Radiotheranostics Today

Oncidium foundation

Voicing the Challenges and Opportunities of Radiotheranostics for Cancer Care

February, 20th 2025

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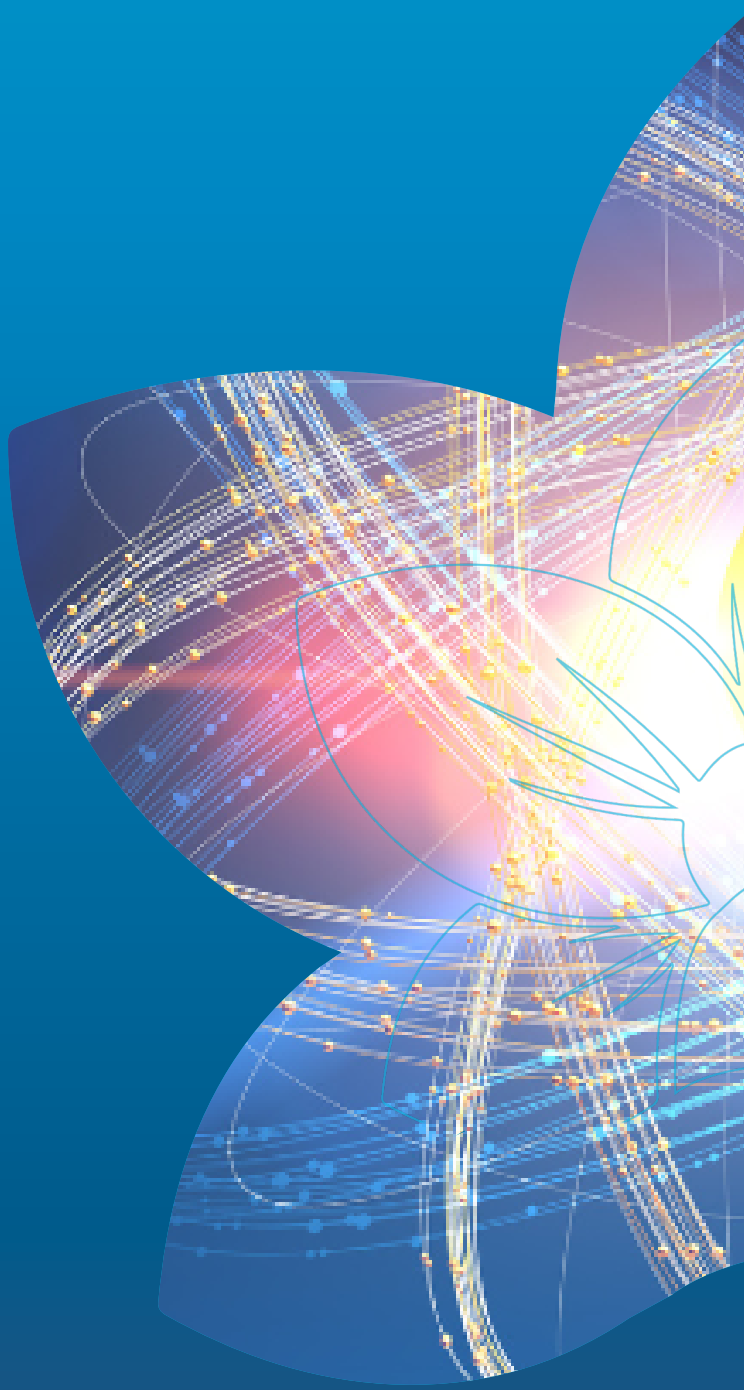

Full Speed Ahead: A Dynamic February!

February is an important month, marked by World Cancer Day on February 4th. This year's theme, "United by Unique," emphasizes placing people at the center of care and their stories at the heart of the conversation.

This principle strongly resonates with the Oncidium foundation's mission and actions, particularly in the field of personalized medicine, where every case is unique and we are united around this shared commitment to support individuals living with cancer. In this review, you will hear diverse voices sharing different perspectives but echoing the same message: we must come together to shape the future of cancer care.

Whether through increased efforts to expand Access, ensuring broader availability of radiotheranostics, upholding GMP standards for quality, safety, and excellence, or prioritizing Education through continuous learning for all stakeholders, collaboration is key. Passionate debates spark new ideas for the future of radiotheranostics, reinforcing the need to unite healthcare professionals around a common goal: providing the best possible care for people living with cancer. Last but not least, by listening, learning, and taking action, we amplify stories of Hope, no matter who or where they come from.

From challenges to opportunities, awareness to readiness, explore what Oncidium's voices have to say about advancing Radiotheranostics Today.

Ready to talk radiotheranostics with Oncidium foundation?

- **Zoom on the radiotheranostics situation in your country**
- **Evolution, projects and challenges in your region**
- **Focus on a particular application**
- **Patient/practitioner interview etc.**

Contact us to contribute to the next edition!

Advancing Alpha Therapy: Dr. Tadashi Watabe on Astatine-211 and its Promise for Patients

January 29th, 2025

Professor Tadashi Watabe is an Associate Professor of Radiology at Osaka University and Principal Investigator for clinical trials on targeted alpha therapy using astatine (^{211}At). His research focuses on developing novel theranostics for cancer, including trials for thyroid and prostate cancer, as well as radiotracers like FAPI and PSMA. In this interview, Professor Watabe joins Dr. Cristiana Gameiro, Scientific Advisor at the Oncidium foundation, in a discussion focusing on the advancements, challenges, and future potential of Astatine-211 in alpha therapy, highlighting its clinical applications, production advantages, and impact on patient care.

Dr. Cristiana Gameiro: *Dr. Watabe, could you please provide an overview of the alpha therapy, its significance and importance for improving patient outcomes? More particularly, what are the advantages of alpha therapy over other forms of radiation therapy for patients?*

Prof. Watabe: First of all, thank you very much for giving me the opportunity to introduce our research activity about targeted alpha therapy using Astatine.

Alpha therapy is still in its early phase, because there is only one drug approved in the world, which is Radium-223, Xofigo®. It is used for bone metastasis in patients with castration resistant prostate cancer. We have other alpha-emitting radioisotopes, such as Actinium, Astatine, Lead, and others with potential medical use. The advantage of using alpha emitters is that it induces highly efficient DNA double-strand breaks due to its high energy transfer. As a result, the treatment efficacy is higher than conventional radiation therapy using X-ray or radioligand therapy with beta emitters.

Currently, we are conducting two clinical trials using NaAt for thyroid cancer and At-PSMA-5 for prostate cancer. In addition, we are developing pan-tumor targeting ^{211}At-drugs. In the near future, I hope we will achieve a true clinical breakthrough with the approval of new Astatine-based alpha emitting drugs.

What makes Astatine-211 particularly interesting for patient treatment?

First of all, one of the main challenges of alpha therapy is the difficulty in producing or securing a stable supply.

However, ^{211}At can be produced by a cyclotron accelerator with natural bismuth as the target material. By establishing accelerator facilities, we can scale up the production of ^{211}At. This represents a significant advantage when compared to other alpha emitters, because we do not have to import it from other countries. For example, Japan, being an island nation without a medical reactor, must import therapeutic radionuclides such as Iodine-131, Lutetium-177 or Radium-223 from abroad. In contrast, ^{211}At can be produced domestically using cyclotrons. In addition, Astatine is a halogen and an iodine analogue, allowing it to bind directly to the carbon or benzene rings without a special chelator. In terms of theranostics, ^{211}At pairs well with fluorine or iodine for diagnostic imaging, making it particularly advantageous for alpha therapy.

> **“The advantage of using alpha emitters is that it induces highly efficient DNA double-strand breaks due to its high energy transfer.”**

In terms of research and trials, can you please describe the current trials you are involved in focusing on Astatine?

At Osaka University, we are conducting two investigator-initiated clinical trials. One is the Alpha-T1 trial for thyroid cancer, and the other is Alpha-PS1 trial for prostate cancer.

Alpha-T1 trial included patients refractory to Iodine-131 therapy. Typically, these patients have undergone radioiodine treatment more than three times, but showed progression. In this trial, we are evaluating safety and efficacy of sodium astatide ([^{211}At]NaAt) which can accumulate in thyroid cancer cells similarly to iodine.

We have completed the administration to eleven patients in our Phase I clinical trial. Although I cannot disclose the detailed results today due to the ongoing patent filing process, but I can say that some patients showed good response to the therapy.

Alpha-PS1 trial is a PSMA-targeted theranostics approach. We have developed a novel compound, ^{211}At-PSMA-5, whose diagnostic counterpart is ^{18}F-PSMA-1007, as both share a very similar chemical structure.

This is a first in-human dose-escalation study, and we are now in the second dosing cohort. In fact, we administered ^{211}At-PSMA-5 into 6 patients and they tolerated the therapy very well.

In December of last year, we published the first in-human image of ^{211}At-PSMA-5, which demonstrated very high accumulation in the local recurrence and metastatic lymph nodes. This provided a proof of concept that ^{211}At-PSMA-5 effectively targets PSMA-expressing lesions, similar to what we have observed with ^{18}F-PSMA-1007 PET.

> **"We certainly need more clinical data for the safety and efficacy to expand their applications."**

You probably do not conduct research alone. I have seen you collaborate, for example, with Professor Giesel from Germany. Are there any collaborations or partnerships with other research institutions that were really beneficial for your research and clinical translation?

Regarding collaboration, at Osaka University, we have strong collaborations across various faculties. For example, within Osaka University, we work closely with the Research Center for Nuclear Physics, which operates several cyclotrons capable of producing ^{211}At and other rare isotopes.

Moreover, we collaborate with the Faculty of Science, where experts in radiation chemistry and organic chemistry contribute to our field. Through these interdisciplinary collaborations, we can seamlessly integrate the entire research process—from the production of the isotopes to the labelling, preclinical evaluation, and ultimately clinical evaluation. Osaka University is an excellent environment to conduct radionuclide research and the clinical translation has been very successful so far.

How about the government support for the advancement of this research in Japan?

The Japanese government is now supporting our clinical trials through Japan Agency for Medical Research and Development (AMED). We also receive support from Alpha Fusion, a startup company from Osaka University.

In addition, the Japanese government is also promoting the domestic production of radionuclides for medical applications. They are now focusing on the domestic production of Technetium-99m Astatine-211, and Actinium-225.

We currently use an academic accelerator, but the supply is limited. Therefore, we need more production sites to conduct Phase II or Phase III clinical trials. Fortunately, we are now building a new production facility at Osaka University with the support of the Japanese government. And we have already finished the construction of the building, and we will install a new cyclotron to expand our production capabilities.

Thank you for emphasizing the role of the government in high technology projects for cancer treatment. Such ambitious endeavors require multi-stakeholder support, not only from small biotechs, companies, or academia, but also from governmental authorities.

I always like to conclude on a positive note. I hear your enthusiasm for ^{211}At, could you elaborate more on how you see it's in Japan?

We started Astatine research 10 years ago. At the beginning, I was a little bit skeptical about the safety and efficacy of ^{211}At as the effectiveness of alpha emitters was still uncertain. However, after we have started the preclinical studies, we could observe its excellent treatment effect, demonstrating greater efficiency than conventional beta therapy.

In addition, we have successfully secured the government funding and, we were ready to go to the clinical phase with two clinical trials ongoing.

I believe that it is very promising therapy. Moreover, usually in Japan, patients typically need to be isolated in a dedicated ward when administering beta therapeutic drugs, such as Lutetium or Iodine. In contrast, alpha therapy can be conducted in an outpatient setting, making it much more friendly for patients. It is true that the short half-life of ^{211}At of 7.2 hours is challenging in terms of delivery or logistics. However, in terms of patient safety, it can be very flexible because we can adjust the dosing regimen by administering smaller, fractionated doses in a more personalized manner.

Another advantage of using a short half-life Alpha emitters is that we don't have to worry about radiation for a long period of time as it decays quickly. When explaining to the medical staff, such as the nurses and the hospital administrators, we can explain that there is very almost no residual radioactivity in the patient body one or two days after administration. This is one of the big advantage as radiation exposure can sometimes be a barrier.

Last but not least, what kind of support do you expect from the Oncidium foundation in your context?

I am expecting the Oncidium foundation to support the promotion of targeted alpha therapy using Astatine, considering the diversity of cancers, clinical application of alpha therapy and radioligand therapy is still limited in general. We certainly need more clinical data for the safety and efficacy to expand their applications. Once again, I hope the Oncidium foundation can support us in raising awareness of this therapy, as it has the potential to be a very safe and patient-friendly treatment option.

It is the core of the Oncidium foundation to raise the awareness and educate patients about these new therapies including alpha therapies with ^{211}At.

Thank you very much. We learned a lot.

Prof. Tadashi Watabe

Oncidium foundation Ambassador - Japan

Dr. Cristiana Gameiro

Scientific Advisor at the Oncidium foundation

Good Manufacturing Practice Standards in Isotope Production: Ensuring Quality, Safety, and Excellence

By Dr. Leila Safavi, PhD
Oncidium Ambassador, USA

The production of isotopes for nuclear medicine is a highly regulated process, governed by Good Manufacturing Practice (GMP) standards to ensure the safety, quality, and efficacy of these critical medical products. These standards apply to every stage of production, from facility design and material selection to process validation and workforce training. As demand for diagnostic and therapeutic isotopes grows worldwide, this article will examine how GMP compliance addresses the challenges of scaling production, optimizing materials, and managing supply chains. By ensuring consistent quality and patient safety, GMP is essential in meeting global healthcare needs and advancing patient care through nuclear medicine.

Designing Facilities for Efficient and Safe Isotope Production

Isotope production facilities are meticulously designed with essential features such as radiation shielding, monitoring systems, and cleanroom classifications to maintain safety and prevent contamination. Strategic workflows are implemented to minimize cross-contamination risks and enhance production efficiency. Adhering to GMP standards ensures compliance with strict safety and quality requirements, while alignment with global regulations, including those set by the United States (US) Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Atomic Energy Agency (IAEA), facilitates the safe production, conversion into radiopharmaceuticals, distribution, and use of isotopes in medical treatments worldwide. This commitment to international standards not only ensures patient safety but also promotes collaboration and advancement in nuclear medicine.

Process Validation and Documentation

Validation ensures that every step of isotope production meets high standards of quality and consistency. Each process, from target preparation to final purification, is standardized and thoroughly tested. Equipment is qualified through installation, operational checks, and performance testing to maintain reliability. Detailed documentation, such as batch records and quality assurance logs, provides traceability, supports regulatory audits, and allows for quick resolution of issues. This approach builds trust in the safety and effectiveness of isotopes used in nuclear medicine.

Target Material Optimization

Selecting the right target materials is essential for ensuring reliable isotope production. These materials must achieve a balance between durability, yield, and cost-effectiveness while withstanding the extreme conditions of irradiation. Sourcing high-quality targets from reputable vendors, including U.S. national laboratories and, historically, even Russia, plays a pivotal role in maintaining production consistency. Recycling irradiated targets offers a sustainable approach to reducing waste and ensuring a steady supply of quality materials, though it requires rigorous validation processes. By optimizing target material selection and maintaining stringent quality control at every stage, the industry can enhance production efficiency and meet the growing demand for nuclear medicine applications.

Workforce Expertise: Building a Skilled Team

A skilled team is essential for GMP-compliant production. This includes chemists, such as radiochemists and analytical chemists, medical physicists, experts in aseptic (sterile) handling, nuclear pharmacists, engineers, technologists, and clinicians who are trained in handling radioactive materials and following GMP standards. Ongoing training ensures the team stays updated on regulations and innovations in the field.

Logistics and Supply Chain Management

GMP guidelines extend to the transportation and delivery of isotopes, with strict rules for packaging and shipping radioactive materials. Just-in-time (JIT) logistics and optimized distribution networks ensure isotopes reach their destinations on time, preserving their quality. The window of use is usually short, ranging from a few days to a week depending on the isotope. Aligning supply chain operations with GMP ensures timely delivery, especially for isotopes with short half-lives, preventing decay losses and ensuring patient safety. In some cases, final quality assurance and product release are conducted during shipment to save time, but all release procedures must be completed prior to clinical use.

Scaling Up Production and Managing Risks Across Platforms

Nuclear reactors and accelerators, including cyclotrons and rhodotrons, play essential and complementary roles in producing isotopes for both diagnostics and therapeutics, each requiring specialized approaches to meet GMP standards. As demand for isotopes increases, producers must navigate challenges such as equipment malfunctions, supply chain disruptions, and regulatory changes, often necessitating redundant systems for reliability. By combining advanced technologies with comprehensive risk management strategies, production processes can remain flexible and dependable, ensuring the timely delivery of high-quality isotopes critical for patient care.

By focusing on GMP compliance, the isotope production industry not only ensures that products meet regulatory standards but also builds trust with clinicians and patients. Aligning with international regulations, such as those from the FDA, EMA, and IAEA, fosters collaboration and innovation, ensuring isotopes consistently meet high-quality standards worldwide. As global demand for isotopes continues to rise, maintaining these high standards is essential for delivering reliable treatments and diagnostic solutions. Embracing GMP principles and regulatory frameworks positions the nuclear medicine sector for sustainable success, expanding global access to medical treatments and reinforcing its pivotal role in advancing patient care.

Radiotheranostics in a Crystal Ball

By Dr. Richard Zimmermann
President and founder of the Oncidium foundation

Everyone in the field could try to describe the future of nuclear medicine on the basis of their own experience and knowledge, and try to predict its evolution, but how many will be right? Thinking outside of the box is a complex exercise and in particular, the influence of competitive fields may be highly underestimated. On the basis of 25 years of experience in the Research and Development (R&D) and business development (BD) field in radiopharmaceuticals, I also tried to do the exercise of predicting the future of radiopharmaceuticals by looking in my own crystal ball. Another 15 years will be needed before knowing if what is written below makes sense. Everything may be wrong, but eventually, it was worth trying.

Beta Emitters

Lutetium-177

The following hypotheses are based on the potential of radiotherapeutics to become a real alternative, or at least equivalent in terms of treated population using chemotherapeutics with a solution for almost any type of cancer. Lutetium-177 (^{177}Lu) is presently (2025) the workhorse on which new radiotherapeutics are based. Almost all new molecules will be labeled with non-carrier added ^{177}Lu, and carrier added ^{177}Lu will disappear from the landscape within five years. Based on the existing and future reactors, which should not increase capacity but only replace aging reactors, the production capacity of ^{177}Lu may be limited by 2034, approximately to producing doses sufficient for about 500,000 patients per year.

This figure seems large but if the use of radiotherapeutics goes beyond third line therapy and even in the case of prostate cancer to become an alternative to first line surgery, the figure is far below the real potential needs. Just as an example, nowadays 12 million men are affected by prostate cancer* and if the industry target is limited to only ten percent of this population, industry will not be able to supply the needs. Fortunately, new technical solutions in the production of ^{177}Lu are under late-stage development (e.g., use of CANDU reactors instead of conventional research reactors) and it is anticipated that their use will cover a capacity much higher than the estimated future research reactor capacity.

Other Beta Emitters

Presently, new drugs based on two beta-emitter alternatives, Copper-67 (^{67}Cu) and Terbium-161 (^{161}Tb), are under development. ^{67}Cu is being developed primarily by a single company, which is working to increase industry investment in analogous molecules. Increased interest in these molecules would contribute to further investment in radionuclide production infrastructure.

Newcomers prefer ^{161}Tb which could unfortunately face the same limitations in terms of production than ^{177}Lu (use of the same technologies). ^{161}Tb shows the same physico-chemical profile (similar half-life), but could make the difference with its additional Auger electron emission which could result in a higher efficacy, provided that the vector is adapted to cell internalization. The improvement in accessing ^{177}Lu will, in parallel, also accelerate access to ^{161}Tb.

Among the older beta emitters, specific physico-chemical properties will make Iodine-131 (^{131}I), Rhenium-188 (^{188}Re) and Yttrium-90 (^{90}Y) available for use only for dedicated indications.

^{177}Lu exclusively based on *nca* ^{177}Lu

^{131}I non metallic atom of interest for Blood Brain Barriers (BBB) crossing

^{90}Y high energy, no gamma - main market in local therapy (liver)

Alpha Emitters

For almost each ^{177}Lu-labelled molecule, an Actinium-225 (^{225}Ac) analogue was synthesized to initiate some preclinical research activities. ^{225}Ac is

*Zhang, Y., et al. Global burden and risk factors of male cancers from 1990 to 2021, with forecasts to 2040. Sci Rep 15, 5123 (2025).

the second workhorse of nuclear medicine with the aim of improved efficacy over ^{177}Lu. On the contrary to ^{177}Lu, based on all the large investments already announced to produce ^{225}Ac, no capacity limitation in the production of ^{225}Ac is expected when these new tools will be operational (beyond 2029).

^{225}Ac is the second workhorse of radioligand therapy

However, even if ^{225}Ac is the most courted alpha-emitter, it might not always be the best fit. In its decay process, ^{225}Ac produces successively 4 alpha particles among which only the first one will really be useful to kill tumor cells. Some alternatives are Lead-212 (^{212}Pb) and Astatine-211 (^{211}At), with respectively 10 and 7 hours half-life, but their production capacities still need to be secured. This seems to be easier and cheaper for ^{212}Pb (less than €100M to reach 100K patients) and almost a dozen companies have entered this challenge. A minimum of €250M will be needed to create the ^{211}At network of cyclotrons (12 units) that will be sufficient to treat about 20-30K patients only. The creation of such industrial networks has been announced very recently, and original ^{211}At-labeled molecules are now reaching clinical trial stage.

Sourcing Raw Material

Access to raw material, and therefore to targets to be irradiated, has been identified as a serious bottleneck. While for producing ^{67}Cu, ^{211}At, and even for ^{212}Pb, this is not an issue, there are still some question marks regarding ^{176}Yb (precursor of ^{177}Lu), ^{160}Gd (^{161}Tb) and ^{226}Ra (^{225}Ac). In fact, as this problem was identified as a serious bottleneck several years ago, some valid solutions are already under development, hopefully, in all three cases, solving the problem of supply before 2029.

Innovation

The chances for other therapeutic radionuclides, besides the ones mentioned above, reaching the market before 2035 are low. The real improvements in the development of the radiopharmaceutical will mainly come from the development of new indications, from the use of radiotherapeutics at earlier disease stages and from the combination of drugs.

Radionuclide Cocktails

Within radiopharmaceutical drugs, an improvement can already be noticed by combining beta and alpha emitters in a same treatment protocol. The evolution of cancer patient treatment could follow the same as for chemotherapies: patients could benefit from different therapies, which could become the standard of care. As soon as different drugs with different radiolabels obtain their market authorizations, physicians will explore the efficacy of combination therapies, combining radionuclides with drugs from other therapeutic classes, but also adjusting with relative doses and timings in injection.

Radionuclide	Therapeutic emission	Radionuclide half-life	Most common production
Lutetium-177	β−	6.6 days	Reactor : Yb-176(n,γ)Yb-177 ->Lu-177
Actinium-225	α	10 days	**Main source:** Generator (Th-229/Ac-225) **Under development:** Radiochemical Extraction from Th-229 Proton spallation of Th- 232 Irradiation of Ra-226
Terbium - 161	β− Auger electrons	6.9 days	Reactor Gd-160 (n,γ)Gd-161 ->Tb-161
Astatine-211	α	7.2 hours	Cyclotron Bi-207 (α,2n) At-211
Lead-212	β−/α	10.6 hours	Generator (Ra-224/Pb-212)
Copper-67	β−	2.7 days	**Reactor** Zn-67(n,p)Cu-67 **Cyclotron** Zn-70(p,α)Cu-67 Zn-68 (p,2p) Cu-67 Zn -70 (p,α)Cu-67 **Photoconversion** Zn-68 (γ,p) Cu-67 **Accelerator** Ni-64 (α,p) Cu-67

Such trials can become cumbersome and finding definitive efficient protocols for mixture may take years. The faster alternative is to work with radionuclides that already show a profile with concomitant emission of at least two types of radiations. There are already two solutions in the portfolio, i.e., ^{161}Tb, which is also an Auger electron emitter and ^{212}Pb, which is first a beta emitter, and only in a second decay an alpha emitter. Both radionuclides could show superiority over all other radionuclides.

Examples of combination studies

Radiopharmaceutical	Oncological Drug	NCT Code
Radium-223	Pembrolizumab	NCT03093428
	Nivolumab	NCT04109729
Lu-177-PSMA ligands	Ac-225-J591	NCT04886986
	Olaparib	NCT03874884
	Enzalutamide	NCT04419402
	Pembrolizumab	NCT03805594
Lu-177-DOTAoctapeptide	Nivolumab	NCT03325816
	Olaparib	NCT06607692
	Fulvestrant	NCT06663072
	Everolimus	NCT06126588

New Technologies

For the next issue we will deep dive in two new approaches. One based on the emitted radiation, Auger electron (AE) and internal conversion electron (CE) emitters could become the third family of radionuclides, probably superior to beta and alpha emitters, provided that the radionuclide is able to enter the nucleus of the cell and to stay close to the DNA strand.

And the other in the property that some atoms (eg. such as Hafnium, Vanadium or Gadolinium) have to generate a cascade of AEs when hit by a beam of any type (external X-ray or gamma beam). In other words, if one saturates tumors with a metal, e.g. (cold) gadolinium and inject a ^{177}Lu based tumor targeting drug, this combination could be much more efficient than that ^{177}Lu alone and this concept becomes the equivalent of a beta/Auger co-injection at very low cost. This approach will take years but also opens new doors for therapy.

Diagnostics

At the level of diagnostics, major changes may arise. In the word theranostic, the first half is clearly pointing at therapy, but the second part of the word stands rather for prognosis than diagnosis. Within the pair of radiotheranostic molecules, the imaging agent is not intended for a diagnostic, which should be confirmed earlier by another modality, but to help select patients that will be positive responders for the therapy, and later to check if the treatment had the expected impact.

Therefore, these imaging analogues are of utmost importance for the development of the drug and must be as close as possible to the structure of the therapeutic, but will not necessarily remain as the molecules used to select patients when the drug will be on the market.

Because it became quickly clear that associated diagnosis agents labeled with ^{18}F or ^{68}Ga needed to be developed. In the pair Lead-203 (^{203}Pb)/Lead 212 (^{212}Pb), the imaging agent labelled with ^{203}Pb will be needed to demonstrate the efficacy of the therapeutic agent, but when on the market, the selection of patients for e.g., PSMA expressing patients, can be made with any PSMA imaging agent. In particular, the PSMA-imaging molecules already on the market, labelled with Fluorine-18 (^{18}F) or Gallium-68 (^{68}Ga) and (soon) Copper-64 (^{64}Cu) or Technetium-99m (^{99m}Tc) will be sufficient to select patients that will go through any new PSMA targeting therapy.

That said, research labs could in priority target new mechanisms of actions and new indications. The first half-a-dozen of molecules on the market for a specific indication based on the same target will block the rest of the development in this field and there are enough unexplored areas for creative teams. This is also applicable for the associated therapeutics.

Long Term Aftermath

What will be the consequences at the treatment center and patient levels if the radiotherapeutic concept becomes a true success,which we certainly hope? Will the expected half a million patients be treated ambulatory or have to stay in shielded rooms at hospitals?

Decision is in the hands of both local politicians and governmental nuclear safety engineers. Solutions will be case by case, country by country. The real problem is not linked to the production lines and industrial waste, but with human waste generated by patients.

Today, hospitals do not have the capacity to collect all the urines and other waste of thousands of patients a year. Hundredths of shielded rooms would also be needed for therapy. If treated in an outpatient setting, what will be the consequence of releasing human waste in nature when hundreds of thousands of patients will be treated yearly? Knowing that this issue is already more restrictive with long half-life radionuclides (^{67}Cu, ^{177}Lu, ^{225}Ac), shouldn't shorter half-life radionuclides (^{212}Pb, ^{211}At) be used in radiopharmaceutical development as early as today?

In a competitive market, if two drugs have the same efficacy, pharmacological profile, and toxicity, the

one with a shorter half-life radionuclide will have an advantage due to growing ecological concerns. This is the most important factor to consider, so it does not poses additional risk to the patient. Economically, ^{225}Ac and ^{177}Lu that are already under development are not at risk, but from 2035 on, a lot of them may be surpassed by shorter half-life analogues.

Production and Logistics

A second issue for large scale production is the access to a production network. This is in favor of long half-life radionuclides which reduces production constraints and facilitates transport. While two manufacturing sites for ^{225}Ac labeled drugs could be sufficient to cover the world market, a minimum of 12 units including a cyclotron each will be needed to supply ^{211}At labeled drugs for the same area. These factors will affect the initial investment level.

The current market trend is that companies will want to control their own network in a verticalized way and the number of existing facilities is already taken by the first players. For example, the four largest USA networks controlling cyclotrons are each engaged with a specific company having developed its own PSMA-imaging agent. Due to their exclusivity contract, they cannot offer this same network to another company if the same indication or radiopharmaceutical needs to be produced. In other words, there is no room today for a new PSMA targeting imaging agent in the USA, unless someone invests in a new network of cyclotrons. This is another reason not to insist on the development "me-too".

For long half-life radionuclide-based drugs, it could be easier for each company to build its own network. For short half-life radionuclides, the companies will have to and must integrate these investments in their budget. Considering that access to ^{161}Tb, ^{177}Lu and ^{225}Ac are secured, there is just a need for all the companies to create their own manufacturing unit. For short half-life radionuclides (^{211}At and ^{212}Pb), they will also have to build their radionuclide production centers, and therefore advantage is given to ^{212}Pb.

In terms of indication, everything is open and radiotheranostics can bring solution in all subtypes of cancers. Exploring new indications should be the priority of research labs such as lung, breast and colon cancers

Last, but not least, it is of utmost importance to anticipate already by now the needs for human resources in this field such as nuclear physicians, radiopharmacists, technologists and nurses, but also radiochemists and other experts for the industry. This challenge should be tackled head-on as early as today.

Summary and conclusions

2034	^{177}Lu	^{225}Ac	^{212}Pb	^{211}At
Chemistry - Radiolabeling				
Indications				
Efficacy				
Waste issues - Ecology				
Precursor availability				
Production capacity				
Transport condition				
Investment needs				
Safety				

- ^{177}Lu- and ^{225}Ac-labeled drugs will continue to progress
- ^{161}Tb and ^{67}Cu will depend upon R&D and investors
- ^{212}Pb will enter the market by 2031
- ^{211}At is best appropriate in development of drugs for orphan diseases (<50K patients)
- ^{212}Pb will put pressure on ^{225}Ac, but ^{211}At will not jeopardize ^{225}Ac or ^{212}Pb
- In any case short half-life radionuclide labeled drugs will gain advantage (^{211}At, ^{212}Pb)

This crystal ball aims at presenting the first elements to anticipate and encourages to work the best way for each area of expertise, company or investment. The final objective remains in prioritizing the patient, but it cannot be accomplished without the financial support and success of the industry, investors being the drivers of this major evolution.

UroTeragLATAM: Pioneering Hope for GU Cancer Patients in Latin America

By Dr. Andrea Luna Mass
MD, Medical Coordinator

By Dr. Danny Mena Cortes
MD, President

In the ever-evolving world of cancer treatment, a beacon of hope shines brightly for patients with genito-urinary (GU) cancers in Latin America. UroTeragLATAM Foundation, a groundbreaking initiative, is set to support education of Spanish native physicians about Theranostics, an innovative, personalized treatment with high therapeutic impact.

This article delves into the details of UroTeragLATAM, its upcoming regional educational event, and the potential impact on patient care.

What is UroTeragLATAM?

UroTeragLATAM Foundation stands as a vanguard organization dedicated to advancing education and practice in GU theranostics across Latin America. Its mission is clear: to foster knowledge exchange and promote best practices among healthcare professionals, ultimately enhancing the quality of care for patients battling urological cancers.

The Landmark Event: A Confluence of Minds and Innovation

Mark your calendars for March 11-12, 2025, as UroTeragLATAM prepares to host a pivotal event at the Cancún Center Convention Center in Mexico. This gathering is not just another medical conference; it's a catalyst for change in the field of GU. Here's what makes this event extraordinary:

1. Focus on Prostate Cancer Theranostics: The event will spotlight the latest advancements in theranostic approaches to prostate cancer, potentially opening doors to more personalized and effective treatments.
2. Educational Partnerships Unveiled: Collaborations between leading institutions will be announced, paving the way for enhanced training and knowledge dissemination across the region.
3. Book Launch: The official presentation of "Theranostics in Prostate Cancer - LATAM" book, the First Book written completely in Spanish by for more than 30 key opinion leaders (KOL) from 7 countries. This book will provide a comprehensive resource for both medical professionals and informed patients.
4. Pre-Congress Course: As part of the XXX ALASBIMN Congress 2025, this course will offer intensive learning opportunities for healthcare providers, directly benefiting patient care.

What This Means for Patients

While the event is primarily for medical professionals, its impact on patients cannot be overstated:

1. Access to Cutting-Edge Treatments: As knowledge spreads among healthcare providers, patients across Latin America may gain access to the latest therapeutic options.
2. Informed Decision-Making: With increased dissemination of information, patients can engage in more meaningful discussions about their treatment plans.

The Oncidium Foundation's Commitment to Amplifying the Message

The Oncidium foundation is supporting UroTeragLATAM in its mission to:

- Improve Access to Radioligand Therapy: This innovative treatment approach could offer new hope for patients who have exhausted traditional options.
- Enhance Information on Uro-Theranostics: By increasing awareness and understanding, patients can become more empowered in their treatment decisions.

See you on March 12, 2025, in Cancun for Efrain Perini's talk on the importance of enhancing awareness and access to radiotheranostics for cancer care, as well as the role of the RLT-Connect platform in facilitating dose donations for patients in the region.

UroTerag® LATAM

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ASOCIACIÓN LATINOAMERICANA DE SOCIEDADES DE BIOLOGÍA Y MEDICINA NUCLEAR

Supporting Cancer Care through European Research Projects Collaboration

The Oncidium foundation is proud to be actively part of two innovative projects led by Innovative Health Initiative (IHI)[1] and the European Commission and focused on advancing precision Oncology and Theranostics in Europe, Accelerate.eu and Thera4care.

In these two projects, Oncidium is focusing on emphasizing patient advocacy, leveraging its ambassador network and patient-centered vision, to ensure the dissemination of the project's results within the patient and oncology communities. Through these efforts, the foundation reinforces its commitment to expanding access to innovative radiotheranostic solutions and improving cancer care globally.

Accelerate.eu is an initiative designed to push the boundaries of cancer therapy research by proposing an innovative radiotheranostic approach using the isotope Astatine-211 (^{211}At) as an alpha emitter.

With promising physical and chemical properties, ^{211}At offers several advantages as an alpha-emitting radioisotope that could be effective at treating cancers that are resistant to standard treatments such as chemotherapy. This project will focus on three highly aggressive cancers, in the pancreas, breast (triple negative breast cancer) and brain (glioblastoma).

Led by Ion Beam Applications (IBA) and Jules Bordet Institute, Accelerate.eu is a collaboration of 17 European institutions from 9 countries, uniting academic and industrial expertise to transform radiotheranostic therapy. The project aims to develop and test new therapeutic agents, and to ensure a robust and sustainable infrastructure for ^{211}At production.

For more information, visit their website

THERA4CARE

Thera4Care aims to establish Europe as a global leader in theranostics by addressing key challenges in the field. It will strengthen the manufacture and supply of radiotheranostics for timely, cost-effective treatment delivery, develop cancer models for preclinical testing, and create a flexible framework for phase 1 clinical trials.

Additionally, the project will enhance the clinical use of radiotheranostics through AI-driven imaging, personalized dosing protocols, and a multi-modal oncology platform to support physicians in treatment decision-making.

Led by GE HealthCare and the Università Cattolica del Sacro Cuore & Fondazione Policlinico Universitario Agostino Gemelli IRCCS (Italy), the project brings together partners from 14 European countries and the United States. By addressing these foundational needs, Thera4Care is setting the stage for Europe to lead the global landscape in theranostic development and application, ultimately improving outcomes and access for patients across the continent.

For more information, visit their website

[1] The Innovative Health Initiative (IHI) is a public-private partnership (PPP) between the European Union and the European life science industries. IHI's mission is to translate health research and innovation into tangible benefits for patients and society, and ensure that Europe remains at the cutting edge of interdisciplinary, sustainable, patient-centric health research (www.ihi.europa.eu).

RLT-CONNECT

RLT-Connect: A Global Treatment Donation Program for Patients in Financial Need

Supporting patients throughout their radioligand therapy journey remains the foundation's primary focus. Recognizing disparities in access based on location and financial resources, the RLT-Connect Platform has been launched. This initiative facilitates the donation of treatment doses for patients unable to afford therapy costs by connecting healthcare practitioners with leading medical radioisotope companies. Emphasis is placed on regions where RLT facilities exist but treatment is not readily available or reimbursed.

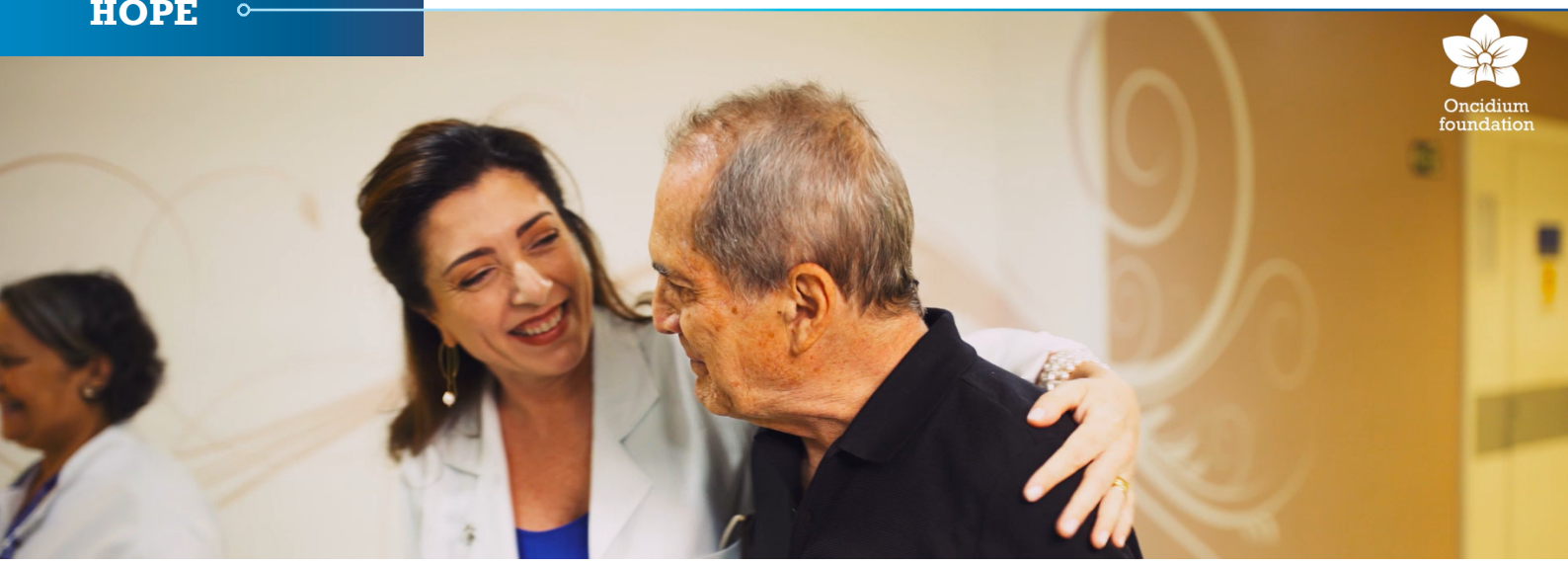
During its first year, RLT-Connect successfully facilitated the administration of 100 doses across six countries. Efforts are underway to expand the program to as many countries as possible. 9 out of 22 patients were treated in Latin America, 2 in Mexico and 7 in Argentina. A major milestone was also reached in Brazil with the signing of an official agreement, paving the way for future initiatives to support Brazilian patients. Over the next two years, access to Lutetium-based treatments for prostate cancer and neuroendocrine tumors will be extended across five additional Latin American countries through collaboration with Ambassadors, industry partners, local therapy centers, and radiopharmacies.

Ultimately, the foundation envisions to help 365 lives over the next five years, which is equivalent to 2000 doses donated.

Key radioisotopes suppliers, radiopharmacies and healthcare professionals are already on board by donating doses, lab time or delivering doses to patients. The foundation can also count on the collective support of individuals and companies that are eager to build a future where accessible cancer care knows no bounds.

Changing Lives, One Patient at a Time

Click to watch the video



Stories of Hope – Meet Edson, Living with Prostate Cancer

My name is Edson. I'm from Brazil, and I'm 69 years old. Seven years ago, I received news that changed my life—I was diagnosed with advanced prostate cancer. The treatment would be very aggressive, and my chances of a cure were almost non-existent.

I underwent treatment for six years, including chemotherapy, various procedures, and hormone therapy, but these treatments were no longer effective. My urologist mentioned a treatment he had heard about in Campinas as part of a research project—Lutetium-177 therapy. I managed to schedule a consultation, where they determined that my type of cancer would be a good fit for this treatment.

The physician leading the project was very attentive and explained everything in great detail, which gave me a sense of security.

The treatment is incredibly simple—just an injection that takes about half an hour. And, thank God, I didn't experience any significant side effects, only a slight dry mouth, which was easy to manage.

> **"People who see me today think I'm a different person. I'm this happy person."**

Three days after the treatment, the bleeding I had been experiencing every single day for nearly three years, finally stopped. Before, my life was extremely difficult. Urinary incontinence made it impossible to reach the bathroom in time. I had to wake up multiple times during the night, and the tumor was compressing my rectum and bladder. It was affecting an area deeply tied to masculinity, which was very challenging.

Now, I can go six or seven hours without needing to use the bathroom, which has been life-changing.

This improvement has truly transformed my life. It boosts self-esteem and changes a man's entire life. For me, no treatment has ever been as effective as Lutetium-177.

I still go for regular check-ups, and I take each moment as it comes. But today, my moment is one of happiness. I feel as if I never had this disease. For the past eight months, I've been living again.

My real birthday is in September, but I think I'll change that because I feel like I was reborn on April 25th—three days after my first dose.

Click to watch this and more Stories of Hope

> **Mr. Edson received one dose, and within five days, the blood in his urine stopped—and it hasn't returned since. His quality of life improved significantly. This is a game-changer. It reintegrates a patient back into society. It's truly impressive.**

Dra. Etchebehere, Nuclear Medicine Physician and Director of MND Campinas, Brazil.

The Oncidium Foundation Expands Radioligand Therapy Access in Brazil

During the Belgian Economic Mission in Brazil, led by Her Royal Highness Princess Astrid, the Oncidium foundation achieved key milestones to expand access to innovative cancer treatments in the country. The signing of an RLT-Connect agreement with MND Campinas marks a historic step in making radioligand therapy (RLT) more accessible. Additionally, a Memorandum of Understanding with important public institutions, INCA and IPEN signal further progress in improving RLT access in Brazil.

These partnerships demonstrate how international cooperation can power efforts to tackle healthcare inequities while providing cancer care equity.

For more information: ***Access here.***

RLT Channel: An Accessible Educational Platform for Radioligand Therapy Awareness and Diffusion

The Oncidium foundation is proud to launch its brand-new media platform: the RLT Channel.

The goal of this new content format is to demystify radioligand therapy (RLT) by providing clear and practical information. It aims to help individuals living with cancer, as well as their loved ones, understand how the therapy works, its potential benefits, and how it can be integrated into the care pathway.

RLT Channel is evolving into one of our key initiatives, providing a safe space to spotlight various cancers and explore treatment possibilities through radiotheranostics. Each episode is designed to provide comprehensive insights, from addressing global challenges to highlighting local perspectives and advancements.

We are convinced that a clear and accessible understanding of the patient journey is essential, as it helps reduce the apprehension and stress that often accompany these challenging stages, supporting patients and their families in making informed decisions among the available options.

Episode 1: Prostate Cancer's New Hope: RLT in Action - Global and Belgium focus

The first episode of the RLT Channel series is designed for individuals living with prostate cancer, their loved ones, and anyone interested in learning more about this treatment option.

Click to watch the video

With insights from experts in the field, this episode explores key topics such as how radioligand therapy (RLT) works and when it becomes an option for prostate cancer patients, challenges in accessing treatment, understanding access barriers, highlighting the importance of supportive care, and sharing patient experiences.

What's next?

The upcoming episode will focus on neuroendocrine tumors (NET), examining the latest developments and challenges on a global scale while offering a detailed look at the current state of NET care with RLT in Belgium.

Stay tuned!

We aim to make this resource widely accessible by producing tailored content for countries or communities that express interest. If you would like to bring similar broadcast to your region, we encourage you to contact the foundation directly.

Together, we can raise awareness and advance the potential of radiotheranostics worldwide.

DUBAI RADIOTHERANOSTICS SUMMIT

How to establish radioligand therapy for advanced cancer care in your region?

The first-ever Dubai Radiotheranostics Summit was a significant milestone in promoting radioligand therapy (RLT) in the region. Organized by the Oncidium foundation with distinguished international experts, the summit brought together leading professionals, hospital decision-makers, healthcare professionals, policymakers, nuclear medicine leaders, and industry partners to discuss expanding access to this transformative treatment.

The day kicked off with a keynote lecture by Dr. Munir Ghesani (USA), who gave a comprehensive overview of radiotheranostics and its impact on cancer care. This was followed by a particularly moving session where patients, along with their nuclear medicine practitioners, Dr. Batool Albalooshi (UAE) and Dr. Yehia Omar (Egypt), shared real-life experiences, highlighting the urgent need for broader access to RLT.

Clinical insights were a major focus, with experts like Dr. Akram Al-Ibraheem (Jordan), Dr. Ghesani, and Dr. Ilya Gipp (USA) discussing the latest advancements in treating prostate cancer and neuroendocrine tumors among multidisciplinary experts and oncologists. The summit also emphasized the role of local and international supporting hubs, such as initiatives within the International Atomic Energy Agency (IAEA) represented by Dr. Valery Radchenko, and the Arabic Nuclear Medicine Society represented by Dr. Batool Albalooshi (President of Arab Society of Nuclear Medicine). Together with industry representatives, they outlined an global call for action, and strategies to establish the corresponding infrastructure, human resources, and regulation guidelines to strengthen the existing ecosystem and pave the way to expand patient access to RLT in the area.

The infrastructure and technology session offered practical solutions for setting up RLT facilities. Insights from Dr. Dmitry Cherkasov (Russia), Dr. Omar Yehia (Egypt), and Dr. Zena Wimana (Belgium) included a compelling case study of the Jules Bordet Institute in Belgium. This led to an interactive panel discussion, moderated by Dr. Alice Viana, where industry leaders debated the key challenges and opportunities in starting, enlarging and enhancing radioligands production and reliable international supply logistics to foster RLT into cancer care in the region.

The summit wouldn't have been possible without the generous support of sponsors like Monrol, Zahrawi,TEMA Sinergie, GE HealthCare, Spectrum Dynamics Medical, as well as the dedication of the scientific committee.

Nuclear medicine is undoubtedly a job of passion, and passion is contagious. This first edition of the Radiotheranostics Summit was driven by this belief. The foundation brought together people from within and outside the RLT community to take action. The enthusiasm and interactions throughout the day demonstrated the power of partnerships and the importance of multidisciplinary teams, all working towards the same goal: transforming cancer care.

As this first edition concludes, the momentum continues. Plans are already underway for the next Radiotheranostics Summit, and we invite you to help shape its future by voting for the next destination. For more to come, stay tuned!

If you missed the event or want to revisit key insights on some featured sessions, head over to our YouTube channel to catch up on the discussions!

Oncidium foundation Expands Operation with a U.S. Subsidiary

By Jean-Luc Vanderheyden

To better serve U.S. patients and reinforce its mission to meet the needs of cancer patients nationwide, the foundation has launched a U.S. subsidiary with a new 501(c)(3) status. This initiative aims to improve access to treatment and advance education while directly engaging with healthcare professionals, industry leaders, and the general public. The 501(c)(3) status enables US donors to benefit from tax-deductible contributions.

One of the foundation's main initiative for improving patient access and raising awareness is the RLT-Connect platform. This unprecedented project provides Radioligand Therapy (RLT) donations to patients, particularly in low- and middle-income countries where such treatments are not yet reimbursed. However, due to specific regulatory constraints, the program is not currently available in the U.S. As a result, the subsidiary will also explore local opportunities to support cancer patients, such as assistance with travel and accommodation during their treatments, easing the burden on patients and enhancing access.

"I have been in the field of nuclear medicine for nearly 44 years. It's exciting to see the progress made, particularly the potential radiotheranostics has to treat patients who previously had little hope. I am eager to bring education, hope, and new treatment possibilities to patients in the U.S., and that's what motivates me."

Jean-Luc Vanderheyden, the dedicated Ambassador of the U.S. subsidiary

> **"Keeping patients front and center"**

Additionally, the U.S. subsidiary will foster collaborations with local universities, companies, patient advocacy groups and healthcare organizations to accelerate the development and accessibility of innovative radiotheranostic treatments. As part of its expansion, the foundation is also looking at growing its local ambassador network, which currently includes eight ambassadors. Volunteers having experienced first-hand the treatments with radiotheranostics, but also reimbursement specialists and all motivated to support the cause.

Our U.S. Ambassador's Team

Calvin Huntzinger

Celia Correa Von Hahn

Leila Safavi

Taylor Kirk

Taylor Prejna

Jess Guarnaschelli

Lake Wooten

Oncidium note: Expanding Regional Impact

With the establishment of its first U.S. subsidiary, the Oncidium foundation aims to build on this experience by expanding its regional presence and partnerships through the network of Ambassadors. In the coming years, the goal is to replicate this model and establish a total of five regional structures across key global regions, ensuring both targeted and effective actions while maintaining a comprehensive global perspective. This approach will enhance geographic outreach and gather specialized expertise, strengthening the foundation's ability to achieve its core mission.

"We are excited to contribute to the growing ecosystem in the U.S. and to provide hope to people living with cancer who can benefit from radiotheranostics as a crucial tool in the fight against the disease."

Rebecca Lo bue, CEO of the Oncidium foundation

Working Beyond Borders with Oncidium foundation Ambassadors

In 2024 we continue to connect specialists all around the world, who have volunteered to increase our already well-established network in leading the foundation's mission locally and internationally. With 110 Ambassadors representing 45 countries, this year promises even greater interactions, shared knowledge, and Ambassador-led Oncidium initiatives and projects.

Join us in making a difference.

Growing Needs, Growing Team

With each new project and initiative, our operational and Ambassador teams continue to expand, a testament to our commitment to advancing radiotheranostics access for people living with cancer.

With new ambitious projects comes greater responsibility. Have you checked your inbox lately? If yes, then you might have come across our new colleagues: welcome to the team, **Gauthier, Shenlan, Efrain & Elisa**

Gauthier Roelants
Director of Finance & Administration

Shenlan Liu
Administrative Assistant

Efrain Perini
Foundation Development Director

Elisa Cannarozzo
Patient Access Coordinator

Our Impact Report is out!

Measuring Impact, Driving Change.

Click Here

See you soon at:

- Economic Mission INDIA – *March 1-8, Mumbai, India*
- 2025 Annual INCA/ENETS Symposium – *March 6, Krakow, Poland*
- Uroteraglatam – *March 10, 12, Cancún, Mexico*
- ALASBIMN - Asociación Argentina de Biología y Medicina Nuclear – *March 13-17, Cancún, Mexico*
- EAU European Association of Urology – *March 21-24, Madrid, Spain*
- PSMA Conference – *March 28-29, Los Angeles, USA*
- 5th Emirates International Annual Conference and Arab Society of Nuclear Medicine and Molecular Imaging – *April 19-20, Dubai, UAE*
- ISRT – *April 10-12, Baku, Azerbaijan*
- BCNM - 12th Balkan Congress of Nuclear Medicine in conjunction with the 17th Panhellenic Congress of Nuclear Medicine – *May 8-11, Athens, Greece*
- Thera4Care Annual Meeting – *May 12-13, Budapest, Hungary*
- ICPO Forum – *May 15-16, Munich, Germany*
- BELNUC'25 Congress – *May 16-18, Brugge, Belgium*
- ANZSNM - 55th Annual Scientific Meeting of the Australian and New Zealand Society of Nuclear Medicine – *May 16-18, Melbourne, Australia*
- BNMS Annual Spring Meeting 2025 – *May 19-21, Glasgow, UK*
- ASCO - American Society of Clinical Oncology – *May 30-June 3, Chicago, USA*
- ZERO Prostate Cancer - Virtual Education Summit – *June 3-5, USA*
- CNIC: Canadian Radiotheranostics Leaders' Summit – *June 12-13, Toronto, Canada*
- SNMMI – *June 21-24, New Orleans, USA*
- UROonco25 – *June 19-21, Seville, Spain*
- RIV – *June, France*
- South African Society of Nuclear Medicine – *July 31-02, Durban, South Africa*

Have you Met Mister Bind and his Companions?

Follow the adventures of the "Life-saving mission of Mister Bind and his companions". Contact us, If you would like to translate our comic for better patient information access or would like to submit the next adventures for better radiotheranostics awareness & reach.

*This translation was possible thanks to our Egyptian Ambassadors

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