# Using RNA Therapeutics to Deliver a Cancer-Free Future

TRANSCODE THERAPEUTICS™

NASDAQ: RNAZ

April 17, 2024

Disclaimer

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# Capitalization (Dec. 31, 2023)

| Source of Capital | Amount |
|---|---|
| Seed Capital *(Angel investors)* | $2,240,000 |
| SBIR Grant | 2,309,000 |
| IPO *(Net Proceeds)* | 25,400,000 |
| Equity Financings – 2023, 2024 *(Net Proceeds)* | 21,707,000 |
| Total | $51,656,000 |

| NASDAQ Symbol: RNAZ | March 20, 2024 |
|---|---|
| Common Stock *(includes PFWs)* | 6,622,053 |
| Options (WAEP $61,911.63) | 6,682 |
| Warrants (WAEP $2.51) | 12,375,096 |
| Total | 19,003,831 |

Cash at December 31, 2023 *(pro forma with $6.2 million from equity offering in January 2024)*: $9.0 million

# Critical Need for An Effective Therapy Against Metastatic Cancer

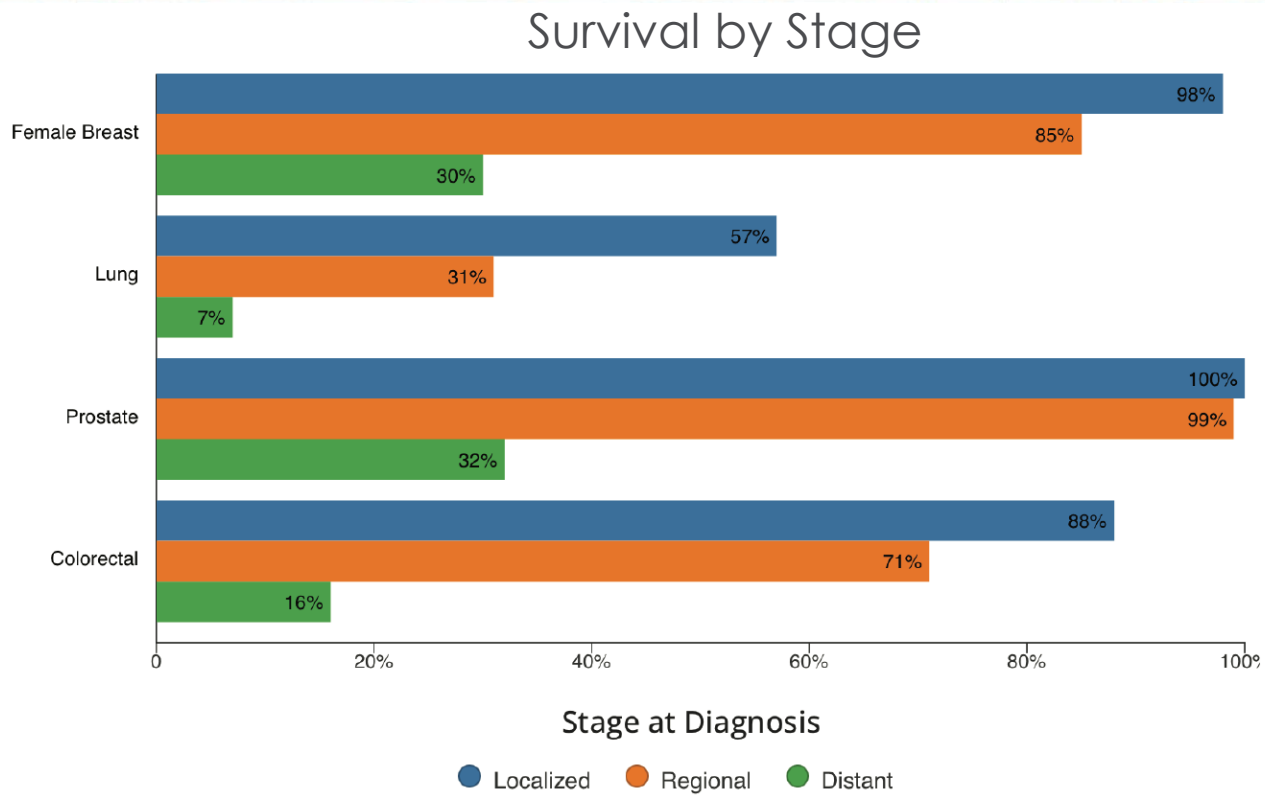
Metastatic cancer is cancer that has spread beyond its organ of origin

Primary tumors are generally susceptible to current treatments

Metastatic cancer is essentially incurable

Of the 10 million cancer deaths annually worldwide, 90% are due to metastasis

$136.9B global market by 2032

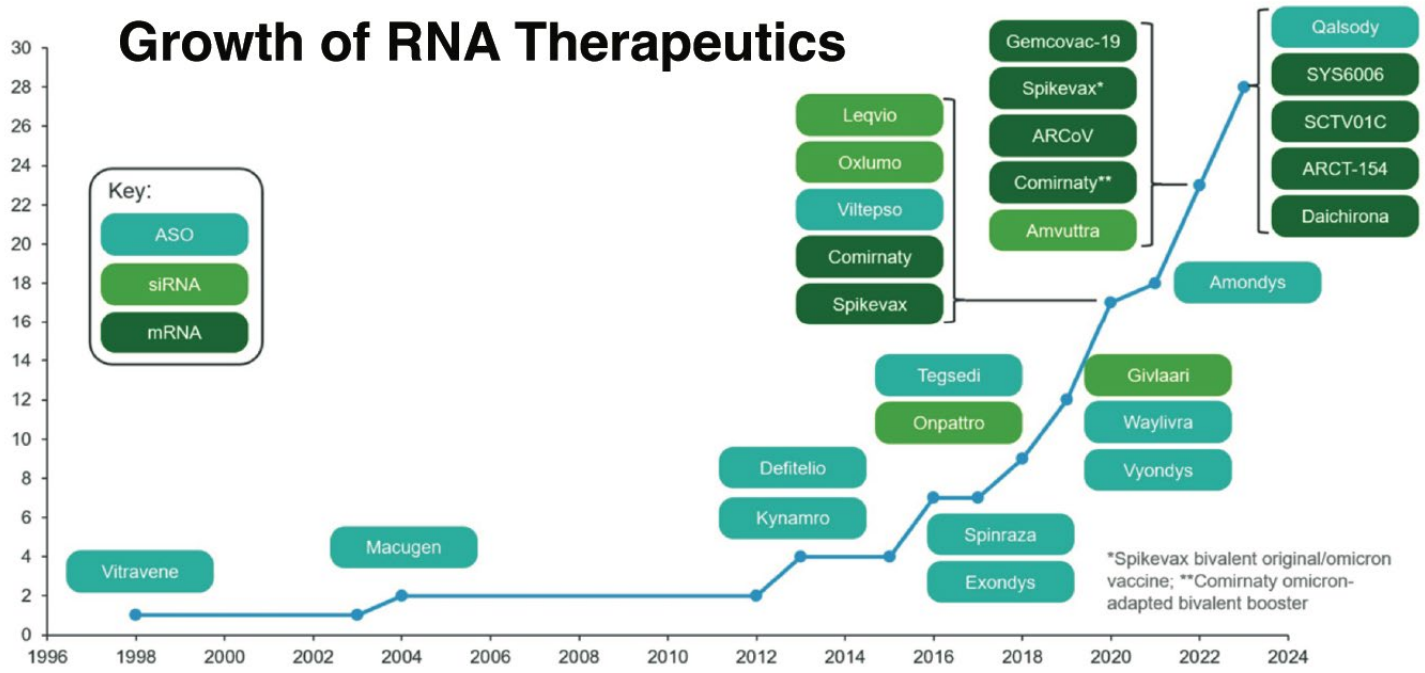


# A Groundbreaking Solution: RNA

RNA therapeutics hold the promise of revolutionizing the way we treat a wide array of diseases

The global RNA market was $4.9B in 2021, and is projected to reach $25B by 2030

The promise of RNA to treat cancer has not been realized because delivery of RNA has remained unsolved – until now




* Source: 2019 American Cancer Society, Inc., Surveillance Research; International Agency for Research on Cancer in its report named GLOBOCAN 2022: Precedence Research January 2022

** Oncotarget, 2023, Vol. 14, pp: 216-218, Therapy drives genomic evolution in metastatic cancer;

# TransCode's Innovative Solution to Metastatic Cancer Using RNA

Breakthrough RNA technology invented at Harvard Medical School designed to treat metastatic disease

Proprietary delivery platform overcomes decades of RNA delivery challenges

FDA authorization for Phase 1/2 clinical trial received April 2024 (expected to start in Q2 2024)

Compelling animal data in multiple models showed evidence of complete cures of metastatic cancer

Science published in over 30 peer-reviewed publications, including *Nature Medicine* and *Cancer Research*

Robust partnerships in place, with more in pipeline

Robust IP: 10 patents in 5 patent families

Highly experienced team of pharma and financial executives, scientists, and clinical experts

# Robust Proprietary Delivery Platform

Most oncology targets are currently undruggable using monoclonal antibodies (mAbs) and small molecules

Engaging these targets with TransCode's proprietary delivery system could revolutionize cancer treatment and open up a vast pipeline of new anti-cancer drugs

TransCode's therapeutic delivery platform, TTX, employs nanoparticles extensively used in imaging that have been repurposed and optimized to efficiently deliver therapeutic payloads to oncology targets

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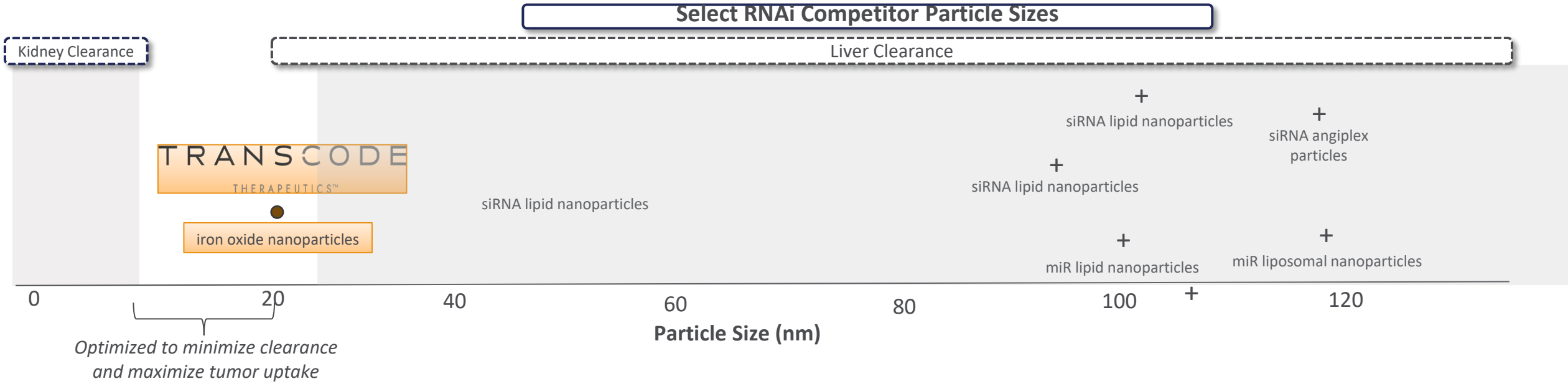
TTX design overcomes long-standing delivery challenges:

- Imaging-capable nanoparticles can quantify delivery to tumors
- Size and surface chemistry "high tunability" to a variety of payloads
- Scalable and cost-effective manufacturing
- Proven safety profile - biodegradability and low immunogenicity

# Unique Particle Size, Exceptional Safety




Stability and optimal PK and biodistribution

Safety and low immunogenicity

Efficient tumor cell uptake and target engagement

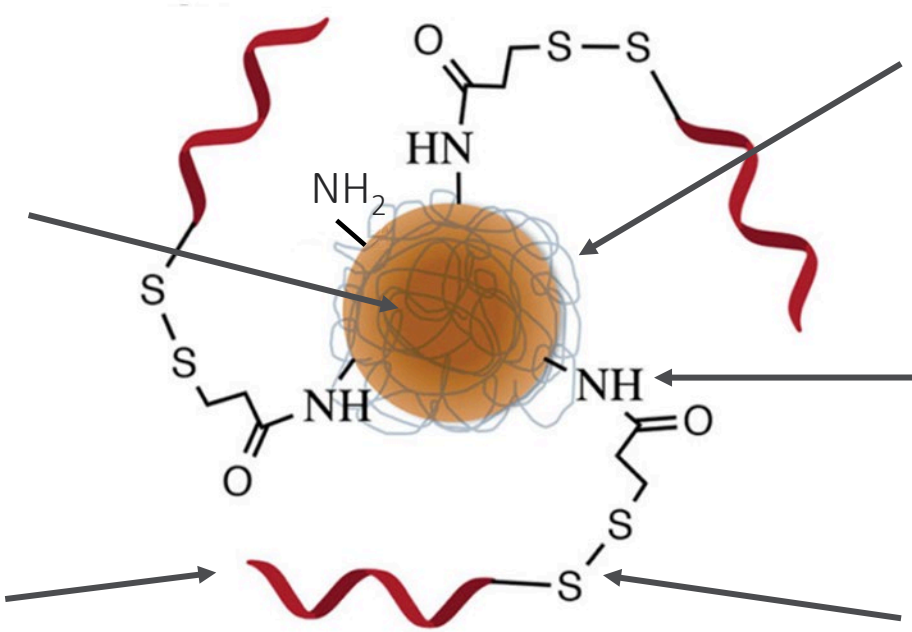
Capability of detection by noninvasive imaging

Source: J Nano Res 2014, J Drug Targeting 2012, Alnylam presentation, Molecular Therapy-Nucleic Acids 2016, Nature Communications 2018, Molecular Therapy 2018, Int J Pharmaceut 2014, Analytical Chem 2013, Large Molecular Therapeutics 2017, Current Pharma Design 2015, Radiology 2018

# TTX Delivery System

## Iron Oxide Nanoparticle Platform

- Long circulation half-life
- Avoids early kidney and liver clearance
- Unique capability to accumulate in tumor cells and metastatic sites
- Image capable via MRI enables quantifiable drug delivery to target
- Highly stable, low toxicity potential; low immunogenicity




## Dextran coating

- Stabilizes nanoparticles
- Protects oligos from degradation
- Promotes tumor uptake and entrapment inside tumor cells

## Amino functional groups

- Provide stabilization

## RNA-targeted nucleic acid

- Strong binding affinity, specificity and stability while minimizing immunogenicity

## Disulfide bond

- Allows oligo to disconnect from nanoparticle in order to bind to RNA/DNA target

# Mechanism of Delivery to Tumors and Metastases

## Hemodynamic targeting

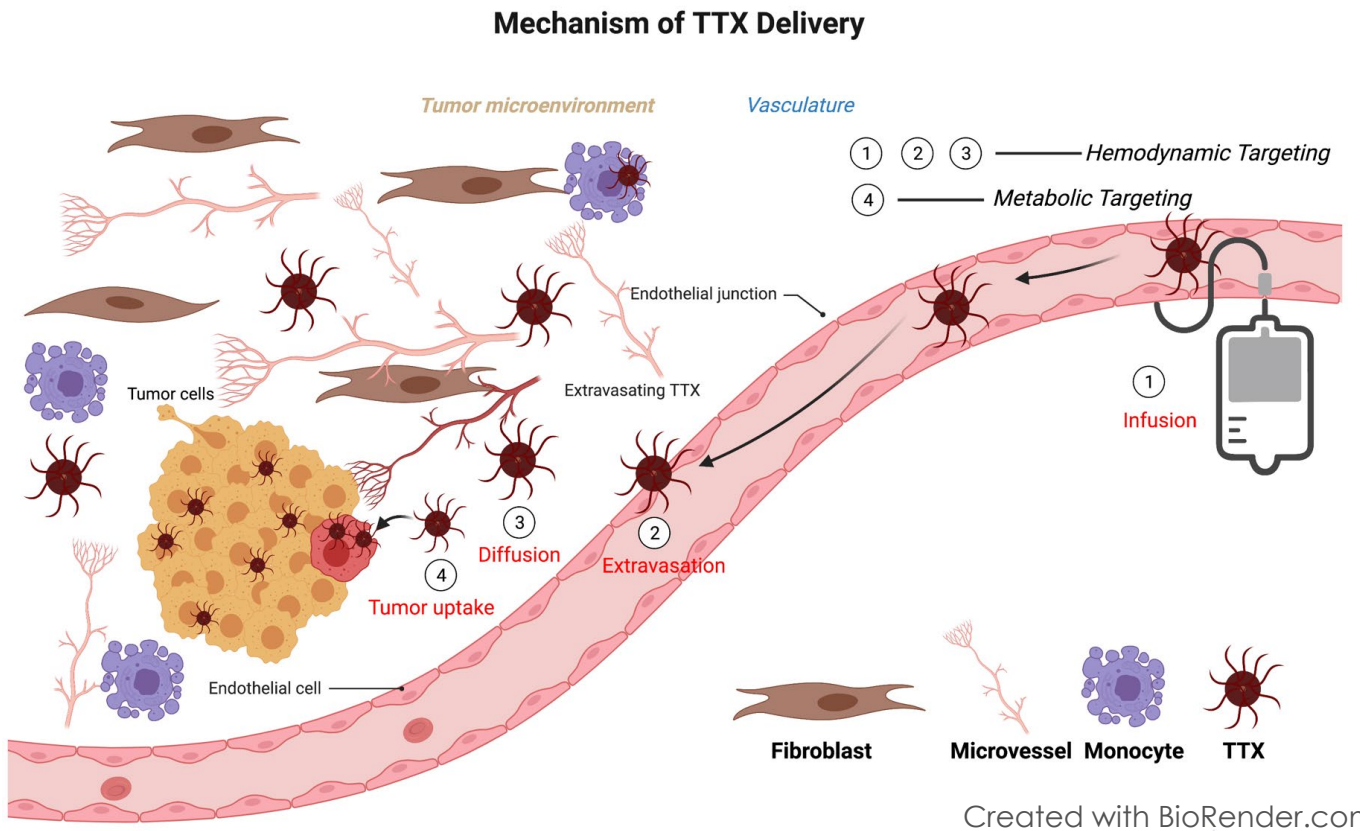
TTX is long-circulating (24-30 hours); allows for distribution throughout the microcirculation of tumors and metastases

Small hydrodynamic size - easily flows from the vascular endothelium (inner cellular lining of veins, arteries, and capillaries) of tumors and metastases and diffuses throughout the tumor tissue

## Metabolic targeting

Tumor cells are metabolically active and require glucose for growth. TTX is coated with a non-metabolizable glucose polymer and is avidly taken up by these metabolically-active tumor cells

The process is similar to the mechanism behind diagnostic PET imaging with fluorodeoxyglucose (FDG), widely used to diagnose and stage metastatic cancer



# Evidence of Delivery to Tumors and Metastases

Delivery to tumors and metastases shown in multiple peer-reviewed publications.

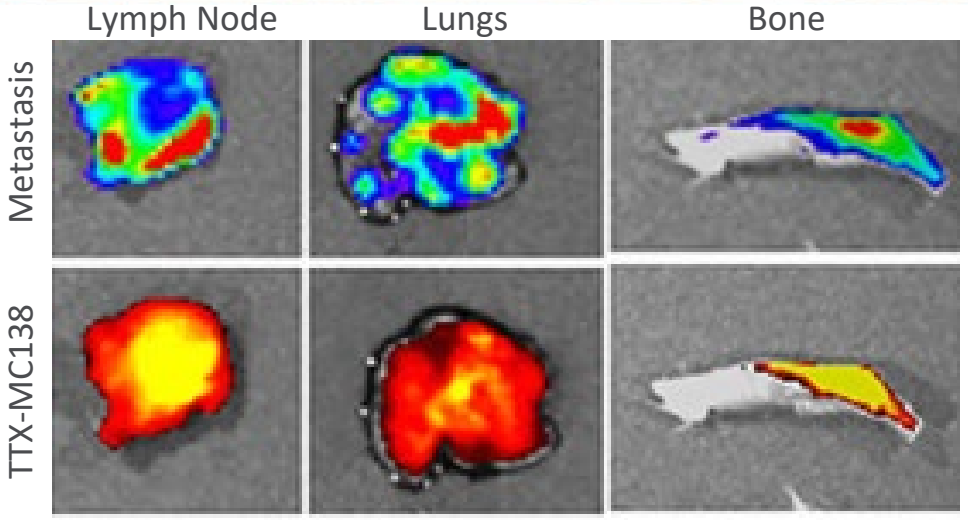
Efficient delivery/pharmacodynamic (PD) activity demonstrated in multiple species (mice, companion animals, and nonhuman primates).

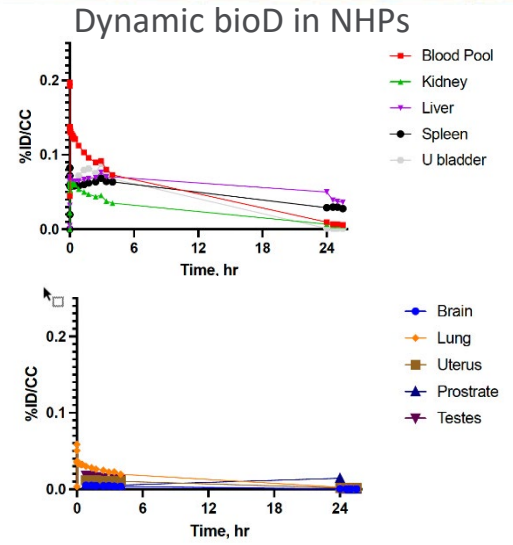
Delivery demonstrated for siRNA, antisense oligonucleotides, immunostimulatory RNA, mRNA, CRISPR, peptides, proteins.

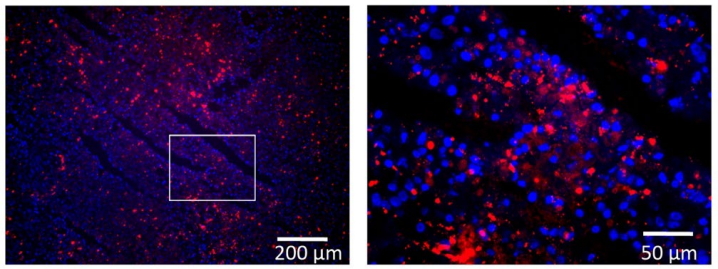
Delivery demonstrated to multiple cancers, including breast, pancreatic, and GBM.

Delivery shown to be highly efficient (>90% in terms of PD activity) and long-lasting (>3 months in spontaneous cancer).

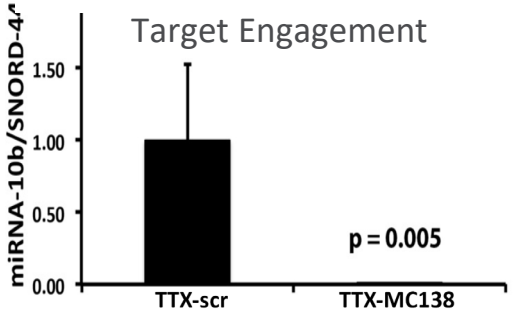
Source: Scientific Reports | 7:45060 | DOI: 10.1038/srep45060, Can Res 2015 and Cancer Nanotechnol. 2021;12(1):16.




Red: TTX-MC138, Blue: cell nuclei

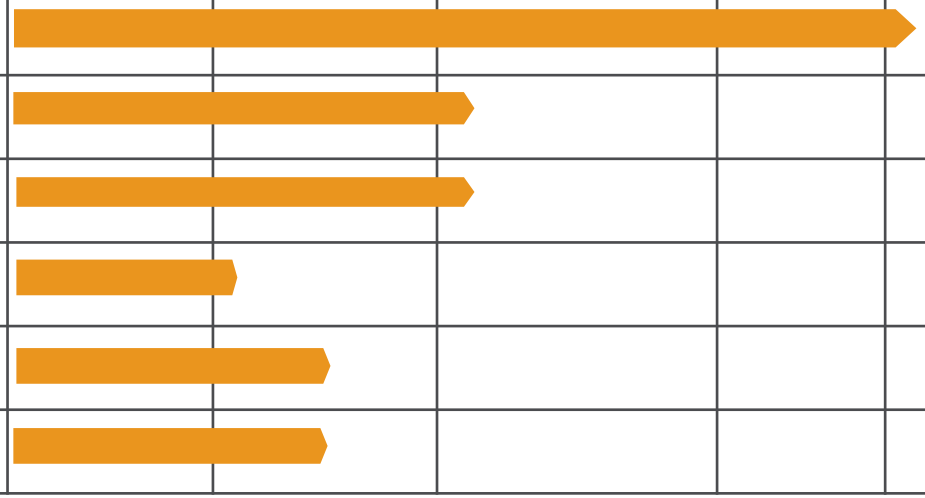


# Therapeutic Candidates

## Advancing Multiple First-in-Class RNA Therapeutics

# Robust Pipeline

| Candidate | Target | Modality | Disease Indication | R&D | Preclinical | IND Enabling | Phase 0 | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|---|---|---|---|---|---|---|
| TTX-MC138 | miR-10b | RNAi | Metastatic Cancer<br>*Pancreatic Cancer | | | | | | | |
| TTX-siPDL1 | PD-L1 | RNAi | *Pancreatic Cancer | | | | | | | |
| TTX-RIGA | Multiple | PRR-RIGI | Cancer Agnostic | | | | | | | |
| TTX-CRISPR | Multiple | CRISPR (Cas9) | Cancer Agnostic | | | | | | | |
| TTX-CRISPR | Multiple | CRISPR (BEC) | Cancer Agnostic | | | | | | | |
| TTX-mRNA | Vaccine | mRNA | Cancer Agnostic | | | | | | | |



* Received Orphan designation status from FDA

# Lead Candidate: TTX-MC138

## A First-in-Class Therapeutic Candidate Targeting Metastatic Cancer

TTX-MC138 targets miRNA-10b, an RNA critical in metastatic cancer

miR-10b is linked to metastatic disease in >200 clinical studies in cancer patients

miR-10b is shown to drive metastatic progression in multiple preclinical models

miR-10b is proven to play a critical role in the survival of metastatic tumor cells

**TTX-MC138 has shown complete regressions of metastatic disease in multiple preclinical studies**

Source: Sheedy et al., Am J Cancer Res. 2018;8(9):1674-1688; Yoo et al., Cancer Res. 2015;75(20):4407-15; Ma et al., Nature. 2007;449(7163):682-8.

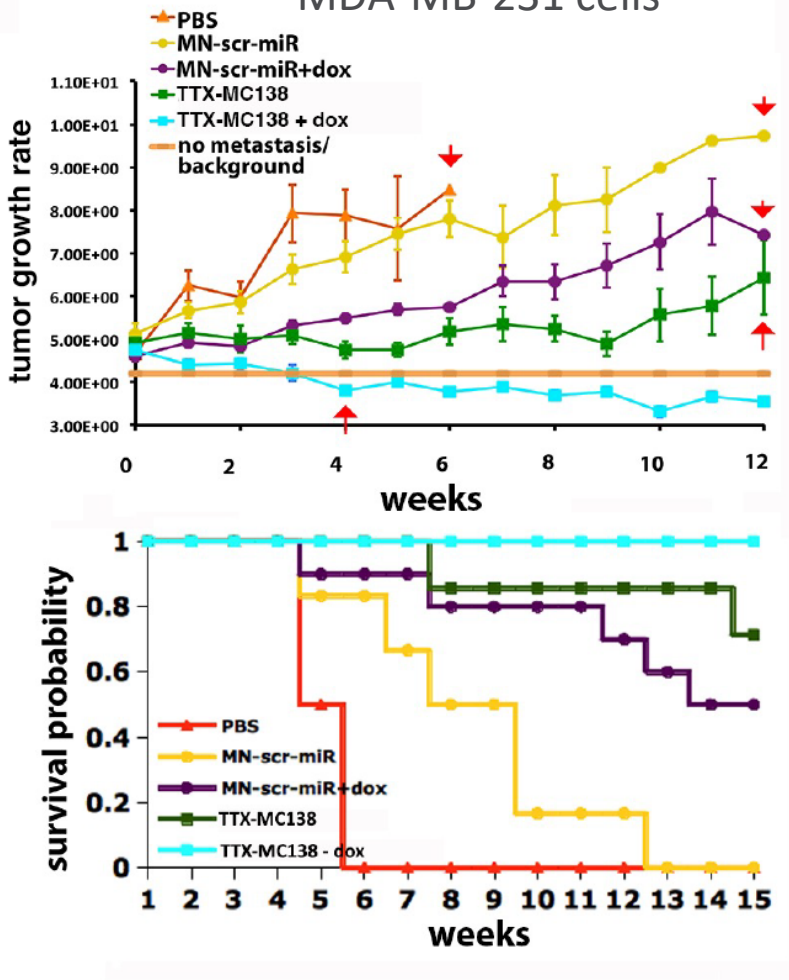
# Evidence of Durable Regressions Preclinically (Murine Models)

Human (Stage II/III) or mouse (Stage IV) triple negative breast cancer cells implanted orthotopically into mice.

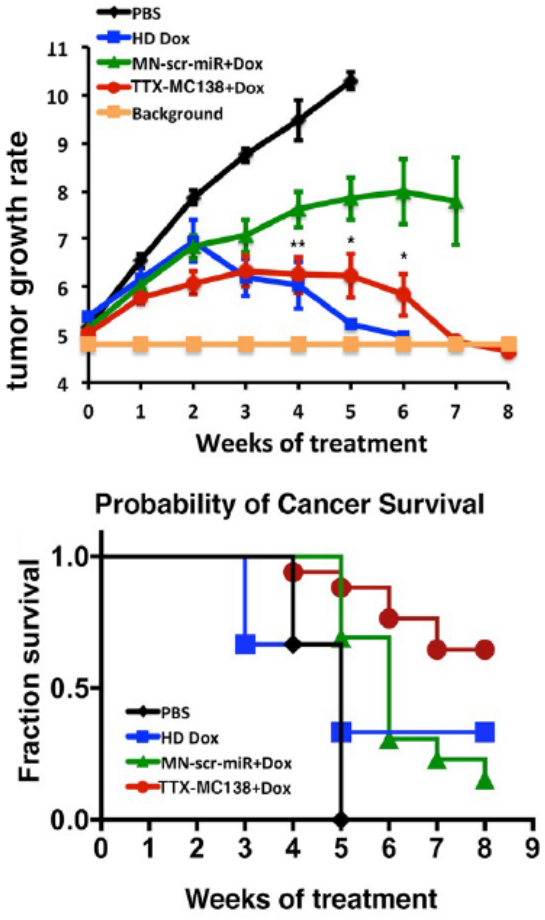
Mice were treated with TTX-MC138 after formation of metastasis.

**100%** (Stage II/III) and **65%** (Stage IV) animals regressed disease completely without recurrence for the animals' natural life.

Stage II/III TNBC
MDA-MB-231 cells

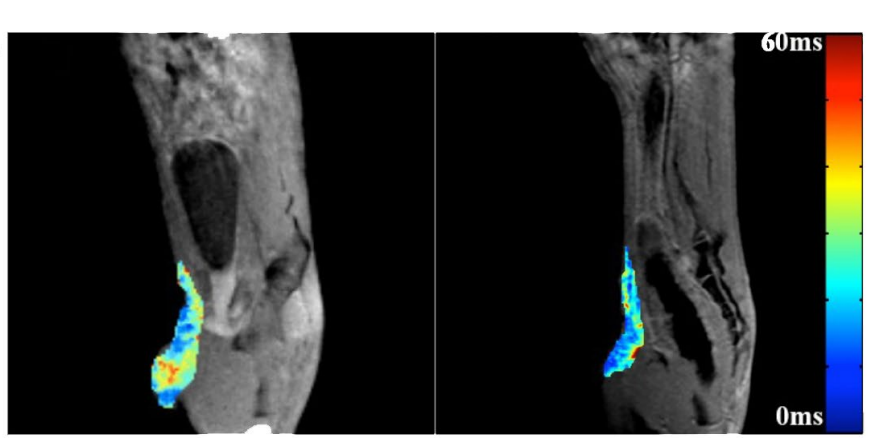


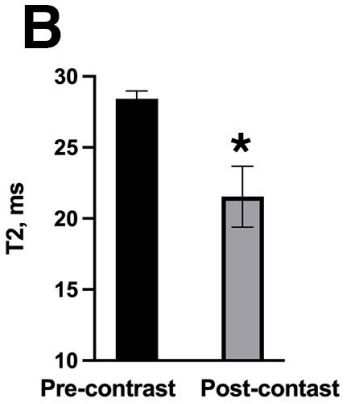

Stage IV TNBC
4t1 cells

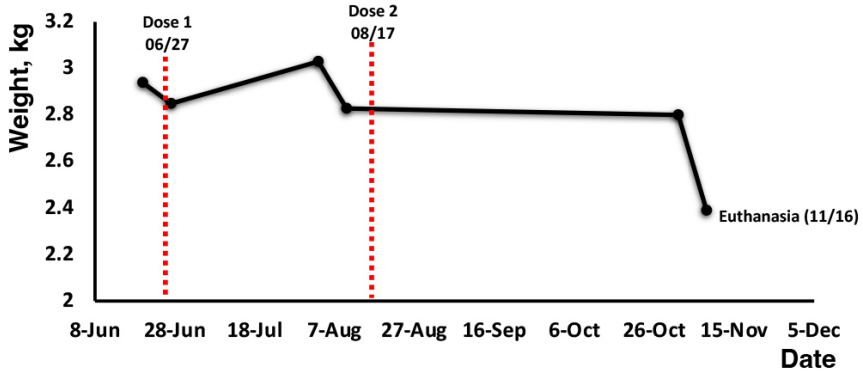


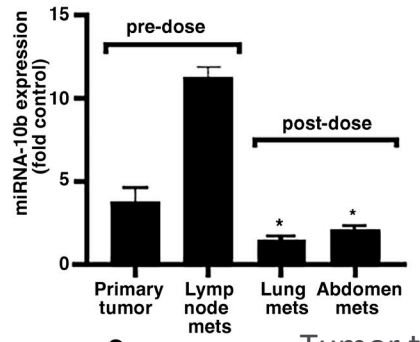

Can Res 2015, Sci Report 2017

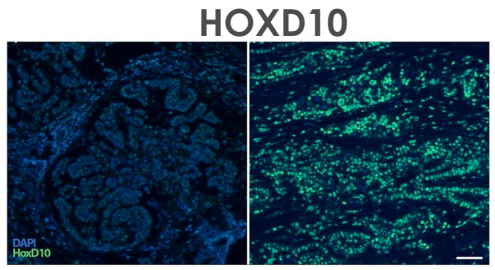
# TTX-MC138 | Evidence of Efficacy in Spontaneous Mammary Carcinoma (Feline Model)

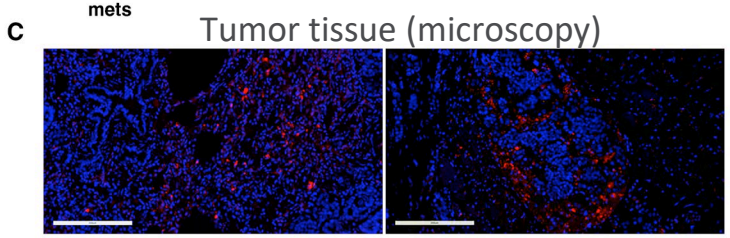



Red: TTX-MC138, Blue: cell nuclei

TTX-MC138 accumulated in metastatic lesions

TTX-MC138 remained in the tumor cells and demonstrated PD activity 3 months after injection

Animal was scheduled for euthanasia the week after initial treatment, but after just one dose, gained weight, resumed eating and drinking, and survived for 5 additional months.

Treatment was found to be safe with liver aspartate transaminase (AST) and creatine kinase (CK) levels slightly but transiently elevated after injection.

Front Oncol. 2022 Oct 26;12:959630.

# Evidence of Pre-Clinical Efficacy in Pancreatic Cancer (Murine Model)

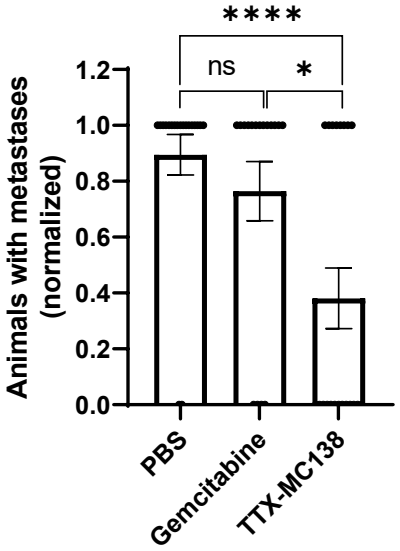
Human pancreatic cancer cells (BxPC3) implanted orthotopically into mice.

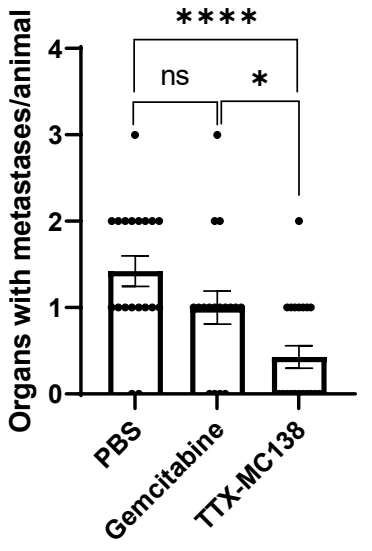
Mice were treated with TTX-MC138 after tumor formation.

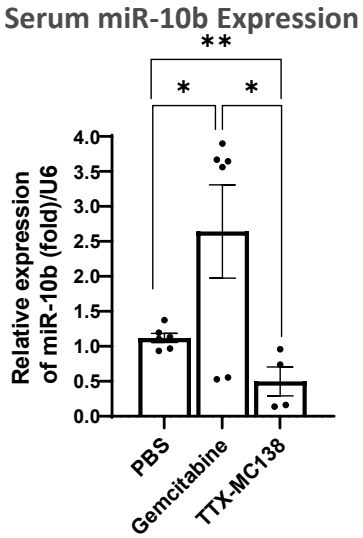
Metastatic incidence was inhibited by 50% relative to standard-of-care chemotherapy.

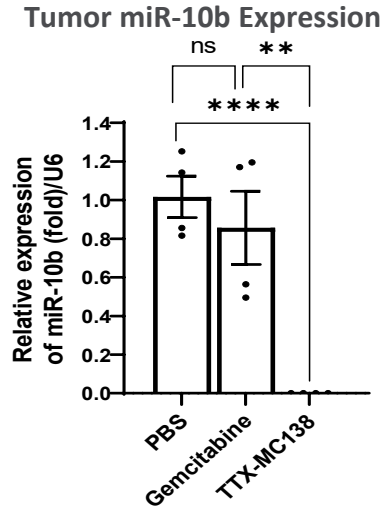
TTX-MC138 displayed remarkable PD activity with target inhibition in tumors over 10,000-fold relative to controls.

Complete regressions observed in up to 40% of animals, depending on treatment dose and schedule.




BxPC3-Red-Fluc cells orthotopically implanted into immunocompromised mice; treatment stopped after 8 weekly treatments

# Clinical Trials With TTX-MC138

First-In-Human (FIH) Phase 0 Study Opened 2023

Phase I Clinical Trial Expected To Commence Q2 2024

# Clinical Trials | Phase 0 Clinical Trial

## PURPOSE

TTX-MC138 (radiolabeled with Cu-64) a microRNA-10b (miR-10b) inhibitor, will be evaluated in a Phase 0 clinical study conducted under an Exploratory IND to evaluate delivery of the molecule to metastatic lesions in subjects with advanced solid tumors by using PET-MRI.

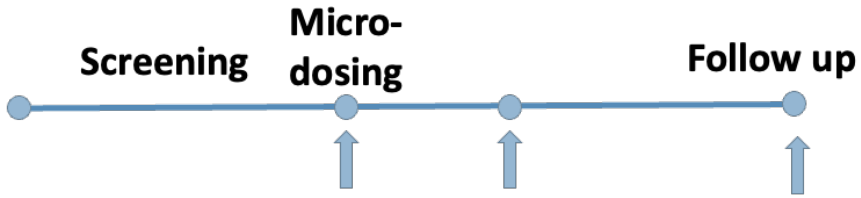
## METHODS

| KEY INCLUSION* | KEY EXCLUSION* |
|---|---|
| • ECOG PS of 0 or 1<br>• At least 1 metastatic solid tumor ≥ 1 target lesion per RECIST 1.1 (≥ 10 mm per MRI from FDG PET-MRI)<br>• Adequate organ function per protocol definitions | • Anticancer therapy (not immunotherapy/Ab therapies) ≤ 14 days or 5 half-lives before study drug<br>• Prior antibody therapy ≤ 28 days before study drug<br>• Clinically significant, uncontrolled cardiovascular disease<br>• Symptomatic CNS metastases or primary CNS tumor associated with progressive neurologic symptoms or requires ongoing corticosteroids to control CNS disease |

**Primary analysis**: Summarize %ID/cc tissue delivered to metastatic lesions
**Safety analysis**: Descriptive statistics to summarize safety data

| OBJECTIVES | ENDPOINTS |
|---|---|
| **Primary Objectives** | **Primary Endpoint** |
| Delivery of TTX-MC138-NODAGA-Cu64 in radiographically confirmed metastatic lesions | %ID/cc tissue of TTX-MC138-NODAGA-Cu64 delivered to metastatic lesions |
| **Secondary Objectives** | **Secondary Endpoints** |
| PK and biodistribution of TTX-MC138-NODAGA-Cu64 | PK of TTX-MC138-NODAGA-Cu64, metabolite analysis, and target engagement |
| Safety of a single microdose of TTX-MC138-NODAGA-Cu64 | Incidence and severity of TEAEs and labs |

## Measurements by Time




| Study Day | -14 to -1 | 1 | 2 | 30 (± 5) |
|---|---|---|---|---|
| Informed Consent | X | | | |
| FDG PET-MRI | X | | | |
| ECOG PS | X | X | | |
| Clinical Labs | X | X | X | |
| ECG | X | X | X | |
| Adverse Events | X | X | X | X |
| Microdosing | | X | | |
| PET-MRI (whole body) | | X | X | |
| PK sampling | | X | X | |

Patient 1
Preliminary Results

# Dynamic Imaging Data (*Data Monitoring Is Ongoing*)

Female, Stage IV, metastatic breast cancer. Primary metastatic sites: bone, liver, lungs

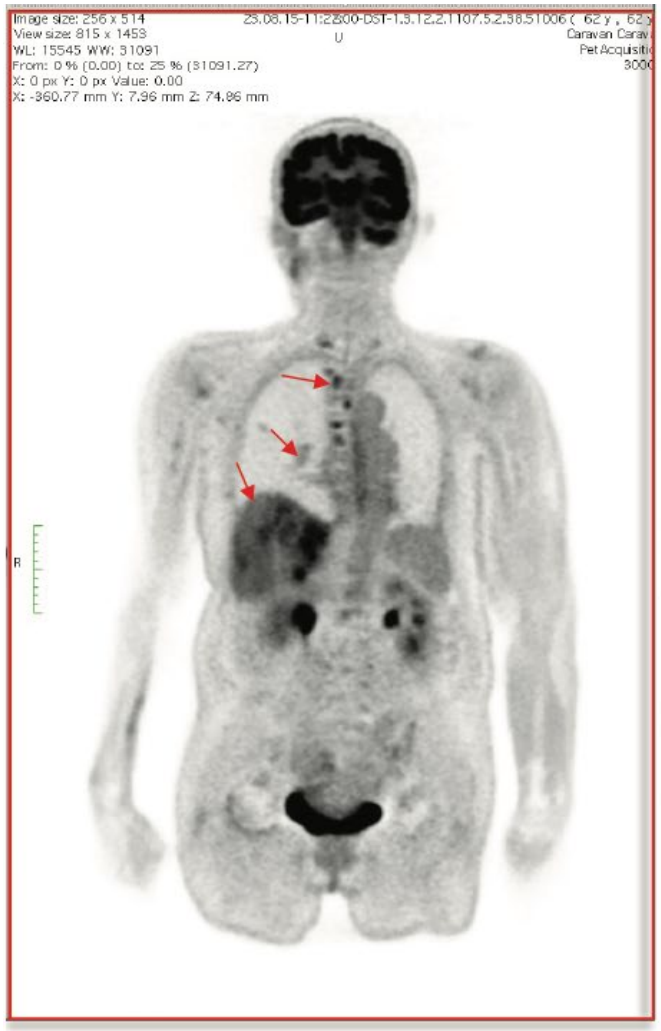
FDG PET-MRI before dosing with TTX-MC138 was used to indicate location of metastatic lesions (red arrows)

PET/MRI at 2, 3, 6 and 24 hours post-dosing was used to detect the presence of TTX-MC138

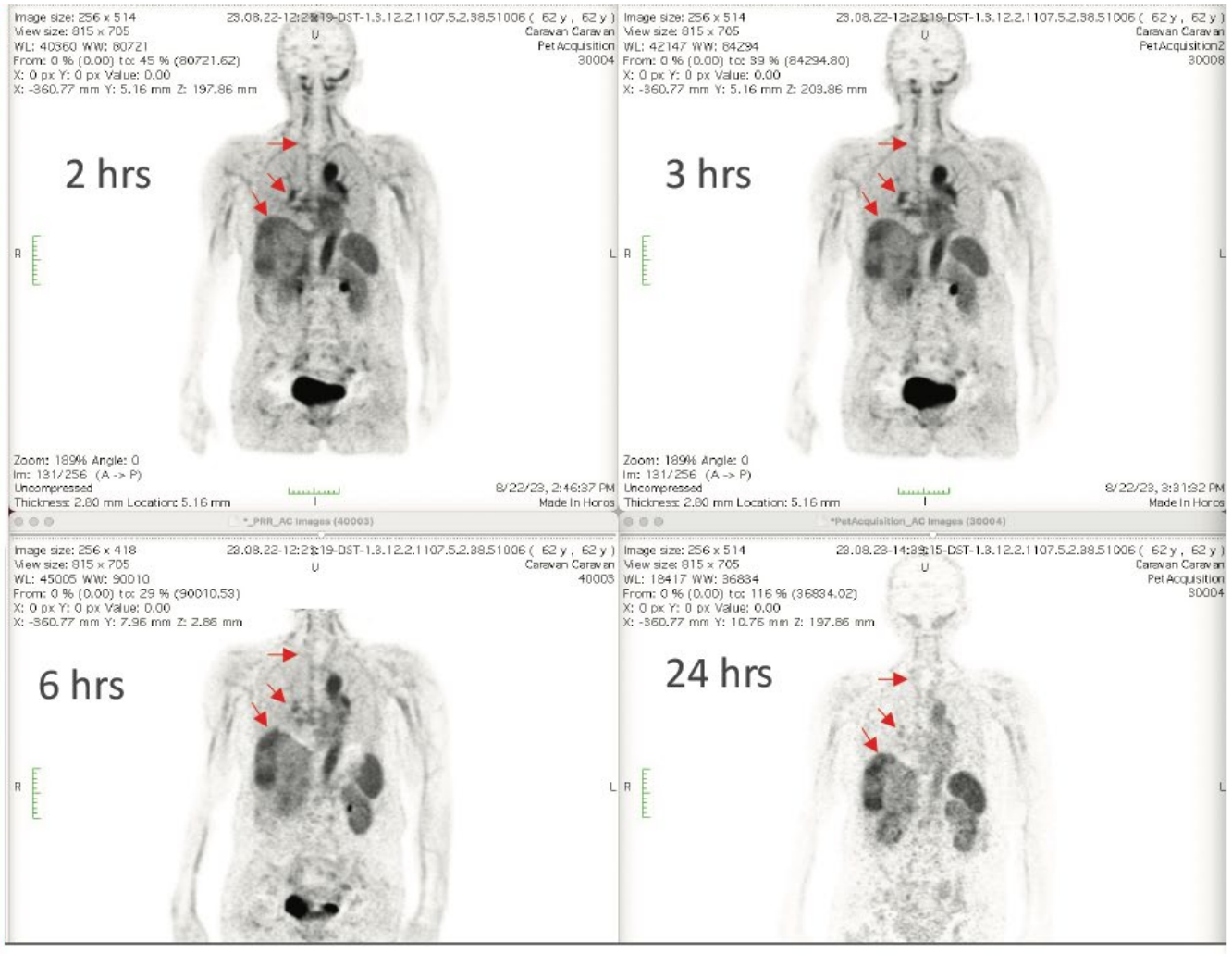
Results show TTX-MC138 accumulation (red arrows) in the metastatic lesions

No safety issues; absence of any allergic hypersensitivity related adverse events

FDG PET-MRI



64Cu-TTX-MC138 PET-MRI



Clinical Trials | Phase I/II Trial Design

Clinical trial design assesses safety, RP2D* and early of anti-tumor activity

| Screening | Phase 1a | Phase 1b |
|---|---|---|
| Advanced Solid Tumors | Escalating Dose Levels<br>Indication: All comers<br>Design: Bayesian Optimal Interval Design (BOIN)<br>N ≤ 32 | Dose Expansion<br>Up to 3 cohorts; indications TBD.<br>Design Scenario: Dose and schedule pending Phase 1 data analysis. |

Phase 1/2: Open-label, multicenter, dose-escalation

Primary Objectives:
- Evaluate the safety and tolerability
- Determine maximum tolerated dose (MTD)
- Select a recommended Phase 2 dose (RP2D).

Secondary objectives: Characterize pharmacokinetics and pharmacodynamics.

Exploratory Objectives: Explore the effect of TTX-MC138 on biomarker expression.

Dose Rationale: Non-clinical data, NHP data, Physiologic PK Model

Dosing Scheme: Up to four dose levels planned for evaluation

Schedule: Screening, treatment 28-day cycles consisting of 1 dose of study drug administered as an intravenous (IV) infusion and Survival Follow Up

Indications: All comers in Phase 1a; Phase 1b tumor types to be determined based on Phase 1a data.

Key Assessments: CT Scan, Biopsy, miR-10b, ct-DNA, RNA Sequencing

*RP2D – Recommended Phase II dose

# Advancing Multiple Partnering Opportunities around TTX Delivery System and Therapeutic Candidates

Partnering | Strategic Collaborations

| Product | Partner | Program; Progress |
|---|---|---|
| TTX-CRISPR (BEC) | Akribion Genomics | Optimizing *in vitro* POC* then move into animals |
| TTX-mRNA | Debiopharm | Successful *in vitro* delivery of mRNA inside tumor cells; next step is optimizing for targeted delivery |
| TCD-miR-10b | LabCorp | Developing assay for clinical measurement of miR-10b in patient samples for clinical trials |
| TTX-MC138 | MD Anderson Cancer Center | Clinical development of TTX-MC138 |
| TTX-MC138 | Massachusetts General Hospital | Clinical development of TTX-MC138 |
| TTX-siRNA | Potential** | Tumor-targeted siRNA delivery |
| TTX-mRNA | Potential** | mRNA delivery to tumors |
| Various | Michigan State University | Preclinical development of pipeline candidates |

* Proof of Concept
** Negotiations in Progress

# Patent Portfolio

## Patent Coverage for TTX Platform and Therapeutic Candidates

Intellectual Property

# Patents and Applicaitons

## Patents/applications cover both composition of matter and methods claims

| Technology | Geography | Expiration | Patents/Applications | Notes |
|---|---|---|---|---|
| TTX IONP for Payload Delivery | US, EU, CA, CN, KR | 2039 | WO2021/113829 | IONP design, payload delivery |
| Nanosensor IONP | 75% of World | 2043 | US10,086,093; EP 2 961 386 | IONP, polynucleotide and polypeptide detection in cells & tissue |
| **Target** | **Geography** | **Expiration** | **Patents/Applications** | **Notes** |
| miR-10b | 75% of World | 2043 | US9,629,812; US9,763,891; US10,463,627; Two Unpublished Continuations | IONP delivery of antagomir, targeting, low dose, sustained release. |
| miR-10b, miR-17, miR-18, miR-19b, miR-21, miR-26a, miR-29a, miR-92a, miR-155, miR-210, miR-221 | US, EU, JP, KR | 2040 | WO2022/147177 | Target sequences form basis of RIG-I activation technology. |
| PDL-1 | US, EU, JP, CN, CA, AU, KR | 2038 | WO2020/068398 | IONP delivery of siRNA |

IONP: Iron-oxide nanoparticle

# Target Milestones

## Potential for Value-Generating Catalysts in 2024 and 2025

Value Inflection

# Potential to Create Multiple Liquidity Opportunities

Advance Existing or Additional Partnerships

## 2023

TTX-MC138:

- Phase 0 clinical trial preliminary results
- Completed final tox testing for Phase I IND
- GMP manufacturing of drug product completed

## 2024

TTX-MC138 – Phase I

- FDA Authorization
- IRB Approvals
- Commence Multicenter Trial
- Preliminary Results

Other IND-enabling studies:

- TTX-RIGA or TTX-siPDL1
- Finalize diagnostic test for miR-10b

## 2025

TTX-MC138

- Expansion Phase I/II dose patients

or, potentially,

- Prepare for Phase III or commercialization (depending on results)

Advance next therapeutic candidate(s) to clinic

- Initiate IND submissions for additional candidates

# TransCode Team

TransCode's senior leadership combines decades of oncology drug discovery and development expertise, adding both scientific insight and valuable strategic perspective.

## Executive Team

Tom Fitzgerald, Interim CEO, CFO, Director

Zdravka Medarova, PhD Founder/Chief Scientific Officer

Susan Duggan, RN, MBA Sr. VP of Operations

Tania Montgomery, Business Development

## Independent Directors

Philippe Calais, PhD Executive Chairman

Magda Marquet, PhD Director

Erik Manting, PhD Director

## Key Advisors

Keith Flaherty, MD Advisor

Frank Slack, PhD Advisor

Lubo Nechev, PhD Advisor

# Potential to Transform the Way Cancer is Treated

| | |
|---|---|
| Value Proposition | Undervalued therapeutic assets with potential for significant return on investment<br>Clinical stage oncology company with a focus on treating metastatic disease<br>Proprietary delivery platform designed to overcome the challenges of therapeutic delivery to tumors & metastases<br>Complete regression of established metastases using TTX-MC138 in preclinical studies<br>Extensive patent portfolio covering delivery system and targeted therapeutics<br>Expanding strategic partnerships |
| Differentiated Delivery System | Tunable chemistry optimized for functionalization against validated oncology targets<br>Size and charge optimized for stability, long circulation, and optimal PK, PD and biodistribution<br>Nanoparticles used in cancer imaging & treatment of iron deficiency anemia repurposed as delivery system<br>Delivery platform is image-capable via MRI – potential for visual confirmation and quantification of delivery |
| Major Unmet Need | ~10 million people died of cancer in 2020*; over 90% attributable to metastasis<br>Virtually no treatment options for cancer patients with advanced disease<br>Metastatic cancer market to reach $136.9 billion by 2032** |

# Additional Slides

# Clinical Validation of miR-10b as a Target

## Hazard Ratios for Overall Survival Based on High vs. Low miR-10b Expression

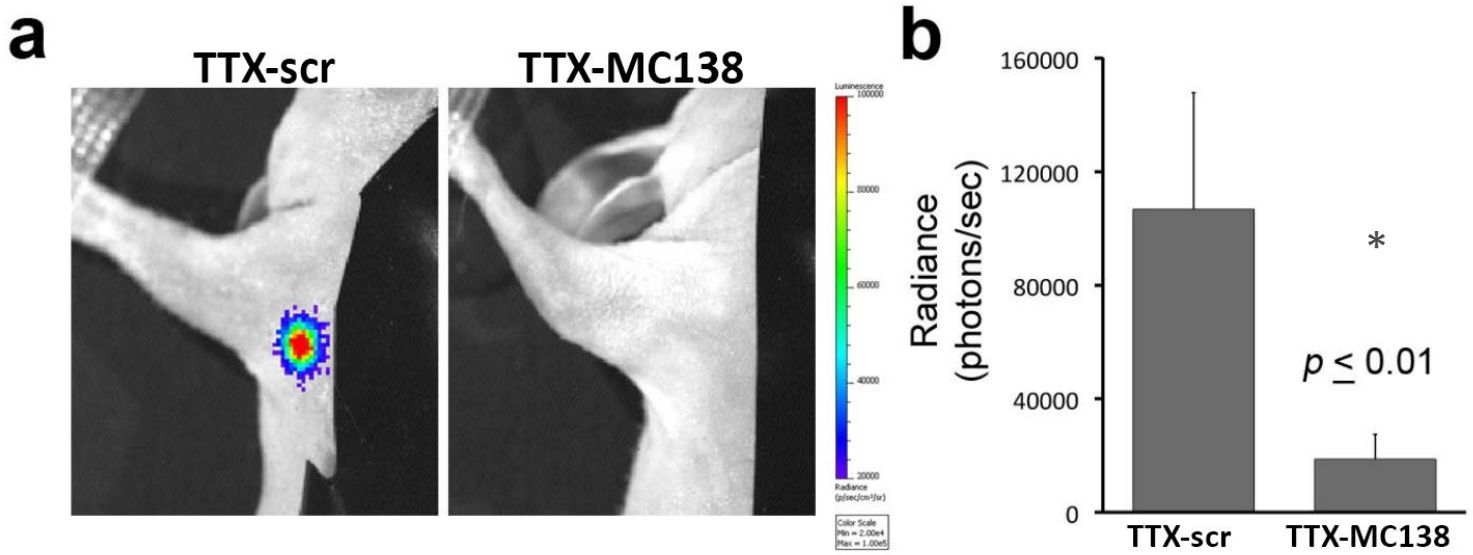


**TABLE 2** Pooled HR for OS according to subgroup analysis

| Categories | Studies (n) | Number of patients | Fixed effects model | | Heterogeneity | |
|---|---|---|---|---|---|---|
| | | | HR (95% CI) for OS | p-value | $I^2$ (%) | $P_h$ |
| OS | 17 | 1,681 | 1.99 (1.51–2.61) | 0.000 | 72.6 | 0.000 |
| Cancer type | | | | | | |
| Digestive system cancers | 4 | 592 | 1.95 (1.46–2.60) | 0.000 | 0 | 0.489 |
| Others | 13 | 1,089 | 2.06 (1.45–2.93) | 0.000 | 77.6 | 0.000 |
| PC | 2 | 210 | 2.47 (1.69–3.60) | 0.000 | 0 | 0.366 |
| NSCLC | 4 | 311 | 1.75 (1.21–2.54) | 0.003 | 0 | 0.930 |
| Glioma | 2 | 223 | 4.84 (3.25–7.22) | 0.000 | 0 | 0.944 |
| CRC | 4 | 592 | 1.95 (1.46–2.60) | 0.000 | 0 | 0.489 |
| BC | 4 | 311 | 1.21 (1.05–1.38) | 0.007 | 0 | 0.972 |
| Cutoff value | | | | | | |
| Median | 8 | 763 | 2.51 (1.76–3.57) | 0.000 | 52.8 | 0.038 |
| Mean | 2 | 174 | 1.80 (1.10–2.97) | 0.019 | 0 | 0.427 |
| Others | 7 | 744 | 1.61 (1.17–2.23) | 0.004 | 55.0 | 0.038 |
| Analysis type | | | | | | |
| Multivariate | 12 | 1,217 | 1.63 (1.32–2.00) | 0.000 | 36.1 | 0.102 |
| Survival curves | 5 | 464 | 3.20 (2.01–5.10) | 0.000 | 54.0 | 0.069 |
| Sample size | | | | | | |
| ≥100 | 6 | 889 | 2.45 (1.99–3.02) | 0.000 | 63.3 | 0.018 |
| <100 | 11 | 792 | 1.35 (1.19–1.53) | 0.000 | 53.6 | 0.017 |

*Note.* BC: breast cancer; CI: confidence interval; CRC: colorectal cancer; HR: hazard ratio; NSCLC: non-small-cell lung cancer; OS: overall survival; PC: pancreatic cancer.

# Prevention of Metastatic Breast Cancer



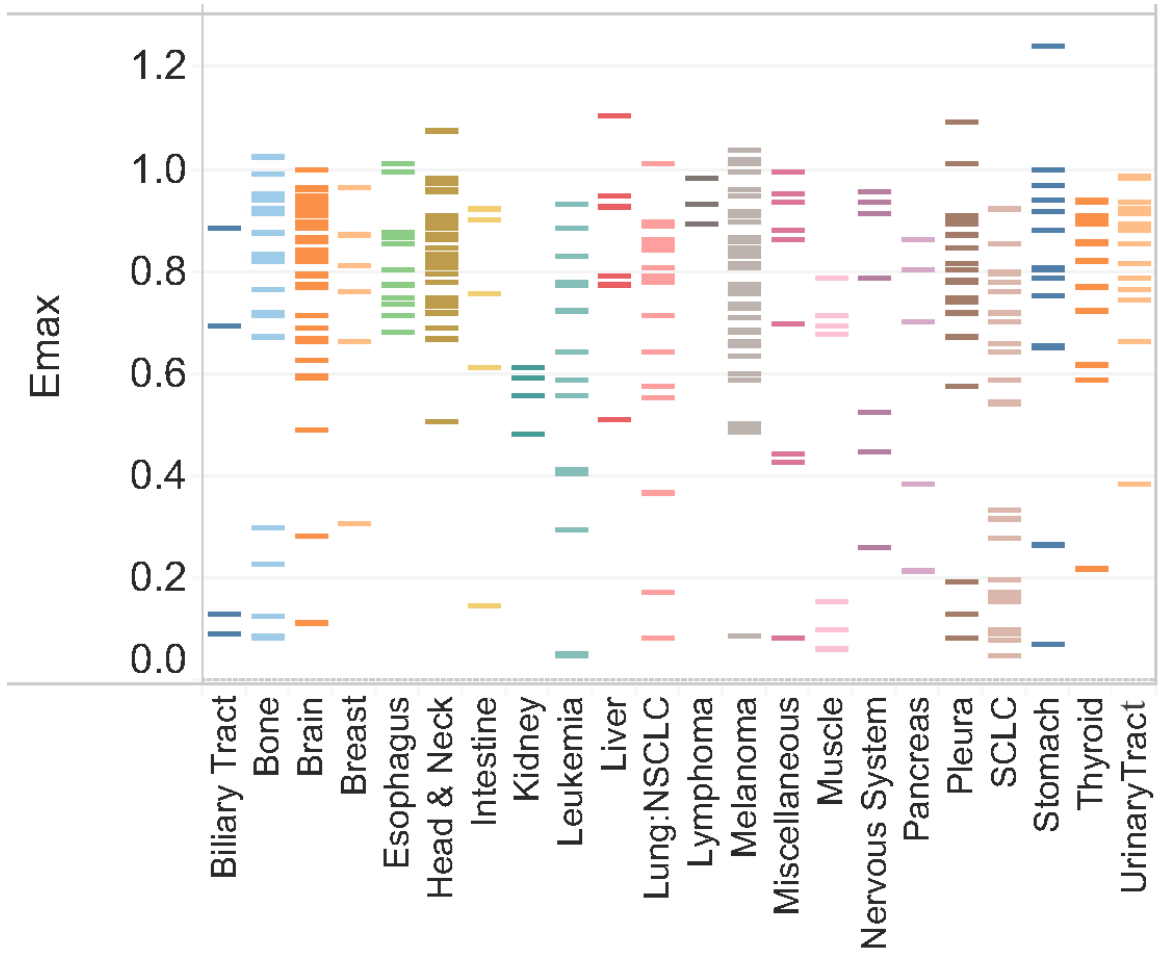

- Human breast cancer cells implanted orthotopically into immunocompromised mice
- Mice were treated with MN-anti-miR10b (TTX-MC138) prior to formation of metastasis
- **None of the treated animals formed metastases**
- By contrast, control animals treated with an inactive form of TTX-MC138 (MN-scr-miR) formed detectable lymph node metastases within 4 weeks

Source: Oncogene 32:1530. 2013.

# Evidence of Efficacy in Multiple Cancer Types

The sensitivity to TTX-MC138 was tested in 624 human cell lines representing metastatic and non-metastatic cancers.

TTX-MC138 elicits strong viability responses in a distinct subset of cell lines




Profile of response across cell lines from different tissues of origin. The response to TTX-MC138 is shown as Emax (maximum effect observed: minimum cell viability observed across the two maximum doses tested).

PLoS One, 2018 Jul 20;13(7):e0201046.

Patient 1 Preliminary Results

# Blood Analysis - Plasma Radioactivity *(Data Monitoring Is Ongoing)*

*p.i. = post injection*

| Parameter/Timepoint | Pre | 15 min p.i. | 30 min p.i. | 1 hr p.i. | 2 hr p.i. | 4 hr p.i. | 10-30 hr p.i. |
|---|---|---|---|---|---|---|---|
| Date of sample Collection (DD/MMM/YYYY) | 22-Aug-2023 | 22-Aug-2023 | 22-Aug-2023 | 22-Aug-2023 | 22-Aug-2023 | 22-Aug-2023 | 23-Aug-2023 |
| Time of sample collection (HH:MM) | 12:36 | 14:16 | 14:36 | 15:03 | 16:03 | 18:08 | 14:00 |
| Metabolite analysis (Percent intact compound %) | - | 90.3 | 93.1 | 93.7 | 96.3 | 98.1 | 95.6 |
| | | | | | | | |
| Plasma radioactivity per volume (kBq/mL) | - | 13.4 | 13.1 | 12.0 | 11.1 | 11.0 | 5.3 |

- Diagnosis – Female, Stage IV, Metastatic Breast Cancer
- Primary Metastatic Sites: Bone, Liver, Lungs
- All sample timepoints collected; pre-dose sample collected but not analyzed
- No adverse events reported

❖ Preliminary Data - data entry and data monitoring are ongoing

# TTX-siPDL1: A First-in-Class siRNA Checkpoint Inhibitor

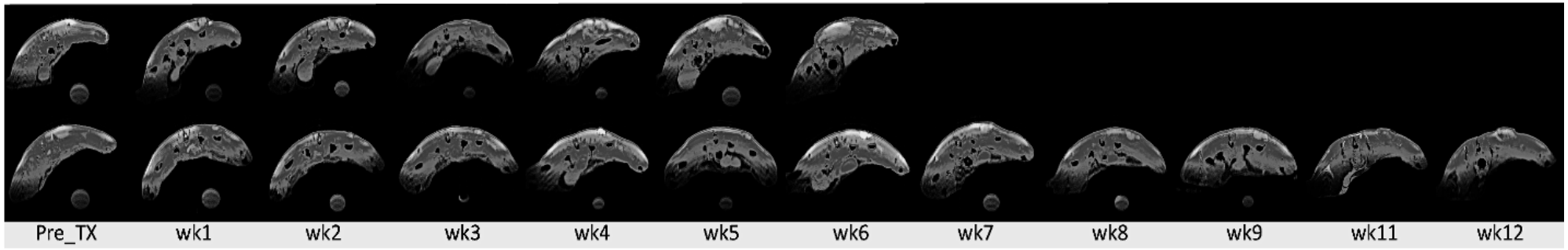
Mechanism of action based on RNA interference with potential to be more efficient that traditional monoclonal-antibody based checkpoint inhibitors

Potential to be applied against multiple cancers, including melanoma, lung cancer, pancreatic cancer, etc.

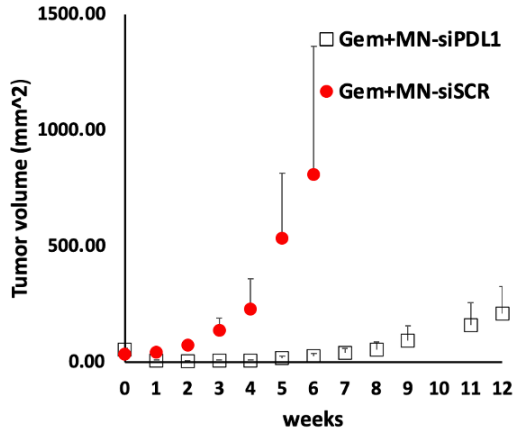
# Efficacy in Preclinical Mouse Model of Pancreatic Cancer (PDAC)

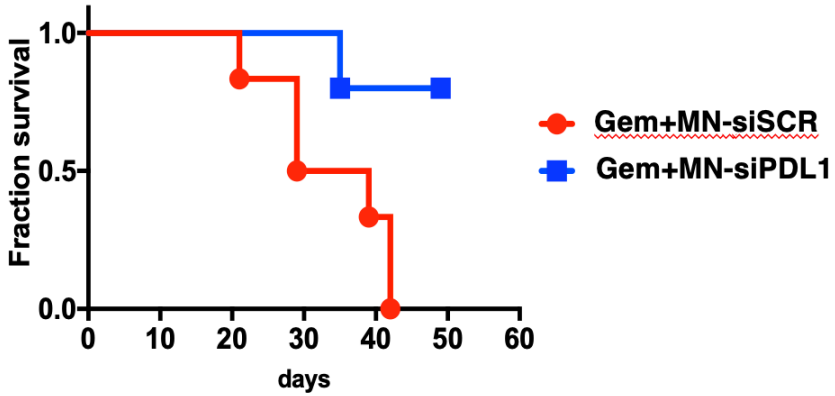
Gem+MN-siSCR

Gem+MN-siPDL1




*MN-siPDL1 - TTX-siPDL1
MN-siSCR, inactive control
Gem, gemcitabine

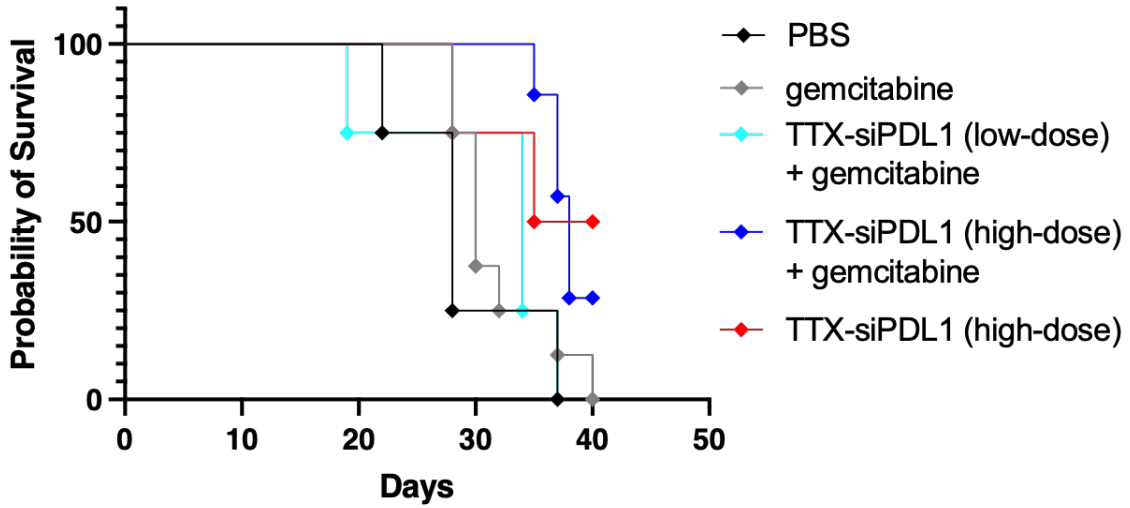



- TTX-siPDL1 + gemcitabine regressed pancreatic tumors by 90% within the first two weeks of treatment and delayed tumor growth.
- Treatment increased survival - 67% of the experimental animals survived for 12 weeks.

Source: Scientific Reports, 9 (1), 4712 2019

# Efficacy in A Highly Aggressive Model of PDAC with Intense Desmoplasia




| HR for OS vs. PBS | HR (95% CI) |
|---|---|
| | |
| gemcitabine | 0.42 (0.082-2.18) |
| TTX-siPDL1 (high-dose) | 0.24 (0.04-1.51) |
| TTX-siPDL1 (low-dose) + gemcitabine | 0.69 (0.11-4.30) |
| TTX-siPDL1 (high-dose) + gemcitabine | 0.08 (0.01-0.56) |

- TTX-siPDL1 + gemcitabine dramatically decreased hazard ratios for survival relative to standard-of-care chemotherapy
- Treatment reduced tumor growth rate relative to buffer-treated controls by 4-fold

Hy15549 cells implanted orthotopically

# TTX-RIGA

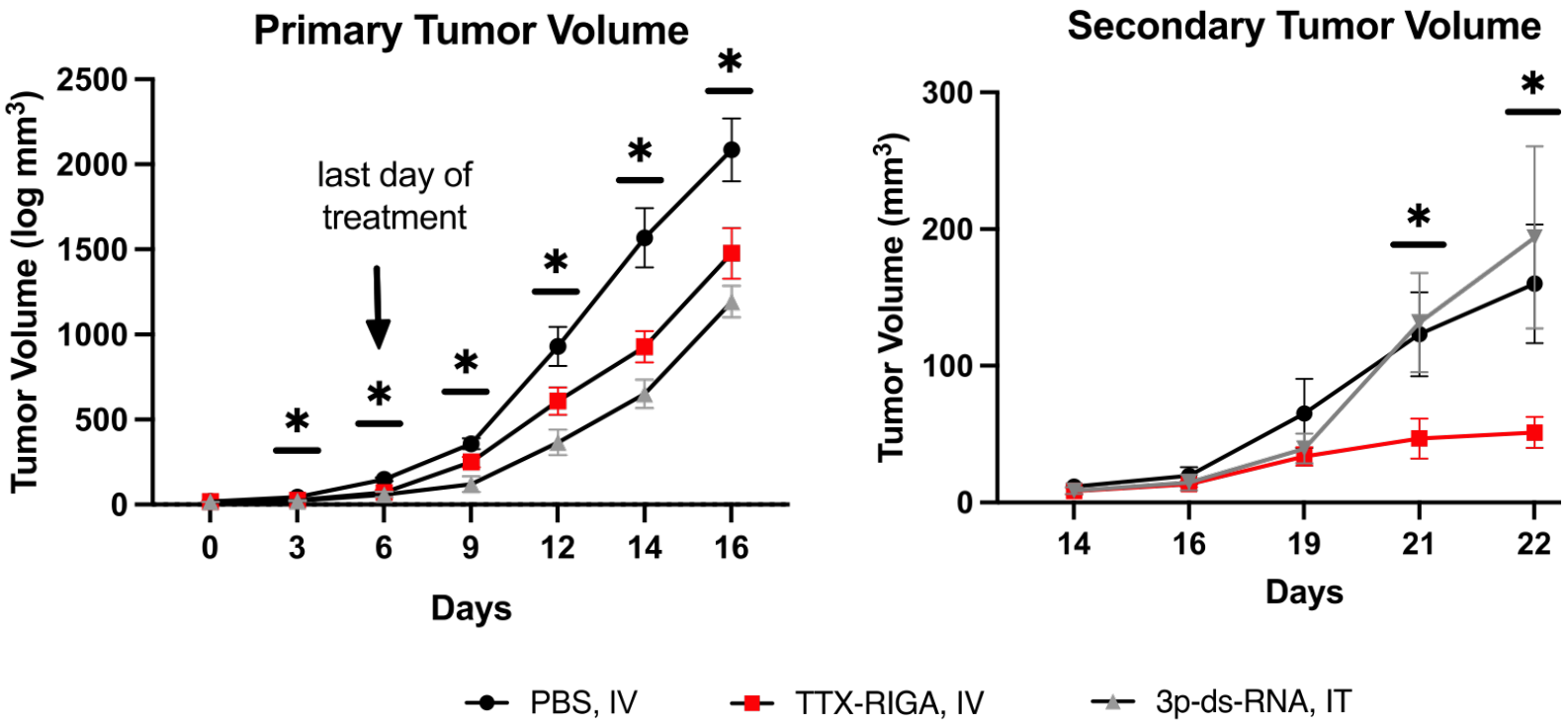
## A Pattern Recognition Receptor Agonist

Potential to trigger the immune system to regress cancer

Treatment applicable to deep-seated or disseminated cancer

Potential to cause immune-rejection of pre-existing or recurrent tumors

# *In Vivo* Efficacy




- Mouse melanoma cells implanted into mice
- Primary tumor growth was inhibited relative to buffer-only control
- Secondary recurrent tumor growth was dramatically inhibited relative to standard-of-care RIG-I agonists

# Achievements

## 2016

Company Founded

## 2017-20

SAB established Execute MGH License File new patents Expand product line

Added 2 Independent BOD

## 2021

IPO - $25.4M (net)

Hired Co-Founder as CTO

Radiolabeled Drug Publication

Added 1 Independent BOD

SBIR Grant awarded from NIH

Hired 7 employees New Lab space at MBI

## 2022

Alliance member of MD Anderson Cancer Ctr

Orphan Drug Designation (ODD) received for siPDL1 in pancreatic cancer

Pancreatic cancer study published - 40% of animals showed complete regression

FDA approves FIH clinical trial

Added 12 employees

Preclinical studies completed in 3 products

# Publications

*Linked references in italics below are authored by TransCode's scientific co-founders*


*Anna Moore, N A. Savan, Paulo V. Saavedra, Alan Halim, Vilma Yuzbasiyan-Gurkan, Ping Wang, Byunghee Yoo, Matti Kiupel, Lorenzo Sempere, Zdravka Medarova: Case Report: microRNA-10b as a Therapeutic Target in Feline Metastatic Mammary Carcinoma and its Implications for Human Clinical Trials. Frontiers in Oncology October 26, 2022 12:959630*

*Le Fur et al.,: Radiolabeling and PET–MRI micro-dosing of the experimental cancer therapeutic, MN-anti-miR10b, demonstrates delivery to metastatic lesions in a murine model of metastatic breast cancer. Cancer Nanotechnology 2021;12(1):16.*

*Byunghee Yoo, Alana Ross, Pamela Pantazopoulos & Zdravka Medarova: miRNA10b-directed nanotherapy effectively targets brain metastases from breast cancer, Scientific Reports volume 11, Article number: 2844 (2021)*

*Sheedy, P, Medarova, Z: The fundamental role of miR-10b in metastatic cancer. Am J Cancer Res 2018;8(9):1674-1688.*

*Yoo B, Greninger P, Stein GT, Egan RK, McClanaghan J, Moore A, et al. (2018) Potent and selective effect of the mir-10b inhibitor MN-anti- mir10b in human cancer cells of diverse primary disease origin. PLoS ONE 13(7): e0201046 2018.*

*Yoo B, Fuchs BC and Medarova Z: New Directions in the Study and Treatment of Metastatic Cancer. Frontiers in Oncology Volume 8, Article 258, July 2018*

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*Yoo B, Kavishwar A, Ross A, Wang P, Tabassum DP, Polyak K, Barteneva N, Petkova V, Pantazopoulos P, Tena A, Moore A, Medarova Z: Combining miR-10b-targeted nanotherapy with low-dose doxorubicin elicits durable regressions of metastatic breast cancer. Cancer Res 2015, 75:4407-4415.*

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*Yigit MV, Ghosh SK, Kumar M, Petkova V, Kavishwar A, Moore A, Medarova Z: Context-dependent differences in miR-10b breast oncogenesis can be targeted for the prevention and arrest of lymph node metastasis. Oncogene 2013;32:1530-1538*