NeuroEndocrine Cancer Australia

The Future of Precision Oncology in Nuclear Medicine

Presented by NeuroEndocrine Cancer Australia and the National Roundtable Steering Committee

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Contents

Statement of Acknowledgement

We acknowledge the Traditional Owners of Country throughout Australia and their continuing connection to the land, sea and community. We pay our respects to them and their cultures and to Elders past, present and emerging.

The Future of Precision Oncology in Nuclear Medicine – National Roundtable
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Executive Summary

Australia has led the way for 25+ years in the field of Theranostics. Theranostics is the term used to describe a unique approach to therapy combining both diagnosis and therapy by utilising a targeting pharmaceutical that is initially bound to a diagnostic isotope and, once adequate binding has been demonstrated, the same pharmaceutical is attached to a therapeutic isotope to treat the patient targeting primary and metastatic sites in the one process.

The ability to acquire a diagnosis and administer therapy in one package has been a game-changer for Neuroendocrine Tumour (NET) patient treatment as we know it, and this is moving into other cancer types such as prostate, ovarian, kidney and brain cancer and lymphoma.

Whilst this report will set out the challenges, solutions, pioneering research and innovation embedded in today's Theranostics landscape, and the need to keep Australia's position as a pioneer in the field, we must not lose sight of the most important aspect that binds everything together, the impact on patients.

Access to nuclear medicine clinical trials and treatments both for imaging and therapy is a matter of life (and being well enough to participate in important life milestones) and death. We have seen first-hand Australian men, women and children presenting with terminal metastatic disease, being able to walk offspring down wedding aisles, watch children graduate from primary school, to secondary school, to university, buy first homes, and take those once in a lifetime overseas adventures.

Australia holds an enviable global position in Theranostics due to our academic centres, high research and development (R&D) standards, universal healthcare, investment from government, industry and Australia Nuclear Science Technology Organisation (ANSTO) and due to the expertise and passion of those in the field. Some aspects of current legislation allows our tertiary hospitals to innovate in this field. Barriers to development exist ranging from funding, to production to access, and with advancements in applications and technologies changing at lightning speed, now is not the time to accept the status quo. We need to have an agile multi-sectoral approach, and a Health Technology Assessment (HTA) and research environment that evolves and nurtures innovation.

We need to ensure that the discoveries made on Australian soil are supported, invested in, and encouraged, and we need to create an attractive destination for inclusion in global clinical trials. Above all, we need to start the conversation today and continue it in the months and years to come. We need to focus on key strategic challenges of integrating Theranostics into cancer planning and patient pathways, political recognition and leadership, professional training, licensing, clinical care guidelines, investment in infrastructure, logistics and up-scaling, to ensure equitable access to all patients who will benefit.

Whilst we are encouraged that nuclear medicine is listed and recognised as one of the “critical technologies” by the Prime Minister and the Critical Technologies Policy Coordination Office (CTPCO), we need to review and contribute to what is planned in this area. We also know that the objectives laid out in the 2022 Critical Minerals Strategy and the actions outlined to support them, align with those of the Theranostic nuclear community. We also acknowledge the commitment to the Australian Precision Medicine Enterprise (APME) with the aim to meet the gap in supply for both traditional and emerging radionuclides. And whilst the focus needs to be on manufacturing, innovation, supply, clinical trials and licensing, we must not lose site of the most important stakeholder in the process and that is the patient. The process to patient access does not stop at reimbursement, but at the point to which treatment is administered safely, effectively and equitably into the patient.

This report brings to together all these key themes that came out of the National Theranostics Roundtable in October 2021. The aim of this report is to present a unified response from across the Theranostics field, to ensure we remain innovative and improve Australian cancer patients’ outcomes for generations to come.

Simone Leyden
CEO & Co-founder
NeuroEndocrine Cancer Australia

Dr Geoff Schembri
Immediate Past President
Australasian Association of Nuclear Medicine Specialists

Dr Daniel Badger
Immediate Past President
Australian and New Zealand Society of Nuclear Medicine

Partners


NeuroEndocrine
Cancer Australia
Champions for early diagnosis and a cure


Australian Government
ANSTO


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Medical Oncology Group of Australia


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Australasian Association
of Nuclear Medicine
Specialists


Prostate Cancer
Foundation of Australia


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AUSTRALASIAN GASTRO-INTESTINAL TRIALS GROUP


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SOCIETY OF NUCLEAR MEDICINE


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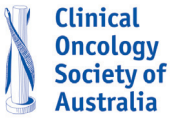
Clinical
Oncology
Society of
Australia


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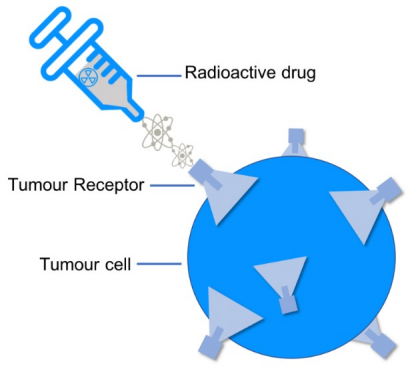
GE Healthcare


NOVARTIS

What is Theranostics?

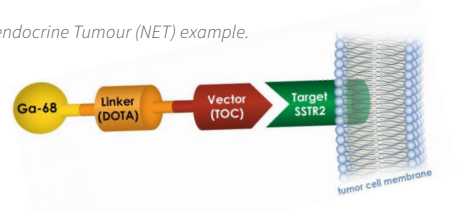
Theranostics is a combination of the term's **thera**peutics and diag**nostics**. Theranostics is the term used to describe the combination of using one radioactive drug to identify (diagnose) and a related second radioactive drug to deliver therapy to treat the main tumour and any metastatic tumours.



The diagnostic phase of thera*nostics*

The key to theranostics is to identify a tumour specific target that we can develop a pharmaceutical to bind to. For example, tumour cells have a range of proteins on their surface on internally that can serve as these targets. Examples are the somatostatin receptor (SSTR2) in neuroendocrine tumours (NETs) and prostate specific membrane antigen (PSMA) in prostate on the tumour cell membrane that can serve as a target for cancer drugs. Typically, a target that is present in much higher concentrations on the tumour cells (over-expressed) than non-tumour cells is chosen. These proteins, as part of their life cycle, are reabsorbed into the tumour cell and can carry the radioactive isotope right into the centre of the tumour cell. The diagnostic isotopes differ from the therapeutic isotopes in that they do not emit radiation that can kill targeted cells, only the level of radiation suitable to safely image/diagnose the patient.

Neuroendocrine Tumour (NET) example.

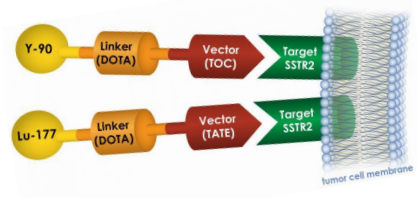


Gallium-68 (Ga-68) DOTATOC is a radioactive diagnostic drug that targets SSTR2. Ga-68 DOTATOC is injected into a patient's vein and travels throughout the bloodstream to all organs and tissues of the body. If the patient has a neuroendocrine tumour with SSTR2 on the tumour cell membranes, the Ga-68 DOTATOC will bind to the SSTR2 and the tumour will light up on a PET scan.[1]

The therapy phase of *Thera*nostics

Neuroendocrine cancer

Once neuroendocrine cancer is diagnosed using a Ga68-DOTATOC PET scan, the Ga-68 can be replaced with another radionuclide, such as Lutetium-177 (Lu-177) or Yttrium-90 (Y-90). These isotopes release short range radiation that can kill tumour cells that have SSTR2 on their membranes.



1 What is theranostics? | University of Iowa Hospitals & Clinics (uihc.org)- M. Sue O'Dorisio, MD, PhD

Therapeutic Y-90-DOTATOC and Lu-177-DOTATATE can both be injected into a patient's veins and will travel to any part of the body that has SSTR2 proteins. These therapeutic agents bind to the SSTR2 proteins like a key in a lock, allowing the drug to enter the tumour cells and kill it by damaging that cell's DNA. This is commonly called **Peptide Receptor Radionuclide Therapy (PRRT)**. Healthy cells around the tumour that do not have SSTR2 proteins on their membrane are not affected by the drug.

Prostate cancer

Once prostate cancer is identified also using a Prostate Specific Membrane Antigen (PSMA) PET scan, the diagnostic isotope can be replaced with a therapeutic radionuclide, such as 177-Lutetium (Lu-177) that can target and kill tumour cells that have PSMA on their membranes anywhere in the body.

Additional new diagnostic agents and therapeutic agents are being developed for use in the identification, diagnosis and treatment of neuroendocrine, prostate, kidney, ovarian, lymphoma and more. These theranostic "agents" will enable doctors to **personalise treatment** based on the specific type of cancer and the specific target that each patient may have.

National Theranostics Roundtable 2021 – Speakers and Agenda

The Future of Precision Oncology in Nuclear Medicine

Thursday October 28

Welcome

Simone Leyden
NeuroEndocrine
Cancer Australia

What is Theranostics?

Prof Rod Hicks
Peter MacCallum Cancer Centre

Prof Louise Emmett
St Vincents Hospital

Clinical Trials andInnovative Technologies

A/Prof Grace Kong
Peter MacCallum Cancer Centre

Prof Nick Pavlakis
Royal North Shore

A/ Prof Ros Francis
ARTNET

Prof Kristofer Thurecht
University of Queensland

Innovative Models of Care

Prof Michael Michael
Peter MacCallum
Cancer Centre

Prof Andrew Scott
Austin Health

Dr Aviral Singh
GenesisCare

Importance of Investment Now for the Future

Dr David Cade
Telix

Daniel Bucki-Smith
Global Medical Solutions

Dr Simon Puttick
AdvanCell Isotopes

Dr Alan Taylor
Clarity Pharmaceuticals

Greg Santamaria
Cyclotek

Dr Keith Hansen
GenesisCare

Soverign Capability, Future Workforce & Infrastructure

Dr Geoff Schembri
Australasian Assoc.
of Nuclear Medicine

Prof Dale Bailey
Royal North Shore

Shaun Jenkinson
ANSTO

Trade Opportunities, Industry Performance & Supply Chain

Amanda Rotger
ITM Germany

MD Rosanne Robinson
ANSTO

Amit Yadav
GE Healthcare

Christopher Sturla
Siemens Healthineers

Matthew Ashton
GMS

Time for a Rethink - HTA Framework for the Future

Prof Dorothy Keefe
Cancer Australia

Prof Robyn Ward
MSAC

Dr Megan Keaney
Dept. of Health

Adj. Prof John Skerritt
Dept. of Health

Patient Experience

Lynda Dunstone
NET Patient

Solutions Discussion

Prof Dorothy Keefe
Cancer Australia

Dr Mike Freelander
Member for Macarthur, NSW

Dr Jane Fisher
Movember

Simone Leyden
NeuroEndocrine Cancer Australia

Elizabeth de Somer
Medicines Australia

Moderator

Paul Cross
Daily Dispatch

Closing

Hon Mark Butler
Shadow Minister for Health and Aging

National Roundtable Steering Committee

Simone Leyden, Professor Rodney Hicks, Professor Louise Emmett, Meredith Cummins, Rosanne Robinson, Professor Michael Michael, Professor Nick Pavlakis, Professor Dale Bailey, Dr Daniel Badger, Professor Nat Lenzo.

Recognition and Leadership

The use of nuclear imaging and therapy has been successfully delivered to patients for many years. Interest in Theranostics in recent years has grown, as its application has expanded into more common cancers and diseases. Global pharmaceutical industry investment has grown exponentially and with that, clinical trials designed with the goal of achieving regulatory approval and reimbursement for patients. Whilst greater industry interest and investment is welcome, academic and Investigator Initiated Trials (IITs) and research, needs to be at the forefront to ensure scientific questions are explored, leading to targeted and personalised delivery to patients.

Australia has the building blocks and capability through ANSTO, the Medical Research Future Fund (MRFF), National Health and Medical Research Council (NHMRC), local biotech companies and academic researchers, to capitalise and lead in this field, however, it requires recognition and leadership from policy makers to achieve this goal. It also requires a collaborative approach bringing all stakeholders together to achieve systemic change.

There needs to be recognition that access and reimbursement for imaging patients, to not only diagnose, but as an integral tool to monitor response to treatment and disease progression along the continuum of treatment. Greater investment in this area will lead to long term benefits for the healthcare system in diagnosing cancer earlier, avoiding unnecessary interventions and keeping patients well.

Australia requires leadership to be at the forefront of discovery of the many new targets and targeting agents. The use of biology to guide treatment, and linking academia with industry in target discovery and validation needs to be encouraged and invested in.

The local scientific community shows leadership in conducting practice changing, globally revered clinical trials, however, government needs to ensure these discoveries get to patients by developing appropriate evidence pathways for Theranostics agents, that are conducive to both pharmaceutical company supported, and non-pharmaceutical company sponsored.

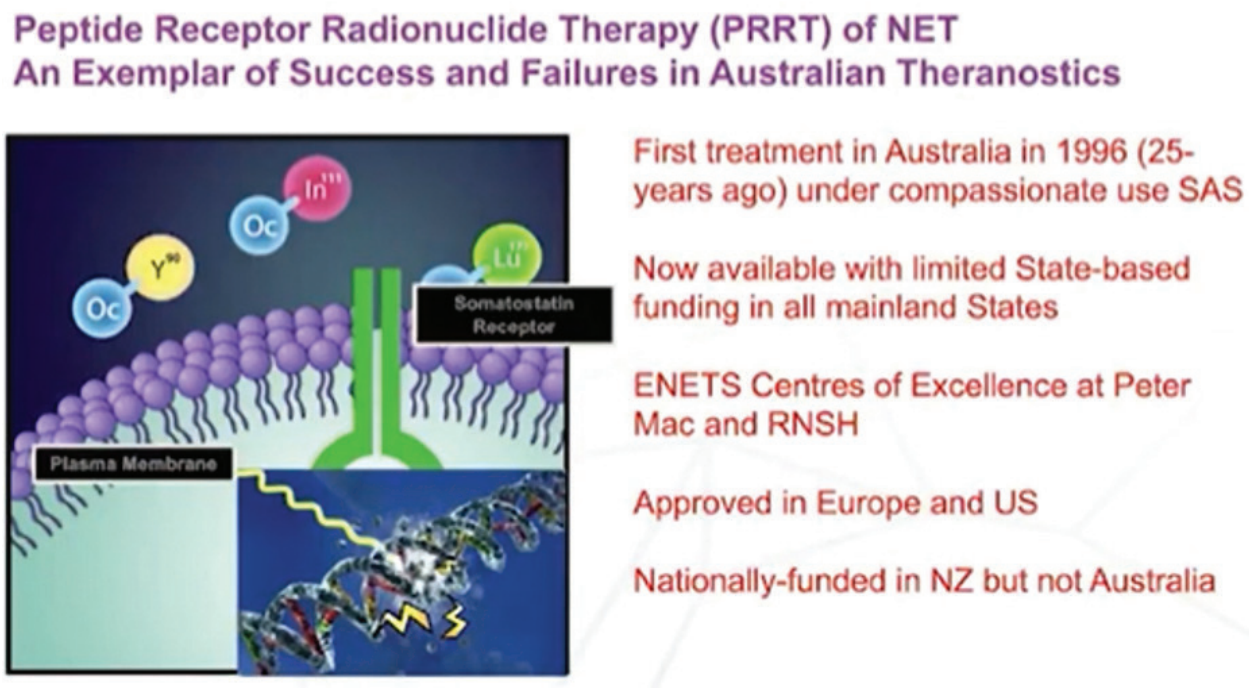
> Therapeutic nuclear medicine grew out of the interaction between scientists and clinicians focused on care of patients lacking treatment options.
>
> Peptide Receptor Radionuclide therapy (PRRT) is the true form of precision medicine, linking diagnostics with therapy to improve patient outcomes through a more personalised approach to medicine.

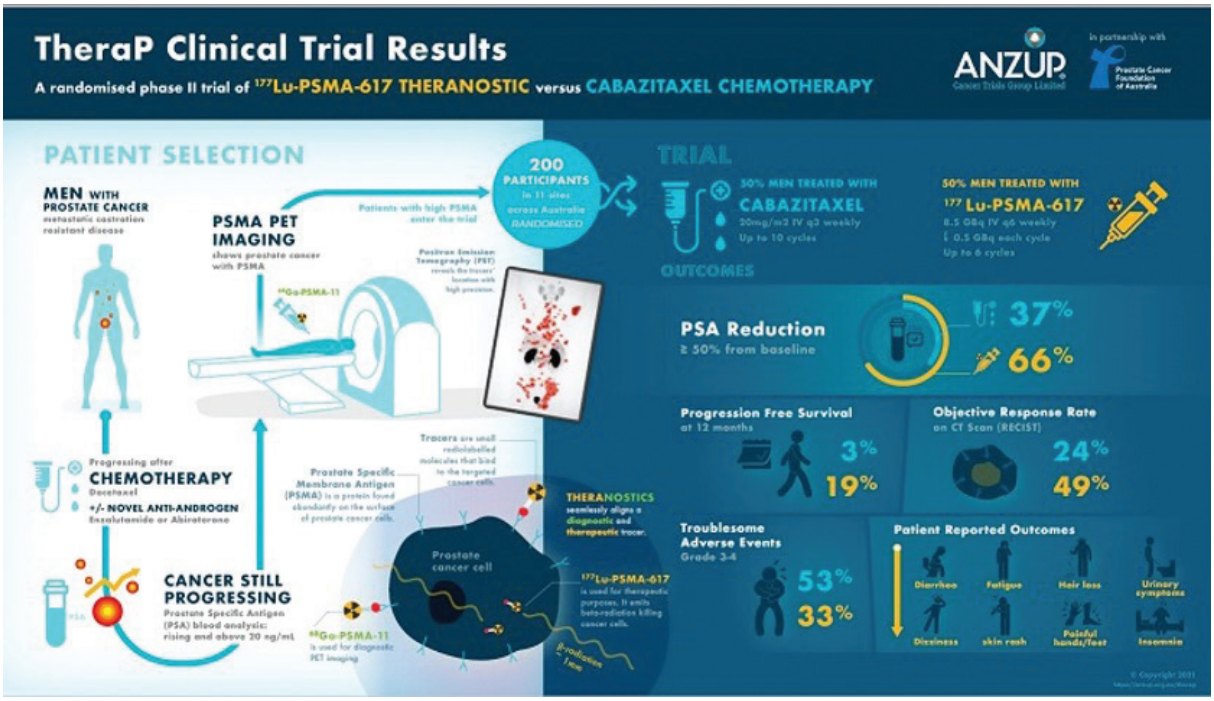
Prof Rod Hicks
Peter MacCallum Cancer Centre

> Inclusion of Theranostics in national cancer plans will be key for creating strategic direction for integration into cancer care.

Prof Louise Emmett
St Vincents Hospital

Australian led trials such as the TheraP study, a randomised phase II trial of 177Lu-PSMA617 theranostic versus cabazitaxel in progressive metastatic castration resistant prostate cancer, is an example of the collaborative approach investigators and hospitals have across the country. The trail included 11 sites and produced unprecedented responses in heavily pre-treated patients. It also provided evidence of Lu-PSMA effectiveness compared to the trationaly standard of care.





Key Points:

1. Australia has a highly trained and educated specialist community.
2. Encouraging the link between academia and industry in target discovery and validation.
3. Government leadership is needed through the development of evidence pathways, both pharma supported, and non-pharma supported.
4. Pathway to implement clinical access to Theranostics treatments for Australians.
5. All stakeholders need to work together to achieve systemic change.

Innovative Technologies & Trials

Benchtop to Bedside Success

Australian academics and researchers are among the best in the world in the field of nuclear medicine, oncology and Theranostics. Whilst our people and our hospitals have the capability, and importantly the collaborative desire to conduct world class research, there is **no reliable funding** mechanism. **Of the 12 recently closed and currently open investigator initiated clinical trials in Theranostics (therapy) across Australia, 10 are either fully or partially philanthropy funded.**

Access to these clinical trials for Australians has traditionally been investigator led because of the many barriers to participation in globally designed trials. These include the differing "hierarchy of evidence" placed on for instance US/FDA designed trials to Australian / TGA trials; red-tape /bureaucracy limiting global collaboration; logistics and supply of "short life" agents; contracts; indemnity, and predominantly the development of non-proprietary Peptide Receptor Radionuclide Therapy (PRRT) through academic centres, versus the propriety product developed by pharmaceutical companies, at usually a much greater cost.

Across the board industry led PRRT trials, and their subsequent commercial success, has been on the back of early academic investment. This is mainly due to the time it takes for submissions into MRFF, NHMRC and the low success rate.

> "The longer the time we have to try and get funding, the more delayed its going to be for the patients to try and be recruited into clinical trials, and potentially getting the right treatment for them.
>
> **A/Prof Grace Kong**
> Peter MacCallum Cancer Centre

> "Despite CONTROL NETs being considered a practice changing clinical trial by international peers…of 17 grant applications 3 were successful (philanthropic).
>
> The healthcare professionals are all here because they are passionate clinicians, investigators and researchers, but we are also at the mercy of fatigue and burn out when you keep hitting your head against a brick wall and not going far. We need to establish processes that are more fruitful and rewarding.
>
> **Prof Nick Pavlakis**
> Royal North Shore

Before and after treatment for a Neuroendocrine Tumour (NET) patient

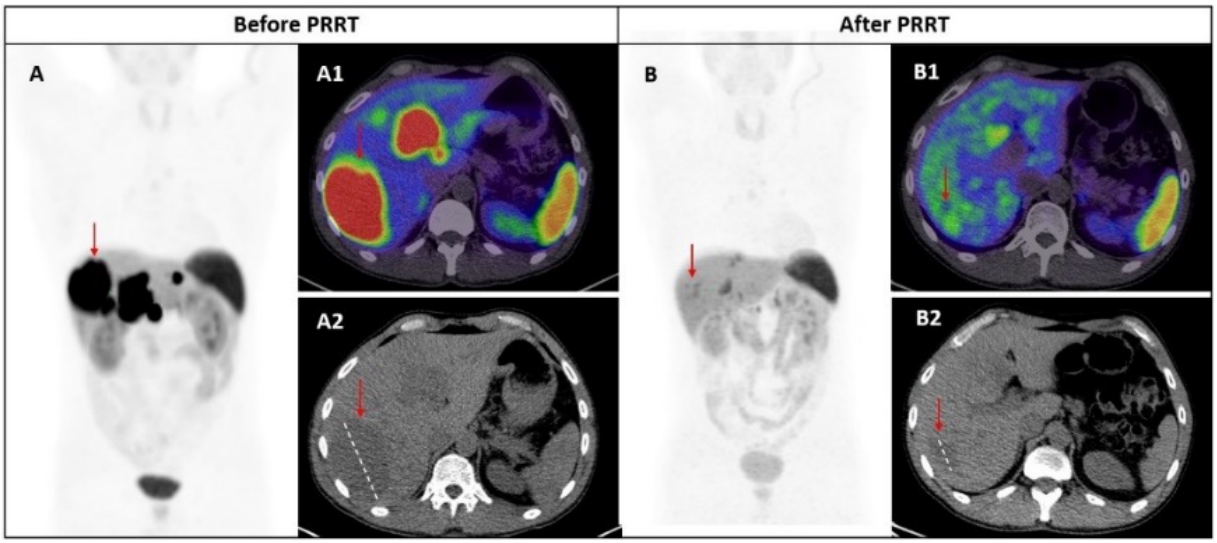


Figure: 50 yo male, presented with unresectable Grade 2 (Ki-67 10%) neuroendocrine neoplasm (NEN), with multiple liver metastases. Somatostatin analogue therapy was commenced. 9 months later, the patient had increasing abdominal pain and weight loss. A Ga-68 DOTATATE PET/CT showed high tracer uptake indicating high somatostatin receptor expression in the pancreatic primary, and multiple liver metastases (Image A). Red arrow highlighting the most dominant liver lesion (A1: trans-axial fused PET/CT images, and A2: co-registered CT). These lesions have all increased in size when compared to the baseline despite somatostatin analogue therapy. Patient was subsequently treated with 4 cycles of Lu-177 DOTATATE PRRT therapy without complications. Images performed 3 months after PRRT showed very marked response (Image B), with lesions only showing mild residual tracer uptake (B1: prior dominant lesion highlighted in red arrow), and lesions have markedly reduced in size (B2). The patient's abdominal pain had completely resolved, and weight returned to baseline after PRRT.

To assist national collaborative clinical research, the Australasian Radiopharmaceutical Trials Network (ARTNET) was formed as a joint initiative of the Australasian Association of Nuclear Medicine Specialists (AANMS) and Australian and New Zealand Society of Nuclear Medicine (ANZSNM) in 2014. ARTNET supports high quality clinical trials through multidisciplinary scientific committee reviews and endorsements of protocols and trial designs, as well as providing quality accreditation across equipment (scanners), radiopharmaceuticals and manuals.

"

As soon as that trial (TheraP) finished, the door was shut and there was no opportunity for patients to access that treatment.

How can we close that gap? We are establishing high quality evidence, how can we then ensure these treatments are available to patients once the trial is finished?

A/Prof Ros Francis
ARTINET

While we have the expertise and the collaborative environment to run world class trials, we also have access to innovative technologies enabling Theranostics in Australia. New target discovery is enabled by next generation genomics/proteomics the capability for discovery in this space to address challenges of the future. Advances in imaging technologies offer far more than just diagnosis, but longer-term prognosis capability and new hardware and artificial intelligence (AI) technologies, will expedite the validation pipeline and multi-centre radiochemistry/radiobiology provides new avenues for rapid translation of new discoveries to clinical assessment, with the cooperation between centres being paramount.

Australia has a strong track record in the arena of Theranostics / radionuclide therapy (NETs, Prostate), with a cohesive clinical multidisciplinary collaborative network pioneering innovative, world-leading, impactful trials. Much of the success has been because of investigator-initiated trials funded through limited research grants and predominantly charity funding. These funds are particularly limited for uncommon or rare cancers such as NETs.

Exciting emerging innovative technologies need to be supported (including funding) to enable further growth, to improve patient outcomes and remain international leaders in this field.

> “There are multiple new leads, there are multiple new drugs sitting in someone’s desk beside them, locked up in someone’s drawer ready to take into clinical translation, and due to the number of factors that have already been talked about today that is not occurring, and it’s actually a good thing that we have this large pool of potential drugs in store.

Prof Kristofer Thurecht
University of Queensland

Key Points:

1. Investigator led trials need access to targeted funding mechanisms and not to rely on philanthropic funding.
2. Support for commercialisation pathways for academic discoveries to stay in Australia.
3. Collaboration in the Theranostics community between hospitals, researchers, industry and societies is strong in Australia.

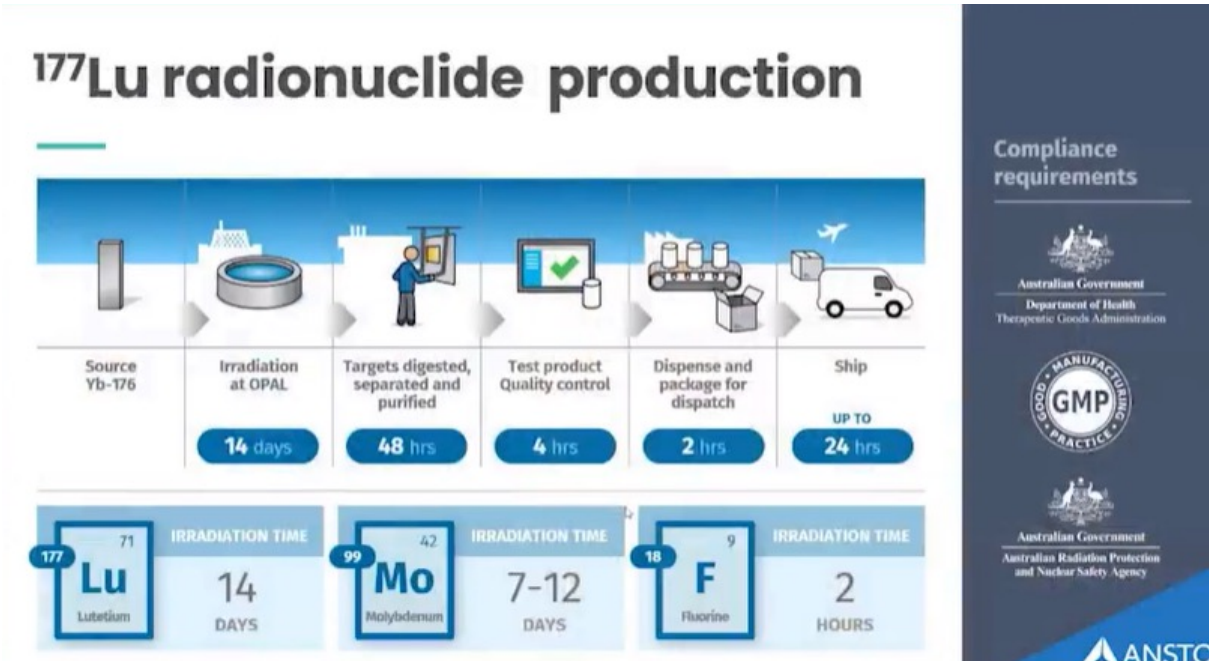
Sovereign Capability, Professional Training and Workforce

Sovereign Capability

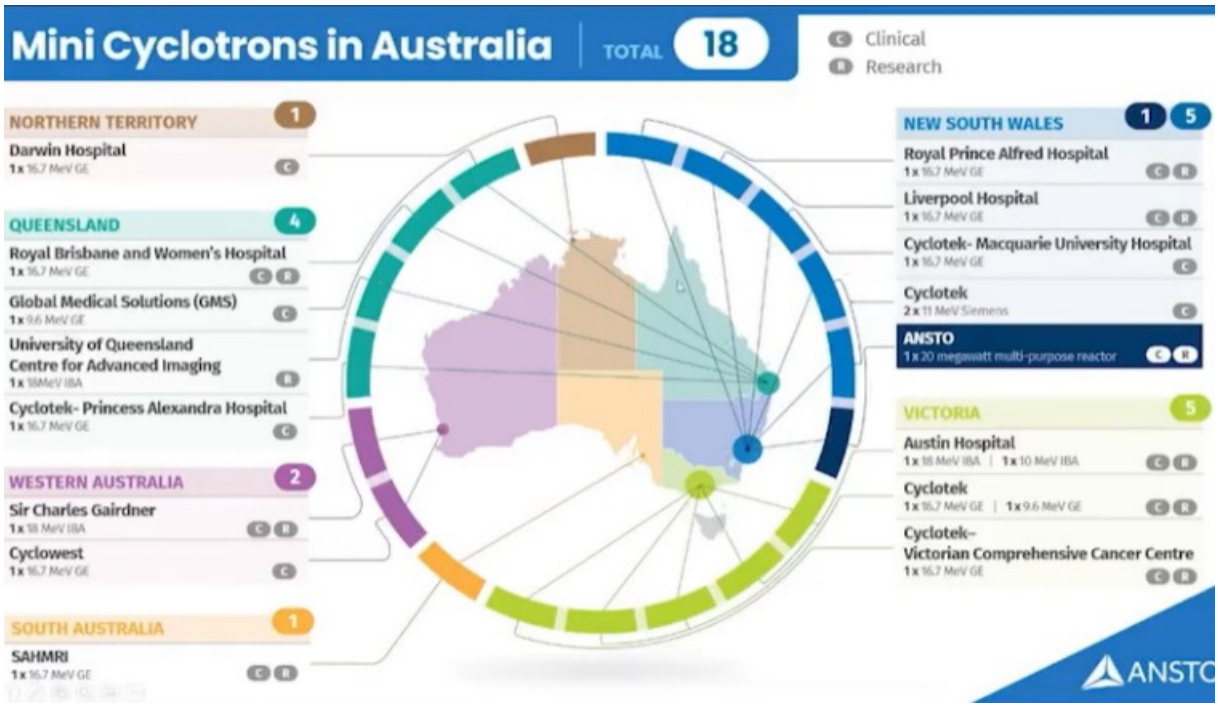
Australia's Nuclear Science and Technology Organisation, (ANSTO) is the home of Australia's most significant landmark and national infrastructure for research. Thousands of scientists from industry and academia benefit from gaining access to state-of-the-art instruments every year.

> To put this into context, out of that facility every week, we deliver all the nuclear medicine – all the Technetium – required for imaging in Australia, – so around 12,000 doses.
>
> **Shaun Jenkinson**
> ANSTO

What is required for radiopharmaceutical production?



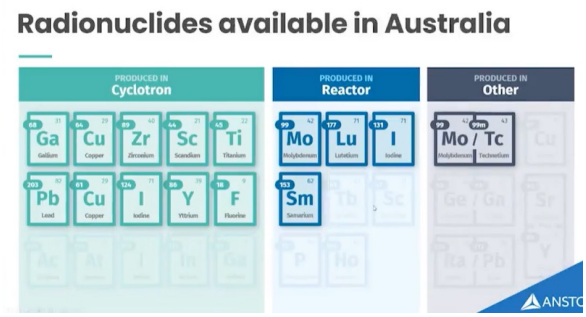
A cyclotron generates particles used in medical imaging techniques such as PET. Radiopharmaceutical production and PET/CT go hand in hand and because of the relatively short half-lives of PET radioisotopes, it's a race against the clock to produce a radioactive isotope, synthesize it into a radiopharmaceutical and get it to the patient. Therefore, access to local cyclotrons is imperative in the delivery of Theranostics.

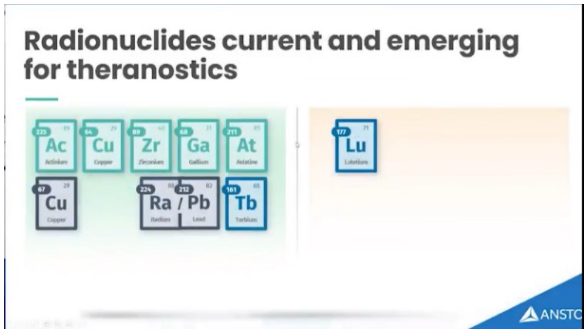


ANSTO has the capabilities to deliver access to world class nuclear medicine through the Molybdenum-99 manufacturing facility, the OPAL multi-purpose reactor, Lu-177 production facility, and the recent $30m investment into the scoping of a new nuclear medicine facility.

Currently ANSTO are manufacturing and supplying Lutetium-177 (on the below right image), however, the emerging demands are for those radionuclides on the below left. There is limited supply of some of these radionuclides from academic centres in Australia, but in other instances they are either imported or not available due to the short half-life, making international supply prohibitive.

ANSTO is working to expand and upgrade its current facilities and undertaking horizon scanning to ensure it can provide what is needed now and what will be needed in the future. This provides an opportunity to not only deliver world class radiopharmaceuticals to the Australian population, but be a leader in the Asia Pacific region.





Maintaining and growing the workforce

Whilst there is excitement in the development of new and innovative radiopharmaceuticals and their application across different cancers and diseases, Australia needs to maintain their highly respected and qualified workforce to meet these demands.

> Maintaining a state-of-the-art national clinical nuclear medicine capability, that attracts the brightest and the best minds is the most important way that government can help maintain the workforce.
>
> **Prof Dale Bailey**
> Royal North Shore

Outside of the site delivering the therapy, we need educators who can train the key personnel, industry suppliers who can provide all of the supporting infrastructure from isotope production to equipment for laboratories, imaging centres and radiation safety researchers and research facilities to ensure the ongoing development of the field and it's wider application to other disease conditions including additional cancers.

> We have been fortunate that several local factors have led to Australia developing a strong and healthy environment for the initial development of Theranostics. Many of the world leading publications in this field come from Australian research sites who have been at the forefront of this new field.
>
> **Dr Geoff Schembri**
> Australian Association of Nuclear Medicine

The Australasian Association of Nuclear Medicine Specialists (AANMS)

The AANMS currently represents 90% of the practicing nuclear medicine specialists in Australia. These are a combination of physician trained and radiology trained specialists who undergo a common final phase of training to interpret the diagnostic component and join with the multidisciplinary team in deciding on the appropriateness, timing and quantity of therapeutic isotope to be administered.

Australian research in this area has been facilitated by the Australasian Radiopharmaceutical Trials network (ARTnet), a collaborative network of all members of the nuclear medicine community and a joint initiative of the Australia New Zealand Society of Nuclear Medicine (ANZSNM) and AANMS.

It is critical to note that Theranostics is a multidisciplinary modality. The team required to deliver therapy at the highest quality levels includes:

- Nuclear Medicine Specialists to assess patients and oversee the whole process.
- Medical physicists to estimate and monitor radiation therapy.
- Radiochemists to produce the therapeutic materials and ensure human grade quality.
- Nuclear medicine technologists to perform the imaging and to assist in therapy delivery, patient scanning and radioisotope dispensing.

There are over 500 nuclear medicine specialists in the country though not all have training in Theranostics. The AANMS with the assistance of the ANZSNM has recently published an initial statement on the Practice of Theranostics in Australia which presents recommended guidelines for all aspects of the provision of Theranostics including training requirements for nuclear medicine specialists wishing to be involved in this field.

The Society are currently developing a training course in Theranostics which is expected to be in place this year.

It is currently expected that most therapies will be for prostate cancer with a smaller number of the equally important but less common neuroendocrine tumours in the immediate term. There are approximately 5-6 million men >40 years in Australia of whom approximately 20/100,000 will suffer from metastatic castrate resistant prostate cancer = 1000/year. This is the initial group that will be eligible to receive Theranostic treatment over the course of their disease. These patients will receive an average 2-4 treatments = 3000.

Currently less than a thousand treatments are given annually for NETs. Hence we are looking at around 4000 treatments/year or less than 100/week.

There is a need to have sufficient sites to ensure there is equitable access to Theranostics across the country (regional and metro), with appropriately trained staff and resources to provide optimal care. It is anticipated that we can manage the initial demand for therapy with the existing workforce while concurrently training new specialists in the field. AANMS are seeking to broaden the existing training scheme to allow radiation oncologists to gain appropriate nuclear medicine qualifications.

To maintain all of the above requires government support and modest investment. The nuclear medicine community is a relatively small one and has been consistently overlooked in many funding reviews while those with larger voices dominate the space. Radiopharmaceutical costs have grown substantially over the last few decades with no provision for this being made in Medicare rebates. We want to attract the best we can into our field. To do so requires an adequately funded specialty with opportunities to contribute in a real way to patient care.

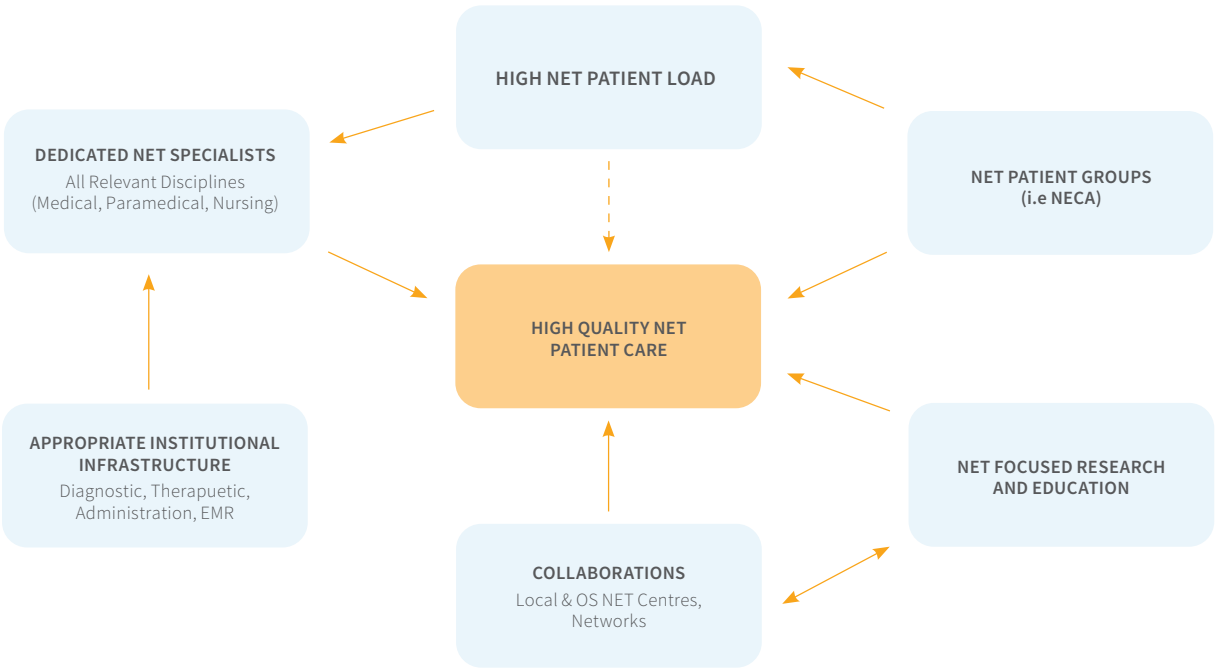
Key Points:

1. Australian Nuclear, Science, Technology Organisation (ANSTO) is re-evaluating its current capabilities and working towards future proofing manufacturing and supply through investment in new and upgraded facilities.

2. Australia has an experienced and respected workforce and through AANMS and ANZSNM and dedicated education modules and workshops will ensure training remains at the highest standards.

3. Australia has the opportunity to be a leader in the field in the Asia Pacific region.

Clinical Guidelines & Care Pathways



Pathways for rare and less common cancers

NETs are a heterogenous, less common cancer which frequently have a delay in the correct diagnosis and present with metastatic disease. The management of NETs is challenging as there is limited patient volume and also limited expertise in the medical community. This results in patient dissatisfaction, psychological impact and reduced QOL. Ultimately, leading to suboptimal care and poorer outcomes (yet to be validated).

> Guidelines can be written, however this does not equate to high quality care as you need the infrastructure with investment to deliver the care.

Prof Michael Michael
Peter MacCallum
Cancer Centre

The coordination of NETs care should be managed in a NET Centre of Excellence (CoE). The European Neuroendocrine Tumour Society (ENETS) has accredited Peter MacCallum Cancer Centre (Vic) and Royal North Shore Hospital (NSW), 2 of only a few sites outside of Europe. There are future plans to establish 3 more sites in Australia to be CoEs (Fiona Stanley Hospital WA, Queen Elizabeth Hospital SA and Royal Brisbane & Womens' Hospital Qld). These facilities have standardised protocols agreed to with the Nuclear Medicine department, Medical Oncology and other disciplines within the NET unit. The PRRT patients are discussed within the Multidisciplinary Meeting (MDM) (templates available for monitoring, investigations) – close collaboration, documentation & Standard Operating Procedure (SOPs). Accreditation and certification (currently carried out by the ENETs) ensure quality by setting standards and following robust and transparent measurement processes. Patients are able to identify and access high-value services and therapy options.

All potential centres who apply for ENETs CoE accreditation must demonstrate governing structure which includes NET multidisciplinary specialists, individual qualifications and NET related expertise, access to relevant resources and collect mandatory quality indicators and key figures annually. Patient volumes are approximately 100 new patients per year and greater than 90% NET patients are discussed at the NET MDM.

Care pathways for Theranostic departments highlight multidisciplinary care and personalised medicine. There is a huge array of potential targets for Theranostics – tumour markers, metabolic, receptors, tumour immune microenvironment. The future is bright for new Theranostics that can be produced in Australia to enable equitable access. However, issues continue to occur in access and availability of radiopharmaceuticals for imaging and therapy, as does the unified approach to rare and less common cancers where evidence is needed from clinical trials so that we can do better.

Credentialing of imaging equipment is needed for national imaging facilities, as is Quality Assurance and image biorepository analysis for Theranostics (e.g ARTnet). It is very important to have levels of evidence which demonstrate health outcomes and enable economic analysis. Funding availability needs to be reviewed, as do the definitions of the roles of regulatory bodies to enable ongoing improvements for patient outcomes.

> "It is very important to have levels of evidence which demonstrate health outcomes and enable economic analysis.
>
> **Prof Andrew Scott**
> Austin Health

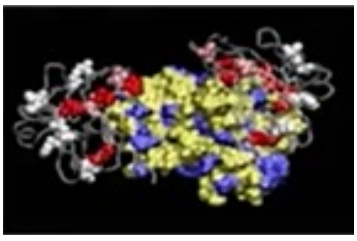
Prof Andrew Scott spoke about the many different areas for targets for imaging and therapy of tumours particularly in:

- Tumour cells (eg. Cell surface receptors, signalling pathways, metabolic processes, mutations).
- Tumour microenvironment (eg. Vasculature, lymphatics, extracellular matrix, fibroblasts).
- Cellular infiltrates (eg. Inflammatory, immune activating, immune suppressive, bone marrow derived).
- Molecular imaging probes can be used to validate targets, confirm suitability of therapeutic drugs, select patients, inform clinical trial design, deliver therapeutic radioisotopes.

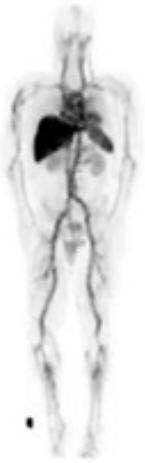
Looking at one target from development in the laboratory that has successfully translated into the clinic is EphA3. EphA3 is expressed in a range of common cancers as well as rarer cancers such as glioblastoma. Prof Scott was able to label this target with Zirconium 89 (Zr89) to show exquisite targeting of glioblastomas, showing few limits in the development of new Theranostics. Prof Scott along with other scientists created a new drug, KB004 (Ifabotuzumap), an antibody which targets the protein EphA3 on the surface of cancer cells and surrounding blood vessels. This product is now licensed to US company, Humanigen with the hope of developing this as a treatment and taking it into trials very soon.

Targeting the Tumour Immune Microenvironment

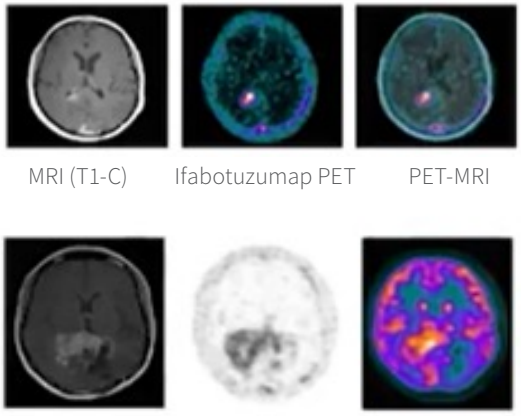
- EpbA3 is expressed in tumour vasculature and some several cells, including MDSCs.
- Ifabotuzumap (KB004) is a non-factorylated IgGlk antibodies targeting EpbA3 receptor.



- Zr-ifabotuzumab demonstrated sensitive, specific and reproducible targeting of the tumour microenvironment is GBM pts.



Targeting EpbA3 in Tumour Immune Microenvironment



MRFF funding can be achieved, however you need a compelling submission with a quality team to do this. In summary, planning and delivery of Theranostics needs to be co-ordination of experts – clinicians, scientists, physicists, technologists, statisticians, health economists, patients and consumers – without this, care is suboptimal, financially burdensome and frequently ineffective.

Health benefits of scaling up imaging and nuclear medicine

Patients diagnosed with **one of 11 common cancers** from 2020-2030:

Projected Cancer Deaths	Averted Cancer Deaths	
With NO scale up: **76 million**	Scale up of treatment & quality of care: **5.4 million**	With imaging added: **9.6 million**

Global scale up of imaging from 2020-2030 would cost **$6.84 billion**, leading to productivity gains of **$1.23 trillion** and a **return of $179.19 for every dollar invested.**[2]

2 Ward ZJ, Scott AM, Global costs, health benefits, and economic benefits of scaling up treatment and imaging modalitiesfor survival of 11 cancers: a simulation based analysis. Lancet Oncol. 2021

From an international perspective Dr Aviral Singh discussed Theranostics in the overseas setting, predominantly Germany.

Germany has one of the oldest and respected healthcare systems in the world with a combination of a statutory contribution system and private healthcare . Whilst this system has served well, access to rapid emerging technologies such as Theranostics, where current market authorisations are lengthy and time consuming, are available to patients through either clinical trials, or compassionate access schemes.

Theranostics application for Neuroendocrine Tumours have kick started a revolutionary phenomenon towards realisation of the goal of precision as well as personalised medicine in Clinical Oncology. Further and ongoing clinical, research, industry and healthcare system effort and support are warranted for the progression of Theranostics in the appropriate direction.

Based on the NETTER – 1 Trial, PRRT for Gastro Entereopancreatic -NET (GEP-NET) is now included in the European and German national clinical guidelines as well as Ga-68 SSTR PET/CT imaging and both are reimbursed by the healthcare system. Theranostics of non GEP-NET is reimbursed by the health care insurance funds in Germany based on clinical indication.

> “Theranostics is at the forefront in the management of various oncological entities and certainly presents itself as the future of Precision Medicine in Nuclear Medicine.

Dr Aviral Singh
GenesisCare

Key Points:

1. For rare and less common cancers a multidisciplinary, centre of excellence model has been proven to provide patients with the best access and outcomes using Theranostics.
2. Inclusion of Theranostics and emerging precision medicines in optimal care pathways.
3. Significant advantages to up-scaling access to imaging for long term improved patient outcomes and healthcare cost savings.

Licensing, Infrastructure & Manufacturing

Think Global Act Local

Telix is a late-stage radiopharmaceutical company developing a broad portfolio of diagnostic and therapeutic ('theranostic') assets using Molecularly Targeted Radiation (MTR).

Telix's product development strategy is to closely integrate and add value to standard care, reflective of the modern team-based approach to managing cancer. Telix's research pipeline aims to address significant unmet medical need in prostate, kidney, brain (glioblastoma), and hematologic cancers as well as a range of immunologic and rare diseases.

Telix is a prime example of an Australian company that is now successful on a global scale. This is due to extensive investment in distribution (80 countries) and manufacturing capabilities (11 countries). Telix has an extensive portfolio of diagnostic and therapeutic assets including 17 countries with market authorisation for TLX591-CDx (illuccix) in progress (FDA & TGA approved) and 17 active clinical trials (7 indications). Radiopharmaceuticals are a unique class of "drug" primarily due to the isotopes shelf life, measured in hours to days.

This is why investment in secure supply chains and local manufacturing is essential.

Key actions needed at a local and global level:

GenesisCare saw the disruptive potential of the Theranostic paradigm particularly in nuclear medicine about 4 -5 years ago. They set a three limb global strategy to support the field and the development of the evidence base. The first step in the strategy was to build out a network of sites to ensure patient access to clinical trials but also to a compassionate use program. They have also been cultivating a relatively unique research capability to be an efficient partner for industry and research organisations looking to develop IP which would include that global network sites. Finally, to back great Australian organisations as they are looking to develop IP developed in this country around the world.

Genesis believe that there is an opportunity to support health tourism in Australia. Prior to COVID up to 70% of patients were coming into Australia for compassionate access particularly from Asia, as Australia is recognised as a world leader in this space. This is something that could definitely be capitalised on after COVID.

Think Global Act Local	*Action*
1. Streamlined ethics, 'pragmatic' research governance	**Maintain**
2. 'Institutional overhead', US-style cost escalation	**Avoid**
3. HTA, public funding framework that 'rewards' theranostic pairs	**Create**
4. Sovereign isotope manufacturing capability	**Build**

"Molecular imaging allows for treatment of those patients we expect to benefit, and avoid treating those patients we expect will derive little to no benefit". "It is ethical for the patient, ethical and fulfilling for the treating physician and even go so far as to say it is ethical for the payer.

Dr David Cade
Telix

"How does Australia realise its full potential? I truly believe we have a global leadership position that we can capitalise on and also build an export industry for Australia. I echo the comments made by other presenters about importance of having sovereign isotope development, I think that would be key.

Dr Keith Hansen
GenesisCare

AdvanCell Isotopes is a clinical stage radiopharmaceutical company developing next – generation therapies for the treatment of cancer. AdvanCell's platform technology, a world-first small footprint medical isotope generator, addresses the fundamental unmet need for cancer radionuclide therapy: the reliable supply of alpha emitting isotopes.

The platform enables the development of a pipeline of alpha radioligand therapies, linking AdvanCell's proprietary and highly scalable isotope production to our in-house pharmaceutical manufacturing and clinical expertise.

AdvanCell is commencing production of their proprietary alpha isotope formulation, alongside launching the Phase 1 trial of ADVC001 – an alpha radioligand therapy for metastatic castrate resistant prostate cancer.

Funding and research partnerships are key for AdvanCell with relationships with CSIRO, University of QLD and University of Adelaide to name a few.

AdvanCell like many in the audience would like to see a dedicated Medical Research Future Fund (MRFF) scheme directed at radiopharmaceuticals/Theranostcs.

> "Collaboration is key. Schemes that encourage collaboration within industries, between industry and academia, and between industries as well, for example we collaborate with the mineral resources industry to source isotopes and that will be important into the future.
>
> **Dr Simon Puttick**
> AdvanCell Isotopes

> "We do really well in phase 1 and 2 of trials but when it moves to phase 3 with funding and looking for regulatory approval, particularly with the FDA which is the largest market, we need to work in the US. It's more difficult to do those sorts of clinical trials in Australia.
>
> **Dr Alan Taylor**
> Clarity Pharmaceuticals

Clarity's mission is to develop next-generation radiopharmaceutical products that improve treatment outcomes for children and adults with cancer.

Clarity is a clinical stage radiopharmaceutical company developing next-generation Theranostic products, based on our platform SAR Technology. The SAR Technology is ideally suited for use with copper isotopes, enabling superior imaging and therapeutic characteristics of radiopharmaceutical products and addressing the current manufacturing and logistical limitations in the growth of the radiopharmaceutical sector in oncology.

Clarity is a global leader in Targeted Copper Theranostics (TCT), developed with its proprietary SAR Technology platform. TCT are the next-generation disruptive platform in radiopharmaceuticals that employ the "perfect pairing" of copper-64 (Cu-64) and copper-67 (Cu-67) for diagnosis and therapy. TCT deliver a compelling combination of high accuracy and high precision in the treatment of a range of cancers, as well as providing supply and logistical advantages over current theranostics.

Clarity has the true experience of "bench-top to bedside", which as a company originally started with funding for basic research out of the Australian National University (ANU) through to translation and lastly just recently closing out the largest IPO for an Australian bio-tech on the ASX.

As Dr Alan Taylor mentions there is a gap in that funding model for translating that initial idea, and basic research through to translation and `in Australia we will have a reticence not just in the nuclear medicine industry but more broadly to focus on the translation of our science. We fail miserably in global terms in translating that intellectual property through for a myriad of reasons.'

Cyclotek is a GMP manufacturer that has been supporting Australian research endeavours for 20 + years. Cyclotek currently produce 11 PET radiopharmaceuticals for clinical, research and clinical trials, including a number of proprietary tracers under contract to pharmaceutical companies. Their facilities are licensed by the Therapeutic Goods Administration (TGA) to manufacture and distribute products throughout Australia, and by the Ministry of Health in New Zealand. Licensing is primarily based on compliance with the Code of Good Manufacturing Practice (cGMP). The company is well placed to develop and expand its operational capacity and to introduce additional PET radiopharmaceuticals.

> “What keeps you up at night – a fear of failure, if one of our facilities goes down, it’s 200 patients that don’t get a scan today. Rescheduling those people could take weeks to get them back in to the system.
>
> **Greg Santamaria**
> Cyclotek

Applied Molecular Therapies (AMT) is a Cyclotek company and joint venture with ANSTO. This is a collaboration between the two organisations to provide cGMP manufacturing and supply for the next generation of radiopharmaceuticals, focused on therapeutic radiopharmaceuticals. Investments in AMT has built robustness in regulatory supports particularly in managing practices around radioactive waste compliance for long lived isotopes and managing the TGA cGMP compliance for their expectations for a multi-isotope facility.

Regulatory Challenges:

The TGA applies a risk-based approach to regulation with sterile injectable products classed as high-risk therapeutic goods.

Consistent regulations applied directly to the “Method of Manufacture” irrespective of the organisation is optimal. Not doing so creates an inconsistent two-tiered regulatory system.

Cyclotek believe Australia has a recognised regulator that is harmonised to international bodies, have methods of supply that cater for a variety of circumstances, whereas the method of manufacture has some ambiguity and inconsistencies. There is a funding gap between good evidence-based products and time line to market, creating financial difficulties for local pharmaceutical companies and patients, wanting to access vastly improved clinical outcomes in diagnostics and treatments. We need to back the science and better patient outcomes. The Australian market is small in comparison to the rest of the world and the cost of early, best in class therapies in diagnostics need to be addressed in a funding model in a collaborative manner of all stakeholders.

Global Medical Solutions (GMS), Ltd. was formed in 2003 to be a leading-edge provider of nuclear medicine and diagnostic imaging products and services. Global Medical Solutions’ mission is to continue the long history of providing quality products and services to the worldwide nuclear medicine community.

GMS supports supply in the Australian market through an extensive network of radiopharmacies in each state, as well as Radpharm Scientific, a Division of GMS the only facility in Australia supplying radiopharmacy “cold-kits”. Three of GMS facilities practice under pharmacy, however, Radpharm operate under GMP. GMS has the current capabilities to provide clinical trial doses on a small scale but need support to scale up.

> Finding that balance between our everyday routine clinical supply which is an important mainstay of nuclear medicine with new clinical trial drugs and being able to put resources to their development…if we can push forward clinical trials it will move nuclear medicine into the future.

Dr Daniel Bucki-Smith
Global Medical Solutions

GMS is addressing the issue around supply of radioisotopes for clinical trials and reliance on overseas through the creation of the Australian Precision Medicine Enterprise (APME) – a joint project between Monash University , Telix and research partners. The aim of APME is to design and manufacture molecules for targeted Theranostics, as well as meet the gap in the market for both traditional and emerging radionuclides. GMS is also upgrading existing facilities to accommodate clinical trial radiopharmaceutical production.

Key Points:

1. Australia has a successful biotech industry that has positioned itself as global players.
2. Australia conducts phase I and phase II trials very well, however, phase III trials are moved offshore to the US due to the regulatory environment, access to patients, funding, and supply of radioisotopes.
3. The Australian Precision Medicine Enterprise (APME) will aim to meet the gap in supply for both traditional and emerging radionuclides.

Logistics

ITM is a privately owned biotechnology and radiopharmaceutical group of companies, who develop, manufacture and distribute globally diagnostic and therapeutic radiopharmaceuticals and radioisotopes. ITM have a robust global supply network, proprietary portfolio and growing pipeline of Targeted Radionuclide diagnostics and therapies for cancer treatment and are a GMP manufacturer.

> We are thankful for the engagement in clinical trials in Australia and are developing strategic alliances in order to ensure supply chains are not broken. It is important that shipments are securely delivered even during difficult times like COVID.
>
> **Amanda Rotger MD**
> ITM Germany

ITM currently has two global clinical trials actively recruiting in Australia:

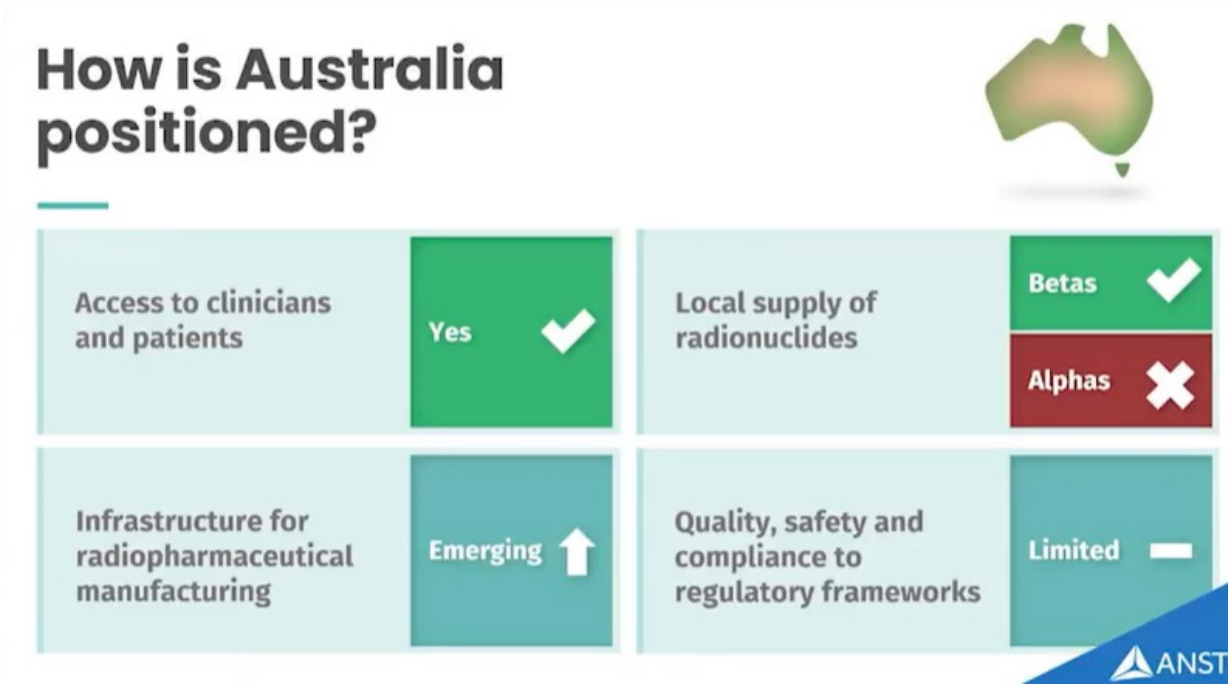
COMPETE: A Prospective, Randomised, Controlled, Open-label, Multicentre Phase III Study to Evaluate Efficacy and Safety of Peptide Receptor Radionuclide Therapy (PRRT) With 177Lu-Edotreotide Compared to Targeted Molecular Therapy With Everolimus in Patients With Inoperable, Progressive, Somatostatin Receptor-positive (SSTR+), Neuroendocrine Tumours of Gastroenteric or Pancreatic Origin (GEP-NET).

COMPOSE: An international, prospective, randomized, controlled, open-label, multi-centre phase III study to evaluate the efficacy, safety, and patient-reported outcomes of first or second-line treatment with n.c.a. 177Lu-edotreotide PRRT compared to best standard of care in patients with well-differentiated aggressive grade 2 and grade 3 (Ki-67 index 15-55), somatostatin receptor-positive (SSTR+), GEP-NETs.

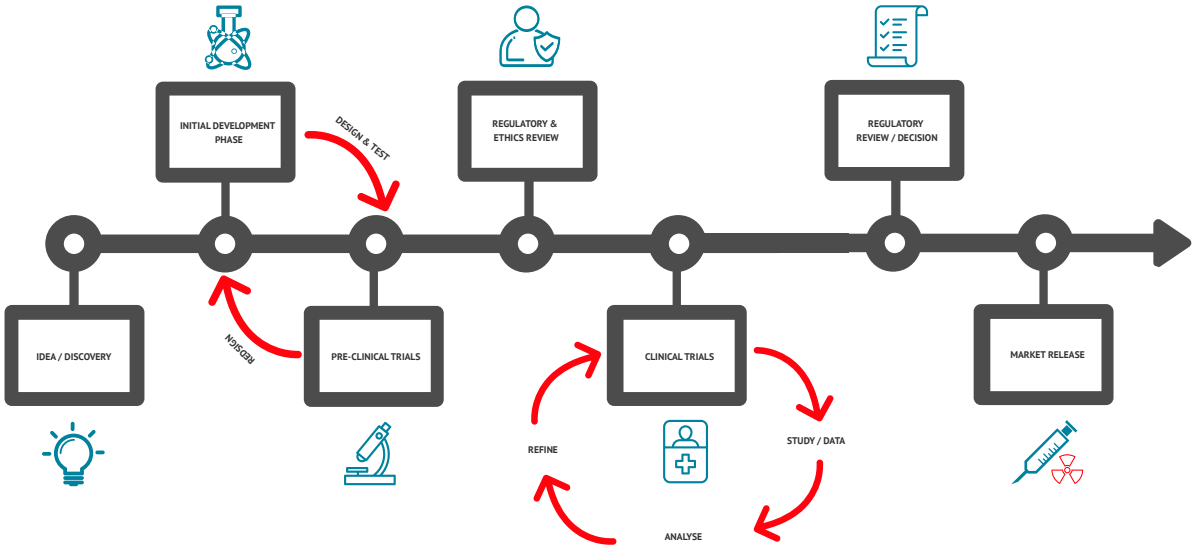
As a global company ITM's long standing relationship with Australia is strengthened through patient advocacy groups including NeuroEndocrine Cancer Australia, key important centres in Radiotheranostics, Key Opinion Leaders (KOLs), clinical trial engagement and strategic alliances. Supply chain access is important and shipment needs to be secured (even in difficult times, COVID) with support from local stakeholders including custom clearance, radioprotection issues and licensing and local authorities.

> We are a high value business…and we are cost effective compared to the US, our clinical trials are 30-50% cheaper to run here. A lot of these international companies have Australian subsidiaries and should also access the R&D tax credit system which can make Australia quite attractive for those trials.
>
> **Rosanne Robinson**
> ANSTO

At the moment the starting material for all radionuclide production in Australia is sourced from overseas, but what we are seeing is this emerging interest in developing business opportunities in taking radioactive waste and turning that in to the starting material for radionuclide production. Turning radioactive waste into starting materials for nuclear medicine is capital intensive but we are well positioned in Australia. We are starting to see mining companies that have radioactive waste try to understand the nuclear medicine market, and whether there is an opportunity. The Australian Government has set up a critical mineral facilitation office as a starting point, to get the engagement with the mining industry.



COMMERCIAL ROLE IN DEVELOPMENT OF THERANOSTICS



The early phase of theranostics production is actually quite a challenge in itself. You may need to look at dose calibration factors that aren't normally considered or a host of new and novel equipment considerations. Moving through the clinical trial phases, these challenges are then compounded in moves to supply to broader market.

The current challenge for Australia comes at phase IIII (true for large-scale cancers like prostate, breast etc but equally for NETs), and these challenges are compounded once rebates start to be applied. This requires not only up-scaled production, but additional TGA/GMP licensing considerations, recruitment challenges and logistical/ supply chain complexities. Generally, the isotopes/ products used in these trials can't be stored long term and have a relatively short expiry, thus any disruptions to commercial airlines, COVID restrictions etc, can make conducting these trials in Australia very problematic if there's a reliance on international supply chains.

Consideration for future concurrent local demand for these products, means that local supply chains need to be secured. Finding redundancy in the supply chains as expanded use occurs is also very important.

If we don't have effective logistics and don't invest in scalable production infrastructure, then maximising supply of these critical radiopharmaceuticals becomes difficult. This needs considered investment now with due consideration for the next 30 years.

> With expanded application and use, a really important point is the inevitable impact of concurrent, increased local demand for these products. Consequently, we have to ensure local supply chains are secure and access to theranostic tracers becomes reliable, with appropriate redundancies built in, as clinical demand increases.
>
> **Matthew Ashton**
> GMS

Siemen's portfolio, spans from in-vitro and in-vivo diagnostics to image-guided therapy and innovative cancer care which is crucial for clinical decision-making and treatment pathways. Siemen's strengths in patient twinning, precision therapy, as well as digital, data, and artificial intelligence (AI), position them to take on the biggest challenges in healthcare. They continue to build on these strengths to help fight the world's most threatening diseases, improving the quality of outcomes, and enabling access to care.

SUPPLY CHAIN, RELIABILITY & REDUNDANCY

SOVEREIGN CAPABILITY

RELIABLE & EFFICIENT LOGISTICS

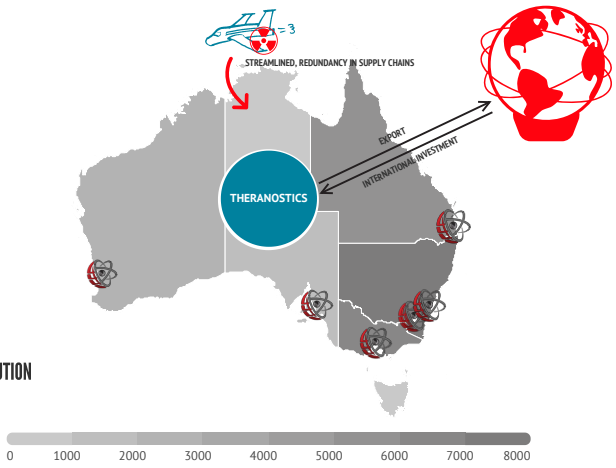
SECURITY & RELIABILITY IN SUPPLY CHAINS

REDUNDANCY IN SUPPLY CHAINS

SCALABLE INFRASTRUCTURE

ECONOMICALLY FEASIBLE PRODUCTION & DISTRIBUTION

PRODUCTION EFFICIENCY - DECAYING ASSETS



WHAT'S NEXT...

INVESTING NOW FOR THE FUTURE

MONITOR & BE GUIDED BY THE SCIENCE

INVESTMENT IN HUMAN RESOURCES

EXISTING FACILITY UPGRADES

INVESTMENT IN NEW SCALABLE INFRASTRUCTUR

MODULAR APPROACH TO PRODUCTION

INDUSTRY ENGAGEMENT IN COST ANALYSIS

SECURE RELIABLE SUPPLY CHAINS

APME

> From an imaging side of things, we have a range of products that can support Theranostics from your corner shop nuclear medicine practice to the top-end academic university hospitals… we need to get the balance right with regional and metro practices.

Christopher Sturla
Siemens Healthineers

According to Siemen's we need to have a "Foundation for Partnership" across research and collaboration; healthcare innovation; education and healthcare delivery. In order to achieve this joint innovation, what is needed is:

- Well defined scope of introducing Theranostic services.
- Development of education partnerships from clinical, pharmaceutical and imaging alliances in Theranostics.
- Continued research and collaboration into new imaging technologies.
- Standardised approaches in Theranostics for the development of products and services.

As a leading medical technology and diagnostics innovator, GE Healthcare enables clinicians to make faster, more informed decisions through intelligent devices, data, analytics, applications and services, supported by its Edison intelligence platform. Within Australia and NZ, GE global appreciates the opportunity to work with the leading clinicians in the field, paired with having access to facilities with the latest technologies such as cyclotrons for diagnostic agents but also treatment agents that are coming online, partnered with the best imaging technologies. GE recognises that the advantages of Australia and NZ include favourable conditions around: digital connectivity; a balanced view on data protection, laws and governance; centralised ethics; and a relatively low-cost base of patient recruitment compared with other countries.

We can improve in some critical areas, COVID highlighted some of those, and some of those things we will never be able to solve locally – like raw materials for every component for every aspect won't be feasible in a country like Australia. What we have done is increased our inventory hold to give ourselves the best chance of meeting those clinical trial requirements that we will need to do. We do need government support, both local and federal to make sure the policy stays based on facts and based on helping the Australian community improve in those areas.

With regards to domestic flights, we can't move goods when those flights don't come through. We also struggle with international freight. It goes beyond the goods and materials, it's expertise that can't also cross geographical borders and a patient is impacted, that slows us all down. COVID saw restriction on flights as well as experts able to travel from overseas and interstate.

State and Federal departments need to work together on nationalising standards. From an engineering perspective there are different radiations standards in each state so the burden of cost, the burden of travel and training that it places on the system at large for us to support trials makes it quite cumbersome and difficult.

Significant delays in the MSAC approval process from moving from a recommendation to a policy to actually getting into policy, it has long lasting impacts both to the patient, their family and friends and the economy at large.

> "Infrastructure and education are the most important…we have to work out a way to get infrastructure and policy national, not state based, that is critical…education from a perspective of where can it be used, where should it be used and in which patients.

Amit Yadav
GE Healthcare

Key Points:

1. Investment in decaying assets and infrastructure.
2. Need secure and strategic supply chains- domestic and international flights.
3. National standards across states and territories from engineering, manufacturing to production.
4. Faster access through MSAC from recommendation to policy.

Equitable Access - HTA framework “time for a rethink?”

Current Theranostics regulatory environment

The current HTA framework encompasses MSAC, PBAC, TGA and PLAC. The application process for approval and reimbursement involves market regulation processes and production – an issue with Theranostics is it has a “just-in-time supply chain” which is dependent on having good infrastructure for production. If there is missing infrastructure in Australia, then production can be affected and then there is a need for sourcing overseas supplies.

> “No one should be left behind, you should not be disadvantaged if you have a common cancer nor disadvantaged if you have a rare one.
>
> **Prof Robyn Ward**
> MSAC

The role of Medical Services Advisory Committee (MSAC) is to inform the Federal Health Minister about services in the context of funding, cost effectiveness and financial impact. MSAC assesses the Medical Benefits Scheme (MBS) and screening programmes, high-cost therapies, blood and blood related products to name a few. In the last year MSAC updated its guidelines (as the guidelines had been previously very segmented) and is now inclusive of technology guidance. Theranostics within HTA framework would be classified as “co-dependent technology”, whereby MSAC works with PBAC and prosthesis listing committee. MSAC assesses value and value for money with the importance of patient relevant outcomes. Importance is also placed that new interventions are available when needed including from the patient’s perspective. MSAC is now assessing genomic technology and CAR T-cell and believes it is fit for purpose to assess these very new technologies.

The Therapeutic Goods Administration (TGA) has the following avenues for review:

- Orphan Drug Status
- Priority Review (150 days)
- Comparable Regulator review (120 days)
- Project Orbis - is an initiative of the FDA’s Oncology Centre of Excellence that provides a framework for the collaborative review of promising new cancer treatments among international regulatory partners. It aims to give patients faster access to promising cancer treatments across the globe.

The TGA is actively reviewing using real world evidence and engaging stakeholders about how to use these patient reported outcomes.

When asked Adj Prof Skerritt believes that any of the above registration pathways will be able to cope with any submissions coming down the pipeline.

The TGA works on a 100% cost recovery model. TGA spoke of potential for more incentives for companies such as fee waivers and discounts, also repurposing for patients. Overseas there are schemes (FDA, North America) which can look at industry fees and cost recovery. This could be a consideration and decision made by Australian government.

The AANMS position statement provides recommendations for the care of patients receiving radiopharmaceutical therapy which supports safe, high quality, targeted care by qualified professionals in this area. The recommendations “include but are not limited to: identifying the optimal workplace and facility requirements, specialist training requirements, patient work flow and MDT requirement.” For Theranostics to be utilised a trained and accredited multidisciplinary workforce is essential. This position statement applies to any HTA approvals.

> “Australia has a flexible model for access where local manufacture, in the hospital setting does not require TGA GMP, however, the TGA is always open to TGA regulated products.
>
> **Adj Prof John Skerritt**
> Dept of Health

Cancer Australia has the role to improve outcomes of people in Australia and reduce the burden, which is largely provided through education. Australia has the best outcomes for cancer in the world. There are areas which are not ideal and this includes rural and remote, Aboriginal and Torres Strait Islanders, some less common and rare cancers. Cancer Australia works in partnership with PBAC and MSAC. Optimal Care Pathways (OCPs) will form the central core to the Australian Cancer Plan and Cancer Australia welcomes new ideas and works with the balance of what is possible and fair.

HTA processes have taken into account less common / rare cancers and the committees are attuned that these cancers should not be disadvantaged. This has been seen in PET scanning and generic review to address rare / less common cancers and improve access for these cancers.

In the case of Theranostics, which is classified as co-dependent (diagnostic and therapeutic), it then goes to Medical Benefits Department (MBD) and works with the craft group (for instance AANMS). An item descriptor and fee for service is decided which includes cost of consumable for this service. This process is done in tandem with MSAC so it can be implemented as soon as possible. Services are funded through MBS and also can be through public hospitals by national health reform agreement.

> “Theranostics is very important, especially for NETs and aligns with the newly created Optimal Care Pathway… These Optimal Care Pathways will form the basis of the Australian Cancer Plan.
>
> **Prof Dorothy Keefe**
> Cancer Australia

Solutions and Next Steps

Since the Roundtable, the Committee that Dr Mike Freelander co-chaired has reported its findings and there are opportunities for the Theranostics community in their recommendations as well as upcoming reviews.

The New Frontier - Delivering better health for all Australians- Inquiry into approval processes for new drugs and novel medical technologies in Australia was released in early December 2021. The inquiry focused on the approval processes for new drugs and novel medical technologies in Australia – regulatory and health technology assessment processes. Many involved in the Theranostics roundtable submitted responses to the inquiry in November 2020 and appeared at public hearings. While it addressed the medicines and medical technology approval processes and reimbursement, looking for more streamlining and simplification/transparency, it also addressed the need for a national approach to clinical trials, supporting the national platform, reformed ethic approvals and a national Clinical Trials register.

The report handed down 31 recommendations and this report will focus on those relevant to the discussion from the roundtable.

Recommendation 1:

Committee recommends the Australian Government **establish a Centre for Precision Medicine and Rare Diseases** within the Department of Health.

- The objective of the Centre should be to ensure that the capacity of the Department of Health is enhanced to provide Australians with timely access to new drugs and novel medical technologies, including for rare diseases, and that the HTA process and government research agenda aligns with this outcome.
- The Centre should provide advice to the Department of Health and the Australian Medical Research Advisory Board on research priorities.
- The Centre should provide education and training information including support for patients and a comprehensive horizon scanning unit for new medicines and novel medical technologies.
- The Centre should provide advice to governments on the establishment of a dedicated regulatory Health Technology Assessment pathway for cell and gene technologies, in consultation with state and territory governments, industry, patients and other relevant stakeholders.
- The Centre should regularly provide advice to government on the effectiveness of those pathways and areas for further reform.

Recommendation 3:

Recommends the Australian Government establish an **Office of Clinical Evaluation** within the Department of Health to assess the best and most effective care for patients in the context of new and emerging health technologies.

- The Office should enable evaluation of both pharmacological and non-pharmacological interventions, combination products and products with different sponsors. It should also establish a "living evidence" function to ensure Health Technology Assessment is based on the most up-to-date global health practices.
- The Office, in consultation with relevant stakeholders, should conduct a review of how the Department's Health Technology Assessment system assesses combination products, particularly combinations with different sponsors, with a focus on:
- Value attribution between the different products.
- Challenges to cooperation between sponsors due to competition law.
- Disincentives for a sponsor with an already listed product to participate in its combination listing.
- The Office should consider collaboration with the National Institute for Health and Care Excellence (NICE) in the United Kingdom to establish similar clinical evaluation processes in Australia that links in with Australian Health Technology Assessment processes.
- The Office should cooperate and share information with the state and territory governments to ensure that patients receive treatment where it is safest and most efficacious for them and that there are no gaps in continuity of care.

Recommendation 8:

Recommends that the Australian Government make the following changes to submission fees for the Therapeutic Goods Administration (TGA) and the Pharmaceutical Benefits Advisory Committee (PBAC) and where appropriate Medical Services Advisory Committee (MSAC) assessments in the following separate circumstances:

- Replace the current orphan drug fee waivers with a HECS-style fee waiver, in which orphan drug application fees are payable on successful application, only once the drug has earned the sponsor a certain amount of revenue. The Department of Health should determine this threshold value in consultation with industry.
- To support smaller companies, HECS-style fee waivers for any sponsor company with revenue at or below $50 million per annum.
- HECS-style fee waivers for Australian start-up companies with a specified amount of revenue in the Australian market to promote innovation.

The Committee also recommends introducing a sliding scale for fees for resubmissions, with fees being lower for resubmissions.

Recommendation 9:

Recommends that the Australian Government establish a fund to support patients, clinicians and non-profit organisations to sponsor registration and reimbursement applications where there is no realistic prospect of a company serving as sponsor, and where the Department of Health is otherwise supportive of the application.

Such a fund should be targeted at treatments for conditions where low patient numbers in Australia serve as a market barrier and where there is a clinical demand and need.

- The fund should be available for applications to repurpose previously listed medicines and technologies.
- The fund should be annually capped with clear and transparent eligibility rules.

Recommendation 13:

The Committee recommends that the Department of Health reform its regulatory and reimbursement processes to enable therapeutic goods to be registered and reimbursed by molecular indication in addition to by disease indication. This should include legislative change if necessary.

Recommendation 27:

Recommends the Australian Government reform data exclusivity provisions in Australia with a view to extending data exclusivity for orphan drugs and vaccines to a period of up to 10 years. The Australian Government should:

- Develop additional reforms to data exclusivity time frames to support research and development into new drugs and novel medical technologies in areas of unmet need.
- Consider future funding initiatives for novel drug discovery and support research and development partnerships in Australia. This would assist new drugs and novel medical technologies in early stage and pre-commercial development.
- In partnership with the states and territories, develop and implement a pilot scheme for value-based payments for new antimicrobial drugs. This pilot should apply the lessons learned from the Australian Government's pilot scheme for payment for Hepatitis C drugs, as well as from overseas antimicrobial drug schemes.
- Promote the recent research and development tax initiatives internationally as a way of encouraging industry to look to Australia for future investments in the healthcare sector.
- Conduct a full review of the patent box scheme every two years after implementation to ensure it is operating effectively and driving increased expenditure and innovation within Australia.
- Collaborate with the states and territories to review the funding of the research and development sector in health care to distribute funding in a methodical way that provides sufficient support throughout the research funding 'pipelines'.
- Noting the work underway through the Modern Manufacturing Program, the Committee supports the development of an updated roadmap to facilitate the manufacturing and commercialisation of novel drugs and technologies in Australia.

Recommendation 28:

Recommends that:

- The Department of Health integrate the patient voice upfront into the Health Technology Assessment system. Earlier patient engagement with the Health Technology Assessment system would include:
- Representation from peak patient bodies that is refreshed every three – five years.
- Representation of Aboriginal and Torres Strait Islander Peoples.
- The Department of Health implement a notification system for all HTA bodies and the TGA to advise relevant patient groups of the receipt of an application.
- The Department of Health provide patients and stakeholders with a concise sponsor's submission summary to help facilitate their own involvement in the Health Technology Assessment process.
- The Department of Health should consider making patient evidence compulsory for certain applications, and should consider the role of patient evidence in the decisions of the Therapeutic Goods Administration.
- The Department of Health should notify relevant patient groups of the outcome of the assessment process by all HTA bodies.
- The Department of Health be funded to implement these recommendations.
- The Australian Government provide funding for organisations to support participation in the HTA process, including for very rare disease patient groups that have limited capacity for fundraising or access to alternative funding.

Recommendation 29:

Recommends that:

- The Committee recommends that the Australian Government amend the National Health Act 1953 (Cth) to formalise the role and powers of the Pharmaceutical Benefits Advisory Committee Executive. The scope of the Executive's role and powers should be determined by agreement between the Executive and the Department of Health.
- The Department of Health produce a pre-submission advice framework for submissions to the Therapeutic Goods Administration, Pharmaceutical Benefits Advisory Committee, Medical Services Advisory Committee and other Health Technology Assessment bodies, explaining the interaction between those bodies and their evidentiary and other requirements, to be provided to sponsors before they make their submissions.
- The independent Health Technology Assessment Review reassess relevant aspects of the Health Technology Assessment process to ensure there are future pathways for treatments and therapies that do not fit neatly into the current system such as rare cancers, antimicrobials, orphan drugs, and precision medicines.
- It is imperative that appropriate clear pathways are considered for inclusion for paediatric medicines and technologies.
- The Committee is of the clear view that precision medicine approval pathways will require a different application assessment than current approaches designed for treatments for common conditions, with large data sets and comparative evaluations.
- The Department of Health publish data on application processing times and positive recommendation rates for the Pharmaceutical Benefits Advisory Committee and other Health Technology Assessment bodies.

In addition:

- The Department of Health should publish Health Technology Assessment processing times annually, benchmarked against other nations with advanced HTA processes.
- The Australian Government, in collaboration with relevant stakeholders, develop a suite of clear and measurable benchmarks to track the Commonwealth's implementations of the recommendations made by the Committee and accepted by the Australian Government.
- These agreed benchmarks along with measurable KPIs/metrics should be developed in such a way as to best facilitate the Department of Health, including its agencies and other relevant statutory bodies, in the tabling of an annual update to the Australian Parliament.

Recommendation 30:

Recommends that the Australian Government's **independent Health Technology Assessment Review (which is scheduled to commerce in July 2022)** consider and develop reforms in the following areas:

- Reducing the frequency and need for applications to HTA bodies to be resubmitted.
- Streamlining the interaction between hospitals and the Health Technology Assessment system.
- Streamlining the interaction of the Therapeutic Goods Administration, the Pharmaceutical Benefits Advisory Committee, the Medical Services Advisory Committee and other Health Technology Assessment bodies.
- Cooperation and harmonisation between Australian Health Technology Assessment bodies and equivalent bodies overseas.
- Improving the measurement of the performance of the Pharmaceutical Benefits Advisory Committee and the publication of data on that performance.
- Improving the mechanisms for communication between sponsors and the Pharmaceutical Benefits Advisory Committee during the submission process.
- Increasing the use of Managed Access Programs to facilitate earlier access to innovative medicines.
- Increasing the use of Real World Evidence in Health Technology Assessment.
- Improving flexibility when choosing a comparator in Health Technology Assessment.
- Introducing a scoping process that includes patients and clinicians at an early stage to agree on the framework that the submission will be considered. This process could draw on the approach taken by the United Kingdom's National Institute for Health and Care Excellence.
- Improving the independent review process for HTA decisions, including the potential for this to be made available to groups of patients and clinicians in addition to sponsors.

Recommendation 31:

Recommends that:

- The Department of Health should consider, in consultation with state and territory governments, industry, patients and clinicians, the introduction of fees for Medical Services Advisory Committee applications on a cost recovery basis, if this is necessary to increase the speed and effectiveness of assessments. If fees are introduced they should have similar features to those recommended by the Committee for Pharmaceutical Benefits Advisory Committee fees (including those arrangements outlined at Recommendation 8).
- The Medical Services Advisory Committee increase the involvement of clinicians in its assessments of technologies with which its members lack relevant expertise.
- The Department of Health introduce an equivalent to the Managed Access Programs for medical devices. The details of this scheme including eligibility criteria and duration should be formulated in consultation with patient groups, clinicians and industry.
- The Therapeutic Goods Administration introduce parallel processing of applications with the Medical Services Advisory Committee.
- The Medical Services Advisory Committee increase opportunities for sponsors of particularly complex applications to present to it at its meetings and expand the opportunities for pre-submission meetings.
- The Medical Services Advisory Committee consider developing international collaboration for complex assessment proposals.
- The Department of Health expand the independent Health Technology Assessment Review in July 2022 to include Medical Service Advisory Committee processes.
- The Medical Services Advisory Committee publish a full calendar time line of meeting agenda and outcomes, including dates when minutes and Public Summary Documents will be made public.
- The Medical Services Advisory Committee publish additional guidance for sponsors of digital health technologies.
- The Department of Health establish a benchmarking system for MSAC assessments, including benchmarking against comparable overseas organisations.

Next Steps

The first National Theranostics Roundtable brought together all stakeholders in the nuclear medicine community including researchers, clinicians, industry, societies, government and most importantly the Australian cancer patient.

In order to maintain the collaborative momentum and ensure that Australia leads the way in precision oncology in nuclear medicine, the author recommends the following next steps:

- As a collective put forward suggested "terms of reference" for the **Health Technology Assessment review** set begin in July 2022, including the addition of MSAC to the review. Put forward submissions to the review.
- As a collective engage in the **National Medicines Policy review.**
- Hold a **Theranostics Horizon Scanning Workshop** in 2022 with the recently elected Federal Health Minister and health department, health technology assessment bodies, as well as representatives from the department of finance, department of industry, science, energy and resources and critical technologies policy coordination office. From this create a policy piece on the future of Theranostics in Australia.

The Theranostics Roundtable committee would like to thank all those speakers who participated on the day in particular **Paul Cross (BioPharma Dispatch)** who did a wonderful job of moderating each session, asking the questions and engaging with everyone to get the best discussions on the day, as well as **Mark Butler MP (then Shadow Minister for Health and Aging, now Health Minister)** for his interest not only in Neuroendocrine Tumours but in Theranostics, where it is at now and into the future. Most importantly we would like to thank **Lynda Dunstone**, a Neuroendocrine cancer patient for sharing her experience from diagnosis and living with an incurable cancer and her reliance on Theranostics to provide good quality of life.

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