Monopar Therapeutics Inc.
Nasdaq: MNPR

March 2024

Monopar Therapeutics

Disclaimer, Forward-Looking Statements

This presentation contains forward-looking statements, which express the current beliefs and expectations of management, within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect Monopar's current beliefs and expectations. Forward-looking statements are not guarantees of future performance. These forward-looking statements rely on a number of assumptions concerning future events and are subject to a number of risks, uncertainties, and other factors, many of which are outside of our control. All statements, other than statements of historical facts, contained in this presentation, including statements regarding future events, including statements relating to our business strategy, our clinical development plans, our ability to obtain the substantial capital we require, our plans to secure strategic partnerships and to build our pipeline, our clinical trials and their projected timeline, the efficacy and toxicity of our product candidates, potential new intellectual property, our plans, objectives, expectations and intentions, are forward-looking statements.

These forward-looking statements can be identified by the use of forward-looking terminology, including, but not limited to, the terms "believe," "estimate," "project," "plan," "anticipate," "expect," "seek," "predict," "continue," "possible," "intend," "may," "might," "will," "could," would" or "should" or, in each case, their negative, or other variations or comparable terminology. They appear in a number of places throughout this presentation and include statements regarding our intentions, beliefs or current expectations concerning, among other things, our product candidates, research and development and clinical trial plans, commercialization objectives, prospects, strategies, the industry in which we operate and potential collaborations. We derive many of our forward-looking statements from our operating budgets and forecasts, which are based upon many detailed assumptions. While we believe that our assumptions are reasonable, we caution that it is very difficult to predict the impact of known factors, and, of course, it is impossible for us to anticipate all factors that could affect our actual results. Moreover, we operate in an evolving environment. New risks and uncertainties may emerge from time to time, and it is not possible for management to predict all risks and uncertainties. Except as required by applicable law, we assume no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. You are urged to carefully review and consider the various disclosures in our most recent annual report on Form 10-K, our most recent Form 10-Q and our other public filings with the SEC at www.sec.gov/edgar.shtml, especially the risk factors detailed therein.

Our Company is Focused on Innovative Treatments For Cancer

Primary Approach: Radiopharma to Illuminate and Eliminate Cancers

Personalized Medicine combined with Precision Oncology

- Develop **radiodiagnostic** to light up an individual's cancer
- Develop **radiotherapeutic** (Ac-225 or Lu-177) to precisely target and destroy the illuminated cancer – ***if we can illuminate… we can eliminate***

Setup for Success

- Lead radiopharmaceutical candidate, MNPR-101-Zr, approved to initiate Phase 1
- Strategic radiopharmaceutical collaboration in place with NorthStar Medical Radioisotopes
- Patent filed on high-yield linker for Ac-225, up to 4x higher yield than widely used DOTA linker

Experienced Team

STRONG MANAGEMENT TEAM WITH A HISTORY OF SUCCESS IN DRUG DEVELOPMENT

Christopher Starr, PhD – Co-Founder, Exec Chairman

- Co-Founder & Former CEO, Raptor Pharma (Nasdaq: RPTP), acquired by Horizon for $800M
- Co-Founder, Former CSO, BioMarin (Nasdaq: BMRN)

Andrew Cittadine, MBA – Chief Operating Officer

- Co-Founder, medical imaging firm Sensant (Siemens)
- Co-Founder, Fmr CEO, American BioOptics (Olympus)
- Stanford BS & MS, Kellogg MBA

Holli Carlson – Director, Clinical Operations

- Clinical leadership in multiple US and EU clinical studies for large and small biopharma
- Senior exec in venture-backed biopharma companies

Chandler Robinson, MD, MBA, MSc – Co-Founder, CEO

- Co-Founder, Tactic Pharma and Wilson Tx; lead drug Decuprate acquired by Alexion for $764M
- Stanford MD, Fulbright and Gates Scholar, published in Science

Kim Tsuchimoto – Chief Financial Officer

- Former CFO, Raptor Pharma
- Former VP, Treasurer at BioMarin

Patrice Rioux, MD – Acting Chief Medical Officer

- Former Chief Medical Officer, Raptor Pharmaceuticals
- Responsible for securing regulatory approval of PROCYSBI® in the US and EU

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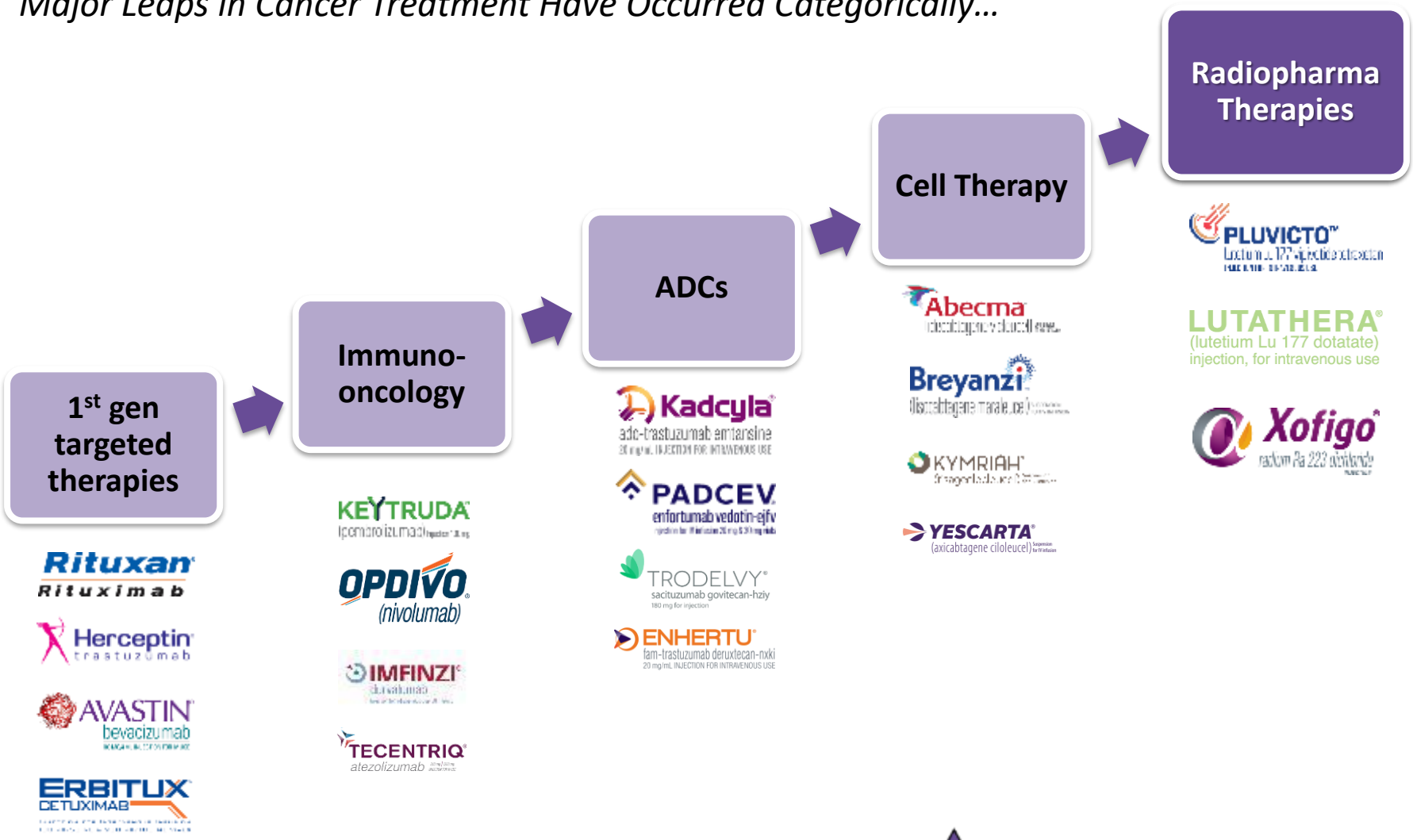
Next Wave in Cancer Treatment: Radiopharma

Major Leaps in Cancer Treatment Have Occurred Categorically…



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Active Emerging Space

NOVARTIS

$2.1B
acquisition

ENDOCYTE

$3.9B
acquisition

Advanced Accelerator Applications

Bristol Myers Squibb™

$4.1B
acquisition

RayzeBio

Lilly

$1.4B
acquisition

POINT BIOPHARMA

AKTIS ONCOLOGY

$161M
series A

MERCK

MPM

EcoR1 CAPITAL

Abdera Therapeutics

$142M
series A-B

Viking

venBio

RTW Investments

Fusion Pharmaceuticals Inc.

$373M
series A-IPO

TPG BIOTECH

VARIAN medical systems

Johnson & Johnson

Components and Mechanism of Action of Radiopharmaceuticals

Radiopharmaceutical Components

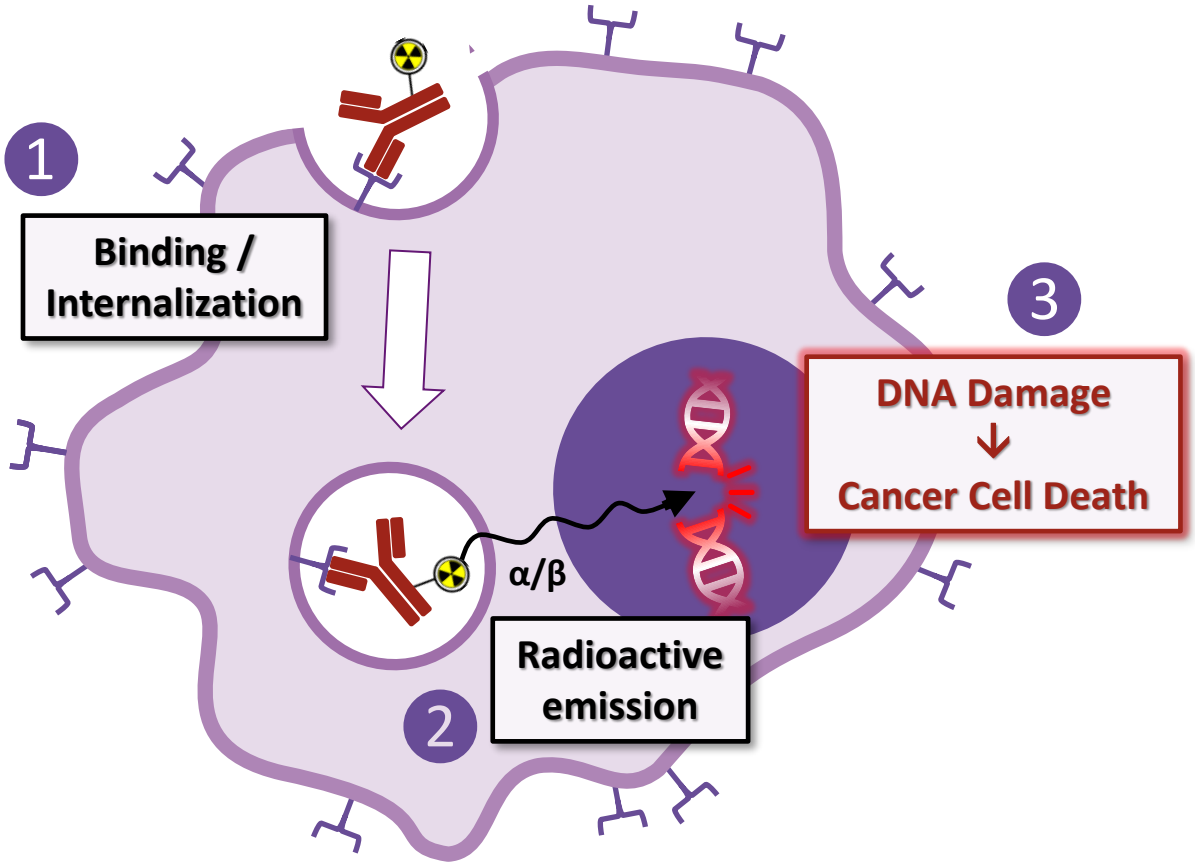
Tumor Marker
High amounts in cancer, rare in normal tissue.

Targeting Agent
Targets marker associated with cancer.

Linker/Chelator
Links Isotope to Targeting Agent

Isotope
Zr-89: *Imaging*
Ac-225 *or* ***Lu-177:*** *Therapy*

Simple Mechanism of Action



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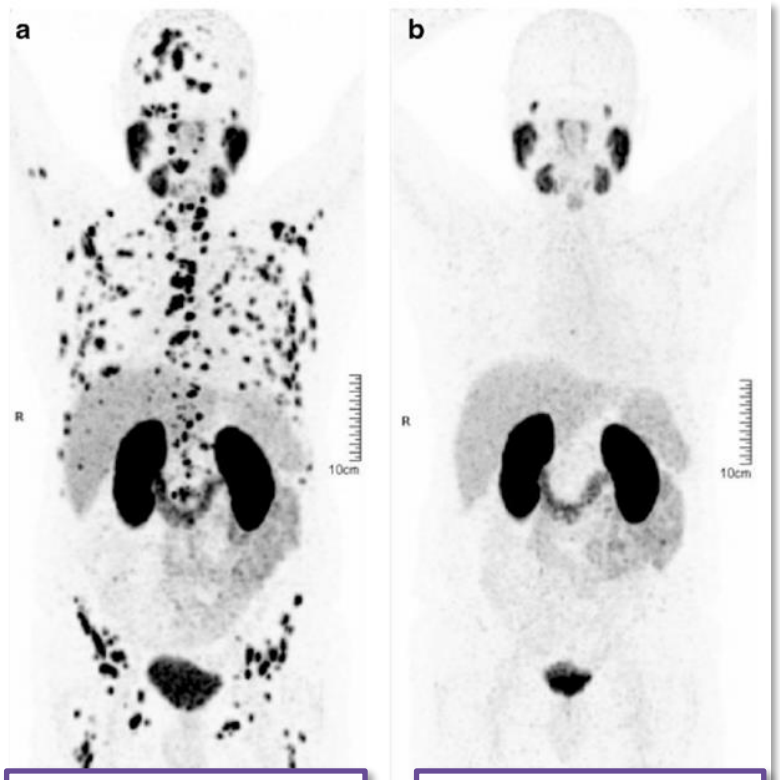
Validated Treatment Approach, Which Has Worked Where ADC's Failed

Novartis' Pluvicto® for mCRPC



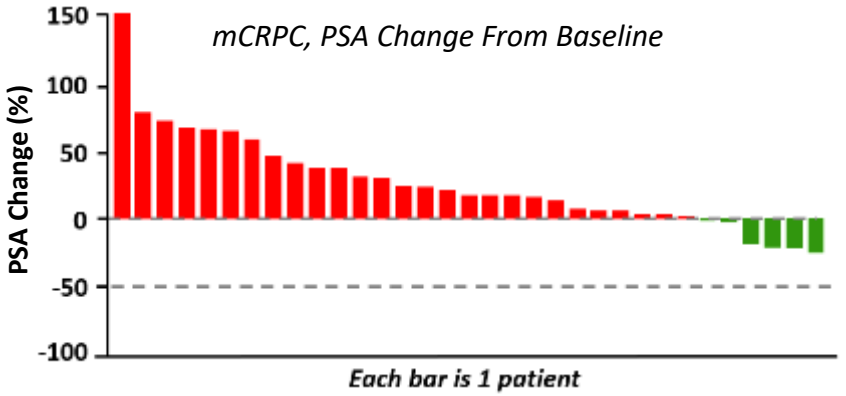
BEFORE TREATMENT

PSA = 50 ng/ml

AFTER TREATMENT

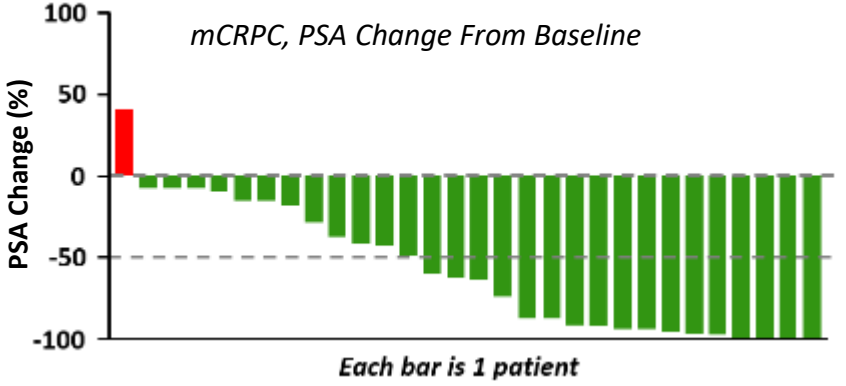
PSA = 0 ng/ml
-100%

PSMA-targeted Drug Conjugate: Failure



VS.

PSMA-targeted Radiopharmaceutical: Success



García-Figueiras et al. Insights into Imaging (2019)
Morris et al., J Clin Oncol, 35, suppl; abstr 5038 (2017)
Hofman et al., Lancet Oncol 19:825-33 (2018)

PSMA – Prostate specific membrane antigen
PSA – Prostate specific antigen
mCRPC – Metastatic castration resistant prostate cancer

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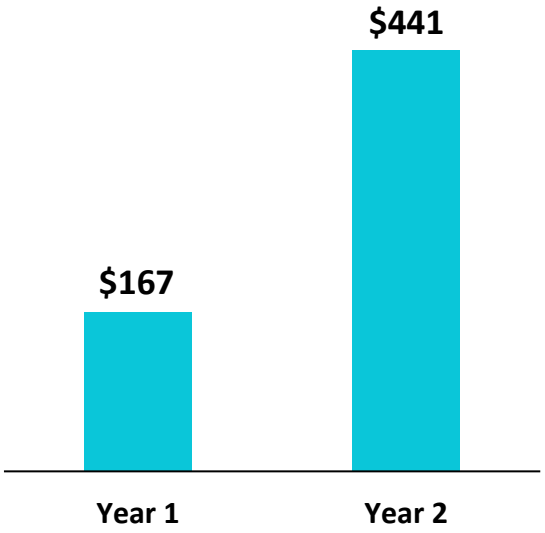
Rapid Market Uptake of Newly Approved Radiopharmaceuticals

Lutathera® (Lu-177 Dotatate)

2-year Post-Approval Uptake ($M)



US Pricing Estimate: **~$230,000**

Pluvicto® (Lu-177 PSMA-617)

Q4 2023 Sales: **$273 million**

US Pricing Estimate: **~$270,000**

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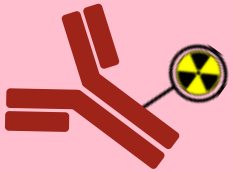
Our Development Program is Streamlined

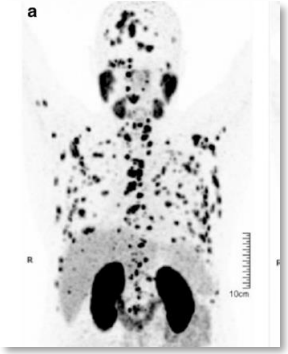
Target Selection

- Discontinued ADC's
- Generics
- Extend life of successful drugs through radiopharma

Generate imaging and therapeutic pair



Imaging + Dosimetry study



Ph I/II trial *or* Direct Ph I/III trial

TRADITIONAL DEVELOPMENT ROUTE = Potentially Years Longer and Riskier

Discovery → Lead optimization → Development Candidate → IND Enabling → Phase 1 → Phase 2 → Phase 3

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Our Radiopharma Advantage

Capital Efficient

Learn quickly if a drug doesn't work (imaging)

Less expensive than CAR-T, gene therapy

+

Fast Development

Modest pre-clinical work

Rapid (FIH) studies, with quick feedback (images)

Standardized Toolkit

+

De-Risked Trials

Poor image = poor efficacy (patient selection)

Potential **toxicities visualized**

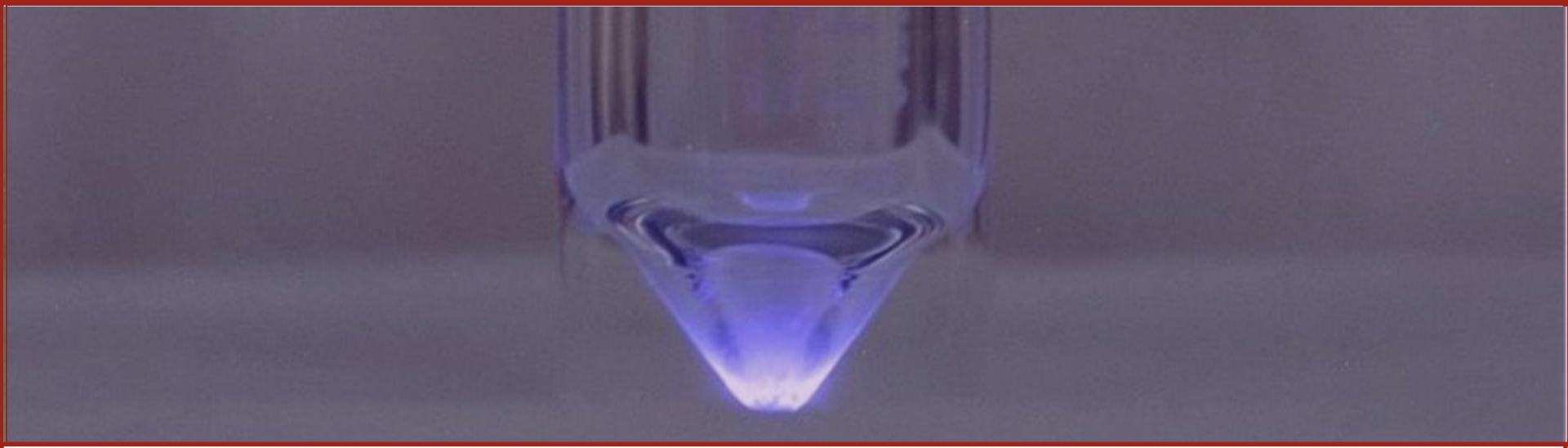
=

HIGH VALUE, LOWER RISK

SUCCESS RATE SHOULD BE HIGHER THAN TRADITIONAL DRUG DEVELOPMENT ROUTE

MNPR-101

Our Lead Radiopharma Candidate



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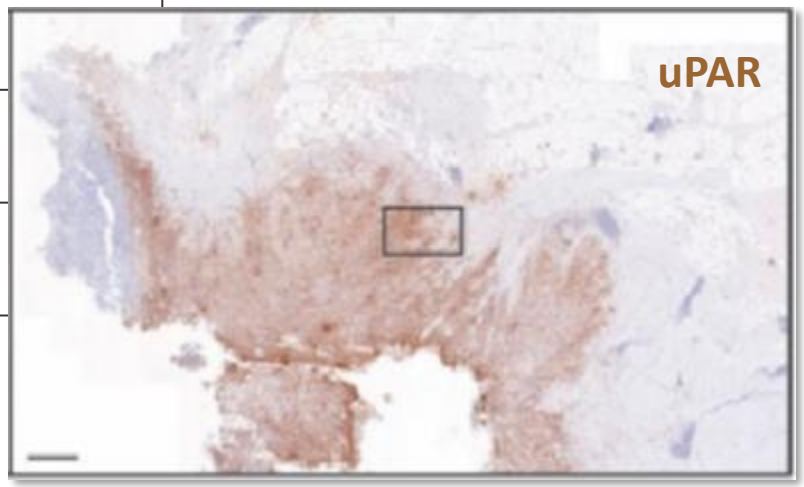
MNPR-101: A monoclonal antibody that selectively targets uPAR

uPAR: a promising target. Highly expressed in several aggressive deadly cancers, but rarely expressed in adult normal tissues

Cancer Type	% Patients with uPAR Expression
Breast[1]	97%
Bladder[2]	89%
Pancreatic[3]	87%
Colorectal[4]	85%



Urothelial cell carcinoma showing uPAR expression in brown[5]

[1]*Dublin et al., Am J Pathol. (2000)*
[2]*Dohn et al., Urol. Oncol, (2015)*
[3]*de Geus et al., Cancer (2017)*
[4]*Boonstra et al., BMC Cancer (2014)*
[5]*Baart et al. , Eur J Cancer (2021)*

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uPAR: A Well Researched Target

uPAR: An Essential Factor for Tumor Development

Tao Lv[1,2✉#], Ying Zhao[1#], Xinni Jiang[3#], Hemei Yuan[1], Haibo Wang[1,2], Xuelin Cui[1], Jiashun Xu[1], Jingye Zhao[1], Jianlin Wang[4✉]

Enhanced expression of urokinase plasminogen activator and its receptor in pancreatic carcinoma

D Cantero[1], H Friess[1], J Deflorin[1], A Zimmermann[2], M-A Bründler[2], E Riesle[1], M Korc[3] and M W Büchler[1]

Urokinase Plasminogen Activator Receptor (uPAR): A Potential Indicator of Invasion for In Situ Breast Cancer

Daniel P. Guyton [1], Douglas M. Evans, Kimberly D. Sloan-Stakleff

Review

The Urokinase Receptor (uPAR) as a "Trojan Horse" in Targeted Cancer Therapy: Challenges and Opportunities

Virginia Metrangolo [1,2], Michael Ploug [1,2] and Lars H. Engelholm [1,2,*]

Urokinase type plasminogen activator receptor (uPAR) as a new therapeutic target in cancer

Nunzia Montuori[1], Ada Pesapane[1], Francesca W Rossi[1], Valentina Giudice[2], Amato De Paulis[1], Carmine Selleri[2] and Pia Ragno[3]

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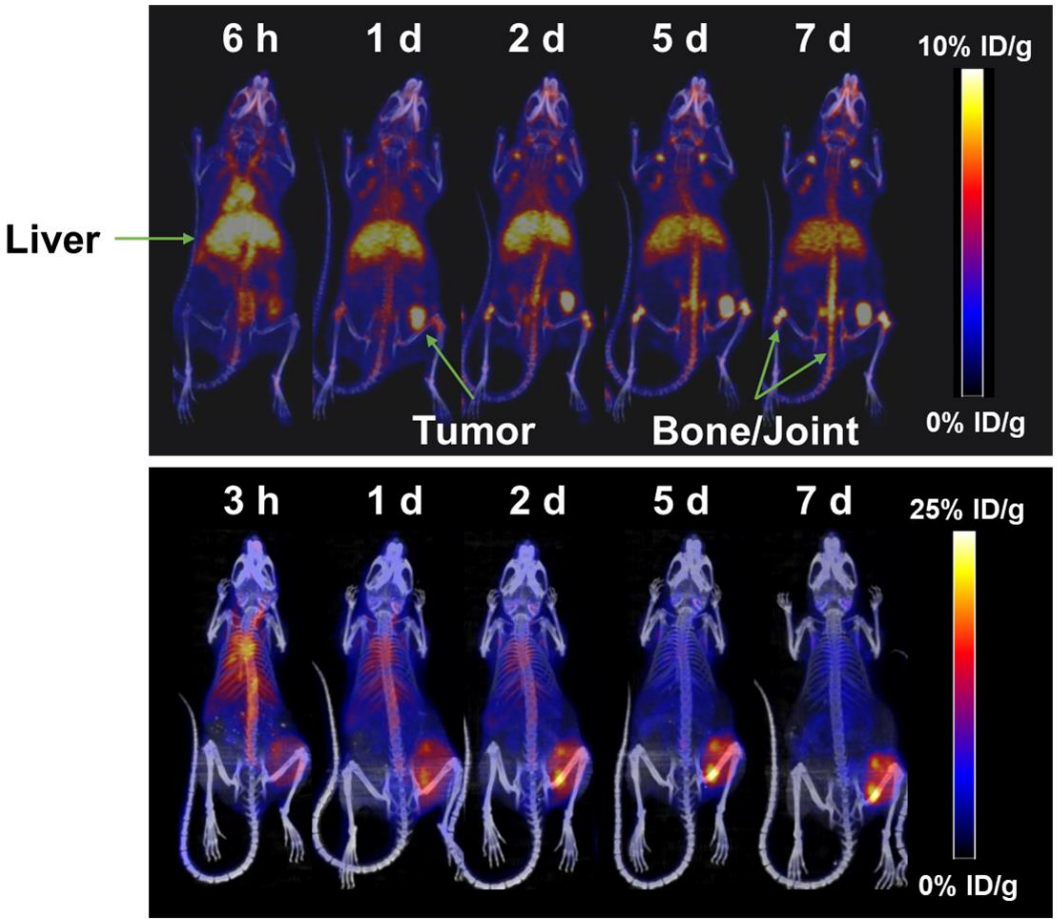
MNPR-101-Zr Radiodiagnostic: Optimization of Biodistribution

In Pancreatic Cancer (MIA PaCa-2 cells) Xenograft

PET imaging time points after injection



Before Optimization

After Optimization

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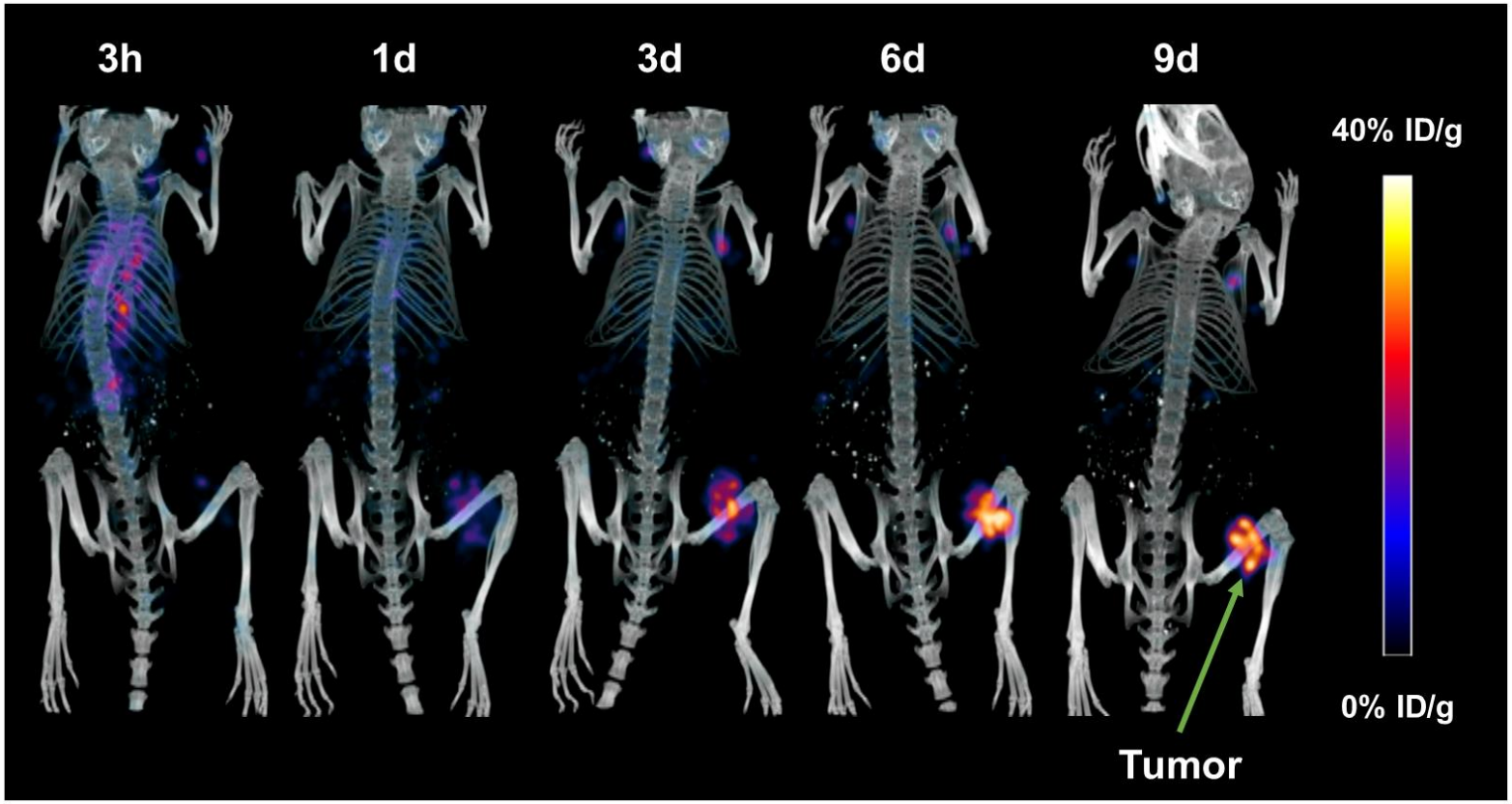
Biodistribution of MNPR-101 with Therapeutic Radioisotope Lu-177

In Pancreatic Cancer (MIA PaCa-2 cells) Xenograft

SPECT imaging time points after injection



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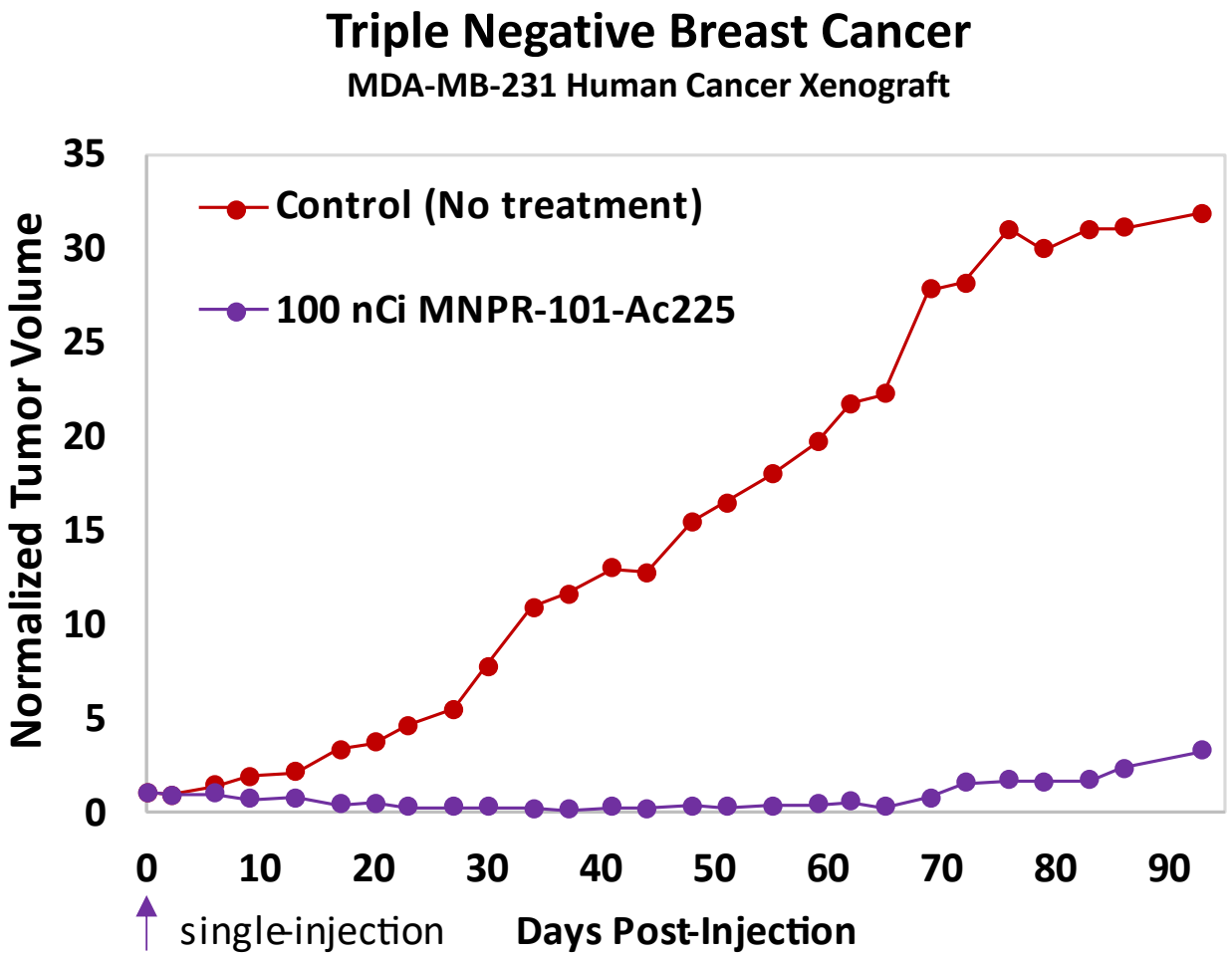
MNPR-101-Ac225 Tumor Efficacy Study



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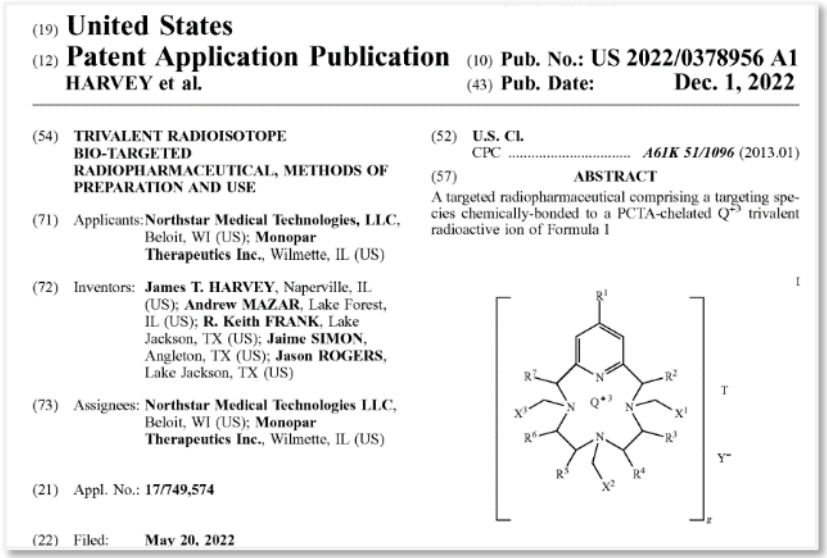
PCTA: Promising Linker for Ac-225, Patent Filed

Chelator (Chelators per Antibody)	Ac-225 Binding Yield
PCTA (12)	**98.8%**
DOTA (12)	21.6%



(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2022/0378956 A1**

HARVEY et al. (43) **Pub. Date: Dec. 1, 2022**

(54) **TRIVALENT RADIOISOTOPE BIO-TARGETED RADIOPHARMACEUTICAL, METHODS OF PREPARATION AND USE**

(71) Applicants: **Northstar Medical Technologies, LLC**, Beloit, WI (US); **Monopar Therapeutics Inc.**, Wilmette, IL (US)

(72) Inventors: **James T. HARVEY**, Naperville, IL (US); **Andrew MAZAR**, Lake Forest, IL (US); **R. Keith FRANK**, Lake Jackson, TX (US); **Jaime SIMON**, Angleton, TX (US); **Jason ROGERS**, Lake Jackson, TX (US)

(73) Assignees: **Northstar Medical Technologies LLC**, Beloit, WI (US); **Monopar Therapeutics Inc.**, Wilmette, IL (US)

(21) Appl. No.: **17/749,574**

(22) Filed: **May 20, 2022**

(52) **U.S. Cl.**
CPC *A61K 51/1096* (2013.01)

(57) **ABSTRACT**

A targeted radiopharmaceutical comprising a targeting species chemically-bonded to a PCTA-chelated Q^{+3} trivalent radioactive ion of Formula I

I

Monopar has demonstrated that PCTA is up to **4x more efficient** at binding actinium than industry-standard DOTA

Patent filed protecting the use of **PCTA for binding Ac-225** in radiopharmaceuticals

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First-in-Human MNPR-101-Zr Phase 1 Dosimetry Clinical Trial

MTIC | Melbourne Theranostic Innovation Centre

MNPR-101-Zr Phase 1 dosimetry clinical trial to be initiated in the near future at MTIC with Prof. Rod Hicks as the lead investigator

The trial will enroll up to 12 patients and will evaluate the tumor uptake, biodistribution, and safety of MNPR-101-Zr

Thank you!

March 2024

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