Matrisome Bio

"*Think outside the cell*"

Noor Jailkhani
Co-founder and CEO

BIO Bootcamp
June 15th, 2025

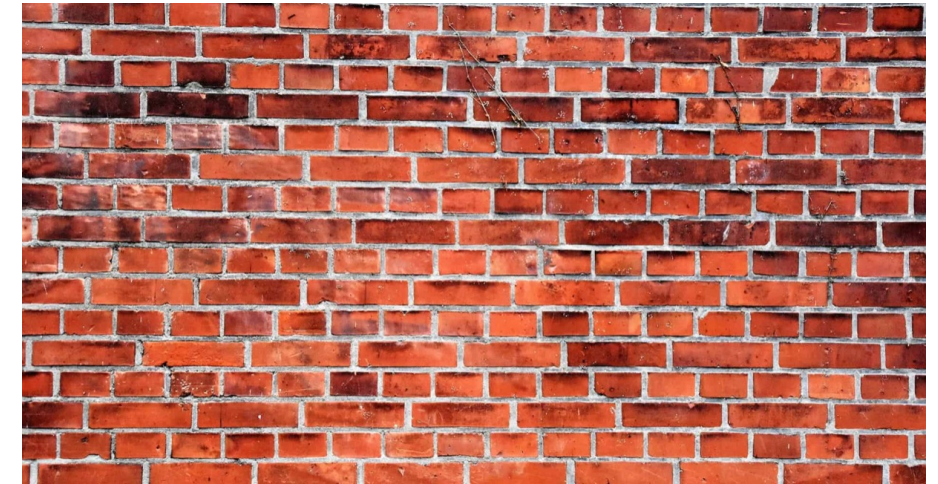https://www.matrisomebio.com

We are harnessing properties of the Extracellular Matrix (ECM)
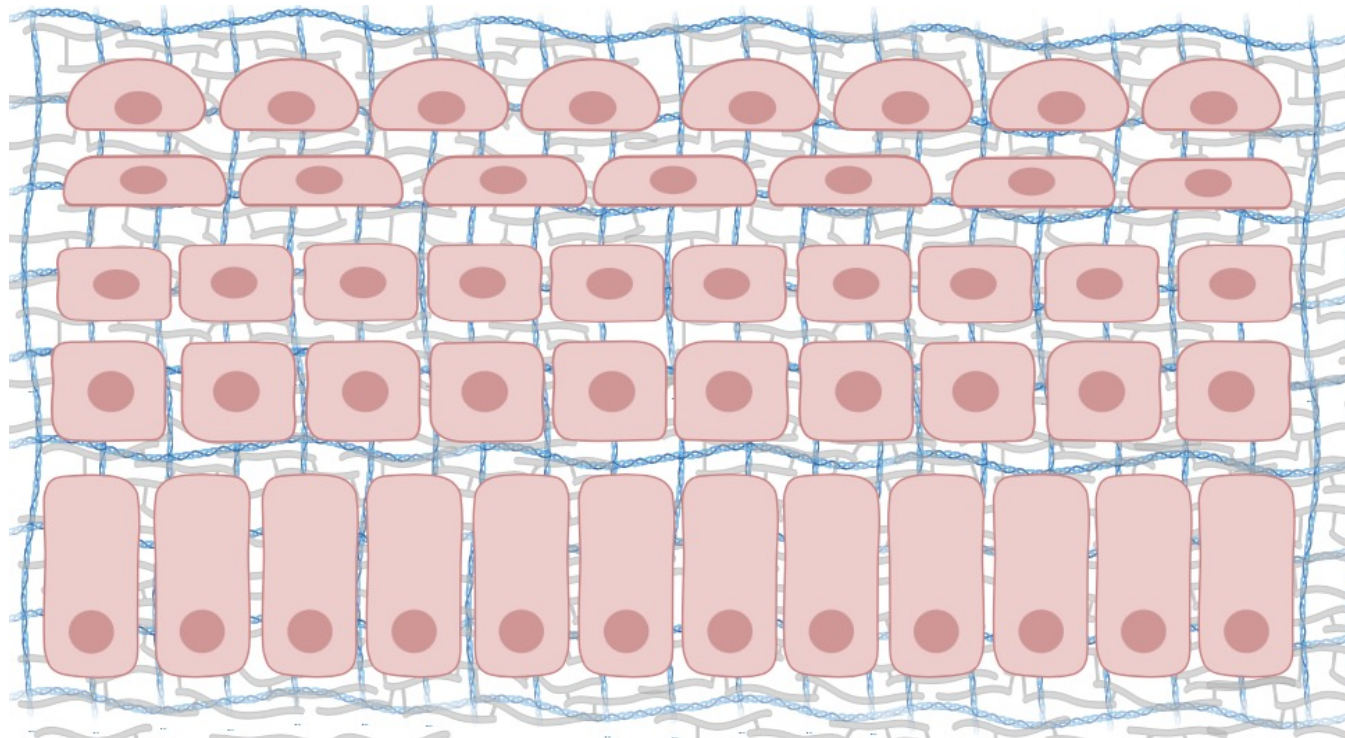
Bricks and Cement

Layer of cells   Extracellular matrix (ECM)
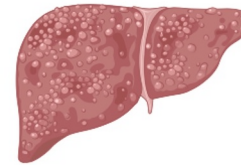
The Matrisome is an underexplored target

The matrix of disease tissues is different from the matrix of normal tissues

Oncology

Cardiovascular disease

Fibrosis

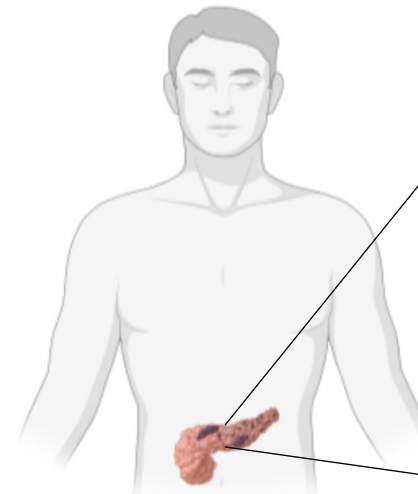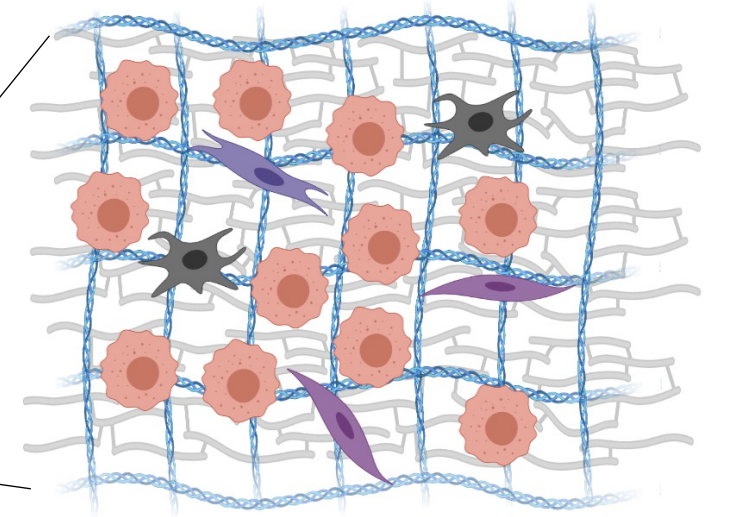| Constitutes a major part of disease tissues | Correlates with poor survival | Selective expression at disease sites |

| Poor T-cell infiltration | Compromised drug delivery | Underexplored target (Universal) |

Pancreatic Cancer

Tumor cells

Stromal cells

Extracellular matrix (ECM)

Vision

Targeting therapies to the diseased Extracellular Matrix using nanobodies

Current solid tumor therapies target cancer cells
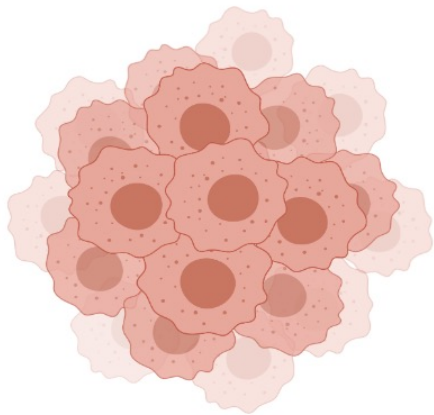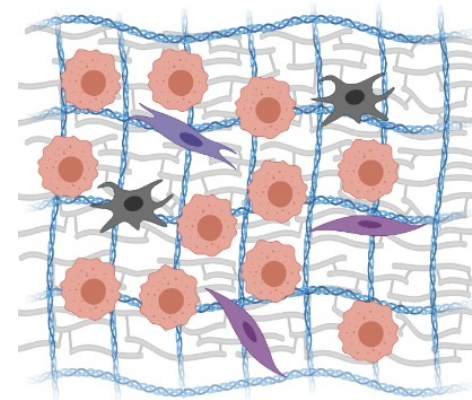

Sub-optimal

Heterogeneity

Genomic instability (mutations)

Large unmet need

We target therapeutics to the diseased ECM

Tumor cells   Stromal cells   Extracellular matrix (ECM)

Disease Selective

Abundant

Extracellular and stable

Cancer agnostic

Our core products are nanobodies that deliver therapies to the tumor ECM

Tools:
Nanobodies

$\oplus$

Targets:
ECM proteins

Validated Nanobodies (2 targets)

Proprietary Nanobody libraries

HcAb — Nanobody

Therapeutic Payload

- Drugs/Toxins
- Radioisotopes
- Cytokines
- CAR T-cells

Nanobody conjugate

- Targeted delivery
- Local enrichment
- Drug persistence

Tumor cells   Stromal cells   Extracellular matrix (ECM)
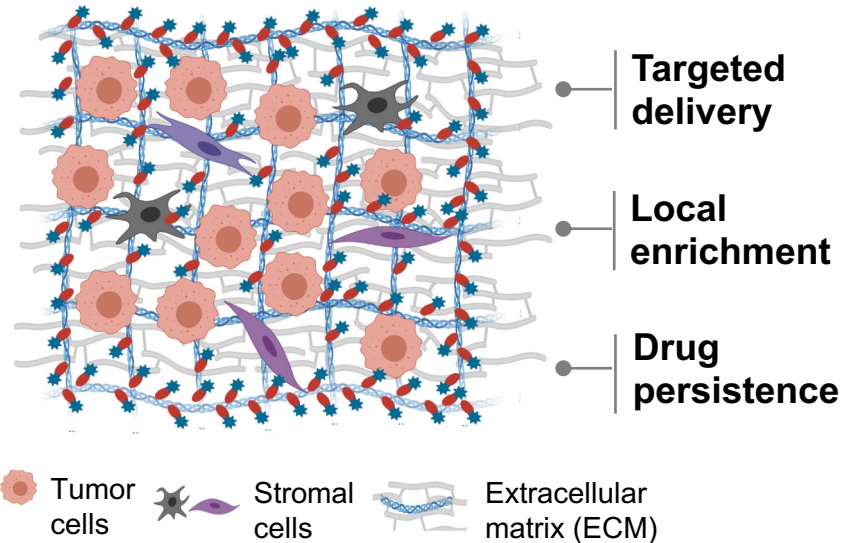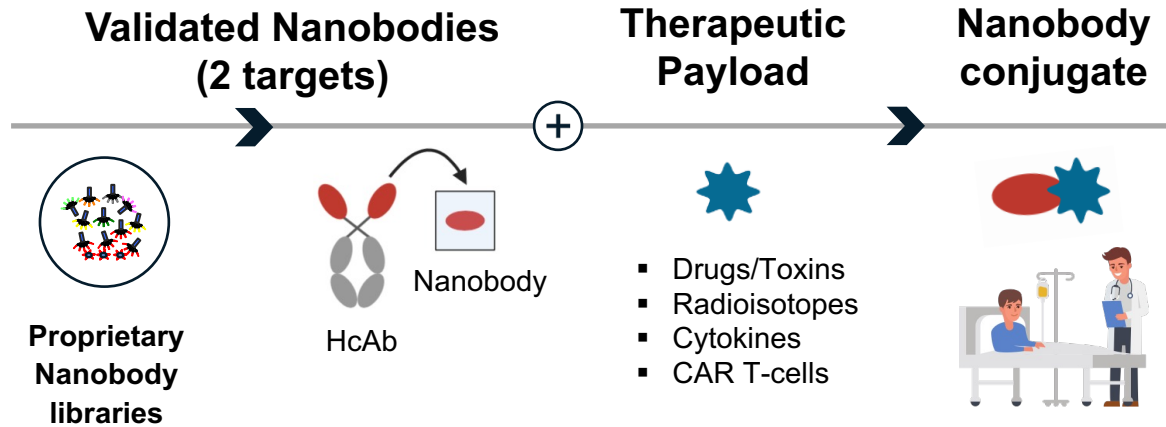
Cancer-agnostic targets

Payload-agnostic nanobodies

- **Off-the-shelf solution, eliminating the need for a patient-specific therapy**

- **We have POC data and IP**

We are the leading experts in ECM biology, with deep expertise in nanobody technology

Proprietary assets and IP

- **Phage-display nanobody libraries** derived by immunizing Alpacas with ECM from human metastases

- **2 validated nanobody leads (two targets)**

Patents

(1) Nanobody based imaging and targeting of ECM in disease and development. Hynes R. O., Jailkhani, N., Ploegh, H.L., Xie, Y.
International patent application PCT/US2019/015290.
United States Patent Application US20190225693A1.

(2) Enhanced-affinity anti-ECM nanobody-cytokine fusions and their applications. Hynes R. O., Wittrup K. D., Jailkhani, N., Momin, N., Lutz E., A.
International patent application PCT/US2023/061658
United States Patent Application US20230295284A1

>50 years of expertise in ECM
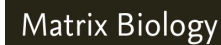
Lasker Award 2022

Matrisome Project

Hynes et. al, Science (2009)
Naba et. al, Mol Cell Prot (2011)
Naba et. al, Matrix Biol (2012)
Hynes et. al, Nature Rev MCB (2014)
Naba et. al, Elife (2014)
Naba et. al, Matrix Biol (2016)
Hynes et. al, CSHL Prospect Biol (2012)
Gocheva et, al, PNAS (2017)
Hebert et. al, Cancer Res (2020)

ECM in Cancer

Tian et. al, PNAS (2019)
Tian et. al, Cancer Res (2020)
Tian et. al, Nature Com (2021)
Rickelt et.al, Clin Cancer Res (2020)
Rickelt et.al, Clin Cancer Res (2022)

αECM nanobody-based tools

Noninvasive imaging of tumor progression, metastasis, and fibrosis using a nanobody targeting the extracellular matrix

Noor Jailkhani, Jessica R. Ingram, Mohammad Rashidian, Steffen Rickelt, Chenxi Tian, Howard Mak, Zhigang Jiang, Hidde L. Ploegh, and Richard O. Hynes

Nanobody-based CAR T cells that target the tumor microenvironment inhibit the growth of solid tumors in immunocompetent mice

Yushu Joy Xie, Michael Dougan, Noor Jailkhani, Jessica Ingram, Tao Fang, Laura Kummer, Noor Momin, Novalia Pishesha, Steffen Rickelt, Richard O. Hynes, and Hidde Ploegh

Maximizing response to intratumoral immunotherapy in mice by tuning local retention

Noor Momin, Joseph R. Palmeri, Emi A. Lutz, Noor Jailkhani, Howard Mak, Anthony Tabet, Magnolia M. Chinn, Byong H. Kang, Virginia Spanoudaki, Richard O. Hynes & K. Dane Wittrup
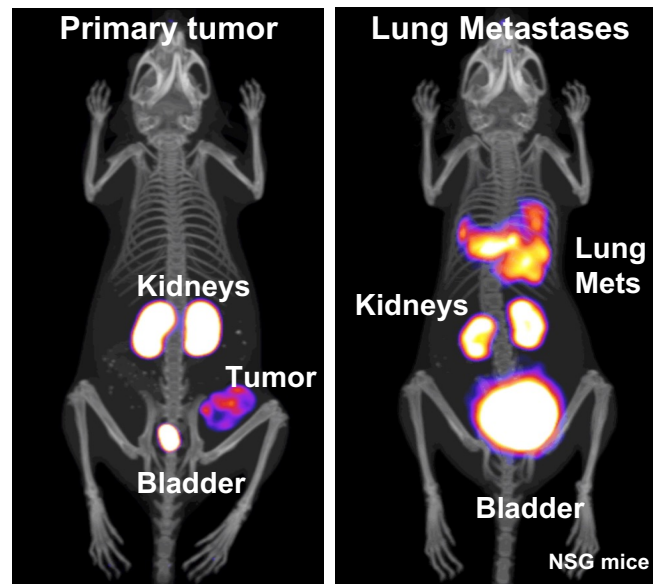
Others:
Lutz EA, Jailkhani N et al, PNAS Nexus, 2022
Jailkhani et. al, (Cancer Res, 2023)

NJB2 homes specifically to sites of disease

LM2 Triple-negative Breast Cancer Model

Primary tumor / Lung Metastases

Primary tumor: Kidneys, Tumor, Bladder

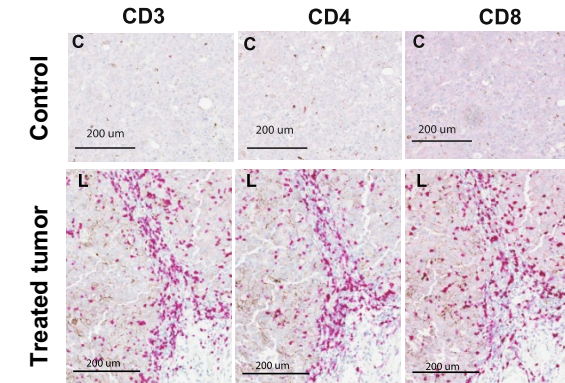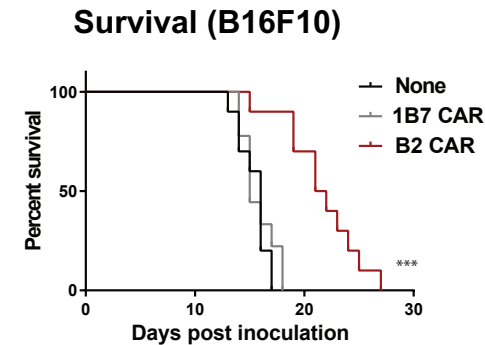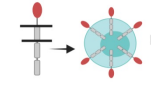Lung Metastases: Lung Mets, Kidneys, Bladder

NSG mice

Jailkhani et al, PNAS, 2019

Similar results in mouse models of:
- PDAC (including early lesions)
- Melanoma
- Lung fibroses

PDAC: Pancreatic ductal adenocarcinoma   TNBC: Triple negative breast cancer

NJB2 delivers CAR T-cells to the tumor ECM and turns cold tumors to hot

CD8

Survival (B16F10)

Percent survival (100, 50, 0) vs Days post inoculation (0, 10, 20, 30)
- None
- 1B7 CAR
- B2 CAR
***

Control / Treated tumor

200 um   200 um   200 um

Xie et al, PNAS, 2019

Nanobody-cytokine fusions enable high cure rates via intra-tumoral delivery

B16F10 survival (%) (100, 50, 0) vs Days (0, 25, 50, 75)

8/11 cures
6/11 cures
1/11 cures

- TA99 (ip) + PBS
- TA99 (ip) + Size matched IL2
- TA99 (ip) + Nanobody1-IL2
- TA99 (ip) + Nanobody 2-IL2

*** ** *** ns

Lutz EA, Jailkhani N et al, PNAS Nexus, 2022

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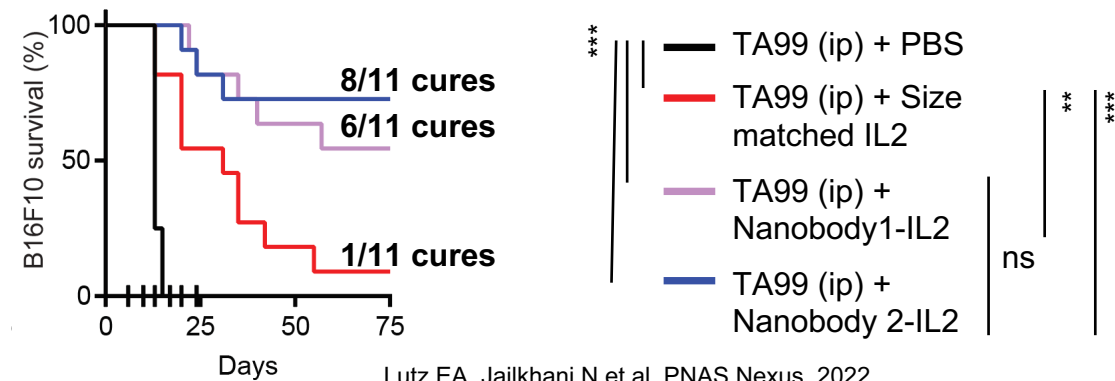
We have a powerful discovery platform for developing novel ECM-specific, nanobody-based therapies…

Disease ECM expertise

Proprietary nanobody libraries

Phage display technology

Nanobody validation & development

Single-step tagging capabilities
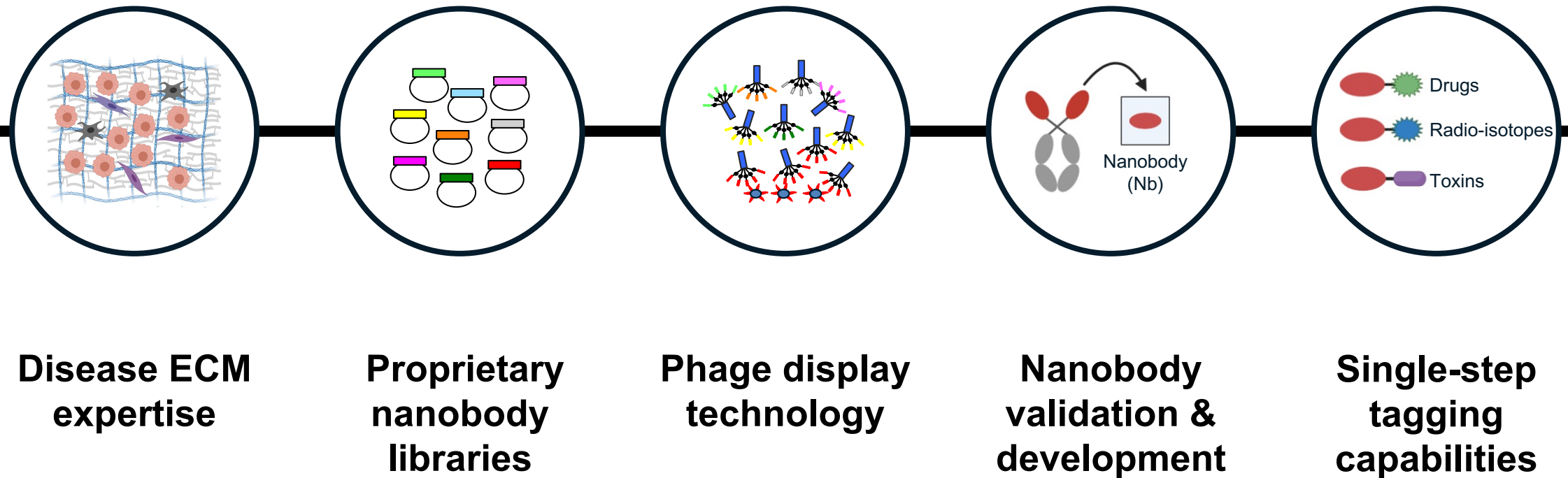
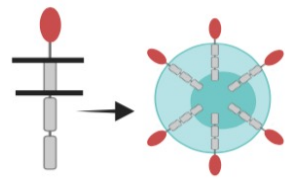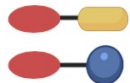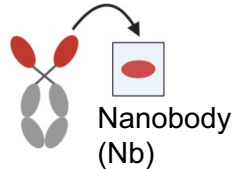# … that can lead to a pipeline of therapeutic programs across solid tumor types

Targeted Immunotherapy

Nanobody-based immunocytokines

CAR T / NK cells

Nanobody (Nb)

Targeted Toxin (drug/radionuclide)

Nanobody-Drug conjugates

Nanobody-nanoparticle-drug conjugates

Nb-drug

Nb-radionuclide

Nb-Enzyme/Toxin

Nanoparticle-drug targeting

Immunoliposomes gene delivery

Multi-specifics

E.g., BiTEs, Function blocking nanobodies (stand-alone therapeutics)

Bivalent

Multivalent

Multispecific

Market size (US)

Estimated to be $5.4 B by 2030

Estimated to grow to $6.1 B by 2030
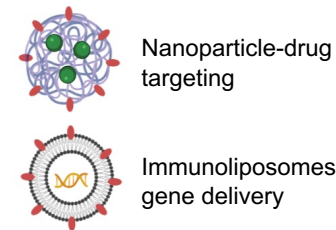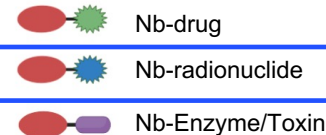
Overall US ADC market projected to grow to $19.8 B in 2028
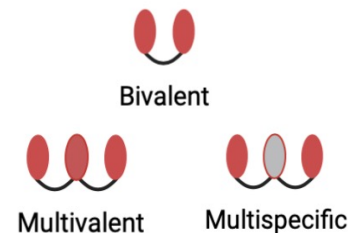
Overall mAB market forecast to be ~$140B by 2024

Our seed strategy is to focus on Radioligand Therapy (RLT) and include experiments that advance the platform.

Our seed strategy is to focus on Radioligand Therapy (RLT)-targeted delivery of radiation to tumors and metastases

Treatment strategy

Receptor targeting monoclonal antibody radiolabeled with Lu-177/Ac-225
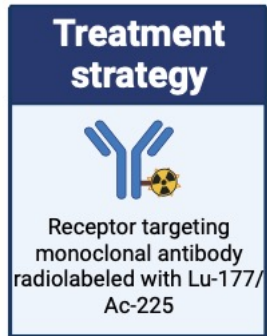
Binders
Antibody
Peptide
Small molecule

Targets
Receptors (PSMA, SSTR)

Our strategy

Matrix targeting nanobody radiolabeled with Lu-177/Ac-225
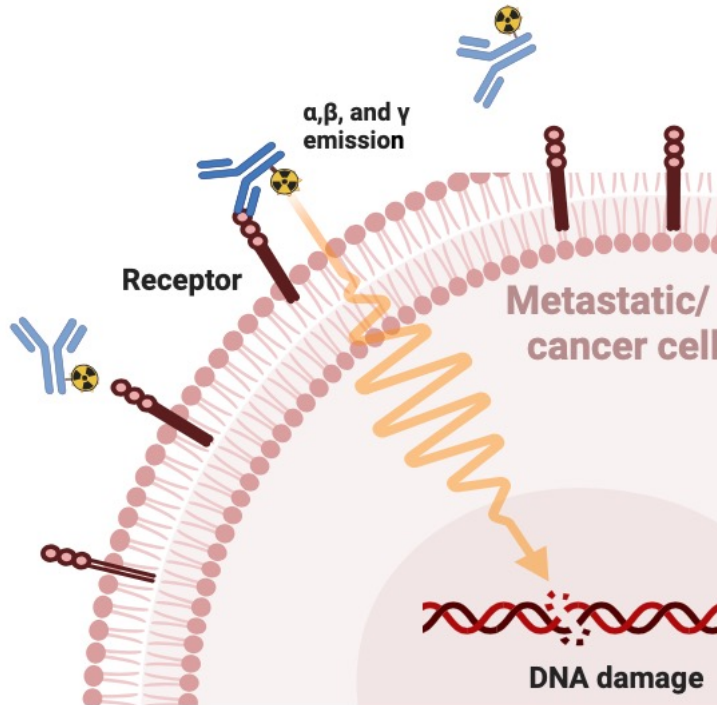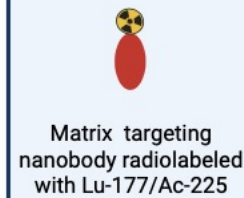
Binders
Nanobody

Targets
Extracellular matrix
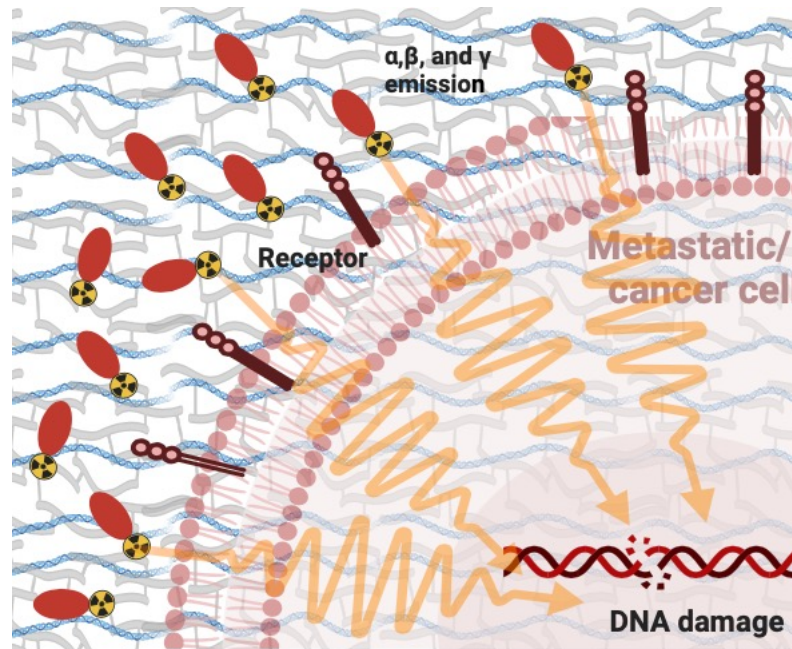
Advantages of our technology

ECM targets	Abundant & stable in disease sites
	Absent from normal tissues
	Cancer agnostic

Nanobody	Deep tissue penetration
	High affinity binders
	Tunable PK & quick systemic clearance

PSMA: Prostate-specific membrane antigen: SSTR, Somatostatin receptors

Radioligand Therapy (RLT) is gaining momentum, and we are highly differentiated by our target (ECM) and binders (nanobodies)

RLT momentum is strong

Recent breakthrough FDA approvals

Large pharma have made multi-billion dollar acquisitions (*Novartis and other examples in appendix*)

$1B+ investments in new radioligand focused ventures in the past ~5 years

We are well positioned to enter the RLT space

Our nanobodies are excellent carriers for radioisotope delivery to tumors and metastases

Primary tumor | Lung metastases | Discrete metastases
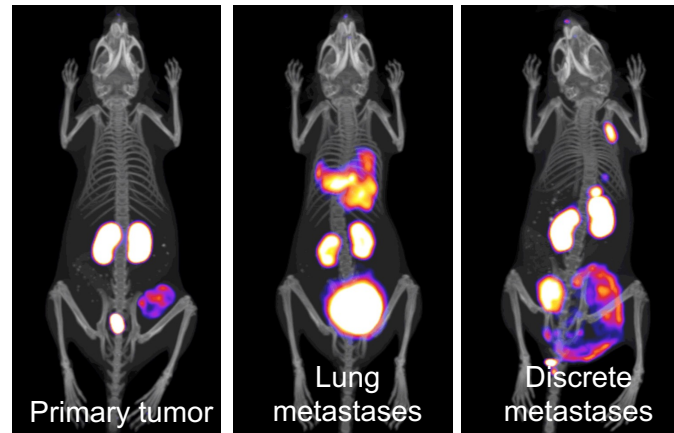
Model: LM2 TNBC model imaged with ^{64}Cu-NJB2

We can deliver therapeutic isotopes Lu-177 and Ac-225...

..to tumors and metastases via ECM-specific nanobodies

Chemistry for conjugation already standardized

We are highly differentiated by our target (ECM) and binders (nanobodies)

Our approach is Theranostic - allowing both detection and treatment of solid tumors and their metastases
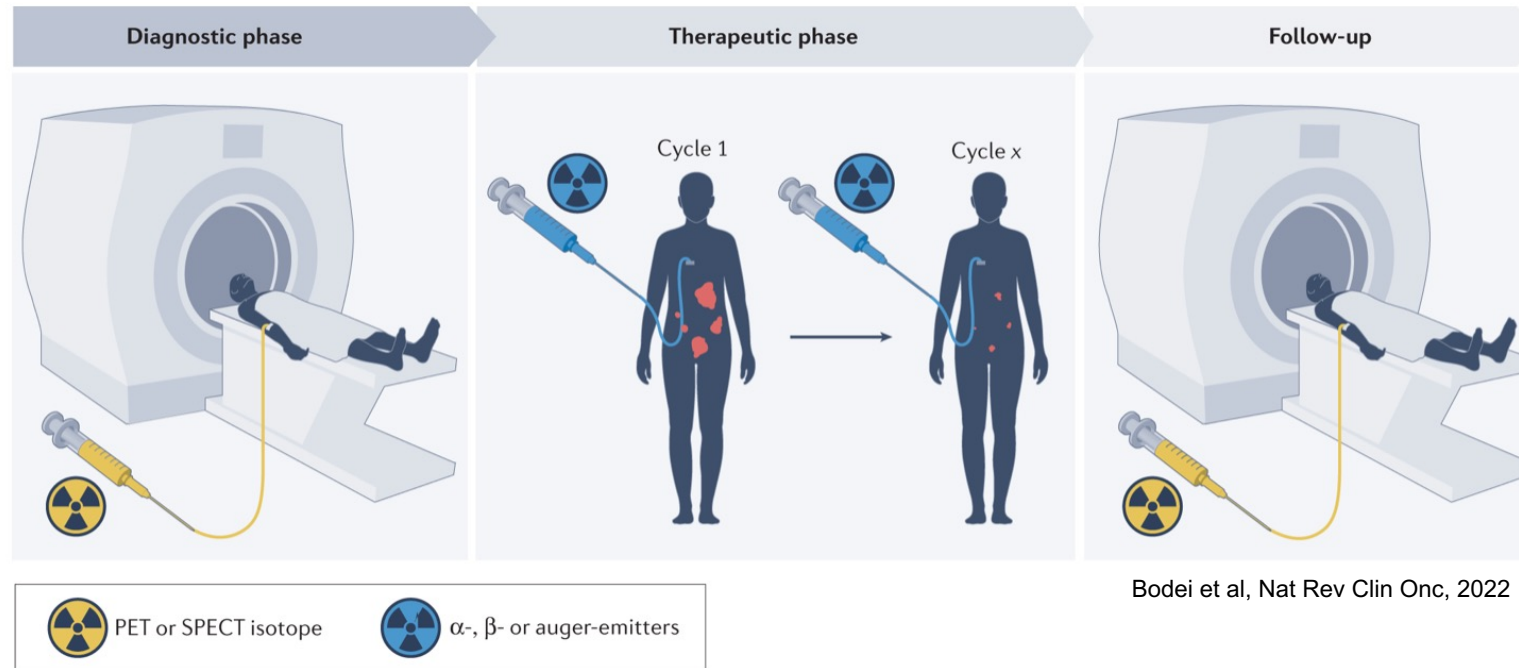
Bodei et al, Nat Rev Clin Onc, 2022

FDA Approved Theranostic in Prostate Cancer

Therapy: ^{177}Lu-PSMA-617
Imaging: ^{68}Ga-PSMA-11

FDA Approved Theranostic in GEP-NETS

Therapy: ^{177}Lu-DOTATATE
Imaging: ^{68}Ga-DOTATATE

GEP-NETs (gastroenteropancreatic neuroendocrine tumors); PSMA (prostate-specific membrane antigen)

Timeline for lead asset and series A raise

Research and Discovery

Preclinical development

Clinical trials

Platform expansion

2022
Matrisome Bio incorporation

2023
Seed funding

THE ENGINE VENTURES

BOLD CAPITAL

PACIFIC 8 VENTURES

Series A

2027
IND submission Lead asset

2027/2028
First-in-human trial data Platform expansion
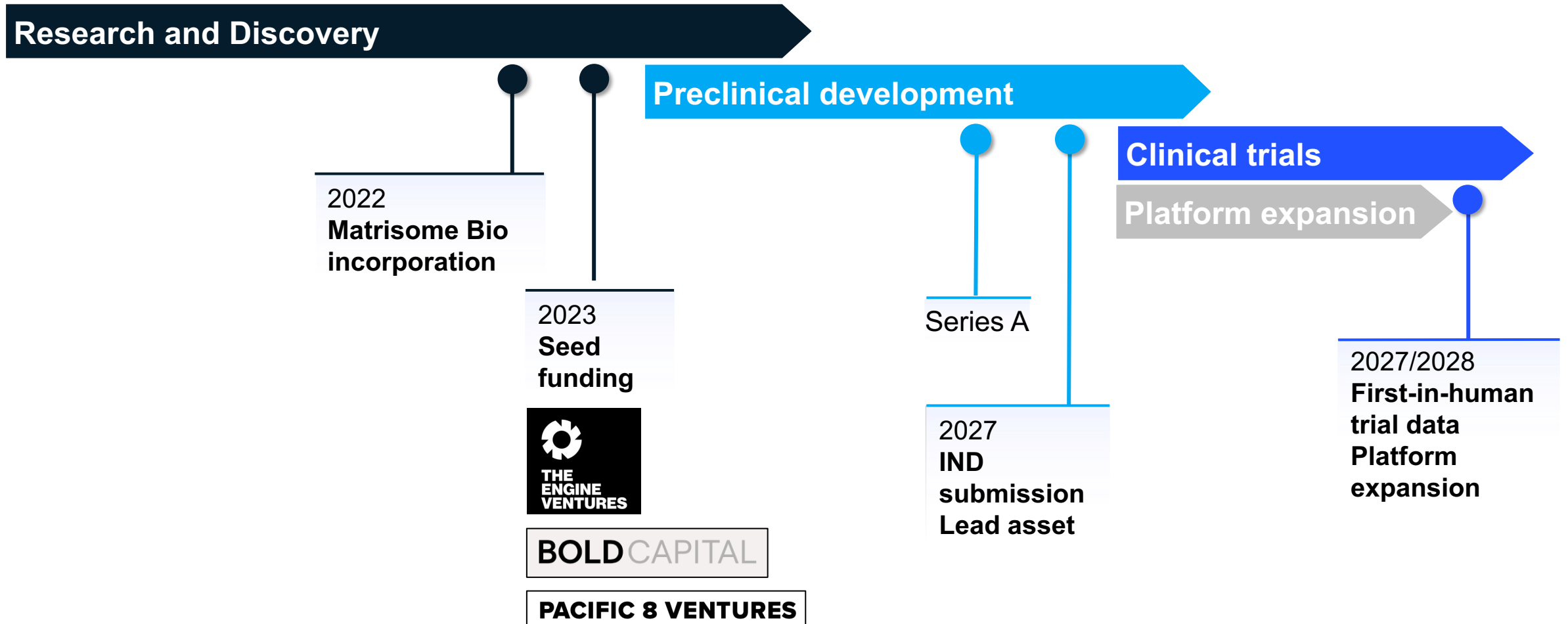
Matrisome Bio is highly differentiated

ECM focus
and expertise

Tumor agnostic

Proprietary anti-ECM
nanobody libraries

Therapeutic
conjugates

Nanobodies

Products

Antibodies/
antibody
fragments

Low   High

ECM focus

☐ Therapeutic focus on oncology +

⬚ Other focus areas – diagnostics, research tools, non-oncology therapeutics

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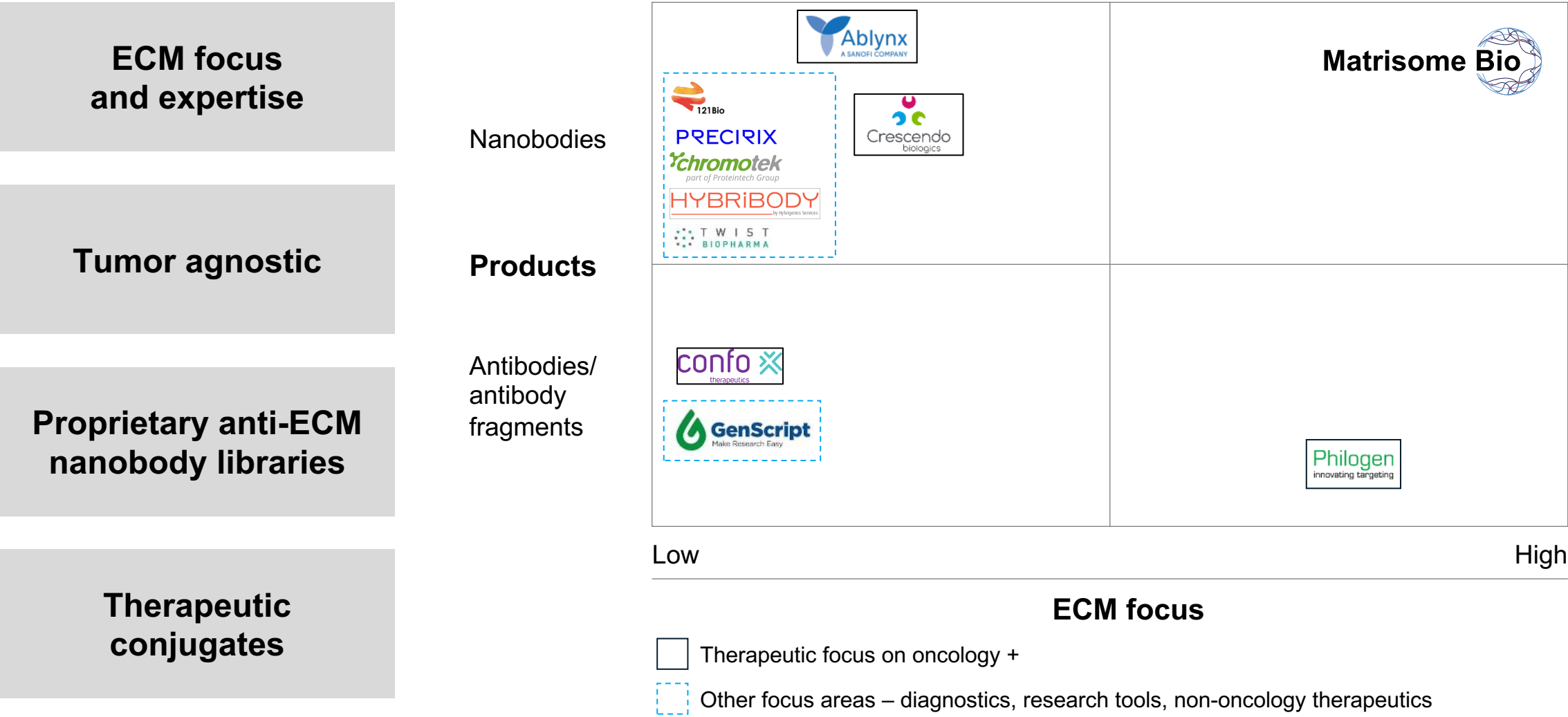
The Matrisome Bio team

Co-founders

Noor Jailkhani, PhD
CEO, Matrisome Bio

Richard Hynes, PhD, FRS
Professor, MIT & HHMI (Alum)
Lasker Award 2022

Sangeeta Bhatia, MD, PhD
Professor, MIT & HHMI

Board Chairman

Tony de Fougerolles, PhD
Ex-CEO Evox, Ex-CSO Moderna
& Ablynx, Ex VP Alnylam

Strategic Advisory Board

Robert Langer, ScD
MIT, Institute Professor
"The Edison of Medicine"

Chaitanya Divgi, MBBS, MS
Former Director, Nuclear Medicine
Columbia University

Padmanee Sharma, MD, PhD
Professor, Medical Oncology
MD Anderson Cancer Center

R&D Team

Dennis Zimmermann, PhD
Associate Director

Alice Desbuleux, PhD
Senior Scientist

Devyn Luden
Research associate

Suma Prabhu, PhD
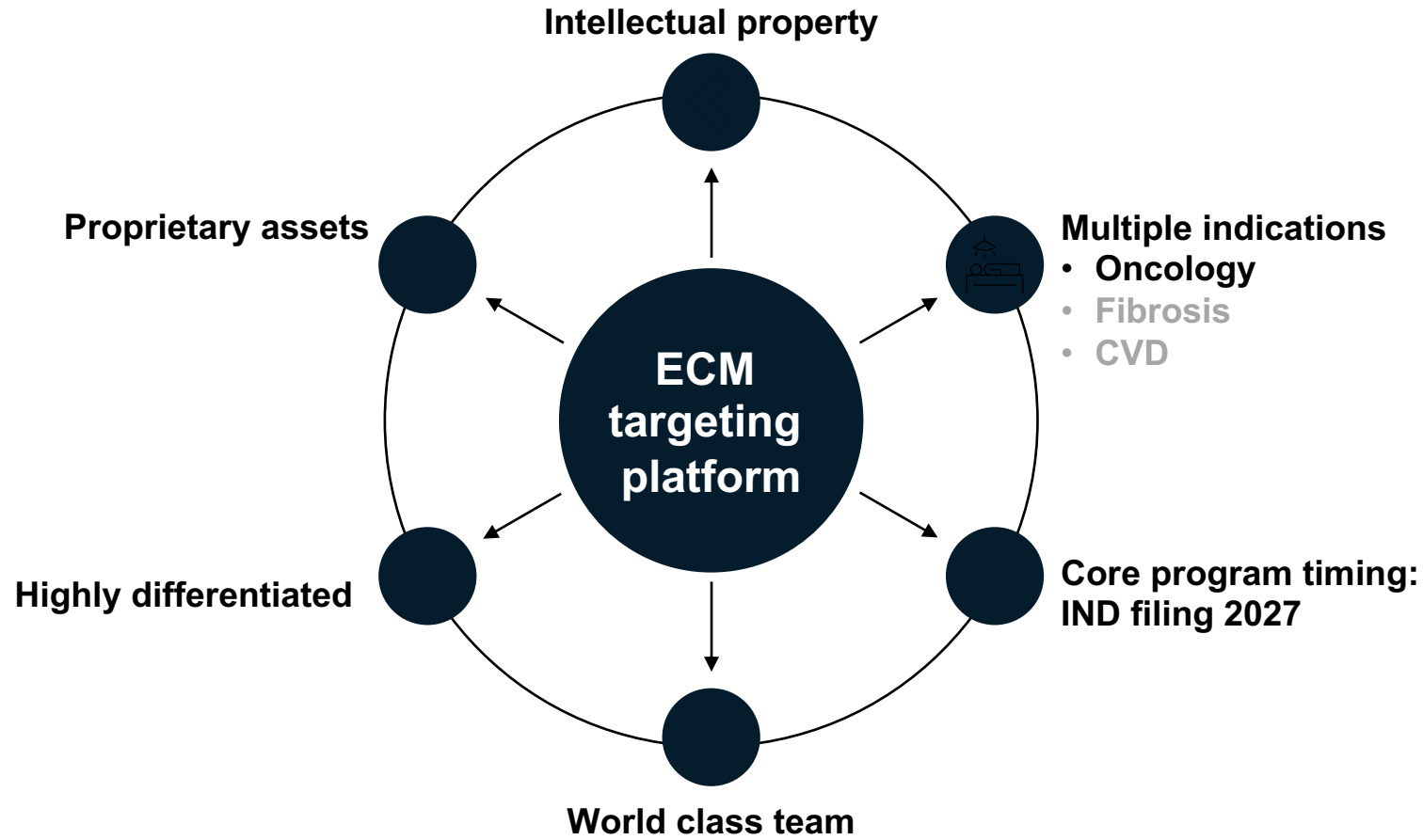Senior Scientist

CBO

Tad Stewart
CBO

G&A Team (fractional)

Precillia Redmond
Chief People Officer
Maeve Consulting

Julie Andriolo
Chief Financial Officer
The Rev Group

Lasker Award

Massachusetts Institute of Technology · HARVARD UNIVERSITY · COLUMBIA UNIVERSITY · Penn University of Pennsylvania · hhmi · MD Anderson Cancer Center · Fusion Pharmaceuticals Inc.

Our mission is to change the landscape of targeted therapies across chronic diseases (multi-billion TAM)

Intellectual property

Proprietary assets

ECM targeting platform

Multiple indications
- **Oncology**
- Fibrosis
- CVD

Highly differentiated

Core program timing: IND filing 2027

World class team

Seed stage milestones:

- **Build the team**

- **Build the core program**

- **Explore partnerships**

Thank you!

Noor Jailkhani
noor@matrisomebio.com