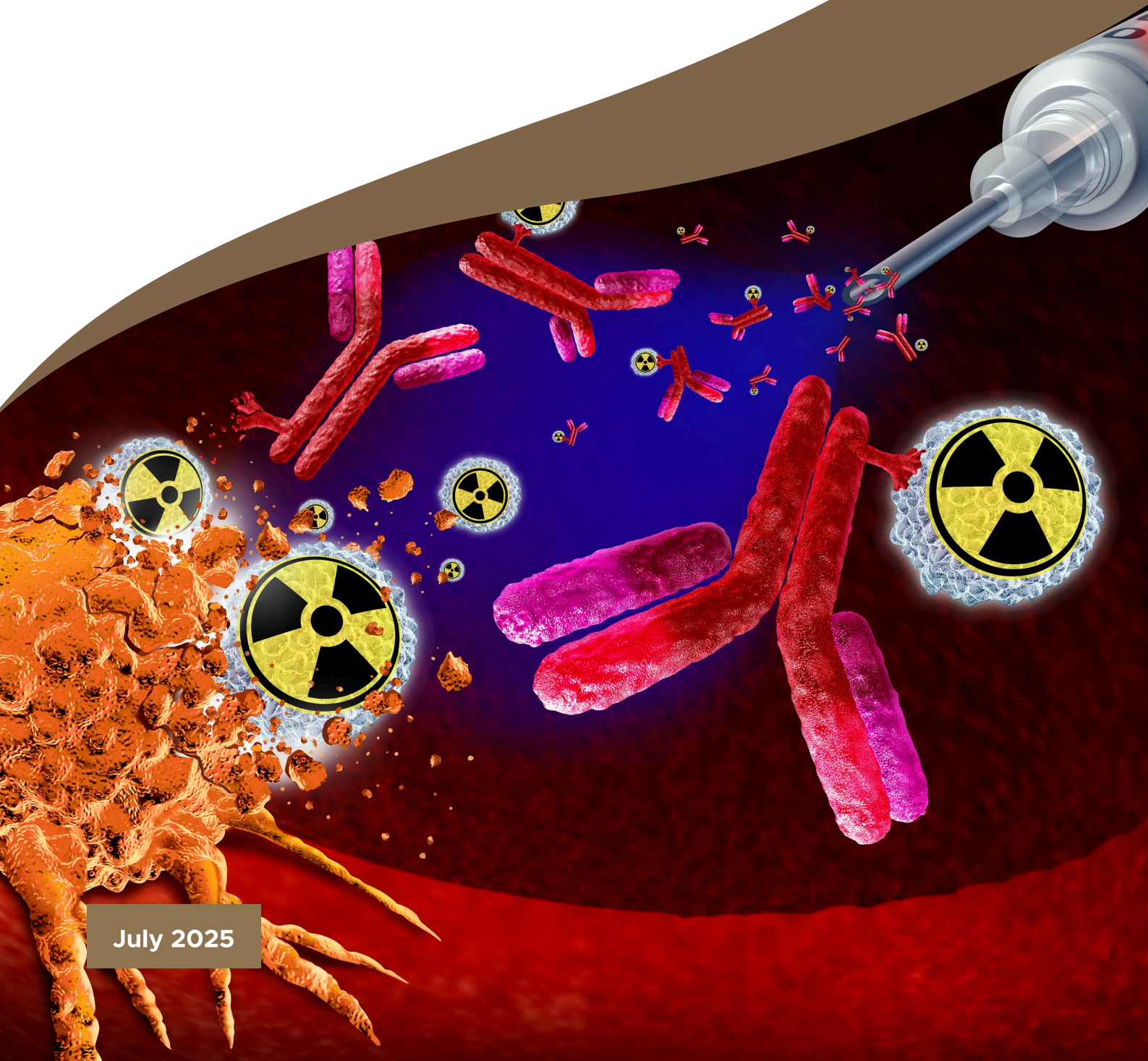




WS AMATI GLOBAL INNOVATION FUND

Innovation Frontier

Radiopharma



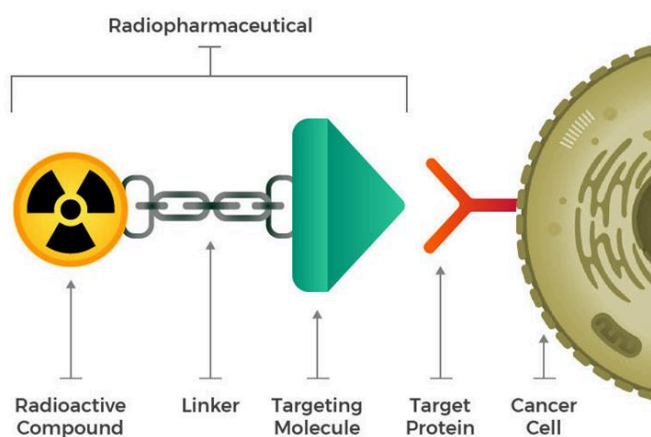
July 2025

Radiopharma



Written by
Dr Gareth Blades

Radiopharmaceuticals are a form of precision medicine, but in this case it's precision medicine gone nuclear. They deliver a radioisotope, a radioactive element, only to a specific target. In the case of a cancer treatment, they are used to light the tumour up to see it (radiodiagnostic) or to deliver enough radiation to kill it (radiotherapy).



National Cancer Institute:

<https://www.cancer.gov/news-events/cancer-currents-blog/2020/radiopharmaceuticals-cancer-radiation-therapy>

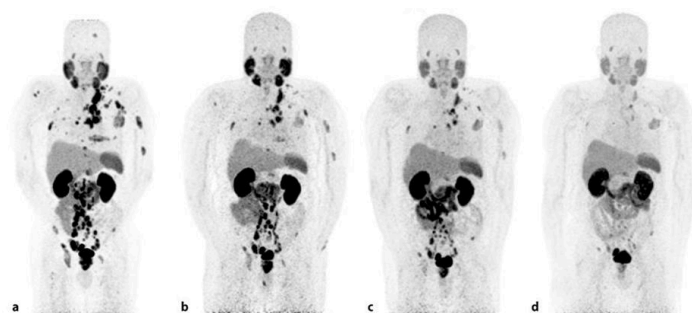
Their structure is like a missile and a warhead, the warhead is the radioactive isotope and the missile is a molecule, like an antibody, that only homes in on its target. The emitted radiation then accumulates only at the tumour site.

The advantage of this approach is that even when the cancer spreads, the missile can still find it and deliver the warhead because of its binding specificity. As a result, patients can experience lower toxicity and lower side effects from higher doses of radiation leading to improved survival rates and better outcomes.

Therapeutics

While this is an emerging field still in a relatively early stage of its growth runway,

radiotherapeutics are already being used to great effect in the treatment of advanced, or metastatic, prostate cancer. Pluvicto, from Novartis, is an example of this. It has shown such excellent results that Novartis has successfully applied to move it earlier in the treatment schedule. This is like moving from economy to business class for a drug. This opens up a new patient pool, increases the demand from treatment centres and boosts manufacturing capacity, thus acting as a catalyst in this space.



National Cancer Institute:

<https://www.cancer.gov/news-events/cancer-currents-blog/2021/prostate-cancer-psma-radiopharmaceutical-vision>

For the treatment of prostate cancer, dark spots highlight the location of radioisotopes. Across pictures a-to-d the tumour burden in this patient is easing over the treatment duration by using Pluvicto.

Diagnostics

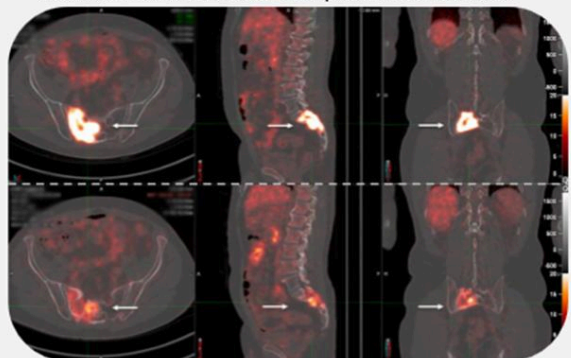
We've jumped the gun here in focusing on a radiotherapy. Before a radiotherapy can be administered patients need a confirmatory PET scan with a radiodiagnostic. PET (positron-emission tomography) is an imaging method, like an x-ray, but instead detecting radiation. The combination of radiodiagnostics with radiotherapy is known as theranostics - catchy.

What radiodiagnostics enable is a clear and definitive picture of cancer. Radiodiagnostics

are thus the gatekeepers of treatment. You can see this in the image above of Pluvicto treatment. What the PET scan is picking up is a radiodiagnostic that is "lighting up the tumour".

These definitive and clear images of cancer are novel. Our due diligence indicates that doctors are keen to leverage this new capability. They are adding more PET scanning sessions per week and planning to buy additional PET machines to accelerate patient throughput. There is growing demand for, and awareness of, these more precise diagnostics and treatments, which will only increase as the market develops further.

TOP: ^{89}Zr -girentuximab PET/CT at baseline showing uptake in a sacral metastatic lesion in a patient with ccRCC.



BOTTOM: ^{89}Zr -girentuximab PET/CT after three cycles of therapy.

Telix Pharmaceuticals investor presentation

A key pioneer in this innovation frontier is Australian listed Telix Pharmaceuticals. It has one of the leading radiodiagnostics for prostate cancer, with a second generation version approved and launched. It's developing a broad pipeline of late stage radio diagnostics and promising radio therapies. These are focused on areas of high unmet needs such as kidney and brain cancer. Following a theranostic approach of having diagnostics paired with therapy for the same target.

A unique part of Telix's business model is vertical integration. Through organic growth and acquisition, it has built capability in research, discovery and development to build a pipeline of medicines and imaging agents. It has secured supply and can even generate isotopes itself. Finally, it is combining missiles and warheads and

delivering these as finished doses to patients via its radiopharmacy network. (These are like normal pharmacies, but they dispense radioactive products). Due to this vertical integration Telix has additional resilience and revenue streams compared to its peers.

What about manufacturing and getting radioactive drugs to patients?

Starting material can be hard to reliably come by and manufacturing can be challenging. For example, global pharma giant Bristol Myers Squibb ran out of supply for its Phase III ACTION-1 trial and halted recruitment. Novartis ran out as it ramped commercial supply of Pluvicto in 2023 because it struggled to get a manufacturing site up and running. This makes reliable supply and manufacturing a valuable part of the value chain for this innovation frontier.

Supply is a key issue and the industry consensus is that there isn't a huge amount of it. Part of the supply dynamic is the low abundance of naturally occurring raw material combined with the typically short half-life of medical isotopes (often just days), the high fixed costs of manufacturing sites, and a shortage of highly skilled labour.

A German listed enabler, **Eckert & Ziegler**, is a leading manufacturer and supplier of both the finished drug and isotopes for diagnostics and therapeutics. It is a rare global-end to-end service provider from production to waste management.

Such is the demand for these rare elements and skills, Eckert & Ziegler has been able to sign long term supply contracts ahead of proving scaled production. The company has the number one position supplying the isotope for the leading radiodiagnostic imaging agent for prostate cancer with its "GalliaPharm" product.

This coffee machine sized box has a shelf life of 18 months and rather than brewing coffee, it brews radioactive Gallium. When this is combined with a targeting molecule (missile) it generates a radiodiagnostic. Due to its rapid decay once created, it has to be sped to PET imaging centres in under an hour. Efficiency in logistics is therefore important

and a key reason why Telix Pharmaceuticals acquired a radiopharmacy network.

Efficiency in logistics is therefore important, and a key reason why Telix Pharmaceuticals acquired a radiopharmacy network.



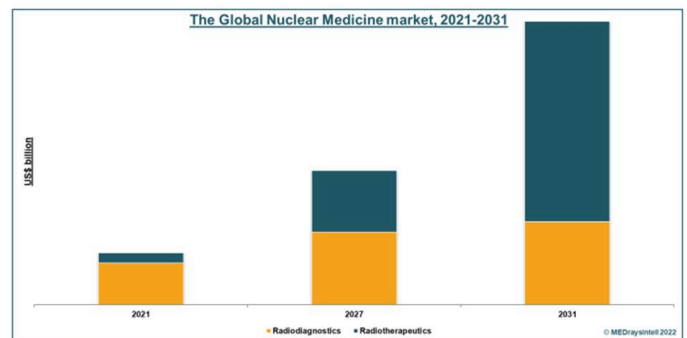
Eckert & Ziegler marketing materials

Manufacturing competition is fragmented and can be niche, from individual biotechs developing their own manufacturing facility such as Rayze Bio (now owned by Bristol Myers Squibb) and individual Pharma manufacturing such as Novartis for Pluvicto. Some suppliers are focused on a single isotope, such as PanTera for Ac-225. Companies with the breadth of Eckert & Ziegler are few and far between.

Market

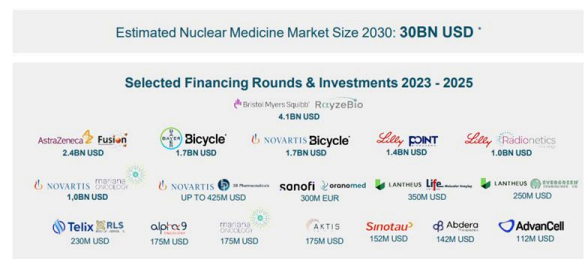
The market for nuclear medicine (both diagnostics and therapeutics) is large and growing, worth ~\$6bn in 2021 and expected to rise to \$30bn-\$35bn by 2031. Therapeutics only make up around 20% of the market value today, with 80% being diagnostics. By 2031 this will flip, with therapeutics estimated to comprise 70% according to market researcher, MedRays. This will be driven by progression of the industry's pipeline, which comprises hundreds of development programmes

according to MedRays. While this shift to therapy doesn't create new patients, what it should mean over time is a move earlier in the treatment journey, as with Pluvicto, which unlocks new pools of patients that diagnostic agents can't do alone.



MedRays

The Nuclear Medicine Market – Development and its Pillars



*MedRays Intel 2020

Eckert & Ziegler, earnings presentation May 2025.

This market research is supported by financing and M&A activity, which totalled more than \$15.6bn since 2023. The industry has seen private funding rounds and consolidation but has also attracted large pharma interest. In the end, whether it is commercial success or acquisition by large pharma, the prize for success is a large one.

The radiopharmaceutical frontier is still in a nascent stage; we are looking forward to seeing it grow and develop and are excited about the patient impact as new therapies and diagnostics are approved and come to market. We own both Telix Pharmaceuticals and Eckert and Ziegler in the WS Amati Global Innovation Fund.

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Should you have any comments, questions or feedback on any of the topics covered, please don't hesitate to contact our investor line on 0131 503 9115 or email

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