Case Study

Targeting the Unknown:
A Full Scope TRT Project with Lead-203/212

How do you turn a bold idea into a viable oncology project when starting from scratch?

With no prior experience in radiochemistry or targeted radiotherapy (TRT), one biotech company set out to explore the potential of Lead-212, a powerful alpha-emitting isotope, to target a common cancer marker expressed across multiple tumor types.

Partnering with Oncodesign Services (ODS) provided the client with a scientific and operational framework incorporating study design to radiolabeling and in vivo testing. Through an integrated approach, the collaboration transformed a high-risk concept into a structured development program, that delivered early biological insights, demonstrated tumor uptake, and defined a clear roadmap for future studies.

This case study examines how tailored support and deep expertise can help biotechs navigate new therapeutic areas and turn ambitious ideas into tangible progress against cancer.

Key Learning Points

This project underscored several key insights:

- **Cold before hot**: Non-radioactive (cold) PK studies are essential. They allow scientists to understand compound behavior, optimize design, and predict performance before introducing high-value and complex isotopes.
- **Iterate strategically**: Early setbacks should be viewed as critical data points. By treating the first 'failure' as a learning step, the team subsequently avoided repeating mistakes and accelerated progress.
- **Integrate expertise**: Success in TRT requires close integration of radiochemistry, biology and pharmacology. No single discipline can solve the challenge in isolation.
- **Enable success for clients**: For teams entering radiopharmaceuticals for the first time, knowledge transfer is as valuable as technical execution. A strong scientific partnership can turn inexperience into informed decision-making.
- **Think ahead**: Changing targeting strategies, translatable oncological model, and careful control of compound concentration are promising potential next steps. These refinements can reduce off-target uptake, improve tumor selectivity, and ultimately shorten the path to clinical translation.

Challenges and Knowledge Gaps

The client entered the project with a clear ambition but limited background knowledge in radiopharmaceutical development. Their interest in alpha emitters, a hot topic in TRT, was driven by the potential of Lead-212 to deliver high-impact results. However, the complexity of the target, the nuances of isotope behavior, and the intricacies of study design presented significant hurdles.

Oncodesign Services' role was to provide end-to-end support, from fundamental education to strategic decision-making. The challenge wasn't just technical - it was about building confidence and capability in a field the client had never navigated before.

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Study Design and Execution

ODS and its partners approached the project as an iterative journey, where each study informed the next.

Phase 1: Feasibility and Early Learnings

The team first demonstrated that radiolabeling with Lead-203 (as a diagnostic surrogate to Lead-212) was technically feasible, achieving stable chelation with the ligands. Compounds were then tested in vivo. However, their short biological half-life (~1 hour) prevented sufficient tumor exposure. Instead of tumor uptake, radioactivity concentrated in the kidneys, confirming that compound profiling and pharmacokinetics were critical hurdles.

Phase 2: Optimized Compound Selection

Building on these insights, the design shifted toward molecules with longer circulation time (1-2 hours and beyond). This modification paid off: in the second in vivo study, two compounds successfully targeted the tumors at 24 hours post-injection. The results provided the first evidence of low to moderate tumor uptake, validating the refined strategy and confirming that careful tuning of compound half-life could unlock tumor targeting potential.

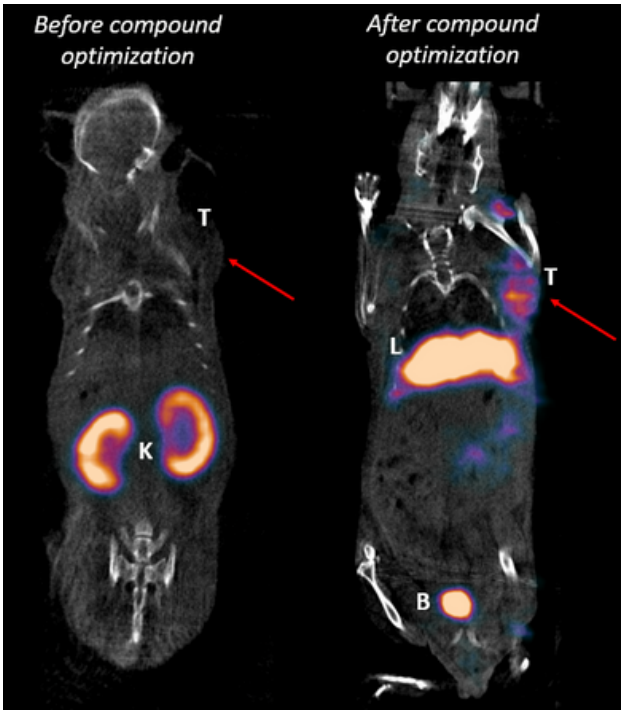

Figure 1. *SPECT scan with Lead-203 radiolabeled compounds*
Tumor location indicated by the red arrow
B = bladder, K = kidneys, L = liver, T = tumor

Collaborative Approach

The project also highlighted the value of collaboration. Through our network of preferred partners' expertise in chelator design and bioconjugation, combined with ODS' radiochemistry and in vivo pharmacology platforms,the experimental team ensured that learnings were rapidly translated into practical adjustments.

With over 30 years of translational experience, Oncodesign Services offers comprehensive preclinical solutions and a strategic pathway to accelerate your immuno-oncology program.

Next steps

Reach out to your relationship manager or contact us at:

- oncodesign-services.com
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More information

Oncodesign Services is a leading CRO specializing in drug discovery and preclinical services. Our mission is to help researchers discover innovative therapies against cancers and serious diseases with high medical need. We have been performing translational science for over 30 years, providing the partnership required to help our clients progress from therapeutic target to advanceable preclinical candidates.

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