Optimizing RNA Therapeutics to Deliver a Cancer-Free Future

TRANSCODE THERAPEUTICS™

NASDAQ: RNAZ

July 11, 2024

Forward Looking Statements

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TransCode's Innovative Solution to Metastatic Cancer Using RNA

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

Proprietary nanoparticle delivery platform designed to overcome decades of RNA delivery challenges

Lead candidate, TTX-MC138, targets miR-10b *(an important oncogene in metastatic cancer)*

FDA authorized IND for Phase I/II clinical study *(anticipated launch July 2024)*

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

Over 30 peer-reviewed publications, including *Nature Medicine* and *Cancer Research*

Several partnerships in place; robust IP *(10 patents in 5 patent families)*

Highly experienced team with pharmaceutical industry expertise in science, clinical trials, management

Capitalization

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: RNAZ	June 15, 2024
Common Stock	7,265,658
Warrants (WAEP/Sh $2.58)	11,731,491
Options (WAEP/Sh $2.43)	1,935,837
Total	20,933,016

Team of Experts

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

Executive Team

Tom Fitzgerald, MBA
Interim CEO, CFO

Zdravka Medarova, PhD
Founder/Chief Scientific Officer

Susan Duggan, RN, MBA
Sr. VP of Operations

Tania Montgomery, MBA,
VP Business Development

Independent Directors

Philippe Calais, PhD
Chairman

Magda Marquet, PhD
Director

Erik Manting, PhD
Director

Key Advisors

Keith Flaherty, MD
Advisor

Frank Slack, PhD
Advisor

Lubo Nechev, PhD
Advisor

Critical Need for An Effective Therapy Against Metastatic Cancer

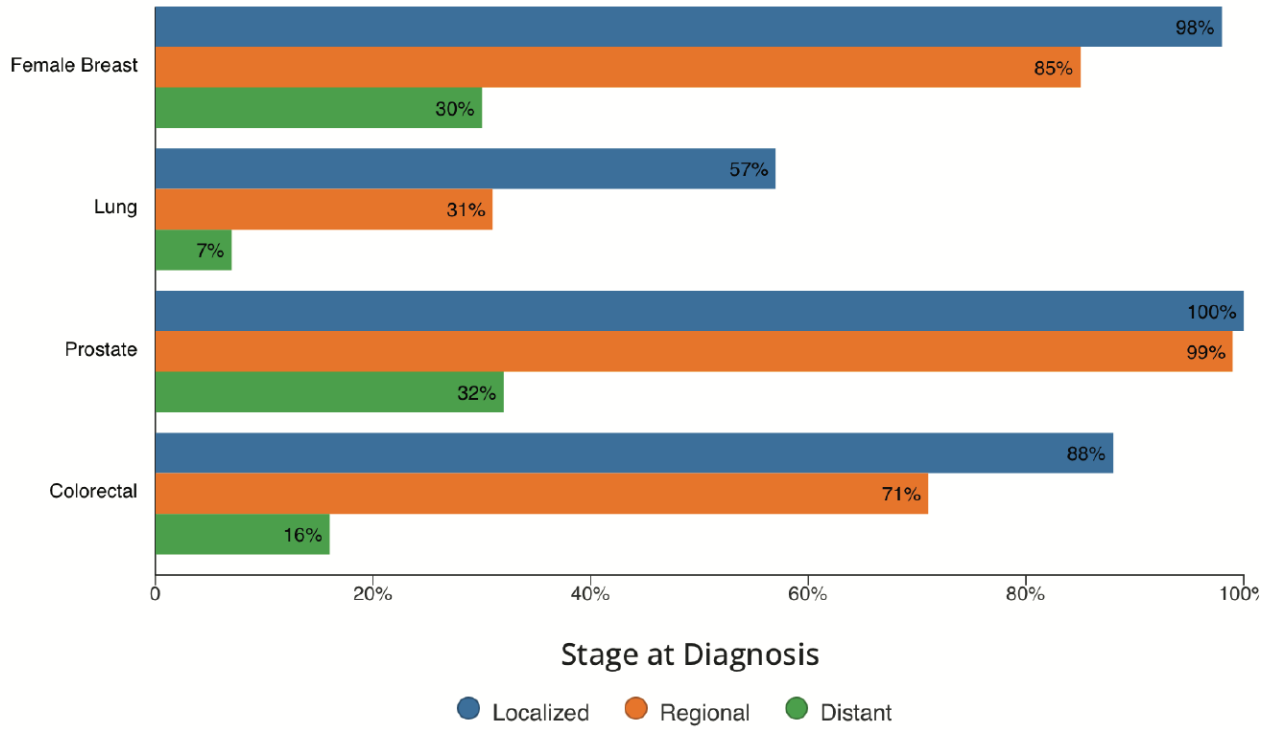
Metastatic (or *"distant"*) cancer is cancer that has spread beyond its organ of origin

Primary tumors generally respond 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



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

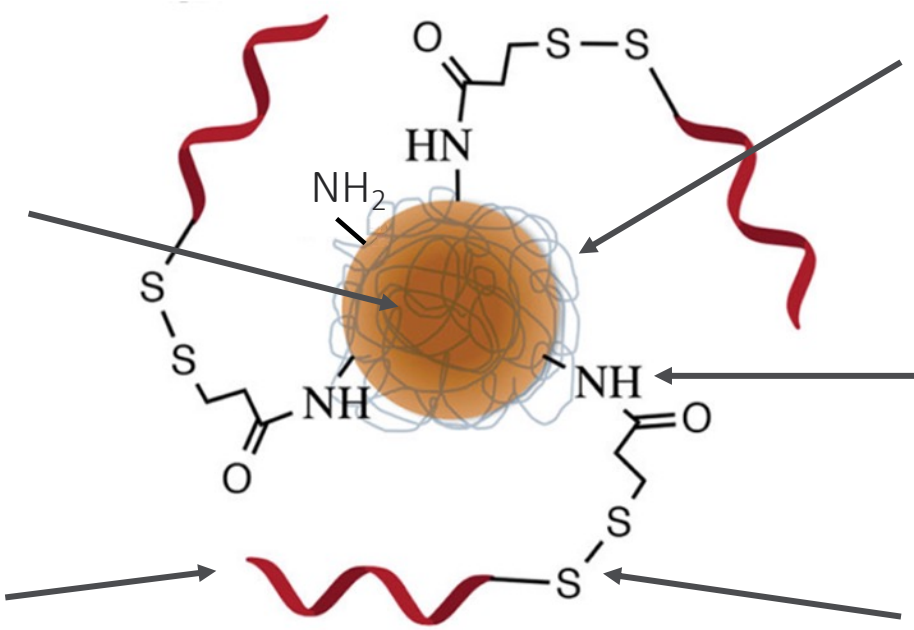
TTX design overcomes long-standing delivery challenges:

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

TransCode's 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

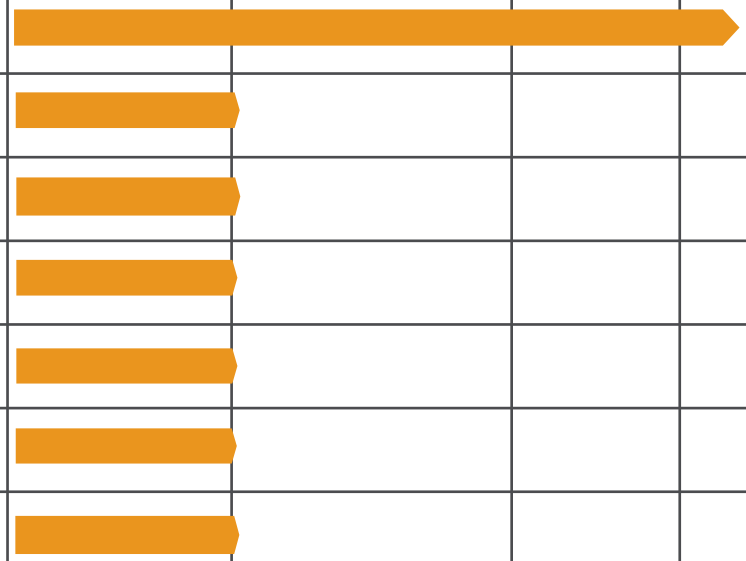
- Strong binding affinity, specificity and stability while minimizing immunogenicity

Disulfide bond

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

Advancing Multiple First-in-Class RNA Therapeutics

Candidate	Strategic Partner	Modality	Disease Indication	Preclinical	IND Enabling	Phase 0	Phase 1	Phase 2	Phase 3
TTX-MC138	Internal	Antisense	Metastatic Cancer *Pancreatic Cancer						
TTX-siPDL1	Internal	RNAi	*Pancreatic Cancer						
TTX-RIGA	Internal	PRR - RIGI	Indication Agnostic						
TTX-CRISPR	Internal	CRISPR (Cas9)	Indication Agnostic						
TTX-BEC	Akribion Genomics	CRISPR (BEC)	Indication Agnostic						
Targeted TTX- mRNA	Debiopharm	mRNA	Indication Agnostic						
TTX- mRNA	Undisclosed	mRNA	Indication Agnostic						



* Received Orphan designation status from FDA

Lead Candidate: TTX-MC138

First-in-Class Therapeutic Candidate Targeting Metastatic Cancer

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

miRNA-10b:

- linked to metastatic disease in >200 clinical studies in cancer patients
- shown to drive metastatic progression in multiple preclinical models
- 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

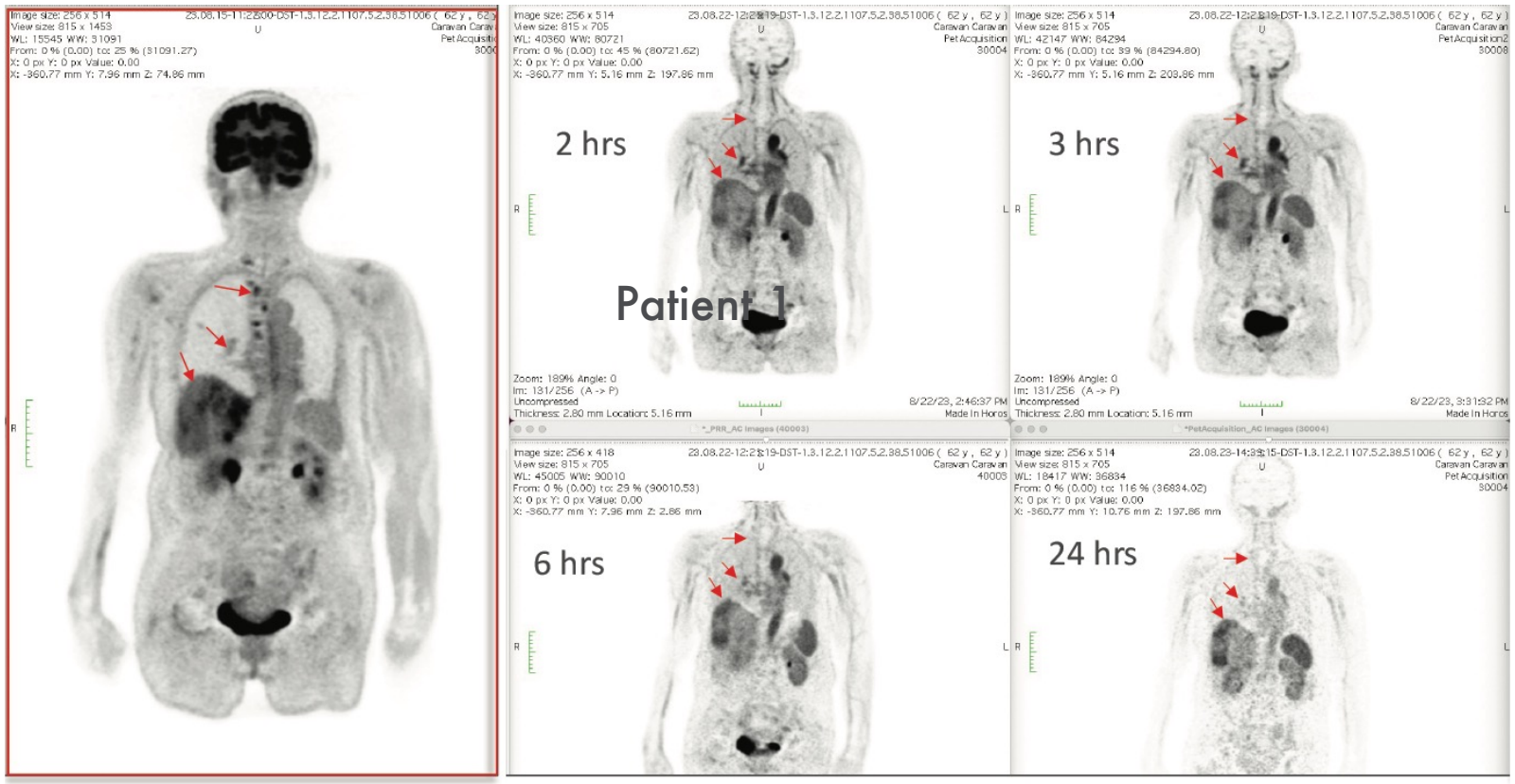
Source: Sheedy et al., Am J Cancer Res. 2018;8(9):1674-1688; Yoo et al., Cancer Res. 2015;75(20):4407-15; Ma et al., Nature. 2007;449(7163):682-8.

Phase 0 Preliminary Results - Patient 1

PET-MRI To Determine Drug Delivery

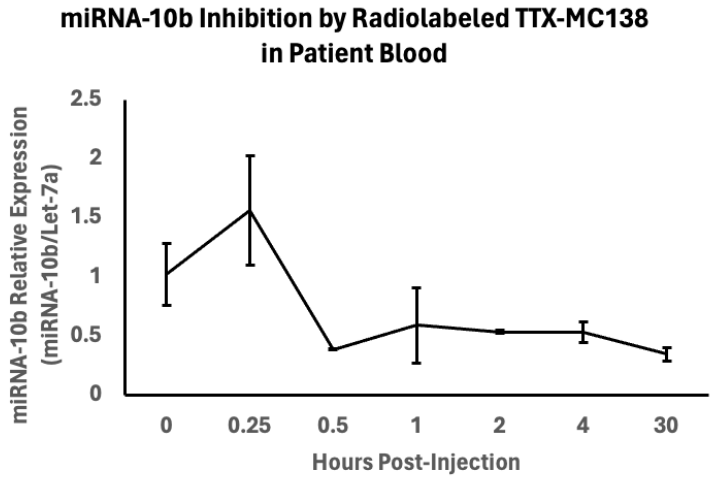
FDG PET-MRI

64Cu-TTX-MC138 PET-MRI



Dynamic Imaging and PD Activity Data

qRT-PCR To Determine Drug Functionality



- Female, Stage IV, metastatic breast cancer. 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**
- **Results show drug functionality/target engagement in patient blood**
- **No safety issues and absence of any allergic hypersensitivity related adverse events**

TTX-MC138 Phase I/II Trial

Clinical trial designed to assess safety, RP2D* and early anti-tumor activity

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

Phase I/II: Open-label, multicenter, dose-escalation

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

Secondary objectives: Characterize pharmacokinetics and pharmacodynamics

Exploratory Objectives: Explore TTX-MC138 effect 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

** Recommended Phase 2 Dose*

RP2D – Recommended Phase II dose

TTX-siPDL1

A First-in-Class siRNA Checkpoint Inhibitor

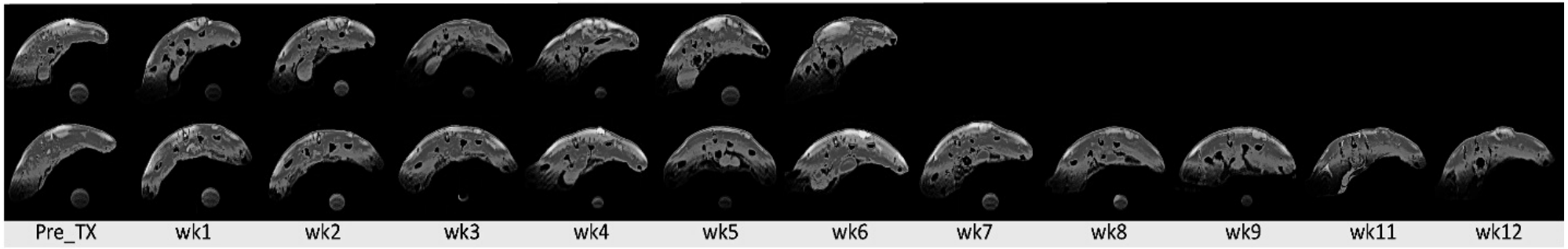
Mechanism of action based on RNA interference with potential to be more efficient than traditional monoclonal-antibody based checkpoint inhibitors

Potential to treat multiple cancers, including melanoma, lung, pancreatic, et al

TTX-siPDL1 Efficacy in Preclinical Mouse Model of Pancreatic Cancer (PDAC)

Gem+MN-siSCR

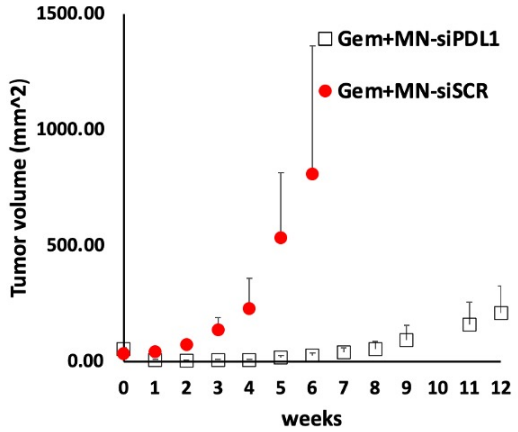
Gem+MN-siPDL1

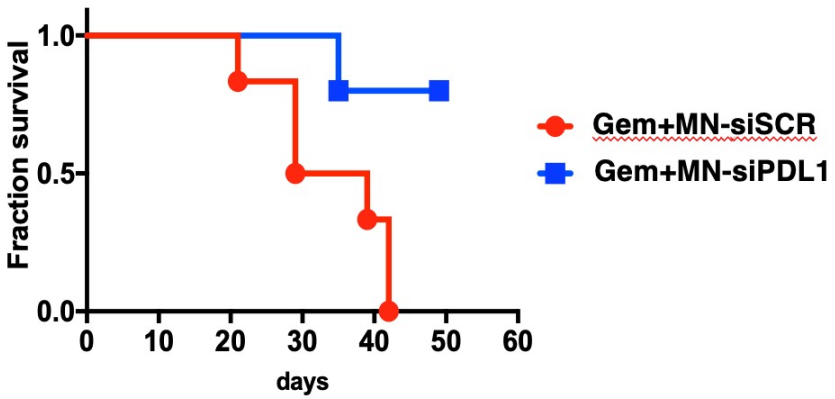


Gem = gemcitabine

MN-siSCR = inactive control

MN-siPDL1 = TTX-siPDL1





TTX-siPDL1 with 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

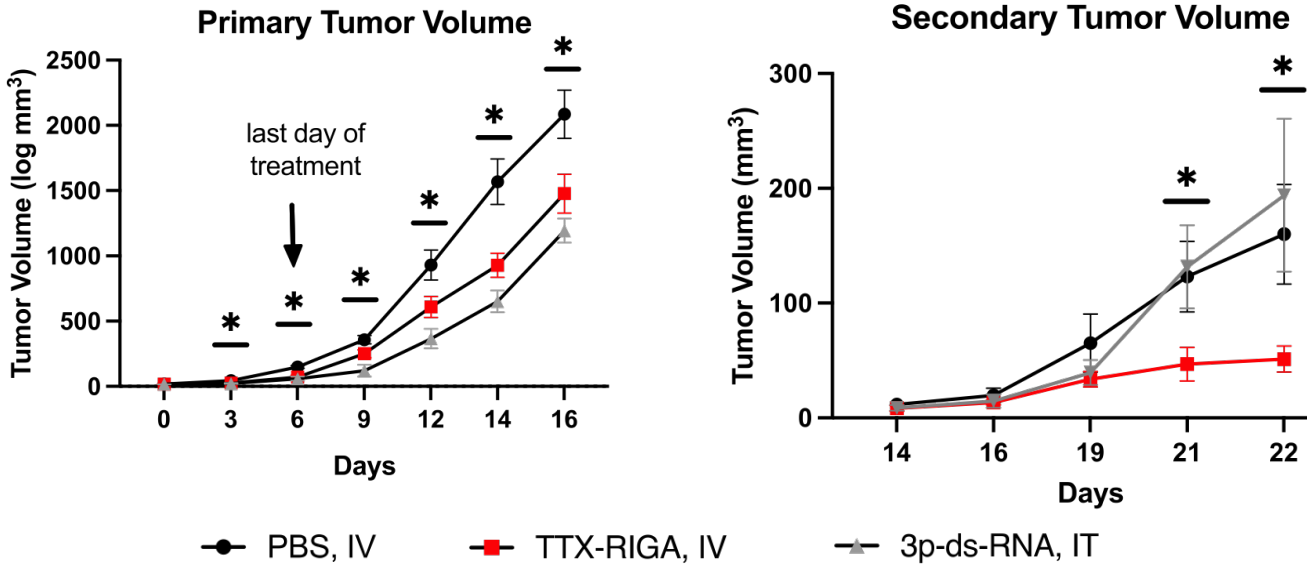
TTX-RIGA

A Pattern Recognition Receptor Agonist

Potential to trigger the immune system to regress cancer

Treatment applicable to deep-seated or disseminated cancer

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



In vivo efficacy in melanoma cells implanted into mice

Primary tumor growth inhibited relative to buffer-only control

Secondary recurrent tumor growth dramatically inhibited relative to standard-of-care RIG-I agonists

Value-Generating Strategic Collaborations

Product	Partner	Program; Progress
TTX-BEC	Akribion Genomics	Optimizing *in vitro* POC* then move into animals
Targeted TTX-mRNA	Debiopharm	Successful *in vitro* delivery of mRNA inside tumor cells; next step is optimizing for targeted delivery
TTX-mRNA	Undisclosed	mRNA delivery to tumors
TTX-siRNA	In Discussion	Tumor-targeted siRNA 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
TTX-MC138	Massachusetts General Hospital	Clinical development
Various	Michigan State University	Preclinical development of pipeline candidates

* Proof of Concept
** Negotiations in Progress

Patents and 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

Potential for 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

- IND Approval
- IRB Approvals
- Launch Multicenter Trial
- Preliminary Results

Other IND-enabling studies

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

Partnerships / Grants

- Debiopharm
- Other

2025

TTX-MC138

- Expand Phase I/II trial
  or, potentially,
- Prepare for Pivotal Trial *(depending on results)*

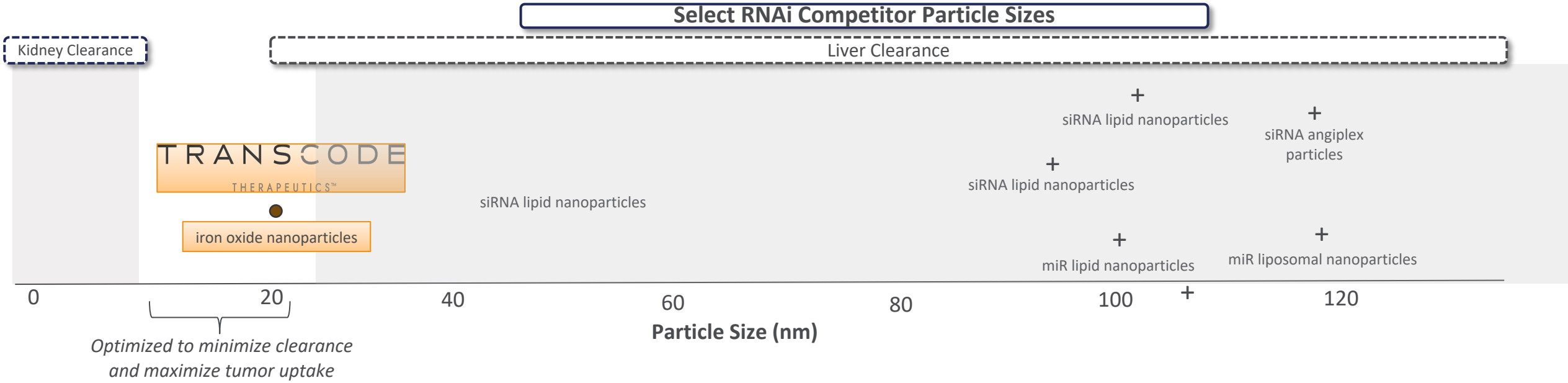
Advance next therapeutic candidate(s) to clinic

- Initiate IND submissions for additional candidates

Partnerships / Grants

Additional Slides

Unique Particle Size, Demonstrated Safety



Stability and optimal PK and biodistribution

Efficient tumor cell uptake and target engagement

Safety and low immunogenicity

Detectable 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

Mechanism of Delivery to Tumors and Metastases

Hemodynamic targeting

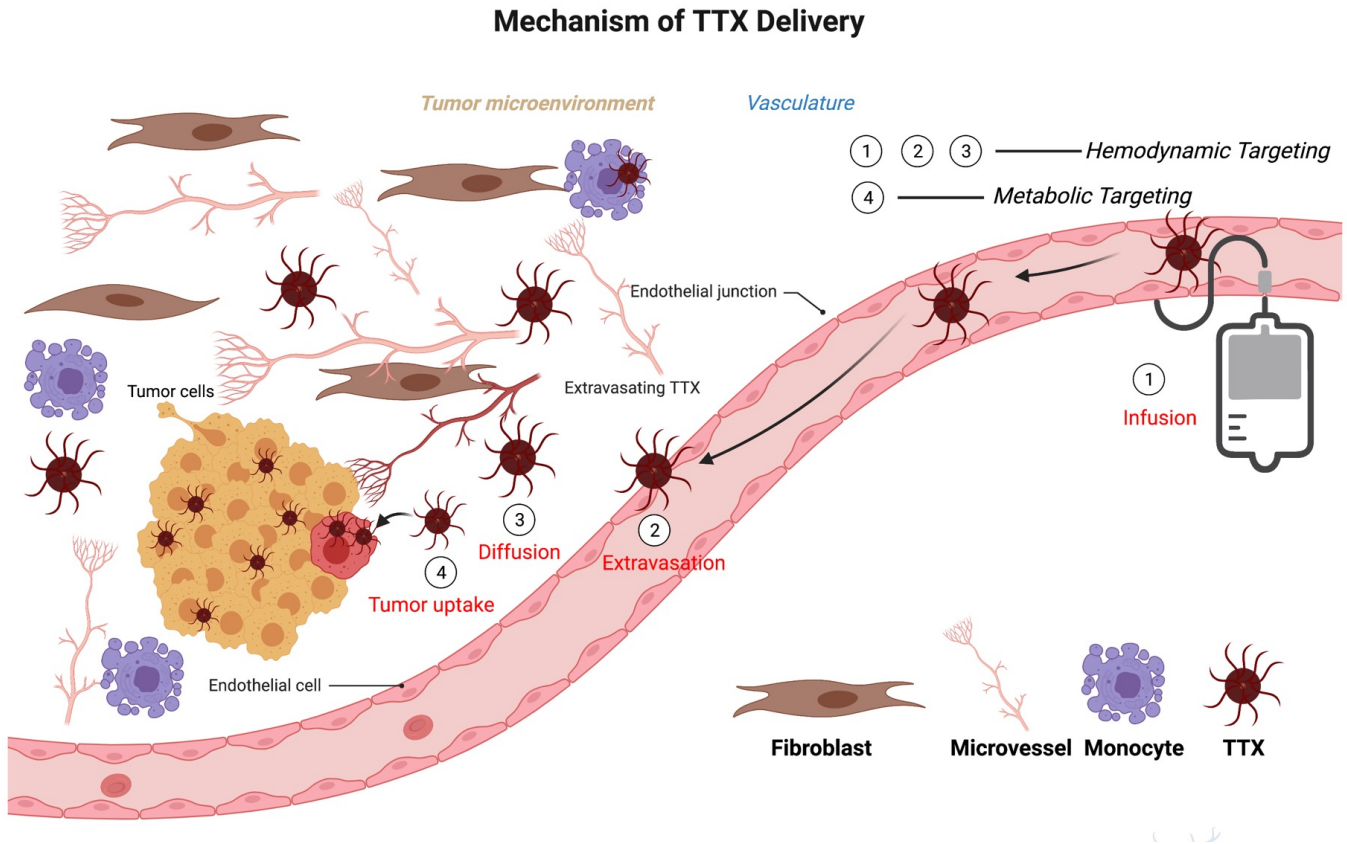
TTX is long-circulating (24-30 hours); allows for distribution throughout the microcirculation of tumors and metastases

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



Mechanism of Delivery to Tumors and Metastases

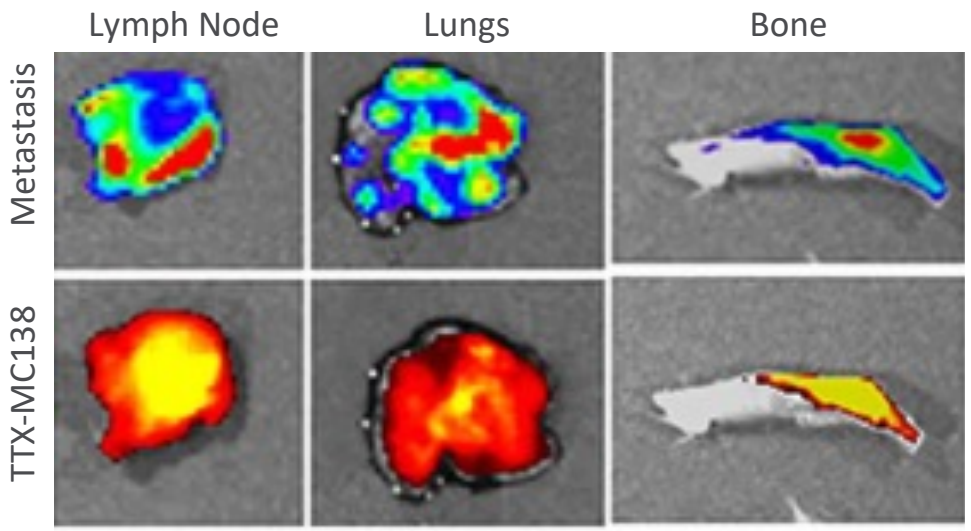
Delivery to tumors and metastases shown in multiple peer-reviewed publications.

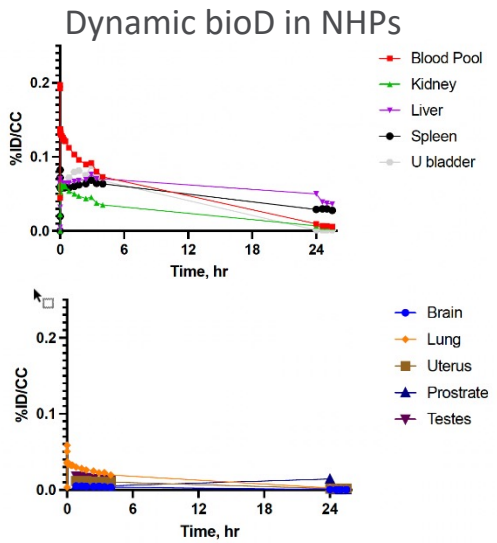
Efficient delivery/pharmacodynamic (PD) activity demonstrated in multiple species (mice, companion animals, and nonhuman primates).

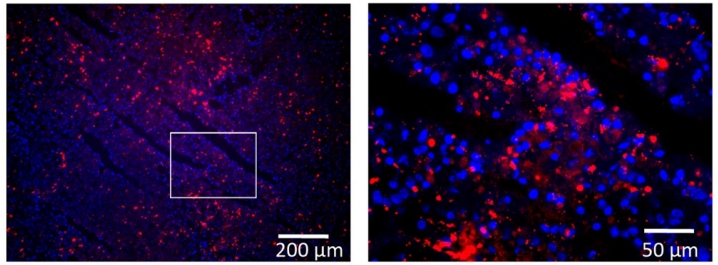
Delivery demonstrated for siRNA, antisense oligonucleotides, immunostimulatory RNA, mRNA, CRISPR, peptides, proteins.

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

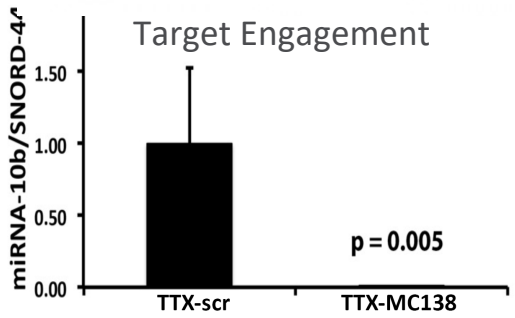
Delivery shown to be highly efficient (>90% in terms of PD activity) and long-lasting (>3 months in spontaneous feline cancer).







Red: TTX-MC138, Blue: cell nuclei



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

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.

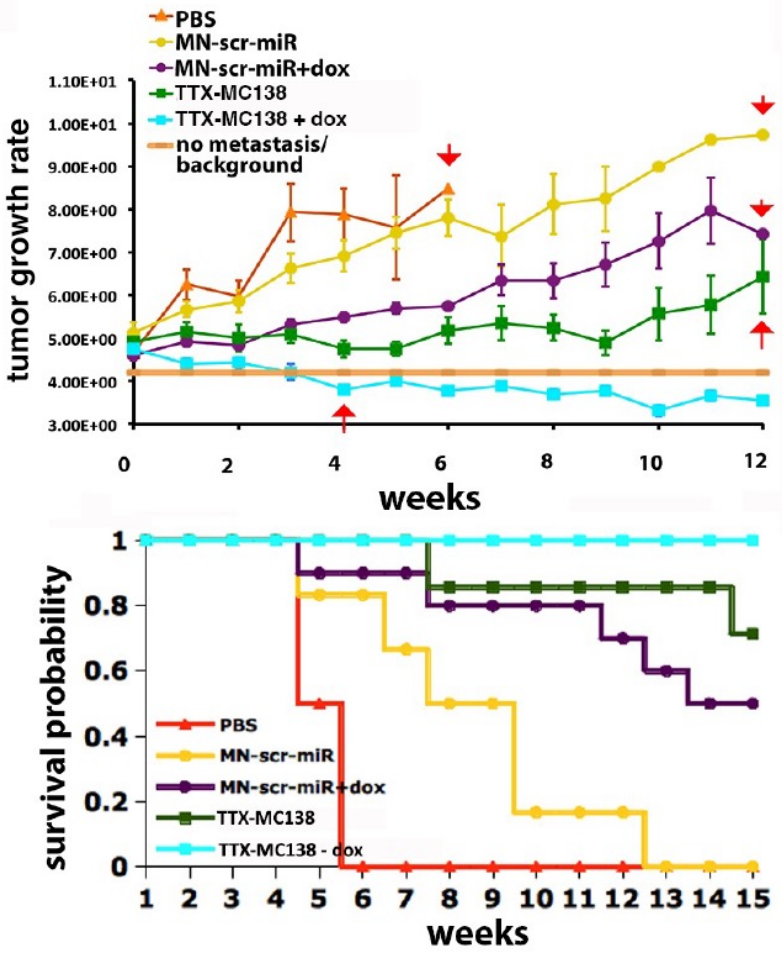
TTX-MC138 Evidence of Durable Regressions (Murine Models)

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

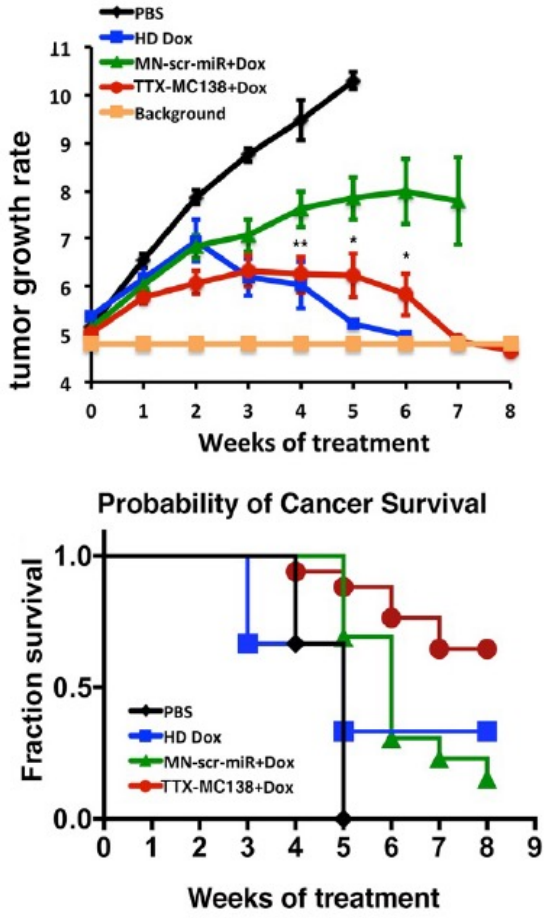
Mice were treated with TTX-MC138 after formation of metastasis

100% (Stage II/III) and 65% (Stage IV) animals regressed disease completely without recurrence for rest of the animals' natural lives

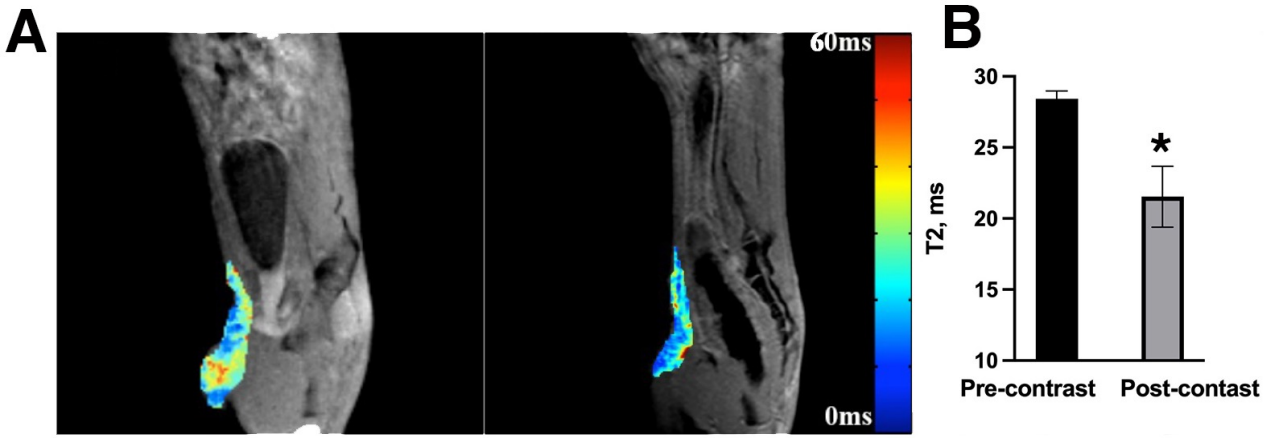
Stage II/III TNBC
MDA-MB-231 cells

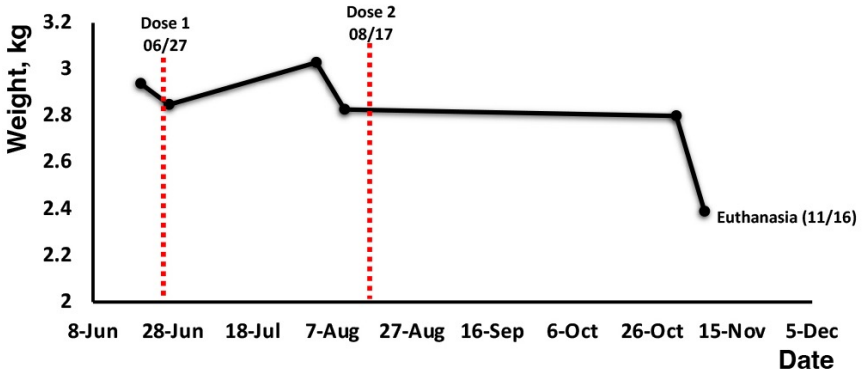


Stage IV TNBC
4t1 cells



TTX-MC138 Evidence of Efficacy in Spontaneous Feline Mammary Carcinoma



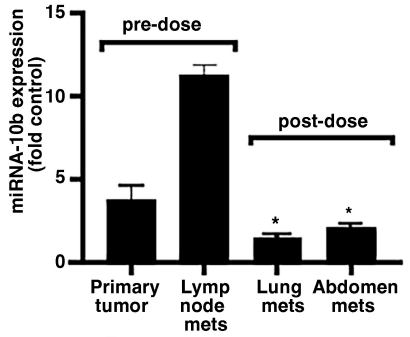


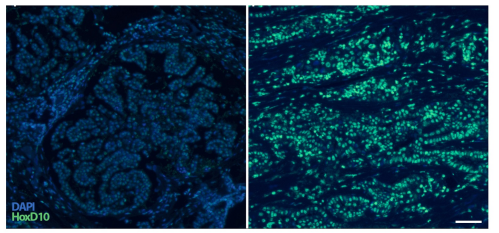
TTX-MC138 accumulated in metastatic lesions

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





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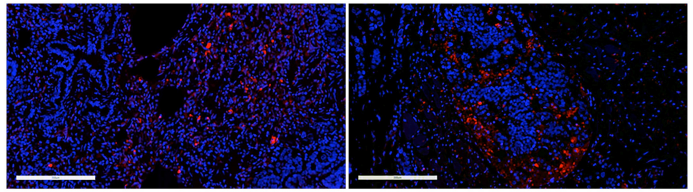


Red: TTX-MC138, Blue: cell nuclei

TTX-MC138 Evidence of Efficacy in Pancreatic Cancer (Murine Model)

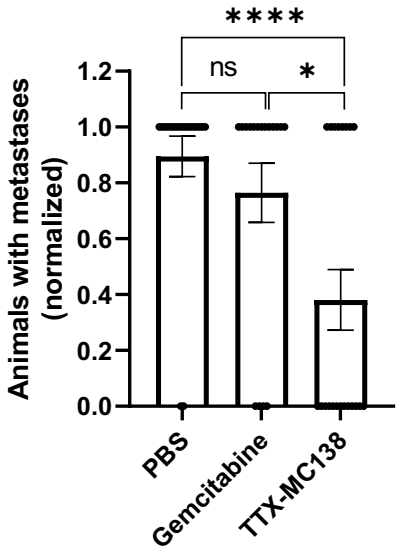
Human pancreatic cancer cells (BxPC3) implanted orthotopically into mice

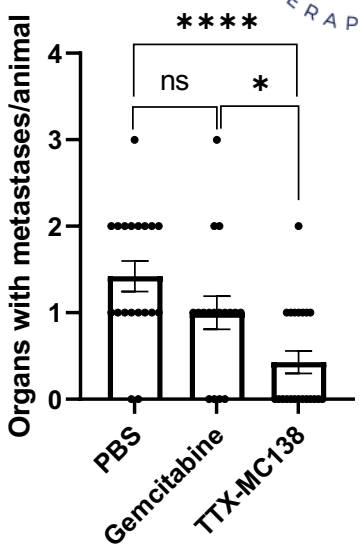
Mice were treated with TTX-MC138 after tumor formation

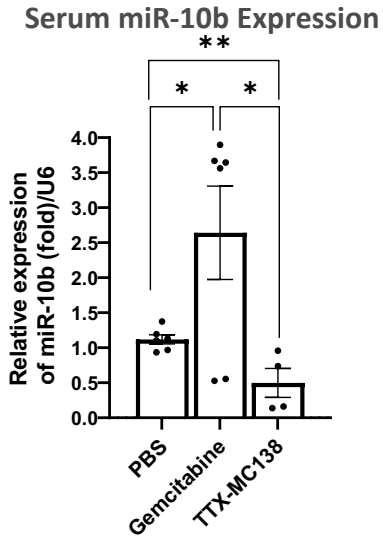
Metastatic incidence was inhibited by 50% relative to standard-of-care chemotherapy

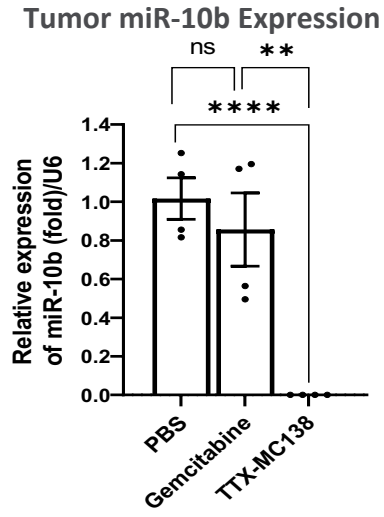
TTX-MC138 displayed remarkable PD activity with target inhibition in tumors over 10,000-fold relative to controls

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



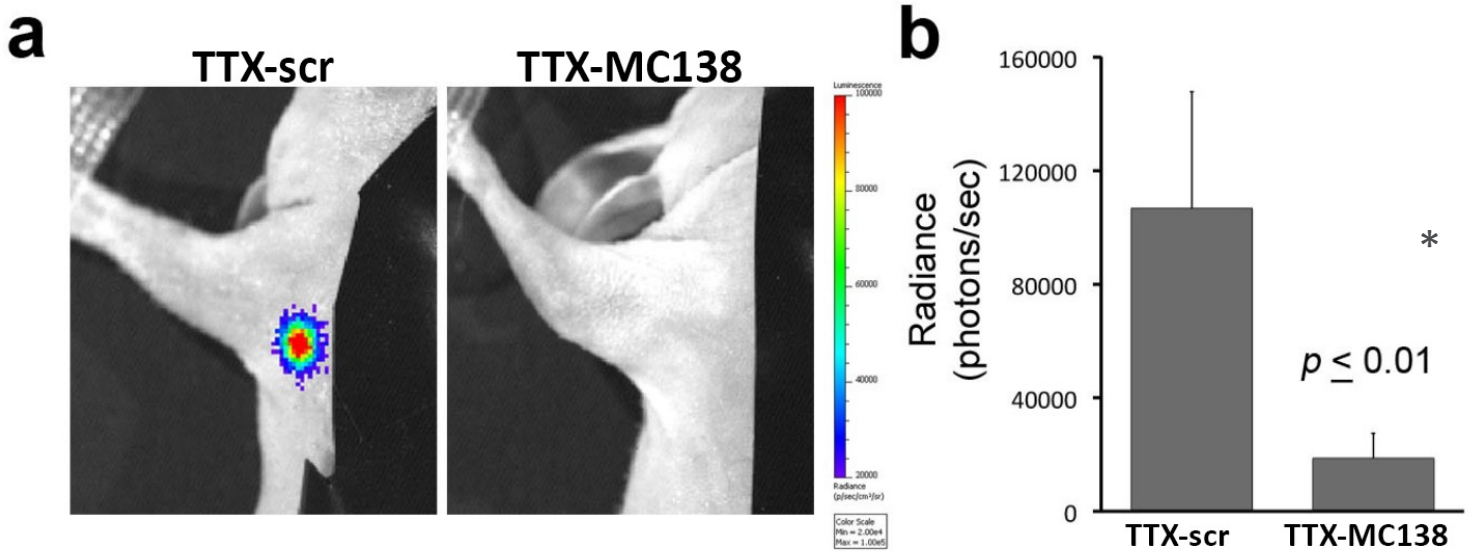






BxPC3-Red-Fluc cells orthotopically implanted into immunocompromised mice; treatment stopped after 8 weekly treatments

TTX-MC138 Prevention of Metastatic Breast Cancer



Human breast cancer cells implanted orthotopically into immunocompromised mice

One cohort then treated with MN-anti-miR10b (TTX-MC138) prior to formation of metastasis

None of the treated animals formed metastases

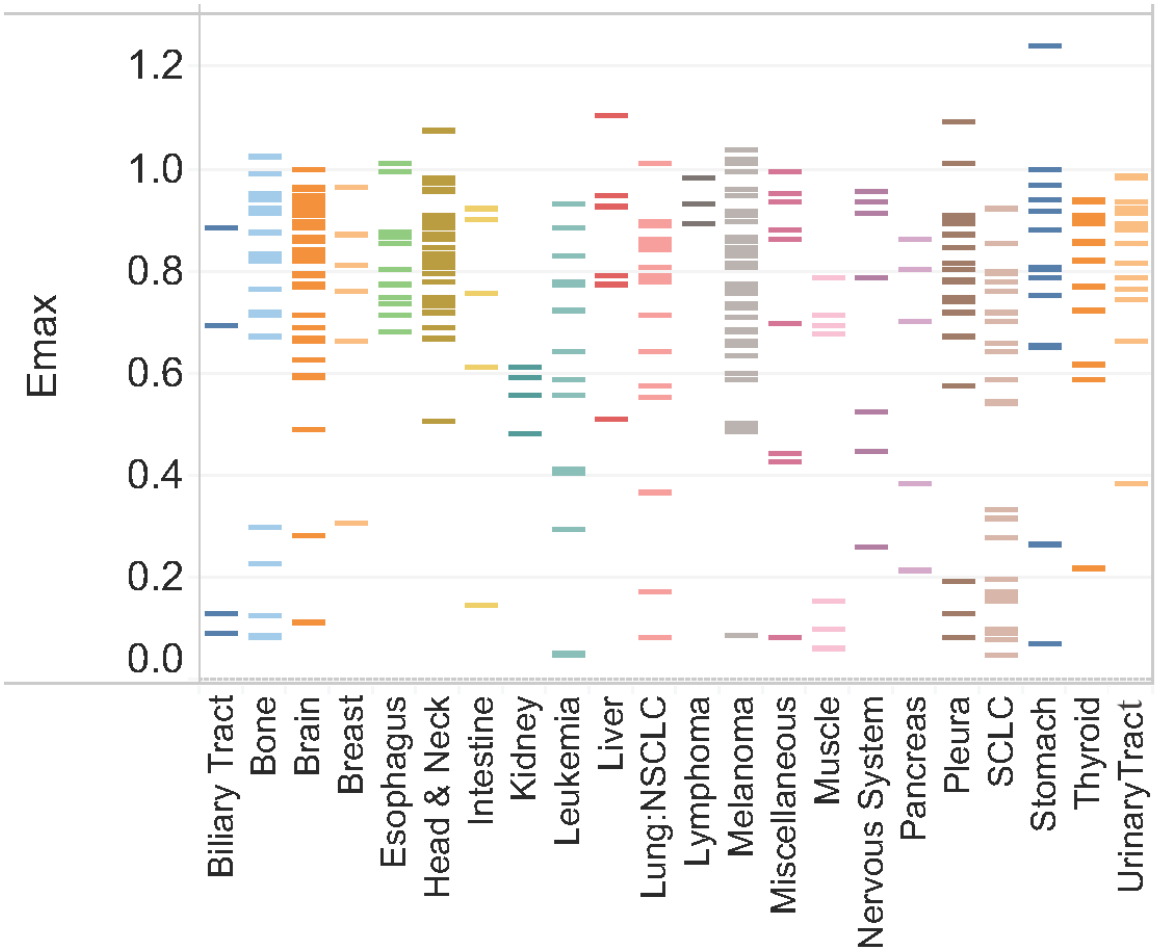
By contrast, control animals treated with an inactive form of TTX-MC138 formed detectable lymph node metastases within 4 weeks

Source: Oncogene 32:1530. 2013.

TTX-MC138 Evidence of Efficacy in Multiple Cancers

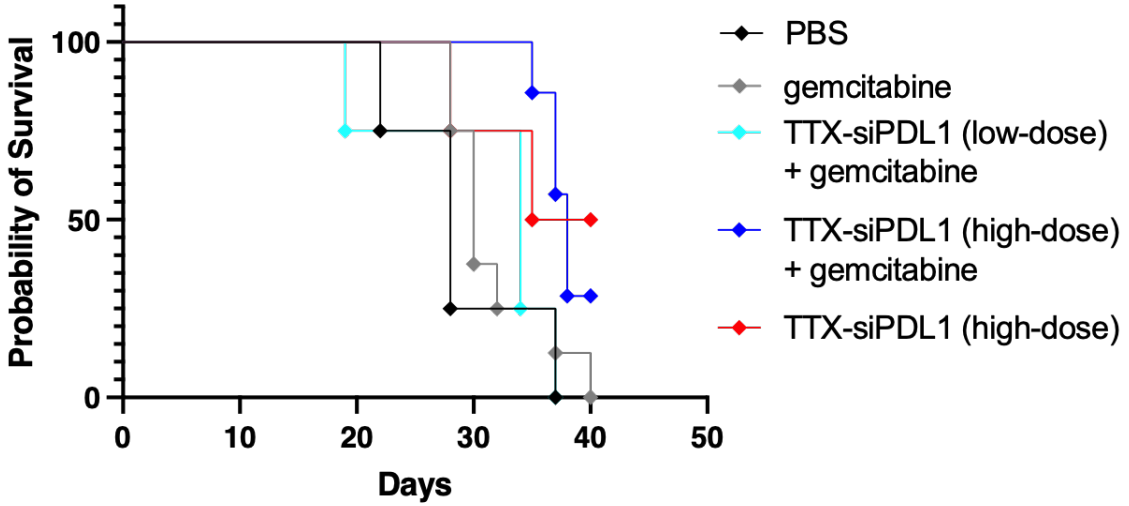
Sensitivity to TTX-MC138 was tested in 624 human cell lines representing metastatic and non-metastatic cancers.

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



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

TTX-siPDL1 Efficacy in a Highly Aggressive PDAC Murine Model with Intense Desmoplasia



Hy15549 cells implanted orthotopically

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 with gemcitabine dramatically decreased hazard ratios for survival relative to standard-of-care chemotherapy

Tumor growth rate in treated animals 80% lower than in buffer-treated controls

Phase 0 Clinical Trial Design

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.

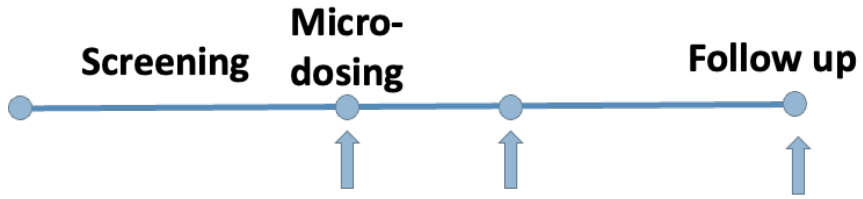
METHODS

KEY INCLUSION*	KEY EXCLUSION*
• ECOG PS of 0 or 1 • At least 1 metastatic solid tumor ≥ 1 target lesion per RECIST 1.1 (≥ 10 mm per MRI from FDG PET-MRI) • Adequate organ function per protocol definitions	• Anticancer therapy (not immunotherapy/Ab therapies) ≤ 14 days or 5 half-lives before study drug • Prior antibody therapy ≤ 28 days before study drug • Clinically significant, uncontrolled cardiovascular disease • 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	

Achievements Since Inception

2016

- Company Founded

2017-20

- SAB established
- MGH license executed
- New patents filed
- Pipeline expanded
- 2 Independent Directors added to BOD

2021

- IPO - $25.4M (net)
- Hired Co-Founder as CSO
- Radiolabeled Drug Publication
- Added 3rd Independent Director
- SBIR Grant from NIH
- New lab space at MBI

2022

- Alliance member of MD Anderson Cancer Center
- Orphan Drug Designation 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.

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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.

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Yoo B, Ghosh SK, Kumar M, Moore A, Yigit MV, Medarova Z: Design of nanodrugs for miRNA targeting in tumor cells. J Biomed Nanotechnol 2014;10:1114-1122

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