



Advancing Nuclear Medicine

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



## Some important radio-isotopes we produce



### Molybdenum-99

NRG is the world's leading producer of <sup>99</sup>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. <sup>99</sup>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 <sup>177</sup>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 <sup>90</sup>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 <sup>166</sup>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?

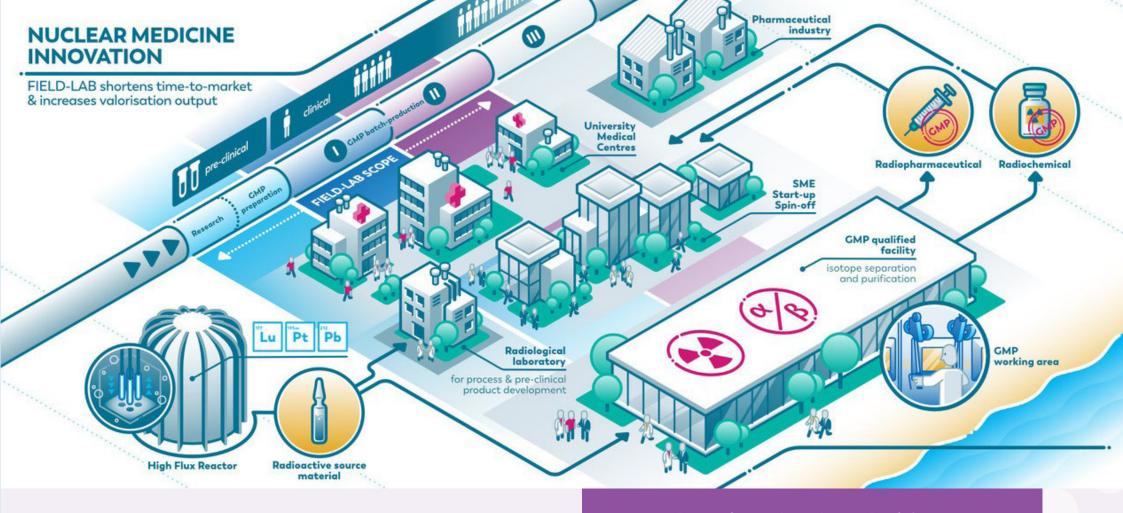
- Supply of radiochemical solutions and radiopharmaceuticals to laboratories
- Both research and GMP grade
- Creation of radiochemical processes using innovative isotopes
- Collaboration between academic and industrial partners
- Portal to a fast-growing network with an open innovation culture

- 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.

# 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.

### Unique proposition from NRG

Through FIELD-LAB, NRG is able to support partners involved in pre-clinical and clinical work & studies related to <sup>177</sup>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 startup 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 <sup>177</sup>Lu n.c.a. chloride

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

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.

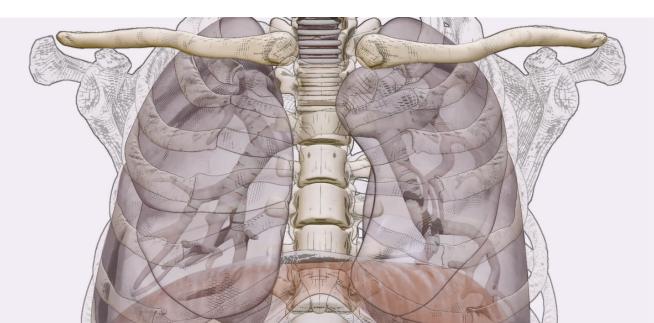
### Why Pt-195m CISSPECT?

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

In case of lung cancer patients, **less than 8%** benefit from this chemotherapy treatment. Many patients suffer from side effects. Therefore, it is very unfortunate that non-responders cannot be identified before treatment starts.

Also, **50% of patients** treated with cisplatin for head and neck cancer in the Netherlands, do not know the outcome before the treatment starts.

With <sup>195m</sup>Pt CISSPECT we may possibly help physicians to select the right treatment for these two patient groups.



# Which solutions will CISSPECT possibly offer?

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

### Unique proposition from NRG

FIELD-LAB assists partners in the application of <sup>195m</sup>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 startup 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 <sup>195m</sup>Pt.

Product description	Pt-195m Cisplatin, or cis- diamminedichloroplatinum-195m(II)
lsotope	Pt-195m
Physical half-life	4.02 days
Decay mode	IT, accompanied by emission of Auger e lectrons E <sub>γ</sub> = 98.9 keV (11.4 %) E <sub>γ</sub> = 129.7 keV (2.8 %) E <sub>X-ray</sub> = 65.1 keV (22.4 %) E <sub>X-ray</sub> = 66.8 keV (38.3 %)
Target material	Metallic Platinum Enriched in Pt-195 (> 97%)
Chemical form	Cis-[Pt(II)(NH <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> ] in 0.9% NaCl solution
Method of characterisation	UVVIS $\lambda_{max}$ : 301 nm, 365 nm; $\lambda_{min}$ : 246 nm Absorbance $\lambda_{max}$ /Absorbance $\lambda_{min}$ > 4.5 UVVIS Spectrophotometer Lambda 365 Perkin Elmer

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 <sup>195m</sup>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 achievability and the potential for medical use:

- 1 alpha-emission in the decay chain, and 11-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

### Pb-212: more effective than <sup>177</sup>Lu, less harmful than <sup>225</sup>Ac

### **Alpha-emitters**

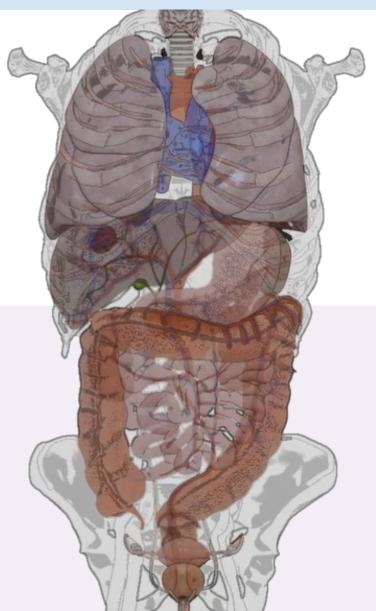
Unstable isotopes that become stable through the release of alpha-radiation. Alpha-radiation consists of highly energetic particles, that do not travel far but can create significant damage on their way.

### Targeted Alpha Therapy (TAT)

Effective cancer therapy by linking an alpha-emitter to a molecule that binds specifically to cancer cells. This so-called "targeting molecule" transports the alpha-emitter to the right location, preventing damage at other locations.

### Why Pb-212?

<sup>\*212</sup>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 <sup>212</sup>Pb for effective cancer therapies."



### Unique proposition from NRG

FIELD-LAB assists in the introduction of  $^{\rm 212}{\rm Pb}$  for customer or partner compounds.

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  $^{\rm 212}{\rm Pb}$ 

Product description	Lead-212 dichloride
lsotope	Pb-212
Physical half-life	10.6 hrs
Decay mode	$E_{\beta, max}$ (Pb-212 à Bi-212) = 573.8 keV $E_{\gamma}$ = 238.6 keV (43.3 %) $E_{\gamma}$ = 300 keV (3.3 %)
	$E_{\beta, max}$ (Bi-212 à Po-212) = 2.3 MeV (64.1 %) $E_{\alpha}$ (Bi-212 -> TI-208) = 6.1 MeV (35.9 %) $E_{\gamma}$ = 727.3 keV (6.6 %)
	E <sub>α</sub> (Po-212 > Pb-208) = 8.8 MeV
	$\begin{array}{l} {\sf E}_{\beta,{\sf max}}\left({\sf TI-208} > {\sf Pb-208}\right) = 1.8 \; {\sf MeV} \\ {\sf E}_{\gamma} = 2614.5 \; {\sf keV}\left(99\;\%\right) \\ {\sf E}_{\gamma} = 860.6 \; {\sf keV}\left(12.4\;\%\right) \\ {\sf E}_{\gamma} = 583.2 \; {\sf keV}\left(84.5\;\%\right) \\ {\sf E}_{\gamma} = 510.8 \; {\sf keV}\left(22.6\;\%\right) \end{array}$
Target material	Enriched Ra-226
Production mode	Th-228 › Ra-224 › Pb-212
Chemical form	Lead-212 dichloride in acqueous HCl solution

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 (+10hrs)
- Reliable supply



### **Advancing Nuclear Medicine**



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 parntnership possibilities.



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