

# ALL THINGS NUCLEAR



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Investment Counsel\*  
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## ALL THINGS NUCLEAR-PORTLAND LIFE UNIFYING SCIENCES NEWSLETTER WINTER EDITION

Dear Friends,

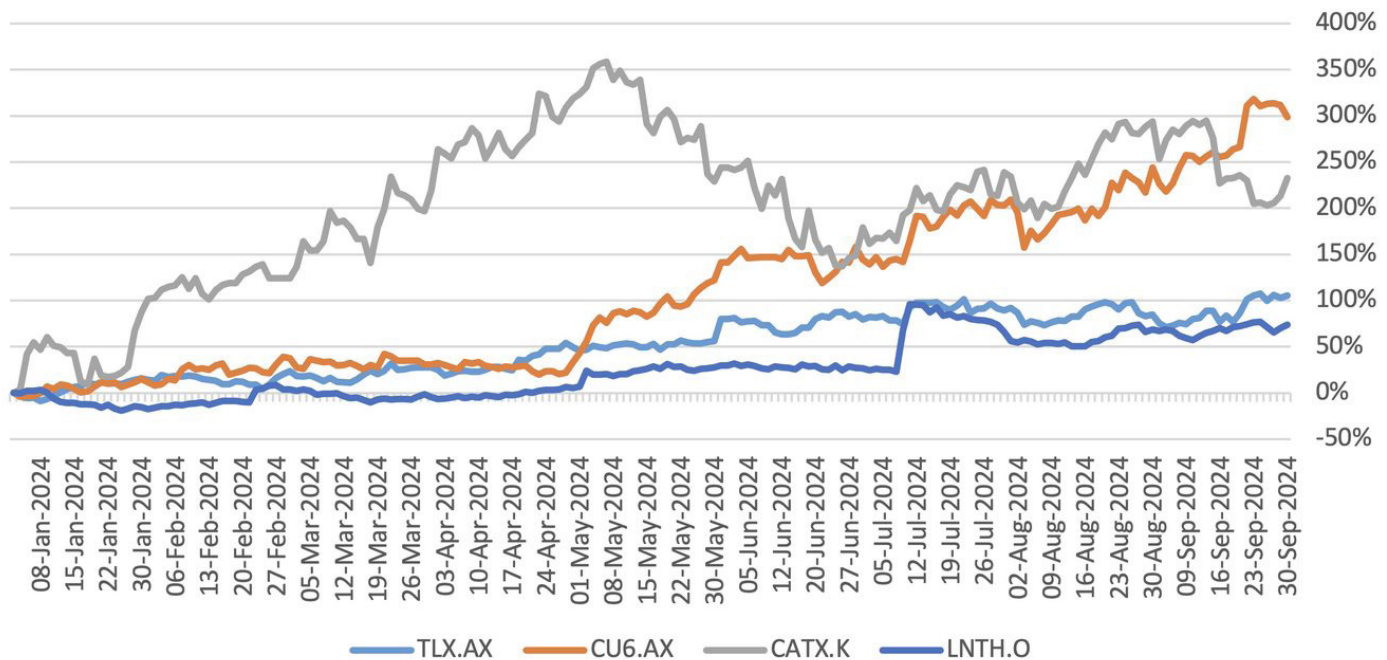
We are pleased to be sharing insights into recent developments in the radiopharmaceutical industry. 2024 witnessed a continuation of robust dealmaking in the healthcare sector. Biopharmaceuticals have continued to be in the crosshairs of acquirors, who demonstrated continued appetite for oncology assets, as marked by an increase of more than 100% in the number of merger & acquisition (M&A) transactions year-over-year<sup>[1]</sup>. We see the strong increase in deal flow over the past few months as being propelled, at least in part, by pressures from impending patent cliffs looming over major pharmaceutical companies. Patent cliffs, a term often used to highlight the impending expiry of patents for key products, are expected to jeopardize tens of billions of dollars in revenue for companies such as Merck, Bristol-Myers Squibb Company (BMS) and Johnson & Johnson<sup>[2]</sup>.

As pharma giants look to replenish their product pipelines, targeted radionuclide therapy companies have reaffirmed their place as a target of top interest through recent market developments. Building on the momentum set by Eli Lilly and Company (Eli Lilly) and BMS, who collectively committed ~US\$5.5 billion to acquire radiopharmaceutical platforms via the acquisitions of Point Biopharma and RayzeBio, respectively, AstraZeneca plc (AstraZeneca) joined the race with its purchase of Fusion Pharmaceuticals Inc. (Fusion). AstraZeneca's investment, which included a \$2 billion upfront payment, came at a substantial 97% premium to Fusion's trading price<sup>[3]</sup>. The acquisition, to our understanding, aims to combine Fusion's platform in radiopharmaceuticals and AstraZeneca's expertise in small molecules to develop follow-on and novel radioconjugates.

In a similar context, Mariana Oncology, a private biotechnology company specializing in radiopharmaceuticals development, was recently acquired by Novartis AG (Novartis) for a significant sum including a US\$1 billion upfront payment, with potential milestone payments totaling up to \$750 million. This acquisition combines Mariana Oncology's radiopharmaceutical pipeline and Novartis's extensive clinical development and commercialization expertise. Mariana Oncology's lead program, MC-339, is in pre-clinical stage and is focusing on small cell lung cancer. The transaction further underscores the attractiveness of the radiotherapeutics approach, with the latest deal being the fourth billion dollar acquisition announced by large pharma companies in the sector since October of 2023. It is our understanding that among the four listed radiopharmaceutical deals from late last year and early 2024, there was considerable interest from parties other than the purchaser, as revealed by regulatory filings.

The widespread interest in the radiopharmaceutical industry extends beyond M&A deals and is also evident in the market performance of publicly listed companies in the sector. Since the beginning of the year, multiple public radiopharmaceutical companies have seen strong appreciation in their share price. Notably, Clarity Pharmaceuticals Ltd. experienced an increase of ~300% year-to-date. Similarly, Perspective Therapeutics Inc. saw gains of about 250% year-to-date, amidst news of clinical assets progression, collaboration deals with large pharmaceutical companies and the announcement of successful private placements, with a number of other industry players also enjoying robust performance since January 1st, 2024, to September 30th, 2024.

### Performance of Select Public Radiopharmaceutical Companies in 2024



Performance of Select Public Radiopharmaceutical Companies in 2024 (As of September 30th, 2024)

The buoyant market sentiment towards radiopharmaceuticals is hardly surprising, in our opinion. In its first full year of sales, Pluvicto, a medicine developed by Novartis for the treatment of specific types of prostate cancer, brought in close to US\$1 billion in revenue, underscoring its sales potential and a robust profile insofar as its clinical efficiency, safety and cost are concerned. According to sell-side industry analysts' projections, the radiopharmaceutical market is poised to reach a market size of \$39 billion by the year 2032. While Pluvicto currently stands as one of the few approved radioligand therapies, the landscape is rapidly evolving with promising candidates from various companies in clinical studies<sup>[4]</sup>.

During the period, the United States Food and Drug Administration (FDA) granted Breakthrough Therapy Designation (BTD) to AlphaMedix, an alpha-emitting radiopharmaceutical product for the treatment of adult patients with unresectable or metastatic, progressive somatostatin receptor-expressing gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who have not previously undergone peptide receptor radionuclide therapy (PRRT). BTD expedites drug development and review for serious conditions, especially when preliminary clinical evidence suggests substantial improvement over existing standard of care therapies. Receiving the BTD has the potential to both increase the medicine's likelihood of success and accelerate its time to market.

Telix Pharmaceuticals Limited (Telix), an Australian company with a global focus on radiopharmaceutical products across various cancers, provided updates on its late-stage programs targeting prostate and kidney cancer during a recent medical conference. These updates highlighted encouraging efficacy and safety signals. Similarly, Clarity Pharmaceuticals Ltd., another Australian-based company, shared initial data from their Phase 1/2 trial. Their diagnostic agent, <sup>64</sup>Cu-SAR-bisPSMA, demonstrated impressive capabilities in detecting smaller tumors. Notably, the diagnostic agent successfully identified a lesion with a diameter of less than 2 millimeters, surpassing the current standard of care for PSMA positron emission tomography (PET) imaging agents. These developments underscore the potential of innovative radiopharmaceutical products in cancer diagnosis and treatment.

Indeed, radiopharmaceuticals are experiencing a renaissance as a treatment modality. With multiple upcoming catalysts – including the potential advancement of Novartis' Pluvicto into earlier line prostate cancer and the impending approval decision of Telix's kidney cancer and brain cancer diagnostic agents – we believe the industry is blooming with opportunities, offering new hope for patients in need.

#### FOCUS ON MANUFACTURING

Manufacturing remains a keystone in radiopharmaceutical development and commercialization<sup>[5]</sup>. Due to the limited half-life of radioisotopes, radiopharmaceuticals must be effectively processed, packed and distributed within a short window of time. Therefore, the

establishment of a reliable supply chain is pivotal, especially in relation to production and distribution of radioisotopes.

The 2024 year-to-date has seen a significant global expansion in manufacturing capacity, fueled by sustained demands for medical radioisotopes. Chiefly, Novartis is investing US\$200 million to expand its radioligand therapy manufacturing capabilities with a new facility in Carlsbad, California – Novartis' third manufacturing site in the US. The company is also expanding its Indianapolis site, which will produce radioisotopes for its therapeutic products, Pluvicto and Lutathera. The investment aims to strengthen the company's manufacturing network and improve delivery of these treatments.

Similarly, ITM Isotope Technologies Munich SE (ITM), a key supplier of radioisotopes for the industry and developer of radiotheranostics, is expanding its production facility throughput. This expansion is facilitated by the installation of a second production irradiation line at Bruce Power's Unit 7. This key collaboration will double the production capacity of Lutetium-177. OranoMed, a company developing targeted alpha-emitter therapy, began construction of its Alpha Therapy Laboratory Valenciennes (AtLab Valenciennes) in Onnaing, France, on the heels of the planned opening of their Indianapolis ATLab facility scheduled for the third quarter of 2024.

Telix has also sought to expand the company's supply chain capabilities through the acquisition of Texas-based theranostics-focused contract development and manufacturing organization (CDMO), Isotherapeutics Group, LLC, establishing a manufacturing presence in North America alongside the company's flagship facility in Liege, Belgium. Telix further acquired RLS Group Inc., America's only Joint Commission-accredited radiopharmacy network distributing PET, SPECT and therapeutic radiopharmaceuticals, further strengthening the company's distribution network.

Similar trends are evident across the radiopharmaceutical industry, with various players engaging in strategic initiatives to strengthen their positions. For instance, isotope suppliers such as Rosatom State Nuclear Energy Corporation (Rosatom) in Russia are undertaking significant infrastructure investments, with plans to finalize the construction of one of Europe's largest radioisotope manufacturing facilities in 2025. At the same time, radiopharmaceutical developers such as Ratio Therapeutics Inc. and ARTBIO, Inc. (ARTBIO) are forging manufacturing partnerships to secure essential radioisotope supply for the advancement of the companies' early clinical programs. PharmaLogic Holdings Corp. (PharmaLogic) and Intermountain Health are partnering to construct a new cyclotron facility in Utah, while in Canada, the BC Cancer Agency in partnership with TRIUMF, announced the construction of a new cyclotron to increase the supply of medical radioisotopes. Eckert & Ziegler Strahlen- und Medizintechnik AG Group (Eckert & Ziegler) announced major partnerships with RLS Radiopharmacies, Inc. (RLS), Nucleus Radiopharma (Nucleus), and Full-life Technologies Limited (Full-Life). The RLS partnership will see Eckert & Ziegler's Gallipharm generator distributed within the RLS radiopharmacy network and Nucleus and Full-life will be supplied with Eckert & Ziegler's Lutetium-177 (Lu-177) as well as Actinium-225 (Ac-225). The flurry of activities underscores the industry's emphasis towards manufacturing. As the industry continues to develop, we believe that the rising demand is likely to fuel ongoing commitments to strategic partnerships and investments in supply chain infrastructure.

Thank you for your continued support as we navigate these exciting developments in the radiopharmaceutical landscape.

Warm regards,

*The PLUS\*\* Team*

## RECENT INDUSTRY DEVELOPMENTS

**ROTOP Pharmaka GmbH (ROTOP) (Germany) – ROTOP CDMO Services** —is expanding to address the rapidly growing radiopharmaceutical market by adding over 15,000 square meters (16,100 square feet) at the Dresden-Rossendorf site. The main focus will be on services for CDMO for clinical studies, as well as on commercial Current Good Manufacturing Practice (cGMP) manufacturing of radiopharmaceutical drugs in the field of cancer diagnostics and therapy. The new premises are substantially enhancing ROTOP's research and manufacturing capabilities, thereby sustaining its dynamic expansion. <https://www.rotop-pharmaka.de/en/>

**RLS (USA)**— announced it has expanded its radiopharmaceutical contract development and manufacturing (rCDMO) capabilities by entering into a strategic agreement with global isotope technology leader Eckert & Ziegler. Under the partnership, all 31 of RLS's radiopharmacies will be equipped with Eckert & Ziegler's advanced GalliaPharm generators, which the radiopharmacy network will utilize to produce high-quality Gallium-68-based (Ga-68) radiopharmaceuticals. Ga-68 is crucial for PET imaging and plays a pivotal role in the accurate diagnosis and subsequent treatment planning for patients with neuroendocrine tumors and prostate cancer. To date, RLS has installed Eckert & Ziegler's GalliaPharm generators within most of its locations and anticipates the remaining radiopharmacies will be operational by the end of June. <https://medical.ezag.com/en/news/rls-radiopharmacies-partnership/>

**PharmaLogic (USA)— Ratio Therapeutics Inc. (Ratio)** announced an expanded manufacturing agreement with PharmaLogic, a contract development and manufacturing organization (CDMO) specializing in radiopharmaceutical production and distribution. The collaboration aims to significantly accelerate the development and commercialization of Ratio's pipeline of next-generation radiotherapies, representing a critical component in advancing Ratio's fibroblast activation protein-alpha (FAP)-targeted radiotherapeutic candidate. Ratio, in collaboration with Lantheus Holdings, Inc. (Lantheus) and PharmaLogic, is currently conducting a Phase I trial evaluating the efficacy of a novel FAP-targeted imaging biomarker, copper-64[Cu-64]-labeled LNTH-1363S (formerly RTX-1363S) for PET imaging in adult healthy volunteers. The company also recently announced a US\$50M Series B financing which will significantly drive the clinical advancement of Ratio's first FAP-targeted therapeutic candidate into clinical trials this year. <https://www.prnewswire.com/news-releases/ratio-announces-expansion-of-manufacturing-agreement-with-pharmalogic-for-fap-targeted-radiopharmaceuticals-302086004.html>

**PharmaLogic—Intermountain Health and PharmaLogic** are partnering to build a new cyclotron facility that will produce radiopharmaceuticals, which are used to diagnose certain medical conditions or treat various types of cancer. This technology is vital in bringing some of the most critical advances in healthcare to the Salt Lake City region. The new facility in Murray will ensure more of these products are available locally to be used for a wide range of imaging applications for certain cancers and other ailments involving the heart and brain. <https://www.prnewswire.com/news-releases/intermountain-health-and-pharmalogic-partner-to-develop-and-expand-access-to-novel-radiopharmaceuticals-at-new-salt-lake-city-facility-302077932.html>

**AtomeVie Global Radiopharma Inc. (AtomeVie) (Canada)**— is proud to announce strategic collaborations with RLS and United Pharmacy Partners, LLC (UPPI), two industry leaders in radiopharmacy and logistics. This strategic move is poised to enhance AtomVie's logistics capabilities within the United States (U.S.), ensuring the widespread distribution of high-quality radiopharmaceuticals by implementing RLS and UPPI as key partners within AtomVie's existing U.S. distribution network. AtomVie specializes in the Good Manufacturing Practices (GMP) and global distribution of radiopharmaceuticals, RLS the only Joint Commission-accredited radiopharmacy network in the U.S., owns and operates 31 radiopharmacies covering more than 80% of the U.S. population, and UPPI, organized as a Group Purchasing Organization (GPO), brings extensive capabilities in logistics and distribution. <https://www.newswire.ca/news-releases/atomvie-global-radiopharma-collaborates-with-rls-amp-uppi-to-strengthen-its-existing-u-s-radiotherapeutic-distribution-network-861845192.html>

**Bayer AG (Brayer)— PanTera, Inc. (PanTera)**, the Belgian joint venture created by Ion Beam Applications S.A (IBA) and SCK CEN (the Belgian Nuclear Research Centre) to secure large-scale production of alpha-emitting radioisotopes, have announced the signing of a capacity reservation agreement with Bayer for the supply of actinium-225 (225Ac) starting in the second half of 2024. <https://www.globenewswire.com/news-release/2024/02/13/2827948/0/en/PanTera-signs-agreement-with-Bayer-for-the-supply-of-actinium-225.html>

**State Atomic Energy Corporation Rosatom (Rosatom) (Russia)**—completed the construction of the building for a new plant for the production of medical isotope products at the Karpov Scientific Research Institute of Physics & Chemistry in Obninsk, Kaluga region. The plant will be largest radio pharmaceutical factory in Europe. Construction began in 2023, and the plant is expected to begin operation in 2025 producing 25 items. The Obninsk plant will produce a range of popular isotopes, including iodine-131, samaria-153 and molybdenum-99. The plant will also develop radiopharmaceutical substances and radiopharmaceutical drugs based on lutetium-177, actinium-225, radium-223 and other isotopes. <https://www.neimagazine.com/news/newsbuilding-for-obninsk-radiopharmaceutical-plant-completed-11494076>

**Eckert & Ziegler and Nucleus Radiopharma (Nucleus)** signed extensive supply agreements for major therapeutic radioisotopes. Eckert & Ziegler will serve as core supplier for high-quality Lutetium-177 (Lu-177) as well as Actinium-225 (Ac-225), both in non-carrier-added form. Nucleus will use the radioisotopes to complement and advance their services for clinical development and manufacturing of



radiopharmaceuticals. <https://medical.ezag.com/en/news/nucleus-ac-225-lu-177-supply/>

**Orano Med (France)**—laid the foundation stone for its Alpha Therapy Laboratory (ATLab) in Onnaing, France. This will be Europe's first industrial-scale pharmaceutical facility dedicated to the production of lead-212 based radioligand therapies. The construction of Orano Med's ATLab Valenciennes is therefore a major step towards making these promising new treatments available to cancer patients with high unmet needs. ATLab Valenciennes, with over 3,000 m<sup>2</sup> of floor space, will represent an investment of €29 million and will create 25 direct jobs. It will focus on the production of lead-212 therapies developed by Orano Med and their distribution in Europe. Orano Med is due to inaugurate a similar facility this year in Indianapolis to serve the US market. This combined capacity will enable Orano Med to manufacture 10,000 doses a year as of 2025, with the aim of producing ten times that number by the end of the decade. Given the short half-life of lead-212 (10.6 hours), the drugs need to be produced close to hospitals. The construction of further ATLabs is therefore envisaged to meet patients' needs worldwide. <https://www.oranomed.com/en/resources/news/2024/orano-med-lays-foundations-for-new-manufacturing-site-for-the-production-of-lead-212-radioligand-therapies>

**BC Cancer Agency/TRIUMF (Canada)**—Construction has begun on a new cyclotron and radiopharmacy laboratory in Vancouver to increase production of clinical radiotracers. British Columbia (B.C.) is investing C\$32 million to support this work through \$21 million to BC Cancer Agency for the new cyclotron and radiopharmacy laboratory and approximately \$11 million to TRIUMF, Canada's particle accelerator centre at the University of British Columbia, to advance research. TRIUMF will also receive funding from B.C. to expand its laboratory capacity to support cancer research as the next generation of treatments for cancer and other diseases are developed, the release stated. The facility was founded in 1968 by the University of British Columbia, Simon Fraser University and the University of Victoria. The new Vancouver laboratory will increase access to PET/computed tomography (CT) scans, which evaluates a body's organs and tissues at a molecular level, can identify abnormalities in cells and can show whether a tumour has grown, shrunk or returned. <https://vancouver.citynews.ca/2024/01/30/bc-cancer-diagnostic-research-funding/>

**Full-Life Technologies Limited (Full-Life)**—and Eckert & Ziegler announced they have entered into an agreement for the supply of Actinium-225 (Ac-225). The agreement provides Full-Life with access to Eckert & Ziegler's high-purity Actinium-225, a radionuclide for use in developing the next generation of therapeutic radiopharmaceuticals. Ac-225 has emerged as a highly promising active agent for the treatment of cancer. The radioisotope releases potent alpha particles with high energy and short penetration depths, allowing for precise targeting of tumor cells, including hard-to-reach micro-metastases, while minimizing impact on surrounding healthy tissue. Based on its potential, clinical and industry experts expect a substantial increase in Ac-225 demand in the coming decade. <https://medical.ezag.com/en/news/full-life-ac-225/>

**ARTBIO—SpectronRx, Inc. (SpectronRX)** a radiopharmaceutical developer and manufacturer, entered into a new partnership agreement with ARTBIO, a clinical-stage radiopharmaceutical company developing a new class of targeted alpha radioligand therapies (ART), to produce a novel prostate cancer therapy, AB001. SpectronRx will use its state-of-the-art facilities in Indiana to serve as a contract developer and manufacturer for the treatment currently undergoing first-in-human trials. The manufacturing processes will start with ARTBIO's AlphaDirect technology for isolation of Pb212. Upon validation, SpectronRx will design, develop, and implement the customized manufacturing line and processes required to scale up production to meet clinical supply requirements. <https://www.prnewswire.com/news-releases/artbio-and-spectronrx-enter-a-collaboration-to-manufacture-key-components-of-artbios-alphadirect-technology-301883562.html>

**ARTBIO—and PharmaLogic** announced a manufacturing and supply agreement for ARTBIO's lead-212 (212Pb)-based radiopharmaceutical candidate, AB001, for the treatment of prostate cancer. Under the terms of the agreement, PharmaLogic will assist ARTBIO with radiochemistry and supply of the finished radiopharmaceutical product for future Phase I and II clinical trials of AB001 from their facility in New York, using ARTBIO's proprietary AlphaDirect 212Pb isolation technology. <https://www.prnewswire.com/news-releases/artbio-and-pharmalogic-announce-supply-agreement-for-lead-212-based-therapeutic-candidate-ab001-for-new-york-and-surrounding-states-302033277.html>

**NorthStar Medical Radioisotopes, LLC (Northstar)**—and Curadh MTR Inc. (Curadh), a global molecularly targeted radiation (MTR) focused clinical, research and advisory organization, announced a long-term strategic collaboration to develop and produce novel radiopharmaceuticals for the diagnosis and treatment of solid tumor cancers. Under the agreement, NorthStar will support the development of select Curadh radiopharmaceutical targets by preparing and distributing Curadh patient doses of Non-Carrier Added (NCA) Ac-225 for its ongoing clinical studies and, upon approval, may manufacture and supply radiopharmaceuticals for commercial use. The new agreement also provides Curadh access to NorthStar's integrated radiopharmaceutical development and manufacturing organization to support development and commercialization of future radiopharmaceutical diagnostic and therapeutic agents. <https://www.northstarm.com/northstar-medical-radioisotopes-and-curadh-mtr-enter-strategic-collaboration-agreement-for-development-and-production-of-actinium-225-ac-225-based-therapeutic-radiopharmaceuticals-for-treatment-of-p/>

**Telix** —announced the completion of the acquisition of IsoTherapeutics Group, LLC (IsoTherapeutics). IsoTherapeutics is a privately held, commercial-stage company that provides radiochemistry and bioconjugation development and contract manufacturing services to numerous companies in the radiopharmaceutical industry, including Telix. The acquisition further enhances Telix's in-house development

capabilities and expands Telix's United States (U.S.) manufacturing footprint with particular focus on bioconjugation and isotope processing. <https://telixpharma.com/news-views/telix-completes-acquisition-of-isotherapeutics/>

**Telix** – announced its acquisition of RLS (USA) Inc., a leading U.S. radiopharmacy network, to enhance its North American manufacturing and distribution capabilities. The acquisition will enable Telix to expand its radiometal production network and improve last-mile delivery of radiopharmaceuticals. With 31 licensed radiopharmacies and over 100,000 square feet of expansion space, RLS provides the infrastructure to meet growing demand and support Telix's future clinical and commercial product rollouts. RLS will continue operating independently within Telix's Manufacturing Solutions division, complementing existing partnerships and production facilities. <https://telixpharma.com/news-views/telix-to-acquire-rls-to-expand-north-american-manufacturing-and-distribution-platform/>

**Eckert & Ziegler**— announced the grand opening of its new Actinium-225 production facility at the Nuclear Physics Institute of the Czech Academy of Sciences. This facility is set to begin commercial production at the beginning of Q3/2024. The customized production line, provided by Eckert & Ziegler Engineering, ensures efficiency and precision. Eckert & Ziegler will also supply the Radium-226 essential for the irradiation process. <https://www.investmentmonitor.ai/news/eckert-ziegler-opens-new-actinium-225-production-facility-in-czech-republic/>

**Novartis**— is putting \$200 million into its radioligand therapy manufacturing capabilities with a new site in California and the expansion of an existing site in Indianapolis. The Indianapolis site will produce radioisotopes for the drugmaker's products Pluvicto and Lutathera. The new location in Carlsbad, CA, will be Novartis' third radioligand therapy manufacturing site in the US, and is part of an effort to "create resiliency in its manufacturing network and optimize the delivery of medicines to patients on the West Coast," according to the company. <https://endpts.com/novartis-expands-radioligand-therapy-manufacturing-in-california-and-indianapolis/>

**Isologic**— is investing US\$29.9 million to support the growth of the radiopharmaceutical industry and to reinforce its critical role in the field of nuclear medicine and the Canadian medical isotope supply chain as part of Quebec's life sciences ecosystem. Approximately \$19 million will be devoted to the expansion and modernization of the Lachine borough site, and \$11 million will be used to purchase state of the art equipment which includes an 18 Mega-electron Volt (MeV) cyclotron which will be operational from the first quarter of 2026. This investment will help add redundancy to the supply chain and meet the growing demand for critically important PET diagnostic radioisotopes in both Quebec and across Canada. The new 18 mEV cyclotron in Montreal will be able to produce emerging diagnostic isotopes such as Zirconium-89 (Zr-89), Copper-64 (Cu-64), Lead-203 (Pb-203) and Gallium-68 (Ga-68), as well as larger quantities of the radiopharmaceuticals F18-FDG and NeuraCeq (F-18-FBB) for the diagnosis of Alzheimer's disease. <https://www.newswire.ca/news-releases/isologic-makes-29-9-million-investment-in-advanced-isotope-production-facility-in-quebec-850041864.html>

**Bruce Power/ITM/Isogen**—celebrate the installation of a second production line that will double the production capacity of the Isotope Production System (IPS) on Bruce Power's Unit 7. The upgrades to the IPS will add a second production line to the existing system in Unit 7, which became the first commercial power reactor in the world to produce lutetium-177 in October of 2022. This second production line, designed and installed by Isogen, will enable Unit 7 to increase production of lutetium-177 to meet increasing demand for the medical isotope, which is used in precision oncology for targeted therapy of a growing number of cancers including neuroendocrine tumours and prostate cancer. The made-in-Ontario IPS, designed and installed at Bruce Power by Isogen, enables large-scale reliable production of lutetium-177, which is transported to ITM in Germany for further processing and global distribution. Expansion of the IPS will provide ITM increased access to this critical isotope, which has been successfully used in various clinical and commercial radiopharmaceutical cancer treatments globally. <https://world-nuclear-news.org/Articles/Bruce-Power-and-partners-to-expand-isotope-capacit>

**\*\*About PLUS:**

*Portland Life and Unifying Sciences (PLUS) is a team within the Portland Holdings group of companies that focuses on healthcare that collaboratively helps the Portland Holdings group of companies to assess investment opportunities. The PLUS team is not a medical team and does not have deep long-standing expertise in TRT or areas relating to precision oncology.*

## Glossary:

**Bioconjugation** means a chemical process of linking biological molecules with other molecules.

**Cyclotron facility** means a facility with particle accelerators.

**Fibroblast Activation Protein-Alpha (FAP)** means a protein highly expressed in some types of cancer cells.

**Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)** means slow-growing neoplasms that arise from the neuroendocrine system of the gastrointestinal tract and pancreas. Gastrointestinal tract is mostly the stomach and intestines.

**Isotope** means each of two or more forms of the same element that contain equal numbers of protons but different numbers of neutrons in their nuclei, and hence differ in relative atomic mass but not in chemical properties; in particular, a radioactive form of an element.

**Metastasis** means the spread of cancer cells from the place where they first formed to another part of the body. In metastasis, cancer cells break away from the original (primary) tumour, travel through the blood or lymph system, and form a new tumour in other organs or tissues of the body. The new, metastatic tumour is the same type of cancer as the primary tumour. The plural form of metastasis is metastases.

**Neuroendocrine tumour (NET)** means a tumour that forms from cells that release hormones into the blood in response to a signal from the nervous system.

**Non-Carrier Added (NCA)** means a pure radioisotope without contamination from stable isotopes.

**Peptide Receptor Radionuclide Therapy (PRRT)** means therapy delivering radiation via peptides that bind to specific receptors on tumors.

**Positron Emission Tomography (PET)** means imaging technique using radioactive tracers to visualize certain activities in the body.

**Precision oncology** means molecular profiling of tumors to identify targetable alterations, is rapidly developing and has entered the mainstream of clinical practice.

**Prostate-specific membrane antigen (PSMA)** means a membrane protein which contributes to prostate cancer's development and is seen in a higher amounts in prostate cancer cells.

**Radioconjugates** means Molecules which generally combine a radioactive isotope with a targeting agent.

**Radioligand therapy** means a targeted form of cancer treatment that delivers radiation directly to cancer cells.

**Radionuclide therapy** means a type of treatment using targeted radioactive elements to destroy cancer cells.

**Radioisotopes** means radioactive versions of elements.

**Radiopharmaceutical** means a radioactive drug composed of a radionuclide and a pharmaceutical that is used for diagnosis or therapy.

**Somatostatin** means a peptide hormone that prevents the release of growth hormone from the pituitary gland.

**Somatostatin receptors (SSTRs)** means receptors that are expressed in high levels in gastroenteropancreatic neuroendocrine tumors.

**Standard of Care (SoC)** medical treatment guideline.

**Targeted Alpha Radioligand Therapies (ART)** means a type of PRRT which utilizes alpha-particle-emitting radioisotopes – same as Targeted Alpha-Emitter Therapy (TAT).

**Targeted Alpha-Emitter Therapy** means a type of PRRT which utilizes alpha-particle-emitting radioisotopes.

**Targeted radionuclide therapy (TRT)** means a form of treatment that delivers therapeutic doses of radiation to malignant tumours, for example, by administration of a radiolabeled molecule designed to seek out certain cells.

**Theranostics** means a new field of medicine which combines specific targeted therapy based on specific targeted diagnostic tests.

### PLUS Team Members

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**Michael Lee-Chin\***  
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Experience: 40+ years



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Experience: 25+ years

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[1] <https://www.leerink.com/articles/analyzing-healthcare-ma-trends-q1-2024-insights/>

[2] [https://www.cNBC.com/2024/01/28/big-pharma-merck-bristol-myers-prepare-to-lose-revenue.html?utm\\_source=Sailthru&utm\\_medium=email&utm\\_campaign=Issue:%202024-01-31%20BioPharma%20Dive:%20Commercialization%20%5Bissue:58698%5D&utm\\_term=BioPharma%20Dive:%20Commercialization](https://www.cNBC.com/2024/01/28/big-pharma-merck-bristol-myers-prepare-to-lose-revenue.html?utm_source=Sailthru&utm_medium=email&utm_campaign=Issue:%202024-01-31%20BioPharma%20Dive:%20Commercialization%20%5Bissue:58698%5D&utm_term=BioPharma%20Dive:%20Commercialization)

[3] <https://www.astrazeneca.com/media-centre/press-releases/2024/astrazeneca-to-acquire-fusion.html>

[4] <https://www.nature.com/articles/s41573-020-0073-9>

[5] <https://www.cNBC.com/2023/02/11/radioligand-cancer-therapy-forces-manufacturers-to-race-the-clock.html>

\*Michael Lee-Chin is a member of the Supervisory Board of ITM.

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