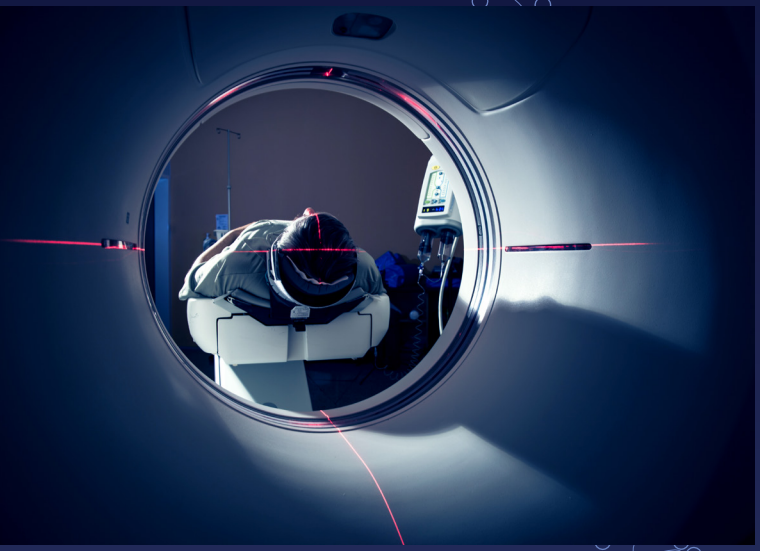
www.rpo-group.com



Radiotheranostic agent *development within reach*

RPO group

Exploring Molecules for Imaging and Therapy

Radiomolecular *Precision Oncology*

RPO Group is an early phase radiotheranostic CRO, situated in the heart of Western Europe, the global epicentre of radiomolecular precision oncology. In our approach, during an interview we begin by listening to our clients and identifying potential challenges, hurdles and bottlenecks. We then provide tailored solutions to help small pharmaceutical and biotech companies mitigate risks in their radioligand therapy (RLT) programs. We enhance the value of early compounds by deriving precise dosimetric insights from limited diagnostic data while also forecasting treatment dose distribution. RPO Group delivers a comprehensive, integrated one-stop-shop solution by partnering with technology providers for dosimetric analysis and image handling, CDMOs for radiomanufacturing, and radiopharmacies for radiolabeling.

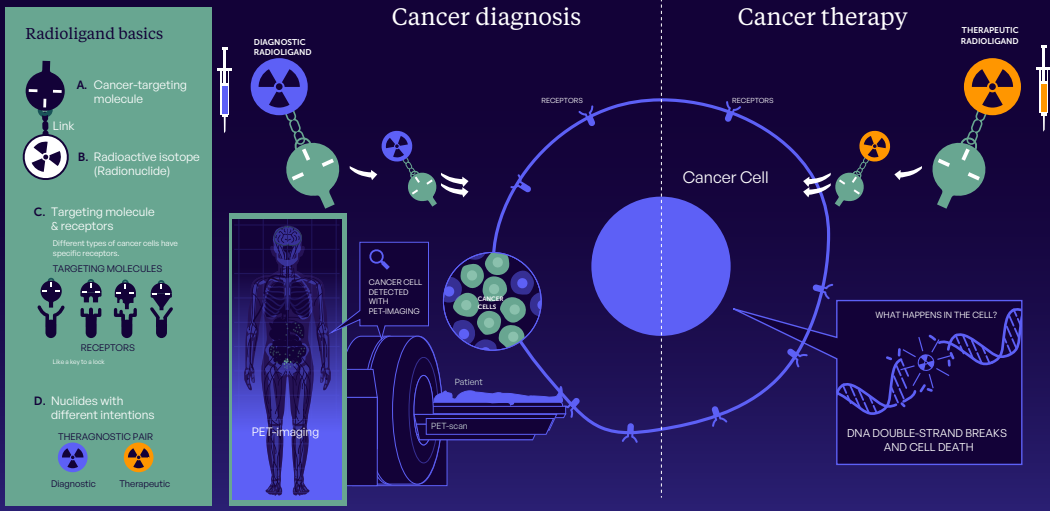
Services

- → Clinical Study Management
- → Radiomolecular Image Handling & Analysis
- → Dosimetric Services
- → Scientific & Medical Consultancy Services
- → Medical Writing
- → Molecule Mapping
- → Hospital & Site Network
- → Safety & Advisory Board
- → Legal Representation for non-EU Companies
- → CDMO Services

The Rise of Radiotheranostics *in Clinical Management*

The current radiotheranostic revolution - primed for a rapid expansion in the coming years - is profoundly changing the multidisciplinary care of (metastatic) cancer patients, and may soon be among the most important pillars in clinical management.

At RPO Group, we enhance the development of radiotheranostics, focusing on surpassing traditional treatments in efficacy and safety. With a high failure rate of over 95% in clinical trials due to safety and efficacy issues, our use of advanced imaging technologies like SPECT-CT, PET-CT, and PET-MRI is key. We precisely identify suitable cancer patients for targeted therapies, leveraging radiotheranostics' unique ability to switch between diagnostic and therapeutic modes within the same molecular structure. This strategy aims to increase the effectiveness of clinical trials and lead the way to safer, more focused cancer treatments.



Tutorial: *early oncology RLT drug development*

The current and future landscape of radiotheranostics is evolving rapidly, with new radionuclides and combination strategies expanding RLT's reach. Radiotherapeutics have the potential to become a real alternative to chemotherapeutics with a solution for almost any type of cancer. At present Lutetium-177 (^{177}Lu) is the workhorse on which new radiotherapeutics are based.

Some emerging RLT strategic insights and considerations are:

1. Other radionuclides:

- Beta emitters: Terbium-161 (^{161}Tb) and Copper-67 (^{67}Cu) are promising due to Auger electrons and improved production scalability. Alpha emitters: Actinium-225 (^{225}Ac) has potency but challenges due to its cascade of daughter radionuclides, while Lead-212 (^{212}Pb) and Astatine-211 (^{211}At) could be viable if production scales up.

2. Combination strategies:

- Tandem therapy (concomitant alpha & beta) to exploit different radiation profiles.
- Cocktail approaches (multiple agents & labels) to customize treatment timing, sequence, and dose. Hybrid approaches combining RLT with chemotherapy, immunotherapy, or cancer vaccines to enhance response rates.

3. Imaging & companion diagnostics:

- The trend toward using theranostic pairs (^{203}Pb/^{212}Pb) ensures diagnostic accuracy while optimizing treatment.
- Predictive imaging will refine patient selection and allow real-time response monitoring.

4. Logistics & production considerations:

- Shorter half-life RLTs will be favored for lower toxicity and waste disposal.
- Longer half-life radionuclides simplify manufacturing and global distribution.

However, the biggest challenge for RLT will probably be target selection and tumor biology. Identifying targets with high receptor density in tumors while maintaining low expression in normal tissues is crucial for delivering an effective radiation dose while minimizing toxicity. Beyond that, other challenges include:

1. Off-target binding & specificity: even when a target is tumor-associated, there can still be risks of non-specific binding, which can lead to unwanted radiation exposure in healthy tissues.

2. Pharmacokinetics & clearance: slow clearance can lead to prolonged radiation exposure in non-target organs, especially the kidneys and bone marrow, which are dose-limiting organs in many RLTs.

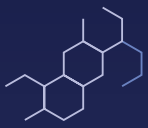
3. Heterogeneous target expression: not all tumor cells within a patient express the target at the same density, which can impact treatment efficacy.

4. Resistance mechanisms: some tumors downregulate receptor expression in response to therapy, reducing RLT effectiveness over time.

Get in touch

Do you have questions or requests? Is there anything you'd like to share? Or would you like to work with us? Don't hesitate to get in touch.

info@rpo-group.com
+32 479 83 87 10
www.rpo-group.com



Molecule mapping. We focus on the 360° profiling of theranostic compounds.

Assessment. We take a critical look at the safety and efficacy of the therapeutic process.

Analysis. We interpret PET-CT and PET-MRI scans of patients using innovative radiolabeled molecules.

Research. We offer the operational capacity for clinical research in Europe, RSA and other specific countries.

Collaboration. We work with leading clinical experts in the field of (radio)theranostic medicine.

Clinical study. We design and deliver clinical studies for theranostic treatment.

RPO group

Exploring Molecules for Imaging and Therapy