White paper: Unlocking the full potential of cancer treatments using targeted radionuclide therapy through Netherlands-UK partnerships

De white paper "Unlocking the full potential of cancer treatments using targeted radionuclide therapy through Netherlands-UK partnerships" is kortgeleden verschenen en wordt in deze editie van het TvNG integraal gepubliceerd (zie pagina 3328-3339). Initiatiefnemers dr. Samantha Terry en dr. Julie Nonnekens introduceren deze white paper en tevens geven ze belangrijke achtergrondinformatie aan de lezers van het tijdschrift.

Introducing this white paper for TvNG

In early 2023, we connected with Marjolein Bouwers, Chief Innovation Advisor at the Netherlands Embassy in London, who expressed a keen interest in fostering Dutch-UK interactions to advance innovative technologies. The Embassy aimed to support collaborations that could lead to significant advancements in healthcare and other fields. Recognizing this opportunity, we applied for a grant to develop a comprehensive white paper on the radiobiology of radionuclide therapy, specifically focusing on how UK-NL collaborations could strengthen this emerging field.

The initiative was led by Dr. Samantha Terry from King's College London and Dr. Julie Nonnekens from Erasmus MC in Rotterdam. With their guidance, we assembled a diverse team of researchers and clinicians from both countries. Our collective expertise spanned the fields of radiobiology, medical physics, and oncology, providing a robust foundation for our collaborative efforts. The team consisted of (in alphabetical order): Steve Archibald (King's College London, UK), Sean Collins (National Physical Laboratory, UK), Bart Cornelissen (UMC Groningen, NL), Mark Gaze (University College London, UK), Wim Oyen (Rijnstate Hospital Arnhem, NL), Mark Konijnenberg (Erasmus MC Rotterdam, NL), Daphne Lobeek (Radboud UMC, NL), Edward O'Neill (Oxford University, UK), Steffie Peters (Radboud UMC, NL), Giuseppe Schettino (National Physical Laboratory, UK), Jane Sosabowski (Queen Mary University of London, UK), Tim Smith (Bangor University, University of Manchester, UK), Alexander Turkin (Oncode Institute, NL), Katherine Vallis (Oxford University, UK) and Jennifer Young (King's College London, UK).

To kickstart the project, we organized a brainstorming session in London, bringing together key stakeholders and experts from the UK and the Netherlands. This full-day session was instrumental in aligning our goals, identifying critical research gaps, and developing a strategic plan to address them. Our discussions highlighted the potential of radioactive cancer-targeted drugs to revolutionize cancer treatment by delivering precise radiation doses to cancer cells while minimizing damage to healthy tissues.

Over the next few months, we worked to draft the white paper. Our primary objectives were to outline the current state of targeted radionuclide therapy, identify the challenges that impede its progress, and propose actionable recommendations to overcome these barriers. We emphasized the need for strategic funding to enhance the mechanistic understanding of targeted radioactive drugs, the facilitation of UK-NL clinical trials, and the coordination of training initiatives to build a skilled workforce in this specialized area.

In February 2024, we published the white paper, which was met with enthusiasm from both the academic and medical communities. The paper underscored the importance of continued investment in scientific research to answer critical questions in radiobiology, dosimetry, and radiation response.

Building on the momentum generated by the white paper,

the Embassy organized an innovation mission in March 2024, focusing on the broader field of nuclear medicine. This event provided a platform for Dutch academics, physicians, and industry representatives to meet their UK counterparts, exchange ideas, and initiate new collaborations. The mission was a resounding success, fostering numerous partnerships that promise to drive forward the field of nuclear medicine.

In conclusion, our collaborative efforts have laid a strong foundation for future advancements in radionuclide therapy. By leveraging the combined strengths of the UK and the Netherlands in science and health technologies, we are poised to make significant strides in optimizing patient care and developing innovative cancer treatments. We invite policymakers, funders, and other stakeholders to download and endorse the white paper to support this crucial area of research.

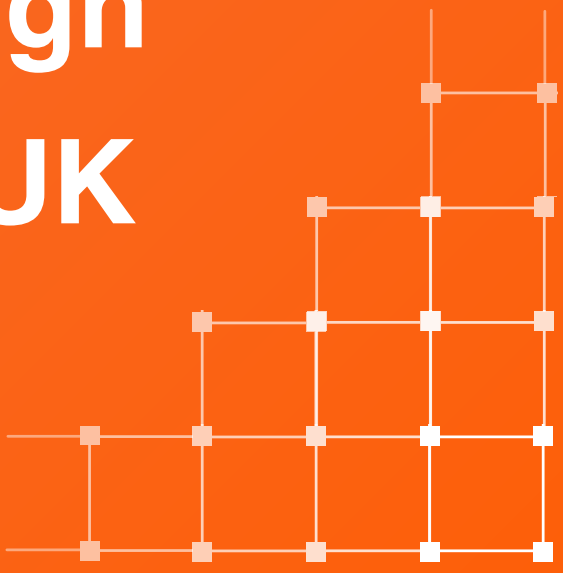
Download and endorse the white paper here: https://subscribepage.io/TRTWhitePaper

Julie Nonnekens
Julie Nonnekens is Associate Professor at the Erasmus MC in Rotterdam. Julie obtained her PhD in cancer biology with the focus on DNA repair mechanisms at the University of Toulouse, France in 2013. After that, she was a postdoc at the Hubrecht Institute working on ribosome biogenesis in cancer and longevity. In 2014 Julie joined the Erasmus MC with a joined appointment at the Department of Radiology and Nuclear Medicine and Department of Molecular Genetics. Her group is studying DNA damage repair mechanisms to better understand the underlying radiobiology of molecular radionuclide anticancer treatment in order to ultimately optimize treatment regimens.

Julie has received several (young investigator) awards and is principal investigator on various research grants including the prestigious ERC starting grant. She is chair of the Netherlands Society for Radiobiology (NVRB). Website of the lab: www.nonnekenslab.com.

Samantha Terry
Samantha Terry is Reader/Associate Professor in Radiobiology at King's College London, UK. Samantha obtained her PhD in Radiation Biology with a focus on the mechanisms of radiation-induced chromosomal damage at the University of St Andrews, UK, in 2010. Her postdoc at the University of Oxford investigated the influence of the density of chromatin packing on the therapeutic efficacy of molecular radiotherapies. Samantha then moved to an industry-funded postdoc on radionuclide imaging of the tumour microenvironment and monitoring therapy response in tumour and arthritis models at the Radboud UMC, Nijmegen, in 2011. Since 2015, Samantha has started her own research group at King's College London, UK, to determine how radionuclides used for therapy or imaging affect the cells they are targeting in order to predict how radionuclides and radiopharmaceuticals can be more efficacious.
Samantha has received many grants from industry partners, several early career grants and is principal investigator on various research grants. She acts on organizing committees for molecular radiotherapy meetings and as editorial board member for Nuclear Medicine and Biology. Website of the lab: www.radlab.uk. ♦

Unlocking the full potential of cancer treatments using targeted radionuclide therapy through Netherlands-UK partnerships



KING'S College LONDON

Erasmus MC
University Medical Center Rotterdam

Radiobiology of MRT
European Working Group

Kingdom of the Netherlands

Executive Summary

Investigating the optimal use of radioactive cancer-targeted drugs presents a unique opportunity to improve cancer treatment, by personalising it to an individual's needs, treating cancer that is spread throughout the body, or has become resistant to other therapies. By combining the strengths of the UK and Netherlands in science and health technologies and prioritising funding towards this research area, there is now the opportunity to accelerate research into optimising these radioactive drugs, and for both nations to maintain global leadership in this field.

Radioactive cancer-targeted drugs stand at the forefront of a paradigm shift in cancer treatment, holding unparalleled promise to not only target cancer volumes visible through scans but revolutionize the very landscape of oncological care by killing tumour cells spread across the body, even those that are resistant to other treatments.

By harnessing the precision of radioactive elements, radioactive cancer-targeted drugs offer a transformative avenue, enabling personalized, potent, minimally invasive treatments that transcend the limitations of conventional cancer therapies and can spare healthy tissues. They can redefine the boundaries of what is possible in cancer treatment.

Expansion of cancer treatment options to enable long, high quality lives for patients is a health priority set out by both the Netherlands and the UK in policy and national manifestos.

This white paper outlines three strategic recommendations to achieve this ambition:

- Strategically allocate funding to enhance mechanistic understanding of targeted radioactive drugs.
- Facilitate UK-NL clinical trials in targeted radionuclide therapies.
- Coordinate training initiatives.

Radioactive drugs can be used to specifically deliver a radiation dose to cancer cells which produces a therapeutic effect.

They can be used to treat not only the disease areas identifiable on medical scans but also can specifically target the microscopic tumour deposits spread across the body, involved in progression of the disease.

Despite its proven efficacy in clinically approved therapies, there is opportunity to fully unlock the potential of these treatments by better understanding the biological mechanisms and radiation dose delivered by these therapies and consequently why some patients respond better than others.

To optimise existing treatments and develop new personalised ones, many unknowns still need to be investigated.

With the development of novel radioactive drugs currently undergoing exponential growth and the global market expected to grow 5-fold by 2032.

> **Now is the time to invest in the science to ensure that when these new radioactive drugs are implemented, we get the treatments right for patients.**

This paper identifies and addresses existing challenges and unknowns in radioactive cancer-targeted drugs and showcases the possibilities afforded through collaborative research in radiobiology and dose measurement between scientists and organisations in the Netherlands and UK.

The big challenge

One in two people will be diagnosed with cancer at some point in their life [1]. As described in the UK Department of Health and Social Care Policy paper [2], “good health should be fundamental to all our lives” and cancer has been selected as one of the top six conditions which should be focussed on.

Targeted radionuclide therapy, or molecular radiotherapy, which is an injected radioactive cancer-targeting drug, can be used to treat a wide range of cancers, including prostate cancer, thyroid cancer, neuroendocrine cancer, and neuroblastoma, which is a cancer type affecting mainly children.

Although remission is possible in some situations, these treatments are mostly used at a late or final stage treatment to alleviate symptoms with patients often having run out of other (curative) options to treat their cancer. The recent success seen with targeted radionuclide therapy has prompted an exponential growth in development of novel radioactive drugs with small and big pharmaceutical companies pushing forward with their latest developments.

> **However, these novel therapies are being used clinically, or proposed for clinical use, without fully unlocking their potential to becoming curative options for cancer patients. For this to happen, many scientific unknowns in radiobiology, dosimetry, and radiation response still need to be answered, which require additional investment in scientific research.**

Photo by Vincent Blinde

[1] Longer, better lives: A manifesto for cancer research and care; https://www.cancerresearchuk.org/sites/default/files/cruk_manifesto.pdf
[2] Major conditions strategy: case for change and our strategic framework, https://www.gov.uk/government/publications/major-conditions-strategy-case-for-change-and-our-strategic-framework/major-conditions-strategy-case-for-change-and-our-strategic-framework--2

Research involving collaboration between the Netherlands and UK is a pivotal step for joint progress in targeted radionuclide therapy.

Now is the time to combine efforts and maximise progress in this field, to best help treat cancer patients and cement the role of the Netherlands and the UK as world-leading experts in this vital area of research. This is well-aligned with both the UK's Life Sciences Vision [3], and the first national action plan to treat cancer in the Netherlands [4].

Photo by Vincent Blinde

Both the Netherlands and UK possess highly skilled individuals across the disciplines relevant to targeted radionuclide therapy, particularly in radiobiological and dosimetry studies. This partnership is rooted in established collaborations (albeit in low numbers) and a rich tapestry of complementary research skills and expertise, both in the lab and clinically.

> ***It holds the potential to revolutionise the field of targeted radionuclide therapy. It will also ensure a comprehensive approach to targeted radionuclide therapy research and application.***

Combining efforts, rather than acting as two siloed countries, will increase the impact and positive outcomes from targeted radionuclide therapy, and leverage existing similarities in the Netherlands and the UK healthcare systems and clinical trial structures. Partnering would also allow for better and faster clinical trials due to increased recruitment possibilities across each country's diverse population.

[3] Life Sciences Vision, https://assets.publishing.service.gov.uk/media/612763b4e90e0705437230c3/life-sciences-vision-2021.pdf

[4] The Dutch Cancer Agenda, https://nederlandskankercollectief.nl/update/persbericht-eerste-landelijke-actieplan-kanker-gelanceerd/

Each nation has complementary skillsets from which the other country would benefit.

Photo by Vincent Blinde

The UK's expertise includes:

- The foundation for precise metrology, ensuring accuracy in dosimetry, activity standards and nuclear decay data, from the National Physical Laboratory.
- Drawing from its nuclear industry experience, the UK National Nuclear Laboratory has successfully identified nuclear waste as a source of therapeutic radionuclides (e.g. radioactive lead) or starting materials and demonstrated these can be separated, which have both health and environmental benefits.
- A rich heritage of radiation biology and radiation medicine research, in particular optimisation of fractionation and dose-response effects for external beam radiation contributing to a deep understanding of the field and providing a solid foundation for applying this to advancements in radionuclide therapy.

The Netherlands' expertise includes:

- The current NRG facility, and FIELD lab stand as a cornerstone in nuclear research, providing a platform for advancements in targeted radionuclide therapy research and application through providing isotopes.
- The new PALLAS nuclear facility in the Netherlands, which is being supported and funded by the Government of the Netherlands demonstrating their commitment to the field of nuclear medicine which includes radionuclide therapy.
- A Dutch dosimetry core unit, showcasing a centralised approach to dosimetry research, which is pivotal in ensuring standardised and accurate dose measurements.
- A heritage in targeted radionuclide therapy research, with the [^{177}Lu]Lu-DOTA-TATE molecule developed in Erasmus Medical Center Rotterdam for the treatment of neuroendocrine tumours, which has contributed significantly to the success and opportunity now available for targeted radionuclide therapy.

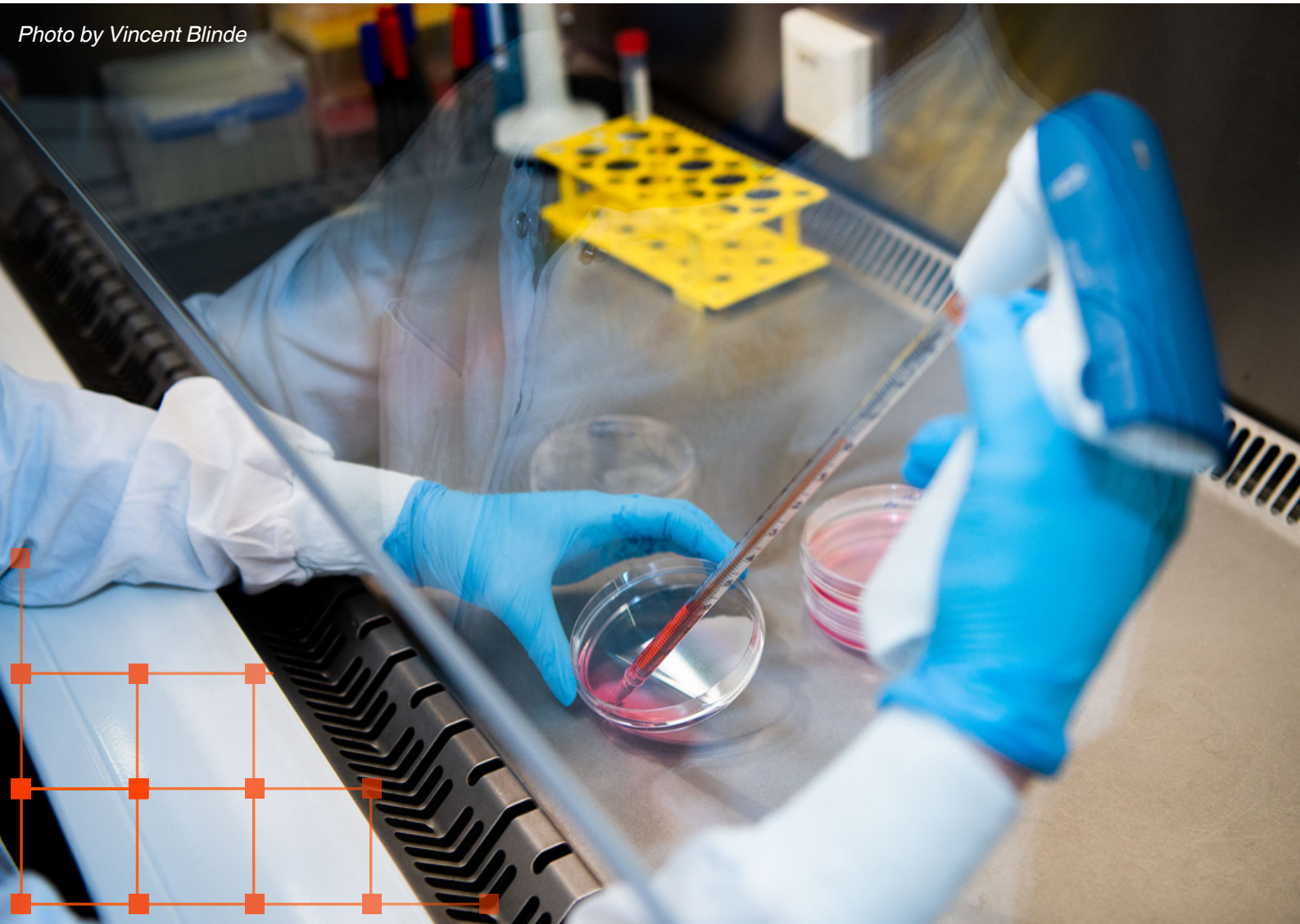


Photo by Vincent Blinde

How do we make this a reality?

We aim to secure commitment from both governments that this is a research area which should be prioritised for funding because of its vast potential to enable targeted radionuclide therapies to be developed into earlier stage and possibly curative options for cancer patients. A synergistic collaboration between the Netherlands and the UK could expedite the realisation of this goal and elevate the global research standing of both nations.

While the Netherlands and UK possess complementary strengths, the collaborative efforts in advancing targeted radionuclide therapy face hurdles. We have created three strategic recommendations to accelerate achievement of this ambition.


Photo by Vincent Blinde

1. Strategically allocate funding to enhance mechanistic understanding of targeted radioactive drugs.

A joint strategy and implementation of resource allocation could ensure investments are strategically directed towards radiobiological and dosimetric research in targeted radionuclide therapies with the aim of significantly improving patient outcomes.

Facilitating joint lab-based and clinical research projects and trials, exchange research projects between labs and countries, and access to radionuclides will further support the production of agents for clinical trials.

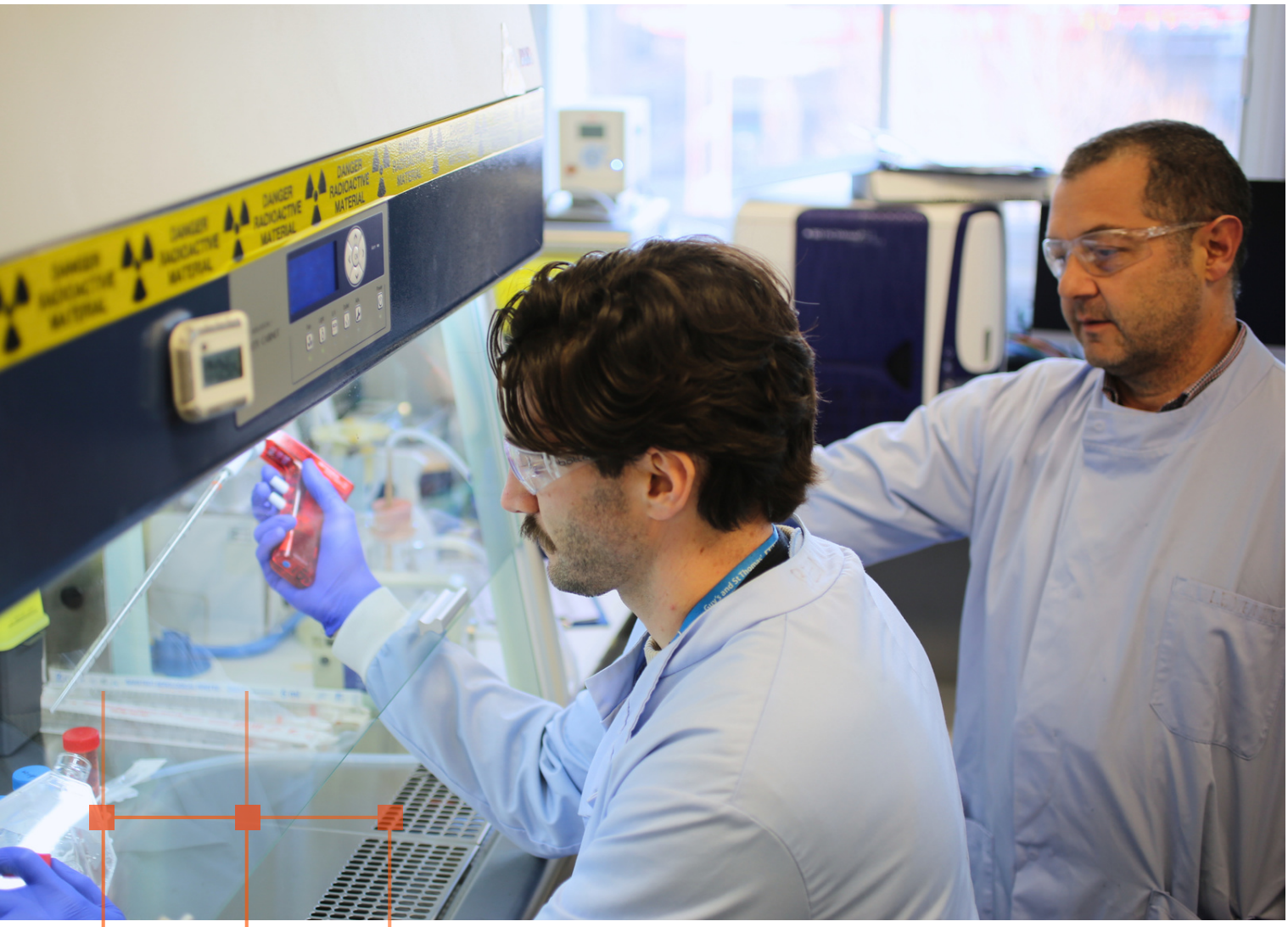
2. Facilitate UK-NL clinical trials in targeted radionuclide therapies.

This will foster cross-country collaborations and ensure the smooth delivery of trials. It could accelerate trials particularly in rare diseases by expanding the patient pool. We propose the process for sharing radioactive drugs, patient tissue or blood samples between sites should be streamlined.

Furthermore, defining and sharing protocols and best practices will improve reproducibility and promote standardization, safeguarding the authenticity of research outcomes. Striving for a balanced partnership with pharmaceutical companies is essential, where research objectives align with the broader goals of advancing targeted radionuclide therapies to improve patient outcomes.

3. Coordinate training initiatives.

There is great skills gap in radiobiology, radiochemistry and dosimetry, and in clinicians using these treatments. Joint initiatives must be developed to enhance training, ensuring a skilled workforce capable of driving advancements in targeted radionuclide therapies. We recommend creating Centres of National Excellence to deliver research and clinical trials. Additionally, fostering knowledge exchange through reciprocal visits by principal investigators, students, and researcher associates to labs will enhance the collaborative learning experience.



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How can you help?

This collaborative call to action invites stakeholders, policymakers, scientists, and funding bodies to actively engage in the implementation of these recommendations.

Therefore, you can:

- ***Promote this message and paper***
- ***Showcase your support and endorse this paper by emailing whitepaperUKNL@gmail.com***
- ***Sign up on our website***