

# Radiotheranostics Momentum

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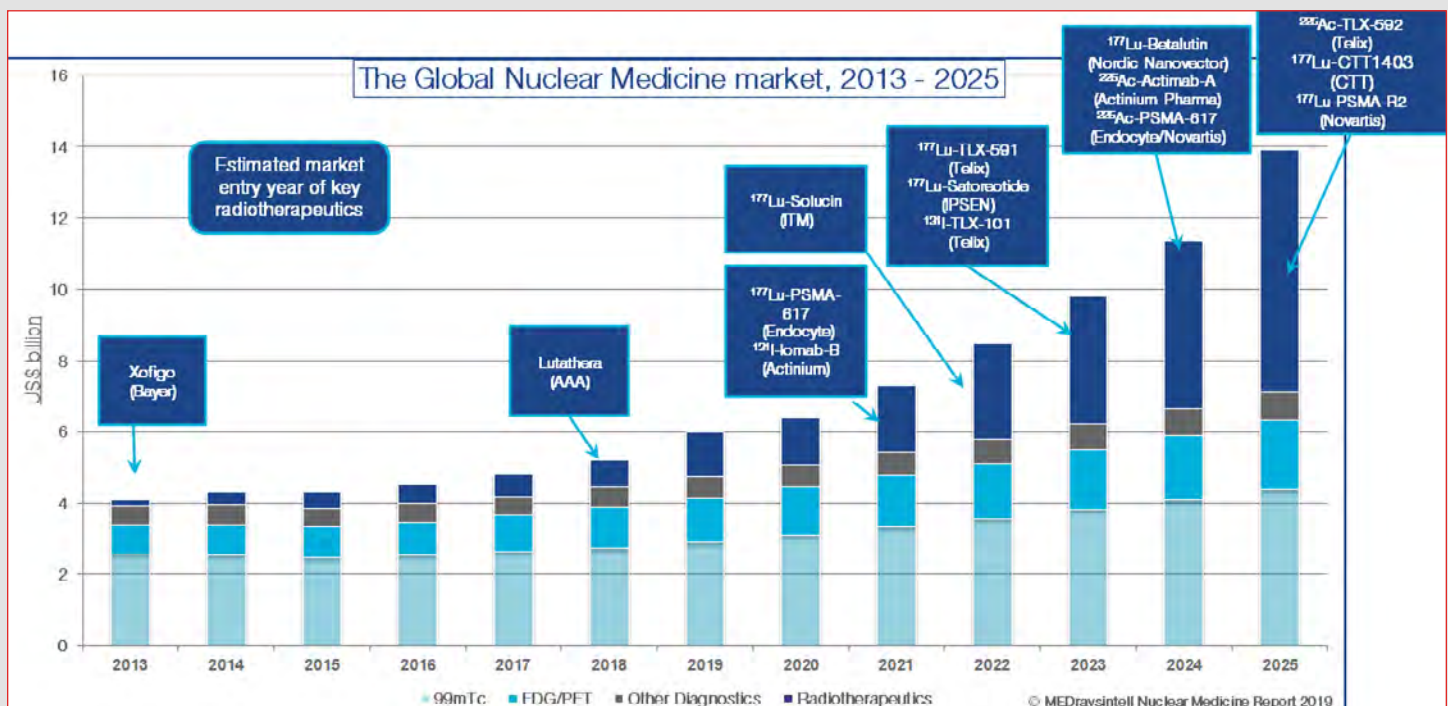
Back in 2011, the availability of radiolabeled drugs for therapeutic application was limited, hence generating the idea of The Oncidium foundation dedicated to the promotion of Radiotheranostics for cancer therapy. But what is it about? These are molecules that can safely carry radioactive isotopes inside targeted human tissues and help physicians get accurate images of tumors, allowing them to more effectively and precisely eliminate cancer cells. At that time, the availability of Radiotheranostics was limited to <sup>131</sup>I-sodium iodide for thyroid cancer treatment, <sup>131</sup>I-Tositumomab (Bexxar) and <sup>90</sup>Y-Ibritumomab tiuxetan (Zevalin) for non-Hodgkin lymphoma therapy, next to several radioactive pain

palliation treatments including samarium-153 or strontium-89 salts. However, the pipeline of radiolabeled drugs under clinical development started to be quite interesting, based on two major technical progresses: on the one hand a very interesting beta-emitter radionuclide for therapy became industrially available, namely Lutetium-177, while on the other hand, the concept of Radiotheranostics became more and more of interest to scientists and physicians.

This concept of Radiotheranostics, already implemented during the development and the application of Bexxar and Zevalin, was simply based on the successive use of a molecule allowing physicians

to select patients that are almost guaranteed to be positive responders to a therapy, followed by the treatment of the patient with the therapeutic form. In Radiotheranostics, the technology allows use of the same molecule targeting a specific tissue or biological mechanism (the vector), to which a gamma or positron emitter is attached respectively allowing SPECT or PET imaging, and upon positive biodistribution, using the same molecule in which the imaging radionuclide is replaced by a particle emitting beta or alpha radionuclide with the aim of destroying these identified cell masses. In other words, Radiotheranostics are pairs of molecules, to see the disease, to decide the treatment, and to destroy

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these tumor masses. The concept of Radiotheranostics was enlarged to a combination of imaging followed by other non-radioactive therapies, of any type, including of course chemotherapy but also (guided) surgery or external radiotherapy. On this basis, Theranostics will not only reduce considerably the patient population needed to complete the trials, and of course the costs of drug development, but also reduce the healthcare expenses by limiting the application of expensive drugs to those who will really benefit from it.

By 2011, several Radiotheranostics were under development, unfortunately with limited budget for late stage development. Only the company AAA with its NET treatment targeting molecule  $^{177}\text{Lu}$ -DOTATATE was at an advanced stage with sufficient funds. Big pharmas started to be interested in these molecules only at that stage when it became obvious that the authorities will not accept much longer molecules that are efficient only for a limited number of patients, but still prescribed to all of them, even non-responders, in absence of alternative solutions. Bayer was the first company investing heavily in a radiolabeled drug ( $^{223}\text{Ra}$ -Xofigo<sup>1</sup>). Although it is not considered a Radiotheranostic, the blockbuster potential of the molecule triggered the interest of other companies. Novartis spent several billions to acquire two other molecules,  $^{177}\text{Lu}$ -DOTATATE, which came on the market in 2018 under the name Lutathera, and  $^{177}\text{Lu}$ -PSMA-617 for metastasized prostate cancer therapy, that could reach the market by 2021. Both molecules are associated with their diagnostic/

patient selection analogue labeled with Gallium-68 for PET imaging.

This success initiated the race for radiolabeled drugs, and nowadays more than half of the top 20 big pharmas have acquired assets in this field or are performing research involving radiolabeled substances, including Roche, J&J, AstraZeneca, GSK, Merck, Pfizer etc. Moreover, some companies entirely dedicated to the development of Radiotheranostics, such as Telix Pharmaceuticals, have been founded over the past three years. Nowadays, in this field more than 20 startups have been created in the world since 2018 with all the potential of AAA.

In terms of drugs (radiotherapeutics), all of them associated to their diagnostic equivalent, it appears that almost all indications are presently covered, and more than 28 molecules are under clinical development with a chance to reach the market before

2026. Most of them are based on  $^{177}\text{Lu}$ , usually associated to  $^{18}\text{F}$ ,  $^{68}\text{Ga}$  or  $^{89}\text{Zr}$  for imaging. The present trend is to use also alpha-emitters such as Actinium-225, which easily replaces  $^{177}\text{Lu}$  in the same molecule for a higher efficacy or an alternative for non-responders to  $^{177}\text{Lu}$ . A successful new approach is to perform tandem therapy in which  $^{225}\text{Ac}$  and  $^{177}\text{Lu}$  labeled drugs are co-injected.

Since creation of the Oncidium foundation, the technology has considerably improved with a high number of Radiotheranostic pairs expected to reach the market. But there is still a lot to do to raise awareness among physicians, oncologists and the general public about this new therapeutic approach, which remains the aim of Oncidium.

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1. Developed for the treatment of patients with castration-resistant prostate cancer (CRPC), symptomatic bone metastases and no known visceral metastatic disease.



*“Before believing in the Foundation, I strongly believe in the technology. But for a technology to be accepted by the largest number, one has first to push and develop this message to the largest number. Therefore, I believe in the important role of a Foundation that can promote a technology with an incredible potential that will benefit this large number.”*

Richard Zimmermann  
President and Founder of the Oncidium Foundation  
Co-Founder of MEDDraysintell



*The Oncidium foundation focuses on promoting Radiotheranostics for cancer therapy and providing support to advance the availability of this innovating and life-saving technology, worldwide. The foundation's priorities include raising awareness about Radiotheranostics among patients, oncologists, practitioners, and the general public, investing in research and scholarships, supporting the development of new radiopharmaceuticals for therapy, supporting clinical best practice, and ultimately improving access to patients.*