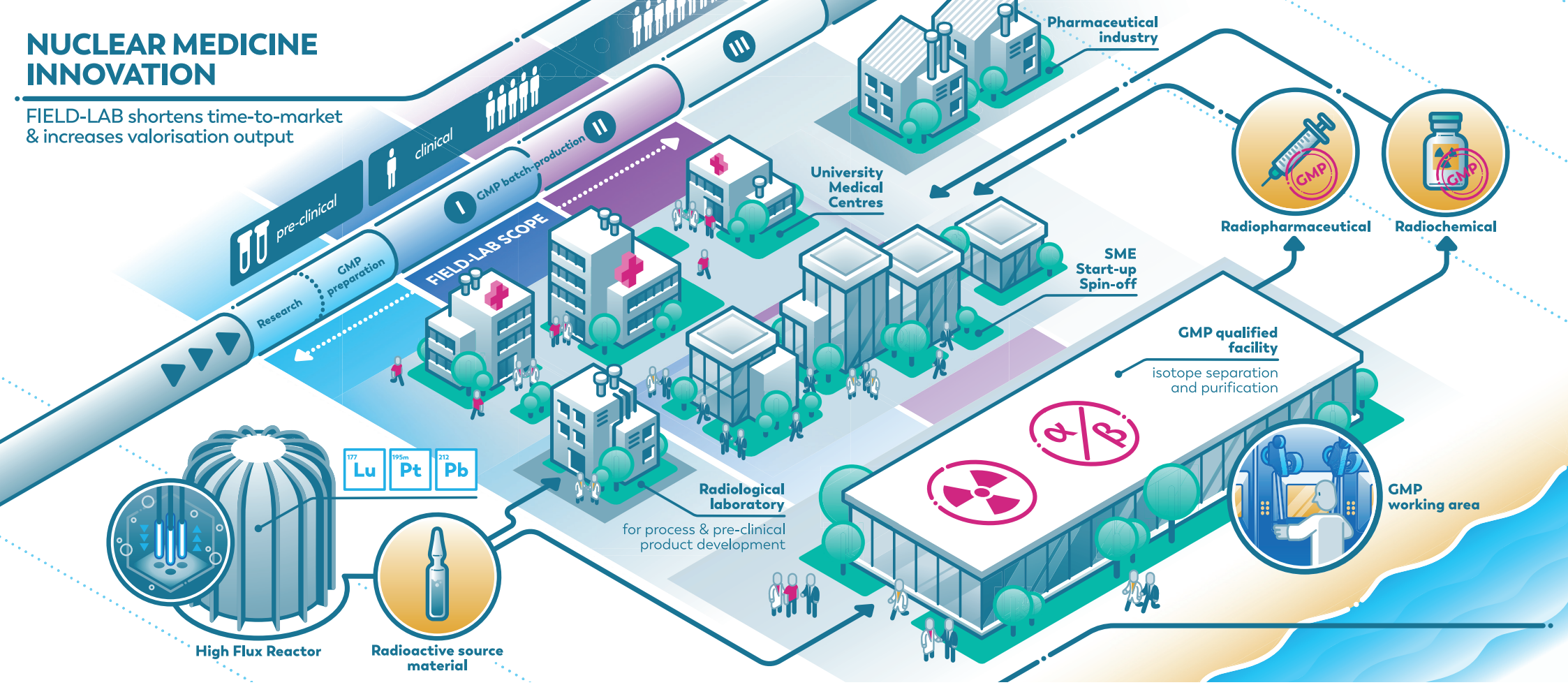


Will you partner with us in our quest for the development of new nuclear medicine?

NRG

FIELD-LAB

Advancing Nuclear Medicine

NRG Advancing Nuclear Medicine

Experts in irradiation, innovation and commercial processing with medical isotopes

NRG Advancing Nuclear Medicine cares for the well-being of people worldwide. Especially for their health. We wish people to live longer, be more vital and feel happier. We believe everybody should have access to advanced treatments. New highly targeted treatments will cause less side effects and improve the quality of life.

We provide solutions to advance nuclear medicine ranging from:

- Complete irradiation services for medical isotope production
- Access to R&D resources to drive the development of new nuclear therapies
- Commercial processing services supporting customers to scale up the production of a radiochemical or radiopharmaceutical.

- **Serving 30.000 patients daily**
- **1 hour away from important European airport**
- **Europe's most complete nuclear infrastructure**

How we can help you

Some important radio-isotopes we produce

Molybdenum-99

NRG is the world's leading producer of ^{99}Mo targets for use in the supply chain of technetium-99m, commonly used all over the world for a broad range of imaging purposes in serious medical conditions. ^{99}Mo forms a significant part of the medical isotopes produced by NRG enabling more than 10 million patient treatments yearly.

Lutetium-177

NRG is a major supplier of ^{177}Lu, primarily for the latest developments in theranostics. NRG was involved in the early production development of Lu-177 for use in Neuroendocrine Tumour treatment. Currently, many clinical trials are being held, and in the future, many patients can be treated with nuclear medicine based on Lu-177.

Yttrium-90

With the production of irradiated ^{90}Y for multiple clients, NRG plays an important role in the supply chain to hospitals worldwide. Among other applications, this isotope is commonly used in radio-embolisation (SIRT) treatment. Our full-service approach includes preparing irradiation capsules, irradiation, waste handling and logistics.

Holmium-166

NRG supplies ^{166}Ho to a business partner who developed a unique radio embolisation method for treatment of primary liver cancer and liver metastases. Firstly, the emitted beta radiation has therapeutic effects. And additionally, the gamma radiation and the paramagnetic effects of holmium allow for imaging with a SPECT or MRI scanner.

Unique location & infrastructure

Our premises in Petten are home to a unique combination of nuclear facilities. Over the past 60 years, the site has expanded to an Energy & Health Campus of international allure. With the knowledge developed in these facilities and the continuous production of medical isotopes, our services and products are improving quality of life globally.

For the future we expect spectacular breakthroughs in the treatment of life-threatening diseases by using targeted radiopharmaceuticals in a personalised approach. To support this, our site in Petten is being overhauled with a significant investment programme. At present a state-of-art R&D environment and supporting facilities are being created to cater for the needs of all pioneers in this exciting field of nuclear medicine.

NRG is located in the Dutch dunes, just north of Amsterdam and only one hour away from Amsterdam Airport Schiphol.

FIELD-LAB

an innovative joint partnership for nuclear medicine development

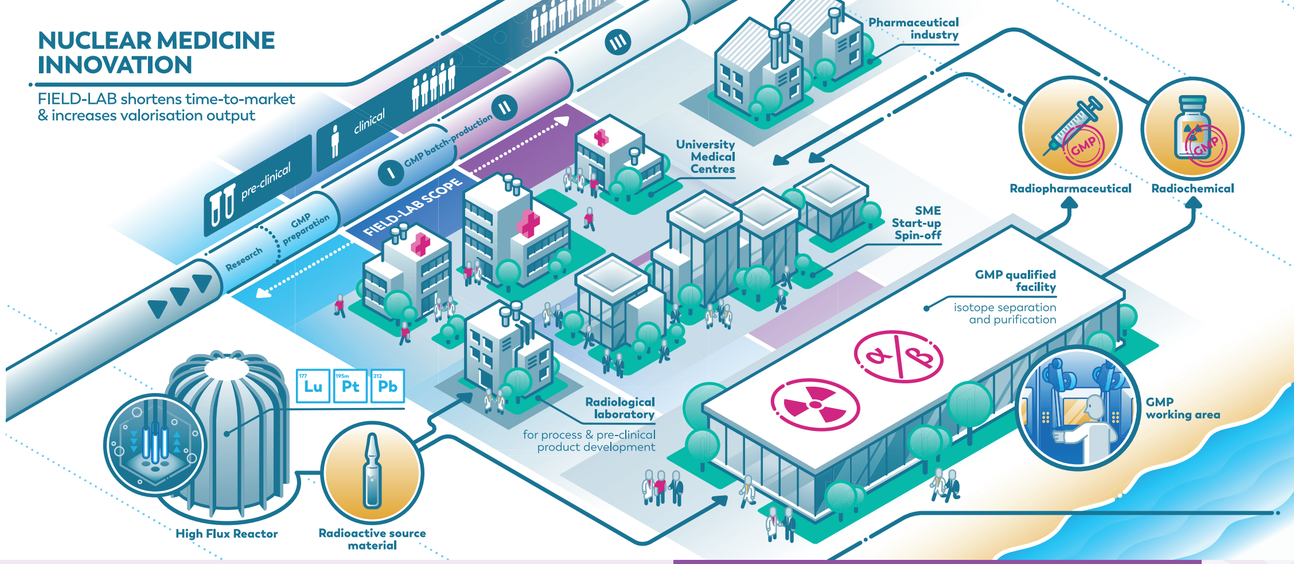
FIELD-LAB is a drug discovery facility that will help you to speed up the development and market launch of new nuclear drugs for cancer treatment. Through supply of small (non) GMP batches of radiochemicals and radiopharmaceuticals, we meet the need of bio pharma scientists and start-up ventures for research materials. This will drive both their ambitions to develop a new drug.

FIELD-LAB is created for and together with partners from different backgrounds. Dutch UMC's have committed themselves to be part of this initiative. They believe in the beneficial results that will be brought to the Nuclear Medicine society. In addition, the partnerships that arise from FIELD-LAB form a portal to a fast growing network, which results in an open innovation environment.

What can we offer you?

- Supply of radiochemical solutions and radiopharmaceuticals to laboratories
- Both research and GMP grade
- Creation of radiochemical processes using innovative isotopes
- Collaboration between academic and industrial partners
- Portal to a fast-growing network with an open innovation culture

- **Supports medical product development**
- **Unique nuclear infrastructure**
- **Supply of promising medical isotopes**



Will you take up the challenge to develop your new cancer treatment solution with us?

Become a partner and get access to unrivalled nuclear resources and a network of renowned academic centres.

Proposition & infrastructure outline

A sound nuclear infrastructure is necessary to produce radiopharmaceuticals. The guarantee for safe production and the handling of radioactive materials rely on it. To ensure that the nuclear materials are safe for patients, FIELD-LAB uses facilities and processes that are in line with Good Manufacturing Practice (GMP) standards. These types of facilities are complex, rare and expensive.

As partner within the FIELD-LAB consortium NRG realises the needed nuclear infrastructure, covering the complete route of nuclear medicine product development.

From nuclear material generation, to radiological laboratories for pre-clinical research, to small scale GMP radiopharmaceutical production for clinical trials.

FIELD-LAB has a unique and complete nuclear infrastructure

- **High Flux Reactor**
- **Radiological laboratories**
- **Hot cell laboratories**
- **GMP small scale production facility**

NRG is a supplier and leading partner within FIELD-LAB. Ánd operator of the High Flux Reactor (HFR) in Petten. A large part of the medical isotopes used worldwide are currently produced in the HFR.

Our nuclear infrastructure is available to partners within FIELD-LAB for research, development, production and distribution of medical isotopes.

n.c.a. lutetium-177 chloride

Small scale supply for preclinical stages and clinical trials

From the very beginning that nuclear medicine started looking into using lutetium for therapeutic purposes, NRG has been involved as important irradiator of this isotope. Moreover, NRG has been at the cradle of the development of Lu-177 for the treatment of Neuroendocrine Tumours (NETs).

In the High Flux Reactor both carrier added and no carrier added lutetium-177 are being produced. FIELD-LAB is developing a process to turn the radioactive isotope n.c.a. Lu-177 into a chloride. The liquid can be used in the development of different radiopharmaceuticals.

Why n.c.a. Lu-177 chloride?

Currently, Lu-177 is dominating the clinical pipeline regarding the innovation of radiopharmaceuticals. Researchers have found numerous possible applications for this radioisotope.

We hope that in the future, many patients with different types of cancer, can be treated with radiopharmaceuticals based on lutetium-177.

Unique proposition from NRG

Through FIELD-LAB, NRG is able to support partners involved in pre-clinical and clinical work & studies related to ^{177}Lu n.c.a.

Test batches of lutetium-177 n.c.a. chloride from the in-house developed Lu/Yb separation method will be made available to potential partners.

For these potential partners we aim at (academic) hospitals and start-up companies.

NRG offers perspective on secure and reliable supply when the products come to market: commitment of mutual benefit

Contact us to see how we can help you with supply of ^{177}Lu n.c.a. chloride

Product description	**No-carrier-added lutetium-177 trichloride**
Isotope	**Lu-177**
Physical half-life	**6.75 days**
Decay mode	**$E_{\beta,\ max}$ = 498.3 keV E_γ = 208 keV (11 %) E_γ = 113 keV (6.6 %) E_α (Po-212 à Pb-208) = 8.8 MeV**
Target material	**Enriched Yb-176**
Production mode	**Yb-176(n,γ)Yb-177 › Lu-177**
Chemical form	**Lutetium trichloride in acqueous HCl solution**

Metastatic castration-resistant prostate cancer

An example of a promising treatment currently under investigation is lutetium-177-PSMA for treatment in patients with metastatic castration-resistant prostate cancer. The advantage of this form of targeted radiation is that the damage is very local and limited to surrounding tissue.

Do you want to get access to n.c.a. lutetium-177 chloride?

Become a FIELD-LAB partner and we will set new standards together in the fight against cancer.

- **Small batches for research purposes and clinical trials**
- **GMP quality**
- **High Specific activity**

platinum-195m CISSPECT

Radioactive cisplatin: an innovative solution to improve treatment outcome.

CISSPECT is the radioactive look-a-like of cisplatin, worldwide one of the most used anticancer drugs. CISSPECT is currently being developed in collaboration with the Netherlands Cancer Institute and Amsterdam UMC, loc. VUmc in the Netherlands. The collaboration is focusing on lung cancer patients and head and neck cancer patients.

CISSPECT can improve cisplatin treatment and save patients from side effects such as kidney failure, loss of hearing, nausea and tiredness.

Why Pt-195m CISSPECT?

Most of the patients treated with cisplatin do not respond to cisplatin therapy.

For lung cancer patients treated with radiation, additional cisplatin chemotherapy could be beneficial. On average, the chances of survival **increase by 8%**. Although these chances can be higher for some, many patients suffer side effects from the cisplatin treatment. Hence it is unfortunate that non-responders cannot be identified before the treatment starts.

Similarly, patients treated with cisplatin for head and neck cancer do not know if the therapy will lead to results.

For all cancer patients treated with cisplatin chemotherapy, about **20-30**% suffer from kidney failure as a side effect.

With ^{195m}Pt CISSPECT we may possibly help physicians to select the right treatment for these two patient groups.

Unique proposition from NRG

FIELD-LAB assists partners in the application of ^{195m}Pt for indications additional to the present lung cancer and head & neck cancer under investigation.

For these potential partners we aim at (academic) hospitals and start-up companies

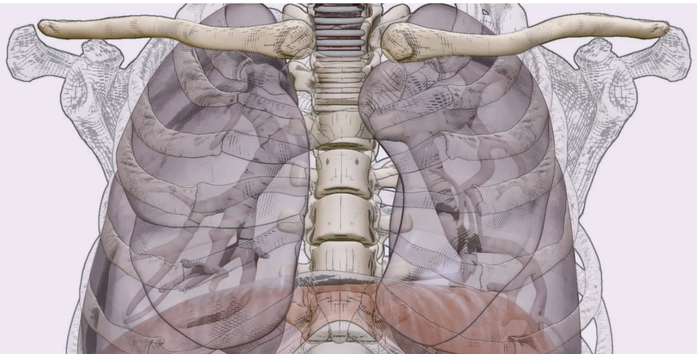
NRG offers perspective on secure and reliable supply when the products come to market: commitment of mutual benefit

Supply

- 2021: GMP supply from VUmc for human pilot study
- 2023: GMP supply from Petten FIELD-LAB facilities

Contact us to see how we can help you with supply of ^{195m}Pt.

Product description	**Pt-195m Cisplatin, or cis-diamminedichloroplatinum-195m(II)**
Isotope	**Pt-195m**
Physical half-life	**4.02 days**
Decay mode	**IT, accompanied by emission of Auger e lectrons E_γ = 98.9 keV (11.4 %) E_γ = 129.7 keV (2.8 %) $E_{X\text{-}ray}$ = 65.1 keV (22.4 %) $E_{X\text{-}ray}$ = 66.8 keV (38.3 %)**
Target material	**Metallic Platinum Enriched in Pt-195 (> 97%)**
Chemical form	**Cis-[Pt(II)$(NH_3)_2Cl_2$] in 0.9% NaCl solution**
Method of characterisation	**UVVIS λ_{max}: 301 nm, 365 nm; λ_{min}: 246 nm Absorbance λ_{max}/Absorbance λ_{min} > 4.5 UVVIS Spectrophotometer Lambda 365 Perkin Elmer**



Which solutions will CISSPECT possibly offer?

- Lung cancer: with CISSPECT, we can possibly identify the patients that will benefit from cisplatin chemotherapy and increase their chances of survival effectively.
- Head & neck cancer: with CISSPECT, we may rightly select the patients that will respond to cisplatin treatment.

Do you have an additional indication to investigate with the use of radioactive cisplatin?

Become a FIELD-LAB partner and learn from the NKI/AvL to speed up your application development.

- **High specific activity of ^{195m}Pt**
- **Reliable synthesis**
- **For in-human use**
- **Chemically identical to Cisplatin**

lead-212

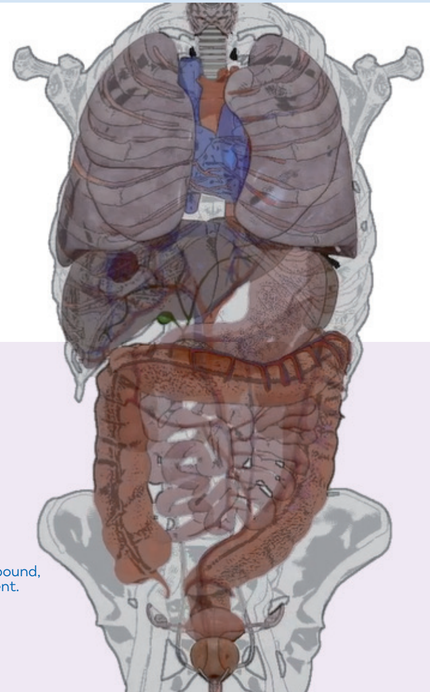
Therapeutic isotope of the future for targeted alpha therapy

The FIELD-LAB team selected lead-212 as one of the key isotopes for nuclear medicine by evaluating technical feasibility and the potential for medical use:

- 1 alpha-emission in the decay chain, and 10,6-hour half-life
  - long enough for targeting purposes
  - short enough and with a single alpha-emission to avoid long term off-target damage
- Favourable production route, strong and up scalable

Why Pb-212?

"^{212}Pb is a very relevant medical isotope with large potential. It is however very difficult to make and have access to. FIELD-LAB allows us to proceed developing and testing the potential applications of ^{212}Pb for effective cancer therapies."



Unique proposition from NRG

^{212}Pb is not readily available, hence the development of ^{212}Pb products has not taken off.

Most urgent needs:

- Sourcing of ^{228}Th mother isotope (either from ^{232}Th or ^{226}Ra neutron irradiation)
- Processing of alpha material (separation and purification) in a suitable alpha- and radon-tight environment with proper nuclear license
- Generator development and availability
- Quality assurance and control (purity) and transport/logistics

With the HFR, NRG's processing expertise, the radiological alpha-tight laboratories, the FIELD-LAB partnership and FIELD-LAB infrastructure, ^{212}Pb has now been regularly produced for preclinical efforts at academic hospitals.

Product description	**Lead-212 dichloride**
Isotope	**Pb-212**
Physical half-life	**10.6 hrs**
Decay mode	**$E_{\beta,max}$ (Pb-212 à Bi-212) = 573.8 keV** **E_γ = 238.6 keV (43.3 %)** **E_γ = 300 keV (3.3 %)** **$E_{\beta,max}$ (Bi-212 à Po-212) = 2.3 MeV (64.1 %)** **E_α (Bi-212 -> Tl-208) = 6.1 MeV (35.9 %)** **E_γ = 727.3 keV (6.6 %)** **E_α (Po-212 › Pb-208) = 8.8 MeV** **$E_{\beta,max}$ (Tl-208 › Pb-208) = 1.8 MeV** **E_γ = 2614.5 keV (99 %)** **E_γ = 860.6 keV (12.4 %)** **E_γ = 583.2 keV (84.5 %)** **E_γ = 510.8 keV (22.6 %)**
Target material	**Enriched Ra-226**
Production mode	**Th-228 › Ra-224 › Pb-212**
Chemical form	**Lead-212 dichloride in acqueous HCl solution**

Pb-212: more effective than ^{177}Lu, less harmful than ^{225}Ac

Targeted Alpha Therapy & ^{212}Pb

Targeted alpha therapy (TAT) offers opportunities for very effective treatment, by localising high radiation damage at the targeted location.

Different alpha-emitters can be considered and selection depends on the application, the targeting compound, and the damage profile combined with half-life and residence time in both tumour tissue and the patient.

For applications which benefit from a moderate damage profile and a relatively short half-life, ^{212}Pb can be the alpha-isotope of choice.

Are you curious if this rare isotope can help you in your R&D efforts?

Become a FIELD-LAB partner and discover with us the most appropriate medical applications.

- **Beta-emitter with limited recoil and a single alpha emission in the decay chain**
- **Ideal half-life (+10,6hrs)**
- **Reliable supply**

FIELD-LAB

Advancing Nuclear Medicine

Financially supported by

European Union
European Regional
Development Fund

We are constantly expanding and look for new partners to help us grow this unique innovation consortium.

- **Are you at the scientific end of nuclear medicine?**
- **Or do you have a venture searching to exploit this great new cancer treatment?**

Contact us to explore the various partnership possibilities.

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