

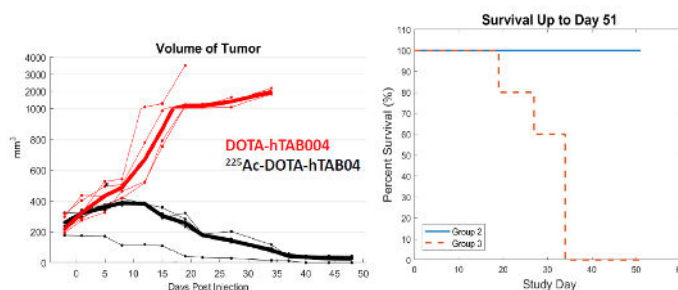
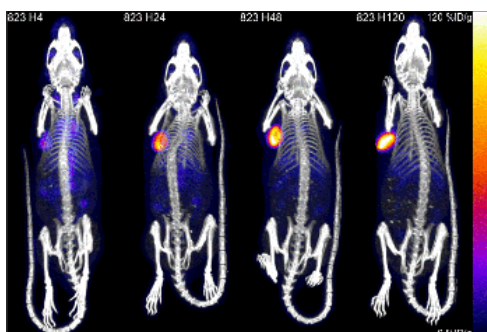
From Concept to Clinic: Key Considerations for Radioligand Therapy Development

When developing radioligand therapies, early-phase considerations are critical for setting the foundation for a successful development trajectory. At Perceptive Discovery, we guide sponsors through each stage, from demonstrating proof-of-concept to optimizing radiochemistry and biodistribution.

Here we outline the factors sponsors should consider and demonstrate how Perceptive Discovery addresses each to ensure your pharmacological, radiochemical, and dosimetry studies are aligned with clinical and regulatory expectations.

Primary Pharmacology

- ▶ Conduct proof-of-concept studies to demonstrate mechanism of action, such as tumor targeting and anti-tumor activity.
- ▶ Assess radiopharmaceutical target binding via in vitro/ex vivo cell and tissue-based binding and internalization assays.
- ▶ Evaluate drug accumulation in normal and tumor regions via in vivo imaging and ex vivo gamma counting and autoradiography assays.
- ▶ Understand efficacy in xenograft, syngeneic and orthotopic models in both immunocompromised and humanized small animals.



A SPECT-CT image reveals high tumor uptake and increasing target to non-target ratio over time with ¹¹¹In-DOTA-hTAB04. Following a single dose of ²²⁵Ac-DOTA-hTAB04, significant tumor shrinkage in a TNBC mouse model was observed, showing an 89% reduction in tumor volume within 48 days. Statistical analysis demonstrated lower tumor volumes and improved survival outcomes in the group treated with ²²⁵Ac compared to controls, propelling this research toward future clinical studies.

Radiochemistry and Immunoreactivity

- ▶ Perform radiolabeling method development to support alpha, beta, and gamma-emitting isotopes conjugated to small molecules and biologics.
- ▶ Conduct high-performance liquid chromatography method development, measure specific activity, optimize formulation, and execute serum stability studies.
- ▶ Complete Immunoreactivity assays for the successful translation of biologic radiopharmaceuticals.
- ▶ Explore good manufacturing practice development, validation and production capabilities along with shipping of tracers and/or setup of chemistry networks to support multi-site clinical studies.

Safety Pharmacology / Toxicology

- ▶ Evaluate radiation exposure and ligand-related toxicities.
- ▶ Visualize the biodistribution of the drug with safety endpoints, such as clinical signs, body weight, complete blood count, clinical chemistry and urinalysis that help guide clinical design and development.

Animal Biodistribution and Dosimetry

- ▶ Run animal biodistribution and dosimetry studies to predict the radiation and dosimetry profile of the radiopharmaceutical in humans.
- ▶ Perform imaging and gamma counting dosimetry studies in small animals and diverse higher animal models.
- ▶ Conduct specialized dosimetry analysis, including voxel-based assessment, advanced spine dosimetry following intrathecal administration and extrapolation from one radioisotope to another.

Streamlined development, evaluation and clinical translation of radiopharmaceuticals requires a partner who has extensive scientific, regulatory and operational expertise.

Translation and First-in-Human Studies

- ▶ Develop a tailored clinical trial design that accounts for radiation safety, dosimetry, and patient selection criteria specific to radioligand therapies.
- ▶ Establish imaging and biomarker strategies to assess target engagement, pharmacokinetics, and early efficacy in human subjects.
- ▶ Ensure GMP-grade production and robust quality control processes are in place to support consistent radiotracer supply for clinical trials.

As in all aspects of drug development, who you partner with matters. Learn why researchers around the world repeatedly turn to the scientists behind **Perceptive Discovery** to help them manage the nuances of early phase radiochemistry and imaging for radioligand therapy development.

Contact hello@perceptive.com to learn how the scientists behind Perceptive Discovery can help you meet your radioligand therapy development goals.



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