[^{225}Ac]Ac-AKY-2519, a B7-H3-Targeted Radiopharmaceutical, in Patients with Metastatic Castration-Resistant Prostate Cancer: The Phase 1b BActinium-1 Study

Gary Ulaner[1], Julio Cordero[2], Brandon Mancini[3], Luke Nordquist[4], Praful Ravi[5], Deepak Kilari[6], Haoran Li[7], Ravi Patel[8], Brian Madajewski[9], Haofei T. Wang[9], Oliver Sartor[10]

[1]Hoag Family Cancer Institute, Newport Beach, CA, USA; [2]Biogenix Molecular, LLC, Miami, FL, USA; [3]BAMF Health, Grand Rapids, MI, USA; [4]XCancer, Omaha, NE, USA; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Froedtert Hospital & Medical College of Wisconsin, Milwaukee, WI, USA; [7]The University of Kansas Cancer Center, Westwood, KS, USA; [8]University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA; [9]Aktis Oncology, Boston, MA, USA; [10]LCMC Health, Metairie, LA, USA

2390eTIP

BACKGROUND

- B7-H3 is highly expressed across multiple solid tumor types, including metastatic castration-resistant prostate cancer (mCRPC), with restricted expression in normal tissues.[1-6]
- AKY-2519 is a highly selective, high affinity, B7-H3-targeting miniprotein radioconjugate that demonstrates rapid plasma clearance with high tumor penetration/retention and limited normal tissue exposure, as evidenced by previously reported in-human imaging using ^{68}Ga and ^{177}Lu **(Figure 1)**.[7]

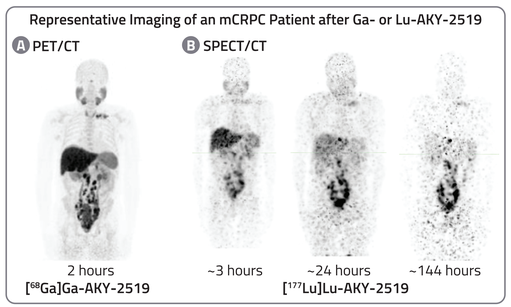


Figure 1. Representative Imaging of an mCRPC Patient after ^{68}Ga- or ^{177}Lu-AKY-2519.
(A) PET/CT, [^{68}Ga]Ga-AKY-2519 at 2 hours. (B) SPECT/CT, [^{177}Lu]Lu-AKY-2519 at 3, 24, and ~144 hours.

- Estimated absorbed doses to normal tissues with [^{225}Ac]Ac-AKY-2519 (using low-adminstered activity ^{177}Lu as a surrogate) are predicted to be below reference clinical benchmarks and compare favorably to approved radiopharmaceuticals.[7]
- AKY-2519 is being investigated in a broad Phase 1b program as a theranostic pair utilizing copper-64 ([^{64}Cu]Cu-AKY-2519) for patient selection and actinium-225 ([^{225}Ac]Ac-AKY-2519) for therapy **(Figure 2)**.

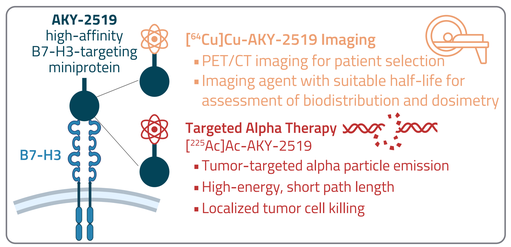


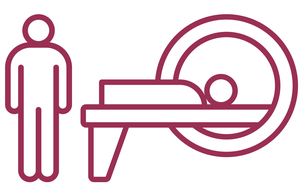
Figure 2. AKY-2519 theranostic pair
[^{64}Cu]Cu-AKY-2519 imaging and [^{225}Ac]Ac-AKY-2519 targeted alpha therapy.

STUDY DESIGN

BActinium-1 (NCT07581184) is the first-in-human study of [^{225}Ac]Ac-AKY-2519 in patients with mCRPC with and without prior ^{177}Lu-PSMA-617 (PLUVICTO™) exposure **(Figure 3)**.

Patient Screening & Imaging Selection

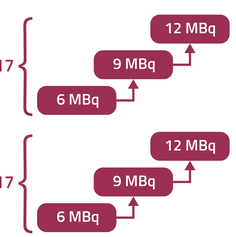
- Target engagement
- Biodistribution assessment



- Metastatic castration-resistant prostate cancer (mCRPC)
- B7-H3 uptake assessed by [^{64}Cu]Cu-AKY-2519 PET/CT
  - Tumor uptake confirms eligibility

Dose Escalation

- Determine MTD/MAD
- Identify cohort-specific backfill dose levels



- Up to 36 patients with mCRPC (18 per cohort)
- Dose escalation guided by BOIN design

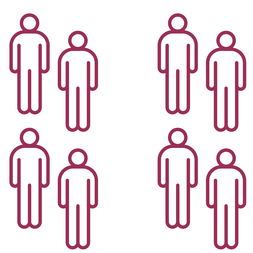
Backfill

Dose Level A
B7-H3 imaging-positive mCRPC (n=30 per cohort)

Dose Level B
B7-H3 imaging-positive mCRPC (n=30 per cohort)

- 2 dose levels explored per cohort

Dose Determination



- Up to 138 patients at 20-25 US sites, in 2 parallel cohorts defined by prior ^{177}Lu-PSMA-617 exposure
- Cohort-specific dose determination

Figure 3. BActinium-1 study design.

OBJECTIVES

Primary Objectives

- Evaluate the safety and tolerability of [^{225}Ac]Ac-AKY-2519
- Determine the MTD and/or recommended dose in each cohort

Secondary Objectives

- Evaluate safety and tolerability
- Characterize pharmacokinetics and dosimetry
- Determine preliminary antitumor activity

KEY ELIGIBILITY CRITERIA

Inclusion Criteria	Exclusion Criteria
• Age ≥18 years with confirmed mCRPC (histologically or cytologically confirmed adenocarcinoma)	• >2 prior ARPIs and/or >1 prior taxane in the mCRPC setting
• Castrate serum testosterone (<50 ng/dL)	• Prior targeted radiotherapy, except ^{177}Lu-PSMA-617 for Cohort B
• Documented progression on the most recent line of therapy, by PSA or imaging	• Prior B7-H3-targeted therapy
• ECOG performance status 0-1	• Systemic anticancer therapy or external beam radiotherapy within 28 days; investigational agent within 28 days or 5 half-lives
• Adequate end organ function	
• Cohort B: ≥2 prior doses of ^{177}Lu-PSMA-617	

CURRENT TRIAL STATUS

- BActinium-1 is actively enrolling in the United States.
- Dose escalation is ongoing.

Figure 4. BActinium-1 study sites

CONCLUSIONS

- BActinium-1 (NCT07581184) is a first-in-human study evaluating [^{225}Ac]Ac-AKY-2519, a B7-H3-targeted miniprotein radioconjugate, in ^{177}Lu-PSMA-617-naïve and -experienced mCRPC.
- The trial aims to define cohort-specific recommended dose and to characterize early clinical activity in B7-H3 imaging positive mCRPC.

Copies of this poster obtained through QR, AR and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.

For more information, contact Janet Horton, MD:
AKY-2519-01Inquiries@aktisoncology.com

References: 1) Seaman S, et al. *Cancer Cell.* 2017;31(4):501–515.e508. **2)** Zhou WT, Jin WL. *Front Immunol.* 2021;12:701006. **3)** Kontos F, et al. *Clin Cancer Res.* 2021;27(5):1227–1235. **4)** Guo C, et al. *Eur Urol.* 2023;83(3):224–238. **5)** Kang N, et al. *Cancer Gene Ther.* 2023;30(10):1382–1389. **6)** Amori G, et al. *Prostate Cancer Prostatic Dis.* 2021;24(3):767–774. **7)** Sathekge M, et al. ASCO 2026, Poster 3097

Abbreviations: ARPI = androgen receptor pathway inhibitor; BOIN = Bayesian optimal interval; CT = computed tomography; ECOG = Eastern Cooperative Oncology Group; MAD = maximum administered dose; mCRPC = metastatic castration-resistant prostate cancer; MTD = maximum tolerated dose; PET = positron emission tomography; PSA = prostate-specific antigen; RBE = relative biological effectiveness; RCT = radioconjugate therapy; SD = standard deviation; SPECT = single-photon emission computed tomography.

Acknowledgments: Medical writing and poster production support were provided by Acumen Medical Communications, funded by Aktis Oncology.

Disclosures: This study is funded by Aktis Oncology. **GU:** Research support: Lantheus, GE Healthcare, Precirix, Nuclidium, Curium, Novartis, Fusion, RayzeBio, POINT; Advisory board/consulting: Lantheus, GE Healthcare, Precirix, Nuclidium; Speaker: Lantheus, GE Healthcare, Blue Earth. **BMan:** Employment and stock ownership: BAMF Health; Consulting/advisory: Lantheus Medical Imaging, MCG Health, RubiconMD; Speakers' bureau: GE Healthcare, Veracyte; Travel/expenses: BAMF Health. **LN:** Stock ownership: Clarity Pharmaceuticals; Travel/expenses: Fusion Pharmaceuticals. **PR:** Advisory board: Bayer, Curium; Consulting: Janssen; Research funding: AstraZeneca, Blue Earth Diagnostics. **DK:** Advisory: Aptitude, Cardinal Health; Speaker: AVEO, Eisai, Pfizer; Consulting: Exelixis, Foundation Medicine, Bayer, J&J, Eisai, Merck, Integra Connect; Research: Genentech, Exelixis, SOBI, Astellas. **RP:** Employment: University of Pittsburgh Hillman Cancer Center; Institutional research funding: Voximetry, Merck; Consulting: RayzeBio; Advisory board: Novartis and Curio (one-time each, 2026), GE Healthcare (ended November 2025). **OS:** Consulting: AbbVie, Abdera, Actinium, Actithera, AdvanCell, Aktis, Alpha9, Amgen, ART Bio, Astellas Pharma, AstraZeneca, Azurna, Bayer, Clarity Pharmaceuticals, Convergent, Curadh, Curium, EcoR1, Full Life, Immunome, Isotopen Technologien, ITM Oncologics, JNJ, Lantheus, Merck, Modex, Norroy, North Star, Novartis, Nucleus Biopharma, NVision, Pfizer, POINT BioPharma, Precede, Progenics, Radiopharm Theranostics, RATIO, Swiss Rockets, Syneos Health, Telix Pharmaceuticals, Wren Laboratories, X-Cancer Software; Data safety monitoring/advisory board: Abdera, Actinium, Actithera, AdvanCell, Alpha9, Amgen, ART Bio, Astellas Pharma, AstraZeneca, Azurna, Bayer, Clarity Pharmaceuticals, Convergent, Curadh, Curium, Full Life, Isotopen Technologien, ITM Oncologics, JNJ, Lantheus, Merck, Modex, Norroy, North Star, Novartis, Nucleus Biopharma, NVision, Precede, Progenics, Radiopharm Theranostics, RATIO, Swiss Rockets, Syneos Health, Telix Pharmaceuticals, Wren Laboratories, X-Cancer Software; Institutional research funding: Amgen, AstraZeneca, Bayer, JNJ, Novartis; Stock/ownership: AbbVie, Actithera, ART Bio, Azurna, Clarity, Curadh, Lilly, NVision, Pfizer, RATIO, Telix; Stock options: Abdera, Actithera, AdvanCell, ART Bio, Asta, Convergent, Radiopharm Theranostics; Patent: Saposin C and receptors as targets for treatment of benign and malignant disorders (US Patent 7,166,691); Expert testimony: Sanofi. BMad and HTW are Employees of Aktis Oncology. HL and JC have no relationships to disclose.