Case Study

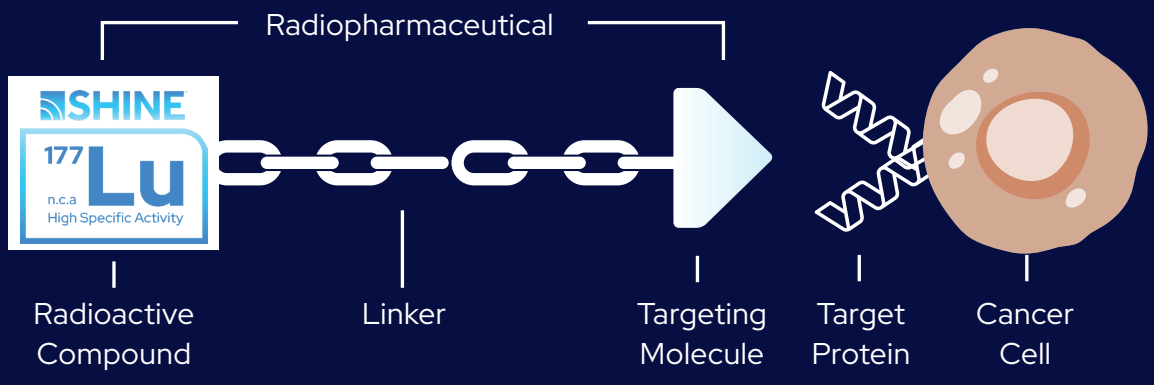
UW-Madison's Cutting-Edge Cancer Research Powered by Ilumira (Lu-177)

Every year, thousands face a diagnosis of advanced kidney cancer (ccRCC) or metastatic prostate cancer (mCRPC), diseases with poor prognoses and limited treatment options. For metastatic ccRCC, the five-year survival rate is just 18%, while mCRPC often develops resistance to existing therapies. Traditional treatments like chemotherapy and radiation often lack specificity, leading to severe side effects and limited efficacy.

At the Advanced Radiotheranostics (ART) Lab at the University of Wisconsin-Madison School of Medicine, Dr. Reinier Hernandez is developing novel radiopharmaceutical therapies (RPTs) to address these urgent needs. RPTs work by combining a targeting molecule with a radioactive isotope, allowing for precise delivery of radiation to cancer cells while minimizing damage to healthy tissue.

Dr. Hernandez's research is supported by WARF Therapeutics, a part of the Wisconsin Alumni Research Foundation (WARF). WARF Therapeutics collaborates with UW-Madison researchers to bridge the gap between academic discoveries and commercial drug development.

> *"The consistently high purity and reliability of SHINE's Lu-177 have allowed us to conduct our studies with a level of precision difficult to achieve before."*
>
> - Dr. Reinier Hernandez, Assistant Professor of Medical Physics and Radiology at the University of Wisconsin-Madison



This illustration shows how Radiopharmaceutical Therapy (RPT) works to target cancer cells. Ilumira, SHINE's n.c.a. lutetium-177 (Lu-177), serves as the radioactive compound, which is attached to a targeting molecule via a linker. This compound seeks out specific proteins on cancer cells, delivering targeted radiation to destroy the tumor while minimizing damage to healthy tissue.

Challenge

The push to optimize RPT efficacy for kidney and prostate cancer patients requires not only innovative targeting mechanisms but also a dependable, highly pure isotope source. This challenge has been a significant hurdle in advancing RPT research, potentially delaying the development of life-saving treatments for patients in desperate need of new options.

Dr. Hernandez's and WARF therapeutic teams have created two promising compounds:

1. ^{177}Lu-WT-7695, a molecule targeting the CA IX protein highly expressed in kidney cancer (WARF Therapeutics)
2. ^{177}Lu-ART-101, a novel compound designed for advanced prostate cancer therapy (ART Lab)

When paired with lutetium-177 (Lu-177), these approaches deliver potent radiation directly to tumors while sparing healthy tissue.

"We like lutetium because it pairs well with our molecules that have long tumor retention," Dr. Hernandez stated. "However, our early supplies of Lu-177 were not pure enough to achieve optimal results. Impurities in the Lu-177 can dilute the potency of the drug, reducing its effectiveness in targeting cancer cells."

Additionally, relying on international suppliers led to logistical issues, disrupting carefully planned experiments due to shipping delays and customs processes.

Without a reliable source of high-quality Lu-177, RPT faces hurdles:

- Reduced potency and efficacy due to inactive isotope impurities
- Radiation safety concerns from long-lived impurities (Lu-176m or Lu-177m)
- Increased costs for lower quality product
- Supply chain vulnerabilities and disruptions from international sourcing
- Inconsistent quality hampering research reproducibility and progress

Solution

When SHINE Technologies began producing Ilumira (non-carrier-added Lu-177), Dr. Hernandez chose to use it for both the kidney and prostate cancer studies. Based in Janesville, Wisconsin and only 50 miles from the UW-Madison research labs, SHINE has North America's largest production capacity for n.c.a. Lu-177.

SHINE committed to providing a reliable, high-quality supply of Ilumira, enabling Hernandez to conduct his studies without concerns over quality or supply chain disruptions.

Results

Kidney Cancer Study (WT-7695)

WT-7695 compound demonstrated remarkable efficacy in preclinical models of kidney cancer:

- 100% survival achieved at a dose of just 1 mCi
- Best-in-class profile with 55%IA/g tumor uptake at 24 hours and 18%IA/g retention at 7 days
- 8-20x greater efficacy in vivo compared to other compounds in development, including DPI-4452 and RAYZ-15710

Prostate Cancer Study (ART-101)

ART-101 compound demonstrated superior performance to the current therapy, PSMA-617:

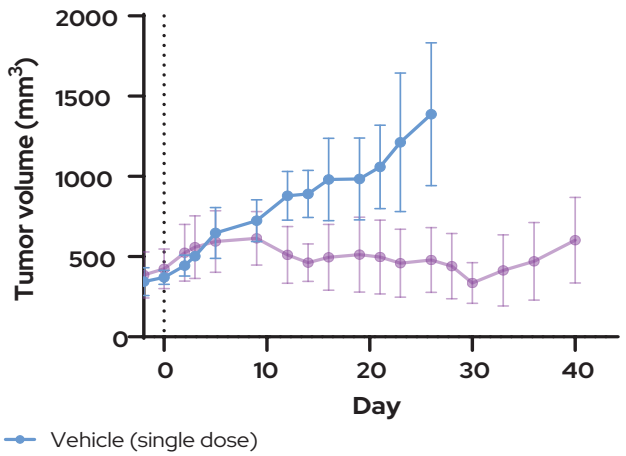
- Remarkably long tumor retention times, with approximately three times more Lu-177 reaching the tumors and remaining there for an extended period
- Demonstrated superior tumor growth inhibition compared to existing treatments
- Maintained efficacy even at lower administered activities, potentially leading to reduced side effects for patients in future clinical applications

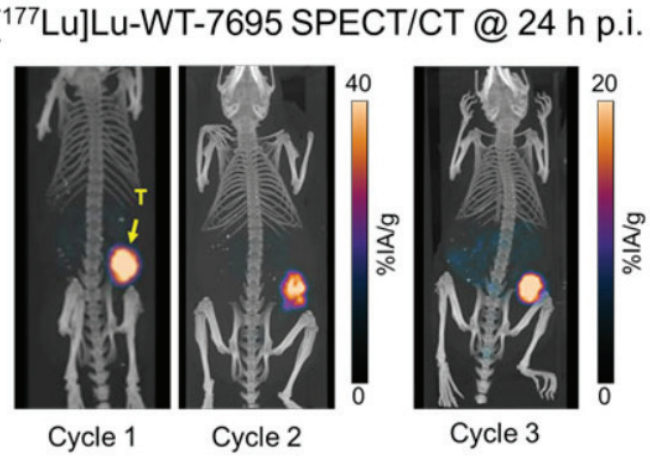
SHINE's consistent, highly pure Ilumira allowed for precise dosing and reliable results, critical factors in developing these promising therapies and moving them toward clinical trials.

WT vs. Debiopharm and RayzeBio

Compound	CA9 potency (nM) / off-rate (min)	CA12 selectivity/ off-rate (min)	% of dose in tumor		177Lu therapeutic 24 h 7 d dose (mCi)
			24h	7d	
PCC WT-7695	0.03 / 490	300 / 31	55%	18%	0.5
DPI-4452	0.25 / 99	NR	10% (4 h)	NR	3.0
RAYZ-15710	0.09 / 27	1500 / NR	6%	<3%	3.0

Mice treated with WT-7695 showed tumor regression starting on day 9-12





The Impact of Reliable, Domestic n.c.a. Lutetium-177

SHINE's ability to provide a dependable, US-based source of high-quality Lu-177 was transformative for this research. Benefits include:

Enhanced Research Speed
No delays waiting for international shipments or customs clearance

Improved Data Quality
Consistent Lu-177 purity leads to more reliable results

Increased Research Scope
Reliable supply allows for more extensive testing and optimization

Streamlined Regulatory Path
Using the same high-quality Lu-177 from research through clinical trials simplifies the regulatory process

> *"We're seeing improved labeling efficiency and better overall results in our preclinical models. This quality and consistency are crucial as we push towards clinical trials and potentially life-changing treatments for patients with kidney and prostate cancer."*
>
> - Dr. Reinier Hernandez, Assistant Professor of Medical Physics and Radiology at the University of Wisconsin-Madison

Looking Ahead: From Lab to Patient Care

The promising results achieved with Ilumira set the stage for potential clinical trials in the near future. WARF Therapeutics is actively seeking partners to advance these compounds through clinical development and eventual commercialization.

For WT-7695 (kidney cancer), the next steps include dose and schedule optimization, isotope exploration, and initiating studies in non-small cell lung cancer (NSCLC) tumor models, along with toxicology studies and preparation for GMP production.

For ART-101 (prostate cancer), the team is preparing for human trials to validate the treatment's potential in improving outcomes for advanced prostate cancer patients. The compound's ability to maintain efficacy at lower doses is particularly exciting, as it could lead to more tolerable treatments with fewer side effects.

The SHINE-UW-WARF Therapeutics partnership exemplifies how collaboration between industry and academia, built on a foundation of reliable, high-quality isotope supply, can accelerate medical breakthroughs. By bridging the gap between cutting-edge research and dependable isotope production, SHINE is helping to illuminate new paths forward in the fight against cancer.

To learn more about WT-7695 or ART-101, visit www.warf.org/warf-therapeutics.

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