ISSN: 2755-0117

Journal of Oncology Research Reviews & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Radiopharmaceuticals and Theranostics: The High Road Ahead

Divya S Mishra

Medical Director, Oncology & Hematology, ICON plc, Singapore

***Corresponding author**
Divya S Mishra, Medical Director, Oncology & Hematology, ICON plc, Singapore.

Received: May 19, 2025; **Accepted:** May 22, 2025; **Published:** June 02, 2025

Keywords: Radiopharmaceuticals, Theranostics, Nuclear Medicine, Precision Oncology, Radio-isotopes

Introduction

Radiopharmaceuticals and Theranostics are transforming the medical landscape by offering precise, targeted diagnostic and therapeutic solutions. Implementing a successful radiopharmaceutical program in any institutional practice or trial setting requires meticulous planning across several domains and seamless integration with oncology workflows for timely and accurate patient care. This article explores the landscape, applications, regulatory considerations, infrastructural and operational requirements along with future directions for expanding these therapies into clinical settings.

Current Landscape

The global radiopharmaceuticals market is projected to grow significantly, with diagnostics leading the charge. It was valued at approximately $6.8 billion USD in 2024 and is projected to reach nearly $19 billion USD by 2035, reflecting a compound annual growth rate (CAGR) of 9.8%. Trends indicate consolidation through mergers and acquisitions, as well as increased interest in novel tumor targets and cancer indications. The growing market reflects the increased demand for targeted therapies in oncology, with pharmaceutical giants like Novartis leading the way. Smaller biotech firms are pushing innovation with new therapies, especially in alpha-emitting radiopharmaceuticals [1].

Evolution of Radiopharmaceuticals and Theranostics

Radiopharmaceuticals have a rich history. The use of radioactive iodine for thyroid cancer emerged in the 1940s, and since then, the field has evolved rapidly from organ specific to cell specific targeting. Radiopharmaceuticals (Figure 1) consist of a target biomarker, a binding ligand (such as peptides or small molecules), and a radionuclide payload. Radioactive isotopes are categorized by their emission type based on imaging (gamma/positron) vs therapy (alpha/beta) and their half-life matching biological clearance rates. Examples of Diagnostic isotopes include (Gallium-68, Technetium-99m) that emit gamma or positron radiation and Therapeutic isotopes include (Lutetium-177, Radium-223) that emit beta or alpha particles.

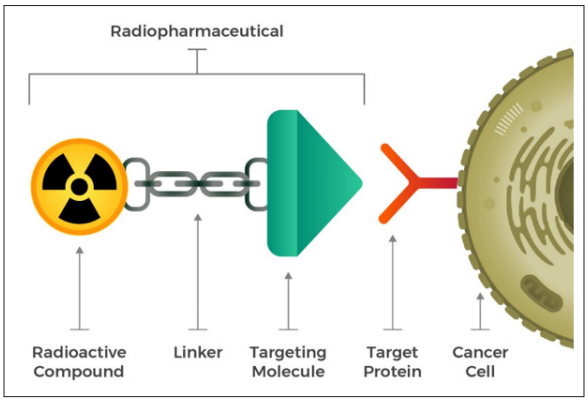

Figure 1: Components of a Radiopharmaceutical (NCI visuals Online)

Recent milestones include the approval of Lutathera (2018) and Pluvicto (2022), marking significant progress in therapeutic applications. Advances in cyclotron technology and the development of more efficient alpha-emitting isotopes continue to open new avenues for radiopharmaceutical therapies, particularly in solid tumors beyond neuroendocrine cancers and prostate cancer [2,3]. Theranostics (Table 1) integrates diagnostics and therapeutics by targeting the same specific biomarker for both imaging and treatment, enabling personalized, precision medicine. For example, PSMA-617 targeting prostate cancer cells allows both imaging and treatment with lutetium-177. This approach improves treatment efficiency and minimizes unnecessary exposure to healthy tissues [4,5].

Table 1: Currently Approved Theranostic Pairs

Diagnostic Agent	Therapeutic Agent	Target	Indication
Iodine 123 or I-131	Iodine -131	Thyroid	Thyroid Cancer
Gallium-68 PSMA-11	Lutetium-177 PSMA-617	PSMA	Prostate cancer
-68 Gallium DOTATATE	Lutetium-177 DOTATATE	SSTR	Neuroendocrine tumors
Technetium-99m MIBI	Iodine-131 MIBG	NET Sympathetic tumors	Pheochromocytoma/ Neuroblastoma
Technetium-99m	Radium -223	Bone	Bone Metastasis

PSMA-Prostate Specific Membrane Antigen; SSTR- Somatostatin Receptors; MIBG- Meta-iodobenzylguanidine; NET-Neuroendocrine tumors

Radiopharmaceuticals primarily cause cell death through direct DNA damage (single- and double-strand breaks) and indirect effects such as immune stimulation. They offer a radiobiological edge in hypoxic tumor environments, thanks to higher linear energy transfer (LET) and reduced oxygen dependency. This results in a more potent and localized therapeutic effect, making them ideal for treating certain difficult-to-reach tumors [6].

Regulatory bodies such as the FDA and EMA provide essential guidelines for the development, clinical testing, and commercialization of radiopharmaceuticals. These guidelines include recommendations for preclinical studies, clinical trial design, and dosimetry practices, ensuring that radiopharmaceuticals are safe, effective, and properly regulated. The rapid approval of new agents like Pluvicto demonstrates the evolving regulatory landscape, which is becoming increasingly supportive of radiopharmaceutical therapies [7].

Infrastructure, Personnel and Pathways

Enhancing infrastructure at clinical sites as well as upskilling to address the talent gap in nuclear medicine through training and recruitment will be essential to meeting the growing demand for these therapies and requires significant upfront investment [8]. Key clinical trial site/institutional requirements include:

- The availability of reactor-produced isotopes (e.g., Iodine-131, Lutetium-177) and cyclotron-produced isotopes (e.g., Gallium-68), as well as portable isotope generators (e.g., Mo-99/Tc-99m or Ge-68/Ga-68 generators) that enable timely delivery for diagnostic purposes [9, 10].
- Appropriate infrastructure that includes Imaging Equipment (Gamma camera, PET and SPECT scanners), shielded injection rooms, radio pharmacy facilities for dose preparation, decontamination areas, radioactive waste storage, and imaging systems capable of PET/CT and SPECT/CT modalities.
- Quality control procedures must be rigorous. Verification of radionuclide purity, dose calibration, and proper documentation are mandatory components of compliance.
- Radioactive waste management strategies are determined based on isotope half-lives. Short-lived isotopes may be managed through decay-in-storage approaches, whereas long-lived isotopes require concentration, containment, or controlled dispersion based on specific regulatory guidelines.
- Trained Personnel in the team delivering radiopharmaceutical therapies includes nuclear medicine physicians, radio pharmacists, trained nurses, medical physicists and radiation safety officers. Training in radiation safety, dosimetry, and safe-handling protocols is essential to ensure compliance with regulatory standards and to guarantee patient safety.
- Integration of nuclear medicine into multidisciplinary tumor boards and establishing clear patient pathways fostering an active collaboration between Oncologists and Nuclear Medicine professionals can help expand access to innovative treatments [11].

Challenges and Emerging Solutions

Despite their transformative potential in precision oncology, radiopharmaceuticals and theranostic programs face a number of systemic, regulatory, and logistical barriers that hinder widespread adoption [2]. The Lancet commission's global survey of nuclear medicine facilities across 82 countries along with IAEA data from an additional 84 countries reveals that supply chains, workforces and regulatory challenges all affect the use of radiopharmaceutical programs across the world [12]. The constraints also include the limited global production capacity for medical isotopes, geographic limitation of uranium ores, besides high logistical costs for secure handling and disposal of radioisotopes. Moreover, there is regulatory complexity with differences across regions causing delays in product development and commercialization.

Overcoming these logistical and regulatory hurdles will be crucial for sustained market expansion and uptake of Radiopharmaceuticals in appropriate indications and trial settings. This section outlines the key challenges and offers emerging solutions informed by current literature, global policy developments, and institutional best practices.

Challenge 1: Regulatory and Approval Complexity

Radiopharmaceuticals occupy a unique hybrid space—simultaneously classified as drugs, radioactive substances, and medical devices. This multi-dimensionality leads to complex, fragmented regulatory oversight.

In the United States, the FDA regulates these agents under both drug and radiological criteria, necessitating coordination between the Center for Drug Evaluation and Research (CDER) and the Nuclear Regulatory Commission (NRC). In Europe, although the EMA has issued a 2024 draft guideline on clinical evaluation of radiopharmaceuticals, implementation across EU member states remains inconsistent. In many low- and middle-income countries (LMICs), regulatory frameworks are either underdeveloped or entirely absent, stalling both market access and research collaboration.

Emerging Solutions

- Regulatory guidance is becoming more refined. The FDA's 2022 guideline for radiopharmaceuticals in rare diseases streamlines preclinical and trial design processes.
- The EMA's 2024 draft guidance aims to harmonize expectations for early-phase trials, combination regimens, and dosimetry validation.
- The IAEA and WHO are supporting national regulatory frameworks in Africa, South Asia, and Latin America.
- Multi-stakeholder working groups led by professional societies such as SNMMI and EANM are advocating for harmonized global regulatory standards and facilitating inter-agency knowledge-sharing [3-10].

A globally harmonized and adaptive regulatory model—one that integrates drug, radiation, and imaging criteria—will be essential to accelerate the safe and timely approval of novel agents.

Challenge 2: Supply Chain and Isotope Production Constraints

The production and distribution of medical isotopes are highly centralized and fragile, often depending on aging nuclear reactors located in North America and Europe. The short half-lives of isotopes like Gallium-68, Actinium-225, and Lutetium-177 complicate logistics and necessitate rapid, local manufacturing capabilities. Transport across borders is hampered by complex licensing under radiation safety laws.

Emerging Solutions

- Investment in compact, regional cyclotrons and generator systems (e.g., Ge-68/Ga-68) decentralizes production [7].
- Accelerator-based production methods offer promising alternatives as nuclear reactor-independent methods for

isotope creation.
- Collaborative manufacturing hubs in countries like Australia, India, and Canada aim to stabilize supply chains [5-20].
- Public–private partnerships with companies like NorthStar and TerraPower are scaling commercial access to alpha-emitters like Ac-225 [16,17].

Establishing resilient, decentralized production and distribution channels will be critical for both. diagnostic and therapeutic radiopharmaceuticals.

Challenge 3: Infrastructure and Operational Readiness
Effective delivery of radiopharmaceuticals requires advanced imaging systems (PET/SPECT), shielded injection rooms, GMP-compliant radiopharmacies, and secure waste management infrastructure. Many Low- and Middle-Income Countries (LMICs) lack these and even in high-resource settings, operational readiness is often challenged by high setup costs, limited real-time dosimetry tools, and integration issues with oncology workflows

Emerging Solutions
- Scalable infrastructure models (e.g., mobile radiopharmacies, modular cleanrooms) can offer adaptable and interim solutions [18].
- Funding programs from national health systems (e.g., NHS in the UK, EU innovation funds) are supporting infrastructure investments.
- Public-private partnerships facilitate shared use of radiopharmacy services between institutions.
- The IAEA has published standardized design blueprints for nuclear medicine facilities, which can accelerate planning and compliance across regions [8,9].

Institutions must consider both short-term implementation costs and long-term sustainability models when adopting theranostic programs.

Challenge 4: Workforce Gaps and Clinical Integration
There is a global shortage of trained professionals including nuclear medicine physicians, radiopharmacists, radiation safety officers, and medical physicists. Moreover, even when personnel are available, radiopharmaceuticals are often poorly integrated into routine oncology workflows, thereby limiting appropriate patient selection and timely care.

Emerging Solutions
- Cross-disciplinary training programs aimed at oncologists, radiologists, and nuclear medicine specialists. Certification and CME modules in theranostic techniques and safety protocols are offered by SNMMI and EANM [10].
- Embedding nuclear medicine experts into multidisciplinary tumor boards to facilitate early and appropriate case identification.
- Deployment of clinical navigators or theranostic coordinators to streamline scheduling, coordination, and patient education.

Upskilling and aligning cross-specialty teams is essential for safe, efficient, and effective deployment of radiopharmaceutical therapies.

Challenge 5: High Costs and Reimbursement Uncertainty
Radiopharmaceutical programs are capital intensive, requiring investment in isotope production, infrastructure, training, regulatory compliance, patient safety monitoring, dosimetry, infrastructure, and workforce training. At the same time, reimbursement models for these therapies are inconsistent, delayed, or entirely absent in many countries with unclear pricing structures, delayed payer decisions, lack of cost-effectiveness data compounded by hesitation among hospital administrators to adopt high-cost treatments without guaranteed return.

Emerging Solutions
- Prospective clinical trials are beginning to incorporate health economics endpoints, such as cost per quality-adjusted life year (QALY) gained. This approach supports payer engagement. Addionally, value-based reimbursement models tied to clinical outcomes are gaining traction in early-adopter countries [18,19].
- Inclusion of radiopharmaceuticals in national oncology treatment guidelines (e.g., Germany, Australia) provides policy backing for coverage decisions.
- Early engagement with payers during the trial phase helps align evidence requirements and accelerates time-to-market.

Health technology assessments (HTAs) and robust economic data will be pivotal for securing broad-based payer support.

Challenge 6: Radiation Perception and Patient Acceptance
Public fear surrounding the word "radiation" persists, despite the safety and tolerability of modern radioligand therapies. Moreover, misconceptions among clinicians often result in delayed referrals and low clinical trial participation.

Emerging Solutions
- Education campaigns highlighting differences between radiopharmaceuticals and external beam radiation therapy.
- Integration of decision aids and transparent risk-benefit discussions into clinical workflow can help to support informed choices by the patients.
- Patient advocacy stories, particularly from neuroendocrine tumor and prostate cancer survivors may help to demystify the approach [11].

Proactive education will be vital to normalize radiopharmaceuticals as mainstream, safe, and effective cancer treatments.

Challenge 7: Limited Access to Clinical Trials
While theranostics is a research-intensive and rapidly evolving field, access to investigational agents is largely restricted to academic centers in high-income countries. This restricts global data generation and perpetuates access inequities.

Emerging Solutions
- IAEA-sponsored training programs are building trial-readiness in emerging healthcare systems.
- CROs with expertise in radiopharmaceutical logistics are creating global trial networks that include LMICs.
- CRO-led networks and AI-based tools are enabling decentralized trial models with real-time dosimetry and remote monitoring [13-20].
- Use of digital tools for patient monitoring, adverse event tracking, and imaging interpretation is improving trial inclusiveness and efficiency.

A globally distributed research ecosystem is essential to ensure the equitable development and validation of radiopharmaceutical therapies.

Conclusion

Radiopharmaceuticals are poised to play a transformative role in the future of precision oncology. Their ability to combine diagnostic accuracy with targeted therapy aligns well with emerging trends in personalized medicine. Rising cancer prevalence globally, regulatory and payer preferences for safer, more tolerable therapies and technological advancements in targeting and delivery means that multidisciplinary collaboration, infrastructure investments, and innovative clinical models are urgently needed. Achieving this potential on a global scale will require concerted efforts to overcome key operational, regulatory, and perceptual barriers. Stakeholders including policymakers, pharmaceutical developers, contract research organizations (CROs), academic medical centers, and payers must align to build scalable, patient-centered radiopharmaceutical programs. With a clear roadmap and collaborative strategy, radiopharmaceuticals can evolve from niche interventions into mainstream oncologic tools with meaningful global impact.

Declarations

Funding: None.

Conflicts of Interest: I declare no conflicts of interest. The views expressed are my own.

Author Contributions: I am the sole author responsible for conceptualization, drafting and revisions.

References

1. KPMG Belgium (2025) Leveraging Opportunities in Radiopharmaceuticals. Brussels: KPMG Belgium https://kpmg.com/be/en/home/insights/2025/03/ls-leveraging-opportunities-in-radiopharmaceuticals.html.
2. Giesel FL (2023) Emerging Radiopharmaceutical Therapies: Opportunities and Challenges. Eur J Nucl Med Mol Imaging 50: 1234-1250.
3. (2022) Guidance for Industry: Developing Products for Treatment of Rare Diseases and Conditions – Radiopharmaceuticals U.S. Food and Drug Administration.
4. European Medicines Agency (2024) Draft Guideline on Clinical Evaluation of Radiopharmaceuticals. EMA.
5. Lassmann M, Eberlein U (2022) The EANM Dosimetry Committee Series on Standardization of Dosimetry. Eur J Nucl Med Mol Imaging 49: 527-538.
6. (2024) World Nuclear Association. Radioisotopes in Medicine. London WNA.
7. O'Connor MK (2022) Overview of Radioisotope Generators and Their Applications. Semin Nucl Med 52: 202-216.
8. EANM (2023) Radiopharmaceutical Dosimetry Guidelines for Clinical Practice.
9. National Institute of Standards and Technology (NIST). Standard Reference Materials for Nuclear Medicine.
10. Society of Nuclear Medicine and Molecular Imaging (SNMMI). Guidelines and Resources for Radiopharmaceutical Therapy.
11. Abdel-Wahab M, Giammarile F, Carrara M, Paez D, Hricak H, et al. (2024) Radiotherapy and theranostics: a Lancet Oncology Commission. Lancet Oncol 25: e545-e580.
12. Haberkorn U (2020) Future directions in radiopharmaceutical therapy. J Nucl Med 61: 331-335.
13. Azzouz F (2024) AI in Radiopharmaceuticals: Trends and Future Directions. J Nucl Med, 2024.
14. (2024) New biotech research and manufacturing hub opens at University of Queensland, Australia. BioSpectrum Asia.
15. (2025) ICPO Collaborating Centers in Eurasia and Latin America. ICPO Foundation.
16. NorthStar Medical Radioisotopes. Supply agreement with PDRadiopharma for Ac-225. Dec 5, 2024.
17. (2024) Clarity Pharmaceuticals and TerraPower Ac-225 Supply Agreement.
18. Algorri M, Michael J Abernathy, Nina S Cauchon, Twinkle R Christian, Celeste Frankenfeld Lamm, et al. (2022) Re-envisioning pharmaceutical manufacturing. J Pharm Sci 111: 593-607.
19. Mancini DP (2023) NHS rejects Novartis cancer drug over cost. Financial Times.
20. (2023) Production and Supply of Medical Radioisotopes. International Atomic Energy Agency.