TRANSCODE

THERAPEUTICS™

The RNA Oncology Company

NASDAQ Symbol: RNAZ

Investor Presentation

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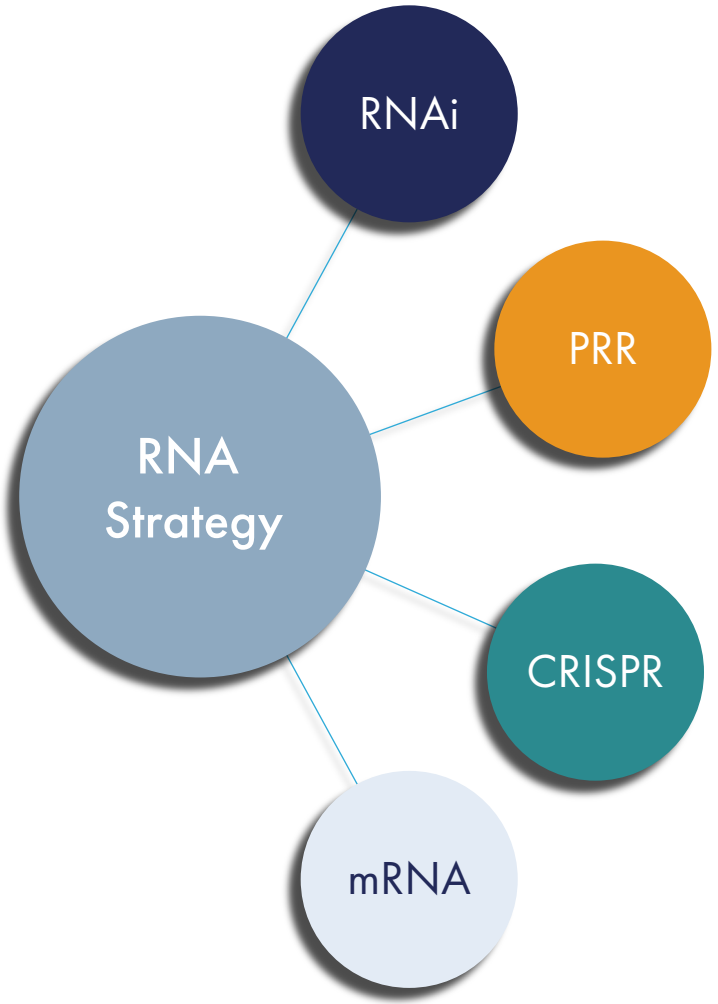
Disclaimer

Forward Looking Statements

Statements in this presentation contain "forward-looking statements" that are subject to substantial risks and uncertainties. Forward-looking statements contained in this presentation may be identified by the use of words such as "anticipate," "expect," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast" or other similar words, and include, without limitation, statements regarding TransCode Therapeutics, Inc.'s expectations regarding projected timelines of clinical trials, and expectations regarding current or future clinical trials. Forward-looking statements are based on TransCode Therapeutics, Inc.'s current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate, including that clinical trials may be delayed; that the data reported may be interim data, conclusions as to which may be superseded by subsequent data we receive in connection with other and/or subsequent clinical trials; and that any anticipated meeting with or presentation to the FDA may be delayed. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in TransCode Therapeutics, Inc.'s prospectus dated July 8, 2021, and other reports filed with the U.S. Securities and Exchange Commission. Forward-looking statements contained in this presentation are made as of this date, and TransCode Therapeutics, Inc. undertakes no duty to update such information except as required under applicable law.

TransCode Therapeutics - The RNA Oncology Company



RNA's power and potential

- Developing multiple RNA approaches in oncology
- Lead therapeutic candidate targeting principal driver of metastasis

TTX Platform: Resolving delivery challenge of RNA therapeutics

- Optimized delivery of RNA therapeutics to genetic targets in cancer
- File eIND FIH (Phase 0) clinical study 1H 2022
- Modular toolbox enabling rational drug design

R&D: Broad and diverse oncology pipeline

- Early programs targeting biomarkers in numerous solid tumor types
- Access to genetic targets previously undruggable without RNA delivery

Corporate

- Robust IP portfolio
- Experienced management, board of directors and advisory team
- Highly capital efficient

PRR- Pattern recognition receptors; CRISPR - Clustered Regularly Interspaced Short Palindromic Repeats

Platform

TTX-Based Modular Design Toolbox

Therapeutic oligonucleotides

Based on phenomenon of genetic complementarity

Nanocarrier delivery mechanism

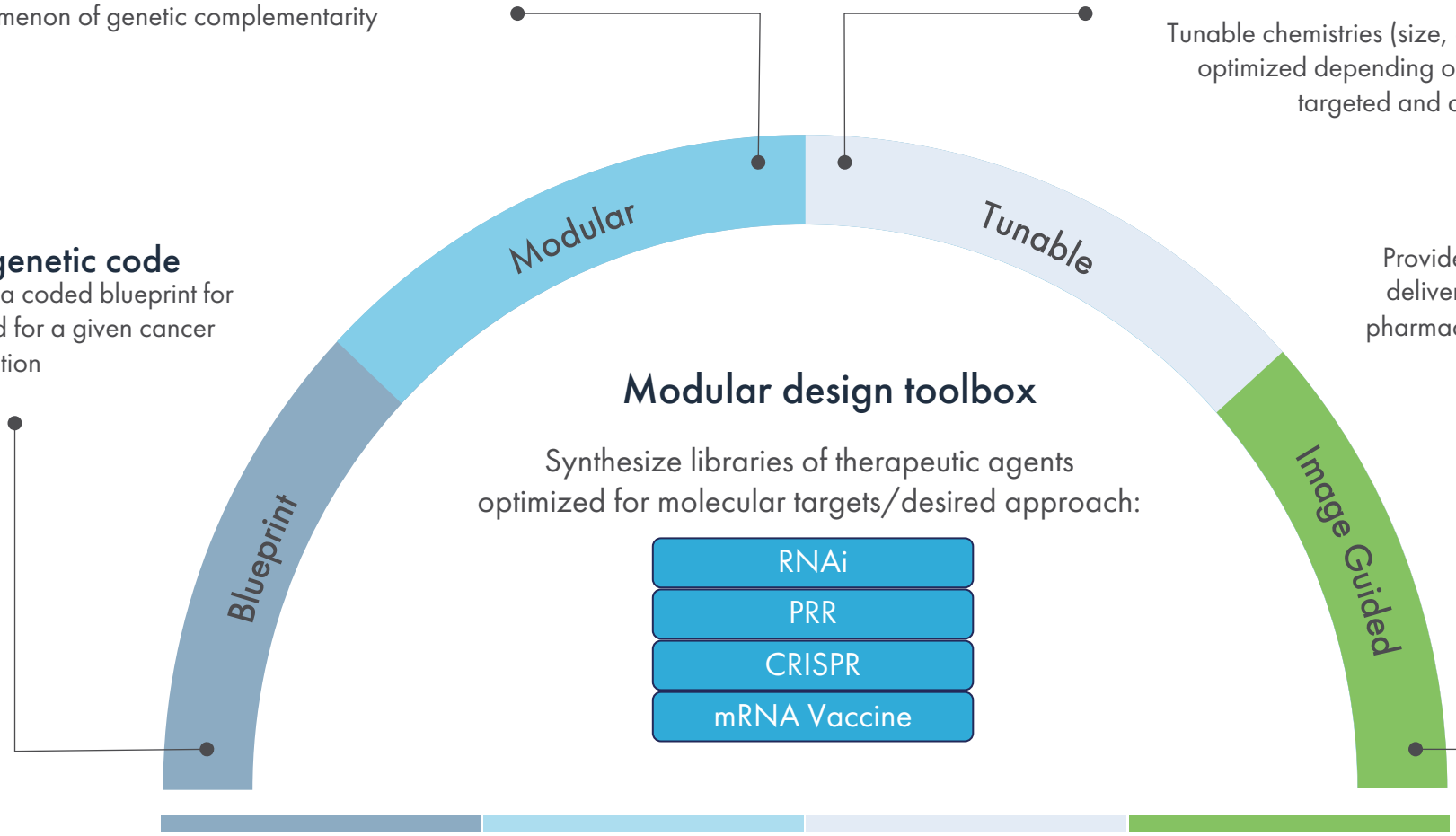
Tunable chemistries (size, charge, surface chemistry) optimized depending on the tissue that is being targeted and approach used

Annotated genetic code

Genetic code provides a coded blueprint for drug design optimized for a given cancer indication

Imaging

Provides specific measurement of drug delivery to target tissue of interest and pharmacokinetics of the drug during drug development



Modular design toolbox

Synthesize libraries of therapeutic agents optimized for molecular targets/desired approach:

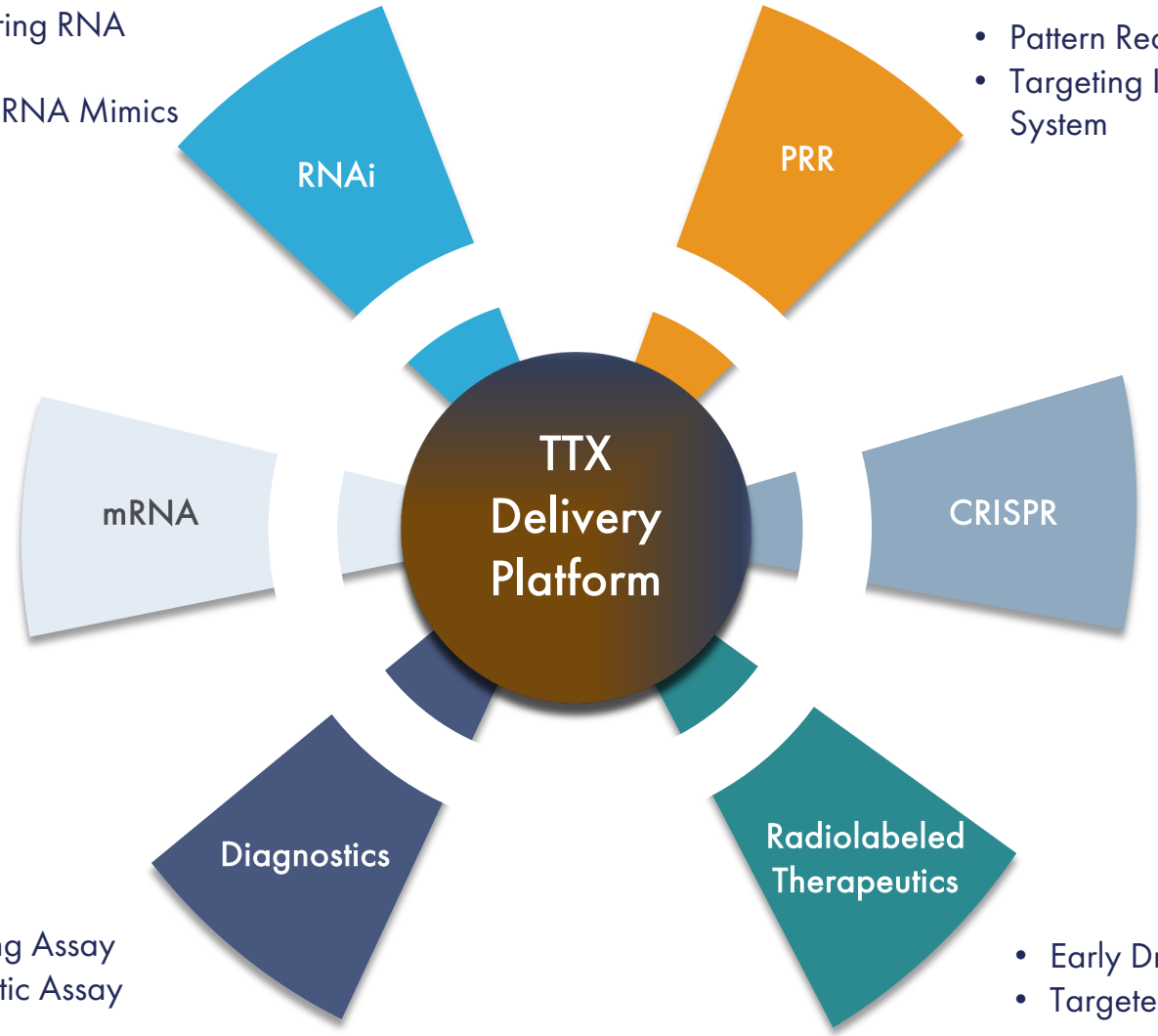
- RNAi
- PRR
- CRISPR
- mRNA Vaccine

Platform

One Delivery System – Multiple RNA Approaches

- Small Interfering RNA
- Antisense
- Non-coding RNA Mimics

- Pattern Recognition Receptors
- Targeting Innate Immune System



- Cancer Vaccines.

- Gene Repair
- Gene Replacement

- Biomarker Screening Assay
- Biomarker Diagnostic Assay

- Early Drug Development
- Targeted Radiotherapy

Pipeline of First-in-Class RNA Therapeutic Candidates in Oncology

Drug Candidate	Target	RNA Type	Disease Indication	Discovery	Preclinical	Phase 0	Phase 1	Phase 2	Phase 3	Key Anticipated Milestones
TTX-MC138	**miR-10b**	**RNAi**	Metastatic Cancer							Tox study 1H '22; eIND filing 1H '22
			Pancreatic Cancer							Complete Preclinical Study 1H '22
			Glioblastoma (GBM)							Complete Preclinical Study 2H '22
TTX-siPDL1	PD-L1	RNAi	Solid Tumors							Continue Preclinical Study 1Q '22
TTX-siLin28b *	Lin28b	RNAi	Solid Tumors							Continue Preclinical Study 1Q '22
TTX-RIGA	Multiple	RIGI	Cancer Agnostic							Continue Preclinical Studies 1H '22
TTX-CRISPR	Multiple	CRISPR	Cancer Agnostic							Commence Preclinical Studies 2H '22
TTX-mRNA	Cancer Vaccine	mRNA	Cancer Agnostic							Commence Preclinical Studies 2H '22

* TransCode signed an Exclusive Option Agreement with The General Hospital Corporation, d/b/a Massachusetts General Hospital, or MGH, for TTX-siLin28b. Under this Option, TransCode has the right to negotiate a license to this asset with MGH. TransCode's decision will depend on the results of a preclinical study it plans to conduct as shown above.

TTX Delivery PLATFORM

A Proprietary Nanoparticle Delivery System for RNA Oncology Therapeutics

The challenge in RNA therapeutics: delivering an oligonucleotide to its target outside of the liver

Our delivery strategy employs a nanoparticle extensively used in imaging that has been repurposed to:

- Deliver oligonucleotides to tumors and metastases
- Achieve robust target engagement in tumor cells anywhere in the body

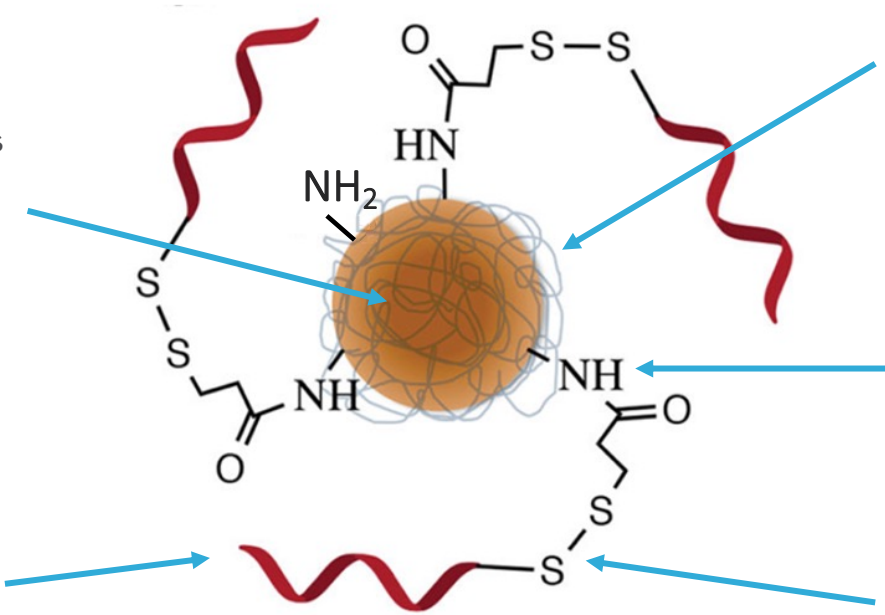
We believe that demonstrating our ability to overcome the challenge of RNA delivery to genetic targets would represent a major step forward in unlocking therapeutic access to a variety of genetic targets involved in a range of cancers

TTX Delivery System: 16+ Years of R&D Optimization

Our delivery system is specifically designed to *access targets inside tumor cells*:

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 – quantifiable drug delivery to the target organ
- Highly stable, low toxicity potential; low immunogenicity



Dextran coating:

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

Amino functional groups:

- Provide stabilization

RNA-targeted nucleic acid:

- Strong binding affinity, specificity & stability while minimizing immunogenicity

Disulfide bond:

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

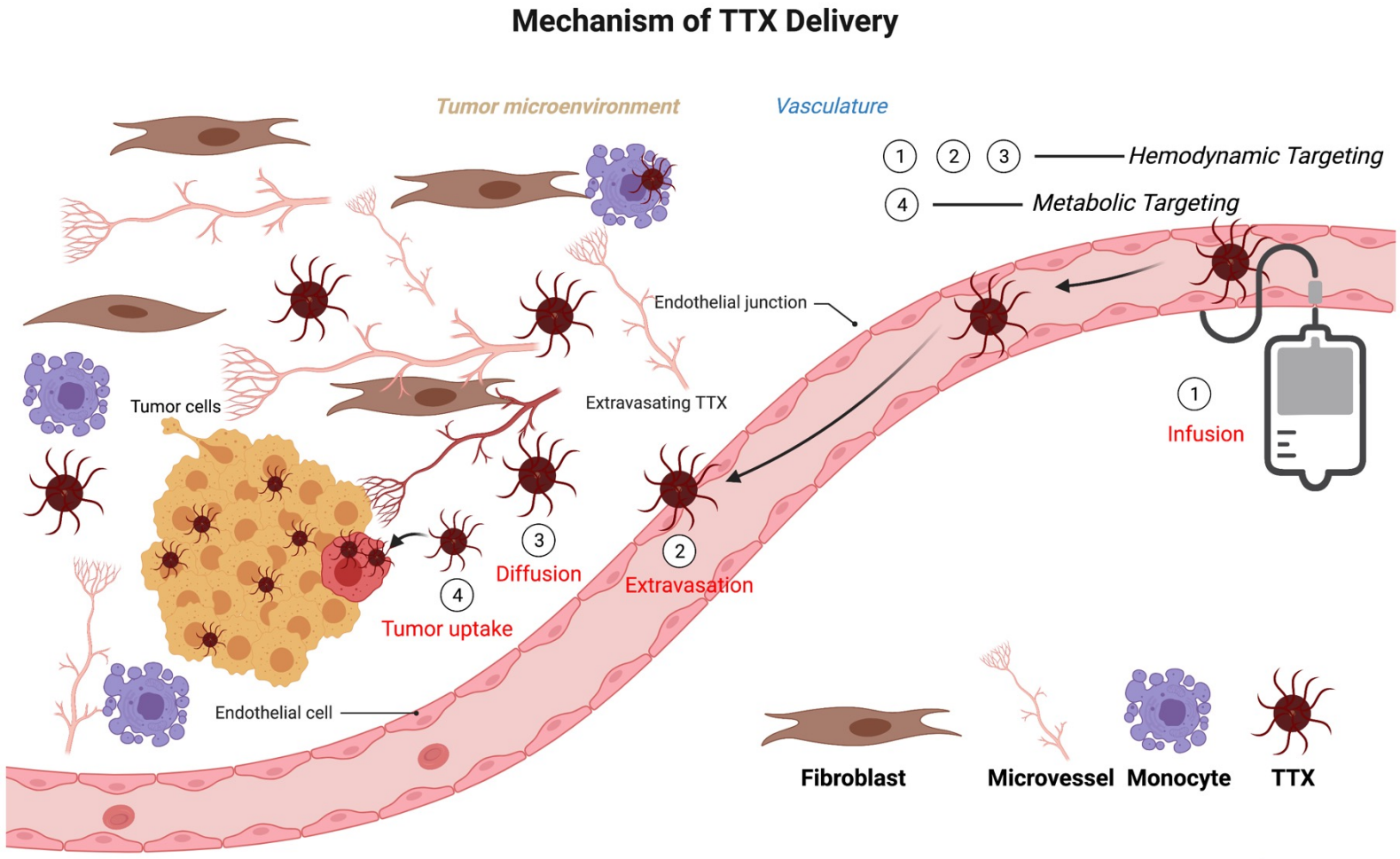
Mechanism of Endogenous Delivery to Tumors and Metastases

Hemodynamic targeting

- TTX is long-circulating (24-30 hours) - distributes throughout the microcirculation of tumors and metastases
- Small hydrodynamic size - easily extravasates from the vascular endothelium (the inner cellular lining of arteries, veins and capillaries) of tumors and metastases and diffuses throughout the tumor tissue

Metabolic targeting

- Tumor cells are metabolically active and require glucose for growth. Once in the tumor tissue, TTX, which is coated with a non-metabolizable glucose polymer, is avidly taken up by these metabolically active tumor cells
- The process is similar to the mechanism behind diagnostic PET imaging with fluorodeoxyglucose (FDG), which is widely used to diagnose and stage metastatic cancer



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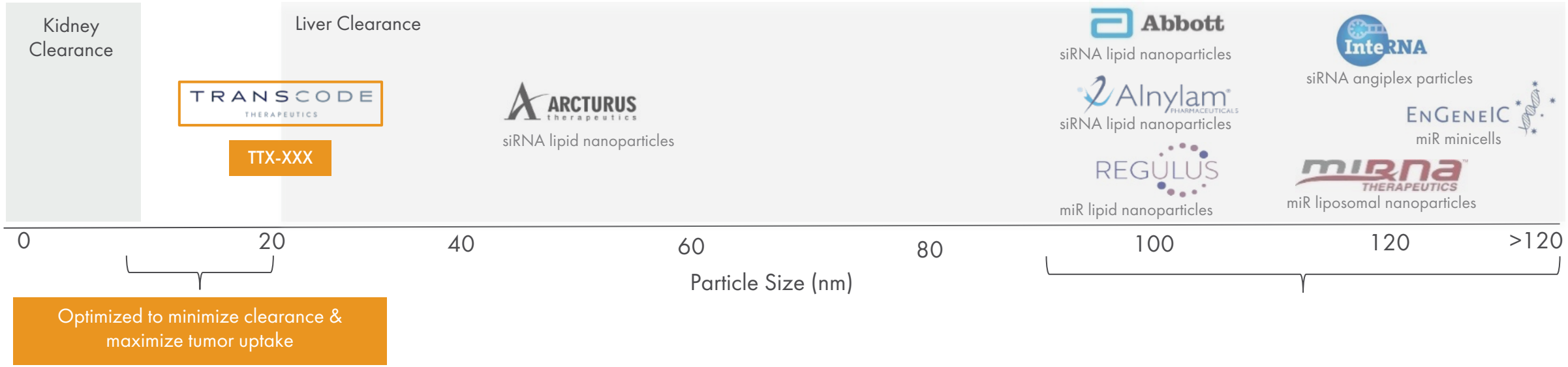
Platform

TTX Delivery Platform is Highly Differentiated



Competition & differentiation summary

- Iron Oxide Nanoparticles were approved for the treatment of iron deficiency anemia & may be used clinically as imaging agents
- Designed for long circulation time & efficient accumulation in tumor cells while minimizing kidney & liver clearance
- Lipid nanoparticles carry a risk of immunogenicity; iron oxide nanoparticles mitigate against this risk

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-MC138

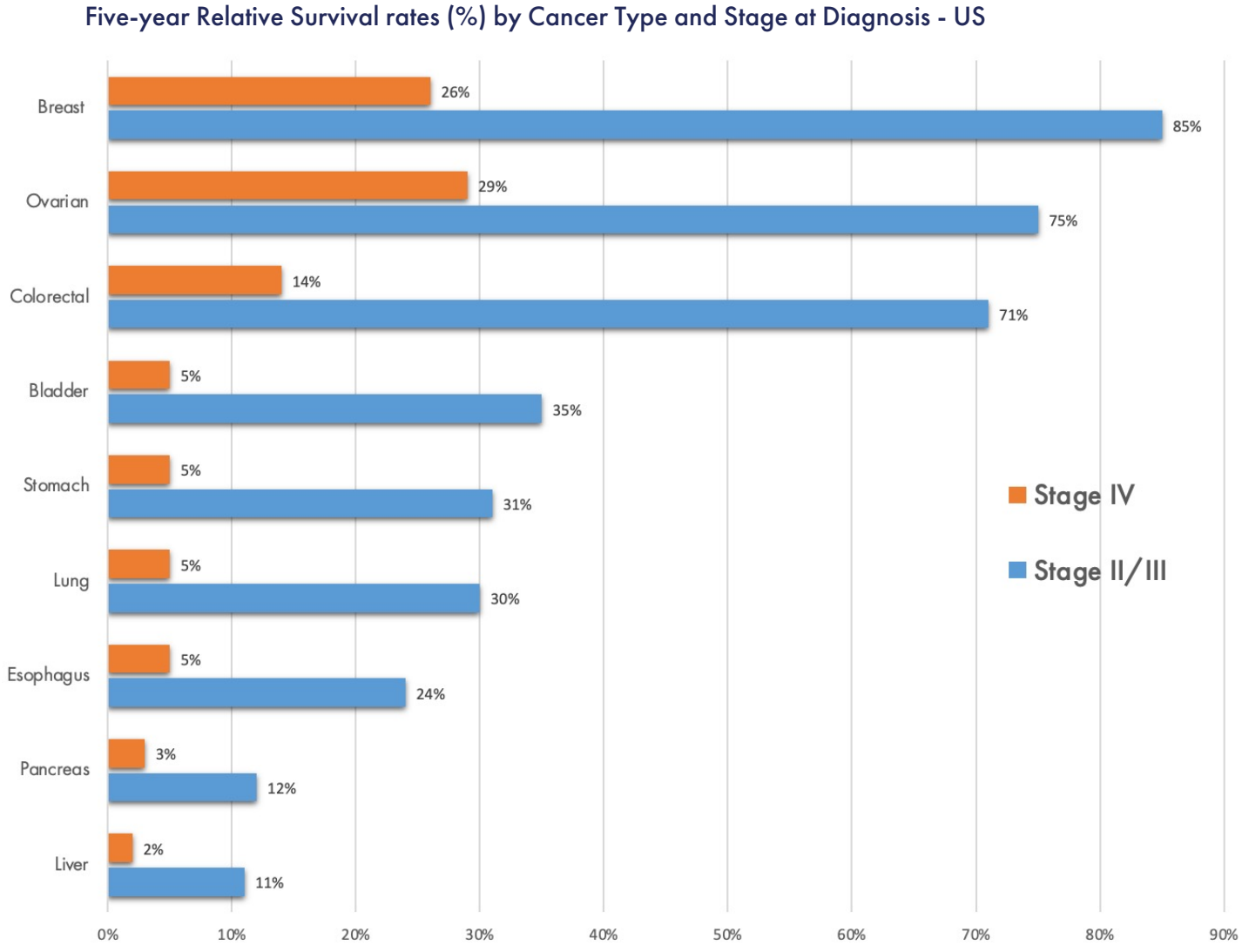
Lead Therapeutic Candidate:
Targeted Therapy Against Metastatic Cancer

Addressing High Unmet Need in Metastatic Cancer

Market	Problem	Solution	Pre-clinical Results	Potential
• In 2021, over 9 million people worldwide died from cancer – the majority of which resulted from metastatic disease	• Current treatments do not specifically target metastatic disease, resulting in high unmet need, offering potential for streamlined development and expedited regulatory path	• TTX-MC138 targets an RNA molecule, microRNA-10b, shown to be the master regulator of metastatic progression in multiple tumor types	• Preclinical studies* using human tumor models in mice linked inhibition of miR-10b with regression of established metastases and no recurrence or toxicity during the length of the studies	• Significant potential due to its broad treatment applicability, as a monotherapy or in combination with SOC, across multiple solid tumor types

* In combination with a low dose cytostatic (doxorubicin), see Figure 10 in S-1.

Metastasis Treatment: Deficiency in the Oncology Market



Metastatic Cancer Reduces 5-year Survival Rate, Highlighting Critical Need for Therapy Targeting Metastasis

90%

of Cancer Deaths Due to Metastasis

$111B

Global Metastatic Cancer Treatment Market by 2027

Source: 2019 American Cancer Society, Inc., Surveillance Research

microRNA-10b (miR-10b) is a Unique, Well Documented Biomarker

Clinical Evidence Demonstrated in >200 peer-reviewed publications over the last ten years

Biomarker of Metastasis

Positive expression associated with *tumor cell migration, invasion and viability of metastatic tumor cells*

Marker of local & distant metastasis

Linked to Higher Cancer Risk - Poor Survival Outcomes

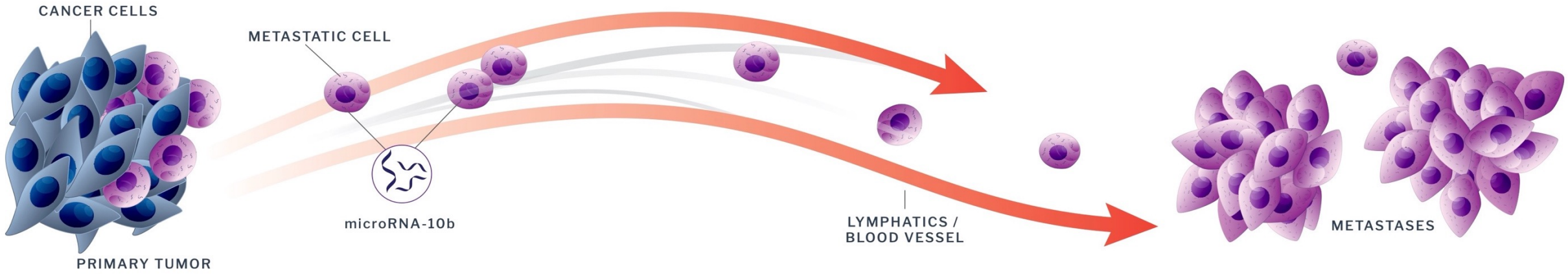
Carcinogenesis, presence of cancer

Poor overall-survival (OS)

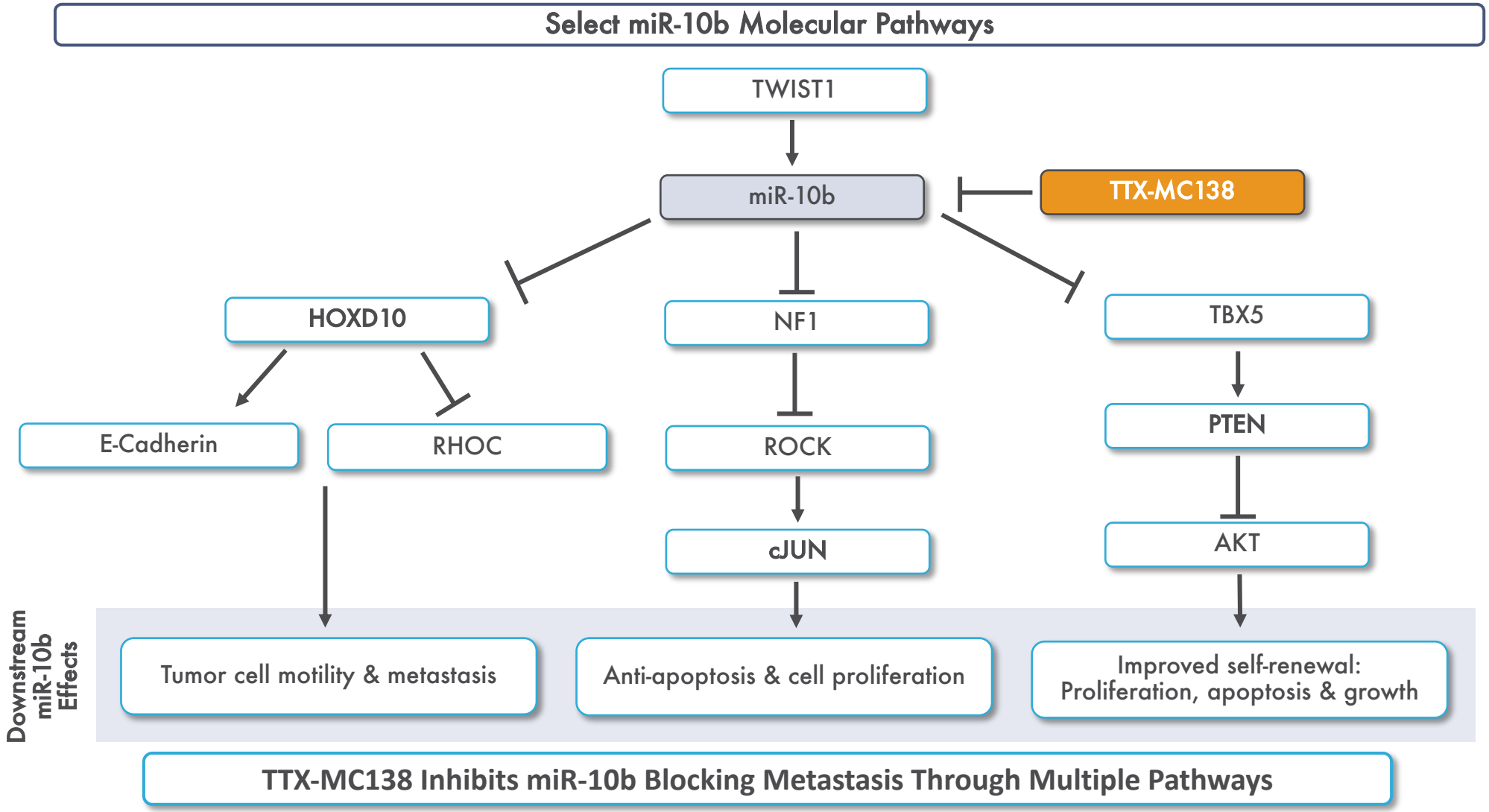
Positive link to greater aggressiveness of disease

Linked to Metastatic Progression in Multiple Cancer Types

Breast, Pancreatic, Non-Small Cell Lung, Gastric, Liver, Ovarian, Colorectal, Prostate, Esophageal cancers as well as Glioblastoma, and others



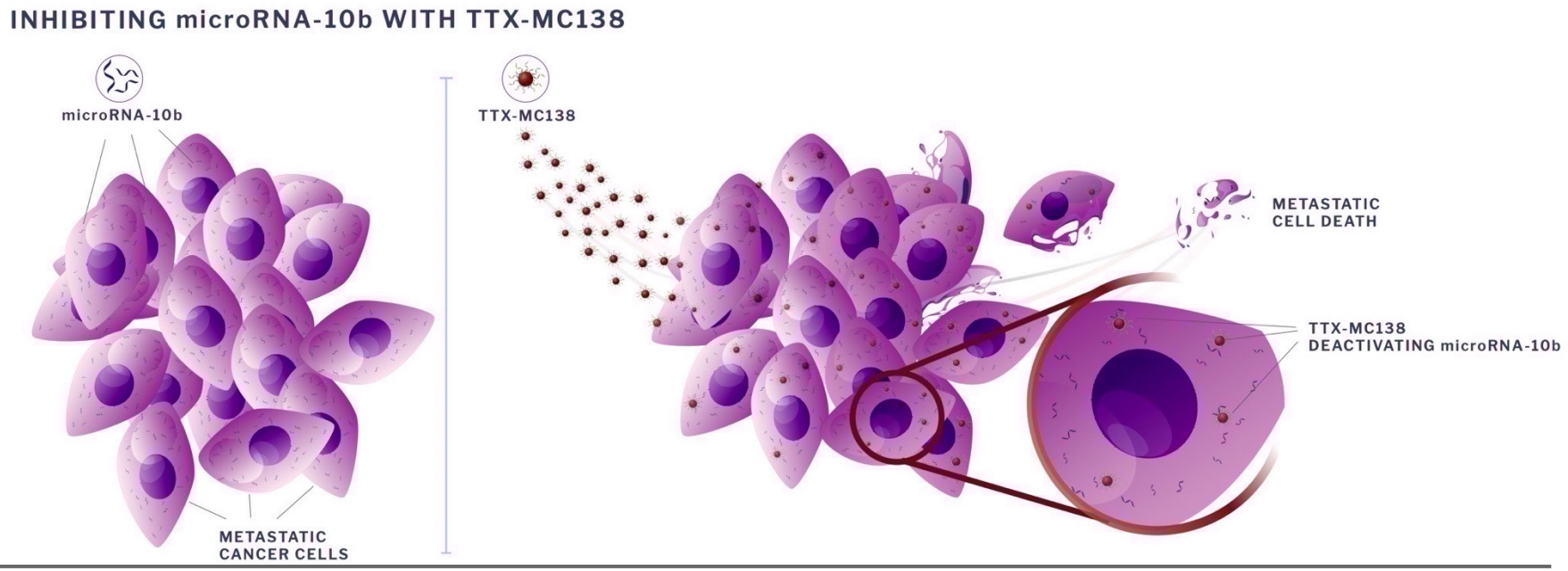
Pleiotropic Effects of miR-10b Driving Metastasis



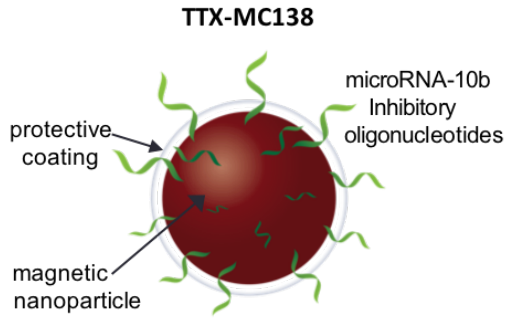
Source: Am J Cancer Res 2018, Oncotarget 2016, Protein Cell 2011, 2(11): 889-898

TTX-MC138 MOA designed to eliminate metastasis by inhibiting microRNA-10b

Mechanism of Action (MOA)



- TTX-MC138 is composed of proprietary nanoparticle delivery system + inhibitory oligonucleotide targeting microRNA-10b, the driver of metastasis
- Delivery system designed to optimize delivery of oligonucleotides to tumor cells anywhere in the body
- Unique capability to accumulate at metastatic sites

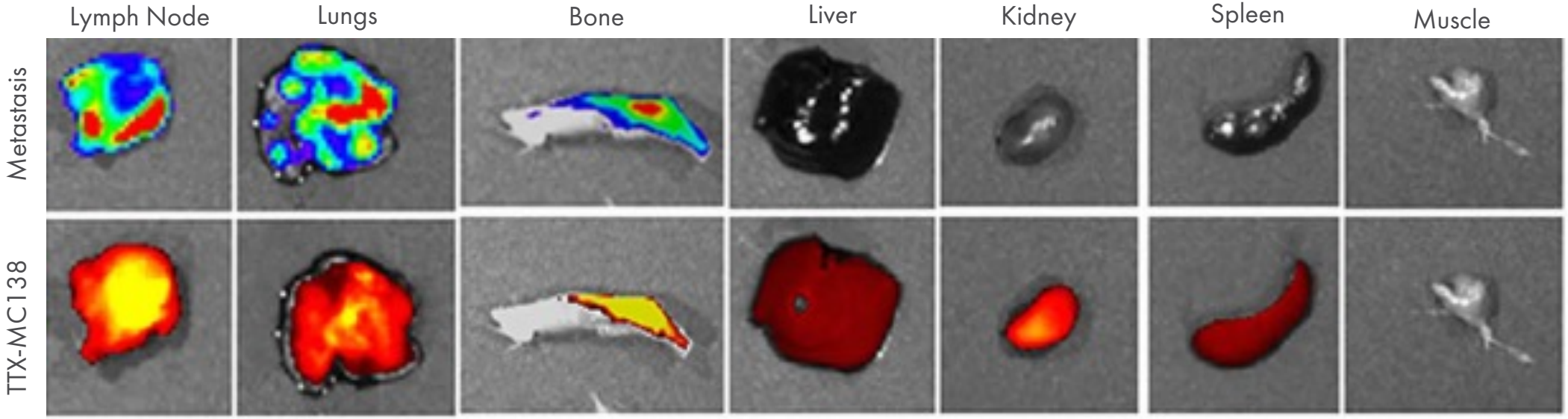


Cancer Res 75, 4407-4415 (2015); Sci Rep 7, 45060 (2017)

Preclinical Evidence of TTX-MC138 Delivery to Metastatic Sites

Accumulation in lymph node, lung, and bone metastases

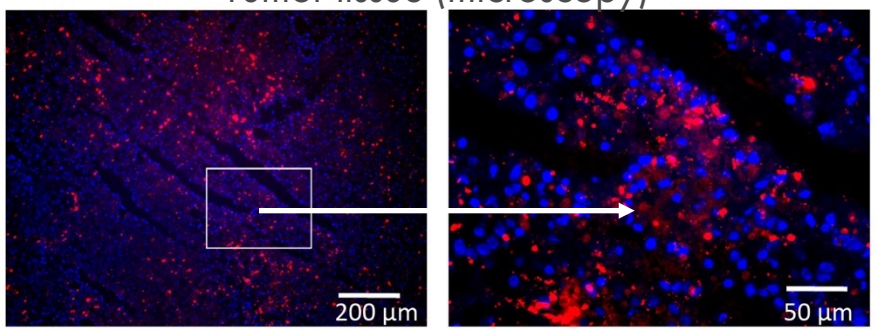
Accumulation in the liver, spleen & kidney as clearance mechanisms



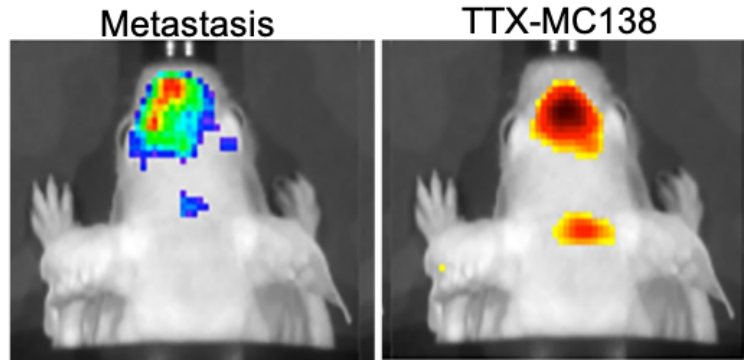
Study results

- Drug accumulated in distant metastatic organs
- Drug accumulation co-localized with the metastatic lesion

Tumor tissue (microscopy)



Red: TTX-MC138, Blue: cell nuclei



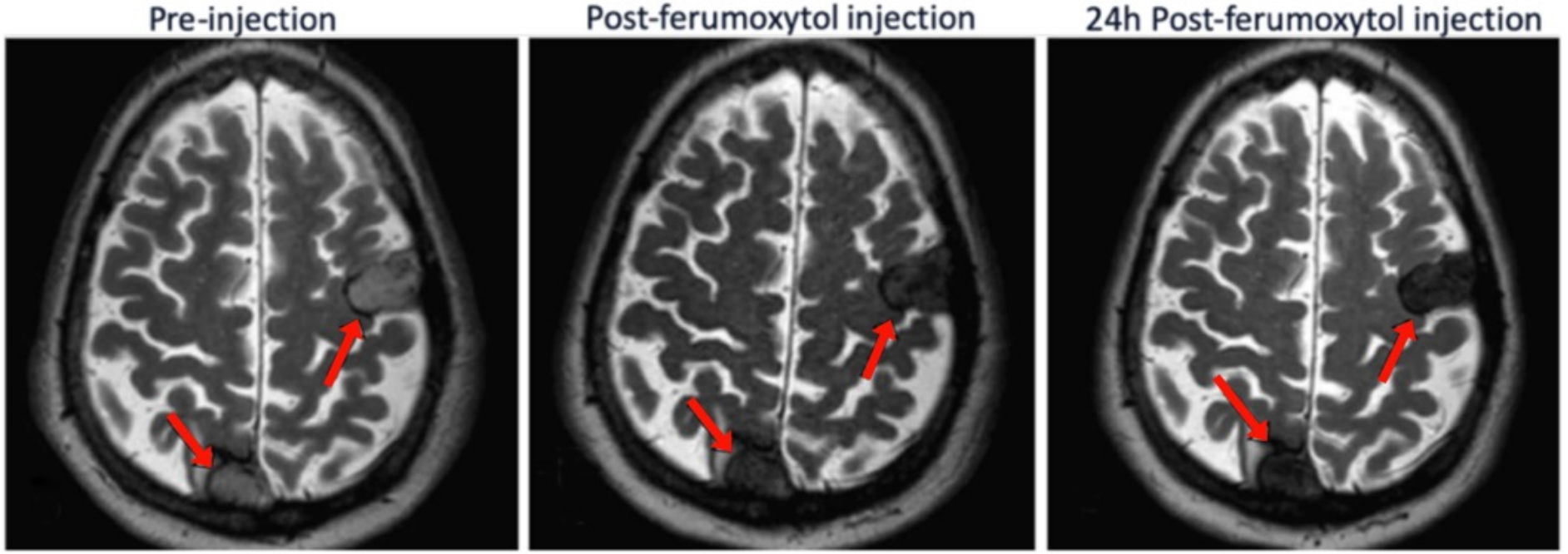
Accumulation in brain metastases

Source: Scientific Reports | 7:45060 | DOI: 10.1038/srep45060, Can Res 2015

Clinical Feasibility of Delivery to Metastases

High confidence of delivery to metastatic sites in patients with TTX-MC138

- Ferumoxytol* accumulates in lesions from multiple cancers
- **Red arrows** point to brain metastases in a patient with pancreatic cancer
- Nanoparticles visualized as darkening on MRI



* Ferumoxytol – iron oxide nanoparticles similar in size to TTX, used to treat iron-deficiency anemia

Sources: Hamilton et al, J Neurooncol 2016; Fredrickson et al, MRM 2017; Ramanathan et al, 2017 Clin Cancer Res

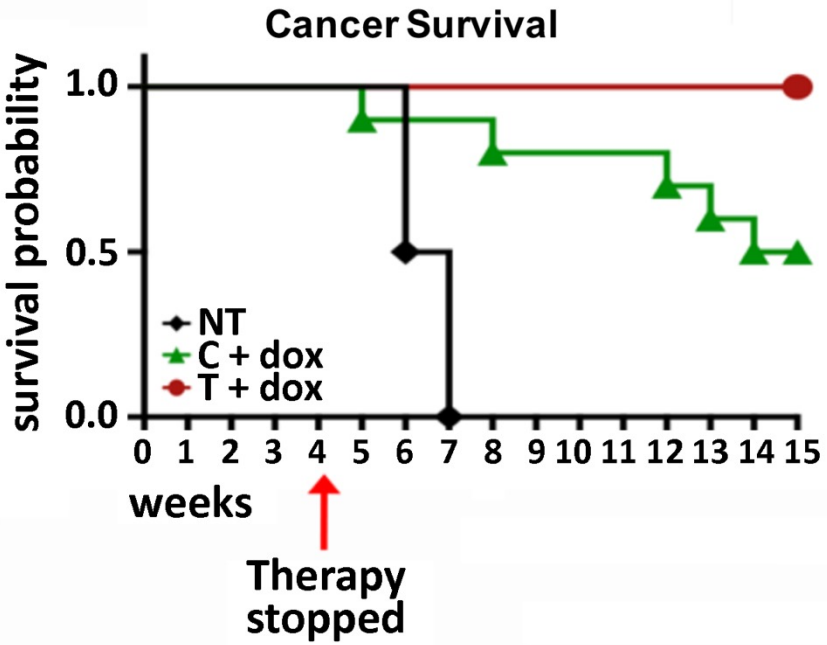
Survival Benefit Observed Preclinically in Multiple TNBC* Models

* TNBC – Triple-negative Breast Cancer

Following cessation of therapy, no recurrence or toxicity observed

Stage II/III
Metastatic Burden

Treatment stopped after 4 weekly treatments once there was evidence (via imaging) that metastases were eliminated

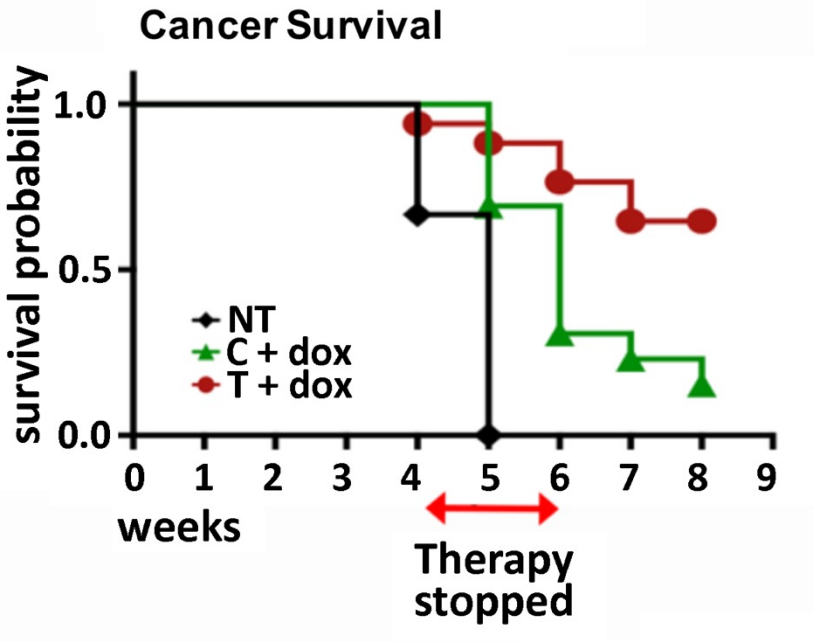


NT: No therapy, C: Control (Irrelevant oligo), T: TTX-MC138, dox: doxorubicin

Study design: mice (n=35) implanted with MDA-MBA-231-luc-D3H2LN
Results: TTX-MC138 eliminated pre-existing **local** metastases in **100% of animals treated**

Stage IV
Metastatic Burden

Treatment stopped after 4-6 weekly treatments once there was evidence (via imaging) that metastases were eliminated



NT: No therapy, C: Control (Irrelevant oligo), T: TTX-MC138, dox: doxorubicin

Study design: mice (n=39) implanted with 4T1-luc2 cells
Results: TTX-MC138 eliminated **distant** metastases in **65% of animals treated**

Sources: Can Res 2015, Sci Report 2017 / Figure 11 in S-1 Preclinical results of TTX-MC138 in models of metastatic breast cancer

First in Human (FIH) Study - Microdosing Study in Breast Cancer Patients

> "A major obstacle preventing widespread usage of oligonucleotide therapeutics has been the difficultly in achieving efficient delivery to target organs & tissues other than the liver."

FIH study has the potential to:

- Demonstrate quantifiable evidence of delivery of TTX-MC138 to metastatic lesions in stage IV breast cancer patients
- Inform Ph I/II clinical trials by measuring pharmacokinetics & biodistribution in vital organs & other tissues
- Extrapolate therapeutic dose level from microdose results
- Validate delivery for the TTX pipeline and open-up additional relevant RNA targets that have been previously undruggable due to lack of RNA delivery challenges

Written guidance by FDA informing proposed FIH (Phase 0) trial

Source: Advances in oligonucleotide drug delivery. Nature Reviews Drug Discovery volume 19, pages 673–694(2020)

Anticipated Study Design for Phase 0 Trial Using Radiolabeled TTX-MC138

Study Design

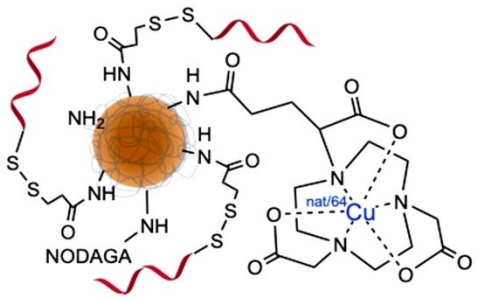
10 Patient Study

- Stage IV breast cancer patients
- Single 100 µg dose
- Investigator sites: Termeer Center and I-3 Institute at MGH

Enrollment criteria

- Positive microRNA-10b expression in blood/tissue
- Stage IV cancer patients with primary tumor resected

^{64}Cu-TTX-MC138



- Precision measurement of pharmacokinetic endpoints by noninvasive imaging (PET-MRI or PET-CT)
  - Quantify delivery* to metastatic lesions
  - Quantify delivery to vital organs
- Measure drug substance disposition by correlating pharmacokinetic imaged measurements to LC-MS/MS
- Intended benefits:
  - Quantitative measurement of amount of TTX-MC138 delivered to metastatic lesions
  - Permits measurement of the pharmacokinetics and biodistribution of TTX-MC138 in metastatic lesions and other tissues of the body
  - Potential to inform dosing for Phase I-III clinical trials.
  - Further informs patient enrollment during Phase I-III trials based on which patients' metastases accumulate TTX-MC138.

*Microdosing study is informed by Dr. Medarova's recent publication: Le Fur et al., Cancer Nanotechnology. 2021;12(1):16.

Quantifying microRNA Expression in Patients

Validated assays for detection of microRNAs

Two Assays for Detection and Measurement of miR-10b in Blood

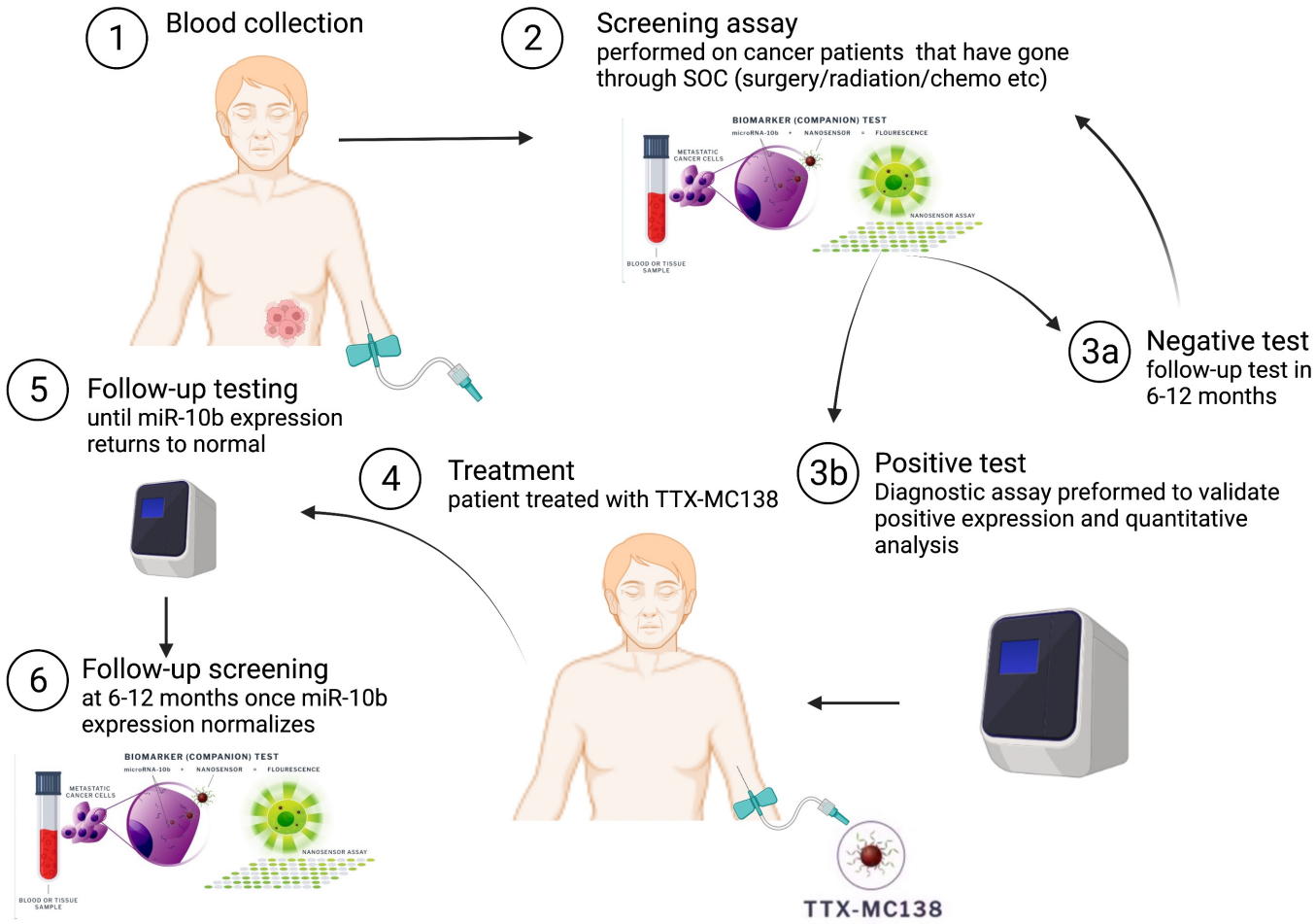
microRNA-10b expression could be useful as 1) a biomarker to detect the presence of metastasis and 2) a biomarker to predict overall survival and disease-free survival in cancer.

TransCode has developed two separate assays that allows for detection of our lead candidate target, miR-10b in patient blood samples:

1. Our screening assay has the capability of detection of miRNA expression. The fluorescent read-out generated by the assay is highly specific and has nanomolar sensitivity.
2. Our quantitative diagnostic assay could be used to confirm miR-10b expression in patient samples that reported positive in the screening assay and measure the level of miR-10b expression.

Potential to:

- Screening assay could identify patients that could benefit from treatment with TTX-MC138
- Screening assay could be used for long term monitoring of disease recurrence
- The diagnostic assay could be used to measure response to therapy



Next Steps & Milestones

Next Steps

Exploratory IND for Ph 0

- Complete CMC processes for radiolabeled Drug Product (DP), ^{64}Cu-TTX-MC138
- Complete eIND enabling studies including Tox
- File eIND for FIH trial
- Conduct Phase 0 study at Termeer Center and Institute for Innovation in Imaging at MGH

IND for Ph I/II

- Complete CMC processes for TTX-MC138 DS and DP
- CMO validation and characterization of DP; sterilization/fill, finish/label DP for IND enabling studies (Ph I/Ph II) and Ph I/Ph II clinical trials
- Manufacturing scaleup of GMP Drug Product (DP) for Phase I/II by our CMO
- Complete IND enabling studies including Tox for IND filing for Phase I/II clinical trial
- File IND
- Conduct Ph I/II at investigator sites TBD

Planned Product Development Milestones

TTX-MC138

2022

- Complete PC* tox study 1H
- File eIND for Phase 0 study 1H
- Initiate Phase 0 study 2H
- Complete non-GMP IND-enabling studies for PhI/II 2H
- File IND for Phase I/II trial 2H
- Complete Preclinical study in Pancreatic 1H
- Complete Preclinical study in GBM 2H

2023

- Dose first patient in Ph I clinical trial 1H
- Continue dosing additional patients in Ph I clinical trial

R&D Pipeline

2022

- Continue PC studies for TTX-RIGA 1H
- Continue PC studies for TTX-siPDL1 in PDAC 1H
- Continue PC study for TTX-siLin28b in PDAC 1H
- Advance TCDx screening assay development 1H
- Advance TCDx quantitative assay development 1H

2023

- File IND for for TTX-RIGA or TTX-siPDL1
- Commence PC studies for TTX-CRISPR
- Commence PC studies for TTX-mRNA

* Pre-clinical

Corporate Information

2022 Corporate Milestones

Intellectual Property:

- File patents for new diagnostics
- File patents for new therapeutics

Regulatory:

- File for Orphan designations

Publications:

- Pre-clinical study results for lead candidate in GBM
- Pre-clinical study results for TTX-siPDL1in pancreatic cancer
- Pre-clinical studies for TTX-RIGA therapeutic

Partnerships:

- TBD

Operations:

- Grow company to 18-20 + employees
- Relocate lab and office

Investor meetings:

- CEO to present at Investor conferences

Marketing:

- Corporate branding
- New corporate website

Capitalization

Source of Capital	Amount
Seed Capital (Angel investors)	2,240,000
SBIR Grant	2,300,000
IPO*	25,400,000
Total	**$29,940,000**

NASDAQ Symbol: RNAZ	
Common Shares	12,904,574
Options (WAEP $0.32)	1,792,672
Underwriter Warrants (WAEP $5.00)	312,500
Total	**15,009,746**

*Net Proceeds

Corporate

Officers and Board

	Name	Experience
	Michael Dudley Co-Founder, President, Chief Executive Officer & Director	• An entrepreneurial senior executive with over 40 years of with diversified industry experience within the biopharma industry and in multiple medical device markets
	Zdravka Medarova, PhD Co-Founder Chief Technology Officer	• Assoc. Professor of Radiology at Harvard Med School • Developed core nanodelivery platform & identified miR-10b as a therapeutic target; also developed the siRNA approach to PD-L1 for our TTX-siPDL1 therapeutic. Authored many publications on targeted cancer therapies
	Thomas Fitzgerald, MBA Chief Financial Officer, VP of Administration & Director	• Extensive CFO and investment banking experience • Former CFO of other life sciences companies • Former founding Managing Director of Leerink Swann & Company (now SVP Leerink)

	Name	Experience
	Philippe Calais, PhD Independent Director, **Board Chair**	• President, CEO and Director MatriSys Biosciences Inc. • 33+ years of biotech & pharma industry experience • Former President & CEO of Isarna Therapeutics, developer of oligonucleotide therapeutics • Former President/CEO Univalor & Ambrilia Biopharma
	Erik Manting, PhD **Independent Director**	• Chief Executive Officer, Immunicum AB, a clinical stage oncology company in the Netherlands; Founder BioEntrepreneur BV; Executive director of life sciences & healthcare at Kempen & Co investment bank '12-'17
	Magda Marquet, PhD **Independent Director**	• Strong expertise in M&A, global commercial development and regulatory strategies. • Serves on multiple boards of public & private companies and is Chair of Micronoma, Matrisys Biosciences & ProciseDx

Addendum

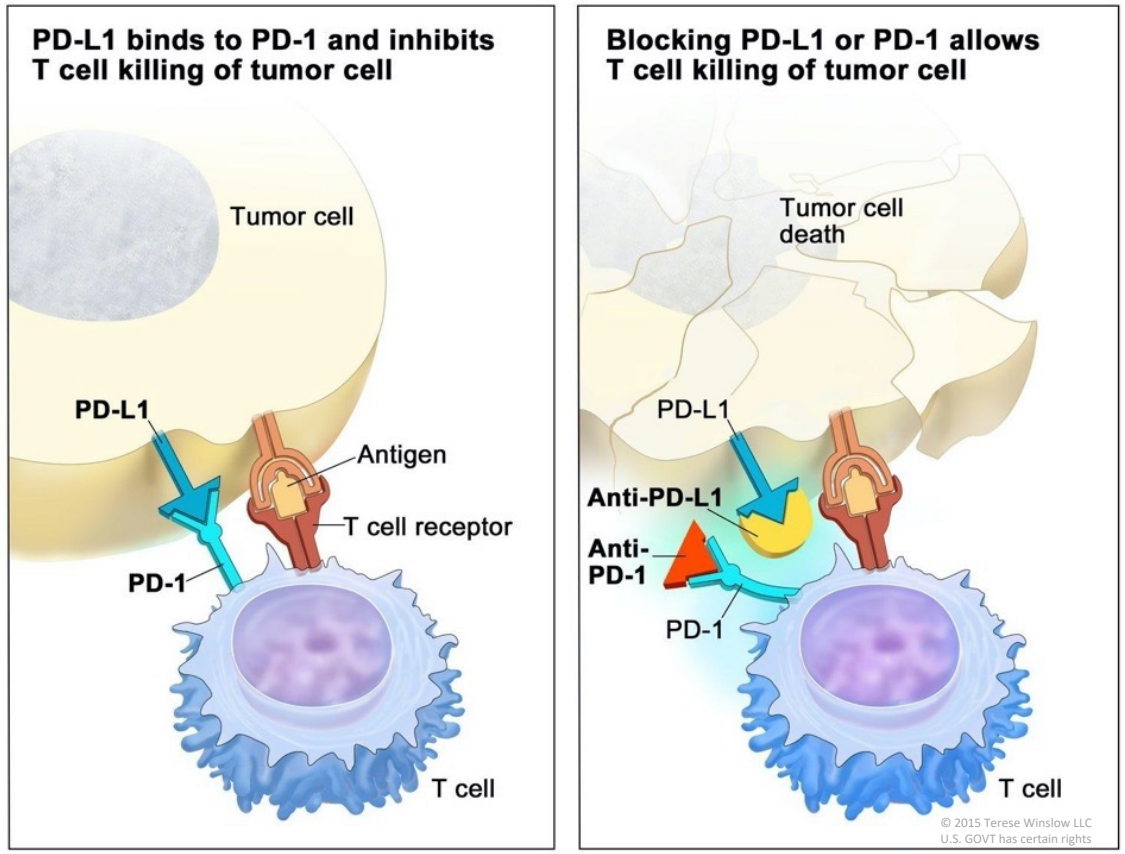
TTX Oncology Candidates in Development

| PD-L1 | Lin28b | RIG-I |CRISPR|mRNA Vaccine

TTX-siPDL1 Targets PD-1/PD-L1 with RNAi

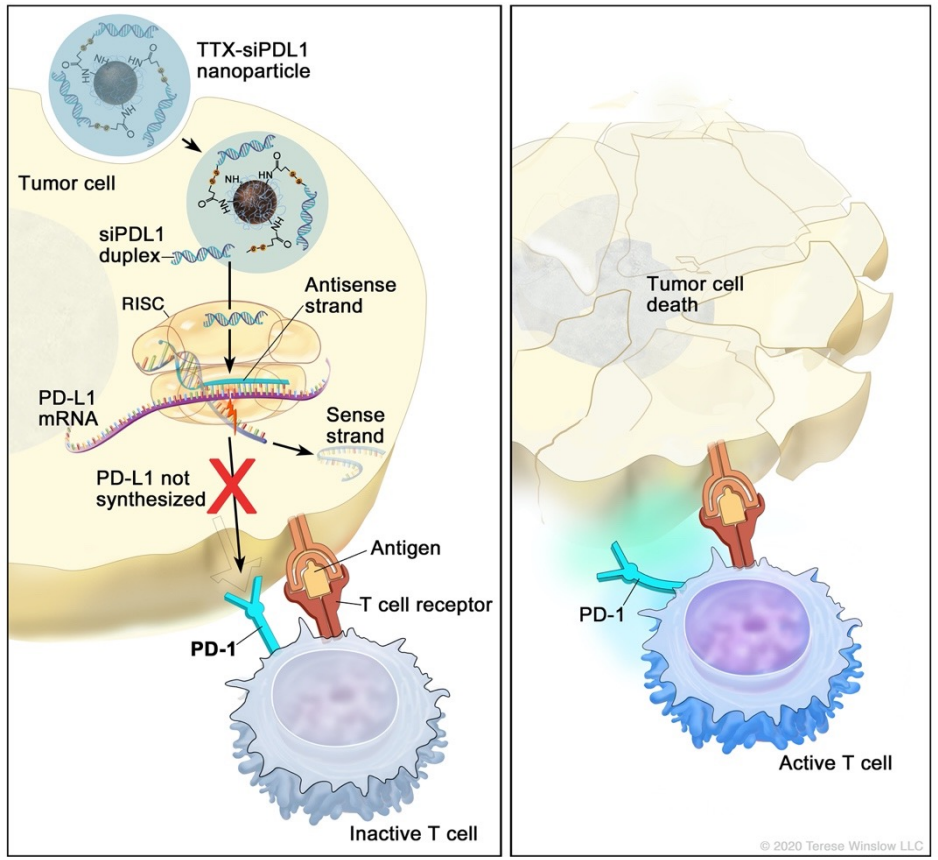
Checkpoint Inhibitors may not be effective in many cancers, including pancreatic cancer:

Traditional checkpoint inhibitors simply block PD-1/PD-L1 from binding each other

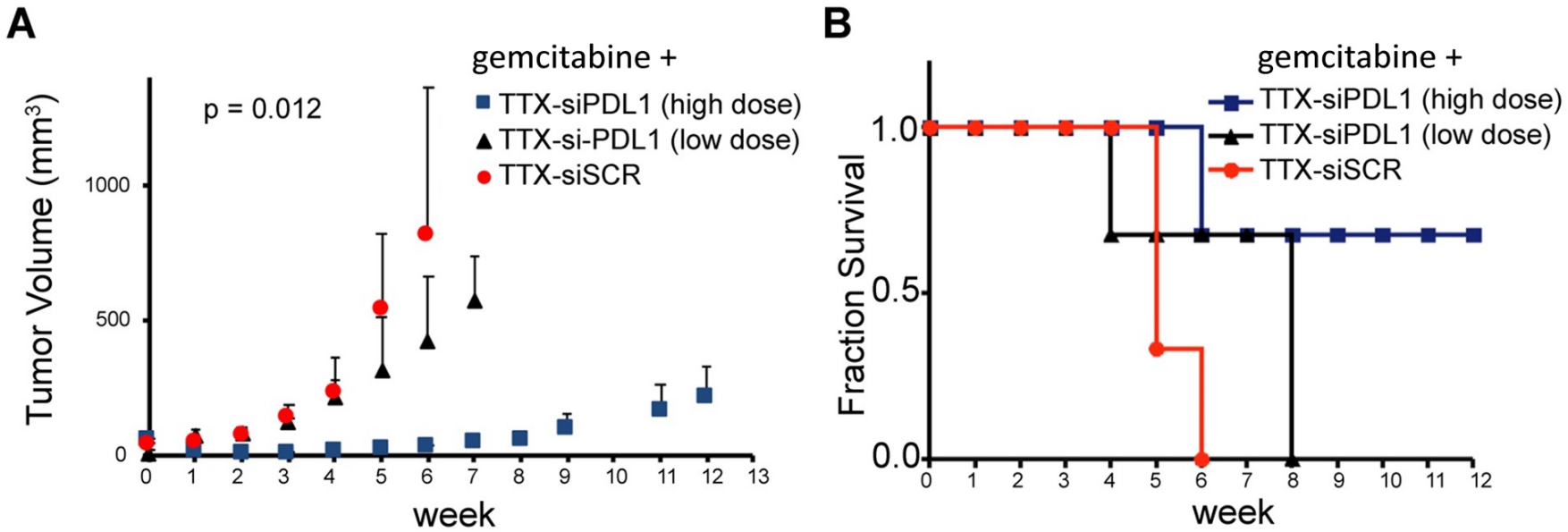


TTX-siPDL1 – (RNAi) advantages:

We employ an RNAi approach which is intended to prevent the synthesis of PD-L1 altogether

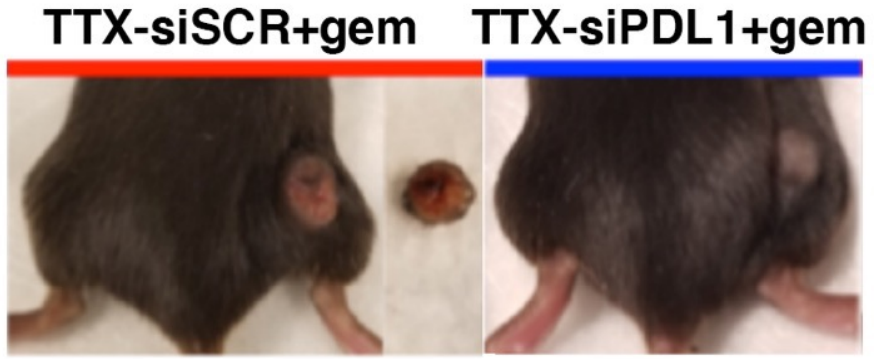


TTX-siPDL1 Generated Robust Preclinical Response in Mice



Results:

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



gem = gemcitabine

90% tumor regression in the first two weeks of treatment

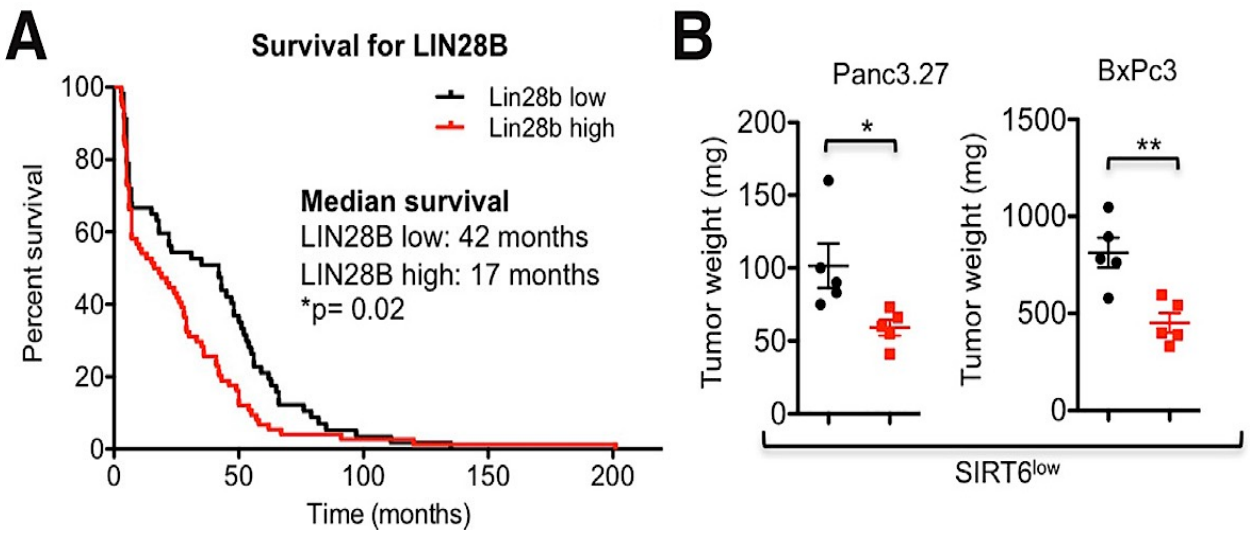
Source: Scientific Reports, 9 (1), 4712 2019

TTX-siLin28b: Lin28b is a Therapeutic Target for Multiple Solid Tumors

Lin28b is a biomarker of tumor survival and an actionable therapeutic target for solid tumors:

- RNA-binding protein that regulates mRNA translation and miRNA *let-7* maturation in embryonic stem cells and developing tissues
- Evolutionarily constrained but aberrantly reactivated with overexpression of oncofetal proteins
- Increasing evidence, it serves as a critical oncogene for SIRT6 deficiency associated with tumor cells
- Believed to have broad applicability in aggressive solid tumors

Key Preclinical Observations



Increased expression of Lin28b correlated with poor survival in Pancreatic Ductal Adenocarcinoma (PDAC) patients (*Figure A*)

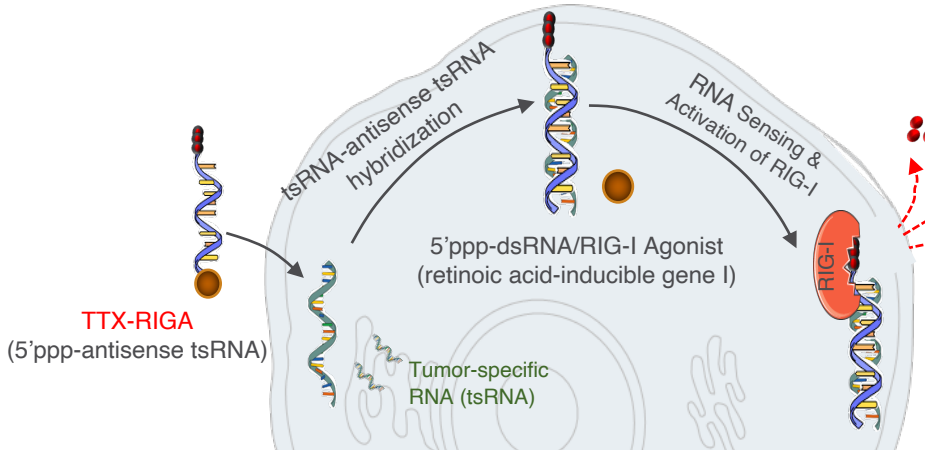
- Lin28b is required for the growth and survival of $SIRT^{low}$ PDAC
- Knocking down Lin28b with both small hairpin RNA (shRNA) and small interfering RNA (siRNA) resulted in potent suppression of cell proliferation and tumor sphere formation
- Knocking down Lin28b inhibited in vivo xenograft growth (*Figure B*)
- Knockdown of Lin28b led to both G1 cell-cycle arrest and induction of apoptosis

TransCode executed an exclusive option agreement with Massachusetts General Hospital (MGH), for TTX-siLin28b, under which TransCode has the right to negotiate an exclusive license for this asset.

Sources: Cell 2016

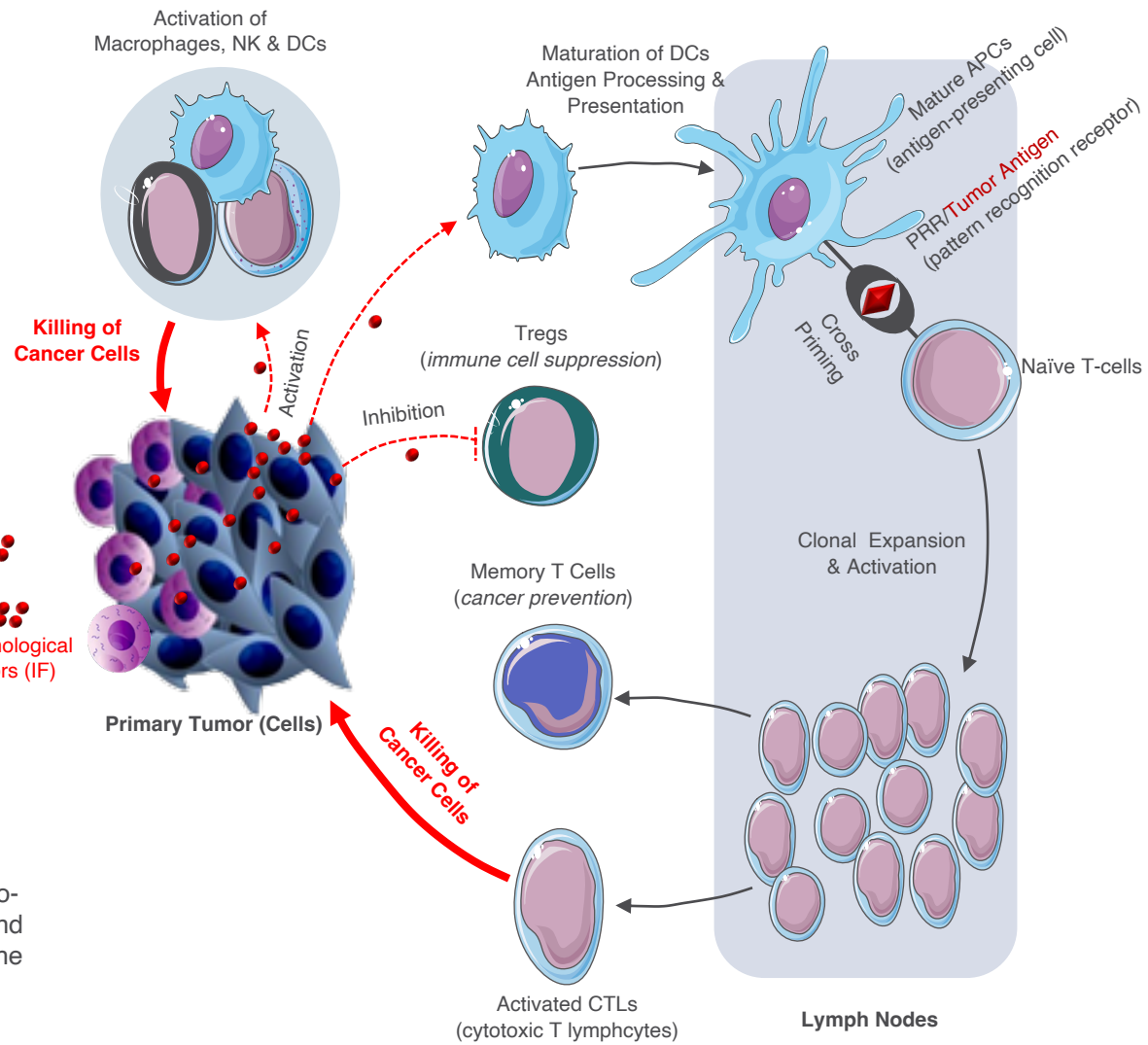
Novel Targeting of Cancer Via RIG-I Signaling Pathway

- Novel delivery of TTX-RIGA inside tumor cells to produce a potent agonist of the RIG-I signaling pathway.
- Activation of RIG-I signaling leads to type I IFN-driven immune response and preferential activation of programmed tumor cell death.
- Tumor cell death through RIG-I has been shown to build immunological memory and would reject tumors as "foreign".



RIG-I Signaling & Cell Death

Release of immunological factors (IF) including type I interferons (IFN), pro-inflammatory cytokines, DAMPs (damage-associated molecular pattern) and tumor antigens that trigger the innate and adaptive immune responses in the tumor microenvironment (TME)

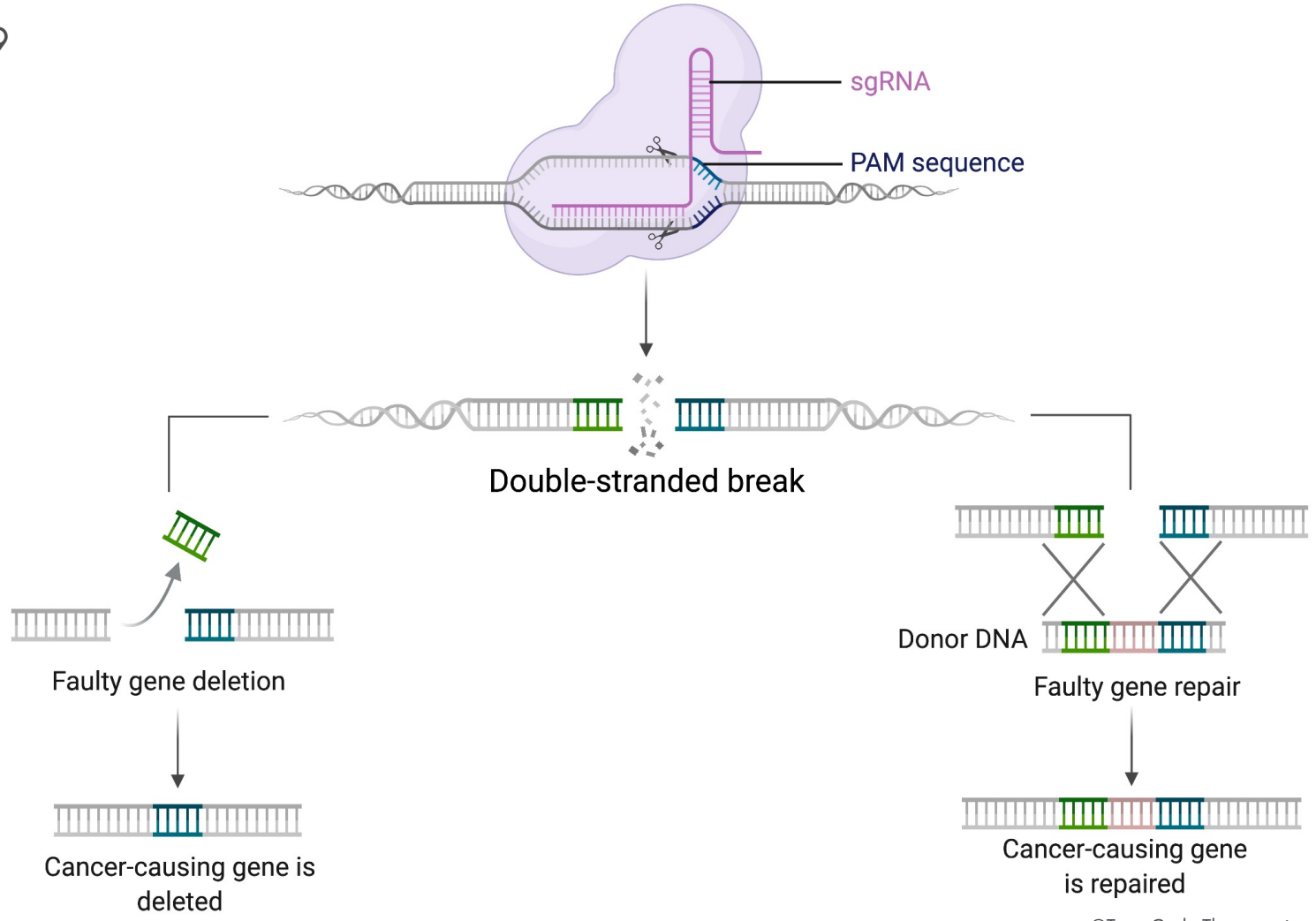


CRISPR/Cas9 Cancer Therapy

TTX can be designed to deliver CRISPR/Cas9 therapy inside tumor cells to:

- Delete cancer-causing gene sequences
- Repair cancer-causing gene sequences

  Important when a gene that protects against cancer is disrupted by mutation and needs to be repaired to function properly



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mRNA Cancer Vaccine

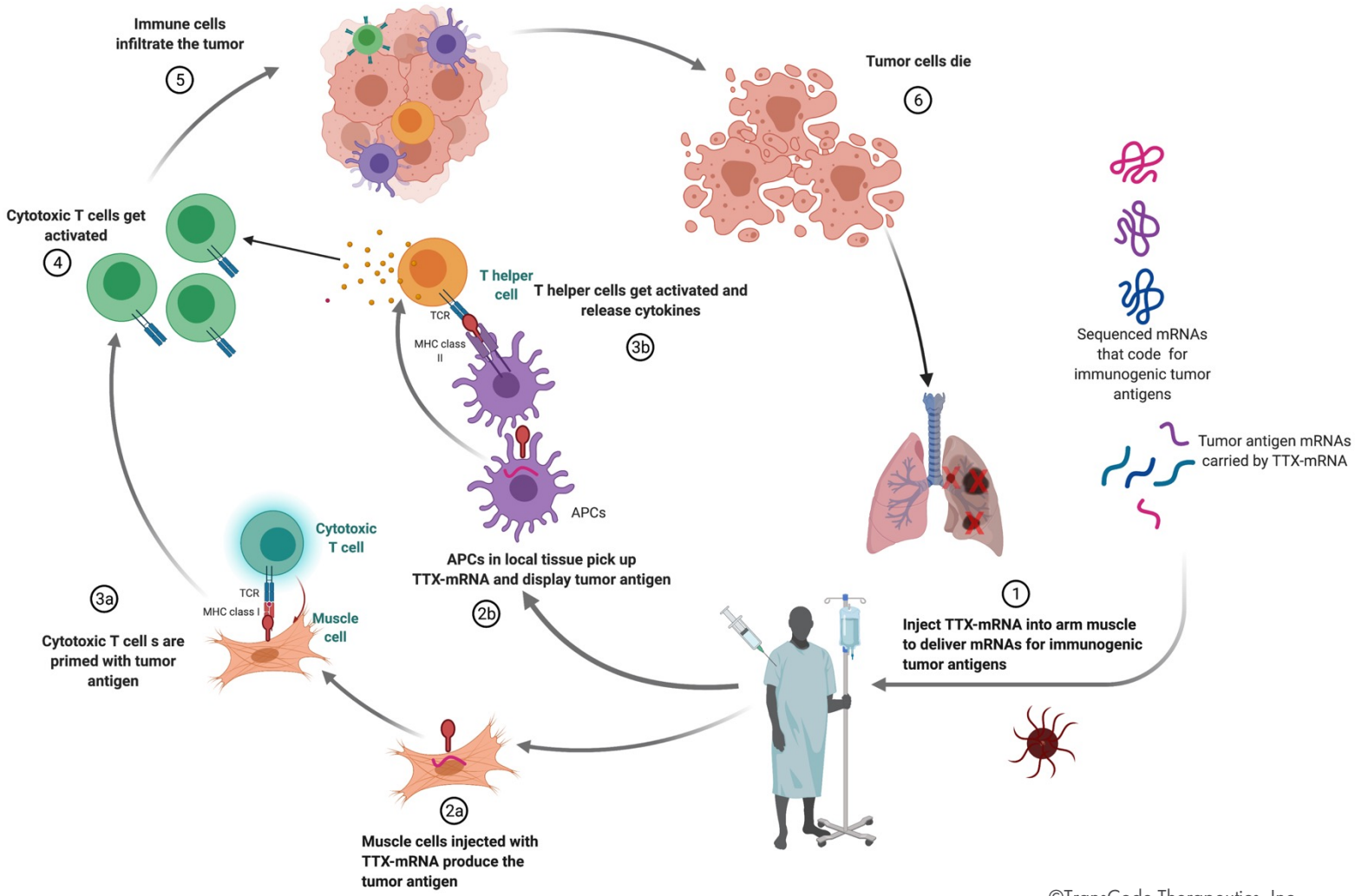
Delivery of TTX-mRNA inside tumor cells to produce an immune response specific to that tumor's immune profile

Activation of cytotoxic immunity against the tumor resulting in tumor cell death

Mechanism behind TTX-mRNA vaccine:

- TTX-mRNA delivers the code for immunogenic tumor antigens
- Once injected into the muscle, TTX-mRNA is taken up by muscle cells (2a) or antigen presenting cells (2b), which synthesize the tumor antigens
- This leads to either direct priming of cytotoxic T cells by the muscle cells (3a) or activation of T helper cells by the APCs (3b)
- Both pathways result in activation of cytotoxic T cells (4), followed by tumor infiltration by the immune cells (5), and tumor cell death (6)

The result of this process is the immune destruction of tumors throughout the body



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