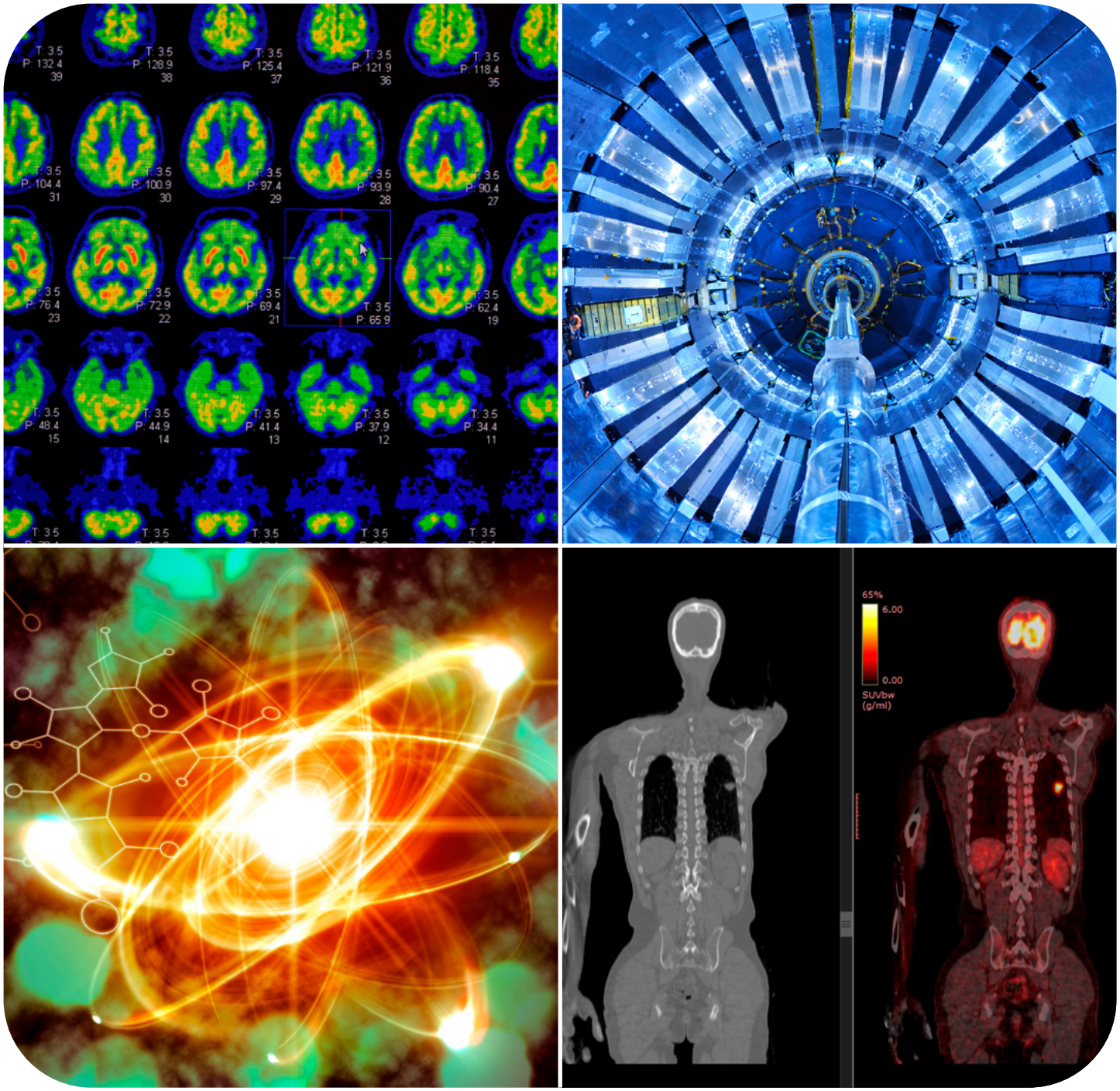
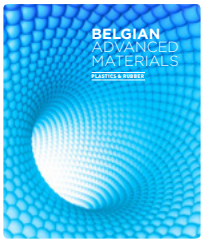
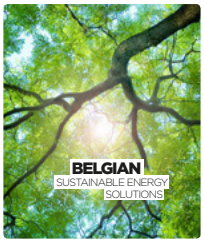
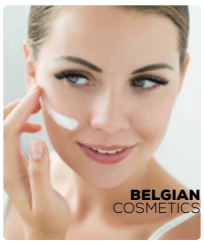


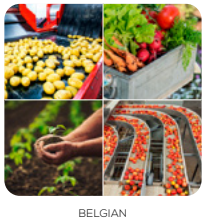
BELGIAN
NUCLEAR MEDICINE

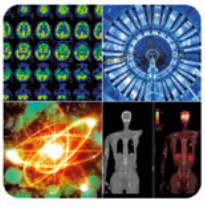
Belgian
Foreign Trade Agency











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The contents of the interviews were approved by the respective companies for use in this publication.

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PRESENTATION OF THE SECTOR

THE 'RADIATING' SECTOR OF NUCLEAR MEDICINE

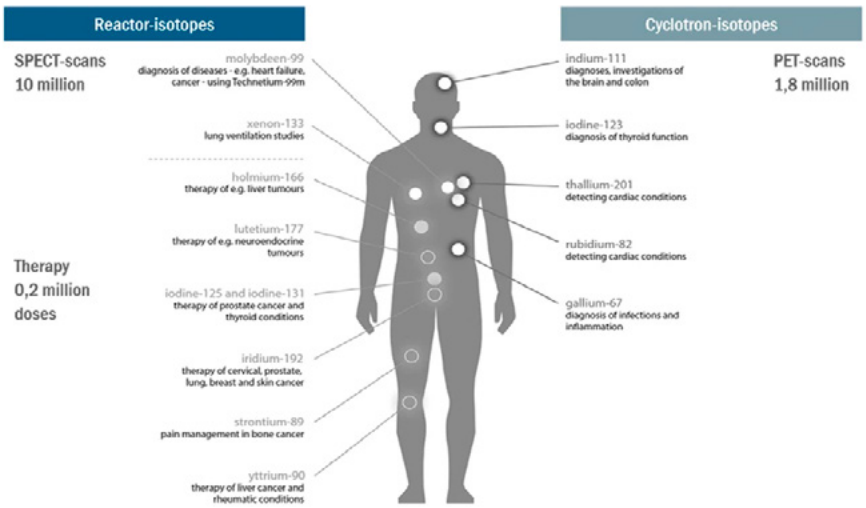
1. Introduction

Given the intricacies of the nuclear medicine sector, this study serves a dual purpose. Firstly, it delves into the technical facets, encompassing the diverse applications of nuclear medicine and emerging technologies within the field. Secondly, it undertakes an extensive examination and elucidation of the Belgian nuclear medicine landscape, emphasizing its global significance.

Nuclear medicine (NM) is a branch of medicine that uses radioactive materials known as radiopharmaceuticals or radiotracers to diagnose and treat a variety of illnesses and conditions. It is a type of medical imaging that provides essential information on how organs and tissues function inside the body. Radioisotopes are used in NM to diagnose and treat a variety of ailments, including some of the most serious, such as cancer, cardiovascular disease, and brain disorders. Diagnostic imaging relies on the introduction of radiopharmaceuticals into the patient's body that emit gamma rays which can be detected by specialized cameras such as PET (Positron Emission Tomography) scanners and SPECT (Single Photon Emission Computed Tomography) scanners. This enables medical professionals to evaluate the structure as well as the function of numerous organs, including the heart, brain, thyroid, bones, and more (National Institutes of Health, 2016).

The required nuclear substances are isotopes, more specifically Molybdenum-99 (Mo-99), the 'parent' isotope of metastable Technetium-99 (Tc-99 and Tc-99m). Tc-99 and Tc-99m are both technetium isotopes used in nuclear medicine, however Tc-99 is utilized largely for radiolabeling compounds to make radiotracers, whilst Tc-99m is often employed for imaging due to its shorter half-life and gamma ray emission, making it suited for diagnostic applications. Mo-99 is necessary for the production of the most widely used radioisotope in NM, Tc-99m (Belgian Science Policy Office, 2022). Furthermore, Europe is the second largest consumer of Tc-99m, accounting for more than 20% of the global market. Other examples of radioisotopes are Caesium-137 and Cobalt-60 which have low-intensity sterilization properties and high-intensity Cobalt-60 which are used to treat brain cancer (Department for Business, Energy & Industrial Strategy, 2018). **Every year, over 10,000 hospitals worldwide employ NM for in vivo diagnosis or treatment of around 40 million patients, 12 million of those procedures take place in Europe.** Of those 12 million, 10 million are diagnostic SPECT scans and 1.8 million PET scans. The remaining 0.2 million NM procedures are related to treatments (NRG, 2022)

Figure 1: Number of procedures with medical isotopes yearly in EU



Source: NRG, 2022

2. About nuclear medicine

2.1 Three phases of nuclear medicine

A) Phase 1: Detection

The medical specialty, known as nuclear medicine, makes use of radioactive materials to diagnose and treat diseases, as previously mentioned. Phase one focuses on the detection and thus the radiation for diagnostic purposes. NM diagnostics, which account for 90% of NM procedures, enable the diagnosis of various types of diseases and evaluate patients' health status in the pre and-post-treatment phase, particularly in oncology where it can play a crucial role in tumor staging or monitoring of suspected tumor relapse. Additionally, the value of NM in early detection has a significant impact on survivability and quality of life (EANM, 2022).

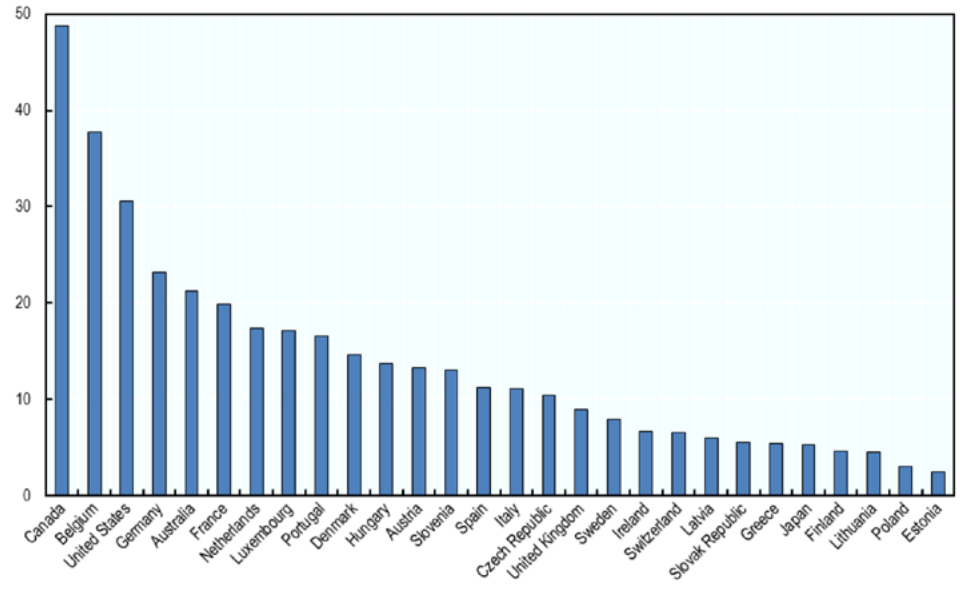
It is important to differentiate NM from radiology. It's a prevalent misconception that NM is included in radiography. NM offers therapy choices in addition to providing diagnostic imaging services, as both specialties do. NM scans are distinct from radiological scans in that they have more of an emphasis on cell function rather than imaging anatomy. NM thus obtains photos of the body's functioning rather than just demonstrating the existence of a tissue structure or organ. Additionally, radiology employs external radiation sources (like X-ray tubes) outside of the body, whereas NM uses internal radiation from the body released by injected radiopharmaceuticals.

Combining therapy choices and diagnostics is better known in the medical world as theranostics. It ensures the best patient outcome by diagnosing and treating a disease with the same chemical structure.

According to the World Nuclear Association (2023), **radioisotope demand is rising at a rate of up to 5% annually, and there are over 40 million NM procedures conducted annually.** Tc-99m makes up 85% of all diagnostic scans performed in NM around the world and is the most frequently used radioisotope for diagnosis. Developing markets account for 16% of the world's demand for Mo-99/Tc-99m and mature markets for 84%. Through 2023, market growth rates are anticipated to be 0.5% yearly for developed markets and 5% annually for developing markets.

Graph 1, on the number of Tc-99m-based NM diagnostic scans per 1,000 population per year, provides a clear oversight of the use of NM in diagnostic scans in different

Graph 1: Number of Tc-99m-based NM diagnostic scans per '000 population per year



Source: OECD/NEA, 2019

countries. Scan rates range from close to 50 scans per 1,000 individuals in Canada, 30 to 40 scans per 1,000 people in Belgium and the United States, to as few as 2-3 scans per 1,000 people in Estonia and Poland (OECD/NEA, 2019).

The absolute number of NM diagnostic scans per year per country (Graph 2) shows that around 10 million Tc-99m-based diagnostic scans are conducted annually in the United States, accounting for more than 50% of all scans performed globally. Together, scans carried out in Canada, Germany, France, Japan, Italy, Spain, Belgium, and the United Kingdom account for another 40% of overall activity, making these 10 nations responsible for more than 90% of scans completed globally. Therefore the OECD Health Division concludes that countries with sizable populations and/or reasonably high NM diagnostic imaging rates account for a substantial portion of the global NM diagnostic activity.

The most commonly used isotopes in Europe for detection or diagnoses are indicated on figure 1 as Indium-111, iodine-123, thallium-201, rubidium-82, and gallium-67 for PET scans and molybdenum-99 (and thus technetium-99m) and xenon-133 for SPECT scans (NRG, 2022).

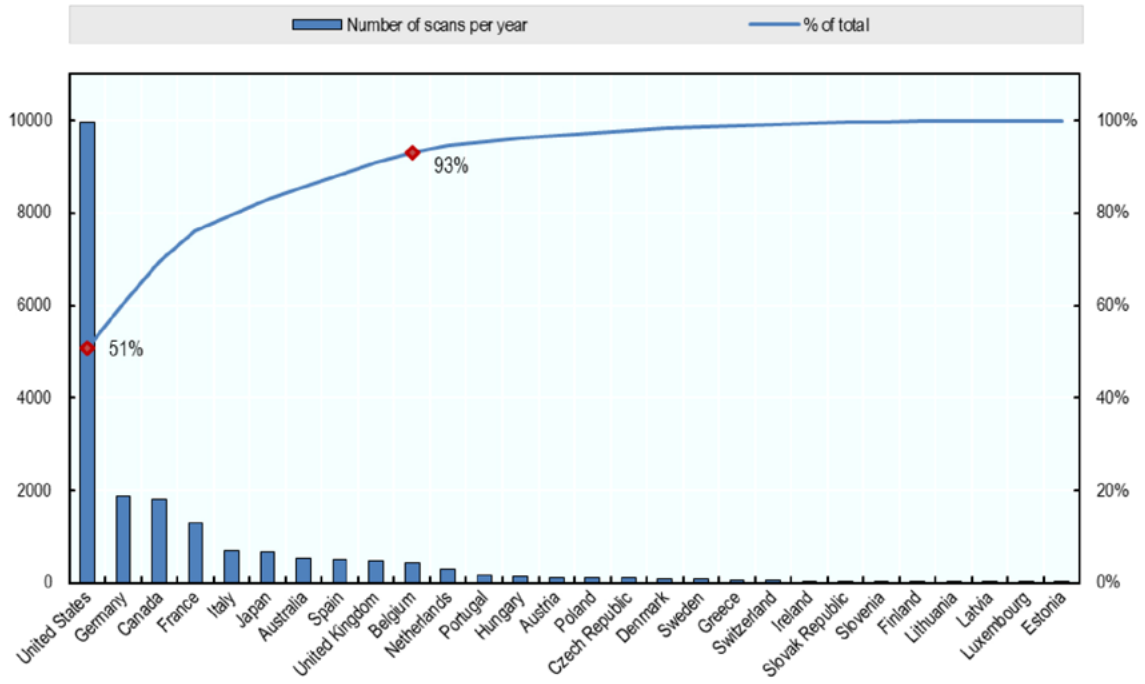
B) Phase 2: Evaluation

A SPECT, or Single photon emission computed tomography, portrays bodily internal biological processes through single photons. These particular scans are designed to discover blocked coronary arteries as well as disorders in bones, gallbladders, and intestinal bleeding.

A PET, or Positron emission tomography, relies on positrons for displaying biological processes occurring inside the body. PET scans are primarily used to identify cancer, track its development, gauge how well it is responding to treatment, and look for metastases.

Once phase one is completed, the results have to be evaluated. The medical term for interpreting these outcomes is imaging. NM employs hybrid imaging, meaning that imaging modalities are based on SPECT or PET devices and are combined with other imaging modalities' scanners (for instance, computed tomography CT or magnetic resonance MR) to enrich the functional imaging properties of NM with the anatomical data obtained from those procedures in a single scan procedure for the patient (Kumar, Bi, Kim, & Feng, 2020).

Graph 2: The absolute number of Tc-99m-based NM diagnostic scans per year by country



Source: OECD/NEA, 2019

Depending on the type of particle or radiation that the radioisotope emits, PET or SPECT scans are employed. While positrons are produced during the radiotracer decay during PET scans, gamma rays are measured by SPECT scans. A positron is an oppositely charged particle with nearly the same mass as an electron.

Figure 1 (p.6) shows that radioisotopes are either produced in a nuclear reactor or cyclotron. *Neutron-rich radioisotopes*, such as molybdenum-99, are best produced in a **nuclear reactor**, whereas *proton-rich radioisotopes* are generated in a **cyclotron**, also known as a particle accelerator. Generally speaking, cyclotron isotopes are short-lived nuclides with only several hours of half-life. Reactor isotopes usually have relatively longer half-lives allowing for a longer, global geographic reach (NRG, 2022).

PET scans solely depend on cyclotron-isotopes while SPECT scans rely on reactor-isotopes.

Innovation in the second phase is crucial since investments in imaging technology have resulted in the introduction of whole-body SPECT imaging, the use of time-of-flight measurements in PET for higher-quality images, and the routine availability of kinetic parameters for more detailed analysis of tumor metabolism, for example. Continuous innovation will enable personalized approaches ensuring the right equipment for the right patient. In short, investments will enhance patient care overall, including radiation dosages, acquisition procedures, scanning durations, and dosimetry. In this phase, the use of AI technology would also have specific benefits towards a future in which NM is more accessible.

All NM applications have an excellent safety profile due to the extreme sensitivity of the scanners and the high efficiency of radionuclides. Radiopharmaceuticals are applied in tracer amounts, only once or a few times in a patient's lifetime and are always administered in a controlled environment by a NM physician.

C) Phase 3: Treatment

Radiopharmaceuticals can also be used to treat diseased tissues, cells, and organs. Treatment accounts for 10% of NM procedures, though this percentage is rising due to recent research that has led to the creation of new radiopharmaceuticals. A therapeutic radioisotope is capable of destroying the harmful cell it is connected to while causing the least amount of collateral damage to the healthy tissue around it. Therefore, targeted radionuclide therapy is a very promising way of treating cancer, particularly in situations where traditional procedures (surgery, external radiation therapy, etc.) cannot be used. In short, **the field of NM provides well-established and innovative possibilities for customized medicine and cancer treatment without the negative side effects of other conventional, non-targeted medicines like chemotherapy.**

Figure 1 (p.6) indicates that the most common radioisotopes for therapeutical purposes are holmium-166, lutetium-177, iodine-125, iodine-131, iridium-192, strontium-89, and yttrium-90 (NRG, 2022).

2.2 Other uses of radioactive isotopes

The radioactive isotopes used in NM are not limited to diagnosing or treating patients. Low-intensity radiation can also be used to kill microorganisms, for example, operational tools. Other medical applications can be found in the sterilization of blood. Since the low levels of radiation can kill microorganisms but remain harmless to people, it is also used for irradiating food. The irradiation not only kills bacteria, it extends the shelf life of products such as tomatoes, sprouts, and berries. As previously described, radioactive isotopes are effective tracers and these features can also be exploited outside a hospital. For instance, leaks in underground water pipes could be discovered by following a tracer through the pipe. A last use of radioactive isotopes can be found in the age determination of various objects and once-living artifacts, such as animal or plant matter (Ball, 2014).

2.3 Revolutionizing nuclear medicine: technology and AI at the forefront

NM is at the intersection of science and technology. The perfect fusion of the latter has resulted in a transformation of the sector. Not only has it led to the introduction of whole-body SPECT imaging and the use of time-of-flight measurements in PET as previously discussed (in Phase 2) but also to developments in tracers and imaging technology. These new tracer concepts are used to image both novel medical treatments and the early phases of Alzheimer's.

In a communication released in 2018 by a high-level, independent expert panel that the European Commission

established, artificial intelligence is referred to as "*systems that display intelligent behavior by analyzing their environment and taking actions — with some degree of autonomy — to achieve specific goals*" (European Commission, 2020).

NM is rapidly utilizing artificial intelligence (AI), which has various advantages for boosting the precision, effectiveness, and efficiency of diagnosis, treatment, and research in this domain. A review article in the European Journal of NM discusses two major components in which AI can play a part in NM. The first component, which is referred to as the "physics" component, deals with picture generation and image processing duties. The second is referred to as the "clinical" component because it is primarily application-driven. It relates to normal tasks and standard clinical outcomes, such as diagnosis, prognosis, and therapy response prediction. AI holds significant promise for enhancing picture quality, customizing dosages (for both therapeutic and diagnostic purposes), and assisting with image interpretation. It paves the path for NM, which is by its very nature a numerical specialty, to realize its full potential—a goal that has gained speed over the past 10 years with the development of radiomics**. AI has the potential to enhance clinical processes in a way that not only boosts overall effectiveness but also makes it possible to practice tailored medicine for the benefit of a patient**. The emergence of total body scanners has resulted in a massive rise in the amount of data that must be processed. Total body scanners and AI look like an ideal combination to solve this issue (Visvikis, Lambin, & Beuschau Mauridsen, 2022).

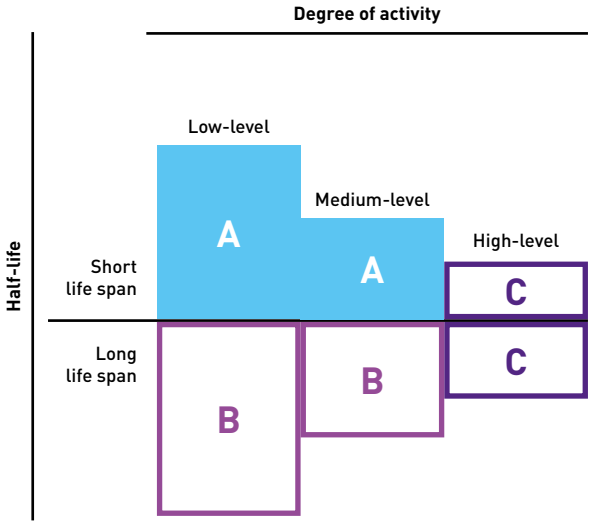
The benefits of AI can be found in the increased accuracy, effectiveness, and efficiency in all phases of NM. More accurate image analysis will help specialists make exact diagnoses. AI could also assist in choosing the best therapeutic strategy by assessing the data, taking into account a patient's medical history, and consequently determining the ideal radioactive dosage for therapy. Other functions of AI include automating routine duties like image processing and data entry for time-saving purposes or by analyzing massive amounts of information from clinical trials and experimental investigations to help hasten NM research.

2.4 Environmental considerations in nuclear medicine

The NM sector has strong legislation of safe limits due to the health risks of exposure to radioactive waste. For example, any future hospital design that calls for the use of radioisotopes for therapeutic and diagnostic treatments must have enough personnel and infrastructure to maintain ambient radiation levels below set safe thresholds. To evaluate the level of radiation safety, regular checks of the hospital setting and radiation personnel are required (Khan, Syed, Ahmad, Rather, Ajaz & Jan, 2010).

Radioactive waste can be divided into three categories. NM is part of category A, meaning that it is low and medium-level short-lived waste. Other examples of category A include maintenance in nuclear plants, industry, medicine, and scientific research. Category B and C represent highly radioactive and/or long-lived waste deriving mainly from the fuel used in nuclear power plants and from the decommissioning of nuclear facilities. A global research project demonstrates that the geological disposal of categories B&C is the most responsible and safest method for handling this kind of waste. The Belgian Research Center for Nuclear Energy Applications (SCK CEN) is a leader in the study of burying these waste materials in thick clay layers. A significant part of that research is done in the underground laboratory HADES in Belgium (SCK CEN, 2023).

Figure 2: Categories of radioactive waste



Source: SCK CEN, 2023

3 The Belgian nuclear medicine landscape

Statistics on the position of Belgian in the world of nuclear medicine prove that it is one of great importance. **Belgium is recognized as a major player since it is the second-largest producer of medical radioisotopes,** after the Netherlands. Furthermore, it is considered a pioneer in research and development and a major player in the transport and distribution of radiopharmaceutical products across the world. **Moreover, one in three of the world's hospitals specializing in nuclear medicine uses Belgian technology**, displaying the expertise and international reputation Belgium has built (IRE & IRE Elit, 2020). Belgium's credibility in the sector is a result of a collaboration between the Institut National des Radioéléments (IRE) and the Belgian Nuclear Research Centre (SCK CEN). **The pair produces 25% of all medical radioisotopes worldwide** (SCK CEN, 2023). As one of the world's leaders in the production of Molybdenum-99, the IRE accounts for an estimated 50% of the European demand for the radioactive isotope. The IRE is world-renowned as the second-largest research institute for nuclear research (Belgian Science Policy Office, 2022). According to the Belgian Nuclear Forum, almost 5,000 people work in the NM sector in Belgium. Jobs in this field are predominantly found in semi-governmental companies and research institutes such as universities and associated hospitals. The growing workforce is qualified through the recognition of Belgian universities in the field of radiology, NM, and medical imaging by the US news and world report. KU Leuven (Katholieke Universiteit Leuven) is currently ranked 24th in the world among universities, according to the latest rankings. Additionally, ULB (Université libre de Bruxelles) is ranked 152nd, and UCLouvain (Université catholique de Louvain) is ranked 174th in the same rankings. A devoted workforce in university labs and research institutes ensures a high level of knowledge in educational areas, ensuring that Belgium continues to succeed at all stages of the value chain (Nucleair Forum, 2023a).

The Belgian nuclear research center SCK CEN produces multiple radioisotopes, for example, molybdenum-99 and iodine-131. Cancer and cardiovascular disorders can be identified with the former. In turn, radioactive iodine is used to combat thyroid cancer. The production process of radioisotopes requires uranium targets that need to be

Overview of facts and figures about the nuclear medicine sector in Belgium

Major supply chain for radioisotopes

- The Belgian Reactor (BR2) has the largest irradiation capacity for Mo-99/Tc-99m production worldwide and is the second Mo-99 producer on yearly basis.
- The BR2 reactor of SCK CEN is one of the 2 most flexible and powerful research reactors in the world, able to satisfy 100% of the worldwide demand of Mo-99 when required.
- IRE is one of the 2 major processing facilities in the world for Mo-99 separation and purification.
- Both SCK CEN and IRE also produce other radioisotopes for medical applications.
- Yearly, Belgium coordinates 35,000 transports of radionuclides for medical applications

High density of nuclear medical imaging equipment for clinical use

- 161 SPECT/CT Gamma cameras: 15 per million inhabitants
- 33 PET/CT cameras: 3 per million inhabitants
- 137 (N)MRI cameras: 12 per million inhabitants
- 8 cyclotrons (7 for production of radioisotopes and 1 for proton therapy) in Belgium

High density nuclear medicine specialists

- ± 350 nudear medicine specialists: 30 per million inhabitants
- ± 5,000 direct or indirect jobs

Source: Rad4Med.be, 2023

irradiated. The scientific breakthrough in Belgium is that all base materials to create radioisotopes now stem from low-enriched uranium in contrast to highly-enriched uranium. SMART, or Source of MedicAl RadioisiTopes, is an intention to generate radioactive molybdenum (Mo-99) from natural molybdenum (Mo-68) for the first time. Mo-68 is the Basic product for many SPECT scans (an imaging test that reveals how blood flows to tissues and organs). Now, uranium-235 is used to make radioactive molybdenum, which may also be utilized in nuclear power plants and nuclear weapons. That necessitates a high level of security as well as a large amount of radioactive waste, which results in soaring expenses. The medicinal isotope molybdenum-99 was successfully produced on a modest scale without the use of uranium in 2022. The director of the SMART project at IRE, Veerle Van de Steen, stated: "*We expect that preparations for the site, which will be the size of a soccer field, will begin in 2023 and we anticipate starting manufacturing in 2028*" (IRE & IRE Elit, 2022).

The Atomium is another enduring representation of Belgium's historical interest in scientific development and the dedication to making it more accessible in people's lives. The clinical acceptance of NM has been undeviatingly growing over the past 10 years. This has led to increased R&D investments, supply chain solutions, cutting-edge technology, and sustainable waste management. The role of Belgian organizations and institutions in the field of NM is pivotal in not only research and production but distribution as well (Atomium, n.d.).

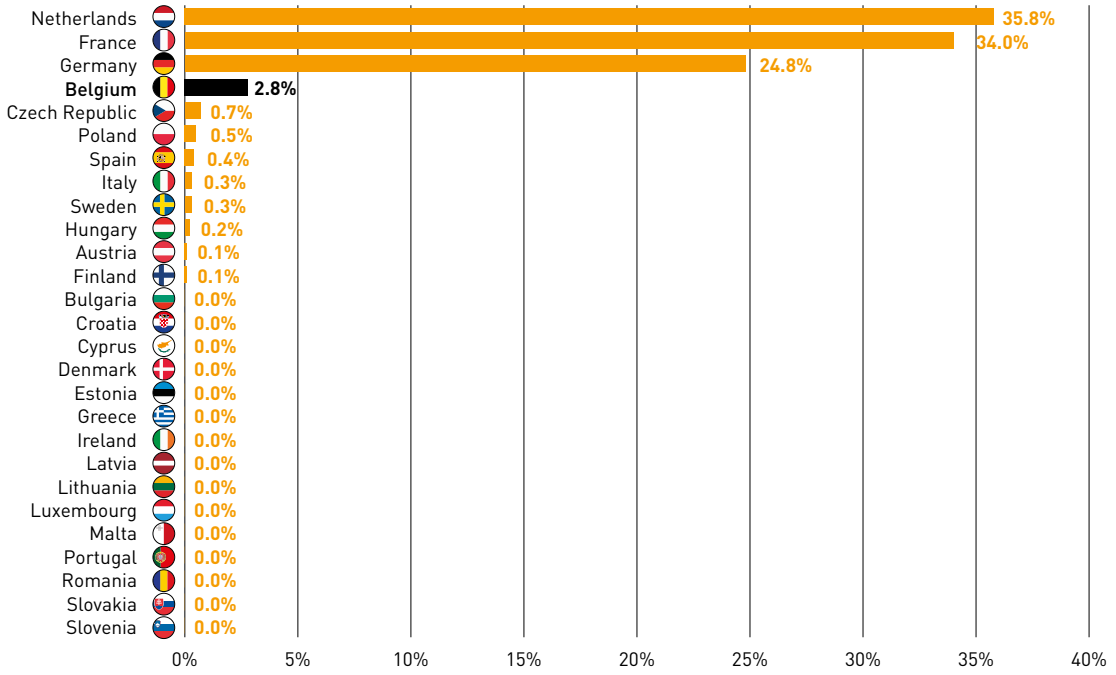
Many stakeholders in the sector work together in order to increase public knowledge of the use of nuclear radiation in healthcare, as well as increasing its visibility. The Belgian Nuclear Research Centre (SCK CEN), the Health Cluster of Wallonia (BioWin), the Institute for Radioelements (IRE), and a privately owned company, Ion Beam Applications (IBA), created an overarching non-profit network called **Rad4Med.be**. With a network of over 80 members, Rad4Med.be is a hub of information regarding the nuclear medicine sector. The key facts and figures on the next page exhibit why Belgium is a force in the world of nuclear science and technology for healthcare (Rad4Med.be, 2023).

3.1 Belgian export industries

Being one of the biggest producers of radioisotopes in the world results in a major responsibility for Belgium to not only supply the domestic market, but foreign markets as well. To give an idea of the domination of Belgium in the NM sector, Tradexplorer.be, a monthly updated website of the Belgian Foreign Trade Agency, publishes and presents data that is released by Eurostat over the last 10 years. The NM sector is represented under the custom code 2844: Radioactive Chemical Elements & Radioactive Isotopes. It is impossible to discuss the evolution of the nomenclature since most of the specific EURATOM custom codes discussed were subject to a readjustment in 2021. Due to the abundance of custom codes, the codes that are represented in this paper are the ones where Belgium plays a significant role in the export of EU27 countries.

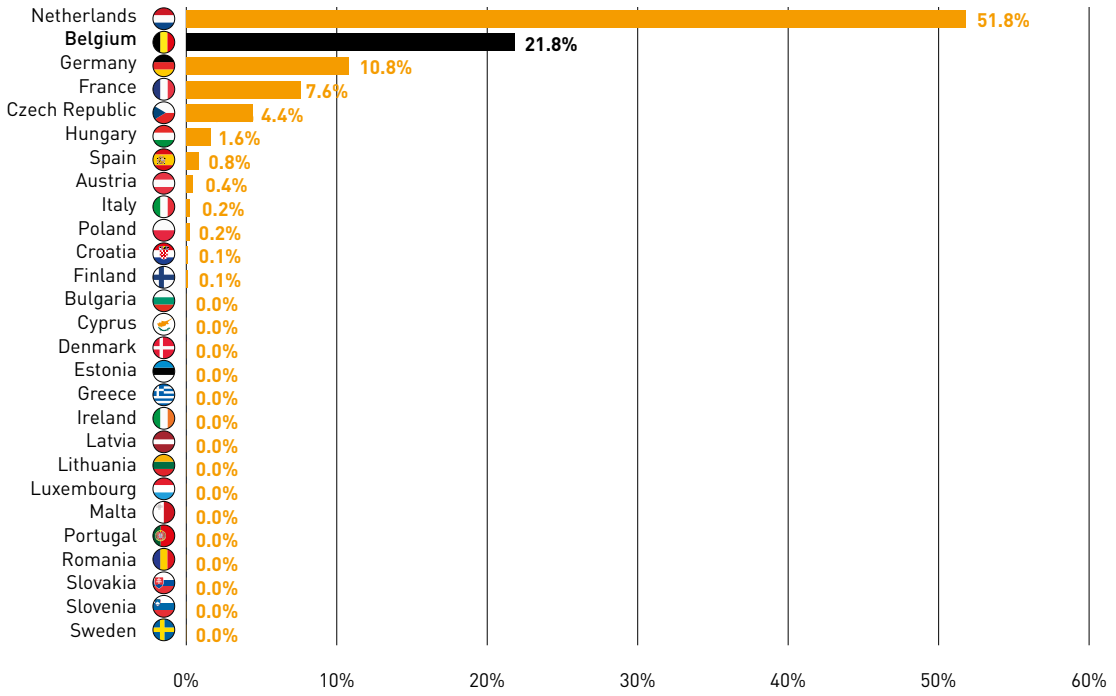
Graph 3 shows that Belgium exports 2.8% of the total of custom code 2844 in the world, equivalent to EUR127,548.0, taking fourth place behind the Netherlands, France, and Germany. The relatively low total can be attributed to the merging of radioactive chemical elements and radioisotopes into one custom code. Belgium has a small share of the radioactive chemical elements exported to the rest of the world. In contrast, the radioactive isotope export, more specifically the artificial radioactive isotopes (28444020) on graph 4, represents a Belgian share of 21.8% of the total export of the EU27 countries. Compared to other EU27 countries, only the Netherlands exports more. Artificial radioactive isotopes are formed when an atom is bombed with an accelerator or when it is exposed to slow-moving neutrons in a nuclear reactor. Tradexplorer.be also indicates that Belgium has a leading export position on three other custom codes within the radioactive isotopes nomenclature. One of those is 28444110 (artificial radioactive isotope and its compounds of tritium), indicating market domination of Belgium with a 68.9% share of the total export of EU27 countries. Tritium is an isotope of hydrogen and is used as a tracer in biomedical and academic research. Radioactive residues (28444400) are another field where Belgium dominates the EU27 export market with a total share of 61.2%. The relatively largest export share of Belgium is attributed to spent "irradiated" fuel elements "cartridges" of nuclear reactors (28445000) with 70.4% of the total EU27 export market. (Tradexplorer.be, 2023).

Graph 3: EU exports of radioactive chemical elements and radioactive isotopes, 2022



Source: Tradexplorer.be, 2024

Graph 4: EU exports of artificial radioactive isotopes, 2022



Source: Tradexplorer.be, 2024

3.2 The nuclear medicine supply chain in Belgium

Only a small portion of the manufacturing process for medical isotopes involves irradiating raw materials (either in a reactor or an accelerator). The irradiation is followed by several purification and processing stages carried out in separate laboratories. Therefore, the extent to which reactors can contribute to the creation of medical isotopes heavily depends on the availability of parties nearby who can promptly produce and deliver the radioactive materials to the hospitals. Due to the isotopes' limited lives, efficient logistics are crucial. Even though the half-life of 6 hours is long enough for convenient supply and same-day imaging studies, interruption of the supply chain can have a large impact on the efficiency of the process (IAEA, n.d.).

Figure 3: Isotopes production chain

Source: Nuclear Netherlands, 2017

The demand for medical radioisotopes is only partially met by a limited number of producers worldwide. One of them is the BR2 research reactor of the SCK CEN. At every operational cycle, it supplies the essential raw materials required to conduct at least one million patient diagnoses and at least 3,000 cancer patient treatments (SCK CEN, 2022). Reliable delivery is essential for achieving a diagnosis or receiving the proper care. The BR2 reactor has not missed one scheduled operating cycle in the previous 45 years, ensuring its status as a reliable supplier. Per operational cycle, BR2 typically generates ten to fifteen distinct radioisotopes. **In 2021, this translated into more than 10 million patients who were assisted as a result of Belgian production** (BioWin Wallonia, 2022)**.**

Only two reactors in the world can now manufacture Mo-99 in sufficient quantities to meet global demand, one of which being the powerful research reactor BR2 from SCK CEN in Mol. SCK CEN generates one-third of the radioisotopes used in cancer detection and therapy globally each year. The isotope is supplied to generator makers by IRE, one of the world's two primary centers for Mo-99 processing. The Ga-68 (Gallium-68) generator is manufactured by IRE. Over 95% of IRE's output is exported. When needed, SCK CEN and IRE can provide 100% of the Mo-99 world's demands (Rad4Med.be, 2023). To illustrate the growing industry, in 2022, more than 11 million patients benefitted from medical radioisotopes made at the BR2 research reactor. These favorable numbers are due to a change in the number of operational days, resulting in an increase of 25% in the production of Mo-99 (SCK CEN, 2023).

In Table 1, on the irradiators of different nuclear reactors, can be seen that **Belgium has the greatest maximum capacity per week with a capacity of 7,800 compared to the Netherlands with a capacity of 5,400.** Although Belgium is leading in the category of maximum capacity per week, the Netherlands is leading in the annual total of world capacity. The numbers can be explained by the average number of Mo-99 production weeks in one year since the reactor in the Netherlands operates for 38 weeks in contrast to the Belgian reactor, which operates 27 weeks annually.

Table 1: Irradiation capacity for Mo-99 production

Reactor	Country	Start of Operation (year)	Reactor Operation License Expiration (year)	Normal Operating Days (days/year)	Mo-99 Production (weeks/year)	Available Production Capacity per week (6-day Ci Mo-99/week)	Available Production Capacity per year (6-day Ci Mo-99/year)
BR-2	Belgium	1961	2026	190	27	7,8	210,6
HFRe	Netherlands	1961	2024	266	38	5,4	228
LVR-15	Czech Republic	1957	2028	210	30	2,4	72
Maria	Poland	1974	2030	200	36	2,7	95
NRU	Canada	1957	2018	280	40	4,68	187,2
OPAL	Australia	2006	2055	300	43	1,75	75,25
SAFARI-1	South Africa	1965	2030	305	44	3	130,7
					Totals:	**27,73**	**998,75**

Source: SCK CEN, 2017

3.3 The transport of radioactive material in Belgium

About 90% of the radioactive material transported in Belgium results from the medical sector. The remaining 10% are radioactive materials destined for research and industrial applications, including food irradiation and electricity production by nuclear power plants. The use of radioactive material requires national and international shipments. Every year, specialized companies transport some 400,000 packages of radioactive materials through Belgium. That corresponds to around 40,000 transports and an average of over 100 packages per calendar day. The transport of radioactive waste produced by all these different applications represents only an extremely small part of the total. We are talking about at most 200 transports per year.

The Belgian medical industry will receive about 350,000 goods or 35,000 shipments of radioactive material. These substances must be transported throughout the rest of the world and in our nation. The transportation is done by both air and land, primarily through Liège and Brussels airports. Road and air transportation are the two primary methods of moving radioactive material in Belgium. Every day, more than 100 transports are made by road, while more than 10 are made by air. 90% of them need to be carried across large distances since they are radiopharmaceuticals with a short life (Nucleair Forum, 2021).

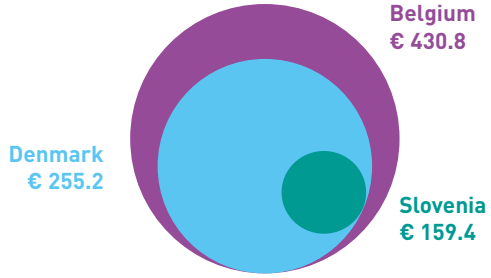
Belgian transportation businesses dominate the industry. Numerous Belgian businesses are well-known across the world for the way they manage all forms of nuclear transport (by land, air, train, and sea). They are equipped with modern transportation and skilled, specially trained personnel. **The most well-known radioactive material transport businesses in Belgium are *Transport Debrouwer, Isotopes Services International (ISI), SDV of the BOLLORE Logistics group, Transnubel, and Transrad*** (IRE & IRE Elit, 2020).

3.4 Belgium, a leader in Europe in terms of R&D and innovation

Nuclear medicine requires a high intensity of R&D spending, which Belgium supports. According to Eurostat (2022), the investment in EU R&D increased to EUR328 billion in 2021. Another significant contribution to European R&D derives from an initiative of the European Commission, also known as the Horizon Europe Work Program 2023-24. The program will allocate a budget of EUR13.5 billion to assist European researchers and innovators in their pursuit of breakthrough solutions to environmental, energy, digital, and geopolitical concerns. The 2023-2024 Horizon program, which is part of the larger seven-year EUR95.5 billion EU research and innovation initiative, will help the EU meet its climate targets, increase energy resilience, and create fundamental digital technologies (European Climate, Infrastructure and Environment Executive Agency, 2022).

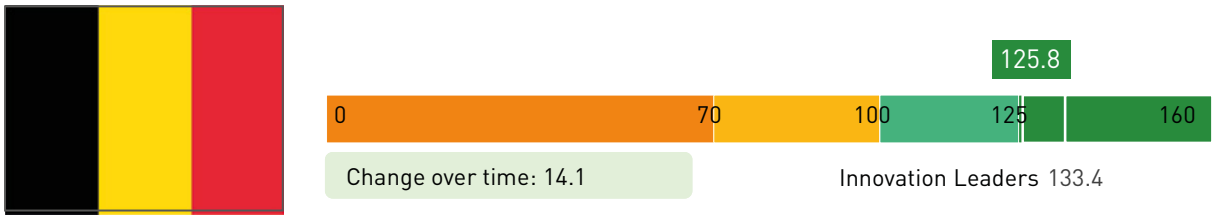
Compared to the R&D expenditures in the EU, Belgium's population and healthcare system allow a proportionately significant investment in biopharmaceutical innovation. The amount of Belgian R&D expenditures in the overarching biopharmaceutical industry are unparalled in the EU. The most recent numbers available, from 2020, place **Belgium eighth in terms of population**, **but second in R&D expenditures** behind Germany and ahead of nations like France and Italy**. Belgium is unquestionably at the top spot when it comes to investment per capita. Our investments in 2020 were about 70% higher than Denmark's, which came in second place, and up to nearly three times higher than Slovenia's, which came in third place** (Pharma.be, 2023; EFPIA, 2023).

Figure 4: Biopharmaceutical R&D expenditures per inhabitant 2020



Source: Pharma.be, 2023

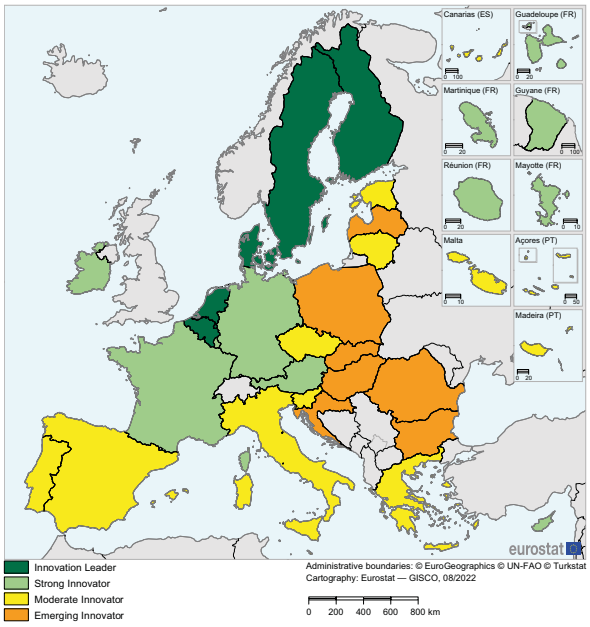
Figure 5: European Innovation Scoreboard of Belgium



Source: European Commission, 2023

In terms of innovation, Belgium has come a long way to become a leader. The result of years of collaboration between academic institutions, business organizations, and governments, led to a 5th place for Belgium in 2022. According to the European Innovation Scoreboard (2022), Belgium performs around 29% better than the EU average and ranks just below Sweden, Finland, Denmark, and the Netherlands. With performance at 128.8% of the EU average, Belgium is an innovation leader (European Commission, 2022).

Figure 6: Map showing the performance of EU Member States' innovation systems

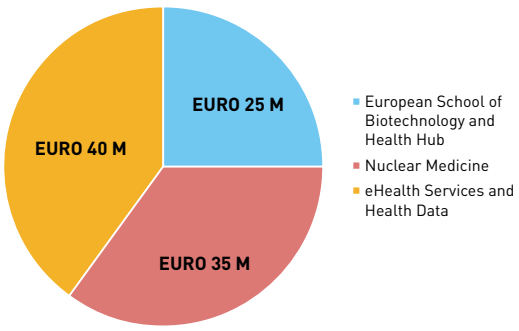


Source: European Commission, 2022

The data on the proportion of GDP spent on R&D also reflect this outstanding innovation performance. The so-called Lisbon objective, which states that 2.5% of the GDP is expected to be reinvested in R&D, was exceeded in 2019 by more than 3%. **Belgium and Sweden are ranked first in the EU in terms of R&D spending as a percentage of GDP in 2020, with a 3.5% share** (European Commission, 2022).

In 2018, the federal government allocated EUR52 million to the research and development phase. Due to Belgium's dedication to research and development, modern imaging systems including PET scanners and SPECT scanners have been developed. This equipment can give medical personnel in-depth knowledge of a patient's condition, facilitating rapid and precise diagnosis. Following the Covid-19 crisis, the Belgian Recovery and Resilience Plan allocated EUR35 million to NM. The investment was part of the EUR99.8 million expenditure in the health sector (European Commission, 2021).

Graph 5: The Recovery and Resilience Plan Belgium for health



Source: European Commission, 2021

The NM sector enjoys of continuous R&D investment within an ecosystem. Future initiatives by the SCK CEN and IRE relate to the upscaling of the radioisotope lutetium-177 to meet world demand. Erich Kolleger, the CEO of IRE, announced that they will collaborate with SCK CEN on the production of lutetium-177 in 2023-2024. This particular medicinal radioisotope, among other things, is promising for the treatment of prostate cancer, the most frequent type of cancer in men. The upscaling is important since additional treatments have been approved, causing a rise in demand. Eric van Walle, former Director General of SCK CEN, claims that the need for lutetium-177 will grow rapidly, from 16,000 patients in Europe and the United States in 2020 to 138,000 patients in 2026. A competition is gaining momentum among a few producing nations worldwide, but Belgium has a major competitive advantage in that we can both make and purify lutetium-177. In order to realize the production and purification of the isotope, a EUR15 million production facility will be build. Two third of the expenses will be provided by the European Recovery Fund. The IRE, which now handles over 2,500 radioisotope shipments each year globally, will offer lutetium-177 to a network of pharmaceutical businesses and hospitals in the near future (De Tijd, 2021a; De Tijd, 2022).

Another promising advancement is the production of novel radioisotopes occuring in Belgium. IBA, the global leader in particle accelerator technology, and SCK CEN announced a strategic R&D collaboration in 2021, PanTera, to allow the manufacturing of Actinium-225 (225Ac), a new radioisotope with tremendous promise in cancer treatment. While experts predict that the usage of lutetium-177 will increase in the future years, its replacement is already gaining traction. Experts consider actinium-225 to be an improvement over lutetium-177. Actinium-225 is nearly unavailable in the market, but numerous studies are being conducted on its potential to treat a variety of cancers, including common cancers such as prostate, lung, colon, breast, pancreatic, blood, and kidney cancers. Despite its medicinal potential, actinium-225 is almost commercially unavailable. It is also referred to as the 'scarcest medicine in the world' since it is produced in only a few countries, including Russia, Canada, and the United States, in levels that reach only 1,700 patients every year. **PanTera**, a joint venture between the two Belgian companies, was formed in late 2022. Construction will begin in 2024, with production beginning in 2027. Pantera may increase manufacturing to include other radioisotopes. Global production is currently just 2 curie (a unit indicating the total amount of isotopes), but it is projected that 200 to 400 curie will be required in the next 10 to 15 years. **Belgium has a distinct advantage in that it has both raw materials and manufacturing know-how on its own soil** (De Tijd, 2021b; SCK CEN, 2021).

Both initiatives are also aligned with the European Recovery plan which disclosed Lutetium-177 and Actinium-225 as promising isotopes. Thomas Dermine, State Secretary for Recovery and Strategic Investments, affirmed that this strategic R&D collaboration is one of the first tangible outcomes of the recovery plan, which commits more than EUR 800 million in additional resources to research and development (SCK CEN, 2021).

3.5 The Belgian approach towards waste management

The adoption of NM has not only improved healthcare outcomes but also has positive economic effects. However, the environmental consequences should not be overlooked in the process. By optimizing production processes, reducing waste, and increasing energy efficiency, Belgium's NM sector is contributing to sustainability goals while bolstering the economy.

The Belgian industry has three solutions for radioactive waste. First, waste stored above ground, also known as surface disposal, is employed for radioactive waste without any risk to the public health of current and future generations. Category A, which includes NM, applies this solution to their waste. In Belgium, the construction of a new surface disposal facility is ongoing. The waste barrels are temporarily kept in special structures while it is being finished. The future surface disposal site is located in Dessel. Meanwhile, Belgoprocess has designated premises where the low and medium-level short-lived waste is kept (SCK CEN, n.d.).

Other categories of radioactive waste require different solutions. The short- and long-term management of all radioactive waste is the responsibility of the Belgian Agency for Radioactive Waste and Enriched Fissile Materials (NIRAS/ONDRAF). The scientific justification of safety files is a major focus of SCK CEN. As mentioned previously, highly radioactive and/or long-lived waste involves geological disposal in deep clay layers carried out by the laboratory HADES, which is located 225 meters underground. To lessen the negative effects on future generations, SCK CEN is researching options for lowering

the risks, costs, and footprint associated with geological disposal. Geological disposal is still required, even though radiochemical process technologies such as advanced separation, also known as partitioning, can divide the different chemical components contained in spent nuclear fuels into distinct fractions. As a result, each fraction may be dealt with in a way that is more focused and effective.

Furthermore, Belgium has started the construction of a facility that enables radioactive waste to be recycled. The RECUMO facility will recycle radioactive residues from the production of medical radioisotopes to recover uranium. The operation to convert and purify radioactive residues to low-enriched uranium will start running in 2026. By giving the radioactive substance a second life, the nuclear sector can contribute and move towards a circular economy. The Belgian facility is a pioneer in a cutting-edge technology that purifies the radioactive substances. In February 2023, the first construction works have been carried out. This European scoop has been made possible by the establishment and operating license granted by the Federal Agency for Nuclear Control and the Flemish region for the environmental permit (World Nuclear News, 2023).

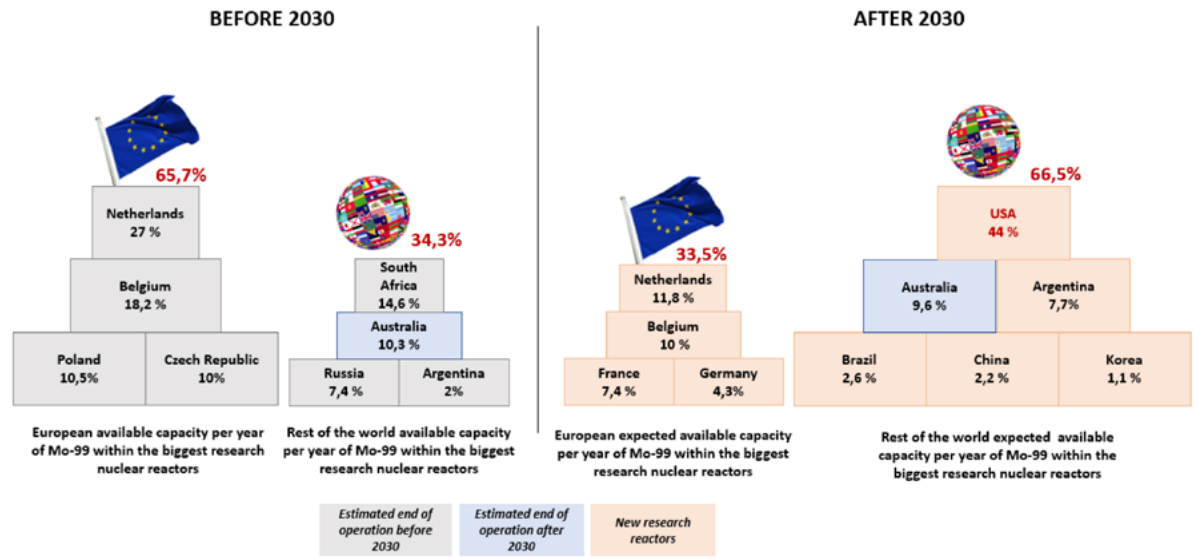
4. How companies are tackling the challenges of nuclear medicine

4.1 Global challenges

In contrast to all the opportunities the NM sector has to offer, facing challenges is unavoidable. Three challenges are identified in the areas of preparation, availability, and production. The first challenge, preparation, refers to the process where medical radiopharmaceuticals have to be prepared in-house since they have a short half-life. If the radiopharmaceutical is prepared, it only has a couple of minutes before it loses its radioactive potential. Therefore, the preparation of such medical products needs to be conducted in dedicated facilities, that are in line with radiation protection standards (EANM, 2022).

The second challenge involves the availability of radiopharmaceuticals since the high diversity of medical radioactive substances and the wide variety of patient-specific indications lead to diminishing commercial interest and bottlenecks in the production process.

Figure 8: Market share of Europe in radioisotope production before and after 2030



Source: EANM, 2022

The last challenge relates to the production of medical radioisotopes. It is vital to keep in mind that the NM industry is not involved in any nuclear energy generation applications. Most radioisotopes used in NM are created in research reactors, which vary from regular nuclear reactors in that they produce neutrons rather than electricity and are solely intended to create medical radioisotopes for academic research. Research reactors are simpler than power reactors because they run at lower temperatures and use significantly less fuel. These are small-scale installations, and the NM industry is now experiencing supply disruptions attributable to the aging of research reactors. This aging equipment will also have a severe impact on Europe's dominant status as a worldwide supplier, putting its self-sufficiency in jeopardy. As indicated on figure 8, before 2030, Europe is said to have a market share of 65.7% compared to an estimated share of 33.5% after 2030 (EANM, 2022).

4.2 The Belgian solution, MYRRHA

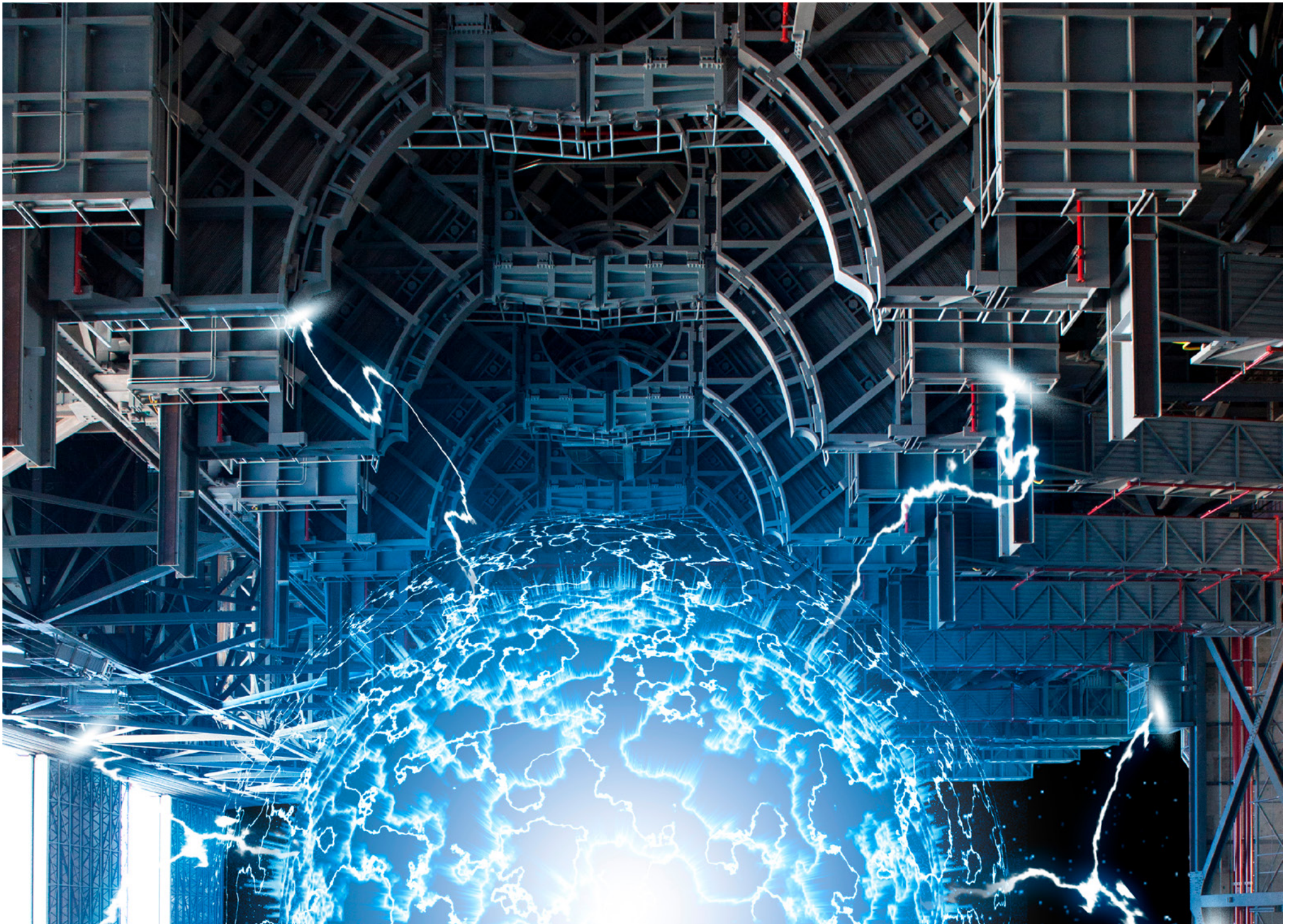
Belgium presents a solution to the last two challenges in the form of a new nuclear reactor called MYRRHA. The reactor will produce theranostic radio-isotopes (for diagnostic and therapeutic purposes) to address this growing demand. SCK CEN also works on the creation of novel therapeutic radio-isotopes that can combat cancer cells in a more focused manner, reducing adverse effects for patients. The accelerator will begin producing radioisotopes for medicinal uses in 2027. In particular, concerning the challenge of availability, the new reactor will provide some solutions. The enormous power of MYRRHA's proton accelerator and dedicated isotope production programs will enable for large-scale manufacturing of these isotopes. Furthermore, MYRRHA permits the creation of distinct isotopes of the same family (for example, multiple terbium isotopes) with extraordinarily high isotopic purity. New radioisotopes and a larger production scale should also reinforce the position of Belgium and Europe in the production of radioisotopes (MYRRHA, n.d.).

MYRRHA, or Multi-purpose Hybrid Research Reactor for High-tech Applications, will be the world's first large-scale Accelerator Driven System project at industrial-scale power levels. MYRRHA provides unprecedented prospects for study in spent nuclear fuel, NM, and basic and applied physics. The Belgian Federal Government agreed on September 7, 2018, to build the MYRRHA project on the SCK CEN site in Mol. The government contributed EUR558 million to the project's phased approach out of a total budget of EUR1.6 billion. Furthermore, the Belgian government announced the formation of an international non-profit organization that will be perfect for attracting investment from new participating nations. MYRRHA is a contender for European Investment Bank financing since it falls within the European Union's ESFRI (European Strategic Forum for Research Infrastructure) and SET (European Strategic Energy Technologies) Plans. The European Commission recognizes MYRRHA as an international innovation project of great social importance. MYRRHA stimulates innovation throughout Europe and plays a role in the development of the knowledge-driven economy. Like the Belgian government, Europe has therefore decided to provide financial support to SCK CEN for this project. MYRRHA will be constructed in 3 phases, phase 1 is set to be completed in 2026. The second phase will be an extension of production capacity whilst phase 3 will involve the construction of the reactor, of which the construction should be completed in 2036. The MYRRHA project draws experts from across the world, which helps to build our worldwide status and reputation for excellence. Aside from teaching future generations of specialists, this world-class initiative provides the potential to connect multiple research institutes, colleges, and businesses in our nation and throughout the world. MYRRHA will provide roughly 2,000 long-term jobs, both directly and indirectly, during the operating period. Furthermore, this dynamic project will be supported by the production of spin-offs and the establishment of new high-tech enterprises in the neighborhood of SCK CEN (Nucleair Forum, 2023b).

Closing thoughts

Belgium's nuclear medicine sector is a testament to the power of innovation in healthcare. Novel technologies have propelled the field forward, enabling precise diagnostics and groundbreaking therapies. As Belgium continues to invest in research and development, its contributions to nuclear medicine promise to have a lasting impact on global health.

In an era where healthcare challenges are ever-present, Belgium stands as a beacon of progress, using science and technology to pioneer advancements that benefit patients, healthcare providers, and society as a whole. The Belgian journey in the nuclear medicine sector is not only a testament to the country's dedication to excellence but also a promising outlook for the future of healthcare worldwide.



SUCCESS STORIES IN BELGIUM

INTERVIEW WITH
Ruth Devenyns,
Former CEO

COMPANY

Precirix

REGION

Brussels

Founded: 2014

Location: Headquarters in Brussels (Jette)

Number of employees: > 30 employees

Investments: Series B financing of 80M EUR in 2022

Prizes, awards:
1/ Series B Finance Raise of the Year 2022 (European Lifestars Awards)
2/ Best Venture Capital Deal – Life Sciences 2022 (M&A Awards)

CEO at the time of the interview:
Ruth Devenyns (December 2023)
Current CEO: Tom Plitz (end of February 2024)

PRECIRIX

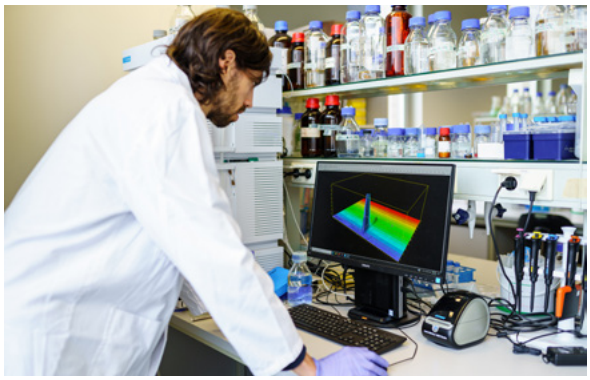
Precirix, a pioneering clinical-stage biotechnology company rooted in Belgium, is revolutionizing cancer treatment through groundbreaking technologies. Focused on radiopharmaceuticals, Precirix sets itself apart with an innovative approach to cancer therapy, utilizing camel-derived antibodies to precisely target cancer cells on a molecular level. "After conducting a first study with our lead compound to assess its safety, we continue our journey on the long path of drug development, Ruth Devenyns, former CEO of Precirix, explains.

UNCONVENTIONAL CANCER THERAPIES

Precirix specializes in developing radiopharmaceutical drugs, distinguishing itself from conventional cancer therapies like external radiation. Their unique modality involves radiating cancer through a drug, enabling unparalleled precision at a molecular level. The company employs camel-derived antibodies, originating from a 1990s Brussels University discovery, known for their human-like characteristics and the ability to specifically target cancer cells. The core innovation lies in using these antibodies as targeting molecules, ensuring a drug's rapid attachment to cancer cells, while non-bound drugs are rapidly excreted from the body. This groundbreaking technology has potential applications in treating various cancer types. Precirix has initiated clinical studies to assess the safety of their lead compound, with a focus on developing a therapeutic approach that minimizes side effects and enhances efficacy.

"This dual-program strategy balances the certainties of validated targets with the potential of groundbreaking, albeit riskier, novel targets."

In their pursuit of developing groundbreaking radiopharmaceuticals, the company strategically navigates the landscape of cancer targets. The initial program, CAM-H2, focuses on the well-established HER2 receptor: a clinically validated target with existing drugs demonstrating its therapeutic potential. The decision to launch their technology development with this proven target reflects a calculated approach, minimizing risks while tapping into a competitive yet validated market. Their second program, on the contrary, centers around FAP (fibroblast activation protein), a novel and less explored target within the radio-



pharmaceutical domain. While FAP exhibits promise by being expressed in a large number of cancer types, its lack of clinical validation introduces an element of risk. However, the company views this risk as an opportunity, capitalizing on the field's openness and reduced competition to forge new avenues in cancer treatment. "This dual-program strategy reflects a nuanced risk-management approach, balancing the certainties of validated targets with the potential of groundbreaking, albeit riskier, novel targets", Devenyns explains.

BELGIUM AND BEYOND

Precirix has a multifaceted approach to their international endeavors. Research and corporate activities take place in Belgium, where the company's lab facilities drive pure research initiatives. Manufacturing activities are conducted in North America, emphasizing the need for optimizing and upscaling the production process to meet regulatory standards for human testing. Clinical activities are also executed in North America, where the company has received CTA/IND approval to conduct studies. Precirix strategically collaborates with global partners, such as AtomVie in Canada and Evergreen in the U.S., to leverage their expertise and facilities in various aspects of the development process.

Belgium serves as an instrumental base for Precirix due to various strengths. Despite high taxation, the country offers support for research endeavors, including deductions for social security contributions. "The supportive environment extends to a robust ecosystem of biotech and pharma companies, providing essential services and expertise. Additionally, Belgium's vibrant investor community facilitates funding for innovative ventures like ours", states Devenyns.

The company also emphasizes the role of Belgian universities, particularly the VUB (Vrije Universiteit Brussel), where research and development activities, including animal testing, are still ongoing. Furthermore, Precirix highlights the country's favorable environment for attracting and retaining talent in the field of cancer research.

TRANSFORMING CANCER TREATMENT

Precirix' long-term vision is ambitious yet focused. The company aspires to transform cancer treatment, specifically in the realm of precision radio pharmaceuticals. "Our mission is to contribute a novel treatment modality to the existing toolbox for cancer patients, aiming to prolong life and improve the quality of life during treatment", declares Devenyns. While acknowledging the complexity of cancer, Precirix envisions offering a unique solution that minimizes complications associated with traditional treatments.

The company's short to mid-term focus revolves around demonstrating the efficacy of their most advanced programs in patients. This includes achieving regulatory approval for testing their second compound in patients, marking a significant milestone. "Additionally, the people at Precirix are keen on identifying specific patient populations and treatment regimens for their compounds, paving the way for future development strategies", highlights Devenyns.

In order to reach these short to mid-term goals, the company can rely on a compact and versatile team. The close-knit nature of a small company provides a powerful advantage, fostering seamless interaction and collaboration among team members. "The dynamic at Precirix allows for a collective approach to problem-solving, where individuals, with their varied skills and perspectives, unite to address challenges collectively", states Devenyns.

Devenyns sees a promising future for nuclear medicine in Belgium, particularly within their niche market. The country's expertise and momentum in this field position Precirix to thrive as the demand for innovative cancer therapies continues to grow. The company's commitment to building on this momentum aligns with the broader outlook for nuclear medicine in Belgium.

The strategic initiatives of Precirix also align with the belief and conviction in the robustness of its technology and its innate capacity to generate impactful products. While harboring aspirations to broaden their scope and build a comprehensive pipeline, the realization of such ambitions hinges on securing additional financial resources. "Selling our technology may take precedence in the future, the company remains pragmatic, understanding the necessity of prioritizing and allocating resources judiciously in the present", Devenyns concludes.

"Our mission is to contribute a novel treatment modality to the existing toolbox for cancer patients."

INTERVIEW WITH

Patrick Flamen,

Doctor, head of the department Nuclear Medicine

COMPANY

Institut Jules Bordet

REGION

Brussels

Founded: 1939

Location: Rue Meylemeersch 90
1070 Anderlecht

Number of employees: 1200

Turnover (2022): 220M EUR

Growth (2022): +20,5%

Investments (2022): Construction of the New Bordet: 400M EUR

Prizes, awards: 2 Nobel Prizes (Jules Bordet et Albert Claude)

In the fast-evolving landscape of medical science, Jules Bordet Hospital emerges as a trailblazer, particularly within its nuclear medicine department. "The hospital is charting new territories in the realm of cancer treatment through its innovative approach: Radioligand Therapy (RLT)", according to Dr. Patrick Flamen, the head of the Nuclear Medicine Imaging and Radionuclide Therapy department of the Jules Bordet Institute since 2003.

REDEFINING CANCER CARE

The institute is revolutionizing cancer treatment through Radioligand Therapy, a groundbreaking method within the domain of precision oncology. The method utilizes radioactively tagged molecules (i.e. vectors) to target specific molecular structures expressed by tumor cells (e.g. tumor specific receptors or antigens). The hospital predominantly leverages Lutetium-177, a beta emitter, for clinical applications, particularly in treating cancers such as prostate cancer and neuroendocrine tumors. The hospital has a distinct preclinical lab dedicated to the development of new applications of Radioligand Therapy, labelled ATENO (Advancing Theranostics in Nuclear Oncology). The beta emitters, such as Lutetium-177 and Iodine-131 are now clinically fully accepted for the treatment of patients. Other radioactive isotopes adequate for marking vectors are alpha emitters, such as Actinium-225, Lead-212 or Astatine-211. These isotopes have alpha emission instead of beta emission, which is more effective in terms of tumor control. The hospital is actively charting an optimistic path in the evolution of radioligand therapy, with a dedicated focus on alpha isotopes. In the early stages of pre-clinical and clinical development, this endeavor represents a promising leap forward in refining cancer treatment strategies.

The dedicated cancer institute also rejoices a distinctive academic status through the affiliation with the University Hospitals of ULB (Université Libre de Bruxelles). The research of

"We have the whole chain to develop new radiopharmaceuticals. From pre-clinical infrastructure to infrastructure in the hospital."

H.U.B HÔPITAL UNIVERSITAIRE DE BRUXELLES ACADEMISCH ZIEKENHUIS BRUSSEL

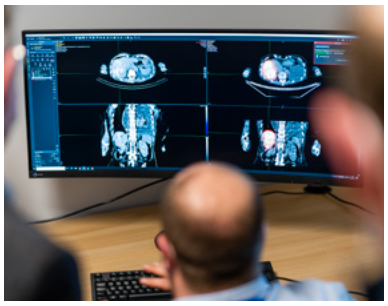
INSTITUT JULES BORDET INSTITUUT

Hôpital Erasme ULB

the early stages of pre-clinical and clinical development can be divided into four strategic pillars that are guiding the department's research initiatives. The first pillar focuses on extending beta therapy to different tumor types where unmet medical needs exist, with an emphasis on triple negative breast cancer, glioblastoma, and pancreatic tumors. The second pillar involves optimizing existing therapies through strategic combinations, such as pairing RLT with immunotherapy, showcasing promising synergistic effects in pre-clinical studies. The third pillar encompasses the development and clinical introduction of alpha therapy, a collaborative effort with industry partners like ArtBio, SCK-CEN and IBA. The fourth pillar integrates artificial intelligence (AI) to refine patient selection for RLT, heralding a new era in personalized cancer care. "We are going to launch 2 major multimillion European projects concerning the development of innovative Radioligand Therapies within a consortium of five major European academic centers and the relevant industries involved, accelerating and activating these research activities in the next few years", states Flamen.

TODAY'S INFRASTRUCTURE IS BUILDING TOMORROW

The hospital, as one of the few, has a perfect infrastructure to create the development of new innovative solutions and to perform the entire spectrum of development. This includes a cyclotron for the production of radioactive isotopes, labs for preclinical in vitro testing and in vivo (small animal)



imaging, as well as a GMP radiopharmacy in line with the highest quality requirements to produce new radiopharmaca. The recent merger of the nuclear medicine services with Erasmus Hospital in Brussels has transformed the institute into the largest nuclear medicine services provider in Belgium, while ranking among the top three in size in Europe. The hospital's relocation from an outdated facility in the center of Brussels to a modern, purpose-built structure positions it as a leader in Belgium. At the same time, this move significantly helps to implement the necessary infrastructure for nuclear developments without extensive renovations. The hospital's Radioligand Therapy, involving radiolabeled molecules, requires specialized isolation rooms and containers to manage radioactive waste, showcasing the hospital's commitment to patient safety and environmental responsibility. The holistic approach of the hospital has the capacity to translate scientific discoveries into tangible medical advancements. "We have the whole chain to develop new radiopharmaceuticals. From pre-clinical infrastructure to infrastructure in the hospital. So from mouse to human, we have everything to start making that happen", explains Flamen. The whole infrastructure is available to the pharmaceutical and nuclear industry to further develop, optimize, and test innovative radioligand treatments. While refraining from direct commercialization, the hospital actively engages in partnerships through contract types like CMO (Contract Manufacturing Organization) or CDMO (Contract Development and Manufacturing Organization) with medium and large-scale industries.

RESONANT AND RADIANT RESEARCH

Collaboration lies at the heart of Jules Bordet Hospital's research ethos. Next to the hospital's close cooperation with the medical faculty of the Université Libre de Bruxelles (ULB), particularly in the development of radiopharmaceuticals, active participation in European consortia fosters collaborations with other hospitals and institutions across Europe, establishing the hospital as a global hub for nuclear medicine research. With a steadfast focus on RLT and a commitment to collaborative research, the hospital is poised to shape the future of nuclear medicine by developing possible new therapies as quickly as possible. "The fight against cancer remains our primary leitmotif, the Jules Bordet Institute certainly has a reputation for bringing innovative new therapies to the patient as quickly as possible", Flamen concludes.

"The fight against cancer remains our primary leitmotif."

INTERVIEW WITH

Philippe Damhaut,

Product Manager Nuclear Medical Applications

COMPANY

Tractebel

REGION

Brussels

Founded: 1862

Location: Brussels, offices in 40+ countries

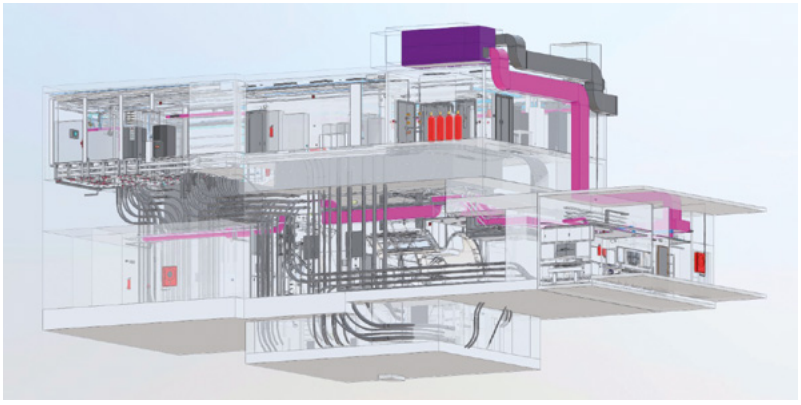
Number of employees: 5.500 employees (1.100 in nuclear business)

Turnover (2022): 518M EUR (170M EUR for nuclear activities)

Growth (2022): 1.5% (versus 2021)

Start of exports for Nuclear Medical Applications: 2015 (PALLAS project)

Share of exports in turnover of Tractebel nuclear medicine (2022): 41% on a total of 8.5M EUR for Nuclear Medical Applications



Tractebel, which is headquartered in Brussels and part of the Engie Group, is a global engineering and consulting company that designs and delivers projects in the field of nuclear power, renewable energy, electricity & gas, electrical grids, hydropower & dams, water resources & supply, desalination, complex & high-tech buildings, transportation infrastructures, and ports & waterways. From 2015, by combining skills in infrastructure, nuclear energy and radiation protection, Tractebel developed an in-house one-stop-shop department for the design of facilities hosting medical radioisotope production, nuclear medicine equipment and radiotherapy. This unique service is based on cross-functional expertise from two of the company's four business lines, infrastructure and nuclear.

Philippe Damhaut, Product Manager Nuclear Medical Applications, is clear: *"If we look at the skills we have developed in-house, such as engineering, particularly in health infrastructure, and nuclear safety, we have the skills to conceptualize nuclear medicine infrastructures. 99% of our nuclear medicine projects are the result of collaboration between our business lines. Thus, it was a no-brainer to offer our expertise for nuclear medicine."*

"Expertise in nuclear buildings, that's what we export!"

The start of the adventure began quite naturally in Belgium. Tractebel was able to capitalize on its country of origin to launch this activity, as Damhaut acknowledges: *"Belgium has a long tradition of developing technologies and skills in nuclear medicine. The development of Tractebel's Healthcare services in nuclear medicine from Belgium offers us proximity to numerous key players in the production of medical radioisotopes and radiopharmaceutical compounds, as well as specific equipment suppliers (cyclotrons, synthesis modules, quality control equipment, radiation protection equipment...)"*.

DELIVERING AN A TO Z ENGINEERING PROJECT IN NUCLEAR MEDICINE

Tractebel's engineering services can be used in all phases of a nuclear medicine engineering project: (1) regulatory assessment, site characterization and feasibility studies, risk analysis and safety reports, (2) project management and technical coordination, (3) design and building information modeling (BIM), (4) operation support and facility upgrade, as well as (5) decontamination and dismantling strategy.

Tractebel wishes to support the development of this sector around the world. In addition to hospitals, its services target key players in the production of medical radioisotopes and radio-pharmaceutical compounds, such as industrial producers, university hospitals and research

centers, research reactors or equipment suppliers.

Nuclear medicine and radiotherapy are demanding disciplines that are rapidly evolving, especially with the theranostic approach and the Targeted Alpha Therapy (TAT). Whether for renovation or new construction, facilities must be built with a design that incorporates nuclear ventilation and radiation protection, as well as new and specific requirements, including bunker(s) for particle accelerators and production laboratories, that comply with nuclear but also pharmaceutical (Good Manufacturing Practices (GMP)) norms and rules. Designing facilities for nuclear medicine thus requires specific cross-disciplinary expertise that Tractebel can offer. Damhaut points out that *"this differentiates Tractebel from its competitors, because we have control of the entire chain when it comes to engineering nuclear medicine installations."*

Tractebel also aims to address concerns about current research reactors used for the production of medical radioisotopes, which are aging and thus require investment in new facilities.

SEIZE OPPORTUNITIES AROUND THE WORLD

One of the group's flagship projects is the UZ Leuven. In partnership with the architectural firm MODULO, Tractebel is responsible for the design and follow-up of the construction site of the new center for nuclear medicine at the UZ. The eight-story building will consist of cyclotron and irradiation vaults, a radiopharmacy, R&D laboratories, offices, and meeting and technical rooms. The new building will be innovative, high-tech and sustainable.

Tractebel also act as owner engineer supporting the PALLAS team in their project to build a new research reactor in the Netherlands. This new facility aims to produce medical radioisotopes.

Another project was completed in 2022, this time a partnership between Tractebel and IBA for the conceptualization and construction of facilities for IBA machines. Tractebel's unique experience in providing engineering services, consulting and training in complex healthcare activities will be a valuable extension to IBA's customer offering, providing customers with support in the construction process specific to proton therapy construction projects. Since co-marketing activities are also involved, this will strengthen their respective international networks. The two companies have already collaborated on several projects, including cost estimation tools for IBA's Proteus facilities, stability studies related to the installation of a Proteus®ONE system in an existing Proteus®PLUS vault, engineering support for the design of proton therapy facilities, including BIM (Building Information Modeling) and seismic and vibration impact studies.

As for foreign trade, Tractebel did not wait for this partnership to sell its nuclear medicine engineering services abroad. Damhaut explains: *"We export brains and hours of work, so we provide services, by means of export licenses for engineering, whether for design, building design or radiation protection calculations. Expertise in nuclear buildings, that's what we export!"*

The markets in which Tractebel Nuclear Medicine is active are divided into four. Firstly, the European market with the Netherlands, France and the United Kingdom, countries where the demand for nuclear medicine is high. Secondly, the international market where Tractebel has local offices and opportunities can be seized, such as South Africa or Brazil (and Latin America). Thirdly, wherever nuclear medicine projects are announced, Tractebel is not far away, as Damhaut explains: *"The monitoring of public procurements is global. Our expertise allows us to meet demands around the world. Mind you, this does not mean that we answer everything, but it does mean that we stay aware of everything, especially through our participation in conferences. You have to be known and recognized internationally. International promotion is essential."*

The department's ambition is to grow thanks to the recognition of its expertise, particularly through its participation in concrete projects around the world.

"You have to be known and recognized internationally. International promotion is essential."

INTERVIEW WITH
Raphael Ortiz,
CEO Telix Europe

COMPANY

Telix

REGION

Wallonia

Founded: 2015, settled in Belgium in 2018.

Location: Global headquarters in Melbourne, Australia with international operations in Europe (Belgium and Switzerland), Japan and the United States.

Number of employees: 320 FTE worldwide, 40 in Belgium (60 expected in 2024)

Turnover (2022): AU$160.1M

Growth (2022): 2,100% (based on comparison with 2021 turnover)

Investments (2022): AU$58M in R&D.

Start of exports: manufacturing and exporting doses for compassionate or magisterial use since 2018. First commercial product launched in the US in 2022

Share of exports in turnover: 99%

Prizes, awards: 2022: Australia's highest achieving company for international growth (AFR Fast Global list) & Australian Biotechnology Company of the Year 2022

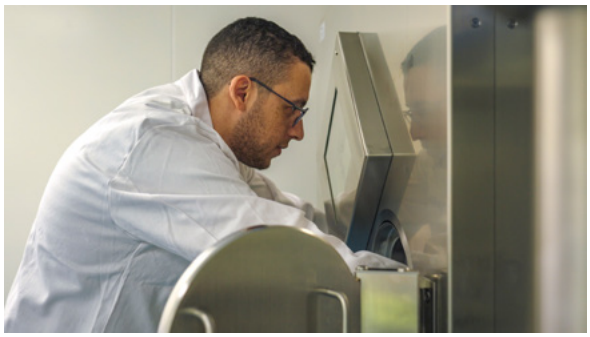
Telix Pharmaceuticals is active in research, development and commercialization of radiopharmaceuticals. Although it was only founded in 2015, the Australian company is already developing integrated solutions for the treatment of cancers with radiopharmaceuticals and associated medical devices. In this regard, Telix is fully committed to the "theranostic" approach, for "diagnostic" and "therapy". Early on, Telix Pharmaceuticals decided to set up several of its activities for Europe in Wallonia and Belgium, in the heart of the *"Radiopharma Valley"*. According to Raphael Ortiz, CEO EMEA of Telix Pharmaceuticals, *"this area encompasses Belgium, Netherlands and Germany"*. Ortiz reminds us that *"in 2018, Belgium was the first country where Telix acquired a company (i.e. ANMI) active in the sector"* before setting up its first European production site in Seneffe, Wallonia, in 2020.

Telix's flagship product, Illuccix®, was launched commercially in 2022 for Australia, Canada and the United States. Illuccix® is composed as an intravenous injection preparation kit based on Gallium (68Ga) PSMA-11, a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA). The commercialization of its flagship product allowed Telix to experience a growth rate of 2,100% in the same year with an annual turnover of 160.1M AUD.

BELGIUM, AT HEART OF THE "RADIOPHARMA VALLEY"

As a fast-growing company, Telix Pharmaceuticals has therefore decided to develop its European platform in Belgium, recognizing the strengths of the country and the Walloon region in terms of nuclear medicine. First, Belgium is recognized as a pioneer in nuclear medicine R&D, with world-class research centres and universities. According to Ortiz, it was important for Telix to include Belgian universities in its research program and establish a partnership with the University of Liège. Second, as Ortiz points out, Belgium is the 2nd largest producer of medical radioisotopes in the world after the Netherlands: *"two Belgian institutions [IRE and SCK-CEN] alone produce 25% of medical radioisotopes worldwide"*. Third, Belgium is a major player in the technological develop-

"Illuccix® is composed as an intravenous injection preparation kit based on Gallium (68Ga) PSMA-11, a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA)."



ment of nuclear medicine, Ortiz stresses: *"Almost one in three hospitals specializing in nuclear medicine uses Belgian technology"*. Fourth, in addition to the local transport of radiopharmaceuticals, Belgium coordinates 35,000 deliveries of radionuclides annually, allowing the production of more than 10 million doses.

Telix has also found the incentives to establish itself in Belgium. At the national level, the company recognizes an attractive tax system, such as the patent-box system, which promotes innovation and the development of medicines. At the Walloon level, the company has been able to find its interlocutors, such as AWEX. Ortiz acknowledges the support provided by the latter: *"we have received extremely strong support from all stakeholders in Belgium, with a valuable partnership with AWEX at its core"*. The AWEX programs, mentioned by Ortiz, are the support that Telix has received for setting up in Wallonia as well as the *Explort* programme, which is a grant for young people taking part in internships in companies focused on developing exports. Finally, still at the Walloon level, the company received financing for the installation of its new production facilities in the Hainaut region through a preferential loan set up by BNP Paribas Fortis and IMBC Group, a Walloon public investment fund.

TELIX'S IMPRESSIVE GLOBAL GROWTH STRATEGY INCLUDES BELGIUM

Telix is counting on its Belgian facilities to support its future development worldwide. The group is developing four key activities in Belgium: R&D, production, radiopharmaceutical services and a hub for innovative nuclear medicine companies in Belgium. As Ortiz explains, this is part of the company's overall strategy, which is to *"integrate with traditional medical oncology and standard of care, to potentially deliver more targeted and personalized therapy and patent-friendly dosing regimens."*

First, Telix is working on the global expansion of Illuccix®. After successfully bringing its new product, "a first-class product", to market in 2022, Telix wants to spread and expand the possibilities of use of its product in countries that have already validated the original use of the product, namely the United States, Canada and Australia. The new markets for which Telix has initiated a validation process are the United Kingdom, the European Union and South Korea. Regarding the EU, Ortiz said the following: *"This is a so-called 'decentralised' procedure, we have submitted our dossier to the German Agency which, on behalf of the EMEA, is the reference and responsible for evaluating the product and sharing the result with the Agency and other national authorities with a view to marketing it in Europe."* At the same time, a validation of the operation of the site hosting the future production line in Seneffe (Wallonia) is also required. For this purpose, Telix is in contact with the competent Belgian authorities, namely the FAMHP and the FANC, to obtain the Good Manufacturing Practices (GMP) of the facility.

Second, following the launch of Illuccix®, Telix is working on the regulatory validation of two new diagnostic imaging agents to establish a clear leadership in urologic oncology: TLX250-CDx (kidney cancer) and TLX101-CDx (brain cancer).

Third, proper to the theranostic approach, they are developing new therapeutic products such as TLX591 dedicated to prostate cancer. The latter was made possible thanks to Telix's research program called ProstACT aimed at treating all phases of prostate cancer, from the first occurrence to the advanced metastatic phase. Telix is also active in research (over 20 clinical studies) to address significant unmet medical needs in kidney, brain or blood cancers, as well as a range of difficult-to-treat immunological and rare diseases.

Fourth, Telix aims to provide an integrated solution for the therapeutic care of patients. The goal is to achieve the next generation of radiopharmaceuticals with personalized and targeted radiation therapy. Telix, having a holistic approach to the solutions offered, is also focusing on the acquisition of new assets that will enable it to offer an integrated processing treatment solution. The most recent example is the acquisition of the Dedicaid platform, in 2023, an AI-driven clinical decision support for diagnosis and therapy planning.

Finally, regarding Telix's facilities in Belgium, which opened in November 2023, the objective is to become the platform in terms of R&D and production of clinical and commercial products for Europe, the Middle East, Africa and beyond. As Ortiz points out: *"Nuclear medicine in Belgium goes from strength to strength and we are very pleased to be part of this world-leading ecosystem"*.

"Nuclear medicine in Belgium goes from strength to strength and we are very pleased to be part of this world-leading ecosystem."

INTERVIEW WITH
Erich Kollegger,
CEO

COMPANY

IRE - IRE ELiT

REGION

Wallonia

Founded: IRE 1971 – IRE ELiT 2010

Location: Fleurus, Belgium

Number of employees: 270 for both companies

Turnover (2022): ± 100M EUR

Growth (2022): Turnover: + 5% y-to-y

Investments (2022): IRE-IRE ELiT: ± 15M EUR

Start of exports: since inception

Share of exports in turnover: over 99%

IRE is a Belgian institute composed of two entities active in three business lines. The parent company IRE specializes in the production and distribution of radioisotopes as Active Pharmaceutical Ingredients (API) for diagnostics and therapy, i.e. radiochemistry. Secondly, IRE-Elit, a subsidiary of IRE, develops finished radiopharmaceutical products for imaging and the treatment of cancer or palliative care, i.e. radiopharmacy. Finally, the Institute is also a reference in the field of consultancy and solutions for the control and analysis of radioactivity thanks to its internal department IRE Lab. Erich Kollegger, CEO of IRE Group, takes the time to explain IRE's various activities and its role in Belgian nuclear medicine.

Mr. Kollegger begins by explaining the process by which radioisotopes are produced: *"IRE's API radioisotopes result from the fission of low-enriched uranium (LEU) thanks to neutron fluxes emitted by a research reactor (such as BR2). During fission, the aim is to target and recover radioisotopes useful for nuclear medicine. The three radioisotopes treated by IRE are molybdenum-99 or Mo-99 [nuclear medicine diagnosis], Iodine-131 or I-131 [treatment for thyroid cancer] and Xenon-133 or Xe-133 [chest radiography]. We combine these radioisotopes or isotopes with a specific molecule to supply them to hospital departments in charge of radiopharmacy or to radiopharmaceutical client companies that convert them."*

Regarding IRE ELiT, Mr. Kollegger also wants to specify its activity: *"It's a slightly different business compared to IRE because we go all the way to the finished product, i.e. we generate Gallium-68 and market it to our customers around the world. Gallium-68 allows for a much more precise radiography enabling possible visualization of very small tumors that are difficult to see with conventional scintigraphy."*

IRE, A NON-PROFIT FOUNDATION IN BELGIUM FOR THE BENEFIT OF NUCLEAR MEDICINE

Originally, IRE (i.e. *Institut national des radioéléments*) was established as a spin-off from SCK-CEN to produce and sell its research results. It has

"It took us 11 years to convert. Since the beginning of 2023, we have been using 100% low-enriched targets."

since developed beyond that. The Institute, a non-profit organization dependent on the Belgian federal government, has a public utility status with a commercial orientation. Profits are to be reinvested in the field of nuclear medicine for the common good, as its CEO specifies.

One of IRE's flagship projects, in collaboration with SCK-CEN, is the complete conversion from enriched uranium to low-enriched uranium, better known as LEU, to produce Mo-99 and I-131. Kollegger says, *"It took us 11 years to convert. Since the beginning of 2023, we have been using 100% low-enriched targets."*

IRE contributes to the biotech ecosystem, a unique ecosystem in Wallonia and Belgium in the field of nuclear medicine. In addition to its strategic position in Europe, its strength also lies in maintaining the SCK-CEN BR2 nuclear research reactor, a reactor with the highest irradiation capacity in the world. Kollegger says: *"I have great respect for what SCK-CEN is doing with BR2. It is an extremely well-managed reactor. That's not insignificant: it is a technological gem that requires a lot of expertise!"*

Mr. Kollegger explains to us the ecosystem that BR2 is part of: *"We are lucky because in Europe alone we have a network of 4 research reactors, whereas there are 6 worldwide. In North America, for example, the last research reactor in Canada shut down in 2015 and has not been replaced since then. As a result, the United States imports almost all of its Mo-99 and I-131, especially with IRE."*

"These are global markets with a few players who are able, like us, to meet demands."

IRE has an international reputation with international competitors, both private and public, such as Curium in the Netherlands, NTP in South Africa or ANSTO in Australia. Unlike the two European players, NTP and ANSTO each have their own on-site research reactor. About the sector, Kollegger points out: *"Whether it's the Mo-99 or the I-131, these are global markets with a few players who are able, like us, to meet demands. The Mo-99 has four players while the I-131 only has three. Our business is very much export-oriented."*

For IRE-ELiT, the main competitors are Germany's Eckert & Ziegler and ITM. Kollegger says, *"When it comes to the production of the Ga-68, we are one of the two world leaders."*

While IRE was founded in 1971, its subsidiary IRE-EliT was formed in 2010. The need arose to create a subsidiary to focus on the radiopharmaceutical activity with end-to-end management from research and development to the marketing of radiopharmaceuticals. As mentioned above, IRE-EliT's flagship products, developed entirely in-house with two patents, are the Galli Ad (European market) and the Galli Eo (North American market), both 68Ge/68Ga generators. This probably would not have been possible without the initial and long-term support of the SFPIM (Belgian Federal Holding and Investment Company) to the IRE, as Kollegger explains: *"The SFPIM is there to help start activities, it doesn't really intend to stay in the capital for years. In the beginning, when you start a business, you consume cash, but you don't generate any. When IRE-ELit was able to generate cash, SFPIM sold its shares to IRE, which became the sole shareholder."*

INNOVATIVE SOLUTIONS TO MEET FUTURE CHALLENGES

Thanks to the recognition of its expertise and the quality of its products, IRE has several projects in the pipeline. The group is working on vertical integration through the acquisition and installation of a 30 MeV cyclotron at its own site in Fleurus, Hainaut, Belgium. It is also looking to expand the Ga-68 market in Asia and Latin America. Finally, IRE is engaged in the research and sale of Lu-177 (lutetium) and other radioisotopes of interest.

Regarding Lu-177, a project in collaboration with SCK-CEN, Kollegger is very enthusiastic: *"Lu-77 will destroy the cancer cell by attaching itself to it. A large number of cancers could be affected by this radioisotope. In the next 10 years, we will have a tremendous development of Lu-177 therapies!".*

Overall, the sector is promising. According to the IRE, the global market was estimated at $6 billion in 2021, and is expected to exceed $30 billion by 2030. Through its various activities and partnerships, IRE is positioning itself as a key player capable of responding to this future growth.

INTERVIEW WITH

Bruno Scutnaire,

President IBA RadioPharma Solutions

COMPANY

IBA

REGION

Wallonia

Founded: 1986

Location: Louvain-la-Neuve

Number of employees: 2,000

Turnover (2023): 429M EUR

Growth (2023): 19%

R&D expenses (2023): 48M EUR

Start of exports: 1987

Share of exports in turnover: 99%

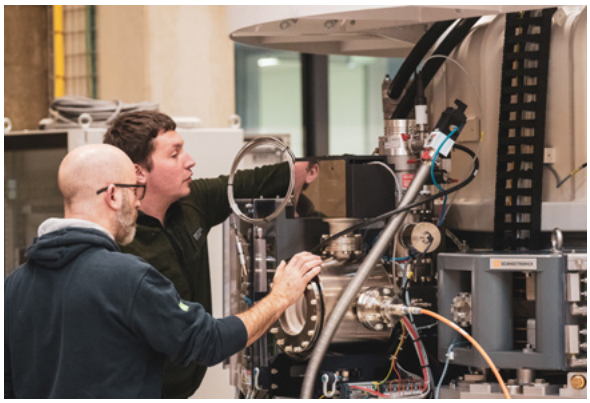
IBA (Ion Beam Applications) is the world leader in particle accelerator technology. The company is the leading supplier of high-technology equipment and high-quality services in the field of proton therapy, radiopharmaceuticals, industrial sterilization and dosimetry.

IBA developed a state-of-art practice for each of the four business units mentioned above. First, since the founding of IBA, **RadioPharma Solutions** has been developing cyclotrons used to produce radio-isotopes and radio-pharmaceuticals specific to nuclear medicine, for cancer diagnosis and therapy, as well as cardiology and neurology. It supports hospitals and radiopharmaceutical distributors to design, build and operate their facilities in order to produce radio-pharmaceuticals according to their speciality and their needs. Second, **Proton Therapy Solutions** enables the most advanced forms of radiotherapy in cancer treatments using ionizing radiation produced by its cyclotrons. Protons deposit most of their energy in a controlled zone affected by cancer, limiting exposure of the surrounding healthy tissues to potentially harmful radiation. Third, **Dosimetry Solutions** offers hospitals a comprehensive range of quality assurance tools and software for the calibration and control of their radiotherapy and radiology equipment. Fourth, **Industrial Solutions** develops solutions and applications such as sterilization. This process is made possible thanks to the Rhodotron®, a state-of-the-art electron accelerator for E-beam and X-ray irradiation.

Bruno Scutnaire, President of *IBA RadioPharma Solutions*, explains the activities and specificities of his business unit specifically dedicated to Nuclear Medicine: "We provide machines that produce radioisotopes, which are then transformed into injectable radiopharmaceuticals. These machines are supplied to hospitals for their own use or to distribution centers supplying nearby smaller hospitals. *We are also involved in the long-term by making their regular maintenance and full after-sales support. Since the beginning of IBA in 1986, we have sold more than 350 machines with more than 90% still in activity."*

He paints a picture of the cyclotron market: *"Today there are two types of markets: mature and emerging. The first market has already experienced the development of nuclear medicine 20 years ago. The United States, Europe and Japan belong to this group. They are looking to produce a larger amount of radiopharmaceuticals in a cost-efficient*

"Those markets are definitely looking for a global solution to develop nuclear medicine facilities. IBA can offer this one-stop shop approach."



way. The second market is represented by Asia – largely China – encompassing tremendous demand. Everyone wants to have access to the same technology that allows a unique type of diagnosis. It has been demonstrated that a early diagnosis leads to a more efficient treatment plan, a higher survival rate and therefore lower healthcare costs. Those markets are definitely looking for a global solution to develop nuclear medicine facilities. IBA can offer this one-stop-shop approach: cyclotrons, hotcells, laboratories equipment complying with high-standard pharmaceutical norms".

In addition to the importance of making their technology accessible worldwide, IBA is also committed to embracing new developments in nuclear medicines, especially considering the theranostic approach. There are several growing applications in therapy (i.e. the use of radioactive injectable radiopharmaceuticals in oncology treatments) such as 223Ra-Xofigo or 177Lu-Lutathera. It is in this context that IBA and SCK-CEN have created PanTera, a joint venture dedicated to the production of a promising radioisotope for cancer treatment: Actinium-225.

BELGIUM, A LONG STORY

Belgium's reputation in the field of nuclear medicine is also a historic legacy, Scutnaire reminds us: *"Pierre and Marie Curie found the process to purify radium used for radiography. This radium came from the Congo where industries extracted it and brought it to Belgium. So everything is connected. It is quite incredible!"*. Later, it was their daughter and her husband, Frédéric and Irène Joliot-Curie, who made a new discovery about radio-isotopes. The Solvay conference will help publicize these discoveries.

Much later, a Belgian researcher at the Catholic University of Louvain, Yves Jongen, came up with the idea of producing cyclotrons more affordably for global nuclear medicine. This is the beginning of the story of IBA, created in 1986 as a spin-off from UCLouvain.

Thus, IBA has flourished mainly thanks to the nuclear medicine ecosystem in Belgium. Today, as a world leading supplier of cyclotrons, IBA has become an important player in this ecosystem. Scutnaire acknowledges this: *"Belgium has always been known for its expertise in nuclear medicine. The density of specific cameras for diagnosis is the highest in the world. There are also a lot of Belgian experts in various fields related to nuclear medicine: radiochemists, radiopharmacists, nuclear physicists, oncologists, etc. Numerous large hospitals are equipped with a cyclotron that contributes to new developments for unique diagnosis or therapeutical applications".*

In addition to the sector's organic growth, IBA also recognizes the support of the public authorities. *"Since inception, we have been participating in international projects supported by Europe, Belgium, and Wallonia. We benefit from the entire ecosystem".*

"PROTECT, ENHANCE AND SAVE LIVES"

IBA's activities are focused on the same goal: to have a positive impact on people's health, as expressed in their mission statement *"Protect, enhance and save lives"*. The company implements this by providing healthcare professionals with the most effective and accurate solutions for diagnosis and treatment, as well as safe solutions for sterilization. According to Scutnaire, this goal is applied in various ways that benefit each of the different stakeholders involved (clients, employees, shareholders, society, and the planet).

"We should not look at what the future will be, but how Belgium will participate in forging the future, both in academia and industry."

IBA RadioPharma Solutions focuses on expanding production capacities for diagnostic radioisotopes and meeting the increasing demand for therapeutics through personalized solutions. Scutnaire specifies: *"This includes enhancing a maximized uptime of our solutions, scaling up production volumes, and ensuring stable operational costs as well as supporting research and less mature technologies, anticipating uncertain clinical trial developments, and adapting to changing therapeutic requirements".*

Regarding nuclear medicine in Belgium, according to Scutnaire, *"We should not look at what the future will be, but how Belgium will participate in forging the future, both in academia and industry"*. He adds, *"Radiopharmaceuticals have a key role to play in critical medical fields such as cardiology, neurology, and oncology. As for radiotheranostics approaches, we have great confidence in their ability to provide tailored and targeted treatments, thereby reshaping patient care standards".*

INTERVIEW WITH
Claude Poliart,
COO

COMPANY

ISI - Isotopes Services International

REGION

Flanders

Founded: 1987

Location: Zaventem

Number of employees: 49

ISI, a Belgian specialist in radioactive shipments for medical use, stands out as a key player in the global market. Headquartered in Zaventem and one of the partners of the Radio Pharma Logistics Group (Isolife and Isovital), ISI has established itself as a reliable freight forwarder, shipping parcels worldwide.

CUSTOMER CUSTOMIZATION AND RELIABLE DELIVERIES

At the heart of ISI's operations lies the transportation of radioactive materials for medical purposes. Collaborating with various global producers of radio nucleates, ISI caters to customers not only in Belgium but also extends its services to the US, Canada, Australia, France, Germany, Spain, etc. The company excels in providing safe and compliant shipments, adhering to stringent regulations for both vehicles and drivers. "We also offer customized charter flights for radiopharmaceuticals and take care of all complex regulations such as ADR, IATA, ISO-9001", Claude Poliart, Group Chief Executive Officer RLG, explains.

Beyond radioactive shipments, ISI boasts a comprehensive storage facility in Zaventem, Belgium. This facility includes dedicated areas for radioactive products and a larger warehouse with temperature-controlled zones, ensuring the prerequisites of pharmaceutical products. With a workforce of 49 in Belgium, employees at ISI handle various roles crucial to its logistics operations. Examples of such roles are dispatchers, logisticians, freight forwarders, warehouse personnel, and drivers.

STRATEGIC PARTNERSHIPS

As part of the Radio Pharma Logistic Groups, ISI collaborates closely with ISO Vital and ISO Life. Although distinct entities, the three companies share common shareholders and work in tandem to optimize deliveries. This collaboration ensures a seamless network for shipments within France, Benelux, and Germany. "Thanks to our own team of drivers and the support of our partners, we can ensure distribution within 24 hours for the Benelux, and distribution within 24-48 hours in Europe", emphasizes Claude Poliart. "ISI holds a market share of 50-55% of radioactive transport in Belgium, whilst ISO Vital and ISO Life hold a market share of 85% in France", he continues.

"The project and integration in Life Couriers is to become number one in the transport of medicine products in the world."

ISOTOPES SERVICES INTERNATIONAL

ISI's global reach necessitates strategic partnerships. Collaborations with logistics giants like DHL and Bolloré Logistics, next to alliances with customs management companies, exemplify the company's commitment to efficient international operations. The close ties with Brussels Airport and other service providers contribute to ISI's role as a critical player in the transport of radioactive materials. A recent integration in Life Couriers will develop a network that will provide medical shipments all over the world. The next project is an expansion to new markets such as Japan and New Zealand. "The project and partnership with Life Couriers is to become number one in the transport of medical products in the world", Claude Poliart explains.

INNOVATIVE SOLUTIONS AND UNIQUENESS

In a field where precision and compliance are paramount, ISI thrives on innovation. The company continually seeks improved solutions, utilizing special packaging for cold and radioactive shipments. ISI is in the process of upgrading its Transport Management System (TMS) to enhance vehicle tracking and temperature monitoring, emphasizing its commitment to quality service. "We ensure our position as market leader due to our unique solutions. Not only do we provide extreme flexibility for our customers by being available 24/7, they can also rely on our experience", declares Claude Poliart.

More than 35 years of experience runs through the company since its inception in Belgium in 1988. The company's presence near Zaventem Airport is also strategic for logistic purposes since the airport is considered the gateway for radioactive shipments. "An estimated 25-30% of all radioactive shipments go through Zaventem Airport", shares Claude Poliart. Belgium is a strategic location for ISI since numerous radio-pharmaceutical companies are based here. Belgium as the radioactive medicine valley will attract many other companies, ultimately fostering growth in the Belgian nuclear medicine sector.

"Not only do we provide extreme flexibility for our customers by being available 24/7, they can also rely on our experience."

FOREIGN TRADE AND INTERNATIONALIZATION

ISI's internationalization is set to amplify with its imminent membership in the Life Couriers group which is focused on life sciences transport. Already well-connected globally, this move is expected to facilitate an even broader palette of services for customers. This membership will allow the company to become the preferred partner for last mile delivery and to increasingly scale up and expand. The definition of last mile delivery at ISI goes as follows: "last mile delivery means personalization for each customer, the essence of personalized services meaning if the product needs to be delivered in the general warehouse or the fourth floor on somebody's desk, we do that", affirms Claude Poliart.

The nuclear medicine landscape is continuously growing and this comes with opportunities and challenges. ISI is not only embracing the former, but is also being proactive in the face of the latter. Due to the growing demand and rising number of requests of its customers, ISI is focused on acquiring a workforce with the right credentials to handle radioactive transport. Poliart states that "it is not easy to find more staff since drivers need to have permits for transport of hazardous goods and need to take an extra training for radioactive products".

Looking ahead, ISI envisions growth not only in Belgium but globally, leveraging its membership in the Life Couriers group. The goal is to become a preferred partner for the last mile delivery. "At ISI, we will further commit to providing specialized services in radio pharma and pharmaceutical logistics as we aim for an 8-12% increase in turnover by 2024", concludes Claude Poliart.

"At ISI, we will further commit to providing specialized services in radio pharma and pharmaceutical logistics as we aim for a 8-12% increase in turnover by 2024."

INTERVIEW WITH
John Zehner,
CEO

COMPANY

SpectronRx

REGION

Flanders

Founded: South Bend - 2004

Location: 2019 - Indianapolis and 2023 Belgium office Grimbergen and production facility SCK Mol

Number of employees: 120-130

SpectronRx

At the intersection between precision and innovation, SpectronRx has solidified its position as a key player in the field of nuclear medicine. Led by CEO John Zehner, SpectronRx specializes in radio-labeling various molecules, navigating the intricacies of radioactivity regulations, drug approvals, and the licensing of radioactive materials. Zehner elaborates on the company's core mission, stating, "We take our customer's product that is labeled to some type of radioactivity, then we help increase the stability, figure out better or more robust ways to manufacture it and finally distribute that to the patients."

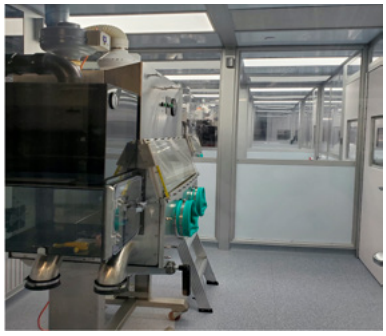
The US-based company has its headquarters in Indianapolis and a branch office in Grimbergen with a production facility on the site of SCK CEN, which is set to be operational in 2024. The new radiolabeling facility will increase the supply of diagnostic and therapeutic radiopharmaceuticals in Europe. Therefore, the new agreement will be of great public interest as medical radio-isotopes remain scarce.

SpectronRx collaborates with a diverse range of pharmaceutical companies interested in radio-pharmaceutical diagnostics or therapy. The company's clientele includes both large pharmaceutical enterprises and innovative startups. Zehner highlights the company's impressive manufacturing space, boasting 140,000 square feet and 24 clean rooms. The commitment to growth is evident as Zehner notes, "We only use about 60 percent of the available space right now", indicating future expansion plans.

INNOVATION AND EXPERTISE IN ISOTOPE LABELING

SpectronRx stands out for its expertise in labeling various isotopes to monoclonal antibodies or fragments. Zehner emphasizes their seven years of experience, stating, "We've developed quite the team that can now handle these and move very quickly through helping companies bring their product to market." Noteworthy isotopes in their portfolio include Actinium-225, iodine-131, Lutetium-177, and many more. The collaboration in Belgium will focus on the potential of Actinium-225 (Ac225). Ac-225 can be combined with multiple types of therapeutic medicines, and

"Our goal is just to maintain our current customer base, enable them, supply them, and meet the ever-rising demand."



SpectronRx is proficient with these Ac-225 therapies. Their achievements ensure the continued growth and extension of Ac 225-labeled radiopharmaceuticals for the benefit of cancer patients worldwide.

THE FUTURE OF NUCLEAR MEDICINE

Zehner foresees tremendous growth for the nuclear medicine sector, citing reports projecting the industry to reach close to USD 30 billion. The focus on therapeutics as a driver for growth is evident, with Zehner stating "ultimately, the driver of the growth will be therapeutics." Important to mention is that regulatory authorities are in favor of diagnostic solutions in order to validate the patients' need for the therapeutic solution. Therefore, diagnostics are expected to grow as well, but the cost and mere complexity of therapeutic solutions will cause a greater financial impact. In addition to the countless opportunities in the sector, Zehner also acknowledges the challenges. Even though it is difficult to maintain a supply of a product that you have to produce daily or weekly, the number of medicines that these isotopes can be labeled to is just scratching the surface.

INTERNATIONALIZATION AND FUTURE EXPANSIONS

SpectronRx continues to embark on its international journey, as Zehner discusses the formation of an entity in Belgium. The company is in talks with Flanders Investment and Trade, emphasizing the importance of establishing a presence in a region known for its expertise in nuclear medicine.

SpectronRx places strategic importance on alliances, with the SCK CEN Alliance opening doors to Europe. Partnerships with R.L.S. for the last-mile delivery and overall white glove services as well as previous collaborations with Arizona Isotopes showcase the company's commitment to expanding its reach and impact.

Looking ahead, SpectronRx aims to maintain its current customer base and extend its reach in theranostic clinical trials. Zehner outlines their role in enabling customers and supplying critical isotopes for therapies. As the company anticipates FDA and EMA clearances for multiple products, Zehner envisions substantial growth, potentially doubling the current workforce towards 300 employees in the next 24 months, a notable change compared to the 6 employees in 2019.

SpectronRx currently has nineteen projects pending for approval, some in early stages of development, but most of the projects will most likely be approved between mid-2025 and 2027. Once a product is approved, hundreds of thousands or even millions of doses can be supplied instead of a few hundred doses for pending projects. Zehner states that "the expansion plan is based on our customer demands. We do not own any of our products and therefore do not compete with our customers. So our goal is simply maintaining our current customer base, enabling and supplying them, while meeting the ever-rising demand."

BELGIUM: A STRATEGIC HUB

Belgium plays a pivotal role in SpectronRx's expansion plans, driven by the country's rich expertise in nuclear medicine. Zehner lauds Belgium's commitment to advancing nuclear medicine, citing ongoing efforts by SCK, IRE, and others in contributing to the nation's prominence in the field. Choosing Belgium as its first overseas location will allow the company to be closer to patients, grow exponentially and be associated with SCK CEN. Other factors that influenced their decision to branch out in Belgium are the efforts of universities in their education programs regarding radiochemistry and the central position in Europe. "The strategic position of Belgium helps to optimize the logistics of the radiopharmaceuticals, thereby streamlining the supply chain", Zehner explains.

Spectron Rx stands at the forefront of nuclear medicine, weaving innovation, expertise, and strategic collaborations into its fabric. As the company navigates the complexities of internationalization, it remains dedicated to its core mission of accelerating the fight against cancer. "Belgium is the top location in Europe for nuclear medicine because it has all the tools to continue to grow", concludes Zehner.

"The strategic position of Belgium helps with optimizing the logistics of the radiopharmaceuticals, thereby streamlining the supply chain."

INTERVIEW WITH
Sven Van den Berghe,
CEO

COMPANY

PanTera

REGION

Flanders

Founded: 2022

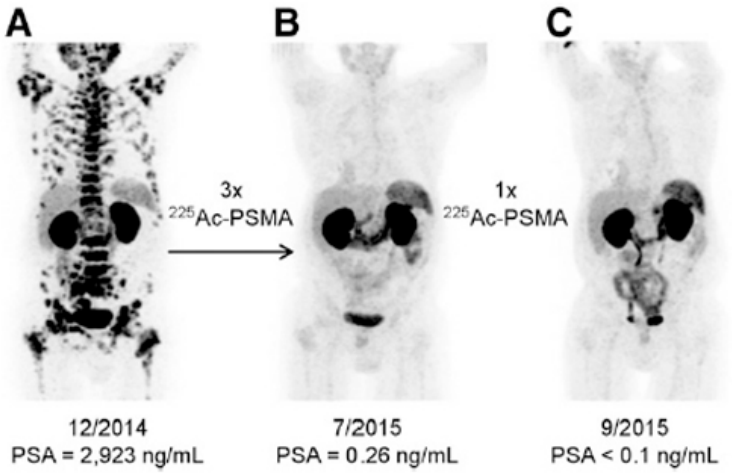
Location: Mol, Belgium

Number of employees: 7, expected to rise to 15 employees in 2024

Investments: An investment round will start in 2024

Start of exports: Early supply 2024, full scale production 2028

Prizes, awards: Present at the core conferences in the field.



In the arena of cutting-edge medical innovation, PanTera, led by CEO Sven Van den Berghe, stands at the forefront, embarking on a mission to address the scarcity of a promising radioactive cancer-fighting agent: Actinium-225. With a robust background of 25 years at the Belgian Nuclear Research Center SCK CEN, Sven brings a wealth of expertise to PanTera's mission.

Actinium-225, emitting alpha radiation, emerges as a potent tool in cancer treatment. Differing from recently developed beta radiation therapies, today mostly based on Lutetium-177 as the radioisotope, alpha emitters like Actinium-225 provide a more lethal and local impact on the cancer cells to which they deliver their radiation. As a result, this effectively kills the malicious cells, while preserving the healthy ones surrounding them. Actinium-225 is currently the most promising and most studied alpha emitter considered for medical applications. This can be attributed to Actinium chemistry closely resembling that of Lutetium, opening avenues for faster and streamlined development processes as more products based on Lutetium-177 currently under development receive approval.

Actinium-225, while not a pharmaceutical product in itself, plays a pivotal role as an Active Pharmaceutical Ingredient (API). In specialized radiolabeling facilities, the API is chemically linked to vectors tailored to bring Actinium to cancer cells. "These vectors are cancer-specific and carry Actinium to the particular type of cancer cells they target. As new vectors are developed and approved for other cancer types, Actinium-225 will be used in tackling increasingly different cancer indications, increasing the demand with every newly approved radiopharmaceutical", explains Van den Berghe.

Unfortunately, the global supply of Actinium-225 is currently limited to approximately two and a half to three curies (2500-3000 patients), hindering advancements in clinical trials. Therefore, it needs to be confirmed in the short and long term that sufficient quantities of Actinium-225 are available. In this way, the pharmaceutical industry can be sufficiently reassured to push their trials to the next phases.

The first pharmaceutical products based on Actinium-225 are expected to be approved for widespread use around 2027, resulting in a first steep rise in the demand for the radioisotope, further increasing with every next radiopharmaceutical based on Actinium-225 reaching commercialization.

PANTERA
A BETTER FIGHT FOR LIFE

"What sets PanTera apart from other players in the field is our meticulous selection of the gamma route for Actinium-225 production."

AMBITIOUS ABOUT ACTINIUM

"What sets PanTera apart from most of the other players in the field is our meticulous selection of the gamma route for Actinium-225 production, a decision grounded in safety, reliability, and scalability", states Van den Berghe. In the gamma route, Actinium-225 is produced as a natural decay product of Radium-225, which derives from the irradiation of Radium-226 with gamma photons generated with an electron accelerator. While alternative methods exist (e.g. proton irradiation of Radium-226), the gamma route minimizes the risks associated with irradiating Radium-226 and ensures a reliable, consistent production of high-quality Actinium-225 at a commercial scale. "The challenge of requiring substantial quantities of Radium-226, which often deters others from selecting the gamma route, is in fact a strength to PanTera. One of our founders (SCK CEN) proudly boast the world's largest stock of this crucial material in a pure form and PanTera can access it exclusively", highlights Van den Berghe.

PanTera's unique understanding of the gamma route for Actinium-225 production also makes the company acutely aware of its complexity and the requirement for specific, scalable and sustainable solutions for the challenges involved. This can be attributed to more than three years of intense R&D by its founders: IBA and SCK CEN. Even with the development of the Intellectual Property (IP) required to implement the production completed today, there are still numerous years of licensing, engineering and construction of a full-scale production facility ahead.

To assure the market is already provided with Actinium-225 before that time, PanTera is currently implementing a temporary small-scale production through a different route. Whereas radium is the base product PanTera is going to use in the gamma route, Thorium-229 is another base product which can be used to produce Actinium-225 through its natural radioactive decay. Yet, the latter is only scarcely available across the globe.

PanTera entered a unique strategic partnership with TerraPower, a company founded by Bill Gates. This collaboration provides PanTera access to sufficient additional Thorium-229 to produce one and a half to two curies (1500-2000 patients) of Actinium-225 per year from mid-2024 onward. That allows pharma and biotechnology companies developing new drugs to overcome their Actinium-225 supply challenges and it ensures a smoother progression of clinical trials beyond the initial phases.

Another key strength that sets PanTera apart lies in its origins: a partnership between its founders IBA and SCK. It provides PanTera with all the building blocks and uniquely suited solutions needed to tackle the challenges posed by its production process. "Having the expertise of handling alpha emitters through SCK CEN, accelerator knowledge via IBA, plus the access to the ideal electron accelerator (the Rhodotron® TT300-HE) and the largest stock of the base material makes us the most credible candidate producer of Actinium-225 out there", declares Van den Berghe.

REVOLUTIONIZING CANCER TREATMENT WORLDWIDE

In terms of expansion, PanTera is exploring both geographical and product diversification. The collaboration with TerraPower open doors to North America, while partnerships in Asia are under discussion. PanTera's international vision aligns with the central location of Belgium and Europe. The commitment to global accessibility to Actinium extends beyond geographical boundaries, with efforts to make it available to patients in Africa and Latin America.

Additionally, PanTera's facility in Belgium has the potential for future expansion in terms of production capacity. PanTera is targeting an initial supply capability of approximately 100 curies annually, enabling the treatment of around 100,000 patients globally. Further diversification is possible by moving into the production of other isotopes, as well as by leveraging byproducts.

Looking towards the future, PanTera envisions a global boom in the demand for medical radioisotopes. The limitations of surgery and chemotherapy and the attention for the patient's quality of life are driving the need for alternative treatments, with nuclear medicine gaining immense support from patient organizations. This represents a wonderful opportunity for Belgium, which provides a full ecosystem in that field.

"Having the expertise, knowledge, and access to materials makes us the most credible candidate producer of Actinium-225 out there."

STAKEHOLDERS

BELGIAN NUCLEAR MEDICINE – ECOSYSTEM

AGENCIES

sck cen

70 years of experience in nuclear research and technology

With more than 70 years of experience in nuclear research and technology, **SCK CEN** is one of the largest research institutions in Belgium. Every day, more than 900 employees dedicate themselves to developing peaceful applications of radioactivity. Our research activities focus on three main areas: innovative nuclear systems, nuclear waste management and dismantling, and the resolute fight against cancer.

For decades, we have been a key player in the global production for medical radioisotopes thanks to our research reactor Belgian Reactor 2 (BR2). To accelerate the fight against cancer, we increase our leading role by taking the next step: actively conducting research on therapeutic radioisotopes. These radioisotopes are a crucial component for radiopharmaceuticals used for Targeted Radionuclide Therapy (TRT), the future of nuclear cancer treatment.

These drugs use carrier molecules to transport radioactive isotopes directly to tumours, precisely targeting and shrinking tumours while leaving healthy tissues intact. This minimises side effects and offers a more humane approach to cancer treatment. We are evolving into a full-fledged pharmaceutical player, in pre-clinical research as well as pilot production of new radiopharmaceuticals for cancer therapies. It's our ambition to help bring new radiopharmaceuticals to life.

Engaging in impactful strides, we have our own cancer research line. That line of research focuses on innovative treatments for three specific cancers: glioblastoma (brain cancer), colon cancer, and ovarian cancer. In addition to our internal research efforts, we actively participate in innovative research assignments for external parties, fostering a collaborative approach.

By seamlessly integrating external collaborations and internal research initiatives, SCK CEN strives to be a global leader not only in nuclear technology but also in advancing the frontiers of cancer research.

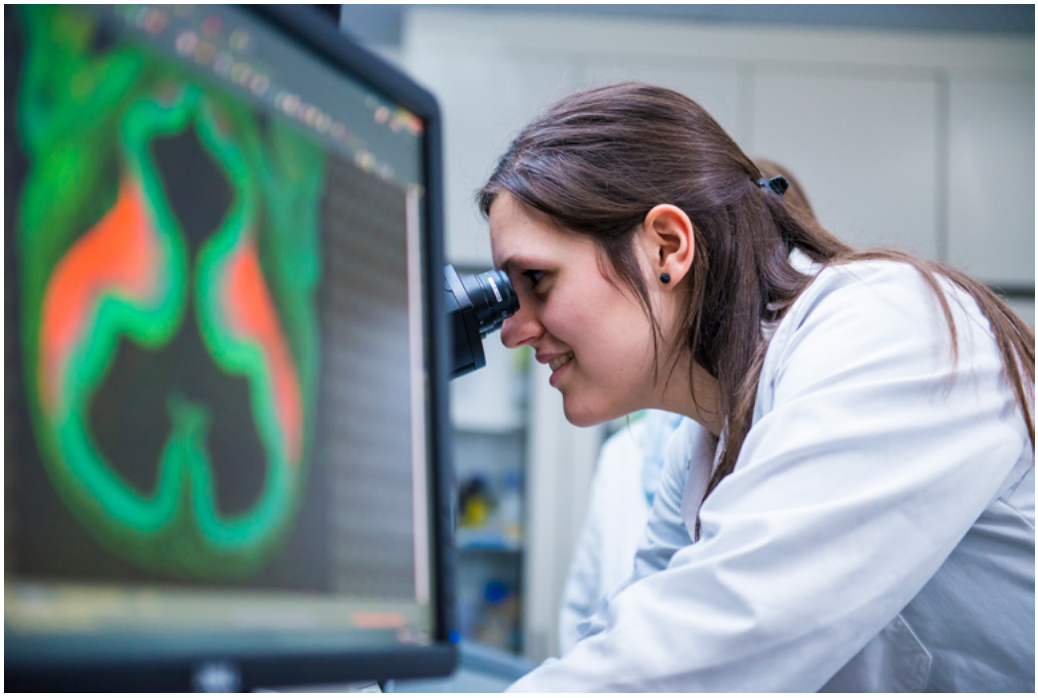
Partnering for personalized medicine

To achieve this goal, we can rely on our unique infrastructure as well as important partnerships across the world. Our state-of-the-art infrastructure serves as a cornerstone for conducting groundbreaking research and pilot production of novel radiopharmaceuticals. Furthermore, SCK CEN has forged impactful collaboration with renowned entities in the field, including SpectronRx, TerThera and IRE.

Improving quality of life

Through these collaborative efforts, SCK CEN remains steadfast in its commitment to ultimately improve patient outcomes. By pioneering advancements in cancer treatment and nuclear technologies, we aspire to contribute to a future where patients facing these challenging diagnoses can experience enhanced therapeutic options, improved quality of life, and, ultimately, better outcomes in their journey towards recovery.

www.sckcen.be



FANC
FEDERAL AGENCY FOR NUCLEAR CONTROL

The Federal Agency for Nuclear Control (FANC) is the Belgian nuclear safety authority responsible for protecting the patient, workers, the public and the environment against the risks of ionising radiation.

Ionising radiation is used in numerous medical applications, including nuclear medicine. In that context, FANC issues licences to the different actors in the complete nuclear medicine chain going from those ensuring the availability of the used radioactive products (production sites, importers, transporters and distributors), the nuclear medicine departments and their physicians using these products for diagnostic or therapeutic (mainly oncological) purposes. The radioactive waste created by these different actors throughout the complete nuclear medicine chain is also monitored by the Agency.

On top of this licensing system, extra measures to guarantee the radiation protection have to be taken by the hospitals and their nuclear medicine department. For instance, FANC imposes the (close) involvement of a recognised expert in medical radiation physics for the organisation and application of the measures necessary to strengthen even more the radiation protection of the patient. Proactive risk analyses, quality control of the equipment and clinical audits have to be performed. Furthermore, when a person is treated by administration of a radioactive product, the responsible physician must give written instructions and a release card to this person, in order to keep the doses and risk of contamination as low as possible for the patient and for people who come into the immediate vicinity of this person or of the radioactive waste the person generates. For diagnosis, optimisation of the activity administered to the patient should be performed through the use of Diagnostic Reference Levels and certain significant events and unintended exposures of patients (or their unborn child) have to be notified to the Agency with the aim of learning from them and preventing them to happen again at the same or at other departments.

That is why FANC aims to be an anticipatory safety authority that can guide its stakeholders in a timely manner on the possible introduction of innovation: we closely monitor nuclear and radiological innovations and new applications to ensure that our stakeholders integrate them into their operations in an efficient, effective and safe manner. It strives to be involved, early on, in new initiatives in order to clarify the expectations of the safety authority at an early stage and to provide interpretation around legislation, qualification of new technology, etc.

www.fanc.fgov.be/nl
www.afcn.fgov.be/fr

famhp
federal agency for medicines and health products

The Federal Agency for Medicines and Health Products (FAMHP) is the Belgian competent authority in charge of ensuring the quality, safety and efficacy of medicines and health products, for human and veterinary use, in clinical development and on the market.

Part of its role is watching over the quality, safety and efficacy by carrying out inspections and controls. Specifically for radiopharmaceutical products, which are covered by a marketing authorisation and thus manufactured by sites holding a manufacturing authorisation, the FAMHP's inspection services are responsible for checking that the Good Manufacturing Practices (GMP) are implemented.

Radiopharmaceuticals can also be prepared in hospitals under the supervision of the hospital pharmacist. Hospitals that do not have the necessary facilities, can obtain the products from other hospitals or can delegate the production to a manufacturing authorisation holder for the production of radiopharmaceuticals. The FAMHP is responsible for checking that legislation applicable to hospital pharmacists is being complied with.

It should be noted that the FAMHP is not responsible for site safety in terms of radioactivity such as protection of workers or the environment.

www.famhp.be/en

PARTNERSHIP

Business

Rad4Med.be
THE BELGIAN NETWORK FOR RADIATION APPLICATIONS IN HEALTHCARE

Belgium is a world leader in medical applications of ionizing radiation. This leadership has been achieved thanks to the creativity and the innovations by hundreds of scientists, clinicians and engineers who built on the very strong foundations provided by the Belgian pioneers in the field.

Belgium is a worldwide leader in all links required for the clinical practice of healthcare applications of nuclear science and technology. From the production and refinement of radioisotopes over transport, generator production, labelling and radiopharmaceuticals, imaging equipment, pre-clinical and clinical studies to daily practice, Belgium excels in all steps of the nuclear medicine value chain. In radiation oncology, it is world leader in proton therapy equipment. Dedicated staff in university laboratories and research centers ensure a strong expertise for educational aspects.

Belgium, ideally located between Northern and Southern Europe, has excellent communication ways, both by road, rail, air and boat to the rest of Europe and the World. This allows for a very efficient and streamlined supply chain for any goods from short-lived medical radioisotopes up to heavy equipment.

Through more than 80 entries, **Rad4Med.be** introduces the impressive Belgian expertise in nuclear applications for healthcare by R&D, E&T, commercial and institutional players.

rad4med.be

NUCLEAIR FORUM NUCLEAIRE

The **Belgian Nuclear Forum** represents the nuclear industry in Belgium. As a sectoral federation of Belgian nuclear players in different applications (energy, nuclear medicine, space exploration, etc.), their mission is to inform and educate the population, the policymakers and the media about nuclear technology and its versatile applications.

It is in the DNA of the Belgian Nuclear Forum to provide rational, reliable and verified information. The Belgian Nuclear Forum gets the recognition of the outside world as a reliable source of information, while promoting the importance and interest of nuclear technology.

Belgium is not only a pioneer in nuclear technology, but also a world-renowned centre of expertise in this field.

This is especially true for nuclear medicine, where our country has established a solid international reputation as a pioneer in research, as well as a major producer of medical radioisotopes and as a major player in the global transport and distribution of radiopharmaceuticals.

Belgium (SCK CEN & IRE EliT) accounts for 20 to 25% of the worldwide production of medical radioisotopes and this can even reach 65% during peak times. Small country, but a major nuclear player! In addition to nuclear medicine, Belgium is a key player when it comes to nuclear power, whether it is the existing nuclear power plants or the nuclear energy of the future (such as the Small Modular Reactor). Our country is actively involved in the development of different types of SMRs, whether they are 3rd generation (water-cooled) or 4th generation (lead-cooled) SMRs. Belgian nuclear businesses are also involved in several nuclear projects that are currently in development all over the world.

www.forumnucleaire.be
www.nucleairforum.be

Research

EORTC
European Organisation for Research and Treatment of Cancer

Patient survival and quality of life are at the heart of **EORTC**'s research.

As an independent, non-governmental, non-profit cancer research Organisation established under the laws of Belgium, its mission is to coordinate and conduct international translational and clinical research to improve the standard of cancer treatment for patients.

EORTC aims ultimately to increase people's survival and quality of life by testing new therapeutic strategies based on existing drugs, surgery, and radiotherapy. EORTC also helps to develop new drugs and approaches in partnership with the pharmaceutical industry and in patients' best interests.

In addition to being independent, EORTC is recognised for scientific and methodological rigor bringing robust datasets to doctors and patients for therapeutic improvement. EORTC covers all disciplines to fight against cancer. EORTC research leaves no one behind and addresses all patients, including patients with rare tumours and specific patient populations.

EORTC is unique:

- International: EORTC manages clinical research activities across more than 35 countries.
- Multidisciplinary: our research spans all aspects of cancer management, from imaging and radiology to surgery and therapeutic innovations, backed by cutting-edge expertise in all fields.
- Multi-tumour: thanks to our broad-ranging network of oncology experts, no tumour is too rare to tackle. Our research is solution-driven, for all types of cancers, leaving no one behind.
- Compliant with regulation: in today's complex regulatory environment, EORTC's experts ensure our activities meet the strictest quality and reliability requirements, everywhere EORTC is active.
- Independent: our research is conducted under conditions of unwavering independence and accountability and all results are made public, to ensure patients and the oncology community benefit from our learnings.

www.eortc.org

Since its establishment in 1978, the primary objective of the **Belgian Association of Nuclear Medicine (BELNUC)** has been to promote the use of radioisotopes in medicine, encompassing scientific research, education, and clinically based applications supported by high-quality data. BELNUC organizes scientific meetings and a National congress every 2 years to foster research, development, and continuous training for its members. It collaborates with interuniversity training programs for young specialist physicians (post-graduate doctors). BELNUC establishes quality assessment tools and programs through dedicated workgroups, such as the radioligand therapy and artificial intelligence workgroups. Over time, BELNUC has transformed into an inclusive organization, welcoming all individuals involved in nuclear medicine. The establishment of a Technologist section in 1998, dedicated to the continuous education of technical staff, marked a significant milestone.

The collaboration between BELNUC for scientific promotion and the Group of Belgian Professional Unions of Specialist Doctors (GBS/VBS) and professional defense, and public authorities like the National Institute of Health Insurance (RIZIV/INAMI) and the Federal Nuclear Control Agency (FANC/AFCN), has significantly contributed to the promotion and advancement of the specialty in Belgium.

BELNUC is represented at the European Association of Nuclear Medicine (EANM) through a National Delegate and a National Deputy. They meet with the EANM Board twice a year at the EANM Delegates' Assembly to exchange ideas and discuss potential synergies on a supra-national level. Additionally, several members of BELNUC actively participate in various Committees or Task Groups of the EANM.

www.belnuc.be

Patient

Pioneering a Future of Hope for Cancer Patients

Dedicated to advancing nuclear medicine therapies, the **Oncidium Foundation** envisions a world where hope and access to leading-edge radioligand therapy are within reach for every individual affected by cancer. This nonprofit organization is committed to making these life-saving treatments accessible to people living with cancer, irrespective of financial means or geographic boundaries.

Boasting a global network of over 70 ambassadors, the foundation operates on three key pillars:

Access: Enhancing global access to radioligand therapies and financing treatment for needy cancer patients is a primary focus. The foundation has initiated the RLT-Connect Platform, an online doses-donation platform connecting healthcare practitioners and leading Medical Radioisotope Companies. This platform facilitates treatment doses for patients lacking access to these vital therapies, especially in low- and middle-income countries.

Education: With a dedication to addressing the gaps in awareness and education within the field, the Oncidium Foundation offers an extensive range of educational materials tailored for patients, oncologists, and the nuclear medicine community.

Hope: Through pioneering research initiatives aimed at broadening access to cutting-edge therapies, the foundation serves as a driving force in the fight against cancer. It actively engages in groundbreaking research to expand accessibility to innovative treatments, fostering hope for those affected by this severe illness.

The Oncidium Foundation serves as both a driving force in the worldwide battle against cancer and a ray of hope for those impacted by this severe illness.

Support the cause at:
www.oncidiumfoundation.org

PUBLIC SUPPORT

Federal

economie
FPS Economy, S.M.E.s, Self-employed and Energy

The production, sustainability and future of medical radioisotopes is a longstanding priority of the **FPS Economy** and to the Minister of Energy and Economy. The FPS Economy has been actively involved in improving the security of supply of medical radioisotopes field through financial and administrative support on different levels in the production cycle (e.g.: BR-2 reactor at SCK CEN and IRE), including the security of supply, research and development (e.g.: MYRRHA), and nuclear waste and fissile material management (e.g.: NIRAS, RECUMO project).

The FPS Economy also represents Belgium in international high-level meetings concerning the production and supply of medical radioisotopes, defending the interests of the Belgian nuclear industry, overseeing the European framework, and coordinating with the public and private actors in the field.

As part of the EU recovery and resilience facility (RRF, 2021-2026) Belgium received funds to invest in different types of projects. As part of this instrument, the FPS Economy oversees the implementation of two RRF medical radioisotope projects. One of these projects is NURA Radiopharmaceutical R&D at SCK CEN for innovative cancer therapies. This entails the development of new, innovative cancer therapies using medical radioisotopes 177Lu and 225Ac, for which some milestones are already achieved in 2023 (e.g.: start of the construction of the Material Treatment Facility (MaT)). The second RRF project covers different R&D projects of IRE and IBA, such as the development of innovative targets for the new generation high current cyclotrons.

www.economie.fgov.be/en

Health
Food Chain Safety
Environment

The FPS Public Health, through the federal Belgian Medical Imaging Platform (BELMIP), works closely together with the National Institute for Health and Disability Insurance (NIHDI), the FANC, the federated entities and the medical field in the matter of medical imaging. The BELMIP aims to improve appropriateness, patient safety and quality in medical imaging. More specifically, nuclear medicine is represented by the participation of the Belgian scientific society of nuclear medicine (BELNUC) at BELMIP.

Faced with rapid evolutions, it is important that there is a good match between the supply and the needs. The FPS Public Health monitors the equipment by means of the "register of heavy medical imaging equipment". For nuclear medicine, this register lists all SPECT-CT devices and all PET devices. An annual overview is published on the FPS Public Health website.

Belgium had 160 SPECT-CT devices and 33 PET-CT devices in 2023. These PET-CT devices are installed in 24 PET centers, in close collaboration with other hospitals. PET-centers are spread across the territory". The federal government monitors whether this program remains in tune with the needs. A possible future expansion of the PET program is currently being examined in consultation with experts from the medical field and the federated entities.

www.health.belgium.be/en

Flanders

DEPARTMENT OF
ECONOMY
SCIENCE &
INNOVATION

The Department of Economy, Science and Innovation (EWI) is a crucial organization of the Flemish Government dedicated to the preparation, follow-up and evaluation of policy within the domain of Economy, Science and Innovation. Positioned as a driving force, our main goal is to transform Flanders into one of the most progressive and prosperous regions worldwide. Our main pillars include promoting excellence in scientific research, cultivating an attractive and sustainable business climate, and nurturing a creative, innovative and entrepreneurial society.

Our approach provides for a harmonious interplay between economics, science and innovation, which provides unique opportunities for the development of a forward-looking long-term strategy. Proactively and responsively, we present policy proposals to relevant ministers based on our insights.

Strong ties with industry provide fertile ground for strengthening our knowledge and expertise, and ensure our added value in decision-making, even on federal and international platforms. Given the increasing impact of globalization, we actively promote Flemish participation in global research and innovation, while aligning economic policy with the international dimension of the Flemish economy.

www.ewi-vlaanderen.be

flanders.bio is a dynamic, member-driven organisation with currently more than 350 members from Belgium and abroad. Our membership base includes biotech start-ups and scale-ups, R&D focused biopharma and agrifoodtech companies, next to research institutes and a diverse community of specialist competence providers and investors (see overview on https://flanders.bio/en/member-directory). As an industry association, flanders.bio provides information tailored to its member companies. The association has a well-developed communication department that contributes to the national and international visibility of its members and the industry in general. In addition, flanders.bio provides a range of strategic business support services for companies to expand their business and access new markets. Facilitation of collaborations between different technology sectors is a key objective of flanders.bio. We do that together with a number of partners in the field of agrifood-tech and in emerging healthcare domains like vaccine development, ATMP and precision medicine.

With its exceptional density of R&D and clinical development actors, as well as a proven track record of companies bringing biotech research to market, flanders.bio and its members are proud advocates of a reputable and growing global impact ecosystem in life sciences in Europe.

Every year this ecosystem gathers during flanders.bio's Knowledge for Growth conference. Over the past 19 years, Knowledge for Growth has grown to become one of Europe's leading biotech and life sciences business conferences. The 2023 edition was attended by over 1000 life sciences actors from Belgium and close to 20 other countries.

www.flanders.bio/en

VIB is widely recognized as an established and world-leading knowledge center in life sciences and biotechnology with an excellent reputation in technology transfer. The unique combination of strategic basic research and a clear focus on innovation and business is one of the major contributors to its success. VIB is highly committed to being the driving force behind the growth of the dynamic life science cluster in Flanders.

VIB operates in close partnership with the five universities in Flanders – Ghent University, KU Leuven, University of Antwerp, Vrije Universiteit Brussel and Hasselt University.

www.vib.be

Wallonia

Wallonie économie SPW

The Public Service of Wallonia (SPW) Economy, Employment, Research, offers subsidies to companies and research institutions. It focuses on technological innovation projects by supporting the development of new products, processes and services, as well as the acquisition and development of new technologies. It also helps companies to file or extend a patent.

www.wallonie.be

MECATECH CLUSTER
WALLOON COMPETITIVENESS CLUSTER IN MECHANICAL ENGINEERING

The MecaTech cluster is Wallonia's mechanical engineering competitiveness cluster. This cluster boasts nearly 300 industrial and academic stakeholders collaborating on mechanical engineering projects in Wallonia. This cluster encourages innovation and cooperation. This initiative aims to create jobs and develop skills with a view to potential internationalisation. The digital cluster works on AI and IoT.

www.polemecatech.be

WE Wallonie Entreprendre

WE contributes to Wallonia's economic development through awareness programs and by supporting and financing Wallonia-based companies in a wide range of sectors, including life sciences, deeptech, energy and aerospace. It provides equity and debt financing to companies of various sizes and at different stages of development, alongside private investors. In this capacity, WE actively contributes to nurturing ecosystems, aiming to foster employment, create value, and attract additional investments.

www.wallonie-entreprendre.be
lifesciences@wallonie-entreprendre.be

BIOWIN
THE HEALTH CLUSTER OF WALLONIA

BioWin is the Health Cluster of Wallonia, Belgium. We are the regional reference holder for all stakeholders in innovative R&I projects in health biotechnology and medical technologies, whether they are companies, research centers or universities. We also aim to promote Wallonia internationally as a world-class life sciences environment for academic, clinical and industrial research.

www.biowin.org

Brussels

hub.brussels lifetech
innovate further, care better

lifetech.brussels is the public Brussels HealthTech cluster. It aims at facilitating and stimulating the attractivity and success of high potential HealthTech solutions with a focus on social and environmental impact. The main goal is to accelerate the availability of innovative healthcare solutions at the service of patients' wellbeing and professionals' needs. The cluster promotes collaborations and synergies between entrepreneurs, researchers, makers, practitioners and industries.

lifetech.brussels is part of hub.brussels, the Brussels Agency for entrepreneurship.

Main services:

- **Clustering activities:**
  - Guidance: the individual coaching is a free of charge personalized guidance to turn innovative idea into a commercial solution (business model, financing strategy, subsidies, partnerships, innovation management, internationalization, regulatory requirements awareness,...); access to hub.brussels expertise (legal, financial, tax, etc.); access to a specialized consultancy network
  - Networking and knowledge sharing: animation of a vivid HealthTech community (workshops, pitching sessions,...)
  - Visibility: promotion of the Brussels know-how and members' activities and projects to increase the visibility of the sector and the members
  - Internationalisation: support the internationalisation of the cluster members through the organization of missions abroad, the support of a broad network of trade advisors worldwide, the access to European funding programs via the network of National Contact Points and search for technological partners via the Enterprise Europe Network

Specific Projects:

- **Collective coaching through the MedTech Accelerator®**: 6-month of a collective and individual coaching program to boost the development of (connected) medical devices with the help of seasoned experts and dedicated coaches. (±60 startups helped since 2016; 8th edition in 2023). For more information: www.medtech-accelerator.eu
- **Prevention Project**: Facilitate testing, validation, and adoption of innovative solutions for primary, secondary, and tertiary healthcare prevention
- **CIMH**: The Center for Medical Innovation in Hospitals aims to provide concrete innovative responses to problems that patients or doctors encounter with medical practices, or obstacles directly related to the quality, safety or organization of health care

www.lifetech.brussels

innoviris .brussels
we fund your future

Innoviris is the public organisation that funds and guides innovation, scientific research and science promotion in the Brussels-Capital Region.

Within this framework, Innoviris co-finances and supports cutting-edge innovation projects and scientific research both at start-ups and large companies, at research centres, the non-profit sector and the public sector to stimulate creative solutions that can contribute to the Brussels region of tomorrow.

Our focus is on research and innovation projects that have the potential to address urban challenges, including in the areas of mobility, nutrition, health and social inclusion, to create quality employment and to contribute to the social and environmental transition of our economy.

To that end, the Regional Innovation Plan 2021-2027 serves as a compass to develop all subsidy and awareness-raising instruments, aligned with the objectives of the Strategy for Intelligent Specialisation and regional strategic plans.

Furthermore, we raise awareness about STEM directions and career opportunities, and about the role of science in society.

While facilitating collaborations within the local ecosystem, we represent the Brussels-Capital Region at national, European and international level in the field of research and innovation.

www.innoviris.brussels

ABBREVIATIONS

- BR2: Belgian Reactor 2
- EANM: European Association of Nuclear Medicine
- EFPIA: European Federation of Pharmaceutical Industries Associations
- ESFRI : European Strategic Forum for Research Infrastructure
- EU: European Union
- EURATOM: European Atomic Energy Community
- FANC: Federal Agency for Nuclear Control
- GDP: Gross Domestic Product
- HADES: High Activity Disposal Experimental Site
- IAEA: International Atomic Energy Agency
- IRE: Institut National des Radioelements or Nationaal Instituut voor Radio-elementen
- Mo-99: Molybdenum-99
- MYRRHA: Multi-purpose Hybrid Research Reactor for High-tech Applications
- NEA: Nuclear Energy Agency
- NM: Nuclear medicine
- NRG: Nuclear Research & consultancy Group
- OECD: Organisation for Economic Co-operation and Development
- PET: Positron Emission Tomography
- SCK CEN: Studiecentrum voor kernenergie or Centre d'étude de l'énergie nucléaire
- SET: European Strategic Energy Technologies
- SMART: Source of MedicAl RadioisoTopes
- SPECT: Single Photon Emission Computed Tomography
- Tc-99: Technetium-99
- Tc-99m: Technetium-99 metastable

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