INSTITUTE @PRECISION

A WHITEPAPER FROM INSTITUTE@PRECISION

Managing Operational Complexity in Early-Phase Oncology Radiopharmaceutical Trials

Overcoming Logistical Challenges to Bring Innovative Therapies to Patients

Geoffrey Kannan, PhD, MD | *VP, Medical Sciences, Precision for Medicine*
Ivan Barrera, MD | *Senior Medical Director & Regional Head, Solid Tumors, Precision for Medicine*
Robert Bauer | *VP, Operational Strategy, Precision for Medicine*

The Institute@Precision is part of Precision Medicine Group, an ecosystem of organizations spanning discovery to commercialization, purpose-built for precision.

PRECISION MEDICINE GROUP®
PRECISION for medicine®
PRECISION AQ™

Executive Summary

Interest in radiopharmaceuticals in oncology is growing rapidly, driven by clinical validation in gastroenteropancreatic neuroendocrine tumors and prostate cancer, theranostic approaches, and improved radioisotope production and supply.

However, early-phase radiopharmaceutical trials present a range of operational challenges that significantly differ from those of other therapeutic modalities. Left unaddressed, these challenges may lead to increased operational friction, timeline expansion, and greater patient burden.

This whitepaper draws on Precision for Medicine's early-phase radiopharmaceutical clinical trial experience across oncology indications to highlight recurring challenges and practical considerations that may help study teams anticipate complexity, mitigate risk, and improve trial execution.

The Rise of Radiopharmaceuticals

Radiopharmaceuticals are an established modality boasting nearly a century of clinical use, beginning with radioactive iodine therapy for thyroid disease in the early 1940s.[1] While early applications focused on organ-specific diagnosis and treatment, recent advances in technology, safety, and accessibility have positioned radiopharmaceuticals at the forefront of oncology.

Such advances have not gone unnoticed. Recent years have seen significant investment within the industry, exemplifying the growing confidence in the modality. For instance, between 2017 and 2023, radiopharmaceutical-focused venture capital funding increased 550% to $408 million, and industry giants such as Ely Lilly and AstraZeneca have announced strategic acquisitions.[2-4]

Developers have also invested significant sums in expanded radiopharmaceutical manufacturing infrastructure. In 2025, for instance, Novartis pledged a $23 billion investment to fund more than seven manufacturing and R&D facilities across the US, including those for radioligand therapies.[5,6]

Multiple factors are driving growth in this sector. First, the FDA approval of several radiopharmaceuticals, including Pluvicto, Lutathera, and Xofigo, has demonstrated the clinical viability of these therapies, driving sector confidence and interest.

Second, theranostic approaches, which integrate diagnostic molecular imaging and targeted radionuclide therapy using a common molecular target, allow providers to "see what they treat". This precision-based framework is attractive to developers, payers, and providers, as it enables biomarker-driven patient selection, improves clinical and economic predictability, and limits exposure for patients unlikely to benefit.

Moreover, increased investment in radionuclide production infrastructure has begun to alleviate historical isotope supply shortages that have limited clinical development.[7,8] Efforts to map current production and supply infrastructure, particularly for alpha-emitting radionuclides, are also helping drive the awareness and collaboration needed to support and expand targeted alpha therapy development.[9]

Finally, although currently approved for prostate cancer and neuroendocrine tumors, radiopharmaceutical therapies have broad applicability across solid tumors, making them an attractive option for developers.

While welcome, these opportunities and industry developments are driving greater competition. Many

more sponsors are advancing similar radiopharmaceutical programs in parallel, making time-to-market increasingly critical. As such, early-phase execution speed can directly impact a developer's competitive positioning and downstream development options. In other words, excellence in clinical trial operations turns a logistical challenge into a critical differentiator. What is more, radiopharmaceutical trials involve unique operational hurdles – hurdles that may be poorly understood by teams without considerable radiopharmaceutical development experience.

In this whitepaper, we provide a comprehensive overview of the key operational challenges specific to radiopharmaceutical clinical trials, along with practical considerations for overcoming them. The insights shared here are the result of lessons learned over years at the forefront of radiopharmaceutical development.

> "Radiopharmaceutical therapy has been around for more than 100 years. What's changing now is our ability to target disease more precisely. As those advances continue to develop, entirely new possibilities for treatment become available, more programs move forward at once, and operational execution becomes the real differentiator."
>
> — Geoffrey Kannan, PhD, MD, Vice President, Medical Sciences, Precision for Medicine

Routine Radioligand Delivery Capabilities Are Insufficient for Phase I Trial Execution

With the FDA approvals of Pluvicto and Lutathera, the number of sites with routine radioligand therapy delivery capabilities is growing. However, the ability to deliver approved radioligand therapies does not ensure Phase I execution readiness. Differentiating between the two – sites that can deliver routine therapies vs those equipped for investigational therapy workflows – is therefore critical.

Understanding the routine-investigational gap

FDA-approved radioligand therapies are typically delivered through predictable, short, and standardized visits, with relatively limited, well-established monitoring and follow-up procedures. By contrast, Phase I clinical trials for radiopharmaceuticals regularly require:

- Extended, multi-day patient visits
- Serial imaging to support dosimetry
- Intensive blood and urine pharmacokinetic (PK) analysis
- More complex sample handling
- Extended observation and monitoring under investigational conditions
- Extensive education and guidance for participants to ensure safety and comfort

These additional requirements increase the logistical burden for both site staff and patients. Site staff, for instance, must maintain coordination across multiple visits and manage increased logistical requirements for radioactive sample handling and timing. For patients, the increased burden of education, safety concerns, extended visits, and rescheduling can negatively impact their experience.

Phase I site requirements

The requirements for radiopharmaceutical trials make it difficult to find appropriate sites. A site equipped for Phase I trial execution must have the following:

Nuclear medicine capabilities	Advanced storage and handling	Just-in-time delivery support	Experienced, multidisciplinary teams	Regulatory compliance
Certified and licensed nuclear medicine departments, PET imaging capabilities, and radiopharmacy expertise	Adequate storage for radiotracers and radiotherapeutic compounds, and expertise in handling and dosing radioactive materials	Point-of-care models may be required due to the short half-lives of isotopes	Staff must demonstrate ongoing training and compliance with radiation safety protocols	Understanding of FDA, OSHA, NRC, and country-specific regulations

Additional site considerations for alpha-emitting radiopharmaceuticals

For teams developing alpha-emitting radiopharmaceuticals, sites must meet additional handling and safety requirements compared to those for beta emitters, including:




Alpha-emitter-specific radioactive materials licenses and radiation-safety committee approvals	Stricter handling and pharmacy preparation protocols, including containment measures to address inhalation risk	Isotope- and protocol-specific dose assay validation (dose calibrator or defined method) and imaging system qualification	IATA Dangerous Goods (Class 7) certification for receiving and materials management staff

Because alpha-emitting radiopharmaceuticals have additional handling requirements and are still investigational, fewer sites are currently licensed and equipped to administer them. This can lead to fewer available sites and longer startup time for alpha-emitter clinical trials.

"A site that can give an FDA-approved radioligand therapy is not automatically ready for a Phase I study. The intensity, monitoring, and logistics need to be at a completely different level."

— Ivan Barrera, MD, Senior Medical Director & Regional Head, Solid Tumors, Precision for Medicine

Key Steps Developers Can Take

To mitigate the risk of delays in site selection and activation, patient loss due to timeline misalignment, and erosion of competitive standing, developers should evaluate sites with the clear understanding that routine radioligand delivery capabilities are insufficient for Phase I trial execution. To bridge the capabilities gap, developers should evaluate sites at least 9–12 months in advance of the first patient in. Doing so allows sufficient time for institutional review board approvals, radiation safety committee reviews, imaging and dosimetry qualification, contracting, and site logistical planning.

Developers must also ensure that trial patient numbers, visit intensity, monitoring plans, and sample handling processes are realistic for the site's capacity. Expert support at this stage can be invaluable, helping teams match site capabilities with study requirements and speed site selection.

Beyond this, developers should consider a site's readiness for subsequent trial phases and how this can impact future timelines. Large institutional centers are more likely to have the licensing, infrastructure, and staffing needed to scale into later-stage studies, whereas smaller or less experienced sites may require additional time to secure license amendments or expand operational capacity. Developers must proactively coordinate with sites to support this transition or plan for site replacement or expansion in later phases.

Radiopharmaceutical Trials Require Diverse Expertise and Increased Multidisciplinary Coordination

Radiopharmaceutical trials demand a diverse range of expertise and greater multidisciplinary coordination compared with other modalities. This can often be overlooked, with sponsors focusing primarily on securing nuclear medicine expertise and investing in equipment.

Global shortages of trained staff, particularly in nuclear medicine, further complicate the assembly of effective multidisciplinary teams.

The key players required for smooth Phase I site operations, along with their functional roles, are summarised in Figure 1.

Key players and responsibilities across disciplines

	Roles	Responsibilties
Nuclear Medicine	• Nuclear medicine physicians • Nuclear medicine technologists • Medical physicists • Radiopharmacists	• Radiopharmaceutical preparation • Dosimetry & radiation safety • Therapy administration
Patient flow/trial progression		
Oncology	• Oncologists • Pharmacists	• Patient selection & treatment strategy • Symptom management • Toxicity management • Long-term follow-up
Cross-Functional Support	• Nurses • Technicians • Pharmacy staff • Operational/administrative staff	• Support therapy delivery and follow-up • Coordinate patient flow, monitoring, and logistics

Figure 1: Summary of key operational players and responsibilities across radiopharmaceutical disciplines. Role definitions and responsibility distribution vary by geography and institution, as workflows are not standardised.

In addition to the need for diverse expertise, the nature of experimental therapies used in Phase I clinical trials introduces a level of uncertainty that requires close, ongoing oversight. Care pathways, especially patient transitions from nuclear medicine to oncology, must include clear and effective hand-offs and expert oversight that account for this added uncertainty.

Without the right expertise and coordination in place, teams risk extending their trial timelines through increased errors and repeated work, and can negatively impact enrolled patient experience through increased repeat visits and loss of confidence in the trial process.

Key steps developers can take

Teams must have a clear understanding of which functional roles are critical for smooth Phase I site operations, and secure those resources well in advance of trial initiation. Developers should carefully assess their internal capabilities to identify any expertise or operational gaps that could be bridged by engaging an experienced contract research organization or other service provider.

Imaging and Dosimetry Considerations

Phase I trials require repeated, protocol-specific imaging to inform eligibility, dosing, and safety assessments. On top of this, regulators increasingly expect dosimetry-informed dose planning and longitudinal safety monitoring, with Phase I trials often carrying the burden of generating this evidence.

However, without proper operational oversight and proactive planning, imaging can quickly become a rate-limiting factor in clinical development, with limited scanner availability and scheduling conflicts representing an on-the-ground reality for many programs. Centralized image review can also introduce additional dependencies that complicate planning.

Key steps developers can take

To set up for Phase I and future trial success, teams must treat imaging execution and interpretation as core operational components, planned with both Phase I intensity and future scalability in mind. Developers should ensure they have:

- Engaged the dedicated nuclear medicine expertise required for imaging and dosimetry, including physician and medical physics support
- Provided the appropriate technical training for both site staff and project teams
- Established robust processes for radiotracer preparation, dose calculation, and administration
- Validated isotope handling workflows and dosimetry processes early, with approaches such as mock shipments, to reduce operational variability and mitigate compliance risk

Together, these measures help ensure imaging and dosimetry are executed with the rigor required for early-phase development while laying the foundation for scalable trial expansion.

Accounting for Time-Sensitive and Patient-Specific Logistics

The rapid decay and limited shelf-life of radiopharmaceuticals mean trials depend on just-in-time manufacturing and delivery models, which are significantly more sensitive to scheduling disruptions than those used for other therapeutic modalities. In some cases, this is complicated by the use of radiopharmaceuticals that need to be manufactured for individual patients.

Crucially, as patient numbers increase across subsequent clinical trial phases, these execution risks grow, increasing the importance of proactive operational planning.

Proactive operational planning should include:

- Initiating structured patient prescreening at the time of the site initiation visit (SIV), where feasible
- Establishing clear timelines for full site activation, typically within 1–2 weeks post-SIV
- Supporting principal investigators in interpreting inclusion criteria and managing washout periods from prior therapies
- Counseling patients on eligibility uncertainty when dependent on confirmatory PET imaging uptake
- Validating site readiness through mock patient simulations and dry-run workflows prior to first patient dosing
- Leveraging experienced operational teams to anticipate and mitigate logistical risks

Taking these steps can help sponsors reduce the risk of compressed scheduling windows, missed imaging or dosing windows, product waste, and patient rescheduling.

Partnerships Help Support Successful Trial Execution

Radiopharmaceutical trials place unique operational demands on developers. Engaging with radiopharmaceutical-specific clinical trial operations experts can support development teams, regardless of their level of experience with radiopharmaceuticals, to better anticipate and plan for this complexity from the start.

Early involvement of radiopharmaceutical trial operations experts, for instance, can support study planning by helping developers distinguish essential clinical trial requirements from nice-to-have elements, which can be challenging. A competent partner can also inform better and faster site selection by efficiently discerning site readiness based on experience and established relationships.

Throughout development, experienced radiopharmaceutical teams can facilitate coordination across multidisciplinary stakeholders, manage vendor interactions, oversee complex logistics, and support smarter regulatory planning, helping to reduce friction and delays and position sponsors for a higher probability of technical and regulatory success.

> "Bringing a novel radioligand therapy to market is a race, but it is more of a marathon than a sprint. If you rush early decisions and planning, you end up paying for it later, usually with time you cannot afford to lose. Taking advantage of operational support early can help developers set a pace that balances speed with acceptable risk."
>
> — Robert Bauer, Executive Director of Operational Strategy, Precision for Medicine

Removing operational barriers to sustainable execution

The operational decisions made during early-phase radiopharmaceutical clinical trial planning can have lasting impacts that determine program success. To effectively mitigate risk, development teams must understand the unique operational landscape for radiopharmaceutical trials and prioritize early, radiopharmaceutical-specific strategic planning.

Working with competent and experienced radiopharmaceutical experts offers invaluable support here, helping sponsors to protect trial timelines, enhance scalability, sustain positive patient experience, and minimize development costs.

Ultimately, developers who effectively address the operational realities of radiopharmaceutical trials upfront will be better positioned to translate scientific promise into therapeutic realities for patients worldwide.

Further Insights from the Institute@Precision Radiopharmaceutical Series

This article is part of the Institute@Precision radiopharmaceutical series, which examines these therapies across the full clinical development-to-access continuum. Additional articles in the series extend the analysis, exploring:

- **Development strategy** — how access constraints intersect with trial design, regulatory expectations, and evidentiary robustness in global radiopharmaceutical development
- **Regulatory strategy** — comparator feasibility, evolving evidentiary expectations, and global alignment for infrastructure-dependent therapies.
- **Commercialization** — pricing and reimbursement dynamics, provider adoption, and market readiness across global regions.
- **Investor perspectives** — commercial and reimbursement realities, globalization tailwinds, upcoming clinical, regulatory and manufacturing milestones, and capital market sentiments

To read more about the unique challenges posed by radiopharmaceutical development and commercialization, and for quarterly expert insights into other timely precision medicine topics, please visit: https://www.instituteatprecision.com/

About Precision for Medicine

Drawing on deep oncology and radiopharmaceutical expertise, Precision for Medicine partners with sponsors to design global trials, accelerate clinical development, and ensure scientific and regulatory integrity.

Authors

Dr. Geoffrey Kannan

Geoffrey Kannan, PhD, MD

Vice President, Medical Sciences, Precision for Medicine

Dr. Kannan is a pediatric oncologist by training and practiced as a pediatric neuro-oncologist prior to his experience in industry. He has over 25 years of experience in oncology, with drug development expertise spanning pediatric oncology, CNS malignancies, and a variety of other solid tumors. At Precision for Medicine, Dr. Kannan leads a team of physicians dedicated to oncology drug development and provides medical and scientific thought leadership to biotech partners.

Dr. Ivan Barrera

Ivan Barrera, MD

Sr. Medical Director & Regional Head, Solid Tumors, Precision for Medicine

Dr. Barrera is a physician with a fellowship in Research GI Oncology and more than 16 years of clinical research experience. He has served as a methodical and strategic contributor within interdisciplinary drug development teams. His experience in solid tumors includes a focus on gastrointestinal oncology, including neuroendocrine tumors, as well as first-in-human and Phase I–IV studies. His industry clinical development experience spans small molecules, antibodies, vaccines, cytokines, oncolytic viruses, radiopharmaceuticals, and cellular therapies.

Robert Bauer

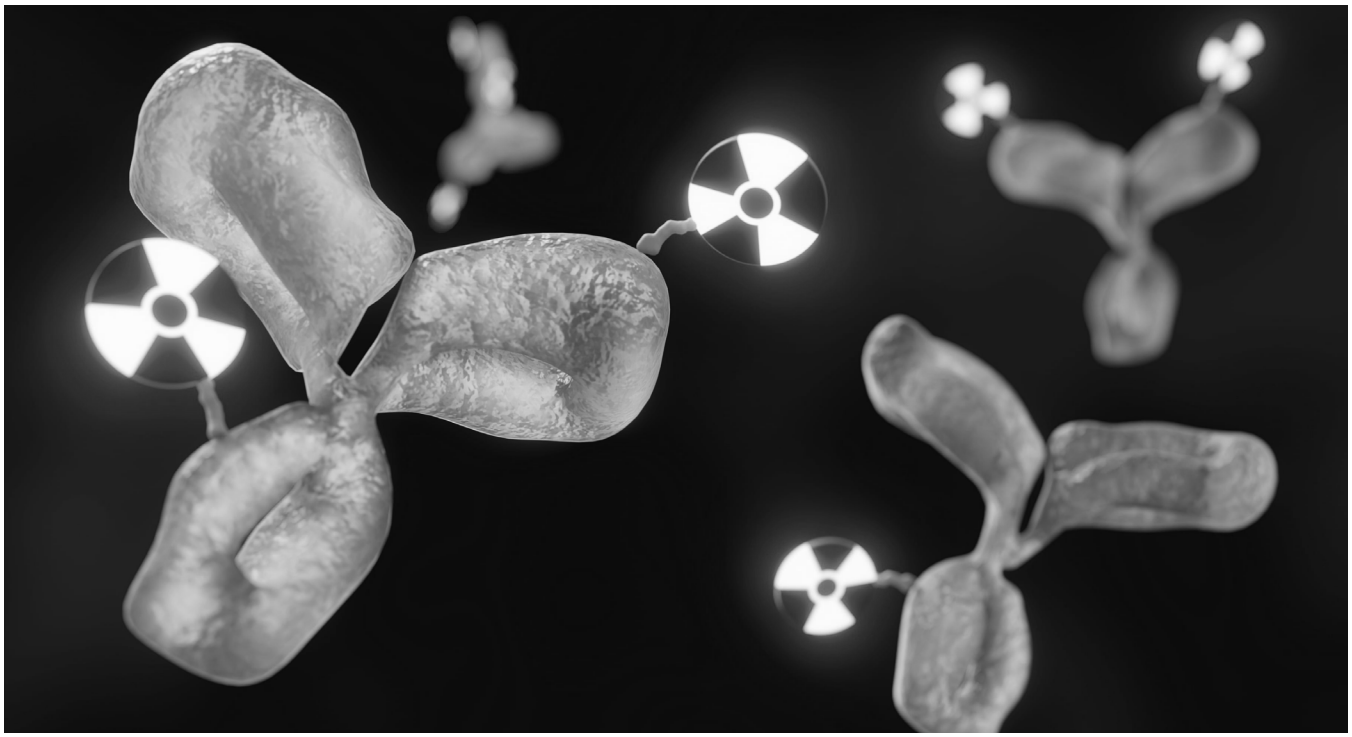
Robert Bauer

Vice President of Operational Strategy, Oncology, Precision for Medicine

Mr. Bauer has 25 years of clinical research experience across both sponsors and contract research organizations. He specializes in developing strategic approaches to support the successful operationalization of complex oncology studies involving theranostics and other advanced therapies.

References

1. Souza PB de, McCabe CJ. Radioiodine treatment: an historical and future perspective. Endocrine-Related Cancer. 2021;28(10):T121-T124. doi:10.1530/ERC-21-0037
2. Radiopharmaceutical-focused VC deals in US see staggering 550% growth to $408 million in 2023, reveals GlobalData. GlobalData. December 8, 2023. Accessed February 11, 2026. https://www.globaldata.com/media/business-fundamentals/radiopharmaceutical-focused-vc-deals-in-us-see-staggering-550-growth-to-408-million-in-2023-reveals-globaldata/
3. Masson G. Lilly enters radiopharmaceuticals with $1.4B Point acquisition. October 3, 2023. Accessed February 11, 2026. https://www.fiercebiotech.com/biotech/lilly-makes-splash-surfing-radiopharmaceutical-wave-14b-acquisition
4. Acquisition of Fusion completed. June 4, 2024. Accessed February 11, 2026. https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2024/acquisition-of-fusion-completed.html
5. Investing in America's Health. Novartis United States of America. Accessed February 11, 2026. https://www.novartis.com/us-en/about/investing-americas-health
6. Novartis to add radioligand therapy manufacturing facility in Winter Park, Florida, fourth in US to serve patients and advance $23 billion investment | Novartis. Accessed February 11, 2026. https://www.novartis.com/news/media-releases/novartis-add-radioligand-therapy-manufacturing-facility-winter-park-florida-fourth-us-serve-patients-and-advance-23-billion-investment
7. Supply of medical radioisotopes - British Institute of Radiology. Accessed February 11, 2026. https://www.bir.org.uk/media-centre/news/2013/april/important-reports-on-supply-of-medical-radioisotopes.aspx
8. Nuclear Energy Agency. Current Trends in the Supply and Utilisation of Medical Radioisotopes. Organisation de Coopération et de Développement Economiques. Preprint posted online 2025. doi:10.82155/X9KB-7J83
9. Tosato M, Favaretto C, Kleynhans J, et al. Alpha Atlas: Mapping global production of α-emitting radionuclides for targeted alpha therapy. *Nuclear Medicine and Biology*. 2025;142-143:108990. doi:10.1016/j.nucmedbio.2024.108990



PRECISION for medicine®

precisionformedicine.com

The Institute@Precision is part of Precision Medicine Group, an organization purpose-built for precision with services spanning discovery to commercialization and featuring experts from:

PRECISION for medicine® PRECISION AQ™