Monopar Therapeutics Inc.
Nasdaq: MNPR

June 2025

Monopar Therapeutics

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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.

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Overview of Monopar Therapeutics

- Clinical-stage biotechnology company developing ALXN1840 for Wilson Disease and MNPR-101 as a novel radiopharmaceutical targeting uPAR for oncology
- MNPR-101-Zr is a PET imaging agent in Phase 1 to illuminate uPAR-positive cancers
- MNPR-101-Lu (Phase 1) & MNPR-101-Ac (late preclinical) are radiopharmaceutical therapies for aggressive cancers
- Team with experience in all phases of drug development and commercialization including CEO who previously led development of ALXN1840 and Executive Chairman who co-founded BioMarin and Raptor Pharma
- Upcoming MILESTONES: Targeting NDA Filing for **ALXN1840** in early 2026, presenting additional ALXN1840 clinical data in 2H 2025

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 – Vice President, 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

Quan Vu – Chief Financial Officer

- Former CFO & CBO, Ocugen
- Senior roles in operations, corporate, and financial strategy at several biopharma companies

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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Pipeline

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ALXN1840

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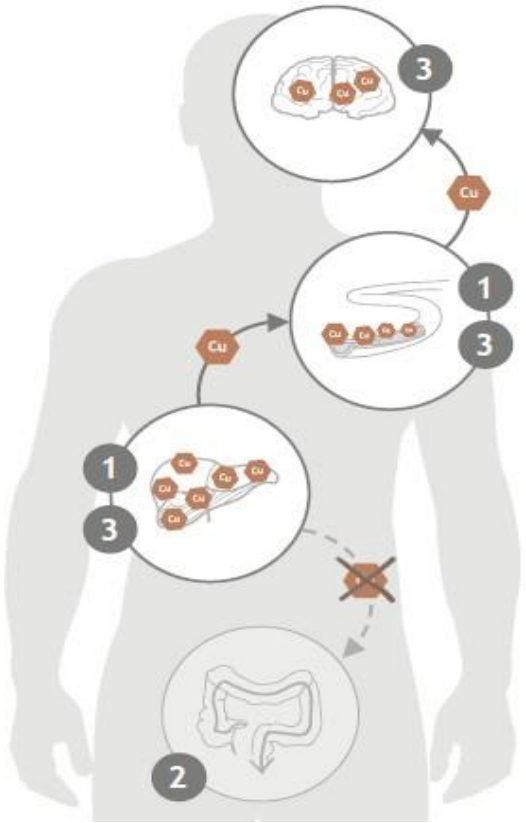
Wilson Disease Background

- **Rare genetic disorder of impaired copper (Cu) transport** with devastating hepatic and neurological consequences that requires life-long therapy
- **Caused by mutations in the ATP7B gene** that leads to excess copper accumulating in liver cells and increased levels of toxic free copper
- **Failure to clear hepatic copper** can have detrimental effects:
  - Jaundice, fluid retention, confusion and synthetic liver dysfunction increased risk of cirrhosis, liver failure, and liver cancer
  - Fatigue, pain, swelling, vomiting and upper gastrointestinal bleeding
- **Neurologic worsening** can be severe:
  - Significant neurological morbidity including problems with movement, gait, speech, and swallowing
  - Psychiatric disorders including depression, mania, irritability, psychosis and personality changes
- **Approximately 5,000 patients treated in the US**, and another 5,000 across France, Germany, Italy, UK, and Spain

Copper (Cu) balance is normally maintained in the body by hepatic excretion of excessive copper in bile. In Wilson disease there is:



1. Diminished loading of Cu onto the ceruloplasmin (Cp) protein in liver leads to suboptimal transport of Cp- bound Cu into blood
2. Diminished excretion of excess Cu through the bile into feces
3. **Increased levels of free Cu (toxic) in blood, liver, brain and other organs**

Sources: Gomes, 2016; Poujois, 2017; Merle, 2007, Beinhardt, 2014

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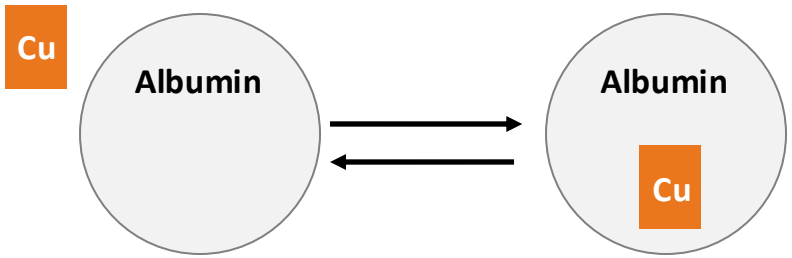
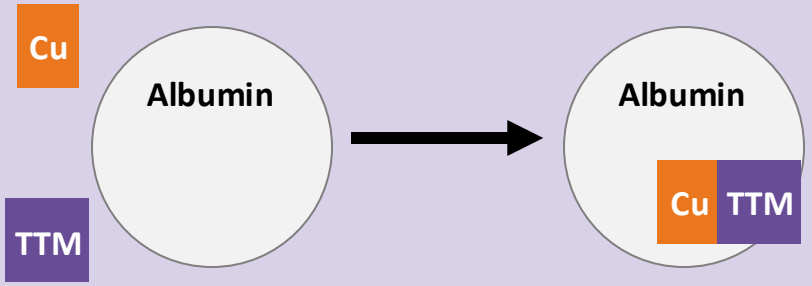
Overview of ALXN1840 for Wilson Disease

- ALXN1840 (bis-choline tetrathiomolybdate, or TTM) is an investigational, once-daily, oral small molecule
- ALXN1840 mobilizes copper and sequesters it as a tripartite complex with albumin, potentially preventing toxic free copper accumulation
- ALXN1840 has been granted Orphan Drug and Fast Track designation in the US and orphan designation in the EU
- ALXN1840 Phase 3- primary endpoint met; Phase 2- mechanism of action studies inconclusive, endpoints not met
- Targeting NDA Submission in early 2026

Without TTM, albumin can carry and release toxic copper



WITH TTM, copper is sequestered in a tripartite complex



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Phase 3 Clinical Trial: ALXN1840 Met Primary Endpoint

ALXN1840 demonstrated superior copper mobilization versus SoC

Primary Endpoint
Daily mean area under the effect-time curve (AUEC) of directly measured non-ceruloplasmin-bound copper (dNCC) from 0 to 48 weeks, ALXN1840 vs SoC

P-value	<0.0001

ALXN1840 has potential to better serve patients by addressing significant unmet needs over current standard of care, including reducing the risk of neurological deficits

More patients had neurologic improvement while fewer worsened on ALXN1840 vs SoC*

MCID Status (IIR Population)	ALXN1840	Standard of Care
Improved	**45%** (22/49)	**20%** (3/15)
Worsened	**5%** (4/74)	**17%** (5/29)

**Minimal Clinically Important Difference (MCID) is based on Standard Error of the Mean (SEM) in UWDRS III scores observed for patients with incomplete and/or intolerant response (IIR) to prior treatment. Trends using the entire Phase 3 study population and MCID = 1/3*standard deviation are similar.*

T. Litwin et al. [abstract]. Mov Disord. 2023

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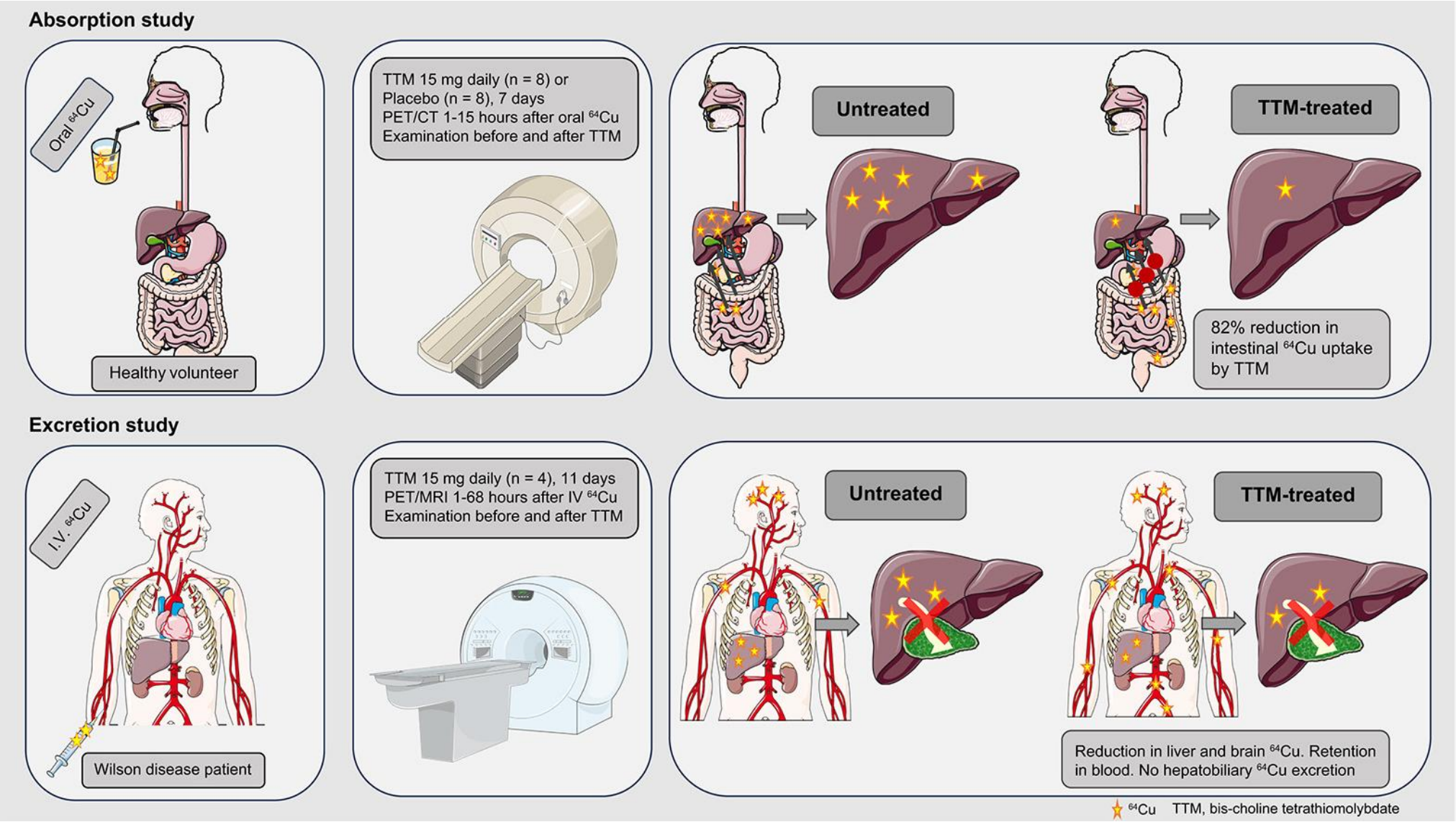
Phase 2 Absorption/Excretion Clinical Trial (1 of 4)



Kirk et al, Journal of Hepatology 2024. vol. 80, 586–595

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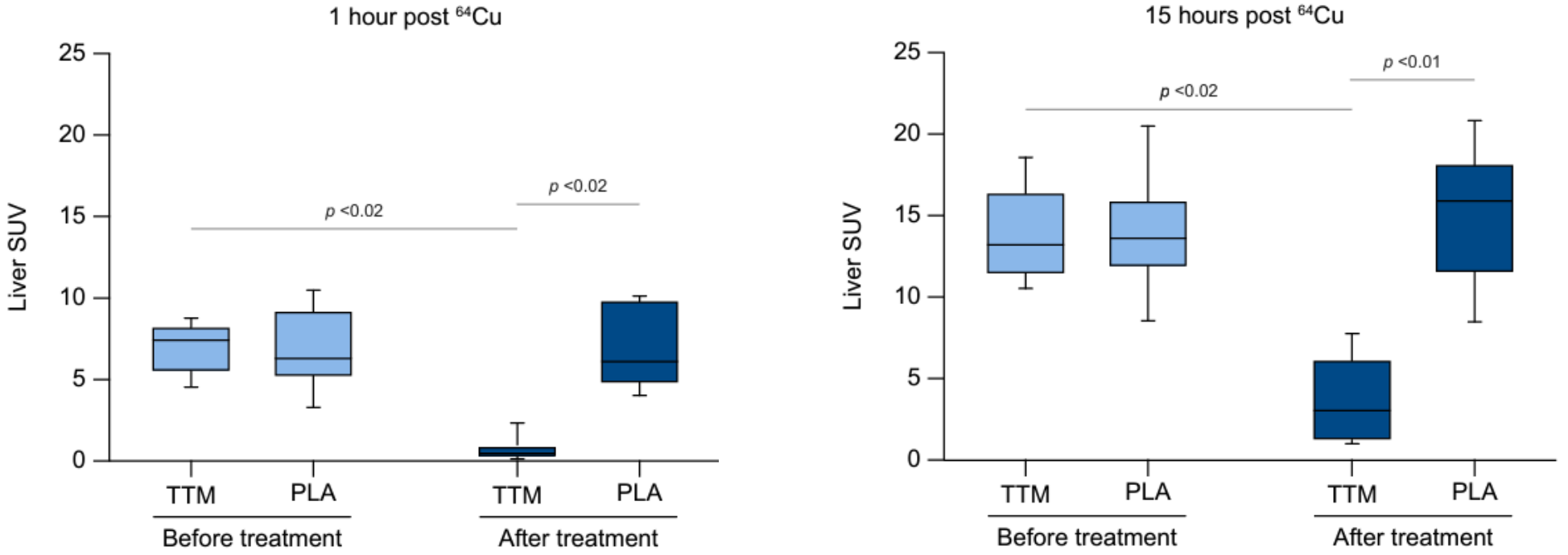
Phase 2 Absorption/Excretion Clinical Trial (2 of 4)

Absorption study: Changes in hepatic SUV



In healthy volunteers, ALXN1840 treatment blocks copper uptake in the liver from an oral dose of copper

TTM – Tetrathiomolybdate (ALXN1840) PLA - Placebo

Kirk et al, Journal of Hepatology 2024. vol. 80, 586–595

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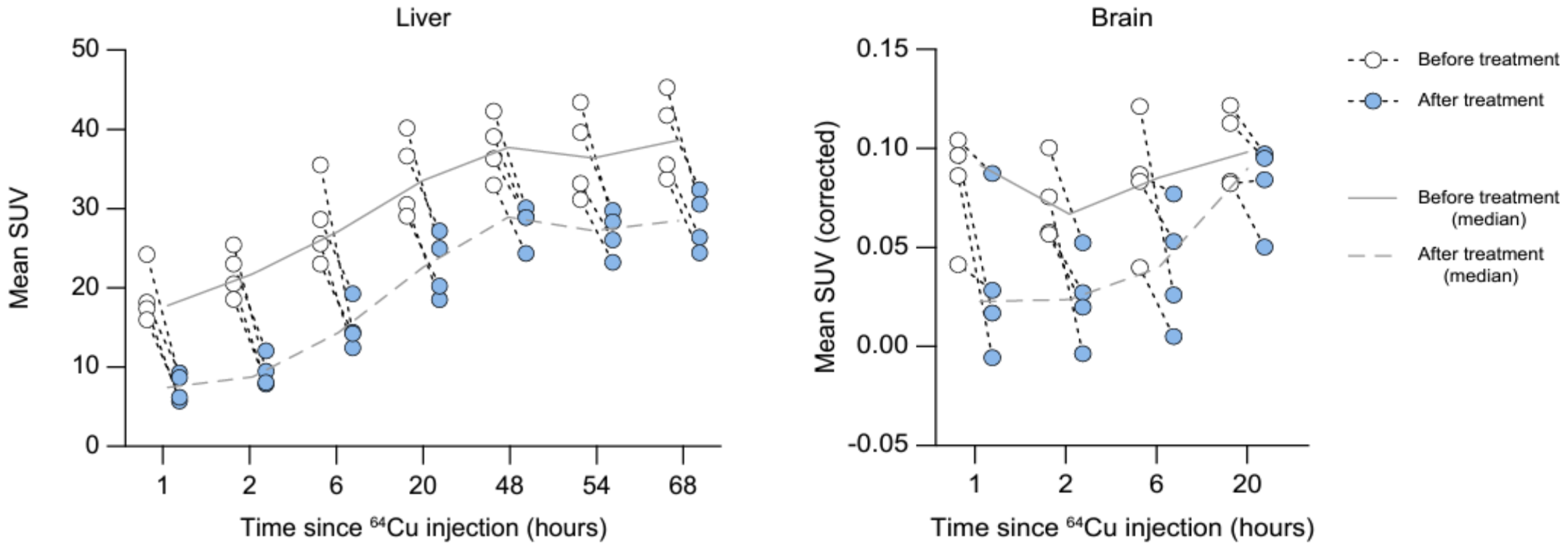
Phase 2 Absorption/Excretion Clinical Trial (3 of 4)



In Wilson Disease patients, ALXN1840 treatment reduced copper accumulation in the liver and brain

Kirk et al, Journal of Hepatology 2024. vol. 80, 586–595

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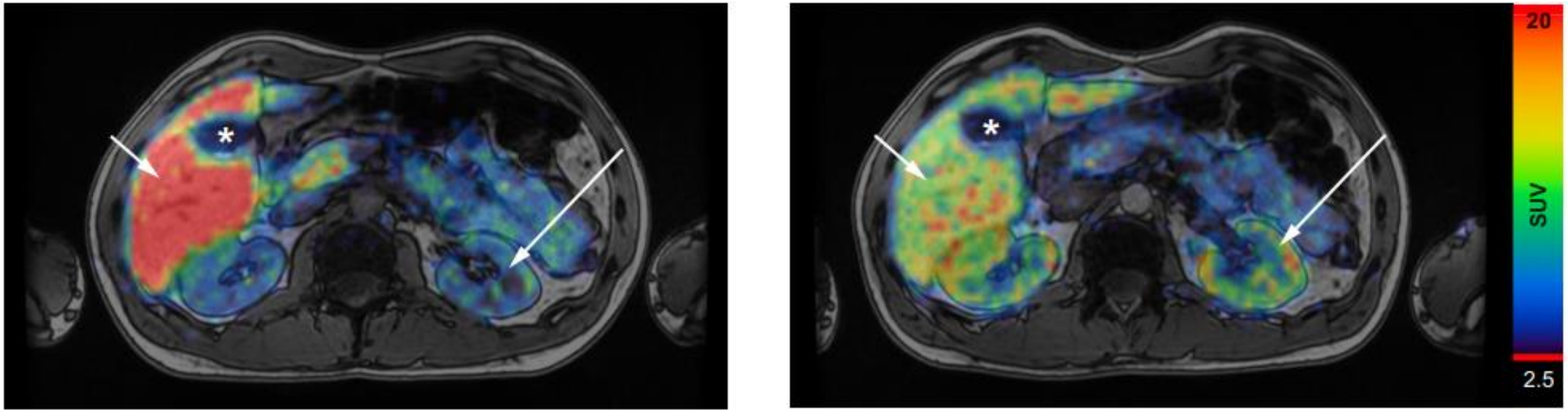
Phase 2 Absorption/Excretion Clinical Trial (4 of 4)



PET/MRI imaging 6 hours post Copper-64 administration to Wilson Disease patients before (left) and after (right) ALXN1840 treatment showing less copper accumulation in the liver

Kirk et al, Journal of Hepatology 2024. vol. 80, 586–595

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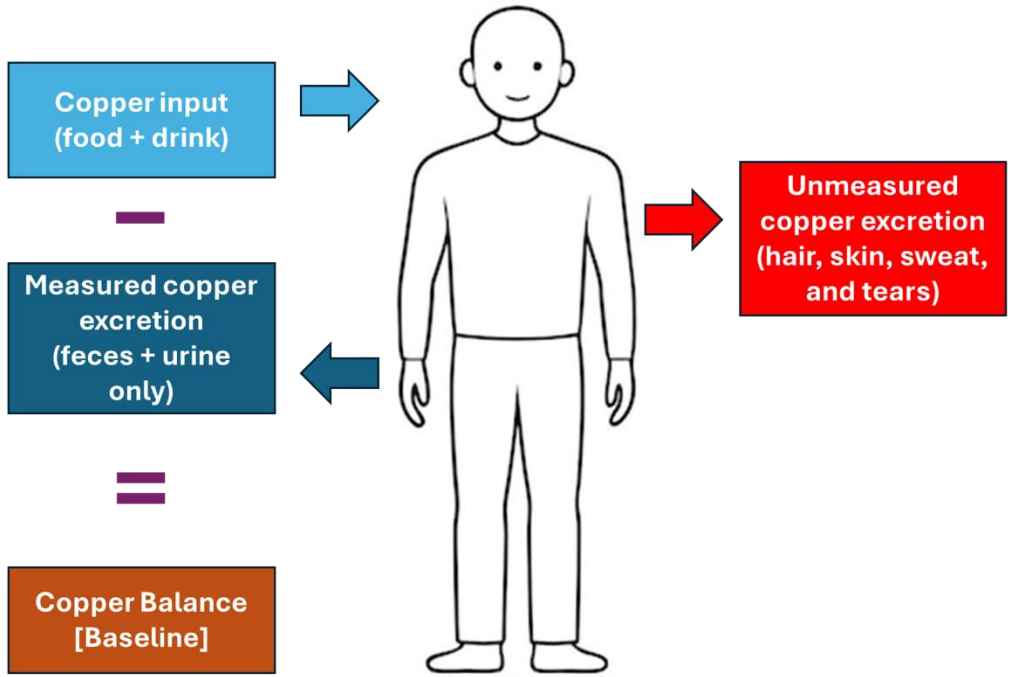
Phase 2 Copper Balance Clinical Trial (NCT04573309)

Change from baseline copper balance

Arm/Group Description	Participants who had received Wilson disease therapy for >28 days prior to enrollment were administered ALXN1840 at a dose of 15 mg/day on Day 1 through Day 28 and then increased to 30 mg/day on Day 29 through Day 39.
Overall Number of Participants Analyzed	7
Day 1 through Day 8 *Mean (Standard Deviation) | Unit of Measure: milligrams/day	-0.3780 (0.14822)
Day 25 through Day 28 *	-0.4697 (0.55770)
Day 31 through Day 35 *	-0.2650 (0.47135)
Day 36 through Day 39 *	-0.1831 (0.44589)

* Mean (Standard Deviation) | Unit of Measure: milligrams/day



For previously treated WD patients, the mean change from baseline in Cu balance remained negative for all time intervals. Despite the small sample size (N=7), it was statistically significant for Days 1-8.

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Sustained Long-term Clinical Improvement over 6-Years

Introduction

Wilson disease (WD) is a rare disorder of copper disposition. ALXN1840 (tiomolybdate choline, TMC) is a novel copper binding agent under investigation for the treatment of WD. ALXN1840 rapidly forms inert tripartite complexes with copper and albumin to prevent toxicities associated with excessive free Cu. Monopar Therapeutics is advancing ALXN1840 toward an NDA filing.

Aim & Objectives

Long-term neurologic and hepatic outcomes of WD patients in ALXN1840 clinical trials were assessed to understand the effects of years-long ALXN1840 treatment.

Method

For efficacy, data from the Ph2 WTX101-201, Ph2 ALXN1840-WD-205, and Ph3 WTX101-301 trials were pooled and analyzed (**n=255**). For safety, data from the Ph2 ALXN1840-WD-204 trial was also included (**n=266**). Median duration on ALXN1840 treatment was **961 days** (2.63 years) and **943.5 days** (2.58 years) for the efficacy and safety datasets, respectively.

Results

ALXN1840 Demonstrates Sustained Copper Mobilization

Table 1: Cu Mobilization on ALXN1840

Study Week	N	Plasma dNCC (µmol/L)
0	250	1.199
48	214	2.949
312	18	3.302

dNCC: *directly measured non-ceruloplasmin-bound copper*

Efficacy

Unified Wilson Disease Rating Scale Results Show Long-term Benefit

Fig 1: UWDRS Part II (Patient-reported)

Least squares mean and standard error – Ph2 & Ph3

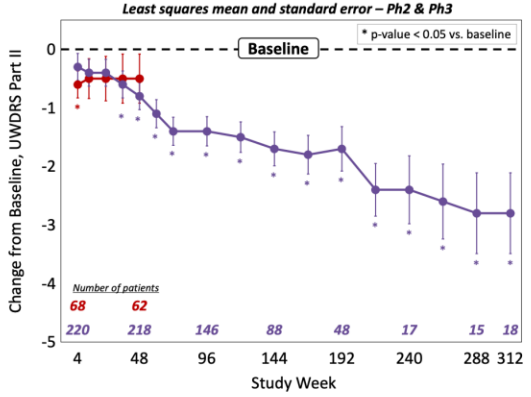
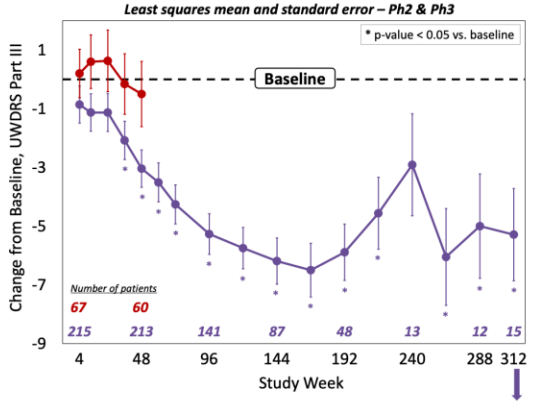


Fig 2: UWDRS Part III (Physician-assessed)

Least squares mean and standard error – Ph2 & Ph3

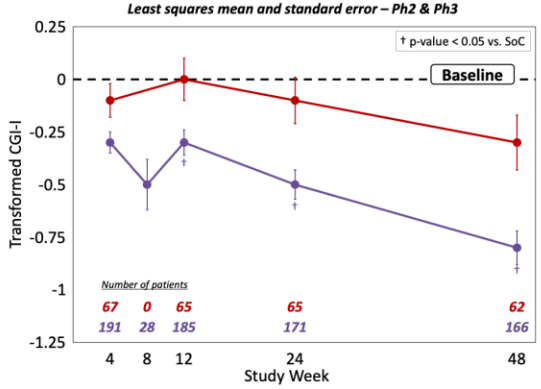


ALXN1840 Standard of Care

CGI-I & TSQM-9 Show Disease Improvement, Patient-Reported Benefit

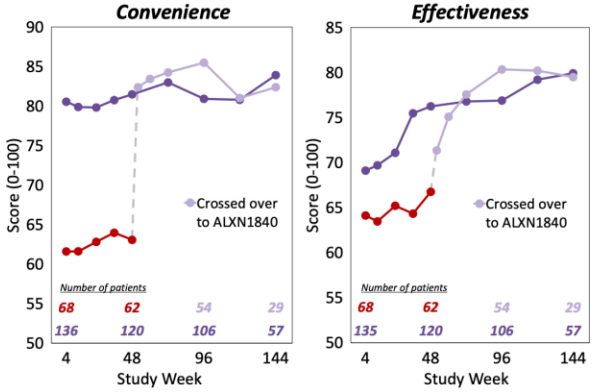
Fig 3: Transformed CGI-I By Visit

Least squares mean and standard error – Ph2 & Ph3



Clinical Global Impression-Improvement 7-point Scale

Fig 4: TSQM-9 Treatment Satisfaction Scores – Ph3



Treatment Satisfaction Questionnaire for Medication-9

Safety

ALXN1840 has a Favorable Safety Profile

Table 2: Serious Adverse Events (SAEs) on ALXN1840

data thru 01-Sep-2022

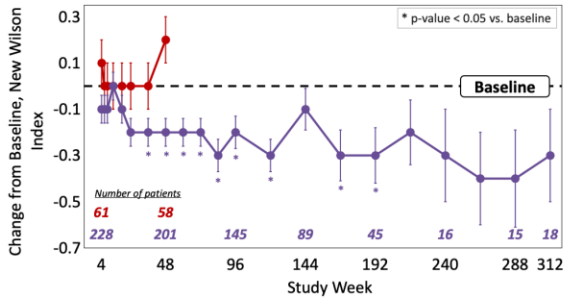
N	266
Patient-years (PYs)	645.6
Patients with any ALXN1840-related SAEs	13 (4.9%)
Renal/Urinary System-related SAEs	0 (0%)
Liver-related SAEs	8 (3.0%)

- Only 2 patients (0.8%) had ALXN1840-related renal/urinary AE
- No deaths occurred due to ALXN1840

61 Ph3 cross-over patients from SoC to ALXN1840 had no change in psychiatric AE rate: 4.3% (3/70, 62.4 PYs) vs. 4.9% (3/61, 55.4 PYs)

Fig 5: New Wilson Index

Least squares mean and standard error – Ph2 & Ph3



New Wilson Index (based on bilirubin, AST, INR, leukocytes, albumin) improved for patients on ALXN1840 treatment over 6 years

Conclusions

Clinical data from 255 WD patients on ALXN1840 treatment show sustained clinical improvement over 6 years of treatment. Combined with long-term safety, this analysis supports the potential use of ALXN1840 as a treatment for Wilson disease.

References & Acknowledgements

The authors would like to thank the patients and their families for their participation in the studies, as well as all participating sites

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Comparison of Important Risks Between ALXN1840 and Standard of Care

- **Tolerability:** Based on the important risks, ALXN1840 may have a better or comparable risk profile
- **Adherence:** ALXN1840 is a once-a-day tablet versus multiple times a day dosing for SoC

Important Risks			
ALXN1840	**Penicillamine**	**Trientine**	**Zinc**
Hepatic effects	Deterioration of neurological function	Worsening of clinical symptoms at tx initiation	Clinical deterioration at the start of therapy
Clinical manifestations of copper deficiency	Serious Hematological Adverse Reactions • Aplastic anemia (Fatal) • Agranulocytosis (Fatal)	Copper deficiency	Copper deficiency
	Acquired epidermolysis bullosa and penicillamine dermopathy	Iron deficiency	
	Pemphigus vulgaris and Pemphigus foliaceus	Hypersensitivity reactions	
	Serious Renal Adverse Reactions		
	Intrahepatic Cholestasis Toxic hepatitis		
	Goodpasture's syndrome		
	Myasthenia Gravis		
	Obliterative Bronchilitis		

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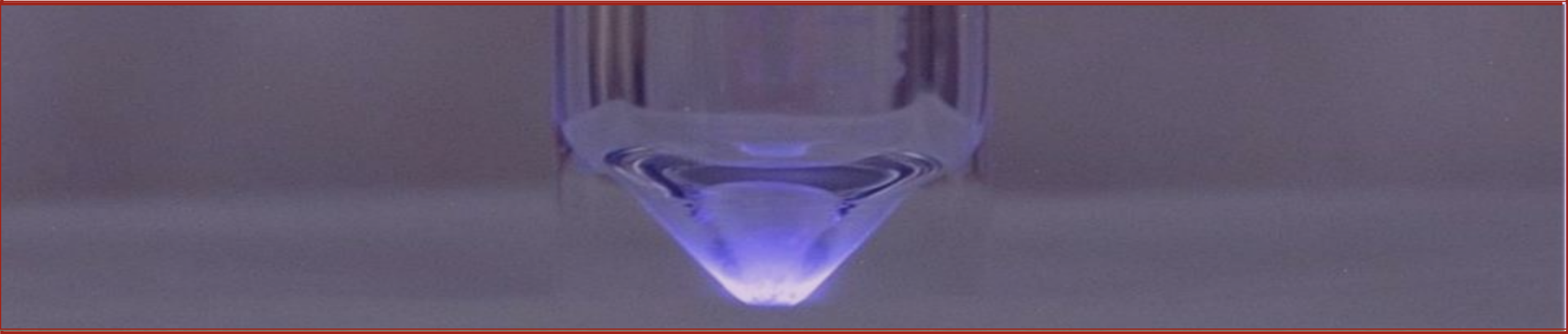
MNPR-101



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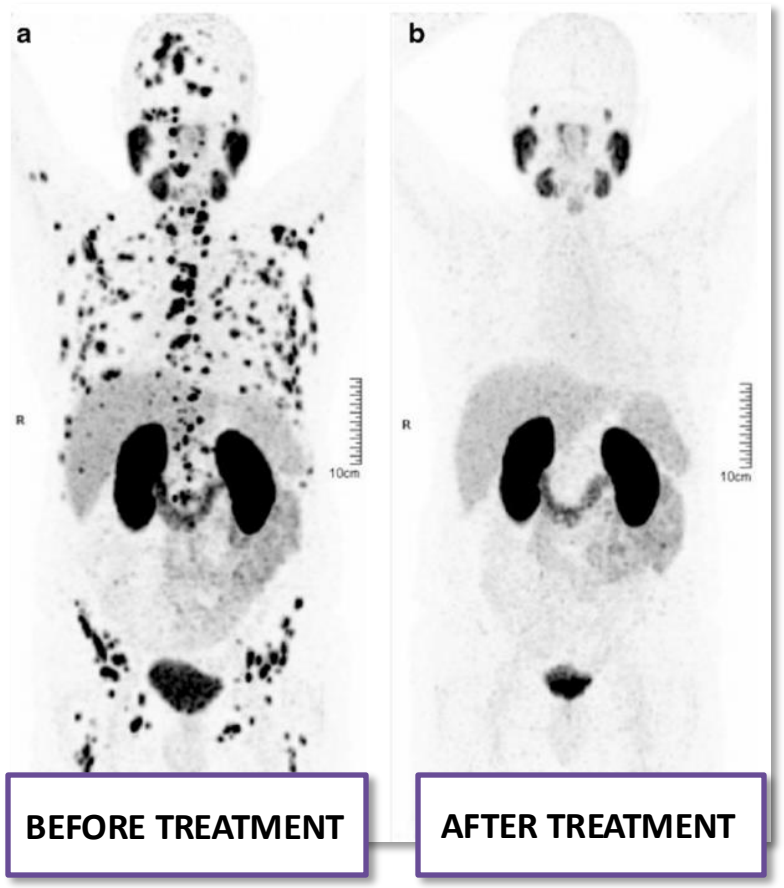
Validated Treatment Approach, Which Has Worked Where ADC's Failed

Novartis' Pluvicto® for mCRPC



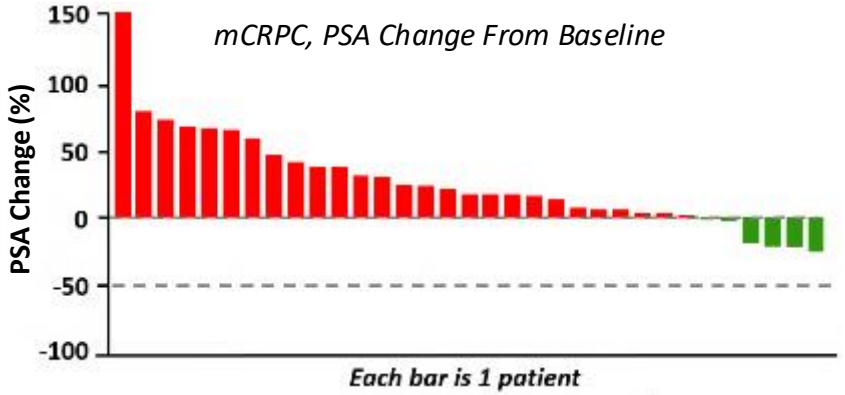
BEFORE TREATMENT

PSA = 50 ng/ml

AFTER TREATMENT

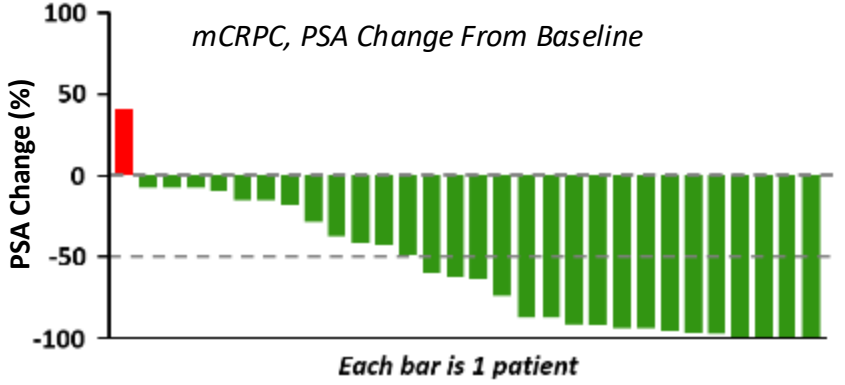
PSA = 0 ng/ml
-100%

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

Monopar Therapeutics

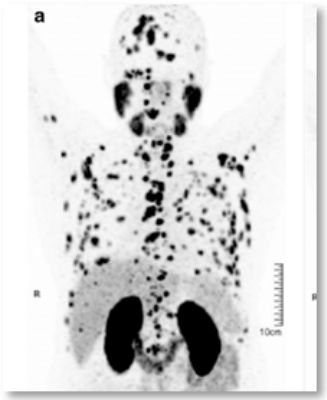
Our Development Program is Streamlined

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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Components and Mechanism of Action of Radiopharmaceuticals

Radiopharmaceutical Components

uPAR

Expressed in multiple aggressive cancers, rarely in normal tissue

MNPR-101

MNPR-101 antibody binds uPAR found in cancer

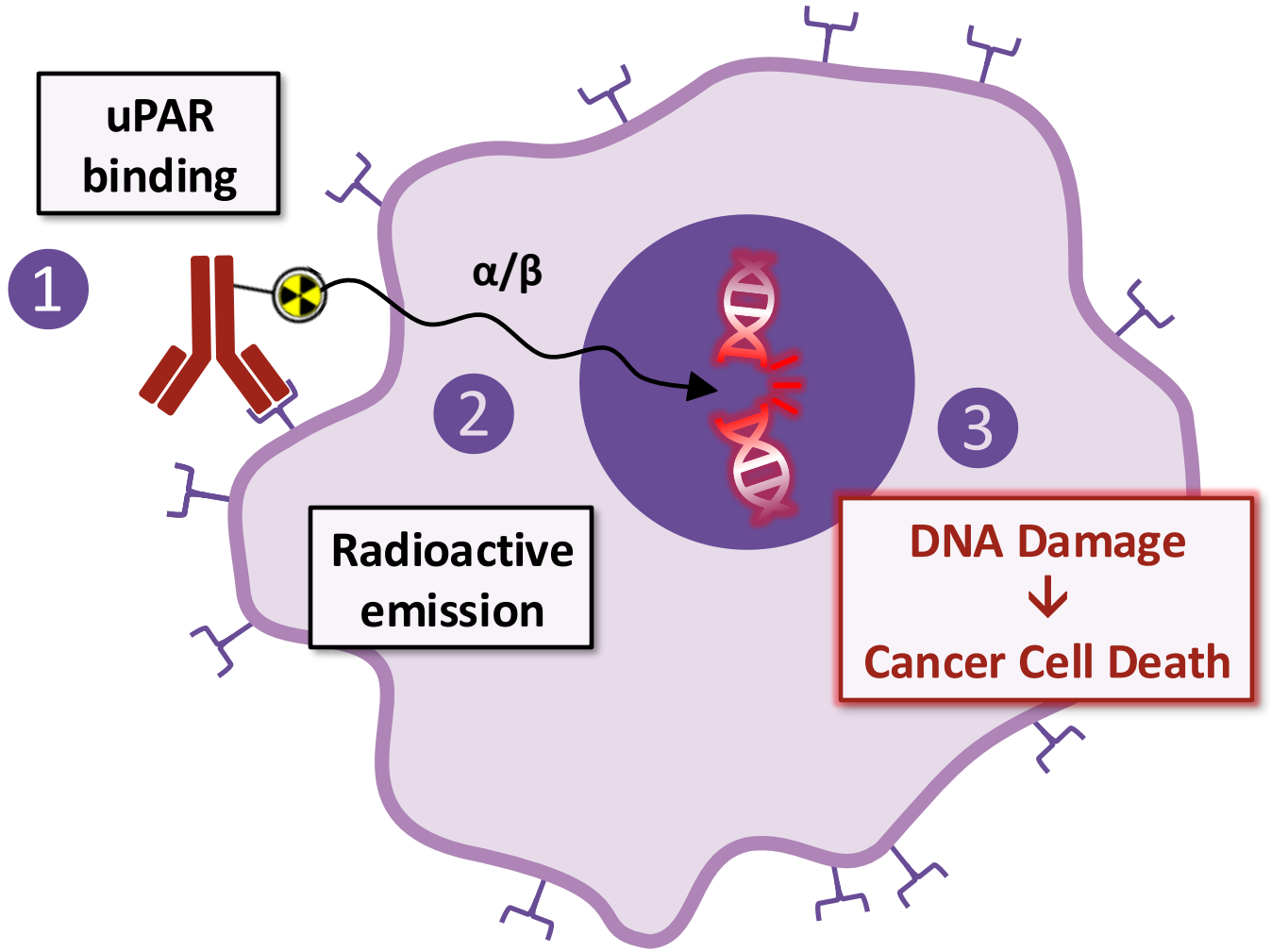
DFO* / PCTA linker

Links Isotope to Targeting Agent for imaging / therapy

^{89}Zr Imaging

^{177}Lu and ^{225}Ac Therapy

Simple Mechanism of Action



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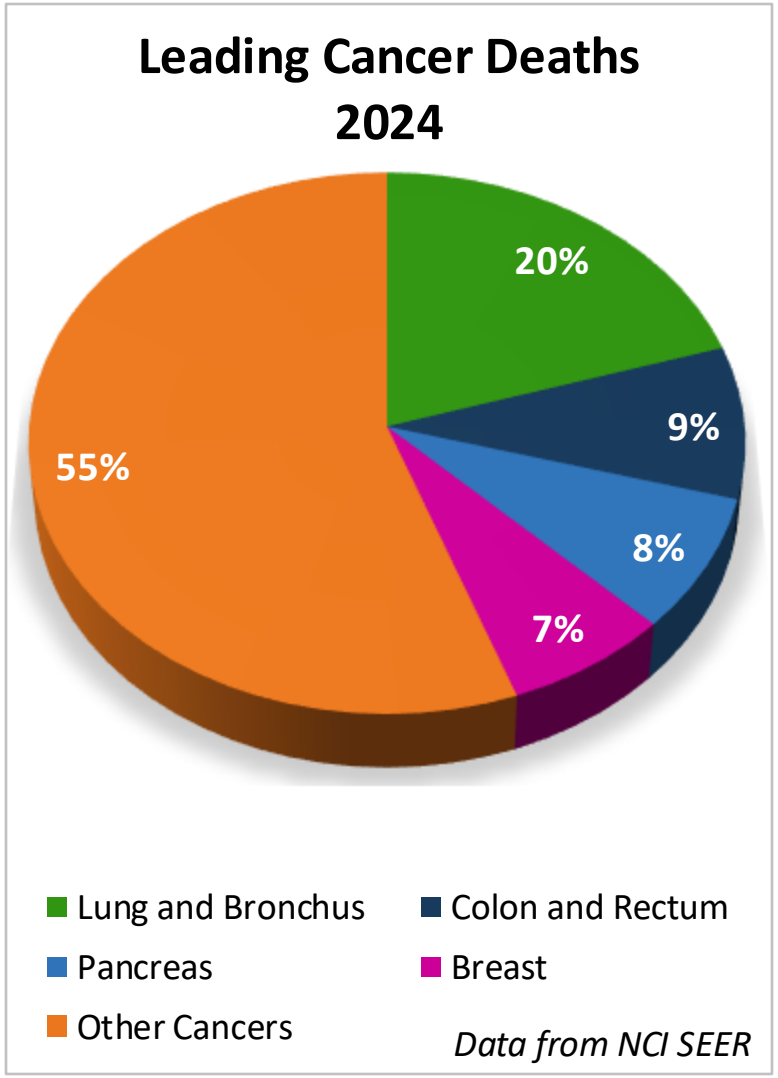
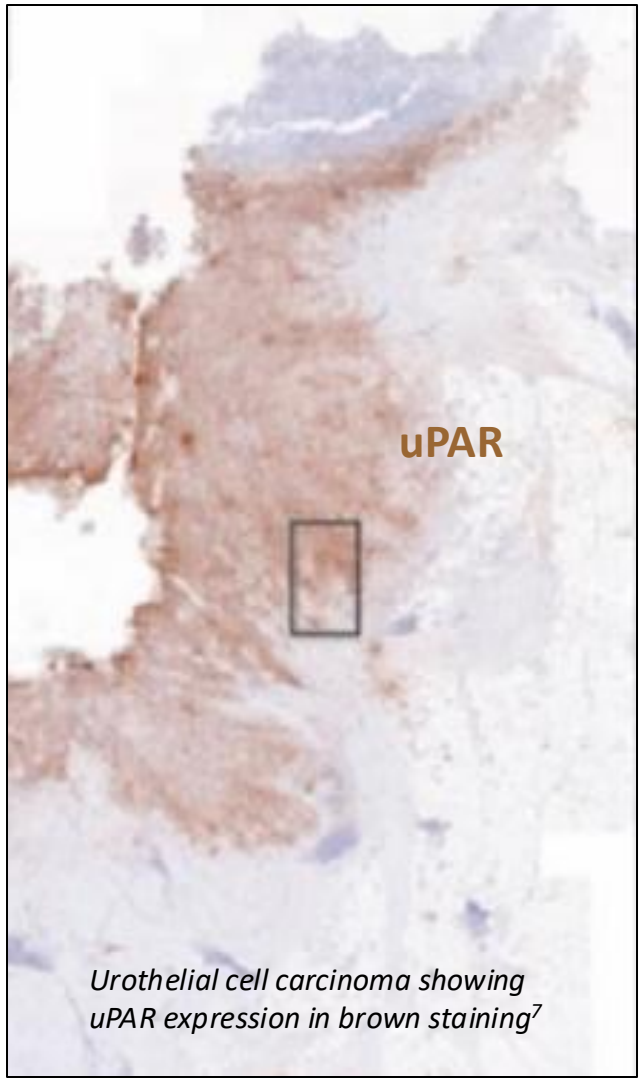
MNPR-101 Targets uPAR



Cancer Type	% Patients with uPAR Expression
Breast[1]	97%
Bladder[2]	89%
Ovarian[3]	88%
Pancreatic[4]	87%
Colorectal[5]	85%
Lung[6]	50%



Urothelial cell carcinoma showing uPAR expression in brown staining[7]

[1]*Dublin et al., Am J Pathol. (2000)*
[2]*Dohn et al., Urol. Oncol, (2015)*
[3]*Wang et al. , Gynecol Oncol (2009)*
[4]*de Geus et al., Cancer (2017)*
[5]*Boonstra et al., BMC Cancer (2014)*
[6]*Salden et al., Annals of Oncology, (2000)*
[7]*Baart et al. , Eur J Cancer (2021)*

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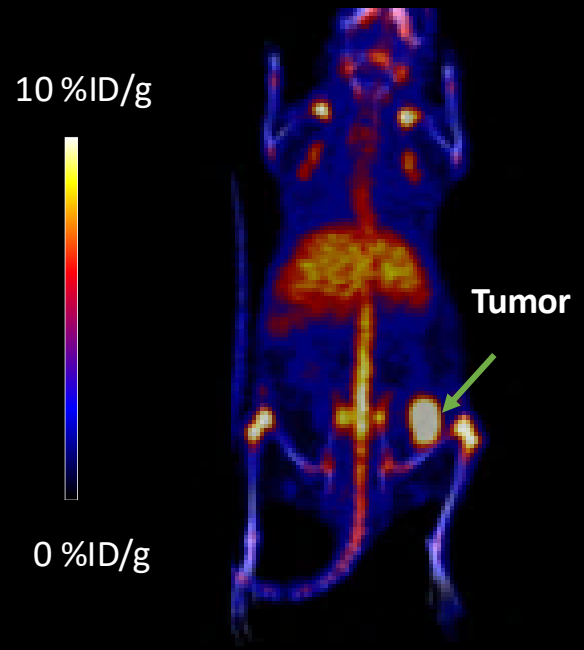
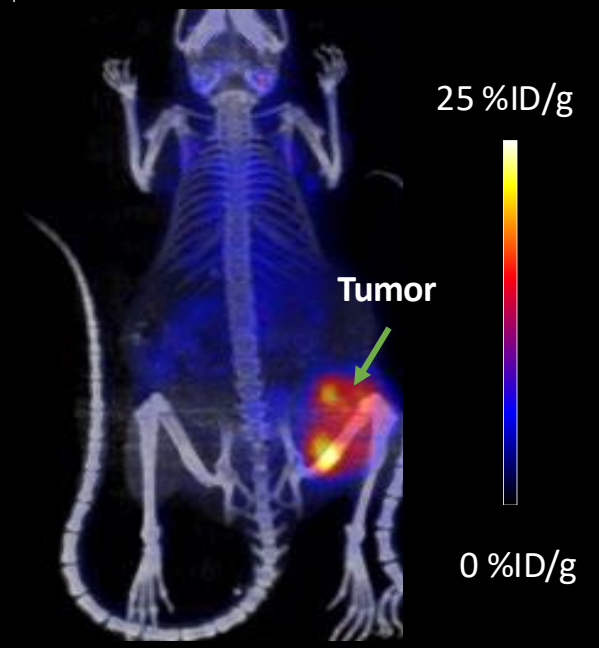
Our Platform Noticeably Improves Biodistribution

BEFORE

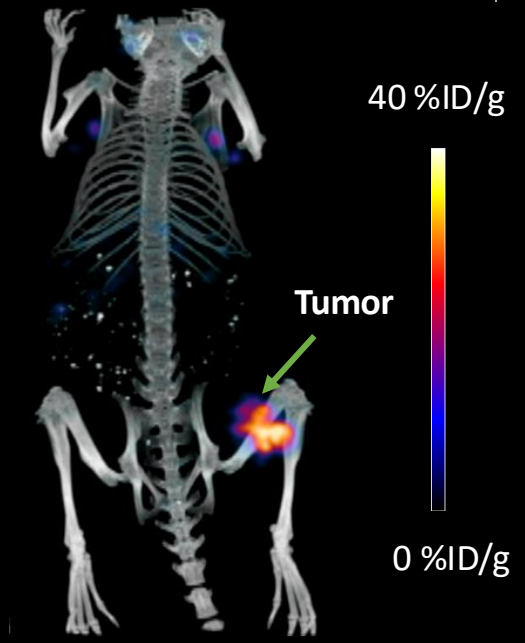


Unoptimized MNPR-101-Zr

AFTER



MNPR-101-Zr



MNPR-101-Lu

Pancreatic Cancer (MIA PaCa-2) Imaging @ 6-7 days post injection

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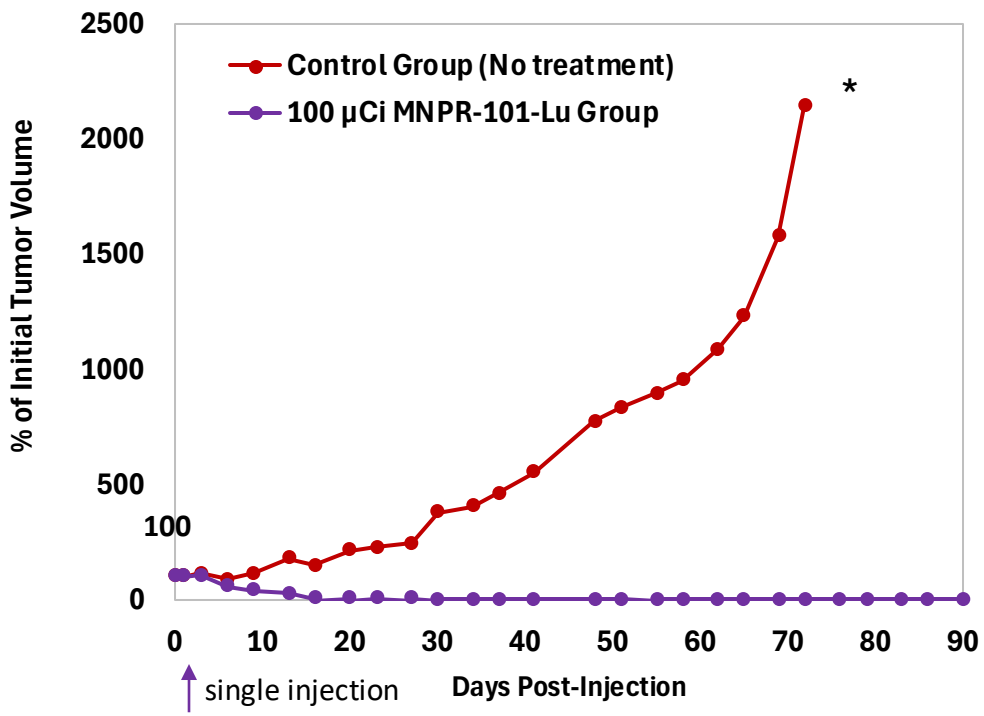
Biodistribution Supports Strong Preclinical Efficacy

Pancreatic Cancer

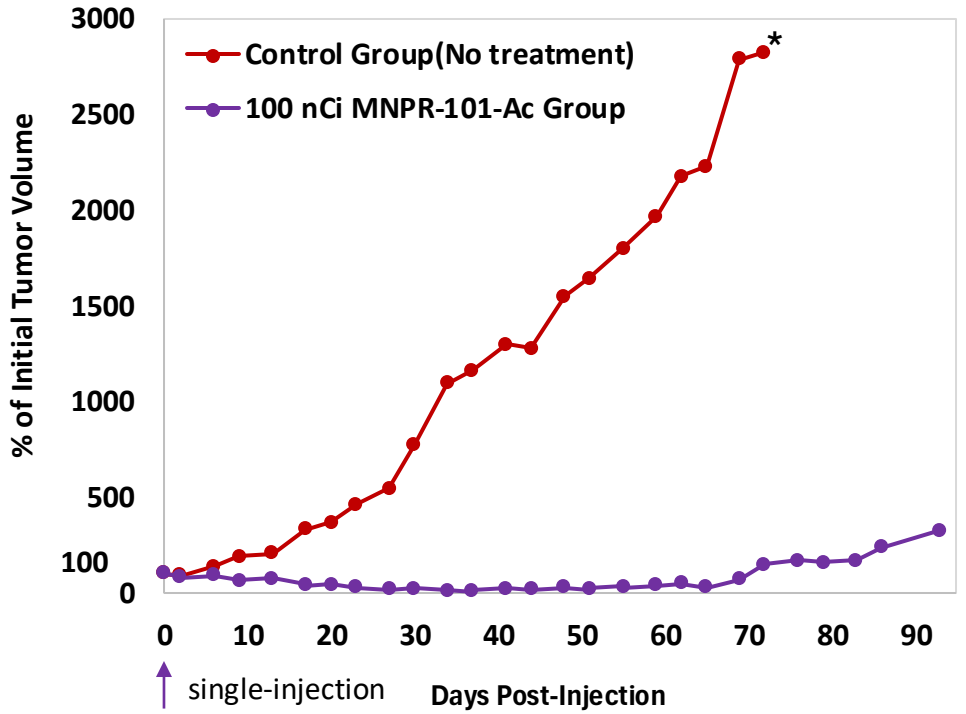
MIA-PaCa2 xenograft mouse model



**Stopped due to tumor volume limit*

Triple Negative Breast Cancer

MDA-MB-231 xenograft mouse model



**Stopped due to tumor volume limit*

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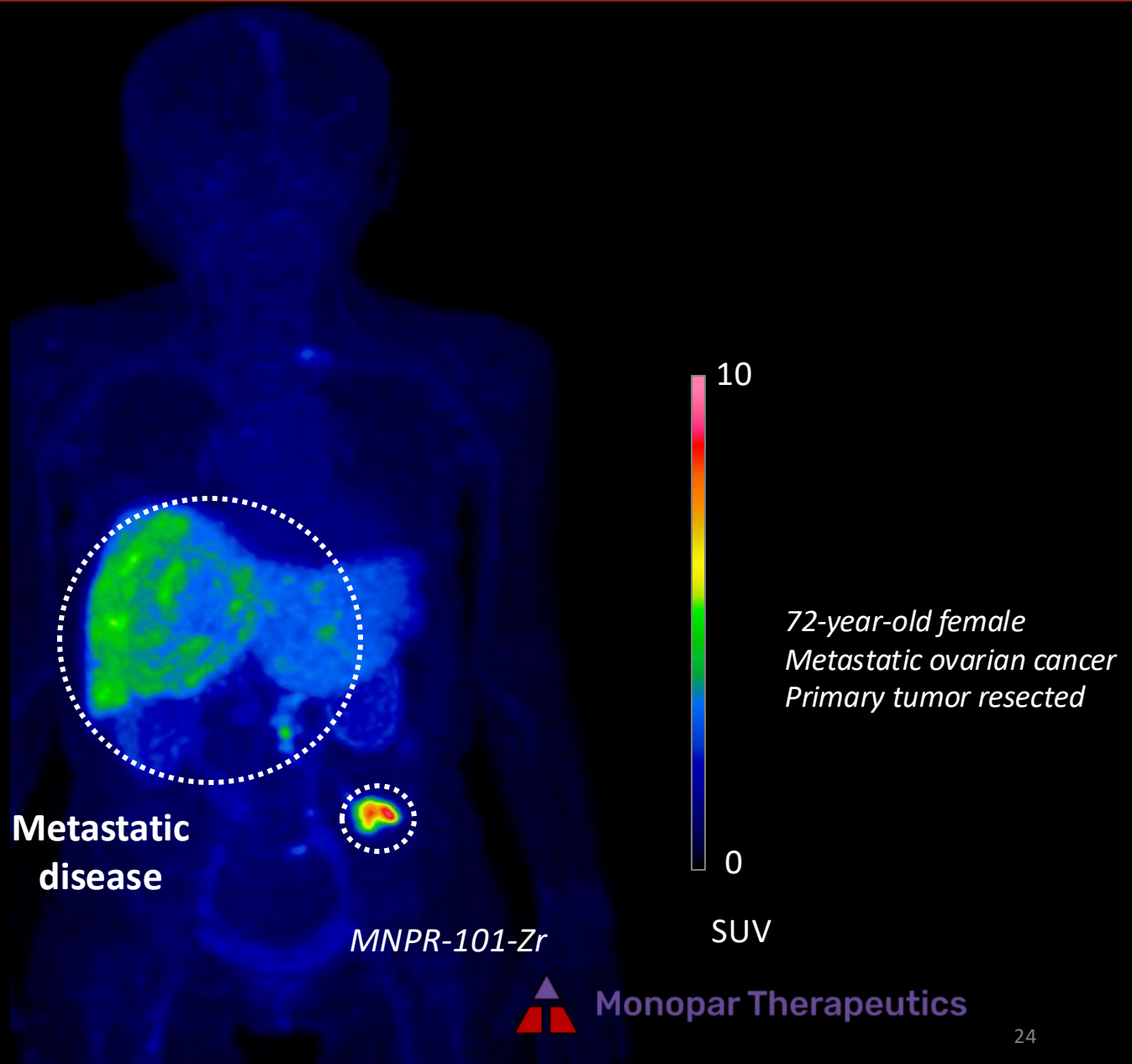
Human Clinical Data Confirms MNPR-101's Tumor Targeting Ability

MNPR-101-Zr Phase 1 – imaging, dosimetry, tumor uptake, biodistribution, & safety

MNPR-101-Lu Phase 1a – therapeutic (efficacy), safety, & dose-escalation

Next Milestone: Ongoing data readouts from these open-label studies



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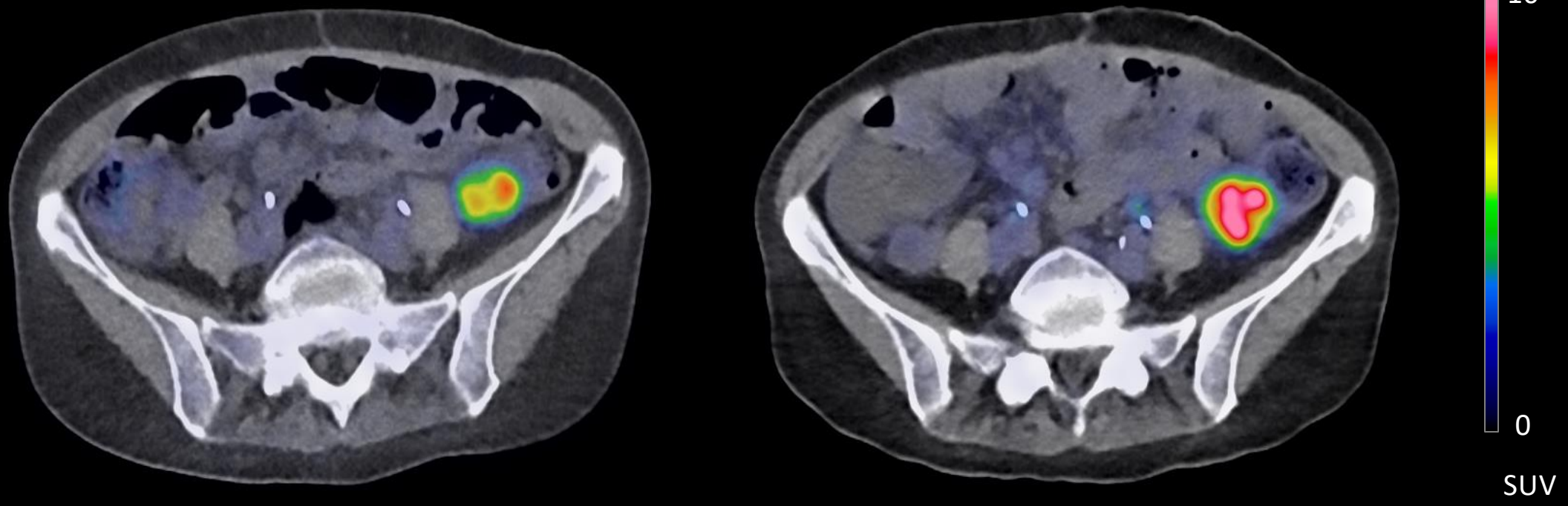
MNPR-101-Zr Comparison with FDG

^{18}F-fluorodeoxyglucose (FDG)

MNPR-101-Zr (72h)



FDG image acquired 14 days prior to MNPR-101-Zr administration on the same Siemens Biograph Vision Quadra™ PET/CT System.

Presented at European Association of Nuclear Medicine 2024

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Favorable Human Radiation Dosimetry Profile

Target Organ	MNPR-101-Zr	Projected MNPR-101-Lu		Organ Safety threshold (Gy)
	Absorbed Dose @43 MBq (Gy)	Dose Coefficient (Gy/MBq)	Absorbed Dose @5624 MBq (Gy**)	
Liver	7.85×10^{-2}	1.63×10^{-3}	9.14	30
Kidneys	5.20×10^{-2}	1.12×10^{-3}	6.30	23
Lungs	3.54×10^{-2}	6.35×10^{-4}	3.57	20
Red marrow*	1.96×10^{-2}	2.73×10^{-4}	1.53	2-3

Actual MNPR-101-Zr and projected MNPR-101-Lu organ dosimetry (at the highest per cycle Lu-177 mAb therapeutic dose we are aware of in the clinic) suggest a favorable safety profile to date in ongoing MNPR-101-D001 clinical trial

Presented at European Association of Nuclear Medicine 2024

* *Blood-based analysis*

** *Lu-177 projected dosimetry uses the highest per cycle dose we are aware of – an ongoing Phase 3 trial of an Lu-177 radiolabeled antibody – 2 fractions @ 45 mCi/m^2 for a standard 1.7 m^2 patient equivalent to 5624 MBq*

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Thank you

June 2025

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