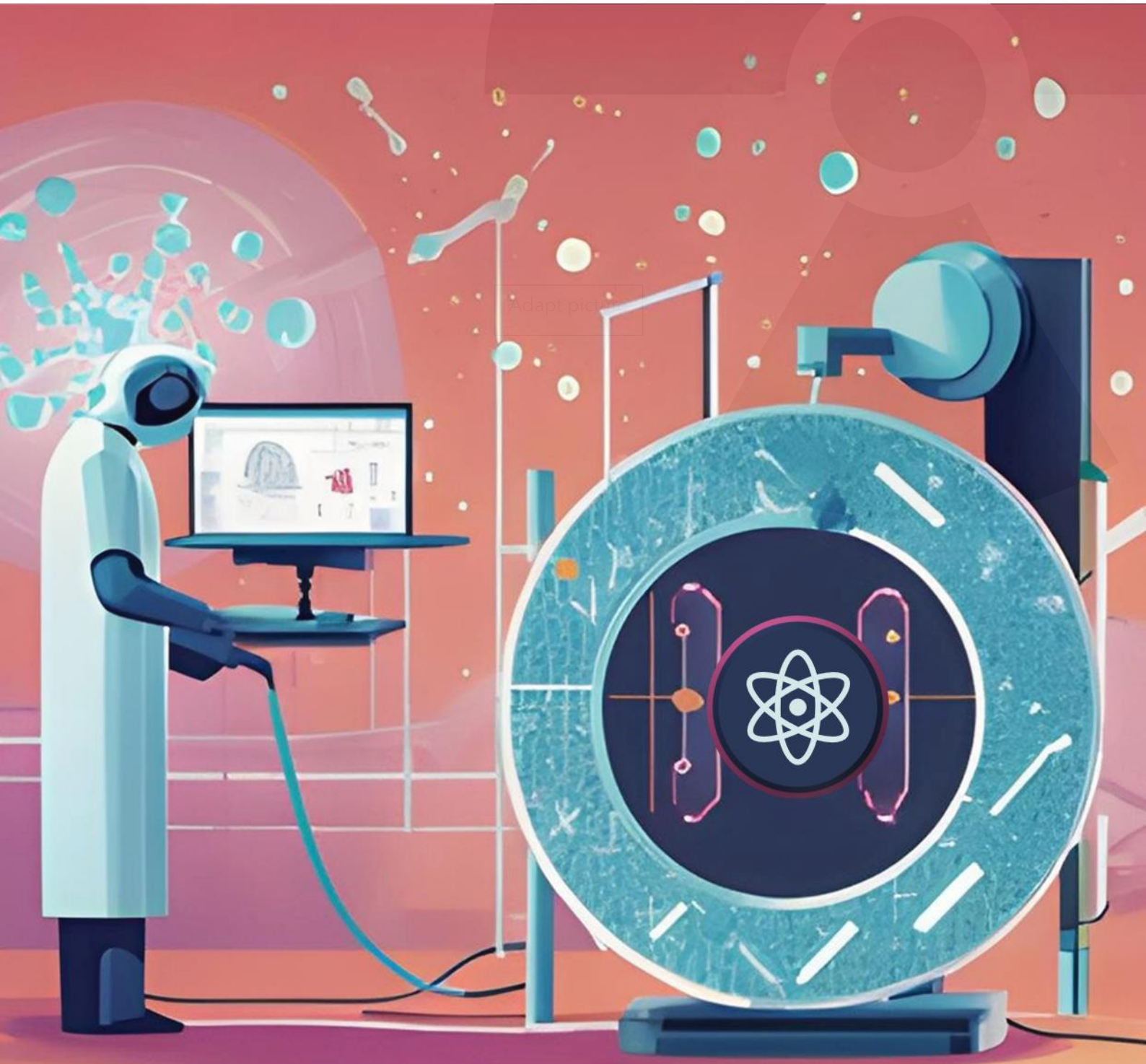
INOVIGATE
achieving outcomes



A radioligand therapy action plan for Belgium

A multi-stakeholder supported integrated solution framework and action plan to be future prepared for radioligand therapy for cancer treatment in Belgium

Policy report

June 2024

Colophon

Title	A radioligand therapy action plan for Belgium
Authors	Ingrid Maes, Eline Kok, Jean Van Nuwenborg, Valerie Debruyn
Expert contributions via interviews	Pedro Facon (RIZIV), Patrick Flamen (Institut Jules Bordet), Zena Wimana (Institut Jules Bordet), Koen Hasaers (SCK CEN), Sarah Baatout (SCK CEN), Bertrand Tombal (UCL Saint-Luc), François Jamar (UCL Saint-Luc), André Deschamps (Wij Ook), Els Verstuyft (RIZIV), Marleen Vandecapelle (FANC), An Fremout (FANC), Roland Hustinx (CHU Liège), Wim Penninckx (FAGG), Guillaume Jean (FAGG), Jean-Luc Golnez (FAGG), Karin Froidbise (FAGG)
Expert contributions via round table participation	Jo De Cock (RIZIV), Marleen Vandecapelle (FANC), Els Verstuyft (RIZIV), Veerle Van de Velde (RIZIV), Charles Vriamont (Trasis), Corentin Warnier (Trasis), Dominique Vanderghinste (UZA), Olivier Gheysens (UCL Saint-Luc), Patrick Flamen (Institut Jules Bordet), Dirk Van Gestel (Institut Jules Bordet), Hendrik Everaert (UZ Brussel), Christophe Deroose (UZ Leuven), Karoline Spaepen (GZA Sint-Augustinus), Olivier de Winter (OLV Aalst), Barbara Brouwers (AZ Sint-Jan Brugge-Oostende), Pieter De Jonghe (AZ Groeninge), Nadia Withofs (CHU Liège), Erik Briers (Europa Uomo), Filippo Serra (pharma.be), Maud ten Haaf (FANC), Koen Hasaers (SCK CEN), Sarah Baatout (SCK CEN), Sigrid Stroobants (UZA), Daan Aeyels (VOKA), François-Xavier Hanin (CHU UCL Namur), Jean-Luc Golnez (FAGG), Freija Verdoodt (Belgische kankerregister), Kristoff Muylle (AZ Delta), Nancy Van Damme (Belgische kankerregister), Robbe Waterschoot (UZ Gent), Vincent Keereman (Xeos), Veronique Le Ray (Stichting tegen kanker), Zena Wimana (Institut Jules Bordet), Jean-Michel Luyckx (Novartis), Rutger Roesems (Novartis), Joao-Louiz Marques (Novartis), Marie-Anne van Lierde (Novartis)
Commissioned by	Inovigate has performed this research and analysis under complete intellectual independence. Inovigate is a strategy and management consulting company for life science industries. This initiative is commissioned by Novartis
Publication date	June 2024
How to refer to this document	INOVIGATE – Maes I., Van Nuwenborg J., Kok E., Debruyn V., A radioligand therapy action plan for Belgium

A radioligand therapy action plan for Belgium

Cancer poses a significant threat to human health, with over 70,000 diagnoses annually in Belgium. Significant R&D efforts have generated breakthrough, often personalised, cancer therapies. More specifically, innovations like **radioligand therapy (RLT) have shown promising efficacy in prominent cancer domains.** RLT is a targeted cancer treatment using radioactive substances that bind to cancer cells, delivering radiation directly to them.

Historically, **Belgium has a strong legacy in RLT** and it has everything it needs to become a worldwide RLT hotspot: research, clinical trials, logistics, production etc. However, it must continue to **invest to maintain this position for the long-term benefit of all Belgian patients.** During multi-stakeholder discussions, we identified and prioritised the six major categories of **challenges to maintain Belgian RLT preparedness**:

Challenges for Belgian RLT preparedness

1. Governance
2. Regulation and reimbursement
3. Identified needs
4. Service provision
5. Health information
6. R&D and innovation

Concrete solutions have been developed to tackle these challenges in the same multi-stakeholder approach. These solutions have been translated into **actions that are allocated to three stakeholder groups to obtain results**: authorities, medical and scientific profiles (healthcare professionals, hospitals and research organisations) and industrial partners. This comprehensive approach culminates in the establishment of the **RLT action plan for Belgium**:

RLT action plan for Belgium

Authorities

- RLT hotspot & leadership vision
- Integration with Belgian cancer plan
- Long-term central planning & management
- Adapted financing instruments
- Adaptive safety regulations
- Adequate reimbursement budget
- Outcomes-related reimbursement
- Regulate hospital and industrial production
- (pre)clinical trial framework to become hotspot
- Centres of excellence

HCP/hospitals/research organisations

- Awareness building & info dissemination
- Inclusion in multidisciplinary cancer treatment
- Clear criteria for referrals & care pathways
- Professional training & licensing for all HCPs
- Evidence-based decisions, guidelines, value
- Predictive models based on registries, RWD
- ST central planning & management of demand & supply
- Sufficient large clinical trials to be meaningful
- (pre)clinical trial framework to become hotspot
- Knowledge pooling
- Data collection & re-use for R&D

Industry

- Inclusion of future technology evolutions
- Companies to provide total solutions
- Adapted financing instruments
- Ensure patient supply

The implementation of this RLT action plan over the period 2024-2026 will ensure that Belgium can maintain its leading international RLT position and Belgian patients can benefit from the most recent important advances in RLT cancer therapy

Preface – Jo De Cock

Radioligand therapies (RLTs) are revolutionising the landscape of cancer treatments, offering new hope, particularly for aggressive cancers like metastatic prostate cancer and gastroenteropancreatic neuroendocrine tumors. In the future and taking into account the global RLT pipeline, RLTs will gain approval for the treatment of many other cancer types. Realising the full potential of RLTs in a growing landscape hinges on ensuring their effective delivery to patients. Realising this effective delivery will lead to a new era in personalised oncology medicine.

To reach this objective, significant challenges remain to be tackled. Delivering RLTs requires multidisciplinary and multisectoral coordination. This necessitates innovative approaches and efforts to integrate these therapies seamlessly into existing treatment protocols and the overall healthcare system. This includes the elaboration of appropriate regulation on safety issues and on reimbursement conditions as well as the development of quality driven models of care, the organisation and development of the necessary capacity and training with regard to service provision and the creation of better awareness and good understanding on the use and added value of RLTs.

Recognising the interconnected nature of these challenges, a multi-stakeholder dialogue has been initiated, engaging authorities, clinicians, patients, experts, research institutions, and industry stakeholders. This collaborative approach aims to develop a comprehensive Belgian Radioligand Therapy action plan, fostering mutual understanding and co-created solutions to overcome barriers hindering RLT implementation. Driving this transformative agenda is a collective endeavour rooted in the principle of equitable access to cutting-edge treatments for all patients in need. It has been my honor to chair this initiative.

The recent interactions on this subject, hosted during a conference under the auspices of the Belgian presidency of the European Union, emphasise Belgium's pivotal role in advancing medical innovation. Leveraging its robust medical infrastructure and recognised expertise in RLT, Belgium is poised to lead the charge in Europe in this transformative journey. The time for action is now! Let us seize this opportunity to shape the future of cancer care to the benefit of all patients.

Jo De Cock

Chairman of the multi-stakeholder initiative
Former Administrator General NIHDI
Chairman of the National Commission of Physicians and Health Insurance Funds and the National Joint Commission of Physicians and Hospitals

June 2024

Table of Contents

Executive summary 6
1. The RLT potential and landscape 8
1.1 Belgium's strengths and value chain 9
1.2 European actions 9
2. Belgian preparedness for RLT 12
2.1 The objective 12
2.2 The approach 13
3. RLT challenges and proposed solutions 15
3.1 Governance 15
3.2 Regulation and reimbursement 16
3.3 Identified needs 18
3.4 Service provision 19
3.5 Health information 20
3.6 R&D and innovation 21
4. RLT solution framework and action plan for Belgium 23
4.1 The RLT solution framework for Belgium 23
4.2 Integration of the Belgian RLT solution framework into the cancer plan 24
5. Implementation of the RLT solutions and action plan 25
5.1 Solution implementation responsibilities for the authorities 26
5.2 Solution implementation responsibilities for HCPs, hospitals and research organisations 26
5.3 Solution implementation responsibilities for companies 27
6. Next steps 28
Table of figures 29
List of abbreviations 30
Supporting literature 31

Executive summary

Cancer is one of the major threats to human health with more than 70,000 individuals being diagnosed every year in Belgium. With advancements in research and technology, the landscape of cancer treatment has witnessed significant progress, offering a range of therapeutic options tailored to individual needs. From traditional approaches like surgery, chemotherapy and radiation therapy to more recent innovations such as radioligand therapy (RLT). Today, RLTs are used in 2 prominent cancer domains, neuroendocrine and castration-resistant, metastatic prostate cancers. First clinical results are underlining RLTs promising efficacy. As Belgium is known for its strong legacy in RLT, our country should be at the forefront of preparedness for the implementation of current and future RLT into clinical practice. This is crucial to maintain and strengthen the Belgian RLT legacy, to position RLT as an established instrument in the cancer treatment instrumentation, and increase benefit for Belgian patients.

To enable this, major challenges and barriers regarding Belgian RLT preparedness have been prioritised based on various multi-stakeholder engagement approaches, including an initial debate, interviews and an e-survey. The challenges and barriers were categorised into 6 different domains: governance, regulation and reimbursement, identified needs, service provision, health information and research and development (R&D) and innovation. Solutions to address these challenges and barriers were developed and proposed during the first multi-stakeholder round table, to reach common ground amongst all stakeholders involved. After two round tables and constructive discussions on some major topics, consensus was reached on all solution blocks. Based on this common ground, the solution framework was developed.

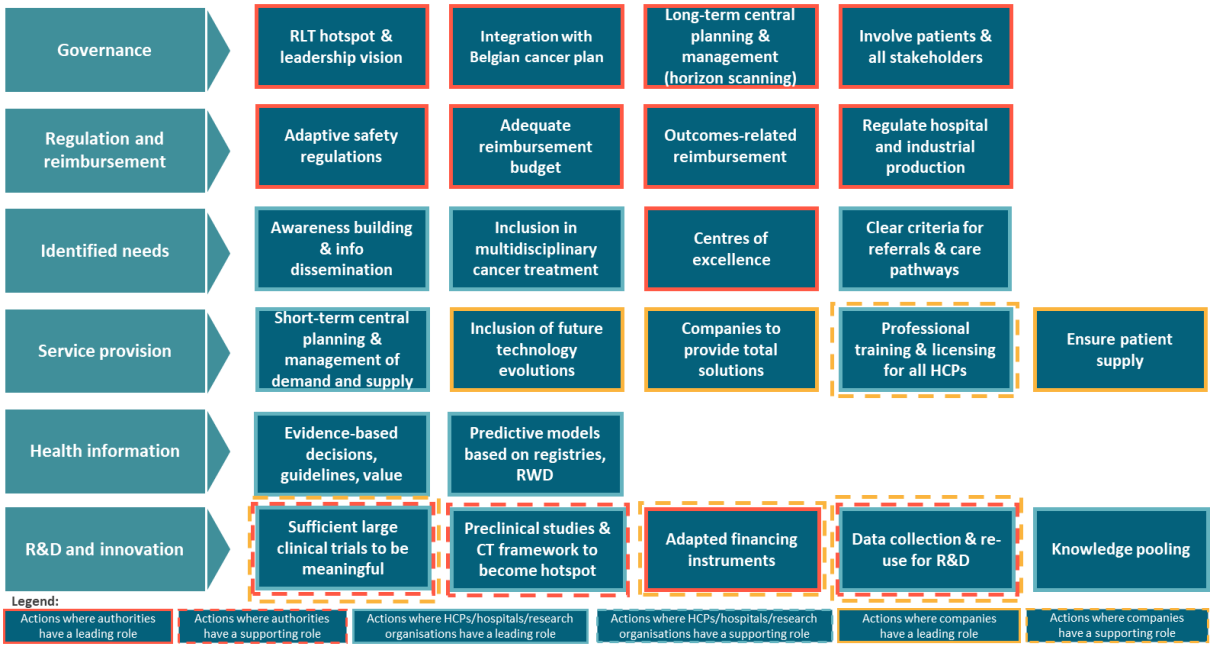


Figure 1: The Belgian RLT solution framework with the proposed solutions in the 6 domains assigned to the responsible stakeholder groups

The objective of the second round table was to finalise the RLT action plan for Belgium formulating concrete actions for all solution blocks, supported by all stakeholders. These actions were assigned to the stakeholder groups (authorities, healthcare professionals (HCPs)/hospitals and research organisations and industrial players/companies), responsible for implementation of the RLT solution framework and action plan for Belgium.

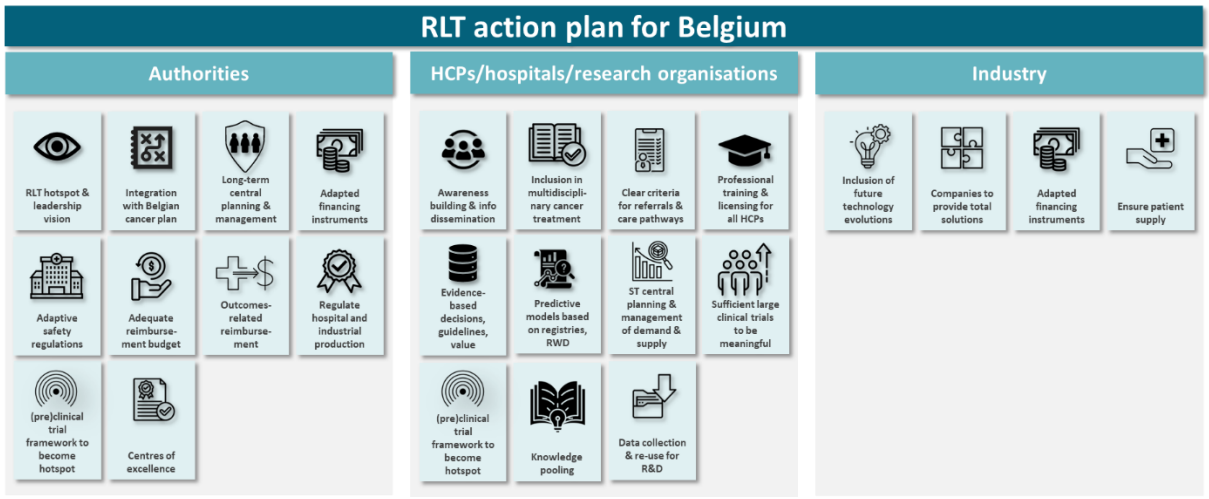


Figure 2: Overview with the list of solutions assigned to the key stakeholders that have to take action or take the initiative to implement the solution

If implementation of the RLT action plan is performed timely, Belgium can maintain its leading international position and Belgian patients can benefit from the most recent important advances in cancer therapy.

1. The RLT potential and landscape

Despite progress in many areas of cancer care, important gaps remain. Many patients do not have effective treatment options, particularly for aggressive or rare cancer types. New strategies are needed to improve both survival and quality of life. One such emerging treatment modality is radioligand therapy (RLT)[1].

RLT is currently used as a precision nuclear medicine therapy for patients with advanced cancers. It operates by selectively delivering radiation to cancer cells based on surface protein recognition. A radioligand is comprised of a radioisotope (radioisotopes are low penetration radiation emitting radionuclides that deposit high levels of energy in the nucleus of the targeted cells to induce DNA strand breaks and activate programmed cell death[2]) paired with a targeted ligand designed to bind specifically to cancer-associated cell markers. By choosing different radioisotopes to attach to the same type of ligand, the process can be used to either diagnose or treat certain types of cancer. As the radiation works over very short distances and can be directed specifically to cancer cells, the treatment is generally well tolerated with self-limiting side effects.

RLT has the potential to contribute to deliver personalised and targeted treatments to cancer patients at an earlier stage in their treatment. It can be targeted to the unique characteristics of the cancer being treated, helping to improve the efficacy of the treatment.

RLT is becoming an important component of cancer care. RLT has proven to improve overall survival and quality of life for patients diagnosed with neuroendocrine cancers and advanced metastatic, castration-resistant prostate cancer. However, it has only recently been introduced into cancer care guidelines for these types of tumours[3]. An increase of cancer types that can be treated with RLT is expected, as globally over 200 clinical trials in RLT are currently ongoing.[4] A few RLTs are already commercialised, and many other RLT therapies are in the final phase of clinical development (see figure 3). The introduction of these diverse therapies (different isotopes, different ligands) on the market in the coming years will cover a broad spectrum of cancers and further propel the RLT market growth. This growth will also be stimulated by the growth of the eligible patient population for these types of treatments.

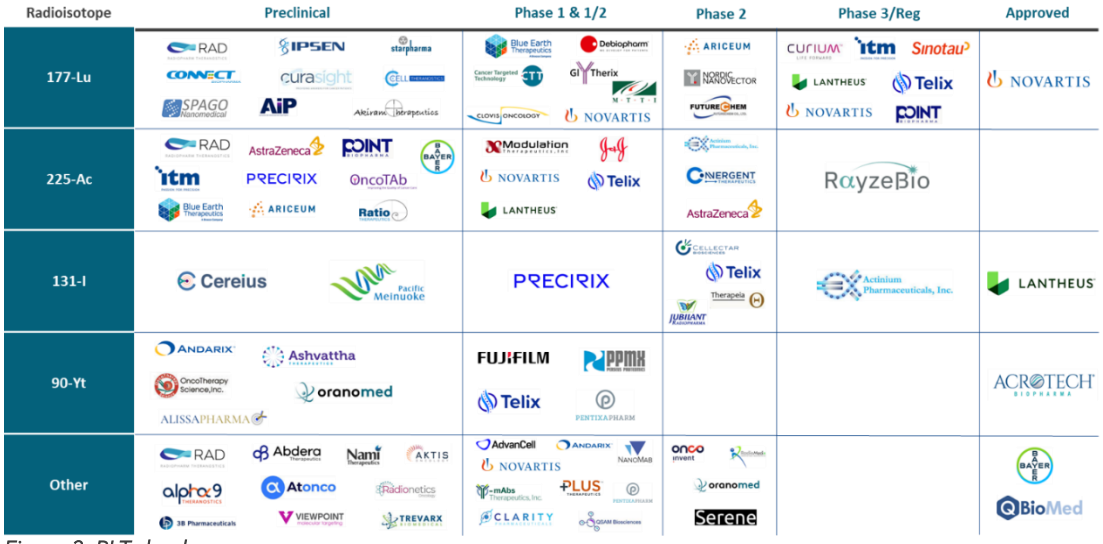


Figure 3: RLTs landscape

[1] The Health Policy partnership 2021

[2] Radiotheranostic definition by: Duan H, Iagaru A, Aparici CM. Radiotheranostics - Precision Medicine in Nuclear Medicine and Molecular Imaging. Nanotheranostics. 2022 Jan 1;6(1):103-117. doi: 10.7150/ntno.64141. PMID: 34976584; PMCID: PMC8671964.

[3] Radioligand Therapy: Realising the potential of targeted cancer care 2020

[4] https://www.linkedin.com/posts/andrewpannu_radiopharmaceuticals-market-map-66-companies-activity-7075122643217117184-Uwog/?trk=public_profile_like_view

1.1 Belgium's strengths and value chain

Belgian nuclear medicine counts more than 5,000 dedicated professionals, amongst whom 350 nuclear medicine specialists.[5] Belgium hosts the global number one manufacturer of cyclotrons both for radioisotope (PET, SPECT and theranostic applications) and proton therapy production. Belgium produces, separates and purifies 20% to 25% of the global medical isotope demand, and this number can even reach 65% during peak periods. The BR2 reactor of SCK CEN is one of the two most flexible and powerful research reactors in the world, able to satisfy 100% of the worldwide demand of 99Mo when required. The Belgian 'Institut des Radioéléments' produces 50% of the radioisotopes needed for approximately 6 million patients. Belgium stands as a global leader in the transport of short half-life materials, facilitating the transportation of approximately 35,000 units of medical radionuclides each year.

In its different renowned universities and associated healthcare centres, Belgium provides the full spectrum of education, training, (pre)clinical research activities as well as all the associated expertise in medical physics and nuclear chemistry, and diagnostic, therapeutic and imaging services. Complementary services like transport, nuclear safety, waste management or engineering link all these partners together, completing the Belgian RLT value chain. The Belgian value chain partners have created the Rad4Med.be network to gather knowledge and expertise, addressing and answering all requests on the use of radioactivity in healthcare in Belgium (see figure 4)[6]. This global approach in every stage makes Belgium very attractive as a global, valuable RLT partner.

Figure 4: The Rad4Med members illustrate the rich Belgian RLT landscape, covering the full value chain

1.2 European actions

RLT is a relatively new treatment approach. Its integration into clinical practice will thus require both national and international efforts. However, these efforts will be necessary to solve the most urgent challenges along the global, European and Belgian RLT value chain and strengthen it.

[5] https://www.nucleairforum.be/topics/belgische-actoren-de-nucleaire-geneeskunde
[6] Rad4Med.be - The Belgian expertise in nuclear science and technology applications for healthcare

In 2020, the European Journal of Nuclear Medicine and Molecular Imaging listed key barriers for RLT, such as:

- Low awareness and understanding on RLT within patient communities and decision-makers
- Limited healthcare professional (HCP) capacity, training and workforce planning
- Unclear models of care (care processes and patient pathways)
- Inadequate physical capacity (a.o., hospital rooms) and resourcing in hospitals
- Evolving legislation, regulation and policy (a.o., integration in national cancer plans, RLT product approval, funding and reimbursement procedures)
- Lack of (real-world) data (RWD) (on patient outcomes and cost-effectiveness) and research

There are many actions that can be taken to address these challenges and build RLT into cancer care plans and encourage its appropriate utilisation in practice. These will require concerted action by decision-makers, nuclear medicine specialists and the broader clinical cancer community, hospital managers, patient organisations, researchers, and companies.

Developing and expanding RLTs requires a coordinated global, European and national approach. European regulatory and policy-making bodies will play a pivotal role, with the European Commission as a leader in shaping the trajectory of RLTs across the continent. The European Commission needs to play a transformative role in advancing RLTs in the context of its mandate to promote scientific excellence, patient safety, and cross-border collaboration. Through the European Commission's Joint Research Center, a series of presentations and multi-stakeholder workshops were organised in 2023 aiming at translating radioisotope-based cancer research into clinical practice in Europe[7]. In these multi-stakeholder workshops, the most essential needs at European and national level were identified, such as:

- A continuous and resilient supply of radionuclides and addressing the criticality and fragility of the supply chain
- Adequately trained medical workforce
- Properly equipped hospitals
- Procedures to be reviewed by national healthcare systems to consider reimbursement eligibility for treatments
- Further research to better understand and predict the treatment outcome and benefits of an earlier treatment and to preclinically develop and test new potential radiopharmaceuticals

From the workshops and discussions, 7 recommendations were formulated:

- Encourage a coordinated approach between programs and initiatives (including Euratom, Horizon Europe, EU4Health and Europe's Beating Cancer plan among others), with solutions for research & development (R&D), preclinical research to scale up to market demand and clinical use
- Strive for EU autonomy for a continuous, stable and uninterrupted supply of medical radionuclides, considering an increasing demand and use of several radionuclides including alpha-emitters
- Harmonise the requirements for clinical trials with radiopharmaceuticals at EU Member States level, in order to enable multicentric European studies, and obtain agile timelines for approval
- Address regulatory issues concerning radiation protection, including harmonisation of guidelines for hospitalisation length after radiopharmaceutical routine treatments
- Join forces on education and training for radiopharmaceutical use to HCPs, radiation protection experts, regulators, decision makers, patients and respective care takers
- Encourage the integration of radionuclide technologies in multidisciplinary clinical boards, addressing also pooling of data for harmonisation of clinical practice
- Support health technology assessments (HTA) and cost-effectiveness analysis of radiopharmaceutical diagnosis and treatments in support of reimbursement decisions

A European strategy to improve access to RLTs in the context of Europe's Beating Cancer plan is needed and advocated by SPARC Europe. SPARC Europe is an independent multi-stakeholder

[7] Goulart De Medeiros M., Holzwarth U., Translating radiotheranostic cancer research into clinical practice in Europe, Publication Office of the European Union, Luxembourg, 2023, doi:10.2760/92392, JRC134480.

European policy initiative (consisting of experts in the field of oncology, internal medicine, nuclear medicine, RLT and patient advocacy), launched in October 2020 and aiming to build a comprehensive policy framework for RLT. The mission of the group is to provide expert knowledge and the necessary guidance for policymakers to support them in the creation of a clear pathway to institutionalise RLT and increase their accessibility for patients.

To realise the full potential of RLT, policy solutions for the barriers for implementation across Europe and a translation of those solutions at a Belgian level are required.

2. Belgian preparedness for RLT

2.1 The objective

Timely and equitable access for an increasing number of patients over the coming years in Belgium needs to be assured. Therefore, the system and the value chain need to be adapted and a future-proof RLT solution framework and action plan for Belgium should be developed. Such an action plan should confirm and further strengthen the Belgian position as the "radiopharmaceutical" valley, build a strong value chain to benefit patients and ensure healthcare system readiness. To reach these objectives and achieve the full potential of RLT for the Belgian cancer patients, the Belgian RLT action plan should present pragmatic solutions to the current challenges and barriers identified along the value chain.

The objective of this publication is to provide a comprehensive overview of the identified barriers and challenges, as well as potential solutions to the accessibility of RLTs in Belgium. These take into account the unique characteristics of RLTs as they require particular healthcare settings and expert coordination to be fully beneficial for Belgian patients. Furthermore, recommendations have been formulated to provide guidance and potential pathways of action for the national institutions, policy makers, clinicians, companies and other stakeholders, to address access barriers, prepare the Belgian healthcare system and value chain to tackle the challenges.

2.2 The approach

To develop an adequate RLT action plan for Belgium, an extensive literature study has been carried out and individual interviews with key stakeholders and multi-stakeholder dialogues were organised. Multi-stakeholder dialogues, involving all relevant stakeholders in decision-making on RLTs, are important to promote the development of balanced and broadly supported solutions. All stakeholders must be involved to improve the understanding and relations among them facilitating to move forward with implementation plans. Stakeholder dialogue generates a common vision, discourages blaming the past and creates a shared future. This project was conducted independently by Inovigate, during 2023.

In the first introductory multi-stakeholder debate, organised on May 22, 2023, the current challenges and barriers for the implementation of RLTs in Belgium were discussed.

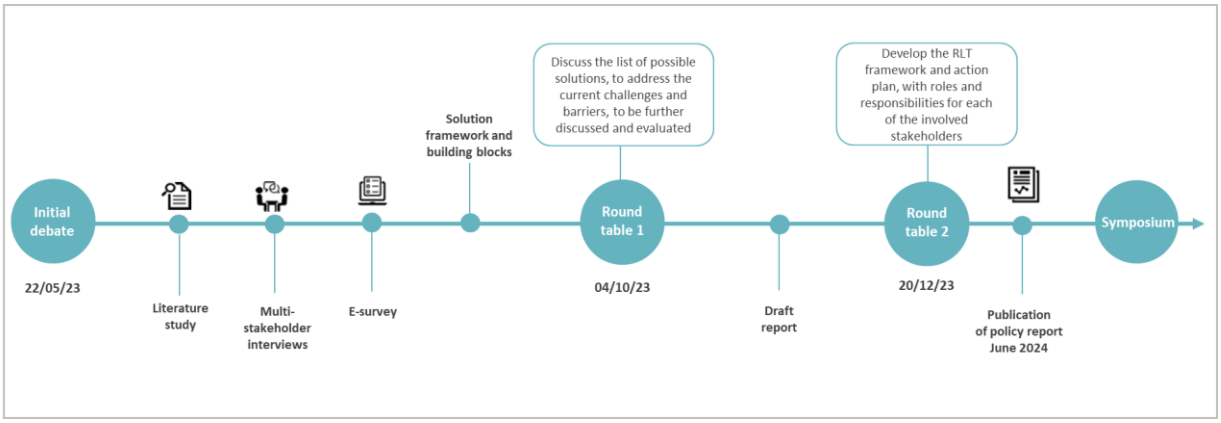


Figure 5: Approach to come to an RLT solution framework and action plan for Belgium

The outcome of this initial discussion has been complemented with an extensive literature study by the Inovigate team, including an analysis of the situation and potential solutions in other countries. Once all challenges and barriers were identified, possible solutions were listed.

This list of challenges, barriers, and potential solutions was further reviewed and discussed with various key stakeholders (patients, patients' organisations, clinicians, researchers, regulators, investors, policy makers, public opinion, …) during one-on-one interviews and in an e-survey, which was widely distributed amongst relevant stakeholders. The list of challenges and barriers and the potential solutions to address them has been prioritised by the stakeholders.

The outcome of the initial debate, the research, the one-on-one interviews and the e-survey was presented in a first multi-stakeholder round table that took place on October 4, 2023, at RIZIV-INAMI (see Figure 6). The round table was chaired by Jo de Cock (former Administrator General of NIHDI and currently chairman of the National Commission of Physicians and insurers and the National Joint Commission of Physicians and Hospitals) with representations of each stakeholder group.

This first round table had two main objectives:

- Confirm the need for an RLT action plan for Belgium by addressing the current challenges and barriers
- Organise a multi-stakeholder discussion on the presented solutions to address those challenges and barriers, as input for the RLT action plan for Belgium

Figure 6: Photo of the first round table at RIZIV

The dialogue aimed at a first evaluation of the proposed solution elements based on multi-stakeholder acceptability and feasibility within the Belgian context, based on two guiding principles:

- Implementability in Belgium
- Practical and short-term implementation focus (the low hanging fruit)

On December 20th, 2023, the second multi-stakeholder round table was organised to finalise the RLT solution framework and action plan for Belgium with a list of recommendations for policy and all other stakeholders. The outcome of the round tables with the RLT solution framework and action plan for Belgium, together with the policy recommendations and actions for all stakeholders, are outlined in this policy report to be shared with the broad stakeholder community.

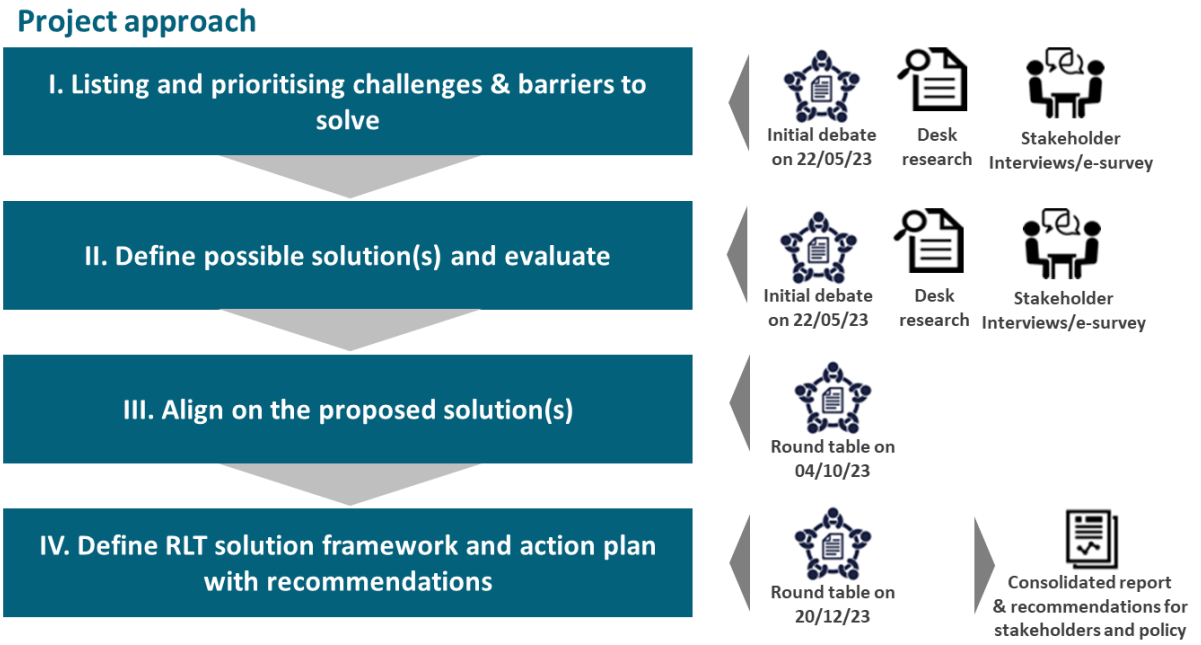


Figure 7: Project steps that have been followed to come to the recommendations for preparing Belgium for RLTs

3. RLT challenges and proposed solutions

The RLT action plan for Belgium will have to respond to the current challenges and barriers. For each of the challenges and barriers, prioritised by the stakeholders in interviews and the e-survey, solutions were formulated. To structure the RLT solution framework and action plan, solutions were grouped in 6 different domains. Together, these 6 domains will form the dimensions of an integrated RLT solution framework and action plan for Belgium.

Domains:	Description:
Governance	Governance refers to a **range of steering and rule-making functions carried out by decision-makers** that directly impact the availability, accessibility and standards of delivery of RLT. Governance comes from health decision-makers in the form of **policy and plans, including guidelines and best practices from the clinical community**
Regulation and reimbursement	Regulation and reimbursement define why, **when and how radioligand therapy should be provided and paid** for. This essential component of the health system is led by various national, and sometimes international organisations and ensures that medicines are delivered safely, effectively and sustainably
Identified needs	Identified need is the potential **need or demand for RLT** among cancer patients. There are many components required to fully understand a need for an intervention, including **epidemiological data, levels of patient and healthcare professional awareness, and referral patterns. Such information is essential in planning services**
Service provision	Service provision encompasses the **inputs and outputs required for the provision of RLT**. This includes the healthcare **workforce and infrastructure** required to ensure RLT services are delivered effectively and efficiently to the people needing them
Health information	Health information refers to **data** that are collected, analysed and synthesised **to support decision-making** around RLT. Comprehensive data collection efforts spanning **clinical, patient, real-world and economic data** points are essential to understand how RLT is used and how services can be improved
R&D and innovation	Research and development, and innovation refer to **academic and industrial research, preclinical research as well as clinical trials and development of innovations in RLT**. It also includes the **public and private funding instruments for research, collaborative R&D**, development of value chains and ecosystems, starting from research and includes valorisation

Figure 8: The 6 domains to be integrated in the Belgian RLT action plan

To integrate RLT in cancer care, there are many challenges that need to be addressed. The next sections outline some of these challenges and the potential solutions to address them per domain.

3.1 Governance

Governance refers to a range of steering and rule-making functions carried out by decision-makers that directly impact the availability, accessibility, and delivery standards of RLT. Governance comes from health decision-makers in the form of policy and plans, including guidelines and best practices from the clinical community.

In the governance domain, three main challenges and barriers were prioritised, based on the initial debate, the e-survey and the stakeholder interviews. Four solution building blocks to solve these challenges and barriers were listed and further detailed, based initially on literature research and further complemented with input from interviews. These solutions were discussed and evaluated during the two multi-stakeholder round tables.

Proposed solutions:

If Belgium wants to stay at the forefront in the RLT field, preserving and even further reinforcing its strong legacy, an ambitious Belgian RLT leadership vision and plan is required. This plan should strengthen the Belgian RLT value chain, supporting RLT across all actors, increasing impact and reinforcing the position of Belgium as an RLT hotspot. The current RLT ecosystem reveals many complexities on multiple dimensions (resources, regulations, supply aspects, …), involving many stakeholders. In today's system, harmonisation and alignment are missing as there are no objectives set and goals formulated. This fragmentation can be solved by an integrated, multi-stakeholder supported RLT vision, strategy and plan for Belgium with clear objectives and evaluation metrics.

RLTs are poorly integrated into the national cancer plan and suffer from limited political recognition and leadership in Belgium. These latter challenges and barriers can be solved by aligning and integrating the Belgian RLT action plan with the national cancer plan and including RLT in European

cancer treatment clinical guidelines (which is already the case). Developing this integrated national plan with all its priorities and decision making, should involve all stakeholders (incl. policy makers, patient representatives and patient organisations). Fast approval or modifications of the plan should be possible based on flexible legislation and regulations. A learn-and-adapt principle should be the basis for this.

Finally, it is proposed to establish an RLT task force with the primary goal of ensuring sustained and equitable patient access. This task force would be responsible for RLT horizon scanning, identifying innovations and facilitating their timely implementation. A comprehensive long-term investment plan spanning the entire supply chain should be devised and implemented, anticipating future RLT growth and demand, to make sure the healthcare system keeps pace with RLT innovations and providing patients timely access to these RLTs. Decision on priorities at Belgian or European level, in hospital infrastructure incl. waste (patient and production) management and in alternative isotopes or production methods to reduce dependency (risk mitigation), are necessary to ensure a future proof RLT supply. Furthermore, the task force is expected to coordinate the efficient utilisation of existing infrastructure by aligning supply with demand.

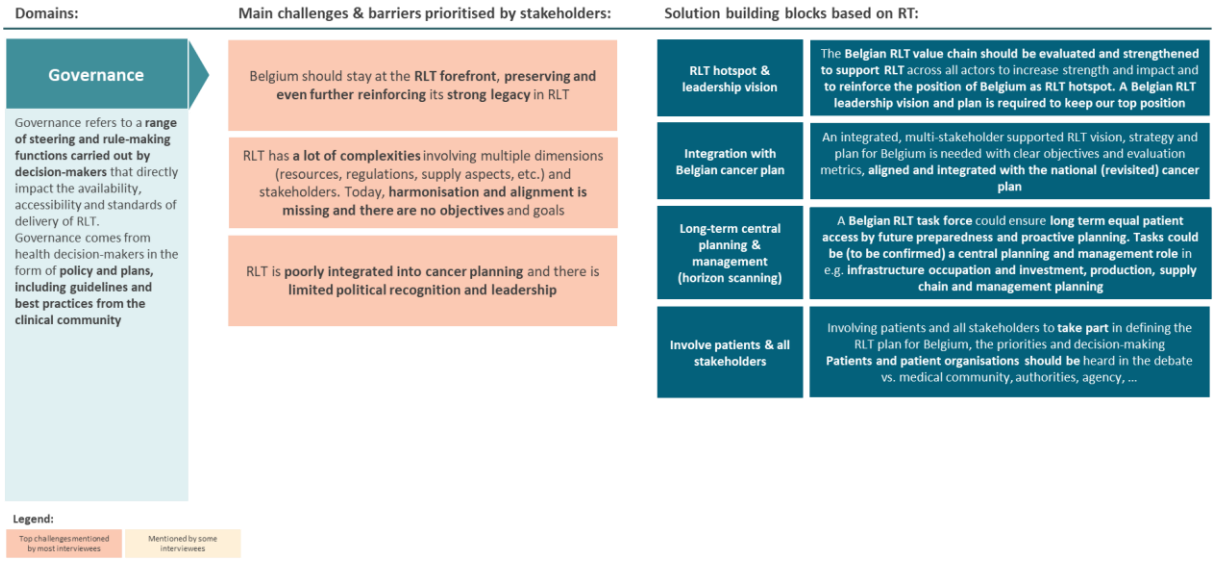


Figure 9: Prioritised challenges and proposed solutions for the governance domain

3.2 Regulation and reimbursement

Regulation and reimbursement define why, when and how RLT should be provided and paid for. This essential component of the health system is led by various national, and sometimes international organisations and ensures that medicines are delivered safely, effectively and sustainably.

In this regulation and reimbursement domain, four challenges and barriers were prioritised based on the initial debate, literature research, the e-survey and stakeholder interviews. Four solution building blocks to solve these challenges and barriers were discussed and evaluated during the multi-stakeholder dialogues.

Proposed solutions:

A first major challenge is the difference in the amount that is reimbursed between hospital and industrially produced RLTs. For both products, the current reimbursement does not adequately cover the cost of all steps in the RLT patient pathway, including the personalised diagnostic approach (theranostic). A revision of the reimbursement procedure should consider the real cost of each step of the RLT patient pathway. This revision should not necessarily impact the total oncology budget. The budget could be transferred from other cancer therapies, as those would be replaced by RLTs. In Belgium the 'Technische Raad voor Radio-Isotopen – Conseil Technique des Radio-Isotopes' (TRRI-

CTRI) is responsible for the reimbursement of radiopharmaceuticals. An objective decision on the reimbursement process is key. On an international level, Belgium plays an important role in the production of isotopes, supplying many countries with radio-isotopes for medical use. However, the invoicing of this supply does not cover the actual production cost. This should be re-negotiated by authorities to justify investments in new production units.

Second, diagnostic and therapeutic reimbursement decisions should be based on clinical value criteria only. Clinical value is determined based on data available via clinical trials and also via real-world data (RWD) registration (if available). This RWD will support HTAs and cost-effectiveness analyses of both radiopharmaceutical diagnosis and treatment, supporting clinical value quantification and reimbursement decisions. RWD registration should be promoted and even be made mandatory by making treatment reimbursement approval dependent on patient RWD registration. RWD registration will facilitate outcome-based reimbursement. This reimbursement can even be slightly higher to compensate for registration of high-quality and structured RWD by hospital HCPs. Automated data registration could remove an important administrative burden associated to data registration and could avoid data errors.

Third, the RLT regulatory framework e.g. on quality, should be clarified between hospitals and industry to create an equal level playing field with a role and opportunities for both producing parties. All round table participants agreed that all RLTs, both for clinical studies or for production under marketing authorisation, should be produced according to GMP standards, with pharmaceutical inspection co-operation scheme (PIC/S) as a solution for hospital magistral preparations (Royal Decree of 30 September 2020, Art. 21. paragraph 2). All stakeholders reached a consensus that early access is essential for patients. This can be either through access to an industrial product under the early access procedure or as magistral preparation by the hospital pharmacy for new RLT products or RLT products without marketing authorisation. All stakeholders expect that future commercial products will be mainly produced by industrial players to warrant global and equal access to patients. RLT reimbursement should be optimised to warrant a high quality supply chain from production over logistics and infrastructure to clinical practice. This optimisation will continue to strengthen the position of Belgium as 'radiopharmaceutical' valley, both in R&D, clinical trial and commercial activities.

Fourth, the current safety regulations, which determine the duration of patient hospital stays after RLT treatment, should be reconsidered and adapted. Whenever possible, the hospital stays should be shortened in order to increase available suitable room capacity. This re-evaluation should be based on a critical evaluation of RWD and latest safety and scientific insights, in line with Directive 2013/59/Euratom and also considering its interpretation in other European member states. The measured dose rate after administration of therapeutic isotopes 177Lu-PSMA; 177Lu-DOTATATE, 166Ho-Spheres shows that the caution period (in accordance with the yet-to-be-published Royal Decree: period taking into account radioactive product, actually administered activity, effective half-life and excretion rate)[8] is in the order of hours, which could perfectly justify treatment via day hospitalisation. Day hospitalisation, given the limited number of suitable rooms available for radionuclide therapy, is essential given the growing number of patients in the near future. This does not alter the fact that patients should always be strictly monitored immediately after administration of radionuclide therapy and that in case of medical necessity and/or in case of excessive dose rate (> 20 mSv/h at 1m distance), overnight hospitalisation in a suitable room is still required. The provision as foreseen in Art 2, paragraph 29 of the yet-to-be-published Royal Decree[6] states that the Federal Agency for Nuclear Control (FANC) can set the parameters determining the caution period. It is expected that FANC will evaluate and publish clear, measurable and scientifically based guidelines to determine the caution period for each radionuclide therapy.

A correct interpretation and implementation of the European Directive and Royal Decree will, while still guaranteeing patient, HCP and population safety:

[8] Federaal Agentschap voor Nucleaire Controle. (2023). Koninklijk besluit tot wijziging van het koninklijk besluit van 13 februari 2020 betreffende de medische blootstellingen en blootstellingen bij niet-medische beeldvorming met medisch-radiologische uitrustingen.

- Avoid hospitals to make substantial but unnecessary investments in overnight hospitalisation rooms, incl. waste management infrastructure, …;
- Provide access to RLTs to a higher number of patients;
- Avoid any potential negative impact on public health.

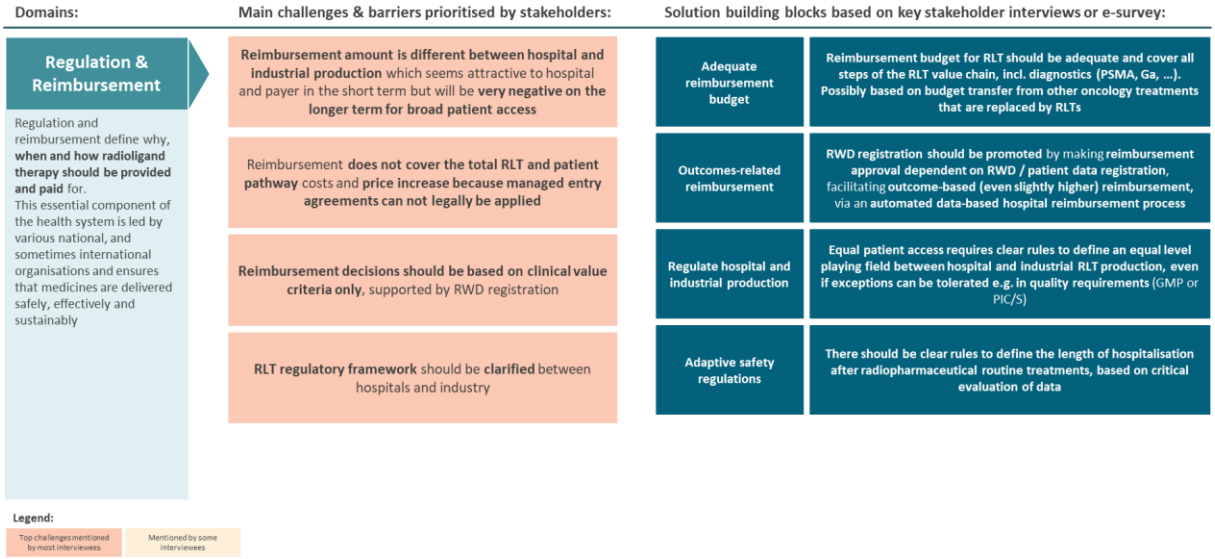


Figure 10: Prioritised challenges and proposed solutions for the regulation & reimbursement domain

3.3 Identified needs

Identified needs are the potential need or demand for RLT among cancer patients. There are many components required to fully understand a need for an intervention, including epidemiological data, levels of patient and HCP awareness, and referral patterns. Such information is essential in planning services.

In the identified needs domain, two challenges and barriers were prioritised based on the initial debate, literature research, the e-survey and stakeholder interviews. Four solution building blocks to solve these challenges and barriers were discussed and evaluated during the multi-stakeholder dialogues.

Proposed solutions:

All RLT stakeholders are confronted with a lack of public understanding and awareness on RLTs. The potential benefits of RLTs are mostly unknown to the general public, hindering their broader acceptance and utilisation. Therefore, initiatives to increase public awareness should be initiated and supported by the entire RLT community, involving all stakeholders and speaking with one voice. BELNUC[9] could take such a coordinating role in this initiative. It could disseminate general information and organise focused and adapted communication to all relevant stakeholders on RLT as a valuable cancer treatment option, preclinical R&D and clinical trials.

This lack of awareness is not limited to the general public. The role of nuclear medicine in cancer treatment is not always very well known in the medical community either, with exception of specialised centres implementing RLT in cancer treatment. However, it is recommended that RLT treatment is administered in a select number of adequately equipped and organised centres of excellence. The organisation of RLT in a limited number of specialised, well equipped, and organised cancer treatment centres guarantees future proof personalised RLT administration related to the best patient outcome. Patients in need of RLT treatment should be referred to these specialised centres for optimal care. An

[9] BELNUC: The Belgian Society of Nuclear Medicine (BSNM, nowadays called 'BELNUC')

additional advantage is that knowledge and experience with RLTs can be better pooled and faster translated in routine medical practice.

Improved awareness in the medical community starts with the oncology HCP's community (medical, radiation and surgical communities), also including nuclear specialists in a multidisciplinary cancer treatment approach. They should all recognise and apply RLT as a full anti-cancer treatment option. This is already the case in many hospitals, but to organise referrals in the most optimal way for the benefit of the patient, the RLT multidisciplinary approach, treatment options and patient inclusion criteria should be clearly communicated to all referring centres by the specialised treatment centres.

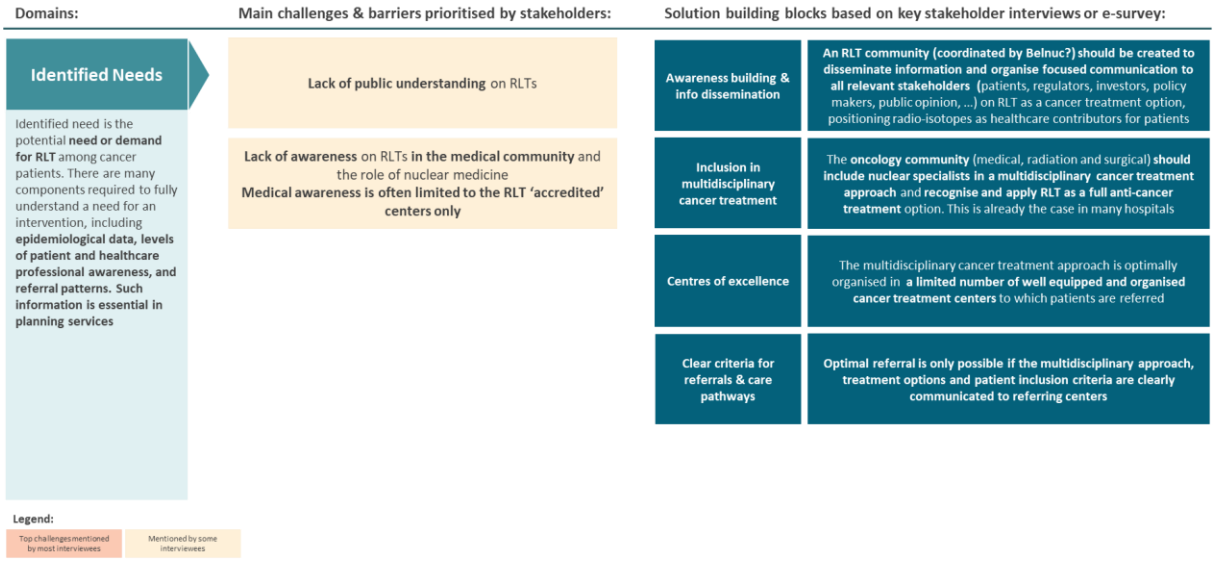


Figure 11: Prioritised challenges and proposed solutions for the identified needs domain

3.4 Service provision

Service provision encompasses the inputs and outputs required for the provision of RLT. This includes the healthcare workforce and infrastructure required to ensure RLT services are delivered effectively and efficiently to the people needing them.

In the service provision domain, two challenges and barriers were prioritised based on the initial debate, literature research, the e-survey and stakeholder interviews. Five solution building blocks to solve these challenges and barriers were discussed and evaluated during multi-stakeholder dialogues.

Proposed solutions:

The forecasted growth of RLT cancer treatments will lead to bottlenecks in each step of the value chain and in the availability of HCPs delivering the RLTs. Therefore, recognising the fragility and criticality of the supply chain is important and adequate solutions are highly needed.

Solutions that were proposed are to optimise the use of available resources based on one-day hospitalisations when possible, a more centralised management of available hospital capacity taking into account patient treatment needs, a centralised management of diagnostic and therapeutic product supply (production and transport) (in close collaboration with European and worldwide coordination and management) and the inclusion of a future product availability criterion in clinical trial designs.

Infrastructural bottlenecks could be solved by infrastructure investments considering expected RLT technology evolutions such as the increased use of alpha-emitters, new isotopes and production technologies… and the specific requirements they impose. Additional investments in reactors,

cyclotrons, accelerators, generators… to ensure projected growth in production capacity will be needed.

Finally, industrial RLT players should, when introducing a new RLT, interact with all stakeholders to provide, in close collaboration and each taking their responsibility, a total RLT solution, pro-actively identifying and/or solving potential issues in the RLT supply chain. An uninterrupted supply of RLTs for authorised and reimbursed products should be ensured for all patients at any time.

Even if the value chain can be organised to be future proof, the lack of trained/certified personnel (medical and other) to meet current and future demand, remains a major threat for the implementation of RLTs in cancer treatment. To solve this issue in the mid-term, RLT education should be organised and promoted, harmonised across Europe for all HCP functions (specialists, nurses, pharmacists, cleaning personnel, …). It should integrate both technical and oncology therapy as well as patient treatment skills. This should increase the inflow of new RLT trained HCPs responding to the growing RLT needs.

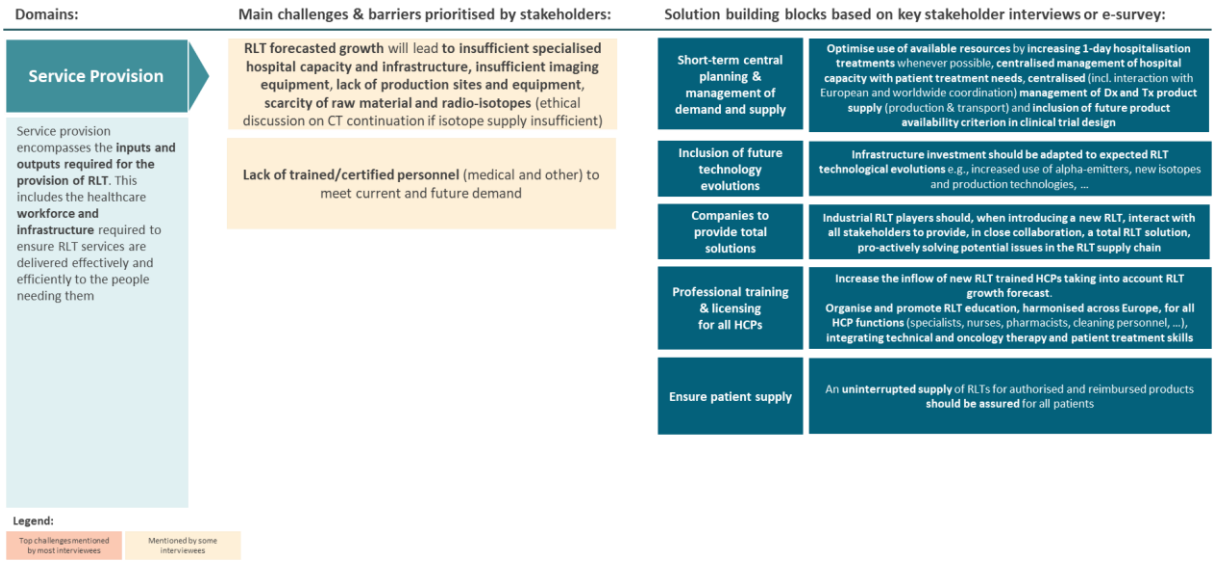


Figure 12: Prioritised challenges and proposed solutions for the service provision domain

3.5 Health information

Health information refers to data that are collected, analysed and synthesised to support decision-making around RLT. Comprehensive data collection efforts spanning clinical, patient, real-world and economic data sets are essential to understand how RLT are used, what clinical results are obtained and what value is created, and how services can be improved.

In the health information domain, two challenges and barriers were prioritised based on the initial debate, literature research, the e-survey and stakeholder interviews. Two solution building blocks to solve these challenges and barriers were discussed and evaluated during multi-stakeholder dialogues.

Proposed solutions:

A first major problem is the lack of sufficient available health data and information to support decision-making. This is reflected in randomised clinical trials (RCTs) that are based on a small number of patients and the limited availability of RWD and central registries to support research and the development of insights to advance the clinical practice and quality of care. As long as this gap subsists, the gap between academic research and clinical practice remains, and the transition from academy to clinic remains difficult.

The implementation of (multi-centric and international) RCTs, both academic and industrial, with an important number of patients will generate robust and convincing clinical evidence needed to approve RLTs. The development of evidence should be based on structured and standardised data and result in the implementation of internationally harmonised RWD and registries. This will support and accelerate the inclusion of RLTs in clinical guidelines and the prescription of RLT products by demonstrating clinical superiority, therapy value and ultimately cost-effectiveness.

A second barrier is that the current data collection systems do not collect adequate data to support evidence-based decision-making. RLT outcomes prediction and personalisation including dosimetry if clinically validated, based on collected patient data, should be improved and financially facilitated in order to better understand and predict patient outcomes. Improved treatment success rates will not only benefit patients but also reduce isotope waste, and will optimise resources accordingly.

RLT clinical trials and RWD registries should become an extension of the current Belgian cancer registry.

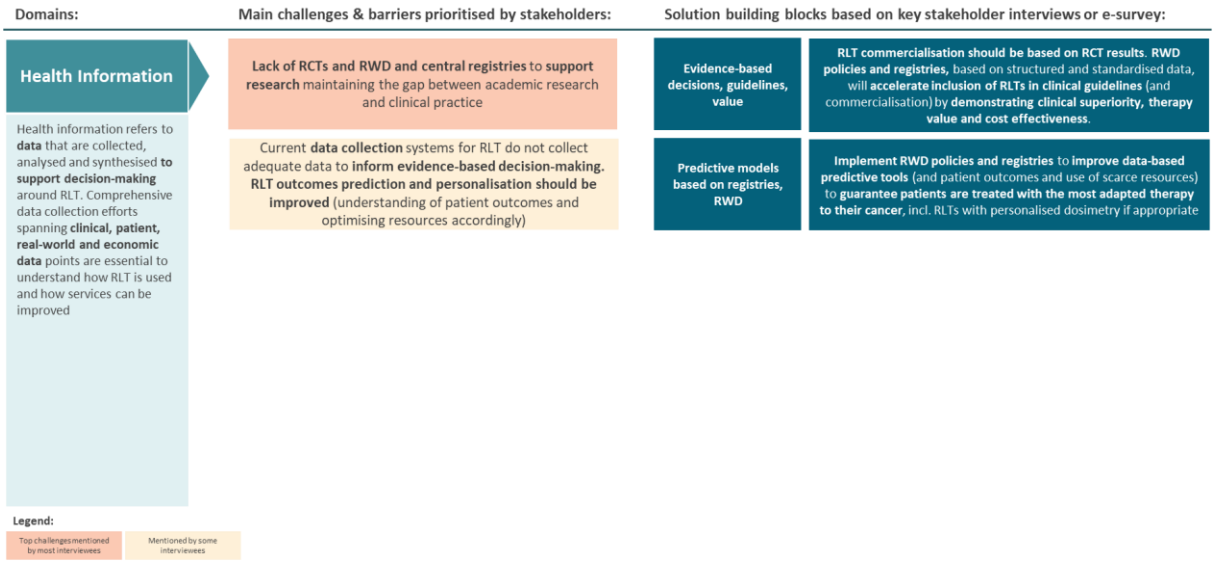


Figure 13: Prioritised challenges and proposed solutions for the health information domain

3.6 R&D and innovation

R&D, and innovation refers to academic and industrial research, clinical trials and development of innovations in RLT. It also includes the public and private funding instruments for research, collaborative R&D, development of value chains and ecosystems starting from research and including valorisation.

In the R&D and innovation domain, three challenges and barriers were prioritised based on the initial debate, literature research, the e-survey and stakeholder interviews. Five solution building blocks to solve these challenges and barriers were discussed and evaluated during the multi-stakeholder dialogues.

Proposed solutions:

Belgium currently is, but should also manage to stay, at the RLT R&D forefront. Preserving and even further reinforcing Belgium's strong legacy in RLT preclinical research, clinical trials and innovation is crucial to benefit our economy and patient care. To reach this objective, the Belgian RLT R&D and innovation ecosystem, including GMP production capacity, should be strengthened to support future RLT R&D, innovation and clinical and commercial development in Belgium.

Despite clinical trials are currently being conducted in Belgium, they are generally too small to result in statistically relevant insights that can be used in clinical practice. All RLT stakeholders should stimulate the conduct of important RLT clinical trials, involving a high number of patients, recruited across hospitals (multi-centric and even international). To increase strength and impact and to reinforce the position of Belgium as European and global RLT clinical trial hotspot, stimulation measures and incentives should be put in place. This could be done based on adapted public and private financing instruments, to support RLT R&D and innovation leadership.

The lack of harmonised high quality, structured RWD and data-based insights complicates the unravelling of the RLT mode of action and the prediction of outcomes. The collection of structured, high quality clinical trial and RWD, and the pooling of knowledge and insights to support research and to accelerate transfer to medical practice and guidelines, are key to identify RLTs mode of action and to predict outcomes. In this process, patient consent to re-use routine care data for research should not be a problem as patient organisations broadly support data registration and (re)use for research purposes.

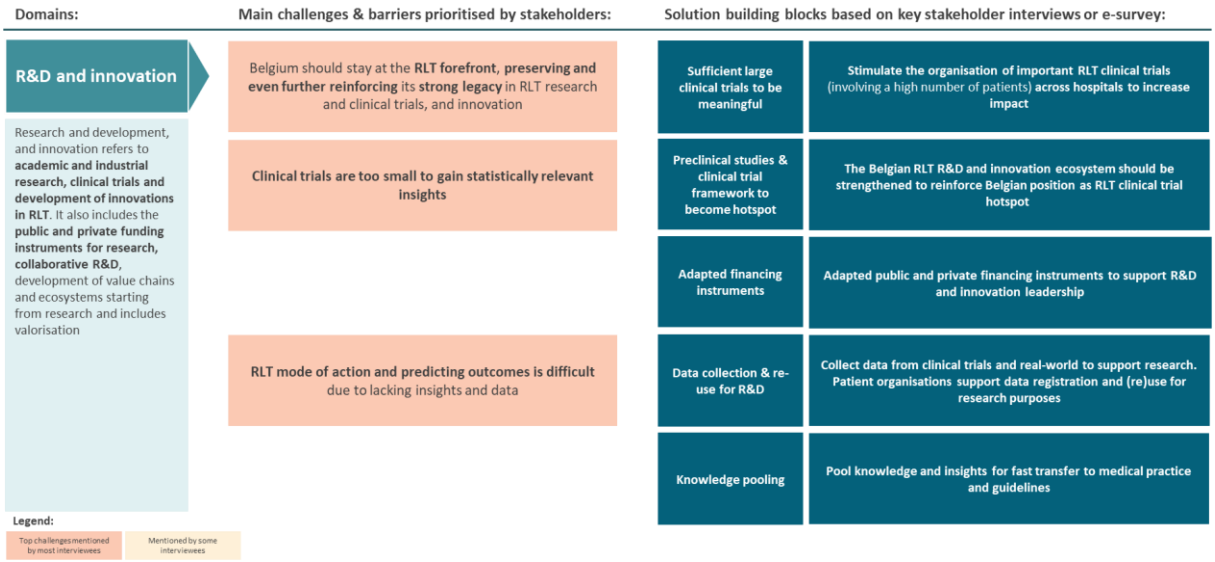


Figure 14: Prioritised challenges and proposed solutions for the R&D and innovation domain

4. RLT solution framework and action plan for Belgium

4.1 The RLT solution framework for Belgium

After the two round tables, consensus was reached on all proposed solutions in the six domains of the Belgian RLT action plan. These solutions are the building blocks for a future proof Belgian RLT action plan, which should be flexible and also dynamically adapted to the emerging developments in the future.

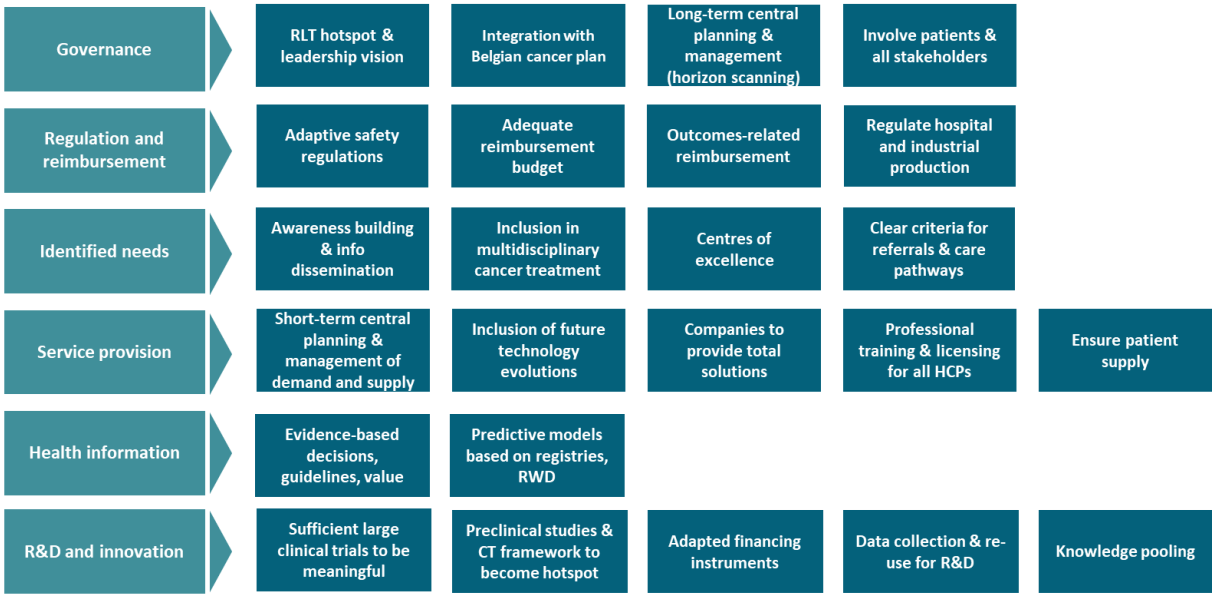


Figure 15: The Belgian RLT solution framework with the proposed solutions in the 6 domains

4.2 Integration of the Belgian RLT solution framework into the cancer plan

The current Belgian cancer plan has been developed in 2008 and is structured around three key pillars: (1) prevention and detection, (2) care, treatment and patient support, and (3) research, innovative technology and evaluation.

All RLT stakeholders agreed on the need to integrate the Belgian RLT solution framework, developed above, as a separate 'chapter' in the Belgian cancer plan, being the ideal opportunity to update the cancer plan. As a start, the proposed RLT solutions in the 6 domains have been mapped against the three key pillars of the Belgian cancer plan (see figure 16).

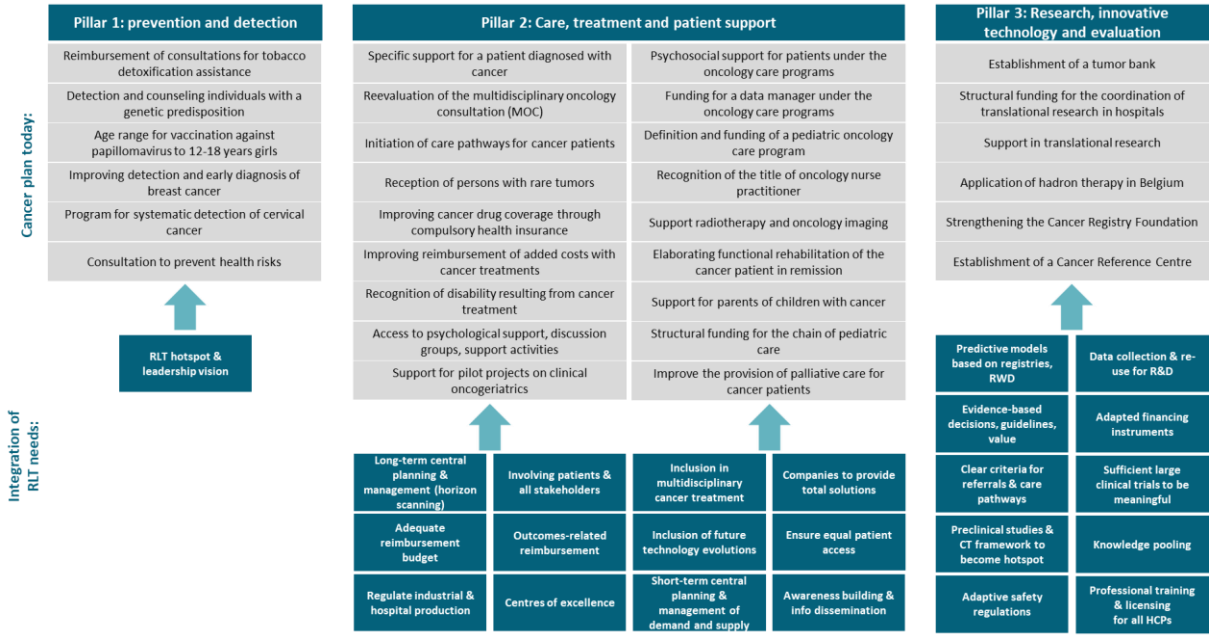


Figure 16: Integration of RLT in the Belgian cancer plan

5. Implementation of the RLT solution framework and action plan

To implement the RLT solution framework for Belgium, roles, responsibilities and concrete actions for implementation have to be assigned to the three involved major stakeholder groups that have to take action, such as:

- The government and the authorities
- HCPs, hospitals and research organisations
- Industrial players/companies

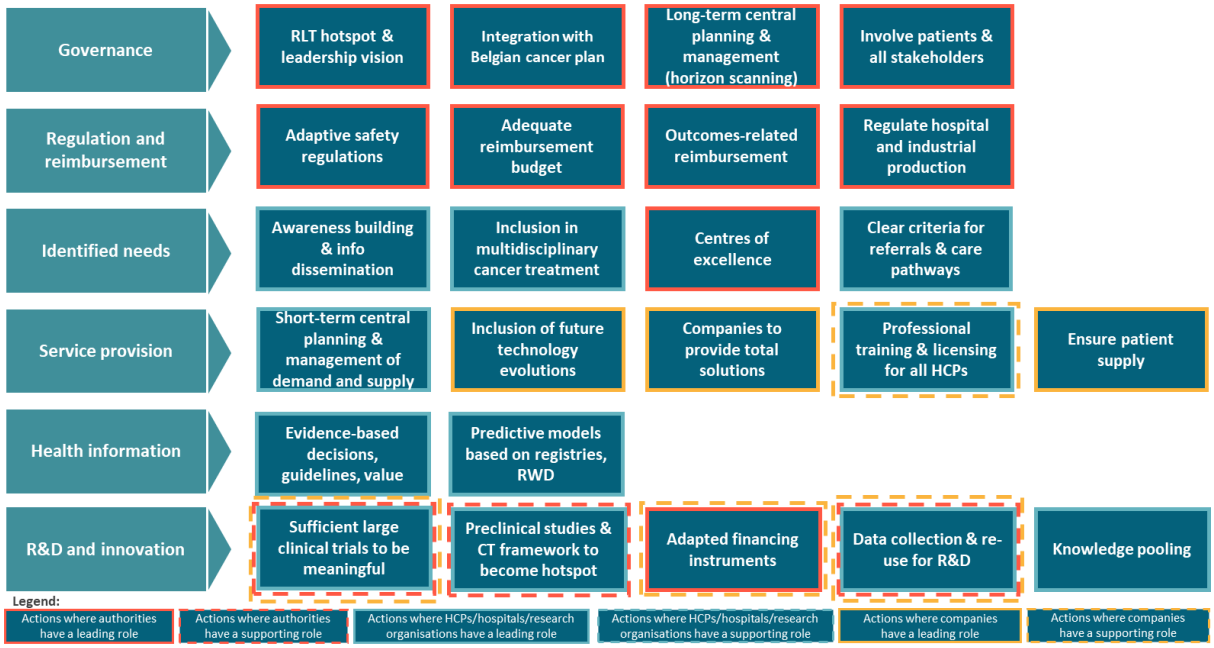


Figure 17: The Belgian RLT solution framework with the proposed solutions in the 6 domains assigned to the responsible stakeholder groups

Per stakeholder group, the proposed solutions have been listed for which the assigned stakeholder must take action or take the initiative to implement the solutions.

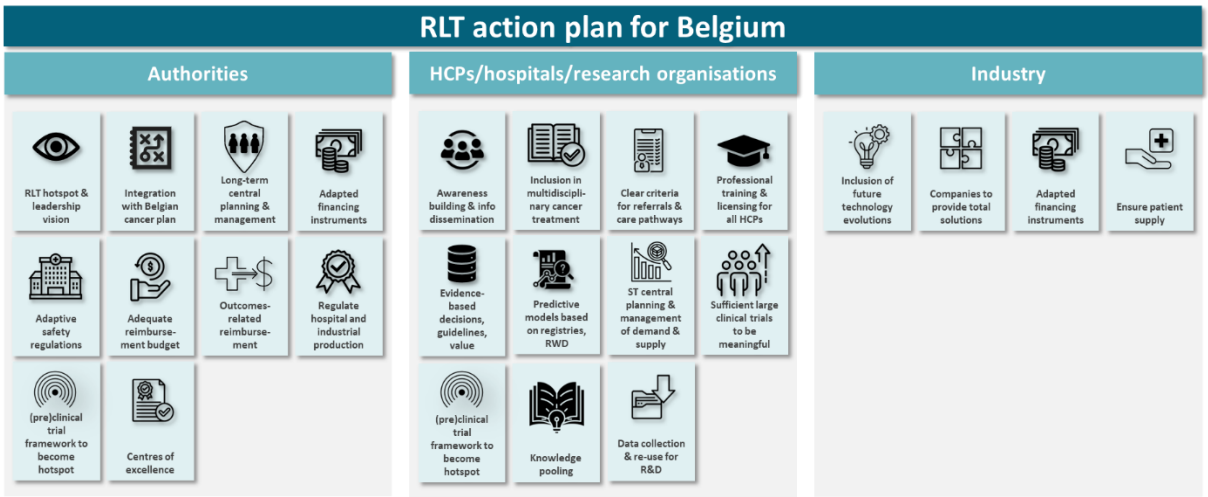


Figure 18: Overview with the list of solutions assigned to the key stakeholders that have to take action or take the initiative to implement the solution

5.1 Solution implementation responsibilities for the authorities

Authorities are responsible for the establishment of clear guidelines and the development of a comprehensive Belgian RLT leadership vision, enhancing the strength and impact of Belgium as a prominent RLT hub. This requires an integrated vision, strategy and plan to harmonise and align on the Belgian RLT objectives and goals. Collaborative discussion based on multi-stakeholder engagement are the basis to build such a plan. The establishment of an RLT task force is recommended to proactively anticipate and plan for RLT growth, with a primary focus on optimising patient access.

The current RLT reimbursement budget inadequately covers all steps of the RLT treatment value chain, necessitating adjustments on both national (TRRI-CTRI responsibility) and international level (cost recovery for radioisotope production). A potential solution involves reallocating funds from other oncology treatments that could be replaced by RLTs (if proven to be superior). To enhance accountability, reimbursement should be linked to clinical outcomes through the establishment of an outcome-based reimbursement pathway based on RWD. All stakeholders agreed that RWD registration for outcome-based reimbursement is feasible, if funding is provided for collecting harmonised, high quality, structured data acquisition and registration.

The Belgian RLT position will be reinforced by combining industrial GMP production for clinical studies or for production under marketing authorisation and PIC/S production for hospitals (by January 2026, based on Royal Decree of 30 September 2020). This combination will warrant global and equal access to patients for all RLT products. Treatment outcomes will be optimised (prediction, treatment results follow-up, …) by organising RLT treatment in well-equipped and recognised centres of excellence (the RLT reference centres). The occupation rate of these centres' infrastructure can be optimised by reducing the duration of hospital stays after RLT treatment, in accordance with FANC and supported by data. Maintaining and developing R&D in these centres to continue to fuel innovation should be facilitated by combining public and private financing, as well as by strengthening the Belgian RLT position as a clinical trial hotspot.

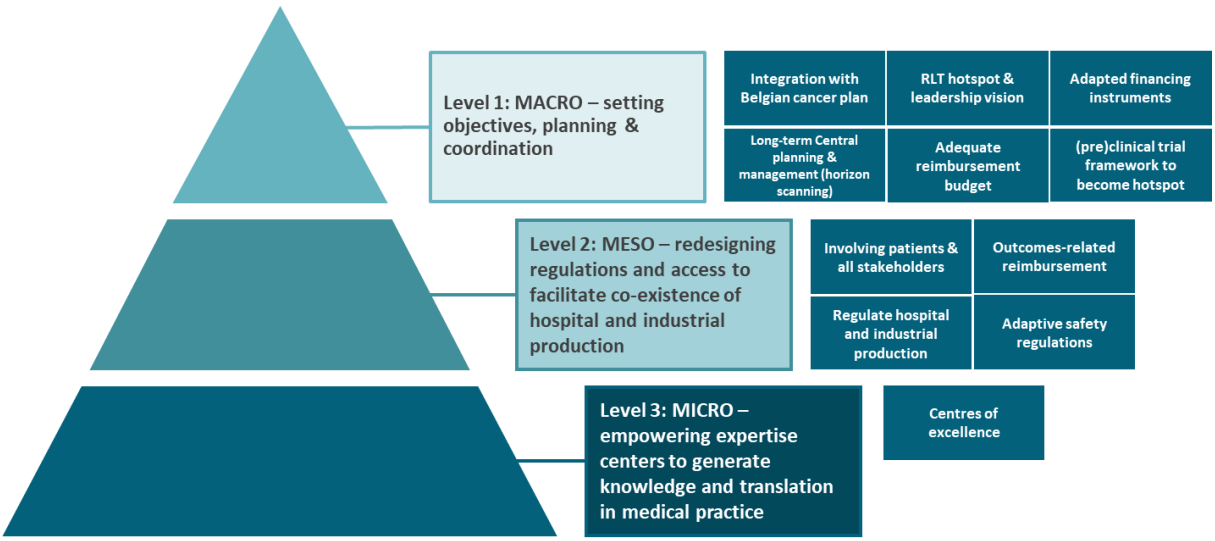


Figure 19: The proposed actions for authorities support macro, meso and micro level RLT preparedness

5.2 Solution implementation responsibilities for HCPs, hospitals and research organisations

The creation of an influential RLT community is essential for increasing public (education of general public and patients) and medical (development of medical practice and guidelines) RLT awareness. Important, (inter)national clinical trials (academic or in collaboration with industrial partners) should be organised. The goal would be to integrate and move up RLT in cancer treatment guidelines and

as a full-fledged cancer treatment, including dose optimisation and personalisation whenever feasible, to increase outcomes.

To cope with forecasted RLT growth, nuclear specialists should be included into multidisciplinary cancer treatment teams, clear criteria for referral centres should be established and harmonised education and training of RLT professionals should be organised at Belgian and European level.

Finally, predictive models have to be developed, to support treatment personalisation and improve patient outcomes. Additionally, further research is required, based on harmonised and structured RWD from clinical trials and medical practice to demonstrate clinical value and cost-effectiveness of RLTs.

5.3 Solution implementation responsibilities for companies

Industrial stakeholders should share their pipeline and technological innovations and developments with the RLT stakeholder community to optimise investment forecast focusing on the co-development of total RLT solutions, rather than pushing stand-alone diagnostic or therapeutic solutions. Based on this long-term view, the appropriate measures and investments could be taken in a timely manner to be ready for the adoption of these new RLTs in routine medical practice. Companies should also ensure individual patient supply for their commercial products.

RLT stakeholders should collaborate to co-finance preclinical R&D, discovery of novel targets, creation of a unified clinical trial registration network facilitating trial design and execution, and collection of harmonised and structured clinical and medical data to support research and innovation.

Moreover, industry can support the other RLT stakeholders in creating awareness, organising trainings for RLT professionals and knowledge dissemination.

6. Next steps

The RLT solution framework and action plan, developed above, are now ready for implementation. Actions to implement the solutions have been assigned to the corresponding stakeholder groups. The current momentum should be seized to realise the implementation in a multi-stakeholder approach, involving physicians and hospitals, research organisations, health policymakers, payers, regulatory and government bodies. That way, the RLT potential for cancer treatment can be fully exploited and can be prepared in time to benefit cancer patients in Belgium.

Table of figures

Figure 1: The Belgian RLT solution framework with the proposed solutions in the 6 domains assigned to the responsible stakeholder groups 6
Figure 2: Overview with the list of solutions assigned to the key stakeholders that have to take action or take the initiative to implement the solution 7
Figure 3: RLTs landscape 8
Figure 4: The Rad4Med members illustrate the rich Belgian RLT landscape, covering the full value chain 9
Figure 5: Approach to come to an RLT solution framework and action plan for Belgium 13
Figure 6: Photo of the first round table at RIZIV 13
Figure 7: Project steps that have been followed to come to the recommendations for preparing Belgium for RLTs 14
Figure 8: The 6 domains to be integrated in the Belgian RLT action plan 15
Figure 9: Prioritised challenges and proposed solutions for the governance domain 16
Figure 10: Prioritised challenges and proposed solutions for the regulation & reimbursement domain 18
Figure 11: Prioritised challenges and proposed solutions for the identified needs domain 19
Figure 12: Prioritised challenges and proposed solutions for the service provision domain 20
Figure 13: Prioritised challenges and proposed solutions for the health information domain 21
Figure 14: Prioritised challenges and proposed solutions for the R&D and innovation domain 22
Figure 15: The Belgian RLT solution framework with the proposed solutions in the 6 domains 23
Figure 16: Integration of RLT in the Belgian cancer plan 24
Figure 17: The Belgian RLT solution framework with the proposed solutions in the 6 domains assigned to the responsible stakeholder groups 25
Figure 18: Overview with the list of solutions assigned to the key stakeholders that have to take action or take the initiative to implement the solution 25
Figure 19: The proposed actions for authorities support macro, meso and micro level RLT preparedness 26

List of abbreviations

Abbreviation	Definition
FANC	Federal agency of nuclear control (Federaal agentschap voor nucleaire controle/Agence Fédérale de contrôle nucléaire)
HCP	Healthcare professional
HTA	Health technology assessment
PIC/S	Pharmaceutical Inspection Co-operation Scheme
R&D	Research & development
RCT	Randomised controlled trial
RLT	Radioligand therapy
RWD	Real-world data
TRRI-CTRI	Technical council on radioisotopes (Technische raad voor radio-isotopen/Conseil technique des radio-isotopes)

Supporting literature

(LinkedIn), r. A. (n.d.). *Radiotherapeutics landscape.*

B. Erlandsson, S. M. (1977, August 25). *Medically used radionuclides in sewage sludge*. Retrieved from Springer Link: https://link.springer.com/article/10.1007/BF00280706

C. Merkel, C. H. (2020). *Realising the potential of radioligand therapy: policy solutions for the barriers to implementation across Europe.*

CANSA. (2017). *Report on the Importance.*

Efpia. (2023). *Joint Position Paper on the Hospital Exemption Scheme for ATMPs*. Retrieved from https://www.efpia.eu/news-events/the-efpia-view/efpia-news/joint-position-paper-on-the-hospital-exemption-scheme-for-atmps/

Euorpean Commission . (2021). *Study on sustainable and resilient supply of medical radioisotopes in the EU.*

Euratom Supply Agency. (n.d.). *Supply of medical radioisotopes*. Retrieved from https://euratom-supply.ec.europa.eu/activities/supply-medical-radioisotopes_en

EuropaBio. (2020). *EU ATMP Hospital Exemption, position paper.*

European Nuclear Society. (n.d.). *Euratom Supply Agency interview*. Retrieved from https://www.euronuclear.org/news/ensuring-the-future-outlook-on-medical-radioisotopes-and-uranium-supply-chains-in-europe/

European Union. (2007). *Regulation (EC) No 1394/2007 of the European parliament and of the council.*

FAGG. (2017). *Ziekenhuisvrijstelling voor geneesmiddelen voor geavanceerde therapie (ATMP).* Retrieved from https://www.fagg-afmps.be/nl/MENSELIJK_gebruik/geneesmiddelen/geneesmiddelen/procedures_vhb/ziekenhuisvrijstelling_voor

Federaal Agentschap voor Nucleaire Controle. (2023). *Koninklijk besluit tot wijziging van het koninklijk besluit van 13 februari 2020 betreffende de medische blootstellingen en blootstellingen bij niet-medische beeldvorming met medisch-radiologische uitrustingen*. Retrieved from https://fanc.fgov.be/nl/system/files/20230317_kb_med_nlfr.pdf

Forschungs-Neutronenquelle Heinz Maier-Leibnitz. (n.d.). *Molybdenum-99 / technetium-99m as the most important radioisotope in diagnostics*. Retrieved from https://www.frm2.tum.de/en/frm2/industry-medicine/radioisotope-production/molybdenum-99/

Goulart De Medeiros M., H. U. (2023). *Translating radiotheranostic cancer research into clinical practice in Europe.* Luxembourg: Publication Office of the European Union.

Health system readiness. (n.d.). *About the international framework*. Retrieved from https://www.healthsystemreadiness.com/rlt-international-readiness-assessment-framework/

Hoge gezondheidsraad. (2015). *ADVIES VAN DE HOGE GEZONDHEIDSRAAD nr. 9218: Ontwerp van koninklijk besluit betreffende de ziekenhuisvrijstelling voor geneesmiddelen voor geavanceerde therapie.*

Inspectie Gezondheidszorg en Jeugd. (n.d.). *Vragen en antwoorden over de hospital exemption voor ATMP's*. Retrieved from https://www.igj.nl/publicaties/vragen-en-antwoorden/vragen-en-antwoorden-over-de-hospital-exemption-voor-atmp's

Institut De Radioprotection et de sûreté nucléaire. (2021). *Nouveaux Radionucleides en medecine nuclaire.* Retrieved from https://www.irsn.fr/sites/default/files/documents/expertise/rapports_expertise/IRSN_Rapport-2021-00083-nouveaux-radionucleides-medecine.pdf

International Commission on Radiological Protection. (2013). *Release of patients after therapy with unsealed radionuclides* . Retrieved from https://pubmed.ncbi.nlm.nih.gov/15571759/

Kankerregister. (2022). *Cijfers over kanker*. Retrieved from https://kankerregister.org/Cijfers_over_kanker

Kelsey L. Pomykala, M. W. (2022, October 13). Tackling the Last Mile: A Major Component to Successfully Establish Radioligand Therapy. *The Journal of Nuclear medicine*.

Koninklijk besluit. (2017). *Koninklijk besluit betreffende de ziekenhuisvrijstelling voor geneesmiddelen voor geavanceerde therapie.* Staatsblad.

Medicines and Healthcare products regulatory agency. (2015). *Advanced therapy medicinal products: regulation and licensing*. Retrieved from https://www.gov.uk/guidance/advanced-therapy-medicinal-products-regulation-and-licensing
Minister van Sociale zaken en Volksgezondheid. (2008). *Nationaal kankerplan*.
Nucleair forum. (n.d.). *België aan de wereldtop in medische isotopen*. Retrieved from https://www.nucleairforum.be/thema/de-kracht-van-nucleaire-geneeskunde/nucleaire-geneeskunde-belgie-aan-de-wereldtop-in-medische-isotopen
Nuclear Medicine Europe. (n.d.). Retrieved from http://www.aipes-eeig.org/
PALLAS. (n.d.). *Where are isotopes produced worldwide?* Retrieved from https://www.pallasreactor.com/en/medical-isotopes/where-are-isotopes-produced-worldwide/
Rad4Med. (n.d.). *The Belgian expertise in nuclear science and technology applications for healthcare*. Retrieved from https://rad4med.be/
République Française. (2022). *Décret n° 2022-193 du 16 février 2022 relatif aux médicaments de thérapie innovante préparés ponctuellement*.
Rijksinstituut voor Volksgezondheid en Milieu. (2018). *De toekomstverwachtingen over ATMP's*. Retrieved from https://www.rivm.nl/publicaties/toekomstverwachtingen-over-atmps
RIZIV. (2023). *List radiopharmaca.* Retrieved from https://www.riziv.fgov.be/SiteCollectionDocuments/list_radiopharmaca_20230701.pdf
RIZIV. (2023). *Radiotherapie: stereotactische bestraling aanrekenen*. Retrieved from https://www.riziv.fgov.be/nl/professionals/individuelezorgverleners/artsen/verzorging/Paginas/radiotherapie-stereotactische-bestraling.aspx
RPP. (2023). *Belgian Forum: the role of radiopharmaceuticals in the future of cancer care in Belgium - event report*.
SCK CEN. (n.d.). *Exploring nuclear medicine* . Retrieved from https://www.sckcen.be/en/expertises/exploring-nuclear-medicine
SNPHPU. (2022). *Décret du 16 février 2022 relatif aux médicaments de thérapie innovante préparés ponctuellement*. Retrieved from https://www.snphpu.org/syndicat-pharmaciens/decret-du-16-fevrier-2022-relatif-aux-medicaments-de-therapie-innovante-prepares-ponctuellement~3453.html#:~:text=Les%20MTI%20(M%C3%A9dicaments%20de%20Th%C3%A9rapie,(EC)%20ou%20commercial).
SPARC Europe. (2021). *High-level position paper: On improving access to radioligand cancer therapies in the context of Europe's beating cancer plan*.
Technopolis group. (2021, October 18). *Study on sustainable and resilient supply of medical radioisotopes in the EU*. Retrieved from https://www.technopolis-group.com/report/study-on-sustainable-and-resilient-supply-of-medical-radioisotopes-in-the-eu/
The Health policy partnership. (2020). *Radioligand tharapy - Realising the potential of targeted cancer care*.
The Health Policy Partnership. (2021). *Health system readiness for.* Retrieved from https://www.healthsystemreadiness.com/app/uploads/Health-system-readiness-for-radioligand-therapy-in-the-UK-Regulation-and-reimbursement.pdf
The Health policy partnership. (2021). *Radioligand Therapy readiness assessment framework: UK.*
(n.d.). *The Supply of Medical Radioisotopes: The Path to Reliability.* OECD 2011: ISBN-978-92-64-99164-4.