# Future of radiotheranostics from an industrial perspective

## Medical Economics in Nuclear Medicine

Chrysalium Consulting
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SOFRA meeting, May 26, 2021

# What to expect in NM within the next 10 years

*…seen from the point of view of investors and industry*

## Three major questions

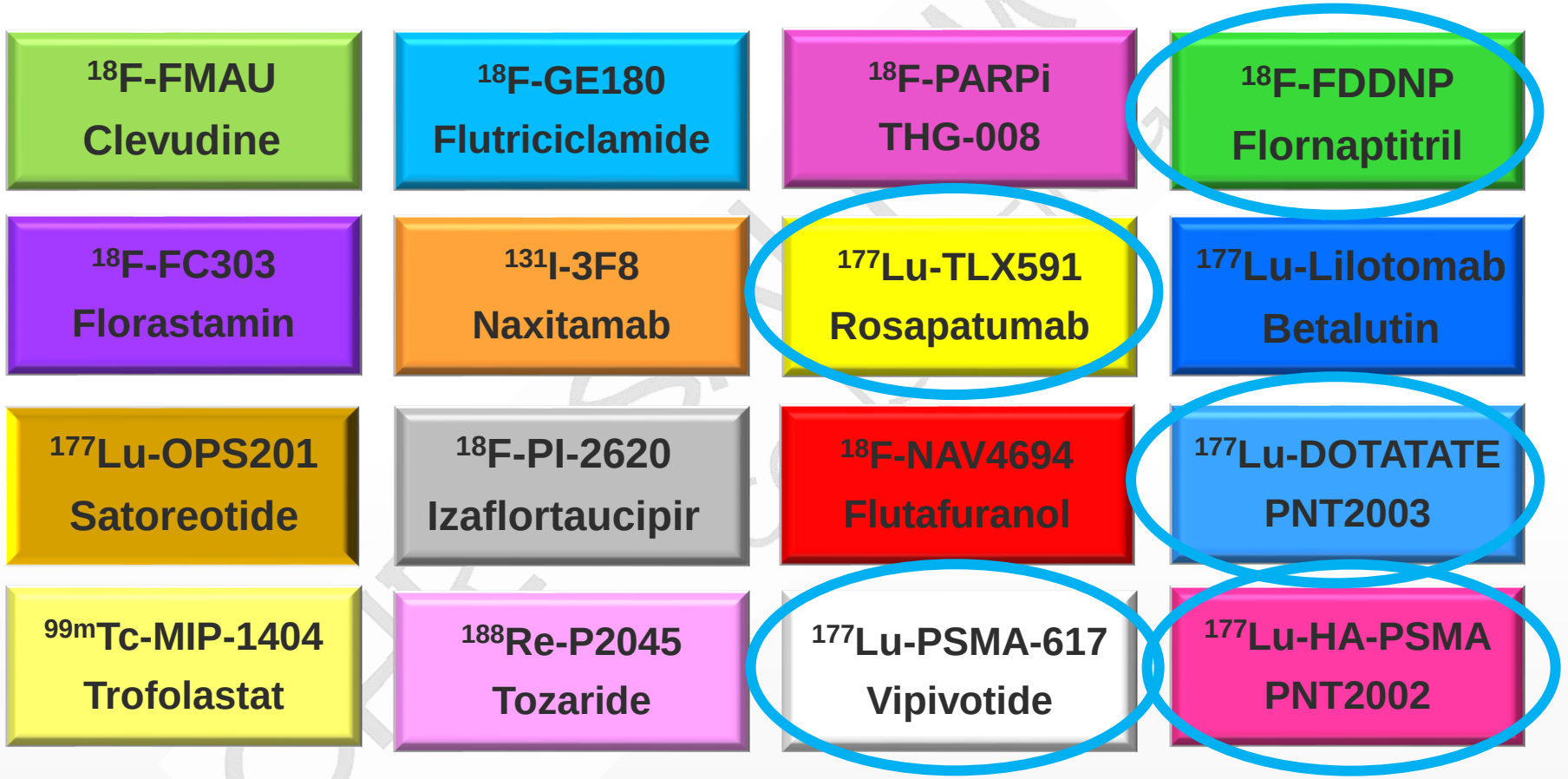
- What will be new for patients ? 2021-2026
- What is of real interest for investors ? 2021-2026
- What is now to expect from research teams ? 2023-2030

**Major aim**: why and where to invest in Radiopharmaceuticals ?

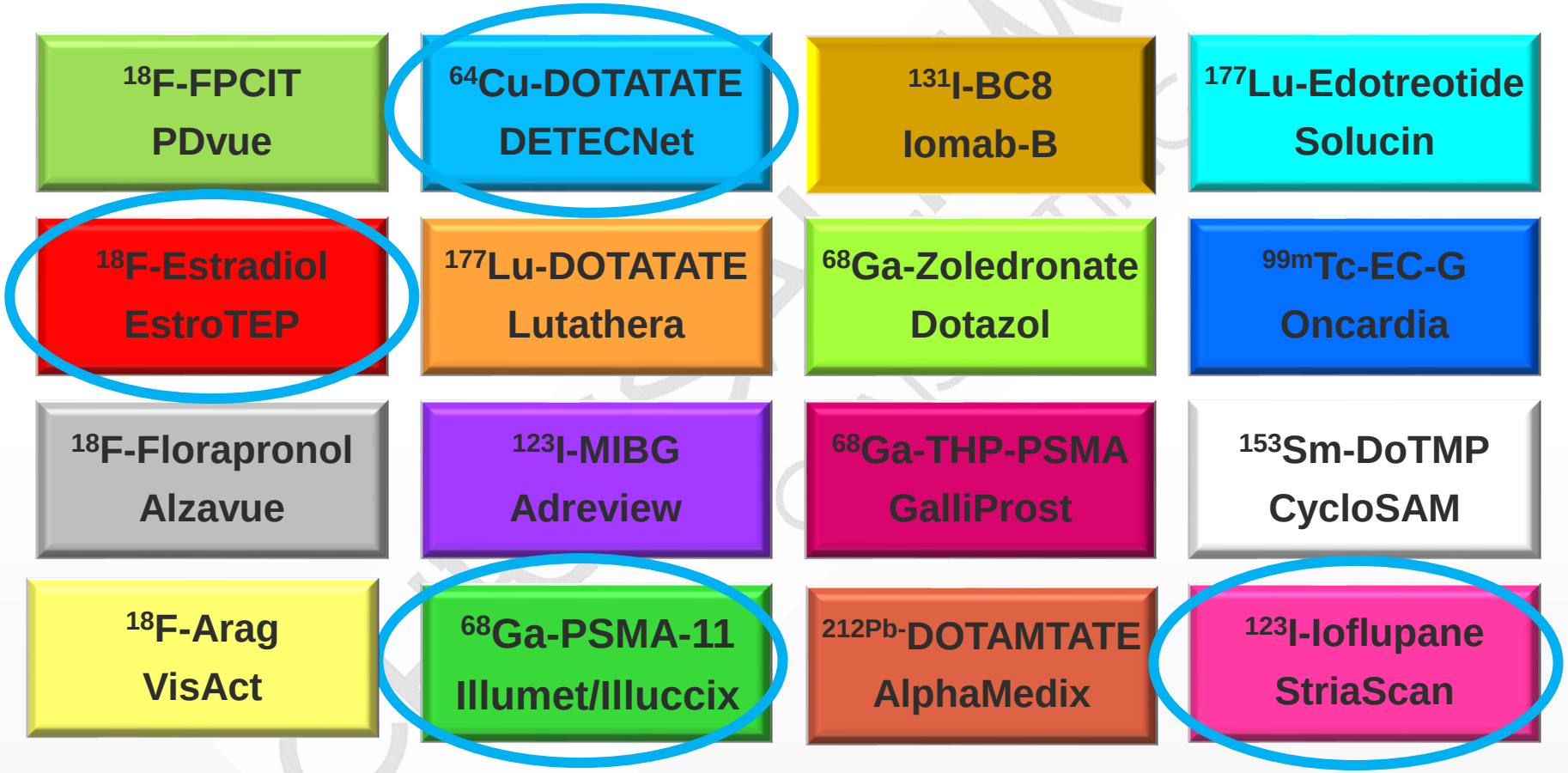
# Message 1

## Do not trust economists, advisors and fortunetellers

# New names (vectors)



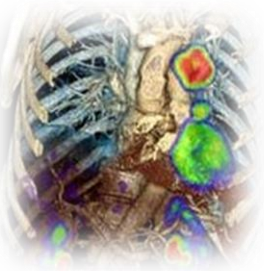
# New tracers/drugs brand names



# New companies

| | | | | |
|---|---|---|---|---|
| Clino | Fuzionaire | Noria Therapeutics | Inflazome | Tracon Pharma |
| Atonco | WWiKY Biosciences | Convetra | Factor 1A | Adeccammas |
| Aytu Biosciences | Andarix Pharma | RayzeBio | Nanogun Technology | Precirix |
| Panacea Pharma | Aktis Oncology | Cassava Sciences | Global Morpho Pharma | Abscint |

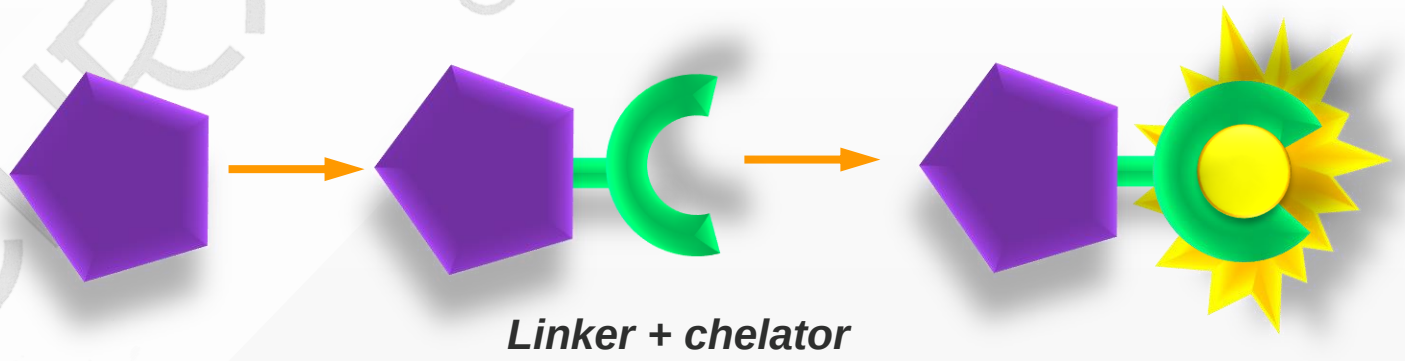
# Investing in radiopharmaceuticals



- Starting point: **Knowledge** about the nuclear medicine field
- Difference between Research tool or Marketed tracer/drug i.e. Publication or Patent
- **Funds availability** => subgroups: from < € 10K up to several €B
  - Stepwise investment: 4F - Business angels - Equity financing - … - Stock funds
- Difference between **Diagnostics and Therapeutics**
- **Expected profitability**: Alternatives to the pharmaceutical business

# Principle of Molecular Targeting


**Imaging** *ex. Labeling with e.g.Gallium-68 (Gamma emitter)*
**Therapy** *ex. with Lutetium-177*



# Message 2

**Global Economics is driving Nuclear Medicine development - not Science**

**Investors will bring money in the radiopharmaceutical industry only if they are sure it can be more profitable than other businesses**

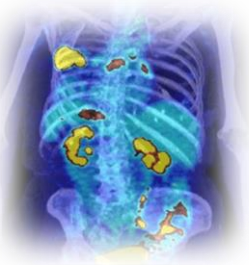
| Primary criteria | **Proprietary molecules (no generics)**<br>**Access to worldwide rights (no local products)**<br>**No 'me-too', no 'me-too+'**<br>**Availability of biodistribution data in man (no early research projects)** |
|---|---|
| Market data and competition | Medical need (at the time of entrance on market)<br>No in-house competition and non-competitive new approach<br>Limited competition with non NM modalities<br>No future competition with non-imaging diagnosis |
| Technical data | Modality is not an issue<br>Type of vectors or indications are not issues<br>Systemic drug, no local applications/therapy<br>Good non-optimized synthesis yields<br>Realistic manufacturing costs<br>**Easy access to starting materials involving GMP grade RNs** |
| Non technical criteria | If possible same day imaging<br>Reimbursement |

# Major basic rule

**Be first sure there is a clean solution to bring your tracer/drug on the market when development is complete (in 5-8 years), before starting investing in its full development**

**Investors need to have trust in the capacity to reach the figures of the business plan before challenging these figures**

# Example of a true issue: new $^{18}$F-tracers



- There is an excess of FDG production centers (800+) and still some countries and location remain underequipped
- Existing centers are not all GMP (probably only 400 are) and most of them are located in hospitals (HRPs)
- Most of them have been built for $^{18}$F-FDG only and cannot handle more than 4 different molecules in parallel
- They cannot expend and they are not able to follow new GMP rules
- New $^{18}$F-labeled tracers are now entering the market and FDG will not disappear
- About 110+ cyclotron equipped centers are still missing in already equipped countries (mainly EU)

# Radionuclides

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# Radionuclides: a kind of ‘natural’ selection

| | | |
|---|---|---|
| 1950’s | Reactor radionuclides: $^{131}$I, $^{32}$P, $^{125}$I , … | Only $^{131}$I survived (thyroid) |
| 1960’s | SPECT $^{99}$Mo/$^{99m}$Tc generator | Still cheapest RN with the largest number of applications |
| 1980’s | First ‘exotic’ radionuclides: $^{89}$Sr, $^{153}$Sm, $^{166}$Ho, $^{169}$Er, $^{188}$Re, … | Limited by chemistry<br>$^{90}$Y and $^{188}$Re interesting decay |
| 1990’s | Small cyclotron: $^{18}$F, $^{124}$I<br>Large cyclotron: $^{123}$I, $^{111}$In, $^{67}$Ga | $^{90}$Y replacing $^{131}$I in RIT R&D |
| 2000’s | New reactor RN’s: $^{177}$Lu<br>$^{89}$Zr - New generators: $^{68}$Ga | $^{177}$Lu replacing $^{90}$Y in R&D<br>$^{99}$Mo shortage issue (solved) |
| 2010’s | $^{64}$Cu and $^{67}$Cu<br>Interest in alphatherapy | All new drugs developed with *nca* $^{177}$Lu<br>Priority given to $^{225}$Ac, $^{211}$At (and $^{212}$Pb) |

Manufacturing capacity (ww) is the limiting factor

# Radionuclide production: Economic considerations

- Value of the PET network ($^{18}$F - half-life 2 hours)
  - France or Germany (homogeneous population): hypothesis 5 centers - 5M€ in average: € 25 M
  - Extrapolation to Europe x 450/70 = € 160M
  - North American market:  approx. same size => World > € 400M
  - $^{124}$I or $^{89}$Zr: about 7M€ /site but only 2-4 required worldwide: € 15-25M

    Exception short half life ($^{123}$I): >10 sites worldwide = >> € 150M
- Reactor: investment of €500M -> €1,000M, but …
- Extension of an existing SPECT or therapy site (e.g. $^{177}$Lu)
  - Estimated 3-5M€/site (2-4 required worldwide): € 10-20M
- Accelerators (production of $^{225}$Ac or $^{67}$Cu): € 40-60M (per site – 2+ sites needed)



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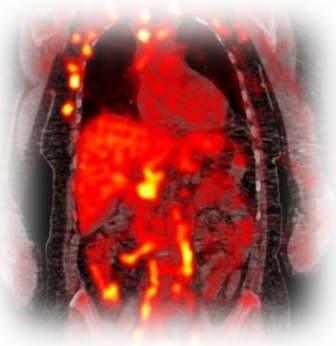
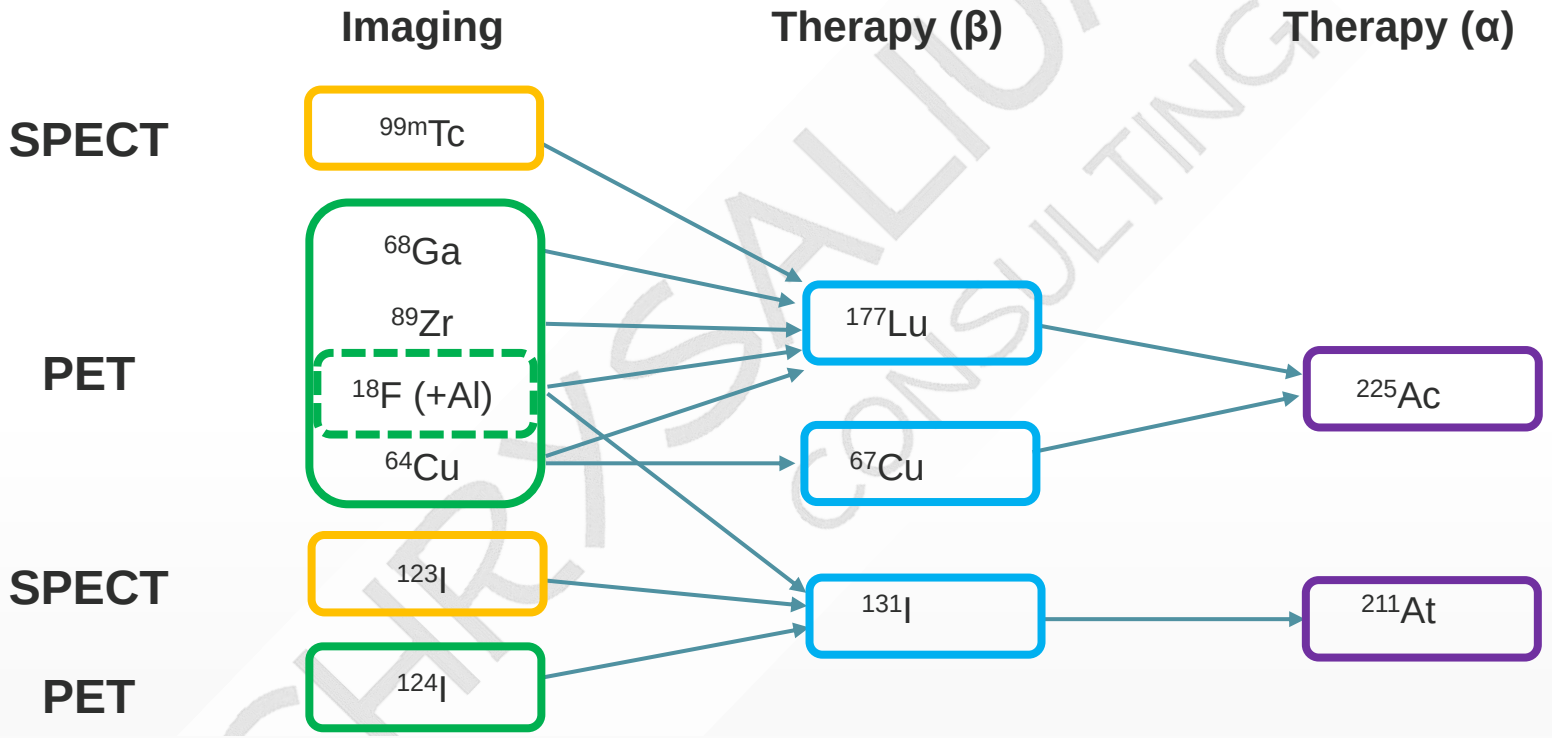
# Lutetium-177



- Two qualities of the radionuclide available
  - Carrier added from direct irradiation of $^{176}$Lu, i.e. low specific activity - contains $^{177m}$Lu (160 d)
  - Non-carrier added from irradiation of $^{176}$Yb and decay of resulting $^{177}$Yb, high specific activity
- Since January 2018, first $^{177}$Lu-drug on the market: $^{177}$Lu-Lutathera (Novartis/AAA) - *ca* Lu
- 17+ $^{177}$Lu-drugs presently under clinical development and 30+ under preclinical stage
- All of them labeled with the non-carrier added form
- 100,000 patients @ 3x 200 mCi dose/year = 60 kCi/y

(200 mCi = EOB, => i.e. 100 mCi in average @ calibration)

# Chemistry driven development



# Radionuclide selection (2020-2026)

**For the next 8 to 10 years, RPs will be based on the following radionuclides**

PET radionuclides

$^{18}F$ , $^{68}Ga$, $^{89}Zr$ and $^{64}Cu$: directly or indirectly cyclotron produced

SPECT radionuclides

$^{99m}Tc$: reactor/generator ($^{99}Mo$)

$^{123}I$: cyclotron (interest declining)

Therapy

$^{177}Lu$ and $^{131}I$ : reactor

$^{211}At$ and $^{225}Ac$ : cyclotron

$^{212}Pb$ : decay product

$^{117m}Sn$ : accelerator

Outsiders (for research purpose)… if….:

$^{67}Cu$, $^{43}Sc/^{44}Sc/^{47}Sc$,

$^{149}Tb/^{152}Tb/^{155}Tb/^{161}Tb$, $^{213}Bi$, ($^{227}Th$)

Declining interest

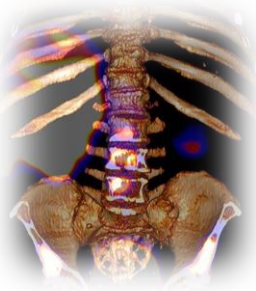
(*from industry's point of view*)

$^{11}C$, $^{124}I$

$^{67}Ga$, $^{111}In$

$^{90}Y$, $^{153}Sm$, $^{166}Ho$, $^{186}Re$, $^{188}Re$

# Message 3



**The selection of radionuclides for the next ten years is complete.**

**Be aware that we still will have to solve the shortage of**

**$^{68}$Ge - $^{225}$Ac - $^{64}$Cu - $^{67}$Cu - $^{211}$At**

# State of the art

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# Worldwide equipment - Summary

## Cameras and cyclotrons

| | USA | EU (geogr. w/o Russia) | World (2019) | World (est. 2025) |
|---|---|---|---|---|
| SPECT (est. 2019) | 12,600 | 4,540 | 25,500 | 29,000 |
| PET (est. 2019) | 2,350 | 1,020 | 6,700 | 8,600 |
| Cyclotrons (est. 2019) (<25 MeV) | 245 | 240 | 1,250 | 1,400 |
| Population (millions - 2019) | 327 | 603 | 7,800 | 8,200 |

*(*) Source: MEDraysintell (2019)*

## Trends

- SPECT: slow evolution in Asia and replacement market
- PET cameras: faster growth but due to filling gaps
- Cyclotrons:  40 new units per year (Asia mainly) - saturation of sites

## Additional issues

- Limited access to shielded rooms

# Message 4

**PET will not replace SPECT**

**MRI will not replace radiodiagnostics**

**SPECT will not disappear nor will the interest for $^{99m}$Tc fade**

**FDG will not disappear either, while bringing a new $^{18}$F-tracer on the market will remain expensive**

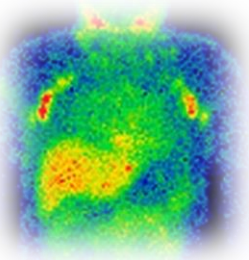
**But $^{68}$Ga (or $^{89}$Zr) will not replace $^{18}$F**

# Pipeline and Chances of Success

| | Diagnostic PET/SPECT | Radio-Therapeutic | Conventional Therapeutic |
|---|---|---|---|
| Chances of success (%) | | | |
| End of Phase II -> Market | 70-80% | 40-50% | 15-20% |
| End of Tox -> Market | 7-10% | 5-8% | 1-5% |
| Budget (M€) | | | |
| Preclinical stage | 2-6 | 2-10 | 5-20 |
| Clinical (theoretical) | 20-30 | 50-80 | 200-300 |
| Total (realistic) | 80-120 | 120-180 | 400-600 |

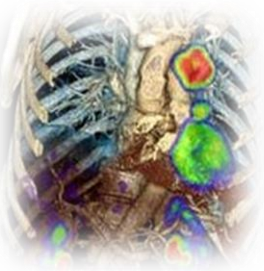
*These €€ figures do not include the failures …*
… and do not include financial costs, marketing budget and manufacturing tools investments

# Message 5



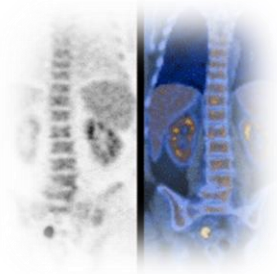
**The development costs of a drug are almost the same if the drug is developed for a limited territory or for the world market**

# Importance of the proprietary aspect



- 93% of all marketed radiopharmaceuticals are generics
  - Including all $^{99m}$Tc labeled tracers (but one) and $^{18}$F-FDG
- More than 50% of all marketed tracers/drugs are (or were) available as at least 3 generic forms
- Generics (or limited IP) include also $^{223}$Ra-Radium Chloride (Xofigo) - $^{177}$Lu-DOTATATE (Lutathera) - $^{177}$Lu-PSMA-617
- But there are possibilities to keep some advantages:
  - Technical process (chemistry, production, formulation, …)
  - Orphan drug status
  - Specific case of Antibodies (exclusive access to the master cell bank)

# Message 6



**Nowadays, no serious investor will bring money for developing generics**

WRONG

**Cf:**

**Telix Pharma**

**Point BioPharma**

# Messages 7 and 8

**Conventional pharmaceutical industry is absolutely not interested in diagnostics**

**The radiopharma industry (RPI) never really had the funds to develop RPs but will continue controlling diagnostics.**

**RPI will also act as CMOs for big pharmas.**

# Radiopharmaceuticals

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# Big Pharmas become interested (in therapy)

## Serious interest

- Bayer Healthcare
- Hoffmann La Roche 2
- Ipsen Pharma
- Johnson & Johnson 1
- Novartis 3
- Sanofi 7

Total M&A in NM > € 17B
(2014-2021)
> 2.5 B (2020-2021)

## R&D program

- Astellas
- Astra Zeneca 11
- Bristol Myers Squibb 9
- Eisai
- Eli Lilly 13
- Genentech
- Janssen Biotech
- Lundbeck
- Merck & Co 4
- Merck
- Merieux
- Pfizer 8

## Wait & Watch

- Boehringer Ingelheim
- Guerbet
- GSK 5
- Otsuka
- Wyeth

*Non-exhaustive list*
***1-15**: Ranking based on revenues 2020*

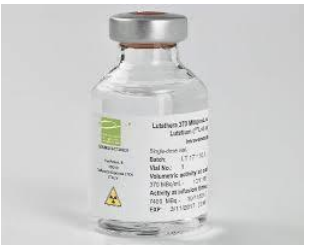
# $^{223}$Ra-Radium Chloride (Xofigo®)


**Bayer's $^{223}$Ra-Xofigo (ex Alpharadin) was supposed to become a blockbuster**

- Indication: treatment of patients with castration-resistant prostate cancer (CRPC), symptomatic bone metastases and no known visceral metastatic disease
- Not only pain palliation, improved life expectancy from 11.3 to 14.9 months
- Price: in the US $ 69K, about € 40K in EU, for a treatment of 6 consecutive injections of 0.1 µCi of $^{223}$Ra
- Sales:

| EUR million | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|---|---|---|---|---|---|---|---|---|
| Xofigo | 41 | 157 | 257 | 331 | 408 | 351 | 303 | 262 |

# $^{177}$Lu-Oxodotreotide (Lutathera)



**Molecule acquired by Novartis in September 2017 - Launched January 2018**

- Indication: treatment of patients with gastro-entero pancreatic neuroendocrine tumors
- Price: in the US, $ 47,500 per dose (full treatment corresponds to 4 consecutive injections of 200 mCi of $^{177}$Lu-labeled drug
- Sales:

| USD million | 2018 | 2019 | 2020 | Q1-2020 |
|---|---|---|---|---|
| Lutathera | 167 | 441 | 445 | (122) |

- **Competition: $^{177}$Lu-PNT2003 (2021+)**

# Somatostatin analogues under development

**33 still active/54**

| | Marketed tracers/drugs | | Clinical development | | Preclinical stage | |
|---|---|---|---|---|---|---|
| Diagnosis | ▪ $^{68}$Ga-DOTATATE<br>▪ $^{68}$Ga-DOTATOC<br>▪ $^{99m}$Tc-EDDA/HYNIC-TOC<br>▪ $^{99m}$Tc-Octreotate<br>▪ $^{111}$In-Pentetreotide | **5** | ▪ $^{67}$Ga-DOTATOC<br>▪ $^{68}$Ga-NODATOC<br>-DOTANOC<br>-HA-DOTATATE<br>-IPN-01070<br>▪ $^{64}$Cu-DOTATATE<br>-SARTATE | **7** | ▪ $^{18}$F-AMBF$_3$-TATE<br>▪ $^{68}$Ga-AM3<br>-EB-TATE<br>-NODAGA-E[c(RGDyK)]$_2$<br>-NODAGA-LM3<br>-SOMA-PK-Dx | **6** |
| Therapy | ▪ $^{177}$Lu-DOTATATE | **1** | ▪ $^{67}$Cu-SARTATE<br>▪ $^{177}$Lu-DOTA-EB-TATE<br>-HA-DOTATATE/PNT2003<br>-DOTATOC<br>-IPN-01072<br>▪ $^{188}$Re-P2045<br>▪ $^{212}$Pb-Ar-RMX | **7** | ▪ $^{67}$Cu-DOTATATE<br>▪ $^{177}$Lu-SOMA-PK-Rx<br>▪ $^{212}$Pb-DOTAMTATE<br>▪ $^{213}$Bi-DOTATATE<br>-DOTATOC<br>▪ $^{225}$Ac-DOTATATE<br>-DOTATOC | **7** |

***Tracer/drugs on hold:***
Diagnostics (9):
Therapeutics (12): **21**

*Non-exhaustive list*

# $^{177}$Lu-PSMA-617 ($^{177}$Lu-Vipivotide)

## Heidelberg University / ABX / Endocyte / Novartis

- **Mechanism**:  anti-PSMA peptide
- **Indications**: metastazed prostate cancer therapy
- **Imaging agent**: $^{68}$Ga-PSMA-11 (Illucix/Illumet)
- **Status**: Phase III completed – NDA filed
- **Expected launch**: 2021+
- **Comments:** partial IP protection > 2030 (some side-effects)
- **Very high potential competition -> $^{177}$Lu-PNT2002**

# PSMA targeting drugs under development

**65 PSMA target/88**
*+27 on hold*

| | Close to market | | Clinical development | | Preclinical stage | |
|---|---|---|---|---|---|---|
| Diagnosis | ▪ $^{68}$Ga-PSMA-11 (*illumet/illuccix*)<br>▪ $^{68}$Ga-THP-PSMA (*Galliprost*)<br>▪ $^{18}$F-DCFPyL | **3** | ▪ $^{99m}$Tc-EC0652, iPSMA, MIP-1404<br>▪ $^{18}$F-CTT1057, rh-PSMA-7, PSMA-1007, PSMA-SR6, RPS-040, RPS-041,<br>▪ $^{68}$Ga-DOTA-FFK, PSMA-R2, PSMA$^{I\&T}$<br>▪ $^{89}$Zr-Df-IAB2M<br>▪ $^{64}$Cu-PSMA-617<br>▪ $^{44}$Sc-PSMA-617 | **15** | ▪ $^{18}$F- AlF-PSMA-11, FC303, HTK01069, HTK01070, HTK01130, JK-PSMA-7<br>▪ $^{68}$Ga-IRDye800CW, P16-093, NOTA-PSMA-BCH,PSMA-PK-Dx<br>▪ $^{64}$Cu-PSMA-ALB-89, PSMA-CC-34, PSMA-BCH-ZL, SarbisPSMA, CA-003, CB-TE2A-FFK<br>▪ $^{111}$In-DOTA-5D3<br>▪ $^{203}$Pb-CA012 | **18** |
| Therapy | ▪ $^{177}$Lu-PSMA-617<br>▪ $^{177}$Lu-TLX591<br>▪ $^{177}$Lu-PNT2002 | **3** | ▪ $^{131}$I-MIP-1095<br>▪ $^{177}$Lu-CTT1403, PSMA-Ab06, PSMA-R2, PSMA$^{I\&T}$<br>▪ $^{225}$Ac-PSMA-617, TLX592 | **7** | ▪ $^{90}$Y-DOTA-EB-MCG, PSMA-617<br>▪ $^{131}$I-RPS-027<br>▪ $^{161}$Tb-PSMA-617<br>▪ $^{177}$Lu-EB-PSMA-617, FC-705, hu11B6, iPSMA, RPS-063, PSMA-ALB-56, PSMA-CC-34, RPS-072, PSMA-PK-Rx, FC315<br>▪ $^{213}$Bi-PSMA-617<br>▪ $^{225}$Ac-hu11B6, RPS-074, TLX591<br>▪ $^{227}$Th-PSMA-TTC | **19** |

***Other approaches:***
Diagnostics (20): Androgen receptors (1), Bombesin/GRPR (11), Lipid metabolism (2), PARP (1), PAT (1), PSCA (1), STEAP1 (1), TAG72 (1), VPAC1(1)
Therapeutics (3): Biphosphonate (1), Bombesin/GRPR (2)

**23**

*Non-exhaustive list*

# PSMA target development approach

PSMA: Prostate Specific Membrane Antigen = GCPII: Glutamate Carboxypeptidase II

PSMA = FOLH1 = FGCP = FOLH = GCP2 = GCPII = NAALAD1 = NAALAdase = mGCP = folate hydrolase

**Potential indications of interest**: CCRC, bladder, adenocarcinoma, NET, GBM, melanoma, pancreas carcinoma, NSCL, soft tissue sarcoma, breast carcinoma

# Message 9

**In a same indication, there is no real sense to develop more than 3 to 5 similar molecules.**

**“Me-too” and “Me-too+” are second options**

**A new proprietary approach must show real advantages and then will displace the existing marketed drug**

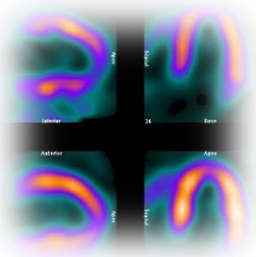
# New Radiotherapeutics under development (2021-2026)

| | |
|---|---|
| **Brain cancers** | $^{131}$I-TLX101 (2024), $^{131}$I-Burtomab and $^{131}$I-Naxitamab (2025), $^{177}$Lu-FF-10158 (2026) |
| **Breast cancer** | $^{131}$I-CAM-H2 (2025), $^{177}$Lu-HP2 (2026), $^{177}$Lu-NM600 (2027), $^{211}$At-ABY-025 (2027) |
| **NET** | $^{177}$Lu-Solucin (2023), $^{177}$Lu-Satoreotide (2024), $^{67}$Cu-Sartate (2026), $^{177}$Lu-DOTA-EB-TATE (2026) $^{212}$Pb-DOTAMTATE, $^{177}$Lu-PNT2003 (2021) |
| **Pancreas** | $^{177}$Lu-IPN-01087 (2024), $^{177}$Lu-MVT-1075 (2026), $^{212}$Pb-AR-RMX (2027) |
| **Kidney cancer** | $^{177}$Lu-TLX250 (2023) |
| **Prostate cancer** | $^{177}$Lu$^{225}$Ac-PSMA-617 (2021/2025), $^{177}$Lu/$^{225}$Ac-TLX591 (2022/2026), $^{177}$Lu-CTT-1403 (2025), $^{177}$Lu-NeoBomb1, $^{177}$Lu-PSMA-R2 (2024), $^{177}$Lu-ZDA (2025), $^{177}$Lu-RM2 (2026), $^{177}$Lu-EB-PSMA-617 $^{177}$Lu-PNT2002 (2023) |
| **Solid tumors** | $^{177}$Lu-DOTAZOL (2024), $^{177}$Lu-Pentixather (2025), $^{225}$Ac-FPI-1434 (2025), $^{131}$I-Metuximab (2020) |
| **NHL** | $^{177}$Lu-Lilotomab - $^{177}$Lu-Humalutin (2022/2024), $^{227}$Th-BAY1862864 (2026) |
| **Blood cancers** | $^{213}$Bi-Lintuzumab/Bismab-A and $^{131}$I-Apamistamab/Iomab-B (2023/2021), $^{131}$I-CLR-131 (2025) |
| **Polyarthritis** | $^{117m}$Sn-Synovetin (2024) |

*Additional research approaches: vulnerable plaque, infection, HIV, …*

*Source: MEDraysintell 2021*

# How about Cardiology ?



**Marketed tracers (20):**

- MPI SPECT (7): $^{99m}$Tc-Sestamibi – $^{99m}$Tc-Tetrofosmin – $^{201}$Tl-Thallous chloride – $^{99m}$Tc Pertechnetate – $^{99m}$Tc-Pyrophospate etc … **and generics**
- MPI PET (4): $^{13}$N-Ammonia, $^{15}$O-Water, $^{18}$F-FDG, $^{82}$Rb-Rubidium - **all generics**
- Miscellaneous (9): blood volume, DPT, blood cell labeling ($^{51}$Cr, $^{99m}$Tc, $^{111}$In and $^{123}$I derivatives) – **all generics**

**Tracers under clinical development (5):**

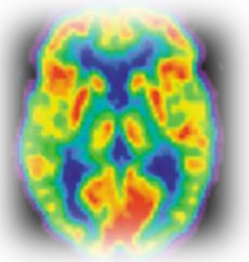
- MPI and CHF (3): $^{18}$F-Flurpiridaz
- Vulnerable plaque (2)

**Tracers under preclinical development (16)**

- MPI and CHF (3)
- Vulnerable plaque (9)
- Miscellaneous (4) : pulmonary embolism, thrombi detection, adrenergic receptor imaging

*Non-exhaustive list*

# How about Neurology ?



**Marketed tracers (19):**

- Brain perfusion SPECT (7): $^{99m}$Tc-derivatives (5), $^{123}$I-Iofetamine  etc … **all generics**
- Brain perfusion PET (2): $^{13}$N-Ammonia, $^{15}$O-Water - **all generics**
- AD (4): $^{18}$F-Florbetaben, $^{18}$F-Florbetapir, $^{18}$F-Flutemetamol, $^{18}$F-Florapronol – **all proprietary –** all plaque imaging
- Parkinson's Disease (5): $^{99m}$Tc-TRODAT, $^{123}$I-Iofetamine, $^{123}$I-Ioflupane, $^{18}$F-FDOPA, $^{18}$F-FPCIT – **all generics**
- Miscellaneous (1): Stroke imaging, epilepsy ($^{99m}$Tc and $^{123}$I derivatives) – **all generics** (also used in brain perfusion)

**Tracers under clinical development (35):**

- AD (23) - Amyloid plaque imaging (2): [$^{18}$F-Flutafuranol, $^{18}$F-Amylovis] -  Tau/tangles imaging (7) [$^{18}$F-Flortaucipir] - miscellaneous (14) : PSBO/PBR
- PD (5): $^{123}$I-Altropane
- Miscellaneous (7)

**Tracers under preclinical development (23)** - not counting pharmacological tools

- AD (14): and 12 on hold
- PD (2): and 4 on hold
- Miscellaneous (7): and 3 on hold

*Non-exhaustive list*

# Thinking out of the box

- **Rheumatoid arthritis**: $^{99m}$Tc-Maraciclamide, $^{99m}$Tc-Chondroitin Sulphate, $^{18}$F-FEDAC, $^{68}$Ga-DOTA-Siglec-9
- **Infectiology**:
  - **Inflammation/Infection**: $^{18}$F-Clofarabine, $^{68}$Ga-DOTA-TBIA10, $^{68}$Ga-NOTA-UBI29-41, $^{99m}$Tc-Ubiquicidine (marketed)
  - **Tuberculosis**: $^{68}$Ga-Tilmanocept
  - **Chronic lung disease**: $^{99m}$Tc-Ciprofloxacin, $^{99m}$Tc-Infliximab, $^{18}$F-FIAU
  - **Cardiac device implantation**: $^{18}$F-Fluoro-Maltohexaose, $^{18}$F-Fluoro-Maltotriose
  - **COVID**: $^{131}$I-CR3022, $^{99m}$Tc/$^{177}$Lu-EC-Amifostine, $^{64}$Cu-NOTA-hACE2
- **AIDS** : $^{64}$Cu-3BNC117, $^{99m}$Tc-F(ab′)2-OKT4A, $^{99m}$Tc-F(ab′)2-CD4R1, $^{123}$I-BNC117
- **Diabetes imaging**: $^{18}$F-Exendin-4, $^{68}$Ga- DO3A-VS-Cys40-Exendin-4, $^{68}$Ga-NODAGA -exendin-4, $^{18}$F-MK6240
- **Veterinary Nuclear Medicine**: $^{117m}$Sn-Synovetin

*Non-exhaustive list*

# Conclusions

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# Pipeline (Therapeutics)

- Molecules under clinical development (Indications) – [May 2021]

| Indication | Prostate | NET | Solid tumors | Oncology (others) [15 indications] | Non-oncology | Total |
|---|---|---|---|---|---|---|
| Number | 18 | 9 | 7 | 26 | 2 | 62 |

- Molecules under clinical development (Radionuclides)

| RN | Lu-177 | Y-90 | I-131 | Ac-225 | Sn-117 | Cu-67 | Th-227 | Pb-212 | Bi-213 | Others: Tb, Re, Ra | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Number | 23 | 9 | 8 | 7 | 2 | 2 | 2 | 2 | 2 | 5 | 62 |

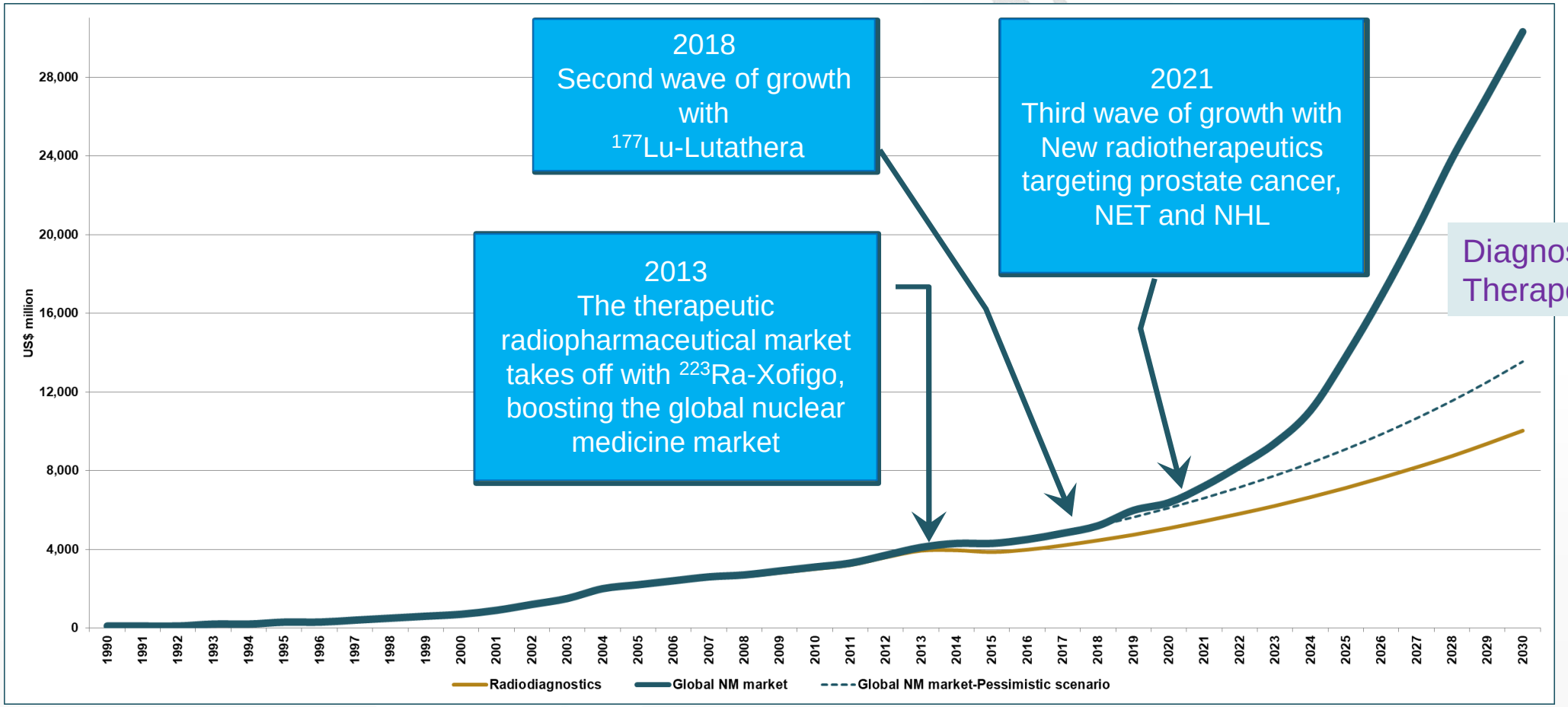
- 6 of them have entered Phase III trial – all of them labeled with $^{177}$Lu
- Number of $^{177}$Lu labeled drugs under advanced preclinical development: 22

# Intense M&A activities

| Date | Event |
|---|---|
| **January 2021** | **Blue Earth/Bracco** buys therapeutic rights to rhPSMA technology from **Scintomics** |
| **January 2021** | **Fuzionaire Radioisotope Tech.** (FRIT) and **Nihon Medi-Physics** (NMP) are teaming up to create a new class of PET RPs. |
| **February 2021** | **Aikido Pharma** invests in **Convergent Therapeutics** for supporting the development of a RP for treating prostate cancer |
| **February 2021** | European Commission okays **Siemens** acquisition of **Varian** |
| **March 2021** | **Lantheus** acquires rights for NTI-1309 (FAP) from **Noria Therapeutics** |
| **March 2021** | **Novartis** acquires exclusive ww rights to develop therapeutics on the basis of a FAP library including FAP-46 and FAP-74 |
| **March 2021** | **Aktis Oncology** announces $72m series a financing to advance breakthrough alpha labeled RPs to treat solid tumors |
| **March 2021** | **Viewpoint Molecular** Targeting signs an agreement with SpectronRx for scaling-up of its $^{224}Ra/^{212}Pb$ generator VMT-α-GEN |
| **April 2021** | **Fusion Pharmaceuticals** acquires the intellectual property and assets related to French firm **Ipsen's** IPN-1087 RP |
| **April 2021** | **EZAG** acquires majority stake in radiopharmaceutical drug developer **Pentixapharm** |
| **May 2021** | **Alpha-9 Theranostics Inc**. announces an $11 million Series A financing |
| **May 2021** | **GEH** acquires the French company **Zionexa** |

# The Nuclear Medicine (RPs) market 1990-2030 (*ww*)

Innovation triggering impressive growth




Diagnostic up 7%/y
Therapeutics up 32%/y

*Source: MEDraysintell 2019*



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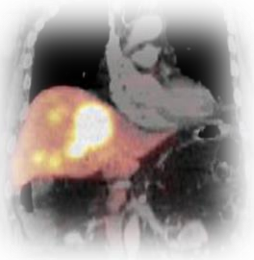
| SPECT | PET | Radiotherapeutics |
|---|---|---|
| **Global Market** | | |
| The global radiopharmaceutical market is expected to reach US$ 30 billion by 2030, showing an annual average growth of 16% from 2020 to 2030. | | |
| The diagnostic radiopharmaceutical market is expected to grow, on average, by 7% a year, mainly driven by volume with limited impact from new tracers. | | The therapeutic radiopharmaceutical market is expected to grow by 32% annually from 2020 to 2030. |
| **Competition** | | |
| There are 77 companies showing revenue in today's nuclear medicine market (sales of radiopharmaceuticals). | | |
| Over 130 companies are currently involved in the development of at least one new radiopharmaceutical. | | |

# Message 10 and conclusion



**There is a bright future for nuclear medicine (and for nuclear physicians and radiopharmacists), mainly driven by radiotheranostics…**

**… if everyone accepts to adapt to the main changes.**

**All based on the natural selection rule: adapt or die**

# Thanks for your attention

www.oncidiumfoundation.org
www.medraysintell.com
www.morphopharma.com