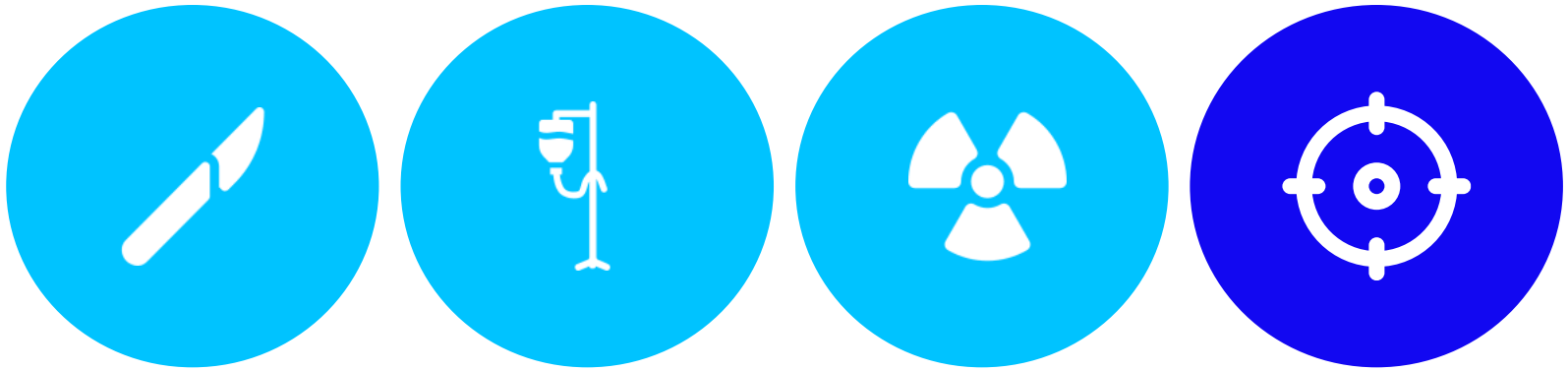
PRECIRIX

precision radiopharmaceuticals

Targeted therapies have revolutionized oncology

Then

Now



150+

approvals in 28 types of cancer since 1997

Frontiers in Pharmacology

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Evolution of targeted therapies for cancer

1990 — 2000 — 2010 — 2020 → Market value by 2025

Immune Checkpoint Inhibitors

3. pembrolizumab (Keytruda), 2014
2. nivolumab (Opdivo), 2014
1. ipilimumab (Yervoy), 2011

$56 B

Small Molecules Inhibitors

3. erlotinib (Tarceva), 2004
2. gefitinib (Iressa), 2001
1. imatinib (Gleevec), 2001

$66 B

Monoclonal Antibodies

3. cetuximab (Erbitux), 2004
2. trastuzumab (Herceptin), 1998
1. rituximab (Rituxan), 1997

$71 B

Allied Market Research, Globe Newswire, Market Data Forecast

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Welcome to

Precision Radiopharmaceuticals

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precision radiopharmaceuticals

EUR 37m Series A in 2018
EUR 80m Series B in 2022

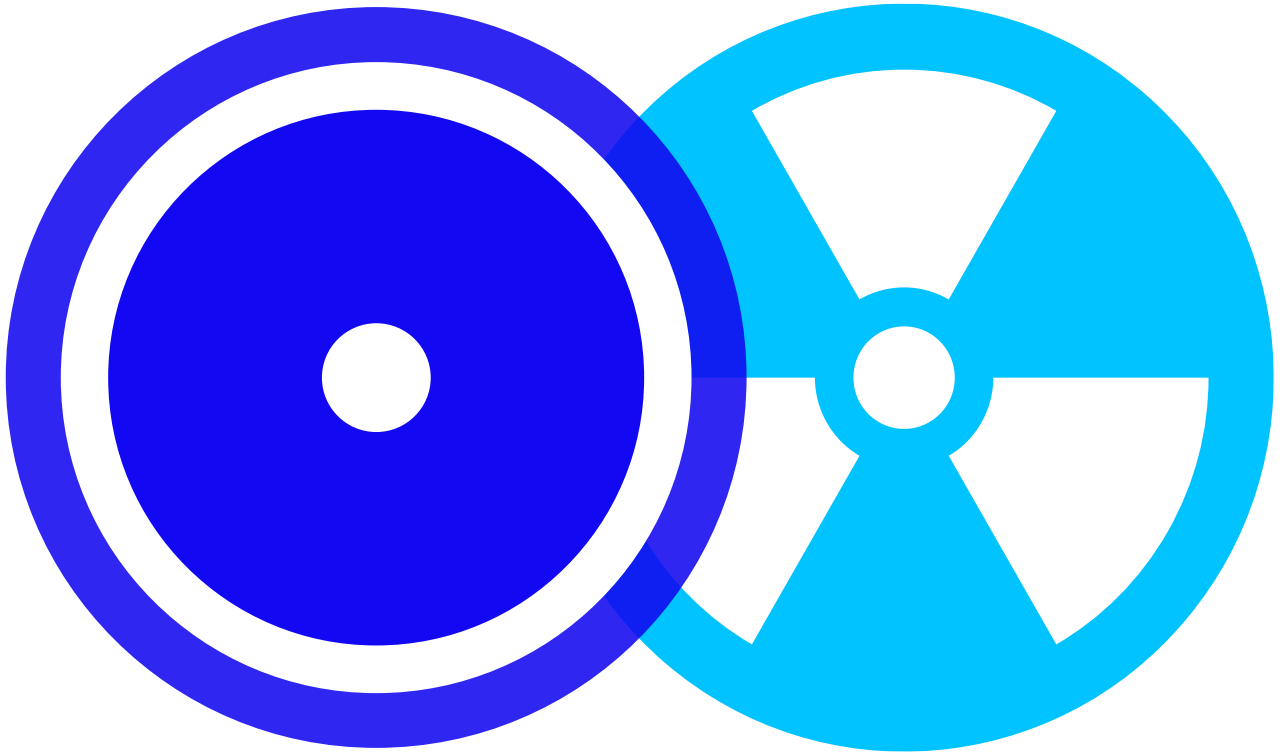
Clinical-stage oncology company developing precision radiopharmaceuticals

Rich preclinical pipeline and discovery platform

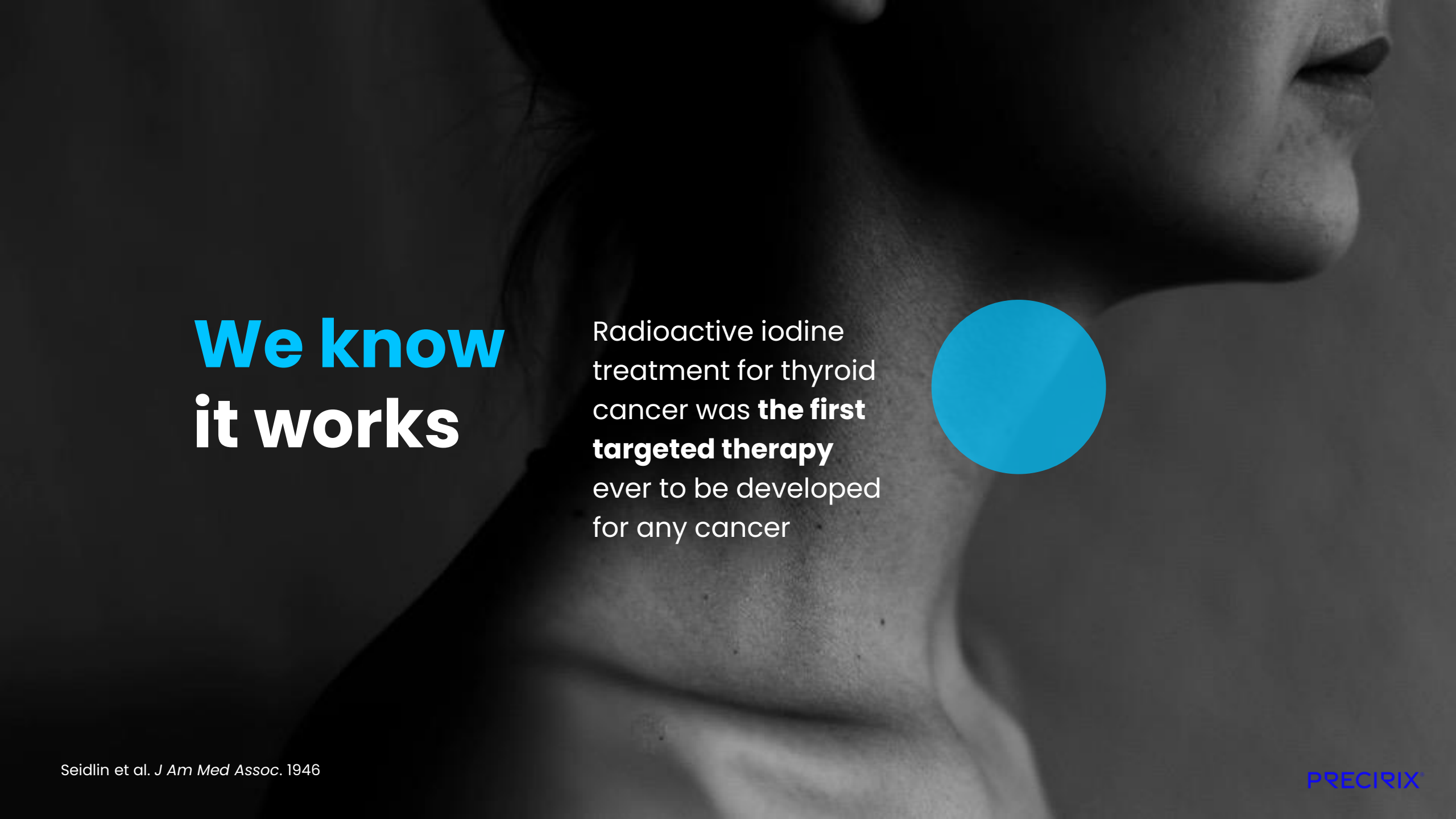
IND approved Phase I/II ongoing with lead compound CAM-H2 targeting HER2-positive metastatic breast & gastric cancer with or without brain metastases

Precirix precision radiopharmaceuticals

single domain Ab



radioisotope



We know it works

Radioactive iodine treatment for thyroid cancer was **the first targeted therapy** ever to be developed for any cancer

Seidlin et al. *J Am Med Assoc*. 1946

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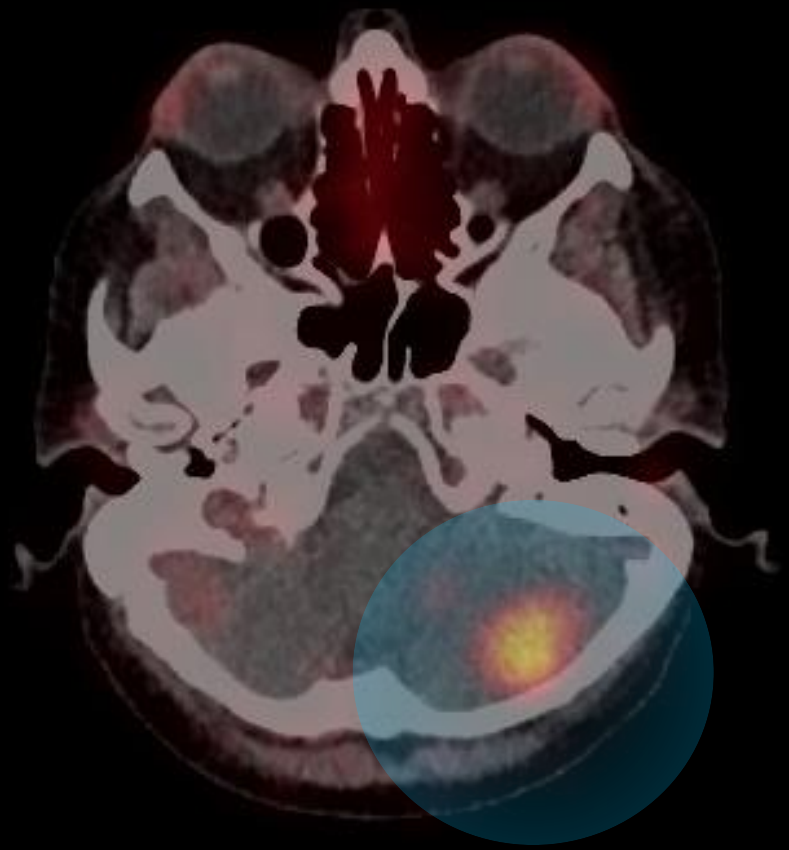

NCT03331601 (Keyaerts et al. UZ Brussel, VUB)

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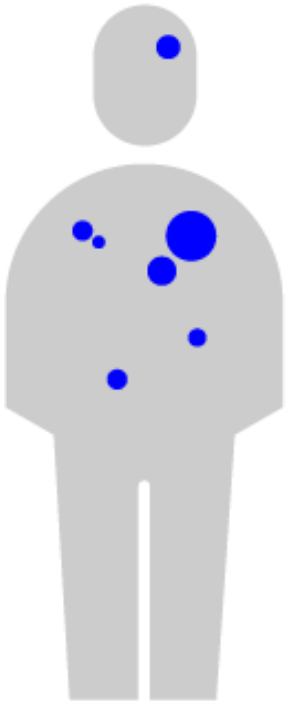
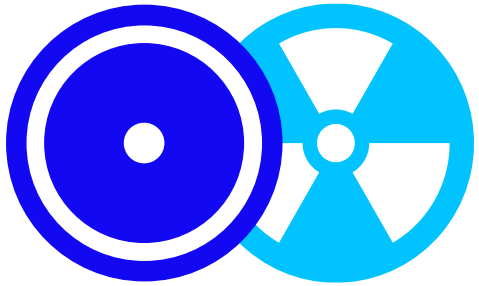
It’s a **platform**

Unique





Radioisotope kills through DNA breaks

Direct cell killing and bystander effects

Single domain antibody targets the cancer

On target in minutes after IV infusion anywhere in the body

Deep tumor penetration and prolonged tumor retention

Rapid renal clearance of unbound product

Flexible

Multiple targets

cancer cells
specific epitopes
tumor microenvironment

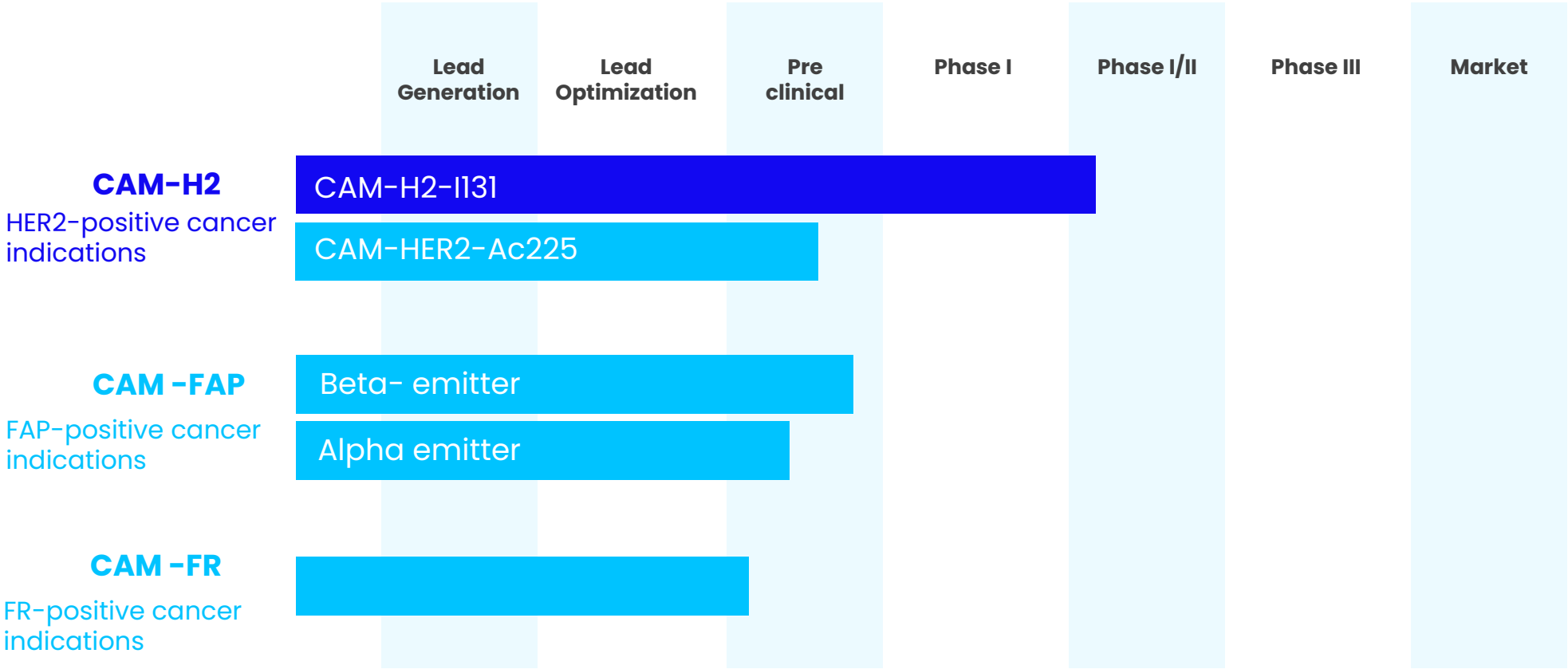
Different isotopes

alpha emitters
beta emitters

Various applications

therapeutic
patient selection
combination therapy

Broad



H2: HER2; **FAP**: Fibroblast Activation Protein: **FR**: Folate Receptor Alpha

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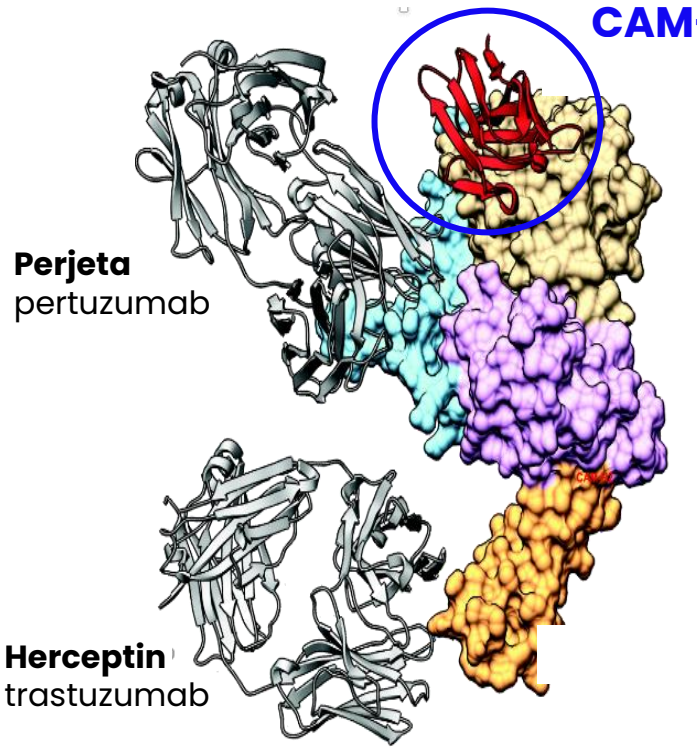
It’s
real

HER2

CAM-H2 clinical candidate



Resistance to HER2 therapy is an issue for approved drugs, CAM-H2 targets a different epitope and brings a new mechanism of action

Intra-tumoral HER2 heterogeneity is associated with poor survival, CAM-H2 has crossfire effect that can target heterogeneous HER2-positive tumors

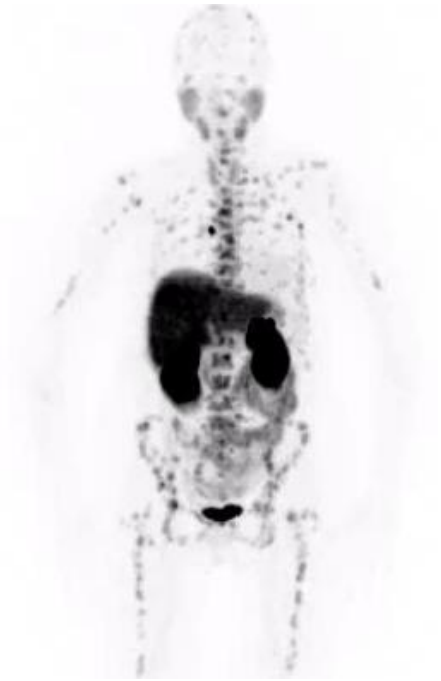
Tissue penetration is an issue for approved mAbs, CAM-H2 penetrates cancer tissues within minutes, including brain lesions

PET imaging analogue supports development

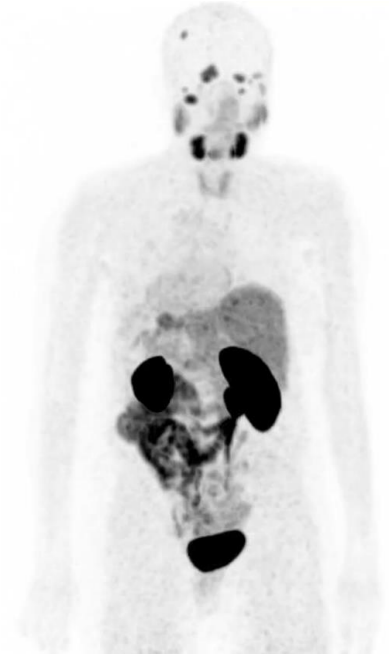
Gallium-68 labeled CAM-H2 in HER2-positive breast cancer

Primary

Metastatic



Brain



Keyaerts et al. (VUB Brussels)

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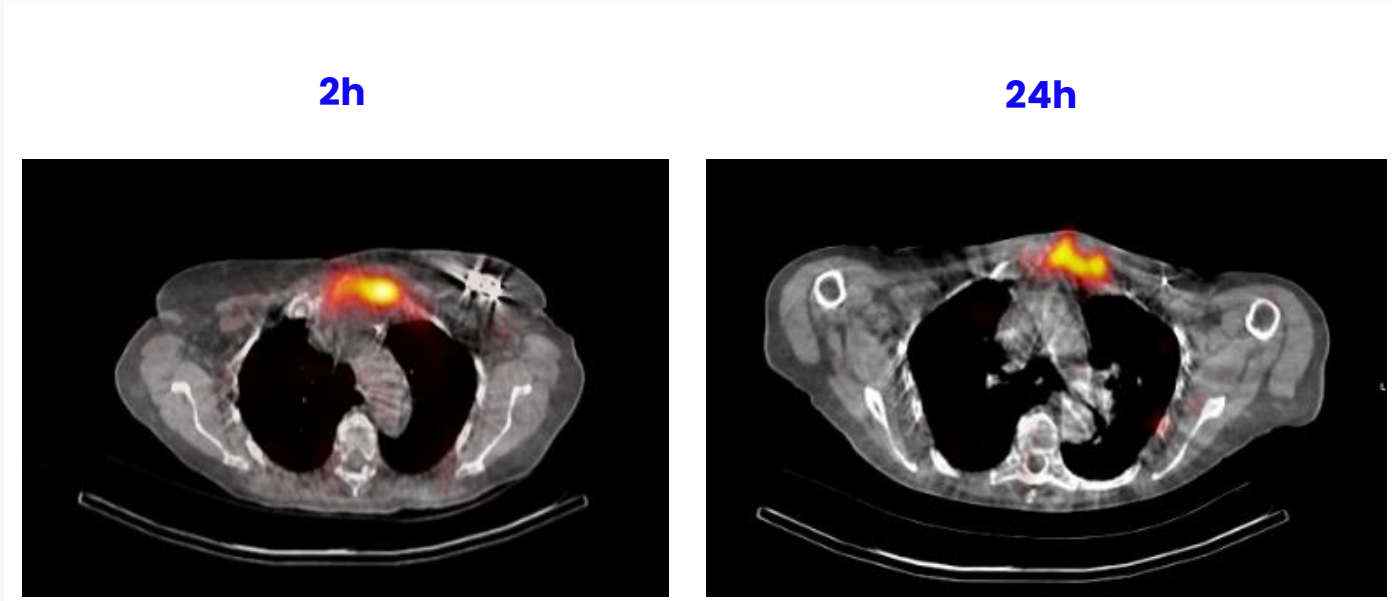
Successful Phase I study

CAM-H2-I131
6 healthy subjects, 3 patients
biomarker dose

No drug-related adverse events
Short biological half-life (7.7 hours)
Kidney is the dose-limiting organ
No accumulation in other organs
Confirmed cancer targeting



NCT02683083

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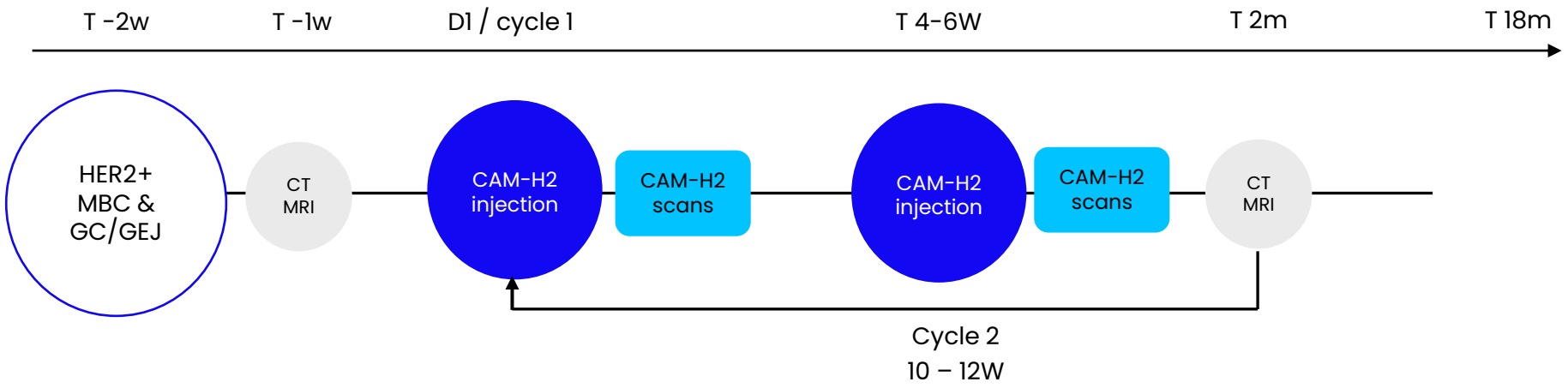
Ongoing CAM-H2 Phase I/II study



Phase I Dose Escalation Phase – Open label 3+3 design

4 cohorts = 1st cycle: 2 IV injections of 50/100/150/(200) mCi each, 4-6 wks apart

2nd cycle: 10-12 wks apart

Phase II Dose Expansion Phase

- CAM-H2 scan at tracer dose for inclusion
- n= 50 patients

NCT04467515

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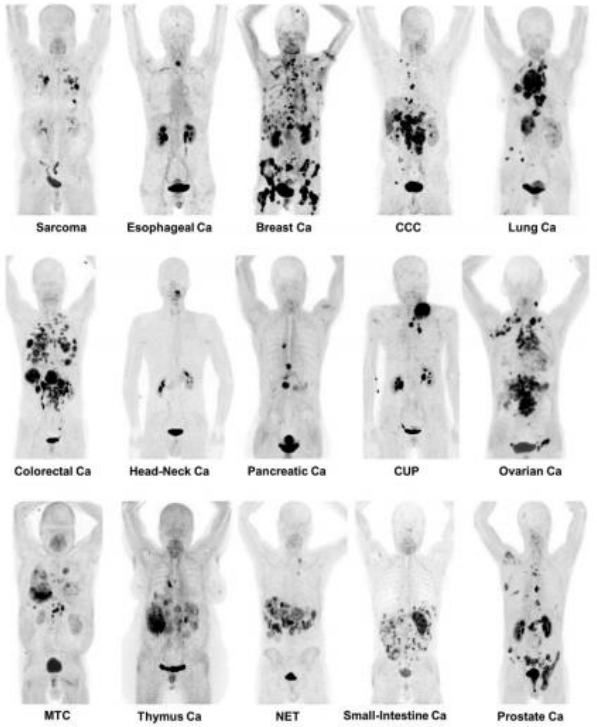
Fibroblast Activation Protein

Targeting the tumor microenvironment

- FAPα is detectable in multiple cancer types, while rarely expressed in healthy adult tissues
- Its expression on cancer-associated fibroblasts makes it an ideal candidate to target the tumor microenvironment
- Some cancer cell types also overexpress FAPα (e.g. glioma)



Kratochwil et al. *The Journal of Nuclear Medicine* 2019

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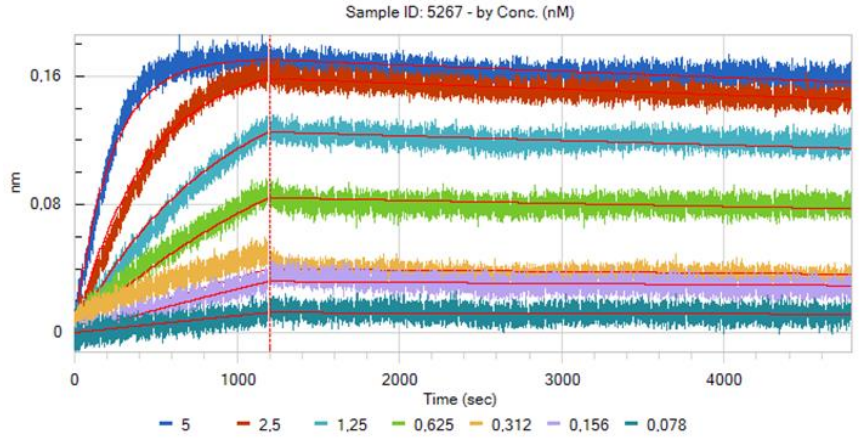
CAM-FAP – Characteristics

FAPα-targeting sdAb: CAM-FAP

- Picomolar affinity for FAPα
- Targets an epitope distinct from the enzymatic active site
- Binding does not interfere with FAPα dimerization

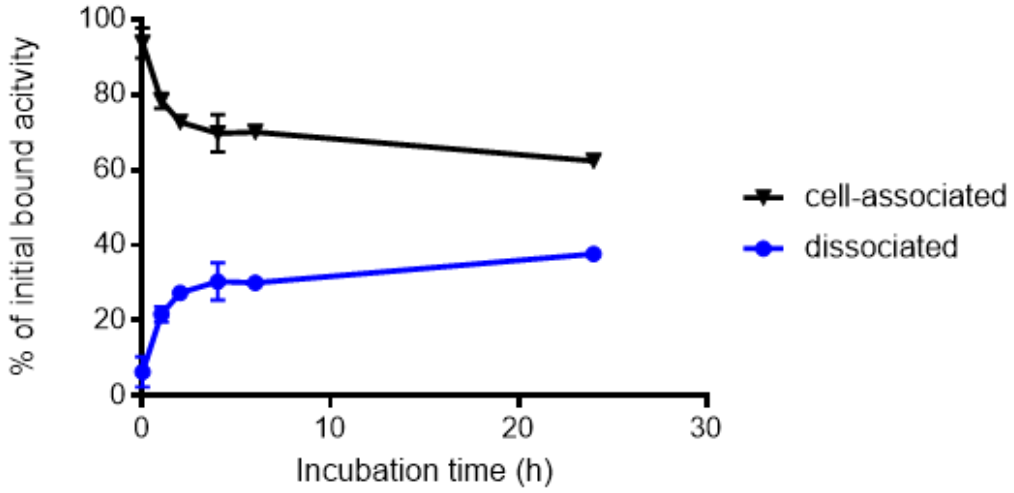
Binding on recombinant FAP



k_{on} = 8.89 10^5 $M^{-1}s^{-1}$
k_{off} = 2.41 10^{-5} s^{-1}
K_D = 27 pM

Biolayer interferometry

Binding on FAP-expressing cells



Radioactive cell binding assay

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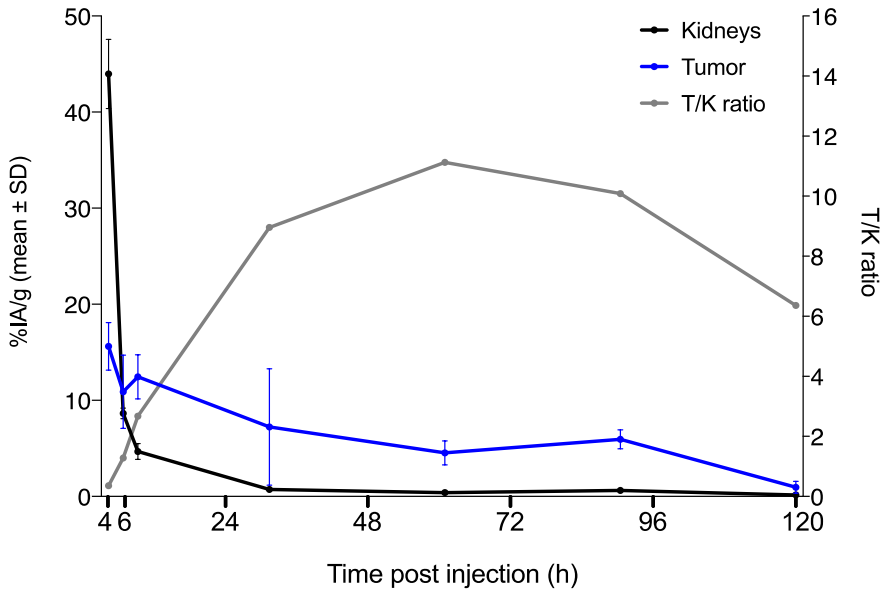
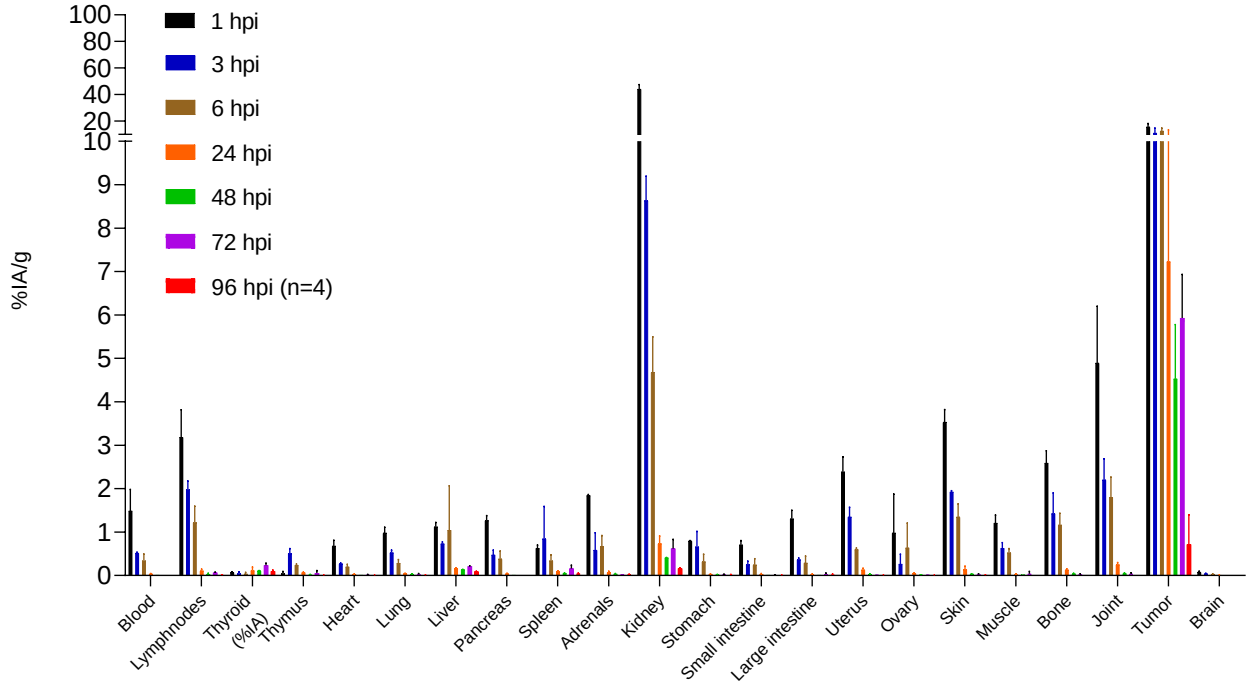
CAM-FAP – Biodistribution

- Superior T/K ratio with CAM-FAP-I-131
- Fast kidney clearance and sustained tumor retention





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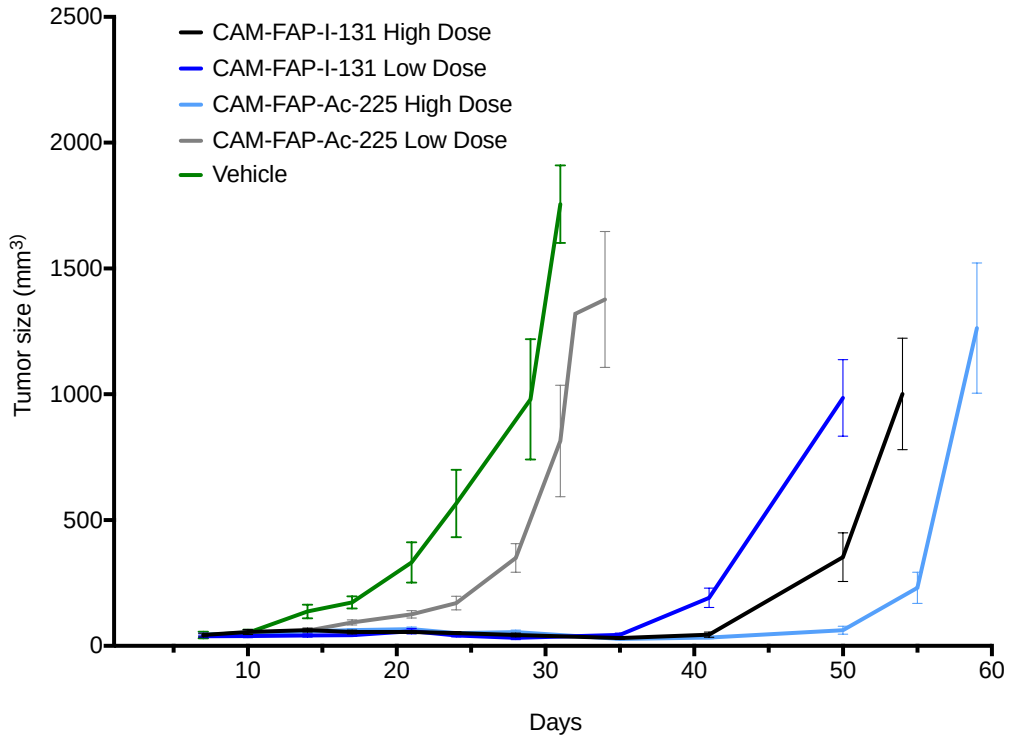
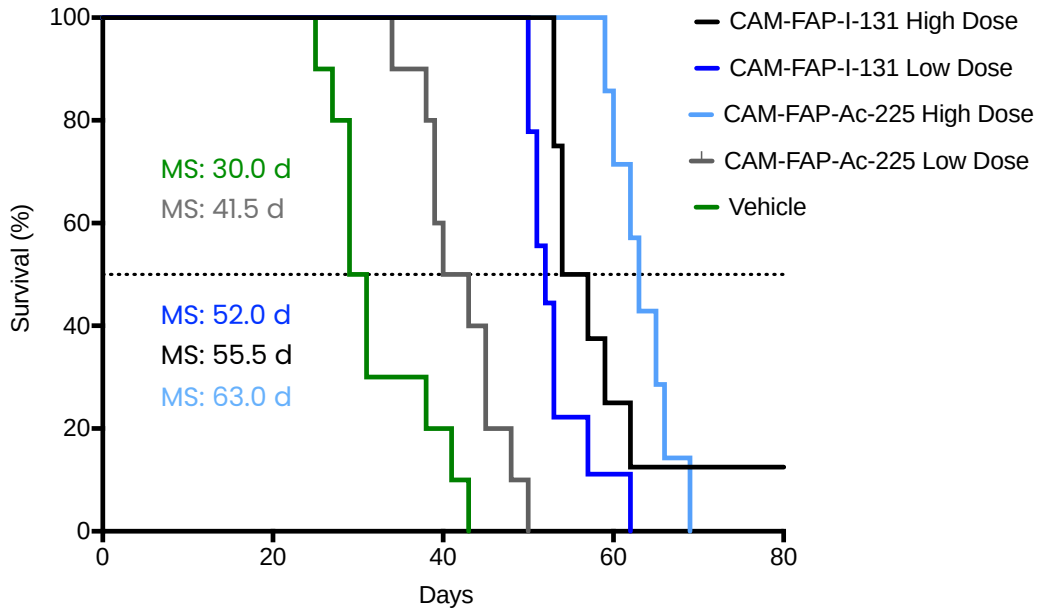
CAM-FAP – Therapeutic potential

CAM-FAP-Ac-225 and CAM-FAP-I-131 are potent in FAP⁺ U87 GM tumor xenografted mice

- Dose-dependent responses
- No signs of acute toxicity in mice





PRECIRIX®

It’s
Precirix

Leadership team

Ruth Devenyns
CEO

25+ yrs healthcare investment banking and VC

Prior Ogeda CFO until acquisition by Astellas

Master in Applied Economics

Tony Lahoutte
CSO

15+ yrs in Nuclear Med Research

Scientific Founder Precirix

MD, PhD in Nuclear Medicine

Niva Almaula
CBO

20+ yrs business development

Prior Head Business Development AAA

PhD Biochemistry and Molecular Biology

Dimitrios Mantzilas
CTO

Former Head of Radiopharmaceuticals Development Bayer

Prior Director Technology Development Algeta

Prior Tech Transfer Leader Clinical Manufacturing GE Healthcare

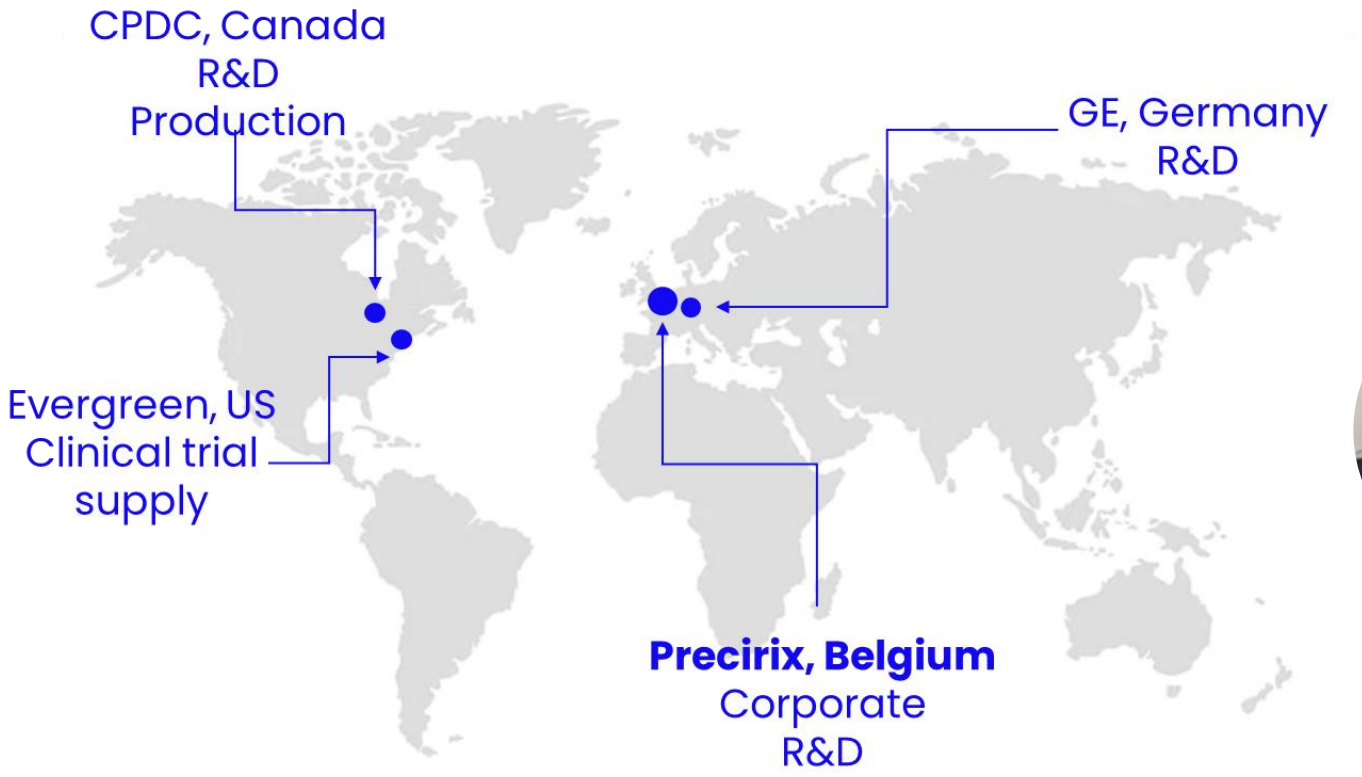
Jennifer Wheler
Consulting CMO

20+ yrs experience as oncologist

Prior associate professor MD Anderson, Clinical Program Leader Novartis and biotech CMO

Medical Oncology fellowships at MSKCC and Yale Cancer Center

Cracking the manufacturing process



2018
- 1-3 mCi yield

2019
- Established radiochemistry team
- 150 mCi yield

2020
- Contracted development partners
- 450 mCi yield

2021
- 1500 mCi yield

2022
- Process replicated to second program

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Strong in-house skills

- sdAb discovery
- Radiochemistry
- Preclinical testing
- CMC
- Clinical development
- Corporate

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IP Portfolio

HER2 – Therapy

WO 2016/016021

Protection of sdAb targeting HER2 linked to radionuclide, and its use for treatment of cancer expressing HER2

Patent granted in US

(US 9,855,348), Japan, S. Korea, Canada, Australia, Mexico, China

Patent pending in Europe, Hong Kong, Brazil.

HER2 – Theranostic

WO 2017/013026

Protection of a method wherein a sdAb targeting HER2 linked to a radionuclide is used as a theranostic (diagnostic, then therapy), for the treatment of cancer expressing HER2

Notification of allowance received in US and EU

Patent pending in China, Brazil, Mexico, S. Korea, Japan, Canada, Australia, Hong Kong.

Preclinical programs

WO 2022/053651

WO 2022/013225

Protection of sdAb as such

Protection of sdAb with any radiolabel for Dx and Rx use in any target-related cancer

Protection of sdAb in non-cancer indications

CMC

First filings in 2020-2021

Protection of methods for radiolabeling