PRECIRIX

precision radiopharmaceuticals

Company presentation
March 2024

PRECIRIX

precision radiopharmaceuticals

- Dedicated to improving the lives of cancer patients by developing novel targeted radiopharmaceuticals
- Unique platform using single domain antibodies (sdAb) as targeting ligands for radionuclides
- Ability to couple any radionuclide to a specific sdAb with theragnostic options possible
- Strong CMC expertise for both protein development and radiochemistry, using multiple radionuclides

CAM-FAP (Ac-225)

- Lead CAM-FAP program progressing towards IND readiness

CAM-H2 (I-131)

- Phase I dose escalation study completed with CAM-H2 in HER2+ metastatic breast & gastric cancer, with or without brain metastases
- Acceptable tolerability and safety demonstrated
- Targets the tumor with limited off-target organ absorption
- Opportunity to increase the dose administered based on dosimetry and clinical safety

Precirix has an experienced leadership team

International 30+ team with a comprehensive skill set

Tom Plitz
CEO

25+ yrs in biotech and pharma

Prior Leadership positions at Wilson Therapeutics, Shire Pharmaceuticals (Acquired by Takeda 2019), and Merck Group

Prior CEO of CHORD Therapeutics (acquired by Merck in 2022)

Advisory roles at RELIEF THERAPEUTICS, and Tribune Therapeutics

Dimitrios Mantzilas
CTO

20+ yrs experience in various academic and pharma R&D roles

Former Head of Radiopharmaceuticals Development Bayer

Prior Director Technology Development Algeta

Prior Tech Transfer Leader Clinical Manufacturing GE Healthcare

Josie Gayton
CDO

20+ yrs experience in various pharma R&D roles

Prior Sr VP Program Strategy, Operations and Chief of Staff at Aeglea Biotherapeutics

PhD Cancer Biology from Institute of Cancer Research in London

Board of Directors

Simon Sturge	Jasper Bos	Simone Botti	Sabine Dandiguian	Morten Graugaard Døssing	Thomas Ramdahl	Mårten Steen	Michaël Vlemmix
Chairman	Forbion	inkef capital	Jeito	novo holdings	Independent Director	HealthCap	Gimv

Precirix has a Scientific Advisory Board with world-leading experts

Jason Lewis – Chair of the SAB

Memorial Sloan Kettering Cancer Center

- Vice Chair for Research, Chief of the Radiochemistry and Imaging Sciences Service, and Director of the Radiochemistry and Molecular Imaging Probe Core Facility at MSKCC
- Published more than 200 papers, books, book chapters, and reviews on cancer imaging

Jean Pierre Pouget

Inserm

- Research Director and Team Leader of the "Radiobiology and Targeted Radiotherapy" team at INSERM (National Institute of Health and Medical Research) in France
- Published more than 60 papers and book chapters dealing with radiobiology and radionuclide therapy and several patents

George Sgouros

Johns Hopkins University

- Professor in the Johns Hopkins Medicine Department of Radiology and Radiological Science, Department of Radiation Oncology and Department of Oncology and a member of the Johns Hopkins Kimmel Cancer Center
- Author of more than 140 peer-reviewed articles on topics including targeted radionuclide therapy, radioimmunotherapy, dosimetry, pharmacokinetic modeling, and alpha-particle emitters

Razelle Kurzrock

Medical College of Wisconsin

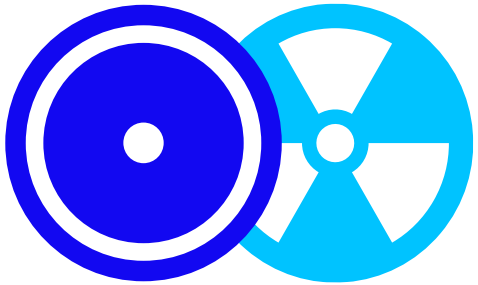
The University of Texas MD Anderson Cancer Center
Making Cancer History®

- Associate Director of Clinical Research for the Medical College of Wisconsin Cancer Center, Associate Director of Precision Oncology at the Linda T. and John A. Mellowes Center for Genomic Sciences and Precision Medicine and the founding director of the Michels Rare Cancers Research Laboratories at the MCW Cancer Center
- Recognized for founding, developing and chairing one of the largest Phase 1 clinical trial departments globally while at the University of Texas MD Anderson Cancer Center.
- Authored over 950 scientific and medical publications and has been principal investigator for more than 100 early-phase clinical trials

Gary Ulaner

hoag

- Director, Molecular Imaging and Therapy at Hoag Family Cancer Institute
- Principal investigator of prospective clinical trials for six novel PET radiotracers for patients with breast cancer, prostate cancer and myeloma. His clinical trials emphasize targeted imaging to guide targeted therapy of cancer, particularly ER, HER2, PSMA and CD38 targeted PET imaging



Precirix capabilities

SdAb generation against any relevant target
Compound maturation for GMP production at scale

Labeling procedures in tune with biologicals
Isotope and chemistry diversification

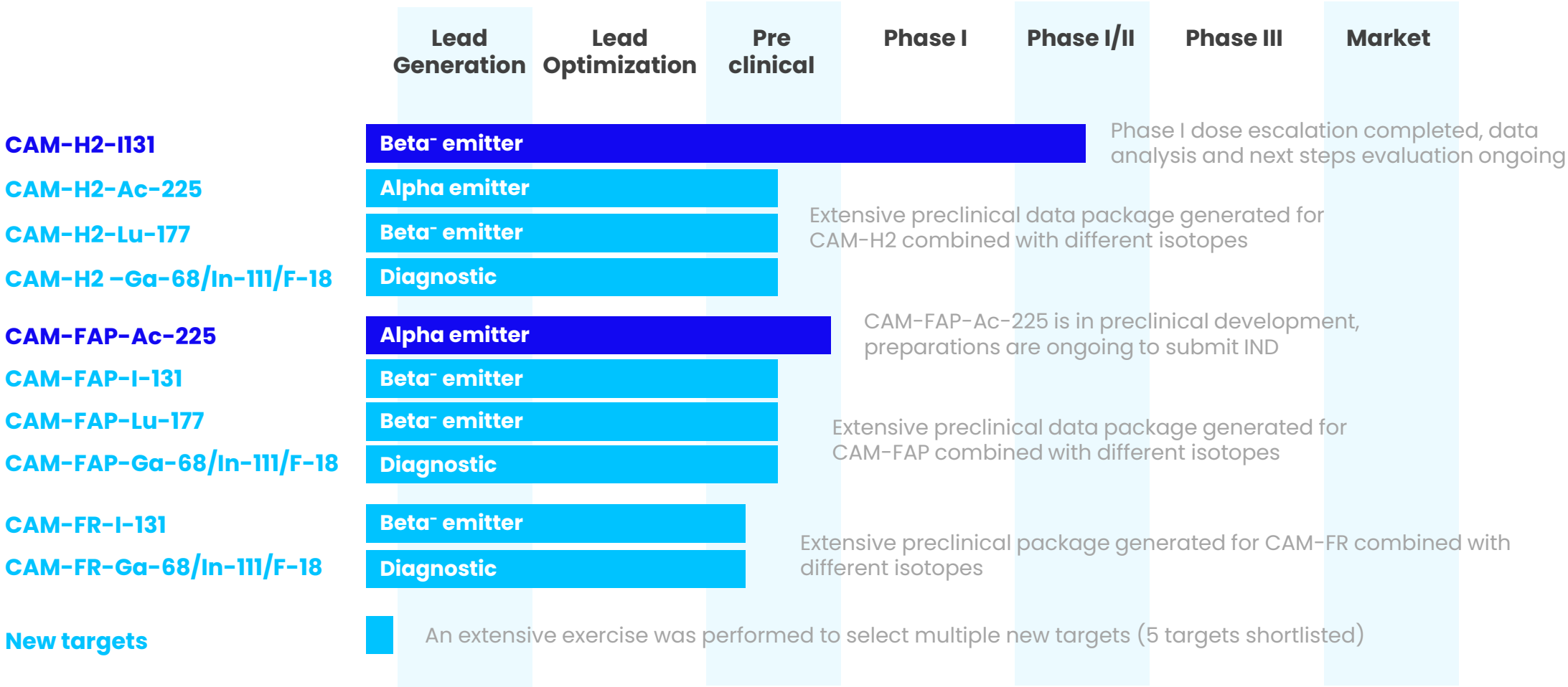
Preclinical imaging and therapy
Focus on rodent models – access to higher animal species
Strong relationships with expert academics and CROs

CMC focus for production and QC
Key partner CMOs for GMP manufacturing
Expertise in place to de-risk biological identity of DPs

Clinical development capabilities with US focus
Sponser driven multi-/single center trials

PRECIRIX®

Pipeline demonstrates strength and diversity of the platform



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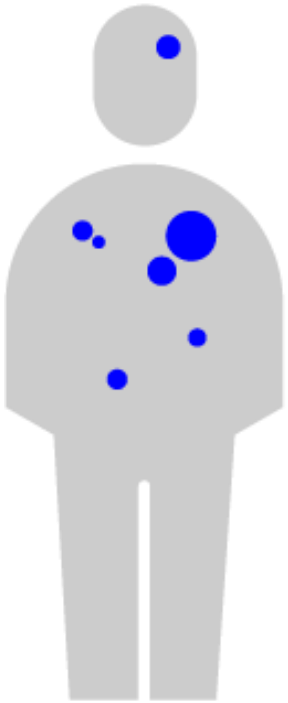
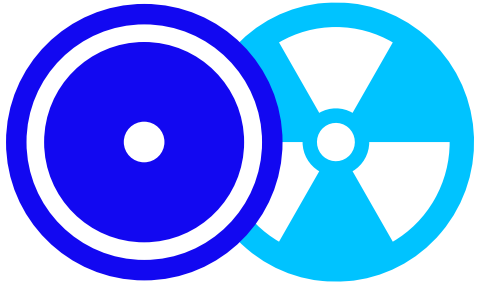
Unique platform using sdAbs as targeting ligands for radionuclides

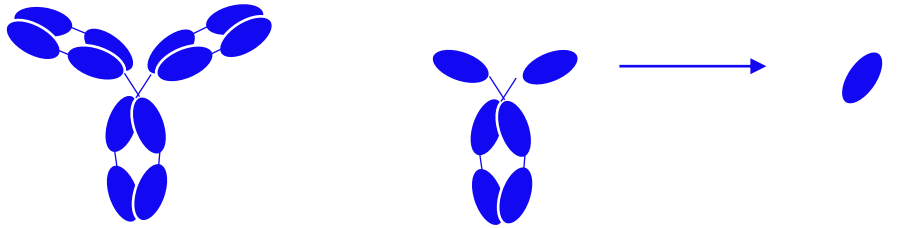




Radioisotope kills through DNA breaks

Direct cell killing and bystander effects

Single domain antibody (sdAb) targets the cancer



Conventional Ab
~150 kDa

Camelid heavy-chain Ab
~96 kDa

Single-domain Ab
~15 kDa

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The sdAb platform combines the benefits of mAb and peptide approaches

sdAbs are perfectly suited as vectors for targeted radionuclide therapy

- sdAbs can be generated against any relevant extracellular structure
- sdAbs are an option for targets not accessible to peptides or small molecules
- sdAbs combine rapid PK, efficient tumor penetration, high specificity, fast clearance and limited immunogenicity
- sdAbs possess superior characteristics in terms of size, high stability, strong antigen-binding affinity, water solubility and natural origin

	Peptide	sdAb	Antibody
Size	0.5–5 kDa	15 kDa	150 kDa
Affinity	pM–µM range	pM–nM range	pM–nM range
Stability	Variable	+	+
Tissue penetration	+	+	-
Blood clearance / Elimination route	Fast / Kidneys	Fast / Kidneys	Slow / Liver
Immunogenicity	-	-	+/-
Production cost	Low	Medium	High
Platform	-	+	+

Adapted from Funeh et al, (Pharmaceutics 2023, 15, 1378)

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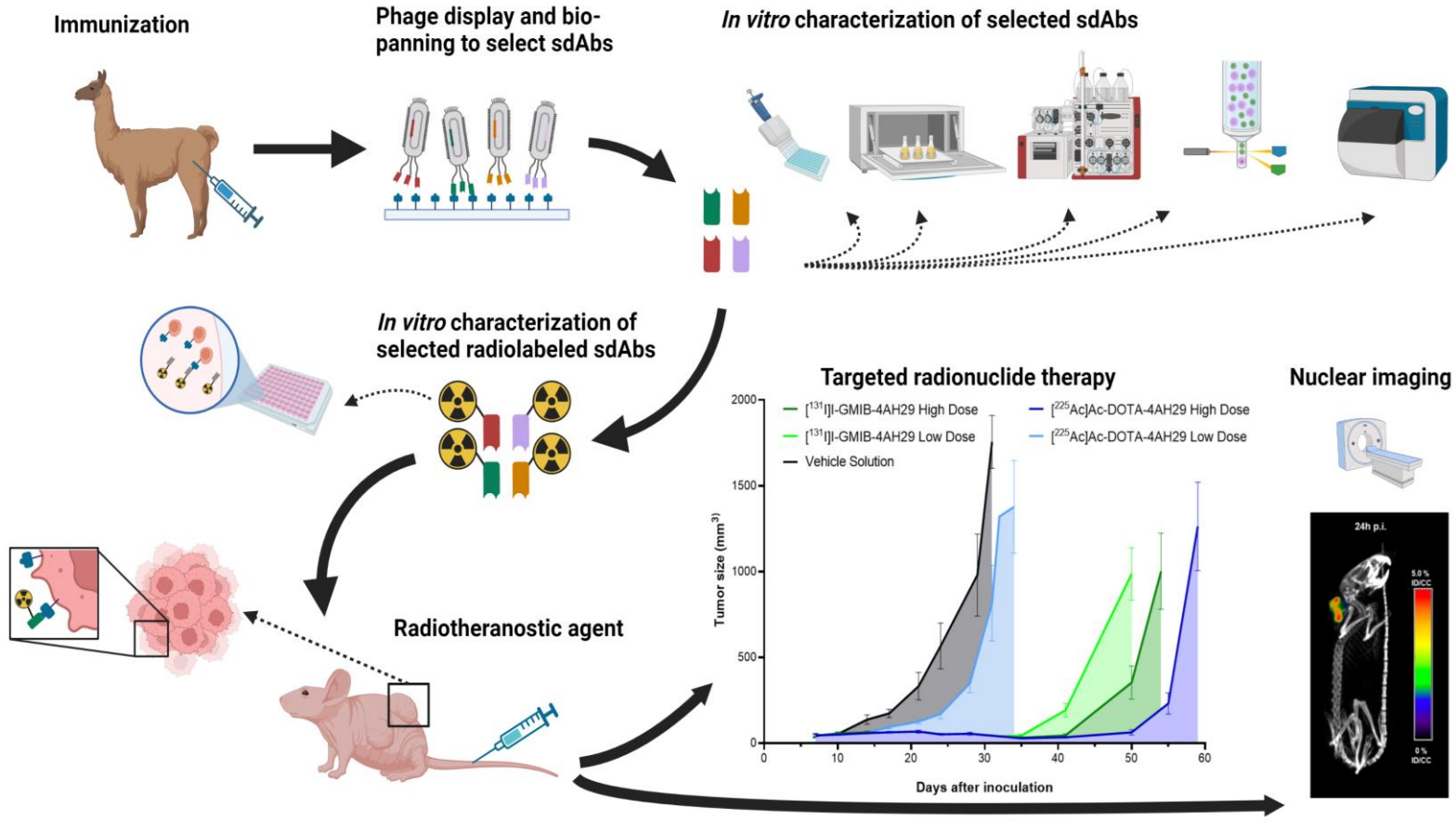
sdAb platform enables quick hit-to-lead selection

- Development **significantly quicker** compared to peptide approaches
- **Reproducible** – resulted in suitable lead compounds after just 1-2 rounds of screening
- **Predictable** characteristics such as PK and stability



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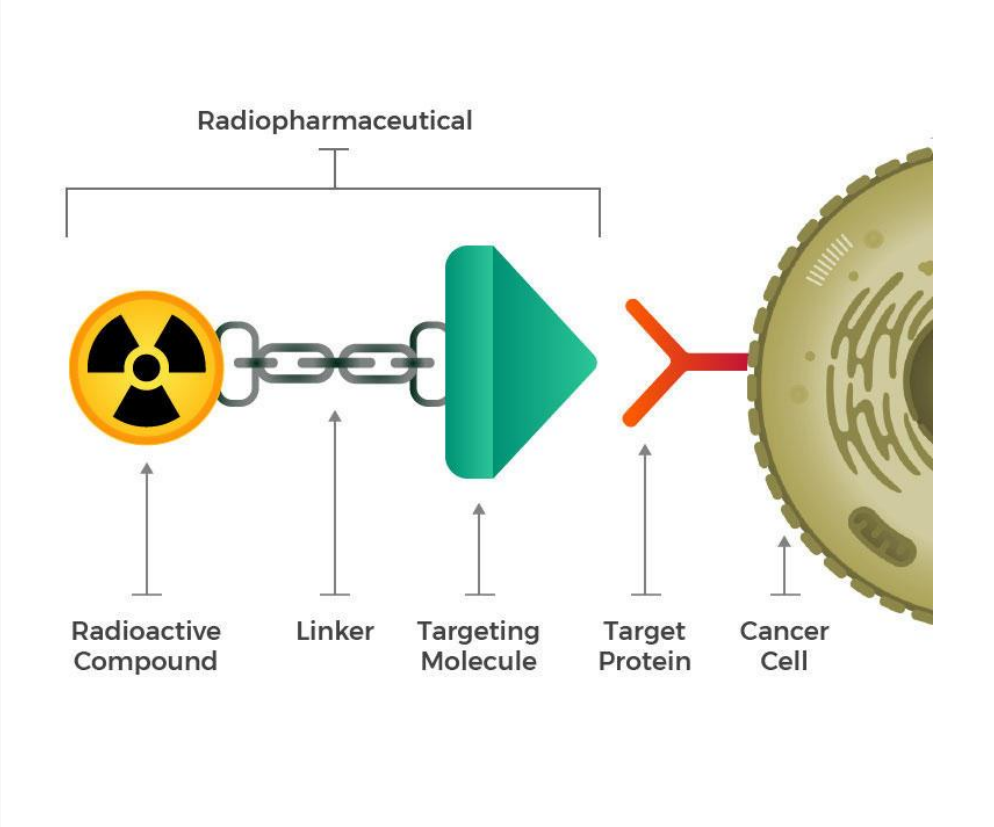
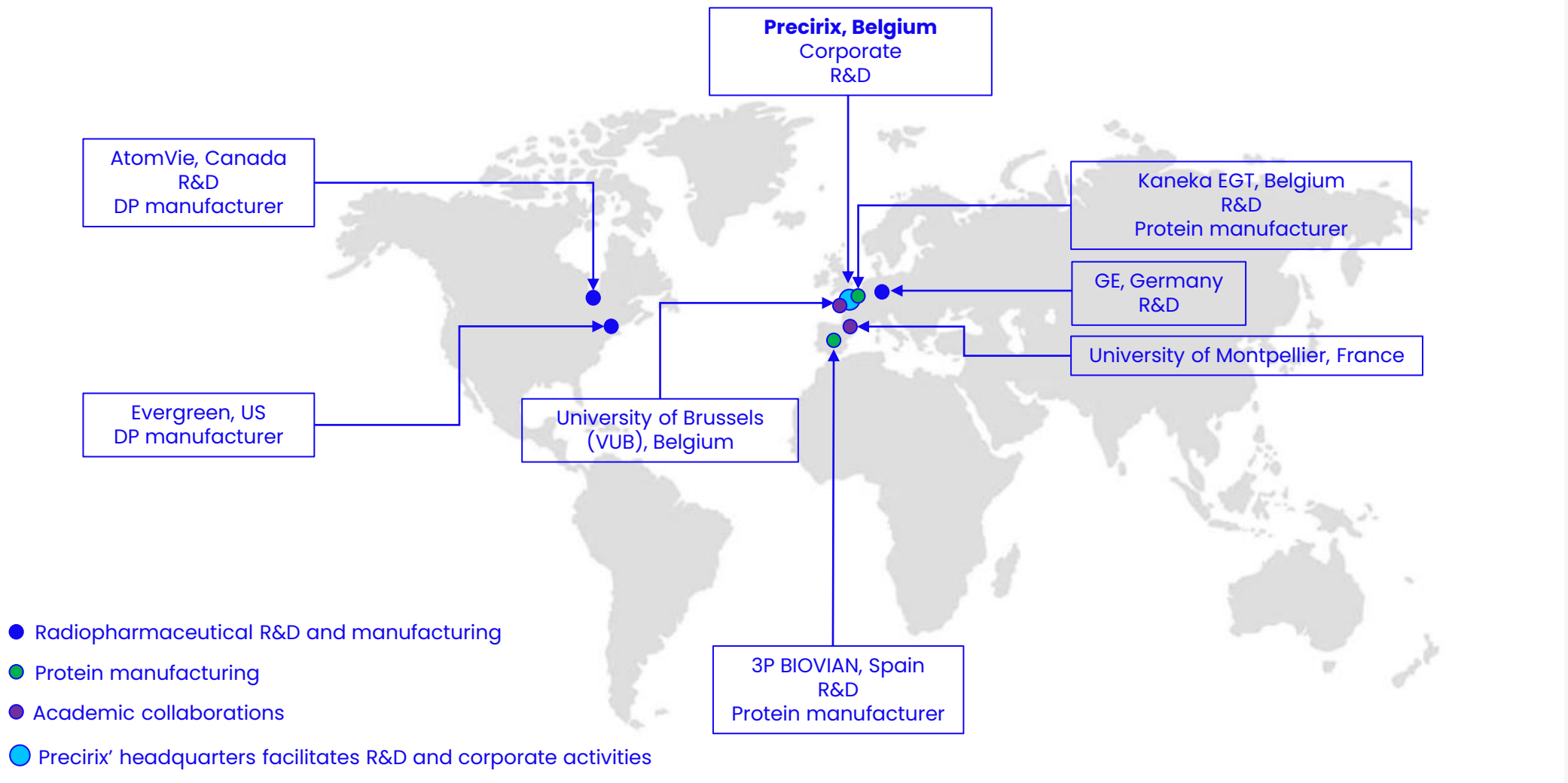
Our platform concept allows for a flexible and modular development approach

Targeting molecule*	Linker	Radioactive compound	Application
CAM-FAP	SGMTB-BOC_2	I-131	Imaging / Therapy
CAM-FAP	SGMTB-BOC_2	At-211	Therapy
CAM-FAP	TCMC	Pb-212	Therapy
CAM-FAP	DOTA	Lu-177 / Ac-225 / Cu-67	Therapy
CAM-FAP	MACROPA	Lu-177 / Ac-227	Therapy
CAM-FAP	DOTA	Ga-68 / In-111 / Cu-64	Imaging
CAM-FAP	NOTA	Ga-68 / Cu-64	Imaging
CAM-FAP	SFB	F-18	Imaging

* The CAM-FAP sdAb is used as an example for a targeting molecule



Global CMC and research network in place



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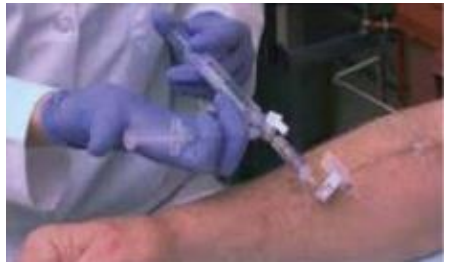
Robust end-to-end supply chain of TRTs

Good control on all elements of the TRT supply chain is a key enabler of our strategic objectives



Isotope Supply

- Reliable external partners
  - E&Z (Ga-68 /Ac-225)
  - Partner X (Ac-225)
  - Partner Y (Ac-225)
  - IRE (I-131)
  - NTP (I-131)

Manufacturing

- Platform technologies leveraging synergies
  - Long shelf life
  - High yields
  - High purity
- Strategic partnerships for handling of activity
  - Evergreen
  - AtomVie

Distribution

- Robust and agile distribution network
- Full coverage of strategic markets (North America)
- Competitive service level on logistics (order to delivery)

Use and Disposal

- Service level as competitive advantage, namely best
  - Commercial format
  - RAM licensing support
  - Dose calibrator set-up
  - Waste handling concepts

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CAM-FAP program

- **Why FAP**
- **Competitive differentiation**

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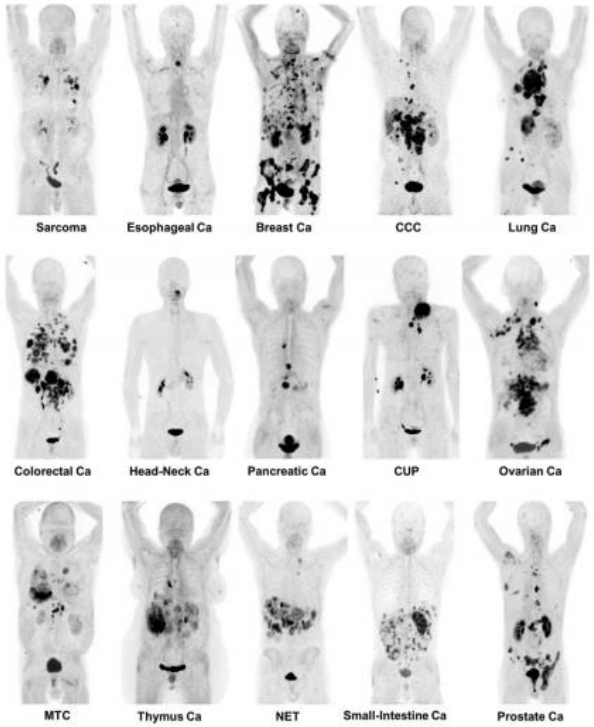
Fibroblast Activation Protein alpha has pan-tumor potential and could be the next multi-blockbuster

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., 2019 *JNM*

HOT TOPICS

FAP: The Next Billion Dollar Nuclear Theranostics Target?

Jeremie Calais[1–4]

[1]Ahmanson Translational Theranostics Division, Department of Molecular & Medical Pharmacology, University of California Los Angeles, Los Angeles, California; [2]Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, California; [3]Physics & Biology in Medicine Interdepartmental Graduate Program, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California; and [4]Institute of Urologic Oncology, University of California Los Angeles, Los Angeles, California

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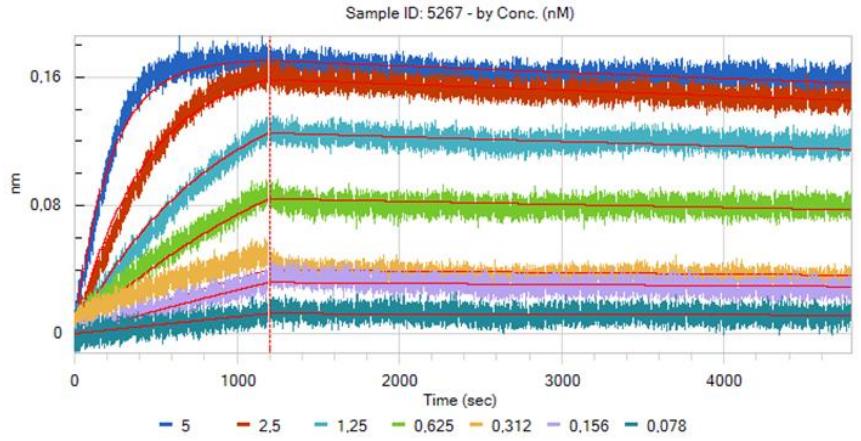
CAM-FAP is differentiated compared to competition

CAM-FAP has picomolar affinity for FAP and remains on target

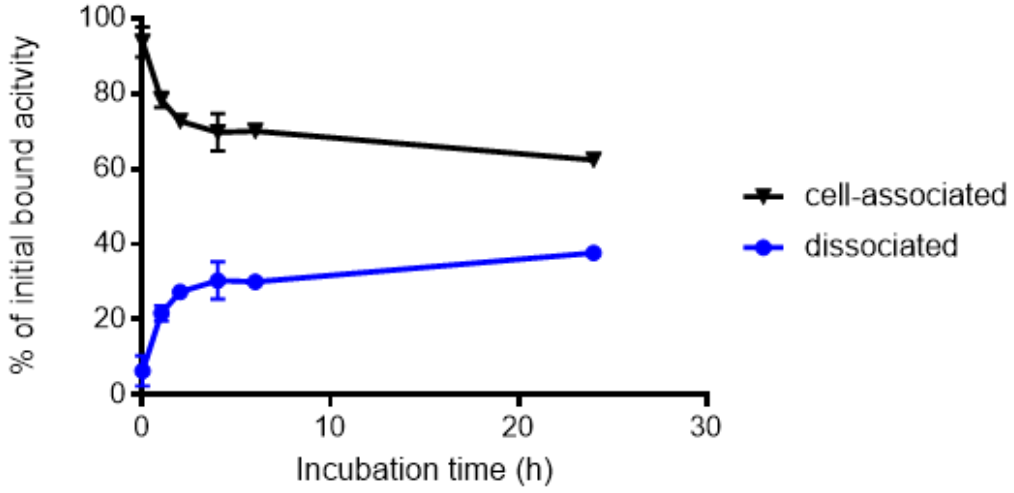
Binding on recombinant FAP



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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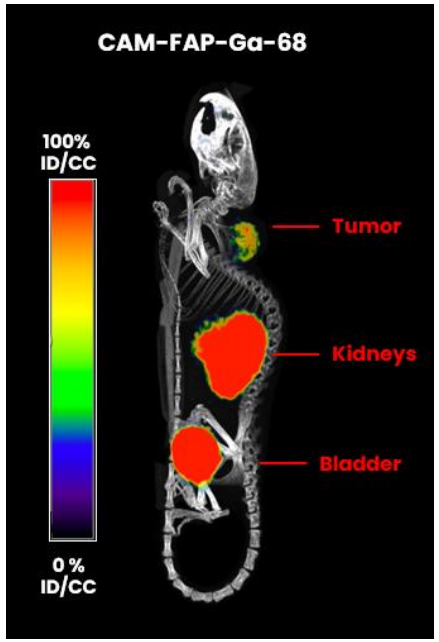
CAM-FAP targets and remains on the tumor

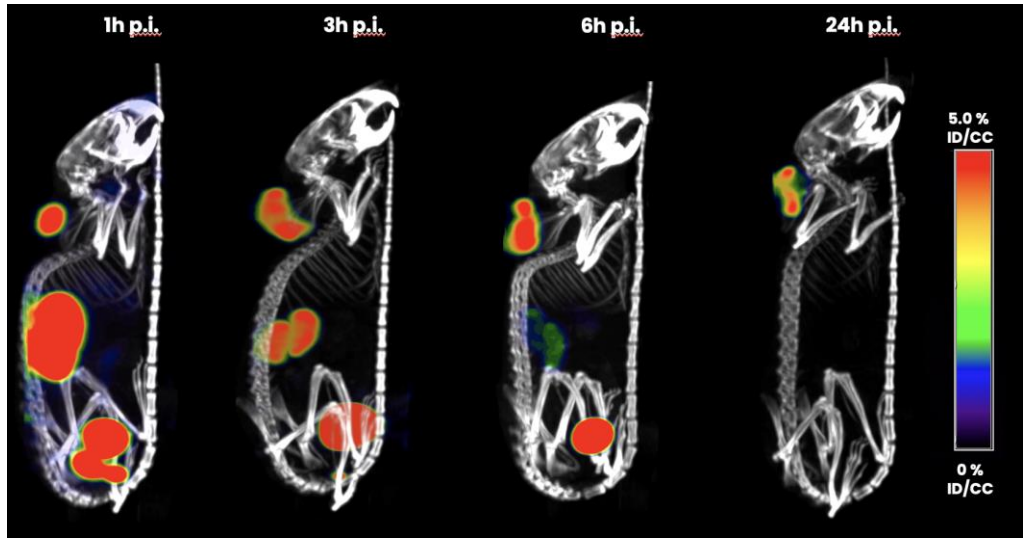
CAM-FAP-Ga-68

CAM-FAP-Ga-68 U87 GM tumor xenografts confirms tumor targeting



Low dose CAM-FAP-I-131

Repeated In vivo imaging of CAM-FAP-I-131 in U87 GM tumor xenografts confirms tumor retention



In vivo micro-SPECT/CT imaging

CAM-FAP has imaging potential allowing a theranostic approach

Dekempeneer et al. 2023, *J Nucl Med*

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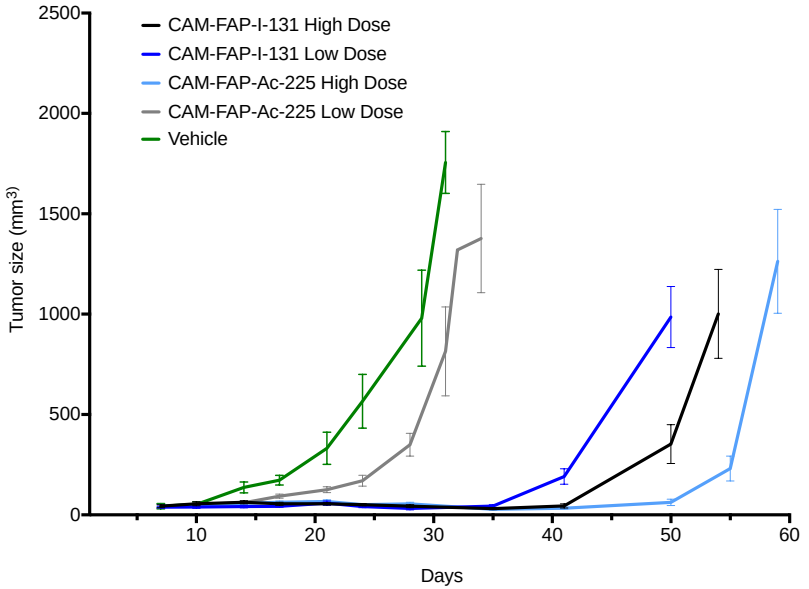
CAM-FAP has therapeutic potential

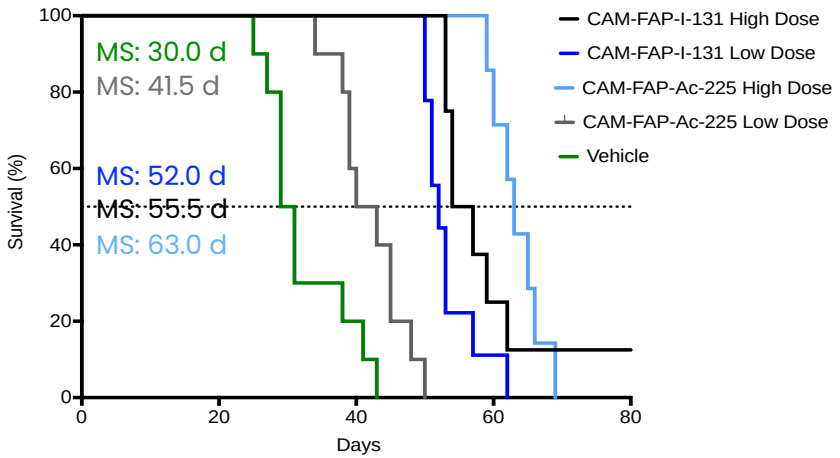
CAM-FAP-Ac-225 and CAM-FAP-I-131 are potent in U87 GM tumor xenografted mice [1]

- Dose-dependent response for both DPs, no signs of acute toxicity in mice

Research focus

- IND enabling nonclinical studies (incl. mice, minipig and NHP)
- Combination studies with immune checkpoint inhibitors
- Combination studies with DNA repair inhibitors
- CAM-FAP therapeutic efficacy in PDX models with stromal compartment
- Differentiation of CAM-FAP from competitors
- Pre-targeting





1 Data published in Dekempeneer et al. JNM 2023

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CAM-H2 program

- **Competitive differentiation**
- **Our progress**

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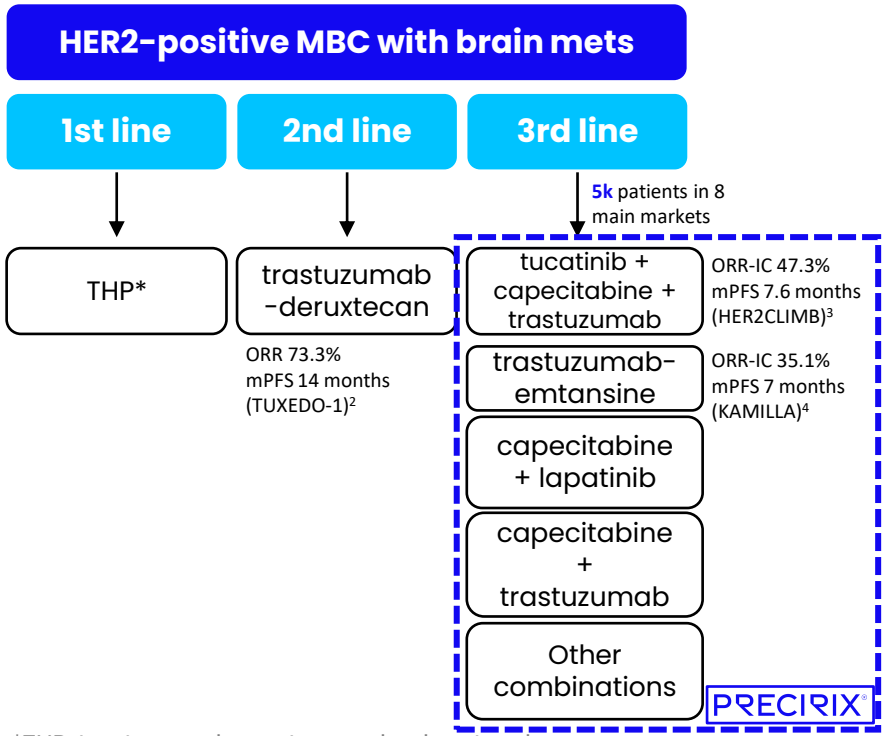
There are currently limited treatment options for patients with HER2+ breast cancer with brain metastases

- Up to **50% of metastatic breast cancer patients** will develop brain metastases[1]
- Enhertu and Tukysa are valuable options beyond standard THP, but come with important side effects and **patients will eventually relapse**
- Potential for **combination therapy**, e.g. stereotactic radiosurgery or whole-brain radiation or standard therapeutic drugs
  - Brain metastases are known to be radiosensitive
  - WBRT and SRS are SoC, they improve intracranial control, but do not improve survival due to dose limitations
  - CAM-H2 can bring additional radiation to target cells



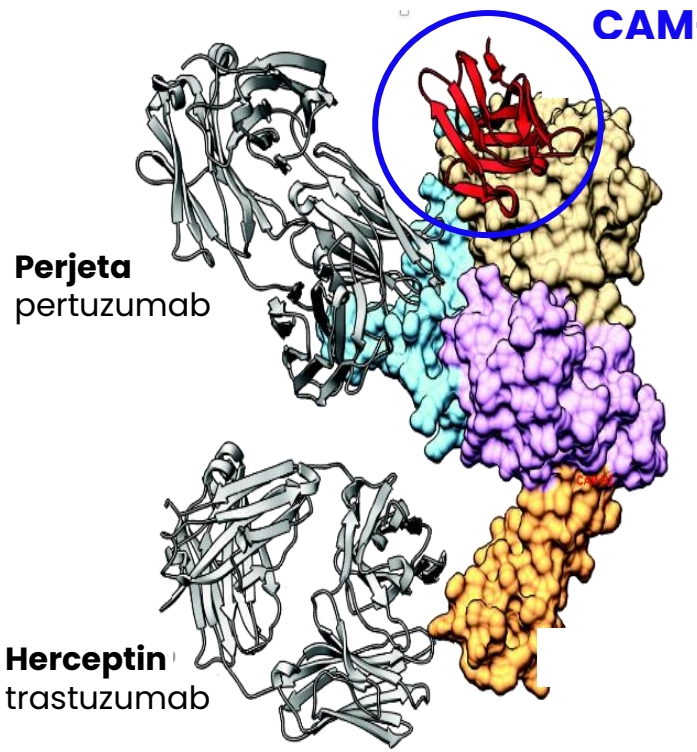
*THP: trastuzumab+pertuzumab+docetaxel

Simplified treatment paradigm derived from ASCO guidelines 2022 (Ramakrishna et al. Journal of Clinical Oncology)

1 Garcia-Alvarez et al. 2021 *Cancers*
2 Bartsch et al. 2022 Nat Med 28:1840-1847

3 Murthy et al. 2020 N Engl J Med 382:597-609; Lin et al. 2020 J Clin Oncol 38:2610-2619
4 Fabi et al. 2018 Breast 41:137-143
Epidemiology data: GlobalData; 8 main markets include US, UK, Germany, Spain, Italy, France, Japan and China

CAM-H2 targets HER2+ tumors including brain lesions and binds to a different epitope to other approved drugs



- **Resistance to HER2 therapy** is an issue for approved drugs, CAM-H2 targets a different epitope and brings **a new mechanism of action**
- **Combination therapy** with standard-of-care feasible
- **Intra-tumoral HER2 heterogeneity** is associated with poor survival, radiolabeled 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

D'Huyvetter M et al., 2017, *Clin Cancer Res*

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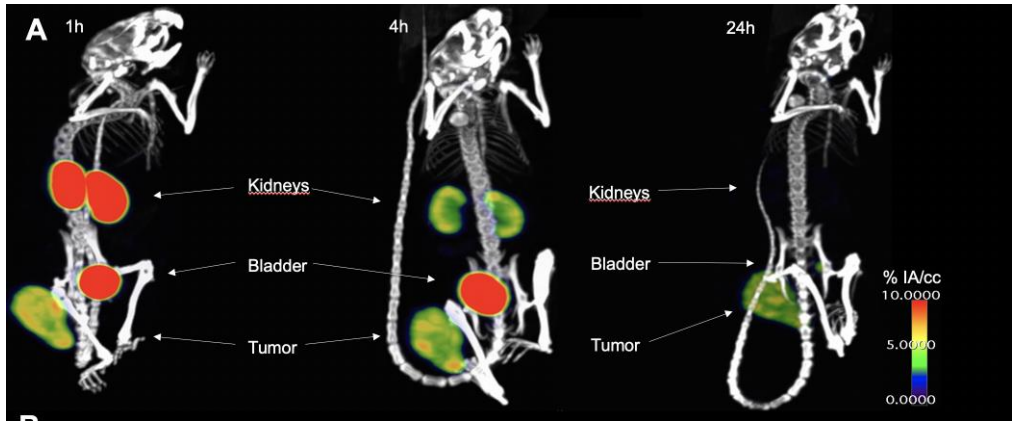
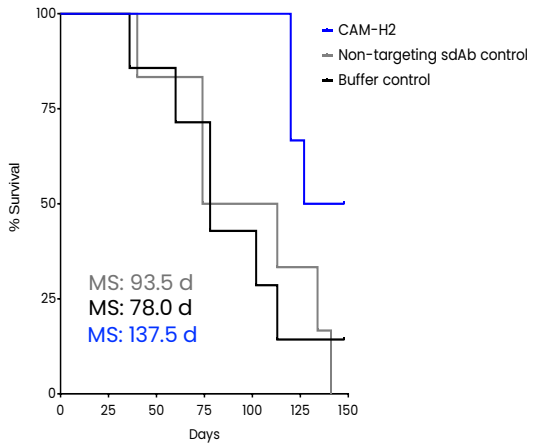
Preclinical validation of theranostic potential for CAM-H2

- **Preclinically validated** as effective theranostic radiopharmaceutical
- **Imaging potential** described using a variety of SPECT and PET isotopes
- CAM-H2 improves survival in preclinical **breast, ovarian** and **brain metastasis** xenograft models in combination with beta- and alpha particle emitters
- Additive effects in **combination with Trastuzumab, Kadcyla, PARP inhibitors**

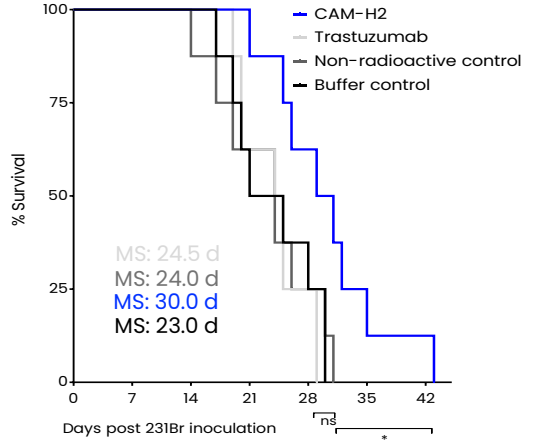
Theranostic CAM-H2-I-131



BT474/M1 xenografts



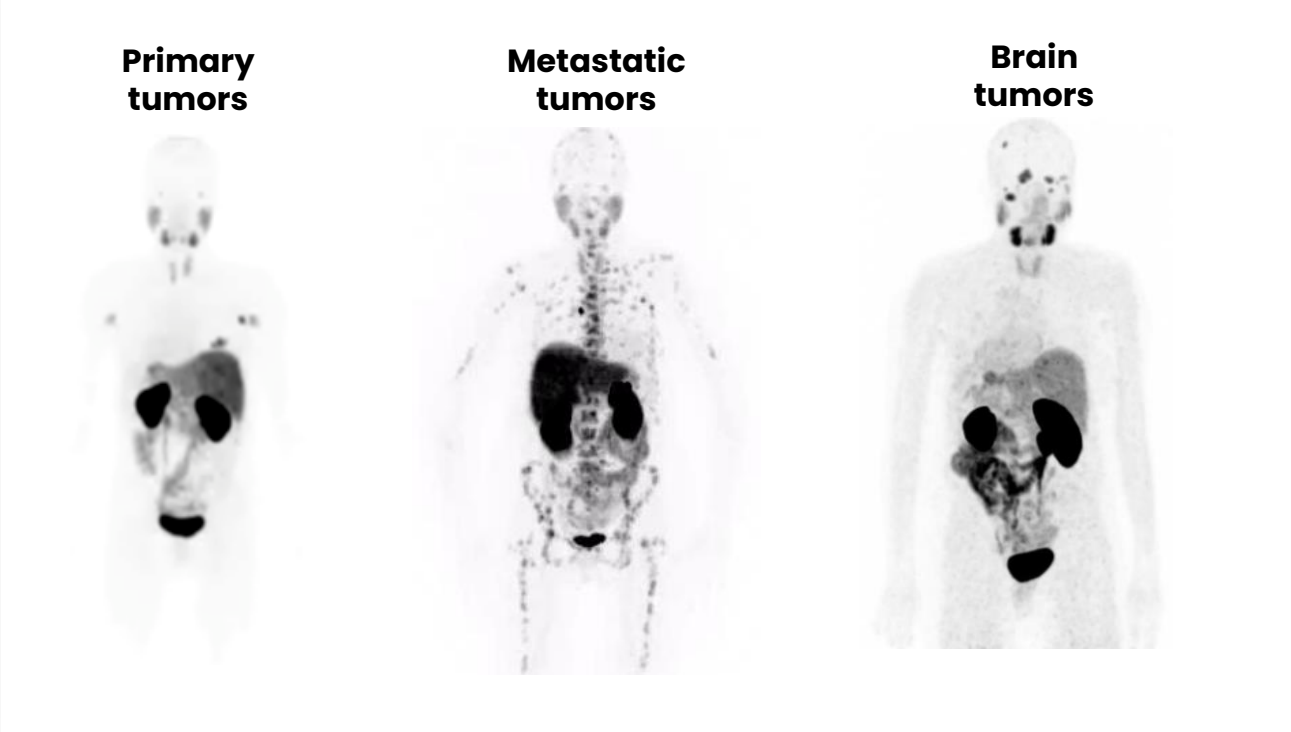
Intracranial 231Br tumors



D'Huyvetter M et al., 2017, *Clin Cancer Res*: N=6/group; 5 weekly injections; 11 MBq/injection
Puttemans J et al., 2020, *Cancers*: N=8/group; 2 injections; 32 MBq/injection on day 7 and 14

Early clinical data provided support for further development

Imaging study



Phase I biomarker study

6 healthy subjects, 3 patients
biomarker dose

- No drug-related adverse events
  - Rapid blood clearance: 2.5h half-life in elimination phase
  - Biological half-life: 7.7h
- Metabolites identified in urine samples (indicating renal metabolization)
- Kidney is dose-limiting organ, no accumulation in other organs
  - A single 400 mCi administration is estimated to deliver 22 Gy to the kidneys (w/o kidney protection through AA)
- Confirmed tumor targeting

Published in D'Huyvetter M et al., *J Nucl Med* 2021 62(8):1097-1105

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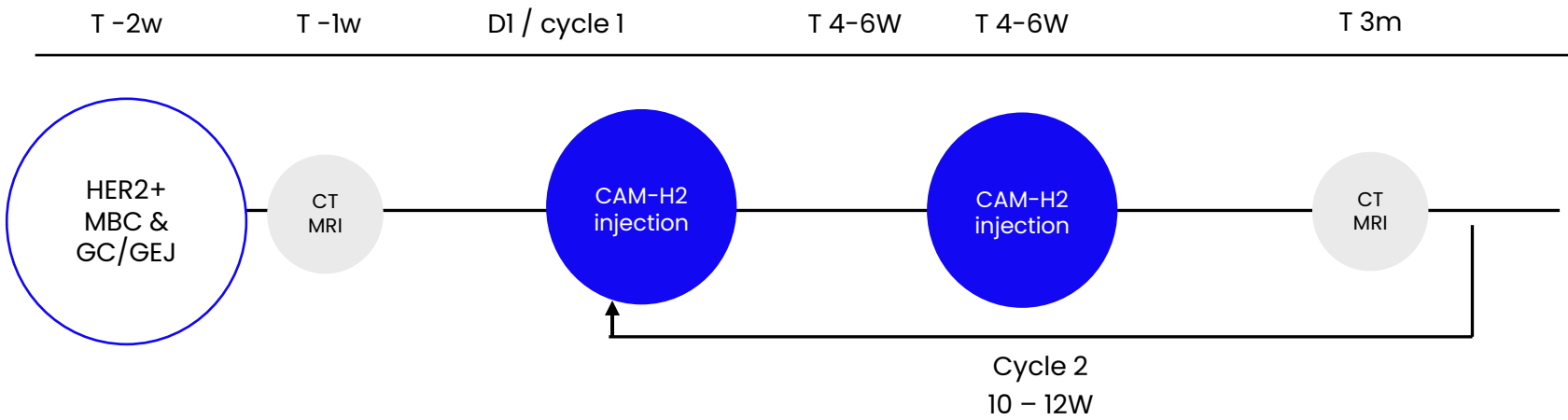
CAM-H2 Phase I dose escalation has been completed



- Multi-center, international trial in Canada and the USA
- Open label dose escalation study with a **3+3 design**
- 3 cohorts have been completed (**50/ 100/ 150mCi**)
  - Each cycle consisted of 2 IV injections of **50/100/150 mCi**, 4-6 wks apart
- 18 patients were screened, of whom 13 were eligible
  - HER2+ metastatic breast and gastric cancer, including 3 patients with brain metastases
  - All patients had been heavily pre-treated
  - Patients were selected based on HER2 status determined earlier in their disease and not via imaging pre-treatment

- **Primary endpoints**
  - Safety, tolerability and dosimetry and PD of ascending doses of CAM-H2
  - Identification of DLTs
- **Key secondary endpoint**
  - Proportion of patients with response (CR, PR, SD)

NCT04467515

CAM-H2 Phase I status update & plans

Key take aways from phase 1 dose escalation study

- CAM-H2 targets the tumour with limited impact on non-target organs (liver, kidney, bone marrow, spleen)
- Tolerability and safety is acceptable at 50, 100 and 150 mCi
- Opportunity to further escalate dose (Independent Safety Review Committee)
  - Absorbed doses across all 3 dose levels did not reach the MTD (as defined by the FDA) for main target organs leaving room for potentially higher doses to be studied
  - Dosimetry extrapolations to hypothetical maximum dose translate to absorbed doses in tumor lesions at therapeutically effective range compared with external beam radiation

Next steps

- Optimising development plan for patients with HER2+ breast cancer with brain mets
- Phase II protocol being developed

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IP Portfolio snapshot

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 and EU

Patent pending in multiple other countries.

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

Patent granted in US and EU

Patent pending in multiple other countries.

Preclinical programs

WO 2022/053651

CAM-FAP – Protection of antibody fragments targeting an epitope of FAP

WO 2022/013225

CAM-FR – Protection of antibody fragments targeting an epitope of FOLR1

WO 2023/213801

Protection of the use of pre-targeting applied to antibody fragments

CMC

WO 2022/053459

Protection of methods for radiolabeling

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Platform
Real
Relevant

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