotoxic in Enzalutamide Resistant PCa Cells and has Combination Activity





In Vivo: ATNM-400 has Durable Efficacy in Enzalutamide Resistant PCa Model and has Combination Activity





ATNM-400 Summary

- **Superior Efficacy:** Demonstrated robust and durable anti-tumor activity in preclinical prostate cancer models, including:
  - Enzalutamide-resistant tumors
  - PSMA-targeted radiotherapy-resistant models (^{177}Lu-PSMA-617 and ^{225}Ac-PSMA-617)

- **Novel Mechanism:** Targets a disease-driving protein linked to progression and resistance that is distinct from:
  - Cell surface-targeting agents (e.g., Pluvicto for PSMA)
  - Other tumor microenvironment-directed therapies that are in Development

- **Translational Potential:** Supports ATNM-400 as a next-generation Actinium-225 therapy - with promise as:
  - Monotherapy in CRPC (pre-Pluvicto)
  - Combination therapy with ARPI's in CRPC
  - Sequential therapy (post-Pluvicto, post-enzalutamide) to fill critical treatment gaps in CRPC

2025: Revamped Strategy, Revitalized Programs To Drive Value Creation

Actimab-A

- ✓ Market expansion with initiation of frontline AML trial under NCI CRADA

TAIHO ONCOLOGY Making the human connection Otsuka

- ✓ Pivotal Phase 2/3 trial with CLAG-M in R/R AML supported by recent publication in *Leukemia*
- ✓ Multiple trials under CRADA to address opportunities approximating 100,000 patients

NIH NATIONAL CANCER INSTITUTE

- ✓ Significant expansion to solid tumors targeting MDSCs with PD-1 inhibitors

KEYTRUDA (pembrolizumab) injection 100 mg OPDIVO (nivolumab)

Iomab-ACT

- ✓ Commercial CAR-T initiated at UTSW, data expected in 2H:2025

UTSouthwestern Medical Center

- ✓ Opportunity to expand the CAR-T market that had sales of over $4 billion in 2024
- ✓ Increased addressable market by 100,000 patients with expansion to Sickle Cell Disease
- ✓ Proof of concept clinical data from sickle cell disease trial at Columbia University expected in 2H:2025

COLUMBIA | COLUMBIA UNIVERSITY HERBERT IRVING COMPREHENSIVE CANCER CENTER

R&D and Capabilities

- ✓ ATNM-400 is a first-in-class, non-PSMA targeting Ac-225 therapy demonstrating poten, durable efficacy in Pluvicto or enzalutamide resistant prostate tumors
- ✓ In-house R&D continues to support expansion of Actimab-A via mutation agnostic mechanism of Ac-225 targeted therapy
- ✓ Focused on establishing in-house radiotherapy production to support clinical success

Continue with value creation via clinical milestones, pipeline advancement and technology deployment

Actinium Pharmaceuticals, Inc.

Thank you

Actinium Pharmaceuticals, Inc.

ATNM:NYSE AMEX